H. Poschenrieder [a], H.-D. Stachel* [a], B. Wiesend [a] and K. Polborn [b]

[a] Department Pharmazie / Zentrum für Pharmaforschung, Universität München, Butenandtstr. 7 – 13, D 81377 München, Germany
[b] Department Chemie, Universität München, Butenandtstr. 7 – 13, D 81377 München, Germany
Received April 25, 2002

Ozonolysis of the pyrrolidinediones **4** afforded the pyrrolidinetriones **5**, which in the presence of Lewis acids were converted into maleimide **6**. Analogously, ozonolysis of the pyrrolidinones **7** gave the pyrrolidinediones **8**, which were converted into the pyridinetriones **11a, b** *via* Lewis acid catalyzed isomerization to yield the trihydroxypyridones **10** and ensuing air oxidation. In solution two tautomeric forms of the pyridinetriones **11** may exist both of which represent hydroxy-azabenzoquinones. In two steps compounds **11** were transformed into the azaquinone derivatives **19**. Representatives of another type of azaquinones are compounds **28a, b**. These were generated in two steps from the pyridones **25**. The azaquinone **28a** reacted easily with acidic compounds yielding the adducts **26**, **27** and **29** or with 2-butenal forming the cycloadduct **30**.

J. Heterocyclic Chem., **40**, 61 (2003).

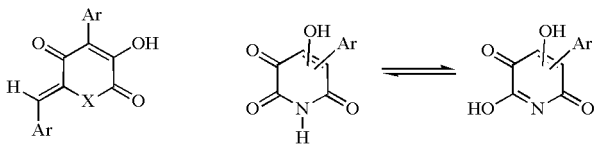
Introduction.

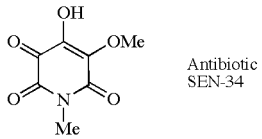
Because of the structural resemblance with fungal pigments named grevellins **1** [1-3] compounds of type **2**, for the sake of convenience, have been called azagrevellins (Scheme 1). It has been claimed that some of the azagrevellins exhibit physiological actions of potentially therapeutic value [4,5]. Recently we have described two methods for the synthesis of azagrevellins and structural isomers by ring enlargement reactions of 2-pyrrolidone derivatives [4,5]. Analogously, starting with 2,5-pyrrolidinediones the synthesis of compounds of type **3a** appeared feasible. Tautomers of **3a** can be regarded as hydroxy-azabenzoquinones (**3b**). Proof of a similar tautomerism was given for dihydropyridones related to **3** [6,7].

The term azaquinones for compounds containing nitrogen atoms as members of the quinonoid ring was introduced in the chemical literature by H. J. Boyer in 1957 [8]. A recent survey on the chemistry of mono- and diazaquinones was given by S. Radl [9]. The significance of azaquinones and derivatives as bacterial pigments and metabolites was summarized by H.-J. Knackmuss [7]. Later on a yellow fungal pigment called incaflavin was recognized as an azaquinone [10,11]. Deviating from the above definition the term azaquinone was sometimes used for quinone imines in the literature [12]. Nomenclatory difficulties also exist with the designation of quinones with fused heterocycles as azaquinones [13].

Up to now, investigations concerning physiological effects of azaquinones are lacking. It should be noted, however, that a compound structurally related to **3** was recognized as an antibiotic [14]. But strictly speaking, this substance named SEN-34 is not an azaquinone because of it posesses a substituted nitrogen.

Scheme 1





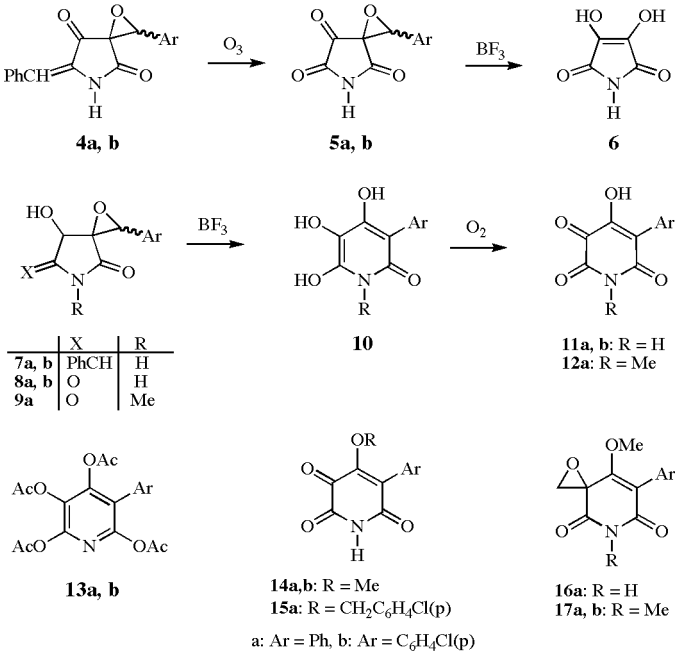
Chemistry.

The azagrevellins **2** were prepared from epoxides **4** (Scheme 2) in a ring enlargement reaction initiated by alkylating agents especially triethyloxonium tetrafluoroborate (Meerwein's reagent) [5]. The isomerization proceeds by an anionotropic 1,2-shift of one of the two acyl groups present after opening of the oxirane ring. Thereby usually the oxo carbonyl group showed a higher migration aptitude than the lactam carbonyl group. It was our aim to apply this ring-expansion reaction to the epoxides **5**.

We planned to produce the unknown imides **5** by ozonolysis from the benzylidene lactams **4** in stock assuming that the oxirane would sustain the procedure [15]. The ozonolysis indeed proceeded as expected. However, the compounds **5** could not be purely obtained because of the rapid hydrolytic cleavage of the oxirane and the ensuing retro-aldol reaction. The maleimide **6** was isolated as final product beside benzaldehyde or 4-chlorobenzaldehyde, respectively. The yield of **6** was better than 50% so that this new synthesis constitutes a convenient and inexpensive alternative to the literature method [16].

The rapid degradation of epoxide **5** may be attributed to an unfavorable molecular geometry enforced by the neighboring carbonyl groups. In consequence, the partly saturated epoxides **8** should be more stable and therefore represent suitable intermediates for the desired ring-expansion. We have found indeed that the premature cleavage of the oxirane can be avoided if the ozonolysis is carried out with the benzylidene lactams **7**. These compounds were obtained by partial hydrogenation of the lactams **5** as

Scheme 2



	X	R
7a, b	PhCH	H
8a, b	O	H
9a	O	Me

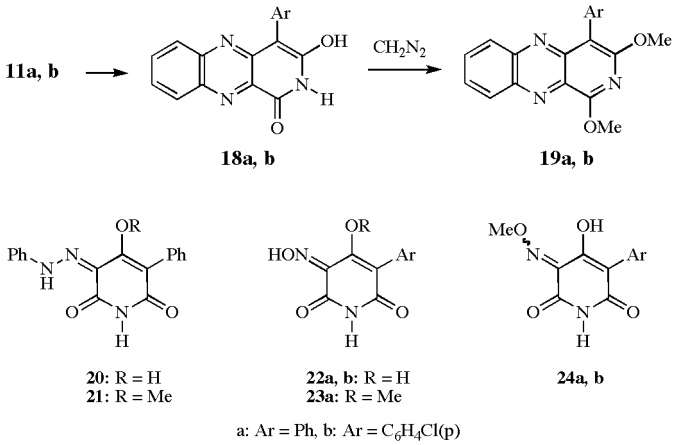
mixtures of two stereoisomers. Therefore the ozonolysis yielded the imides **8a**, **8b** as mixtures of two isomers each. The separation of the stereoisomers proved unnecessary. Addition of boron trifluoride to the solution of either epoxide initiated the ring enlargement reaction and finally the formation of the pyridones **10**. These compounds are best formulated as endiols because they are easily oxidized by air oxygen yielding the yellow pyridinetriones **11**. In between a transient red color appeared. The color might be attributed to intermediate radicals or radical anions as it was demonstrated to be the case during the oxidation of a similar system [6,17].

Some physical and chemical properties of compounds **11** are consistent with a tautomeric azaquinone structure. The compounds prove to be relatively strong acids with pK_a values of 3.7 in aqueous dioxane. Owing to ionization the solutions appear reddish in solvents containing water. Upon addition of bases the color changes to the deep red of the respective anions. The same behavior was reported as typical for hydroxyquinones [18]. On the other hand the compounds **11** are weak bases and dissolve in concentrated sulfuric acid with red color owing to the formation of *N*-protonated azaquinones. Likewise the compounds **11** typically exhibited a red color on silicagel during chromatography.

Some information on the tautomeric equilibrium of compounds **11** can be drawn by comparison of their spectra with those of the *N*-methylated pyridone **12a** which was prepared for this purpose from epoxide **9a**. The ir spectrum of **11a** did not allow the clear identification of *NH*-absorptions because of several *OH*-association bands in the same region [6], which also showed up in the ir spectrum of **12a**. The strong absorptions at 1730 – 1700 cm^{-1} in the spectra of both **11a** and **12a** can be addressed as imide carbonyl bands. Likewise the ^{13}C nmr spectra of **11a** and **12** were essentially identical. From this it must be concluded that the tautomeric equilibrium of compounds **11** is shifted to the trione system. Likewise other azaquinones capable of tautomerism appear to exist largely in the imide form [7]. The only reference to partial enolization of compounds **11** was found in their uv spectra. While the uv spectrum of **11a** showed two absorption maxima at 272 and 379 nm the long wave maximum was missing in solutions of **12a**. Therefore compounds **11** can be considered as azaquinonoids but are written here as pyridinetriones (Scheme 2).

To further confirm the structure of compounds **11** we have prepared a number of derivatives. Although the reduction of compounds **11** can be carried out easily with sodium dithionite we did not succeed in the isolation of the corresponding azahydroquinones **10** in pure state. Reduction of compound **11a** with zinc and acetic anhydride led to the tetraacetoxypyridines **13**. The reactions of compounds **11** with diazomethane proceeded in three steps. First the enol ethers **14** were formed very rapidly. These were then converted into the epoxides **16** and finally into the *N*-methylated epoxides **17**. From the reaction of the trione **11a** with the less reactive *p*-chlorophenyldiazomethane only the benzyl ether **15a** was isolated which formed crystals suitable for X-ray structure determination. The single crystal diffraction analysis (Figure 1, Tables 1a, 1b) confirmed the structure of **15a** and with it the structures of the progenitor **11a** as well as of **11b** by analogy.

Scheme 3



The pyridinetriones **11** reacted with *o*-phenylenediamine in 3- and 4-position yielding the violet quinoxalines **18** (Scheme 3). By reaction of compound **18** with diazomethane the azaquinone derivatives **19** were obtained.

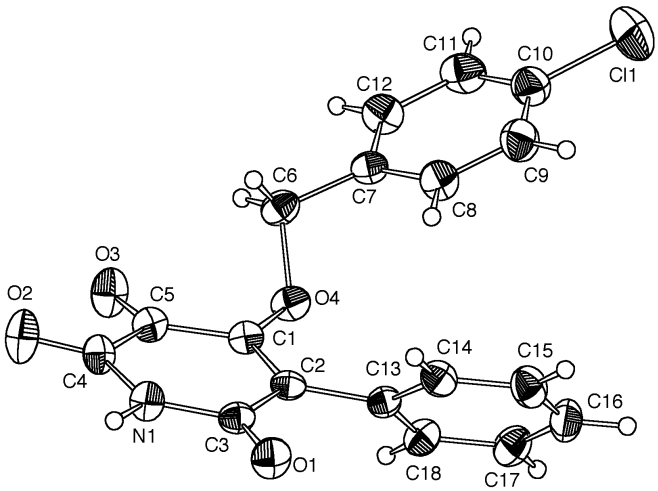


Figure 1. ORTEP plot of Azaquinone **15a**.

Table 1a

Single Crystal X-Ray Crystallographic Analysis of **15a**

A. Crystal Parameters

Formula	$C_{18}H_{12}ClNO_4$ (341.74)
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	orthorhombic
Space group	Pbca
Unit cell dimensions	a = 11.832(2) Å
	b = 7.661(2) Å
	c = 35.362(10) Å
Volume	3205.6(13) $Å^3$
Z	8
Density (calculated)	1.416 Mg/m^3
Absorption coefficient	0.260 mm^{-1}
F(000)	1408
Crystal size	0.53 x 0.43 x 0.13 mm
Theta range for data collection	2.30 to 22.97º
Index ranges	0<=h<=12, 0<=k<=8, -38<=l<=0
B. Refinement Parameters	
Reflections collected	2226
Independent reflections	2225 [R(int) = 0.0820]
Observed reflections [I>2σ(I)]	1598
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2225 / 0 / 217
Goodness-of-fit on F^2	1.086
Final R indices [I>2σ(I)]	R1 = 0.0510, wR2 = 0.1098
R indices (all data)	R1 = 0.0775, wR2 = 0.1270
Largest diff. peak and hole	0.168 and -0.267 $e.A^{-3}$

Table 1b

Bond Lengths [Å] and Angles [°] for **15a**

Cl(1)-C(10)	1.736(4)	C(1)-C(2)-C(13)	122.4(3)
O(1)-C(3)	1.211(4)	C(1)-C(2)-C(3)	118.8(3)
O(2)-C(4)	1.201(4)	C(13)-C(2)-C(3)	118.7(3)
O(3)-C(5)	1.207(3)	O(1)-C(3)-N(1)	118.9(3)
O(4)-C(1)	1.363(3)	O(1)-C(3)-C(2)	122.2(3)
O(4)-C(6)	1.452(4)	N(1)-C(3)-C(2)	118.9(3)
N(1)-C(4)	1.361(4)	O(2)-C(4)-N(1)	123.4(3)
N(1)-C(3)	1.381(4)	O(2)-C(4)-C(5)	121.3(3)
C(1)-C(2)	1.348(4)	N(1)-C(4)-C(5)	115.2(3)
C(1)-C(5)	1.460(4)	O(3)-C(5)-C(1)	123.1(3)
C(2)-C(13)	1.475(4)	O(3)-C(5)-C(4)	118.5(3)
C(2)-C(3)	1.486(4)	C(1)-C(5)-C(4)	118.4(3)
C(4)-C(5)	1.523(4)	O(4)-C(6)-C(7)	108.7(3)
C(6)-C(7)	1.497(4)	C(12)-C(7)-C(8)	118.3(3)
C(7)-C(12	1.381(4)	C(12)-C(7)-C(6)	120.1(3)
C(7)-C(8)	1.383(4)	C(8)-C(7)-C(6)	121.6(3)
C(8)-C(9)	1.372(5)	C(9)-C(8)-C(7)	121.1(3)
C(9)-C(10)	1.371(5)	C(8)-C(9)-C(10)	119.4(4)
C(10)-C(11)	1.364(5)	C(11)-C(10)-C(9)	120.7(4)
C(11)-C(12)	1.379(5)	C(11)-C(10)-Cl(1)	119.8(3)
C(13)-C(14)	1.384(4)	C(9)-C(10)-Cl(1)	119.5(3)
C(13)-C(18)	1.391(4)	C(10)-C(11)-C(12)	119.7(4)
C(14)-C(15)	1.372(5)	C(11)-C(12)-C(7)	120.7(3)
(15)-C(16)	1.374(5)	C(14)-C(13)-C(18)	118.9(3)
C(16)-C(17)	1.374(5)	C(18)-C(13)-C(2)	119.4(3)
C(17)-C(18)	1.376(5)	C(15)-C(14)-C(13)	120.2(3)
C(1)-O(4)-C(6)	115.7(2)	C(14)-C(15)-C(16)	120.7(3)
C(4)-N(1)-C(3)	126.2(3)	C(17)-C(16)-C(15)	119.7(3)
C(2)-C(1)-O(4)	120.9(3)	C(16)-C(17)-C(18)	120.1(3)
C(2)-C(1)-C(5)	121.9(3)	C(17)-C(18)-C(13)	120.4(3)
O(4)-C(1)-C(5)	117.0(3)		

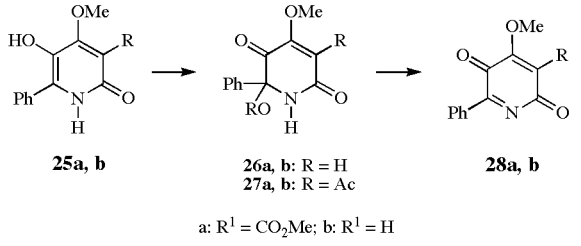
The structure of **19b** was secured by X-ray diffraction analysis (Figure 2**,** Tables 2a, 2b). In the reaction of compound **11a** with excessive phenylhydrazine only the poorly soluble monohydrazone **20** was formed. Compound **20** yielded the enol ether **21** upon reaction with diazomethane. The oximes **22** and their derivatives **24** were all obtained as mixtures of syn/anti isomers by reaction of the triones **11** and hydroxylamine hydrochloride or *O*-methylhydroxylamine, respectively. The oxime **23a**, a structural isomer of compound **24a**, was formed analoguosly from enol ether **14a**.

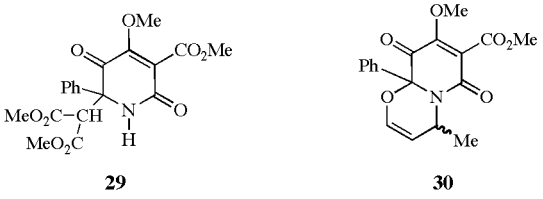
Recently we have reported on the synthesis of the hydroxypyridones **25a, b** (Scheme 4) by a ring-expansion reaction [19]. These compounds can be viewed as azahydroquinones and were easily oxidized to the corresponding azaquinones by dichlorodicyanoquinone or silver nitrate. The red solutions of the azaquinones went colorless upon addition of protic solvents like water during work-up. In the latter case, adducts **26** were obtained the structure of which was secured by *NOE* and CH-COSY experiments. Adducts **26** were converted upon heating with acetic anhydride into the acetates **27**. Solutions of **27a** in dioxane reversibly turned red on heating thus indicating a temperature dependent equilibrium of adduct **27a** and its components, the azaquinone **28a** and acetic acid. The thermolysis of both adducts **27** as solids under reduced pressure led to the corresponding red azaquinones **28**.

The high reactivity at the eletron-deficient imine double bond is a characteristic of azaquinones [9]. Accordingly, the azaquinone **28a** reacted with dimethyl malonate in the presence of pyridine to give the adduct **29**. The reaction of **28a** and the heterodiene 2-butenal yielding the cycloadduct **30** was reversed upon heating under reduced pressure. According to the ^1H nmr spectrum compound **30** was

uniform and therefore evidently the product of a stereoselective Diels-Alder reaction. The configuration at C-4 bearing the methyl group is still to be determined.

Scheme 4





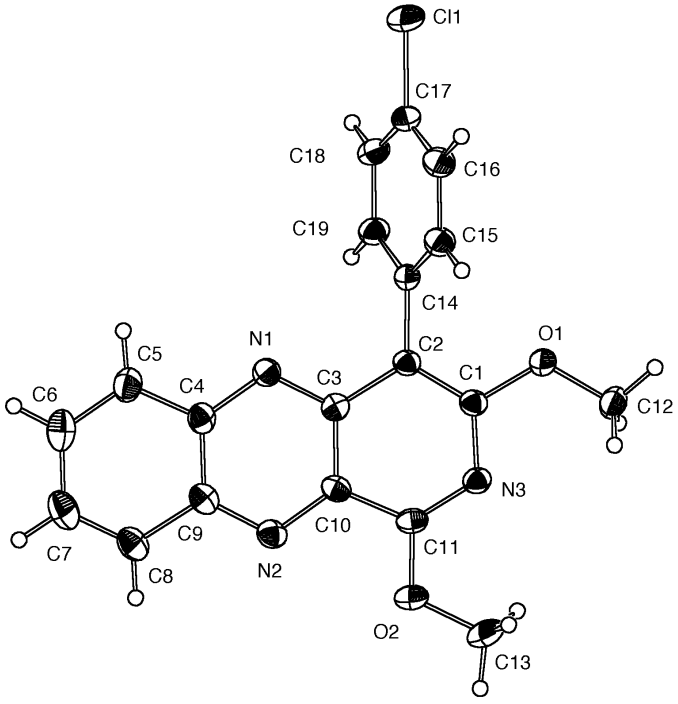


Figure 2. ORTEP plot of Quinoxaline **19b**.

The oximes **22** and **23a** as well as the azaquinones **11** contain partial structures which are present in some substances with known antagonistic action at the physiologically important NMDA receptor [20] and played a role in the development of a pharmacophor model [21]. Representative members of the compounds described here are being tested pharmacologically.

Table 2a

Single Crystal X-Ray Crystallographic Analysis of **19b**

A. Crystal Parameters

Formula	$C_{19}H_{14}ClN_3O_2$ (351.78)
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	triclinic
Space group	P-1
Unit cell dimensions	a = 7.152(2) Å alpha = 92.96(3)°
	b = 11.152(4) Å beta = 97.35(3)°
	c = 10.759(3) Å gamma = 93.84(3) °
Volume	847.6(5) $Å^3$
Z	2
Density (calculated)	1.378 Mg/m^3
Absorption coefficient	0.243 mm^{-1}
F(000)	364
Crystal size	0.53 x 0.20 x 0.13 mm
Theta range for data collection	2.57 to 23.98°
Index	-8<=h<=0, -12<=k<=12, -12<=l<=12
B. Refinement Parameters	
Reflections collected	2530
Independent reflections	2345 [R(int) = 0.0133]
Observed reflections [I>2σ(I)]	1696
Absorption correction	Semi-empirical
Max. and min. transmission	0.9983 and 0.9448
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2345 / 0 / 228
Goodness-of-fit on F^2	1.007
Final R indices [I>2σ(I)]	R1 = 0.0581, wR2 = 0.1343
R indices (all data)	R1 = 0.0828, wR2 = 0.1511
Largest diff. peak and hole	0.190 and -0.210 $e.A^{-3}$

Table 2b

Bond Lengths [Å] and Angles [°] for **19b**

Cl(1)-C(17)	1.716(4)	C(11)-O(2)-C(13)	114.8(4)
O(1)-C(1)	1.390(5)	C(3)-N(1)-C(4)	118.7(3)
O(1)-C(12)	1.414(4)	C(9)-N(2)-C(10)	118.0(3)
O(2)-C(11)	1.313(4)	C(11)-N(3)-C(1)	118.7(3)
O(2)-C(13)	1.428(5)	N(3)-C(1)-C(2)	123.3(4)
N(1)-C(3)	1.337(5)	N(3)-C(1)-O(1)	117.3(3)
N(1)-C(4)	1.375(5)	C(2)-C(1)-O(1)	119.4(3)
N(2)-C(9)	1.328(5)	C(1)-C(2)-C(3)	117.9(3)
N(2)-C(10)	1.363(5)	C(1)-C(2)-C(14)	120.4(4)
N(3)-C(11)	1.325(5)	C(3)-C(2)-C(14)	121.6(3)
N(3)-C(1)	1.334(5)	N(1)-C(3)-C(10)	117.1(4)
C(1)-C(2)	1.348(5)	N(1)-C(3)-C(2)	122.0(3)
C(2)-C(3)	1.460(5)	C(10)-C(3)-C(2)	120.8(4)
C(2)-C(14)	1.460(5)	N(1)-C(4)-C(9)	123.0(4)
C(3)-C(10)	1.395(5)	N(1)-C(4)-C(5)	121.1(4)
C(4)-C(9	1.387(6)	C(9)-C(4)-C(5)	115.9(4)
C(4)-C(5)	1.415(6)	C(6)-C(5)-C(4)	122.1(5)
C(5)-C(6)	1.394(6)	C(7)-C(6)-C(5)	121.7(5)
C(6)-C(7)	1.377(7)	C(8)-C(7)-C(6)	118.0(5)
C(7)-C(8)	1.339(7)	C(7)-C(8)-C(9)	122.2(5)
C(8)-C(9)	1.458(6)	N(2)-C(9)-C(4)	118.7(4)
C(10)-C(11)	1.434(6)	N(2)-C(9)-C(8)	121.1(4)
C(14)-C(15)	1.340(6)	C(4)-C(9)-C(8)	120.2(4)
C(14)-C(19)	1.409(6)	N(2)-C(10)-C(3)	124.3(4)
C(15)-C(16)	1.361(6)	N(2)-C(10)-C(11)	122.3(4)
C(16)-C(17)	1.395(7)	C(3)-C(10)-C(11)	113.4(4)
C(17)-C(18)	1.325(6)	O(2)-C(11)-N(3)	121.9(4)
C(18)-C(19)	1.362(6)	O(2)-C(11)-C(10)	112.3(4)
C(1)-O(1)-C(12)	120.4(3)	C(15)-C(14)-C(19)	119.2(4)

Table 2b (Continued)

C(15)-C(14)-C(2)	117.9(4)	C(18)-C(17)-Cl(1)	116.1(4)
C(19)-C(14)-C(2)	123.0(4)	C(16)-C(17)-Cl(1)	121.8(4)
C(14)-C(15)-C(16)	117.7(5)	C(17)-C(18)-C(19)	115.8(5)
C(15)-C(16)-C(17)	121.7(4)	C(18)-C(19)-C(14)	123.5(4)
C(18)-C(17)-C(16)	122.1(4)		

EXPERIMENTAL

Melting points were determined by using a Büchi Melting Point B-540 apparatus and are uncorrected. Uv analysis was performed in methanolic solution if not stated otherwise on UV/VIS Spectrometer Lambda 20 (Perkin Elmer) or UV/VIS Spectrophotometer Jasco V-530. Infrared spectra were measured as potassium bromide plates by using a FT-IR-Spectrometer PARAGON 1000 (Perkin Elmer). ^{1}H nmr spectra (internal standard tetramethylsilane) were recorded on FT NMR Spectrometer Elipse 400 (JEOL) or FT NMR Spectrometer Elipse 500 (JEOL). The solvent was hexadeuteriodimethylsulfoxide if not indicated otherwise. Mass spectra were recorded with a Hewlett Packard 5989A Mass Spectrometer. Microanalyses were carried out with an Analysator CHN-O-Rapid (Heraeus). CC: By flash column 250 ml (Baker) with silica gel 0.040 – 0.063 mm (Merck). Ozone was generated by the Ozongenerator Fischer 502, capacity: 4.3 g ozone/h at an oxygen flow rate 60 L/h.

3,4-Dihydroxy-pyrrole-2,5-dione (**6**).

Ozone was passed through a solution of 1.0 g (3.4 mmol) of compound **4a** [4] in dichloromethane (50 ml) and methanol (150 ml) at –15° over a period of 4 minutes. The solvent was removed *in vacuo* at a temperature not exceeding 10° (danger of explosive decomposition of by-products). The residue was stirred with 1 ml of trifluoroacetic acid. After a short time the product started to crystallize. Yield 0.30 g (52%), light yellow crystals, mp >165° (dec), ref. [16]: mp 180° (dec).

6-Benzylidene-7-hydroxy-2-phenyl-1-oxa-5-aza-spiro[2,4]heptan-4-one (**7a**).

To a stirred and cooled suspension of 2.90 g (10 mmol) of compound **4a** in aqueous methanol (1:2, 45 ml) were added 0.55 g (15 mmol) of sodium borohydride. After continued stirring for one hour the mixture was acidified with diluted sulfuric acid and the precipitate collected and washed with methanol. Yield 2.0 g (68%), colorless crystals (mixture of two stereoisomers), mp 200-203° (methanol); ir: ν 3477, 3231, 1728, 1685 cm^{-1}; uv: λ max (log ε) 218 (4.365), 272 nm (4.348); ^{1}H nmr: δ 10.84 (s, 0.6 H), 10.53 (s, 0.4 H), 7.44-7.29 (m, 10 H), 6.35 (d, J = 8 Hz, 0.4 H), 5.74 (s, 0.4 H), 5.68 (s, 0.6 H), 5.44 (d, J = 8 Hz, 0.6 H), 4.96 (d, J = 8 Hz, 0.4 H), 4.79 (d, J = 8 Hz, 0.6 H), 4.51 (s, 0.4 H), 4.42 (s, 0.6 H); ms: m/z 293 (M^+).

Anal. Calcd. for $C_{18}H_{15}NO_3$ (293.32): C, 73.70; H, 5.15; N, 4.77. Found: C, 74.00; H, 5.02; N, 4.82.

6-(4-Chloro-benzylidene)-7-hydroxy-2-phenyl-1-oxa-5-aza-spiro[2,4]heptan-4-one (**7b**).

This compound was prepared analogously to **7a** from 3.25 g (10 mmol) of compound **4b** and 0.55 g (15 mmol) of sodium borohydride. Yield 2.80 g (85%), colorless crystals (mixture of two stereoisomers), mp 170-173° (methanol); ir: ν 3470, 1730, 1685cm^{-1}; uv: λ max (log ε) 220 (4.364), 272 nm (4.347); ^{1}H nmr: δ 10.85 (s, 0.45 H), 10.56 (s, 0.55 H), 7.54-7.34 (m, 9 H), 6.32 (d, J = 8 Hz, 0.45 H), 5.74 (s, 0.45 H), 5.66 (s, 0.55 H), 5.45 (d, J = 8 Hz, 0.55 H), 4.96 (d, J = 8 Hz, 0.45 H), 4.80 (d, J = 8 Hz, 0.55 H), 4.52 (s, 0.45 H), 4.44 (s, 0.55 H); ms: m/z 327 (M^+).

Anal. Calcd. for $C_{18}H_{14}ClNO_3$ (327.77): C, 65.96; H, 4.30; N, 4.27. Found: C, 65.73; H, 4.35; N, 4.17.

7-Hydroxy-2-phenyl-1-oxa-5-aza-spiro[2,4]heptane-4,6-dione (**8a**).

Ozone was passed through a solution of 1.0 g (3.4 mmol) of compound **7a** in dichloromethane (50 ml) and methanol (150 ml) at -15° over a period of 4 minutes. The solvent was removed *in vacuo* at a temperature not exceeding 10° (danger of explosive decomposition of by-products) and the oily residue extracted with petrol ether (30 ml). The solution was discarded and the solid residue was crystallized from diethyl ether. Yield 0.52 g (70%), colorless crystals (mixture of two stereoisomers), mp 161-163° (dec); ir: ν 3432, 3271, 1802, 1719 cm^{-1}; uv: λ max (log ε) 220 nm (4.038); ^{1}H nmr: δ 11.84 (s, 0.6 H), 11.52 (s, 0.4 H), 7.48-7.29 (m, 5 H), 6.48 d, J = 8 Hz, 0.4 H), 5.51 (d, J = 8 Hz, 0.6 H), 4.82 (d, J = 8 Hz, 0.4 H), 4.76 d, J = 8 Hz, 0.6 H), 4.51 (s, 0.4 H), 4.42 (s, 0.6 H); ms: m/z 219 (M^+).

Anal. Calcd. for $C_{11}H_9NO_4$ (219.20): C, 60.27; H, 4.14; N, 6.39. Found: C, 60.03; H, 4.21; N, 6.42.

2-(4-Chlorophenyl)-7-hydroxy-1-oxa-5-aza-spiro[2,4]heptane-4,6-dione (**8b**).

This compound was prepared analogously to **8a** from 1.0 g (3 mmol) of compound **7b**. Yield 0.45 g (60%), colorless crystals (mixture of two stereoisomers), mp 172-176° (diisopropyl ether/ethanol); ir: ν 3453, 3204, 1802, 1720 cm^{-1}; uv: λ max (log ε) 229 nm (4.216); ^{1}H nmr: δ 1.85 (s, 0.6 H), 11.53 (s, 0.4 H), 7.50-7.37 (m, 4 H), 6.44 d, J = 8 Hz, 0.4 H), 5.54 (d, J = 8 Hz, 0.6 H), 4.80 (d, J = 8 Hz, 0.4 H), 4.76 (d, J = 8 Hz, 0.6 H), 4.51 (s, 0.4 H), 4.45 (s, 0.6 H); ms: m/z 253 (M^+).

Anal. Calcd. for $C_{11}H_8ClNO_4$ (253.64): C, 52.09; H, 3.18; N, 5.52. Found: C, 52.19; H, 3.11; N, 5.62.

7-Hydroxy-5-methyl-2-phenyl-1-oxa-5-aza-spiro[2,4]heptane-4,6-dione (**9a**).

Compound **8a** (1.10 g, 5 mmol) was added to an etheral solution of excessive diazomethane. After the evolution of nitrogen had ceased the solution was evaporated to dryness and the residue crystallized from diisopropyl ether/ethanol 1:1. Yield 0.45 g (38%), colorless crystals, mp 163°; ir: ν 3452, 1732, 1710 cm^{-1}; uv: λ max (log ε) 228 nm (4.097); ^{1}H nmr: δ 7.37-7.30 (m, 5 H), 5.55 (d, 1 H, J = 8 Hz), 4.77 (d, 1 H, J = 8 Hz), 4.49 (s, 1 H), 2.95 (s, 3 H); ms: m/z 233 (M^+).

Anal. Calcd. for $C_{12}H_{11}NO_4$ (233.22): C, 61.80; H, 4.75; N, 6.00. Found: C, 61.13; H, 4.51; N, 5.87.

4-Hydroxy-5-phenyl-pyridine-2,3,6-trione (**11a**).

A solution of 1.10 g (5 mmol) of compound **7a** and 1 ml of boron trifluoride diethyl etherate in dioxane (50 ml) was heated at reflux for one hour. The solution was concentrated to a volume of 10 ml, poured into ice water (30 ml) and extracted twice with ethyl acetate (70 ml). The combined organic layers were dried with sodium sulfate. The solvent was removed *in vacuo* and the residue crystallized from diisopropyl ether/ethanol 1:1. Yield 0.44 g (40%), yellow crystals, mp 230° (dec); ir: ν 3434, 3192, 1735, 1712, 1669 cm^{-1}; uv: λ max (log ε) 272 (3.761), 379 nm

(3.372); ^{13}C nmr: δ 173.4, 164.7, 155.6, 147.5, 130.9, 130.5, 127.8, 127.3, 117.7; ms: m/z 217 (M^+).

Anal. Calcd. for $C_{11}H_7NO_4$ (217.18): C, 60.83; H, 3.25; N, 6.45. Found: C, 60.83; H, 3.42; N, 6.30.

5-(4-Chlorophenyl)-4-hydroxy pyridine-2,3,6-trione (**11b**).

This compound was prepared analogously to **11a** from 1.0 g (4 mmol) of compound **8b** and 1 ml of boron trifluoride diethyl etherate. Yield 0.50 g (50%), yellow crystals (diisopropyl ether/ethanol 1:1), mp 185° (dec); ir: ν 3471, 3183, 1752, 1703, 1663 cm^{-1}; uv: λ max (log ε) 273 (3.829), 378 nm (3.342); ms: m/z 251 (M^+).

Anal. Calcd. for $C_{11}H_6ClNO_4$ (251.62): C, 52.50; H, 2.40; N, 5.56. Found: C, 52.13; H, 2.51; N, 5.72.

4-Hydroxy-1-methyl-5-phenyl-pyridine-2,3,6-trione (**12a**).

This compound was prepared analogously to **11a** from 0.46 g (2 mmol) of compound **9a** and 1 ml of boron trifluoride diethyl etherate. Yield 0.16 g (35%), yellow crystals (diisopropyl ether/ethanol 1:1), mp 155°; ir: ν 3543, 1701, 1647 cm^{-1}; uv**:** λ max (log ε) 281 (3.863); ^{1}H nmr: δ 11.32 (s, 1 H), 7.40-7.33 (m, 5 H), 3.14 (s, 3 H); ^{13}C nmr: δ 172.5, 164.3, 155.9, 153.1, 130.4, 127.8, 127.4, 127.3, 118.3, 26.6; ms: m/z 231 (M^+).

Anal. Calcd. for $C_{12}H_9NO_4$ (231.21): C, 62.34; H, 3.92; N, 6.05. Found: C, 62.14; H, 4.02; N, 5.96.

Acetic Acid 2,3,6-Triacetoxy-5-phenyl-pyridine-4-yl Ester (**13a**).

A solution of 0.22 g (1 mmol) of compound **11a** in acetic anhydride (10 ml) was heated with powdered zinc (1.0 g) for 5 minutes to 100°. After cooling the mixture was diluted with ethyl acetate (50 ml) and filtered. From the solution obtained the solvent was removed *in vacuo* and the residue crystallized from diisopropyl ether/ethanol 1:1. Yield 0.15 g (40%), colorless crystals, mp 137°; ir: ν 1784, 1760 cm^{-1}; uv: λ max (log ε) 240 (3.967), 269 nm (3.883); ^{1}H nmr ($CDCl_3$): δ 7.41-7.39 (m, 2 H), 7.29-7.27 (m, 3 H), 2.32 (s, 3 H), 2.30 (s, 3 H), 1.97 (s, 6 H); ms: m/z 387 (M^+).

Anal. Calcd. for $C_{19}H_{17}NO_8$ (387.34): C, 58.91; H, 4.42; N, 3.61. Found: C, 50.81; H, 3.63; N, 4.34.

Acetic Acid 5-(4-Chloro-phenyl)-2,3,6-triacetoxy-pyridine-4-yl Ester (**13b**).

This compound was prepared analogously to **13a** from 0.25 g (1 mmol) of compound **11b**. Yield 0.12 g (30%), colorless crystals (diisopropyl ether/ethanol 1:1), mp 151°; ir: ν 1790, 1765 cm^{-1}; uv: λ max (log ε) 243 (4.076), 267 nm (3.975); ^{1}H nmr ($CDCl_3$): δ 7.39, 7.23 (d, each, 2 H, J = 8.1 Hz), 2.32 (s, 3 H), 2.30 (s, 3 H), 2.06 (s, 6 H); ms: m/z 421 (M^+).

Anal. Calcd. for $C_{19}H_{16}ClNO_8$ (421.79): C, 54.10; H, 3.82; N, 3.32. Found: C, 54.03; H, 3.85; N, 3.31.

4-Methoxy-5-phenyl-pyridine-2,3,6-trione (**14a**).

An ethereal solution of diazomethane was added in several portions to a solution of 0.22 g (1 mmol) of compound **11a** in methanol (25 ml) until the red color disappeared. The volatile components were removed *in vacuo* and the residue was crystallized from diethyl ether. Yield 0.10 g (45%), yellow crystals, mp 153°; ir: ν 3233, 1761, 1686 cm^{-1}; uv: λ max (log ε) 275 (3.818), 385 nm (3.240); ^{1}H nmr ($CDCl_3$): δ 8.60 (s, 1 H), 7.46-7.39 (m, 5 H), 3.94 (s, 3 H); ms: m/z 231 (M^+).

Anal. Calcd. for $C_{12}H_9NO_4$ (231.21): C, 62.34; H, 3.92; N, 6.05. Found: C, 61.82; H, 3.3.92; N, 5.96.

5-(4-Chloro-phenyl)-4-methoxy-pyridine-2,3,6-trione (**14b**).

This compound was prepared analogously to **14a** from 0.25 g (1 mmol) of compound **11b**. Yield 0.10 g (40%), yellow crystals (diethyl ether), mp 167°; ir: ν 3229, 1762, 1686 cm^{-1}; uv: λ max (log ε) 224 (4.192), 276 nm (3.768); ^{1}H nmr ($CDCl_3$): δ 8.51 (s, 1 H), 7.45, 7.34 (2d, each, 2 H, J = 8.3 Hz), 4.01 (s, 3 H); ms: m/z 265 (M^+).

Anal. Calcd. for $C_{12}H_8ClNO_4$ (265.65): C, 54.25; H, 3.03; N, 5.27. Found: C, 54.37; H, 3.14; N, 5.14.

4-(4-Chloro-benzyloxy)-5-phenyl-pyridine-2,3,6-trione (**15a**).

A solution of 0.39 g (3 mmol) of 4-chlorophenyldiazomethane [22] in hexane (10 ml) was added to a stirred solution of 0.43 g (2 mmol) of compound **11a** in dioxane (50 ml). After one hour the excess of 4-chlorophenyldiazomethane was destroyed by addition of acetic acid (0.2 ml). The volatile components were removed *in vacuo* and the residue was crystallized from ethyl acetate. Yield 0.13 g (20%), yellow crystals, mp 197°; ir: ν 3441, 1741, 1678 cm^{-1}; uv: λ max (log ε) 219 (4.446), 267 nm (3.891); ^{1}H nmr: δ ($CDCl_3$): δ 11.97 (s, 1H), 7.38-7.19 (m, 9 H), 5.10 (s, 2H); ms: m/z 341 (M^+).

Anal. Calcd. for $C_{18}H_{12}ClNO_4$ (341.75): C, 63.26; H, 3.53; N, 4.10. Found: C, 63.41; H, 3.72; N, 4.02.

X-ray Diffraction Analysis of **15a**.

Data collection: CAD4 Diffractometer, crystal mounted in a glass capillary, cell constants from 25 centered reflections. Mo-K_α radiation, λ = 0.71073 Å, graphite monochromator, ω-scan, maximum measuring time 60 s, intensity of three standard reflections checked every two hours. Structure solution by SHELXS-86 [23] and refinement by SHELXL-93 [24], non-hydrogen atoms refined anisotropically, hydrogens with $U_i = 1.2 \times U_{eq}$ of the adjacent non-hydrogen atom. Full-matrix refinement against F^2. Weight: SHELXL-93. Maximum and minimum of the final difference Fourier synthesis 0.168 and –0.267 e Å^{-3}. The drawing (Figure 1) was made by ZORTEP [25]. Selected data are given in tables 1. The complete data are available from the Cambridge Crystallographic Data Centre [26]. The deposition number is CCDC 183746.

8-Methoxy-7-phenyl-1-oxa-5-aza-spiro[2,5)oct-7-ene-4,6-dione (**16a**).

An ethereal solution of diazomethane was added in several portions to a stirred solution of 0.22 g (1 mmol) of compound **11a** in methanol (25 ml) until the red color disappeared. After 5 minutes the volatile components were removed and the residue was crystallized from diisopropyl ether/ethanol 1:1. Yield 0.05 g (20%), light yellow crystals, mp 192°; ir: ν 3053, 1736, 1667, 1624 cm^{-1}; uv: λ max (log ε) 217 (4.337), 275 nm (3.758); ^{1}H nmr ($CDCl_3$): δ 8.22 (s, 1H), 7.43-7.31 (m, 5 H), 3.57 (d, J = 7.5 Hz, 1 H), 3.53 (d, J = 7.5 Hz, 1 H), 3.37 (s, 3H); ms: m/z 245 (M^+).

Anal. Calcd. for $C_{13}H_{11}NO_4$ (245.23): C, 63.67; H, 4.52; N, 5.71. Found: C, 63.53; H, 4.58; N, 5.59.

8-Methoxy-5-methyl-7-phenyl-1-oxa-5-aza-spiro[2,5]oct-7-ene-4,6-dione (**17a**).

An ethereal solution of excessive diazomethane was added to a solution of 0.22 g (1 mmol) compound **11a** in methanol (25 ml). After one hour the solvent was removed *in vacuo*. The residue was crystallized from diisopropyl ether/ethanol 1:1. Yield 0.065 g (25%), light yellow crystals, mp 86°; ir: ν 2952, 1707, 1661, 1639 cm^{-1}; uv: λ max (log ε) 225 (4.310), 277 nm (3.659); ^{1}H

nmr ($CDCl_3$): δ 7.41-7.31 (m, 5 H), 3.57 (d, J = 7.5 Hz, 1 H), 3.51 (d, J = 7.5 Hz, 1 H), 3.35 (s, 3 H) 3.31 (s, 3 H); ms: m/z 259 (M^+).

Anal. Calcd. for $C_{14}H_{13}NO_4$ (259.26): C, 64.86; H, 5.05; N, 5.40. Found: C, 64.55; H, 5.32; N, 5.07.

(4-Chlorophenyl)-8-methoxy-5-methyl-7-1-oxa-5-aza-spiro-[2,5]oct-7-ene-4,6-dione (**17b**).

This compound was prepared analogously to **17a** from 0.25 g (1 mmol) of compound **11b**. Yield 0.90 g (30%), light yellow crystals (diisopropyl ether/ethanol 1:1), mp 126°; ir: ν 2953, 1711, 1654 cm^{-1}; uv: λ max (log ε) 226 (4.388), 275 nm (3.700); ^1H nmr ($CDCl_3$): δ 7.41-7.27 (m, 4 H), 3.56 (d, J = 8 Hz, 1 H), 3.50 (d, J = 8 Hz, 1 H), 3.39 (s, 3 H), 3.31 (s, 3 H); ms: m/z 293 (M^+).

Anal. Calcd. for $C_{14}H_{12}ClNO_4$ (293.70): C, 57.25; H, 4.11; N, 4.76. Found: C, 56.80; H, 4.18; N, 4.67.

3-Hydroxy-4-phenyl-2*H*-pyrido[3,4-*b*]quinoxalin-1-one (**18a**).

A solution of 0.21 g (1 mmol) of compound **11a** und 0.11 g (1 mmol) of 1,2-diamino benzene in methanol (10 ml) were heated at reflux for 15 minutes. The product precipitated while cooling. Yield 0.17 g (85 %); violet crystals (methanol), mp 270° (dec); ir: ν 3153, 2983, 1698, 1605 cm^{-1}; uv: λ max (log ε) 226 (4.334), 291 (4.443), 538 nm (3.784); ^1H nmr: δ 11.30 (s, 1 H), 10.84 (s, 1 H), 7.48-7.33 (m, 9 H); ms: m/z 289 (M^+).

Anal. Calcd. for $C_{17}H_{11}N_3O_2$ (289.29): C, 70.58; H, 3.83; N, 14.52. Found: C, 69.59; H, 3.67; N, 14.44.

4-(4-Chloro-phenyl-3-hydroxy 2*H*-pyrido[3,4-*b*]quinoxalin-1-one (**18b**).

This compound was prepared analogously to **18a** from 0.25 g (1 mmol) of compound **11b**. Yield 0.26 g (80%), violet crystals (methanol), mp > 280°; ir: ν 2976, 2836, 1703, 1603 cm^{-1}; uv: λ max (log ε) 291 (4.447), 535 nm (3.769); ^1H nmr: δ 11.34 (s, 1 H), 10.93 (s, 1 H), 7.78-7.25 (m, 8 H); ms: m/z 323 (M^+).

Anal. Calcd. for $C_{17}H_{10}ClN_3O_2$ (323.74): C, 63.07; H, 3.11; N, 12.98. Found: C, 62.13; H, 2.98; N, 12.01.

1,3-Dimethoxy-4-phenylpyrido[3,4-*b*]quinoxaline (**19a**).

An ethereal solution of excessive diazomethane was added to a solution of 0.14 g (0.5 mmol) of compound **18a** in acetone (25 ml) and methanol (25 ml). After 5 hours the solvent was evaporated and the residue purified by column chromatography using diethyl ether as eluent. Yield 0.11 g (70%), orange crystals (ethyl acetate); mp 249°; ir: ν 2944, 1618, 1587, 1521 cm^{-1}; uv: λ max (log ε) 275 (4.610), 472 nm (3.647); ^1H nmr ($CDCl_3$): δ 8.29 (d, 1 H, J = 8.4 Hz), 8.05 (d, 1 H, J = 8.4 Hz), 7.64-7.43 (m, 7 H), 4.39 (s, 3 H), 4.10 (s, 3 H); ms: m/z 317 (M^+).

Anal. Calcd. for $C_{19}H_{15}N_3O_2$ (317.35): C, 71.91; H, 4.76; N, 13.24. Found: C, 71.62; H, 4.70; N, 13.11.

4-(4-Chlorophenyl)-1,3-dimethoxypyrido[3,4-*b*]quinoxaline (**19b**).

This compound was prepared analogously to **19a** from 0.16 g (0.5 mmol) of compound **18b**. Yield 0.13 g (75%), orange crystals (diisopropyl ether/ethanol 1:1), mp 248°; ir: ν 2938, 1618, 1586, 1518 cm^{-1}; uv: λ max (log ε) 272 (4.561), 470 nm (3.585); ^1H nmr ($CDCl_3$): δ 8.30 (d, 1 H, J = 8.5 Hz), 8.04 (d, 1 H, J = 8.5 Hz), 7.80-7.46 (m, 8 H), 4.39 (s, 3 H), 4.11 (s, 3 H); ms: m/z 351 (M^+).

Anal. Calcd. for $C_{19}H_{14}ClN_3O_2$ (351.79): C, 64.87 ; H, 4.01; N, 11.94. Found: C, 65.03; H, 3.98; N, 11.69.

X-ray Diffraction Analysis of **19b**.

Data collection: CAD4 Diffractometer, crystal mounted in a glass capillary, cell constants from 25 centered reflections. Mo-K_α radiation, λ = 0.71073 Å, graphite monochromator, ω-scan, maximum measuring time 60 s, intensity of three standard reflections checked every two hours. Structure solution by SHELXS-86 [23] and refinement by SHELXL-93 [24], non-hydrogen atoms refined anisotropically, hydrogens with $U_i = 1.2 \times U_{eq}$ of the adjacent carbon atom. Full-matrix refinement against F^2. Weight: SHELXL-93. Maximum and minimum of the final difference Fourier synthesis 0.190 and –0.210 e $Å^{-3}$. The drawing (Figure 2) was made by ZORTEP [25]. Selected data are given in tables 1. The complete data are available from the Cambridge Crystallographic Data Centre [26]. The deposition number is CCDC 183747.

4-Hydroxy-5-phenyl-3-(phenylhydrazono)-3*H*-pyridine-2,6-dione (**20**).

A solution of 0.24 g (2.2 mmol) of phenylhydrazine in methanol (5 ml) was added to a stirred solution of 0.43g (2 mmol) of compound **11a** in methanol (25 ml). After 1 day the precipitate was collected and recrystallized from methanol. Yield 0.37 g (60%), orange crystals, mp 252°; ir: ν 3010, 1648, 1597 cm^{-1}; uv: λ max (log ε) 260 (4.317), 431 nm (4.500); ^1H nmr: δ 14.24 (s, 1 H), 11.38 (s, 1 H), 10.12 (s, 1 H), 7.79-7.36 (m, 10 H); ms: m/z 307 (M^+).

Anal. Calcd. for $C_{17}H_{13}N_3O_3$ (307.31): C, 66.44; H, 4.26; N, 13.67. Found: C, 66.21; H, 4.19; N, 13.96.

4-Methoxy-5-phenyl-3-(phenylhydrazono)-3*H*-pyridine-2,6-dione (**21**).

An ethereal solution of excessive diazomethane was added to a solution of 0.31 g (1 mmol) of compound **21** in methanol (50 ml). After vigorous evolution of nitrogen had ceased the solution was evaporated to dryness and the residue crystallized from methanol. Yield 0.27 g (90%), yellow crystals, mp 248°; ir: ν 3014, 1661, 1643, 1589 cm^{-1}; uv: λ max (log ε) 259 (4.235), 427 nm (4.522); ^1H nmr: δ 14.27 (s, 1 H), 11.65 (s, 1 H), 7.54-7.30 (m, 10 H), 3.81 (s, 3 H); ms: m/z 321 (M^+).

Anal. Calcd. for $C_{18}H_{15}N_3O_3$ (321.33): C, 67.28; H, 4.70; N, 13.07. Found: C, 67.34; H, 4.92; N, 12.97.

4-Hydroxy-5-phenylpyridine-2,3,6-trione-3-oxime (**22a**).

A solution of 0.22 g (1 mmol) of compound **11a** and 0.21 g (3 mmol) of hydroxylamine hydrochloride in methanol (20 ml) was heated at reflux for 30 minutes. The solvent was evaporated and the residue extracted with acetone (20 ml). The solution obtained was filtered and again freed of the solvent. The residue crystallized from diisopropyl ether/ethanol 1:1. Yield 0.12 g (50%), yellow crystals, mp 191°; ir: ν 3171, 3028, 2844, 1662 cm^{-1}; uv: λ max (log ε) 253 (4.121), 366 nm (3.606); ^1H nmr: δ 11.51 (s, 1 H), 10.61 (s, 1 H), 7.36-732 (m, 5 H); ms: m/z 232 (M^+).

Anal. Calcd. for $C_{11}H_8N_2O_4$ (232.19): C, 56.90; H, 3.47; N, 12.06. Found: C, 56.60; H, 3.89; N, 11.97.

5-(4-Chlorophenyl)-4-hydroxy pyridine-2,3,6-trione-3-oxime (**22b**).

This compound was prepared analogously to **22a** from 0.25 g (1 mmol) of compound **11b**. Yield 0.16 g (60%), yellow crystals (diisopropyl ether/ethanol 1:1), mp 183°; ir: ν 3154, 3022, 2841, 1680, 1660 cm^{-1}; uv: λ max (log ε) 255 (4.285), 368 nm (3.634); ^1H nmr: δ 11.52 (s, 1 H), 10.79 (s, 1 H), 7.40-7.35 (m, 4 H); ms: m/z 266 (M^+).

Anal. Calcd. for $C_{11}H_7ClN_2O_4$ (266.64): C, 49.55; H, 2.64; N, 10.50. Found: C, 48.82; H, 2.94; N, 10.33.

4-Methoxy-5-phenylpyridine-2,3,6-trione-3-oxime (**23a**).

This compound was prepared analogously to **22a** from 0.24 g (1 mmol) of compound **14a** and 0.14 g (2 mmoles) of hydroxylamine hydrochloride. Yield 0.10 g (40%), light yellow crystals (diisopropyl ether/ethanol 1:1), mp 180° (dec); ir: ν 3038, 1668, 1590 cm^{-1}; uv: λ max (log ε) 225 (4.082), 262 (4.083), 338 nm (3.669); ^1H nmr ($CDCl_3$): δ 8.33 (s, 1 H), 7.50-7.30 (m, 5 H), 3.73 (s, 3 H); ms: m/z 246 (M^+).

Anal. Calcd. for $C_{12}H_{11}N_2O_4$ (246.22): C, 58.54; H, 4.09; N, 11.37. Found: C, 58.19; H, 3.99; N, 10.73.

4-Hydroxy-5-phenyl-pyridine-2,3,6-trione-3-(*O*-methyloxime) (**24a**).

A solution of 0.22 g (1 mmol) of compound **11a** and 0.25 g (3 mmol) of *O*-methylhydroxylamine hydrochloride in methanol (20 ml) were heated at reflux for one hour. The solvent was evaporated, the residue extracted with ethyl acetate (20 ml) and the solution obtained filtered. The product crystallized in the refrigerator as a mixture of syn/anti isomers. Yield 0.06g (25%), yellow crystals (ethyl acetate), mp 193-195°; ir: ν 3186, 1707, 1660, 1572 cm^{-1}; uv: λ max (log ε) 262 (4.271), 365 nm (3.754); ^1H nmr ($CDCl_3$): δ 9.05 (s, 0.75 H), 8.15 (s, 0.25 H), 7.42-7.37 (m, 5H), 4.41 (s, 2.25 H), 4.37 (s, 0.75 H); ms: m/z 246 (M^+).

Anal. Calcd. for $C_{12}H_{10}N_2O_4$ (246.22): C, 58.54; H, 4.09; N, 11.37. Found: C, 58.37; H, 4.34; N, 11.30.

5-(4-Chlorophenyl)-4-hydroxypyridine-2,3,6-trione-3-(*O*-methyloxime) (**24b**).

This compound was prepared analogously to **24a** from 0.25 g (1 mmol) of compound **11b**. Yield 0.08 g (30%) as a mixture of syn/anti isomers; the more soluble isomer was removed by recrystallization from ethyl acetate.Yellow crystals, mp 220° (dec); ir: ν 3353, 3191, 3083, 1724, 1698 cm^{-1}; uv: λ max (log ε) 259 (4.284), 3.66 nm (3.782); ^1H nmr ($CDCl_3$): δ ($CDCl_3$): 9.12 (s, 1 H), 8.11 (s, 1 H), 7.40-7.35 (m, 4 H), 4.42 (s, 3 H); ms: m/z 280 (M^+).

Anal. Calcd. for $C_{12}H_9ClN_2O_4$ (280.67): C, 51.35; H, 3.23; N, 9.98. Found: C, 51.86; H, 3.40; N, 10.07.

6-Hydroxy-4-methoxy-2,5-dioxo-6-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylic Acid Methyl Ester (**26a**).

A solution of 0.50 g (1.8 mmol) of compound **25a** [19] and 0.45 g (2 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dioxane (20 ml) was heated at reflux for 10 minutes. After 1 hour at room temperature the hydroquinone had separated from the red solution. After filtration the solvent was evaporated and the residue purified by column chromatography using diethyl ether (containing water) as eluent. Yield 0.20 g (38%), light yellow crystals (diisopropyl ether/methanol 1:1); mp 155°; ir: ν 3346, 3251, 1731, 1650, 1621 cm^{-1}; uv: λ max (log ε) 207 (4.171), 260 nm (4.011); ^1H nmr: δ 9.29 (s, 1 H), 7.50 (s, 1 H), 7.46-7.38 (m, 5 H), 3.80 (s, 3 H), 3.77 (s, 3 H); 13C nmr: 189.3 (C-5), 163.3, 160.5 (C-2), 151.0, 138.6 (C-1´), 128.6 (C-4´), 128.1 (C-3´), 126.3 (C-2´), 120.1 (C-3), 84.3 (C-6), 58.9, 52.6; CH-COSY: H-1/C-3, H-1/C-5, H-2´/C-6; NOE: H-1/H-2'. ms: m/z 291 (M^+, 1%), 105 (100).

Anal. Calcd. for $C_{14}H_{13}NO_6$ (291.26): C, 57.73; H, 4.50; N, 4.81. Found: C, 57.43; H, 4.49; N, 4.58.

6-Hydroxy-4-methoxy-6-phenyl-1,6-dihydropyridine-2,5-dione (**26b**).

This compound was prepared analogously to **26a** from 0.39 g (1.8 mmol) of compound **25b** [19]. Eluent: chloroform/methanol 10:1. Yield 0.19 g (45%), colorless powder (diisopropyl ether/methanol 1:1), mp 151°; ir: ν 3320, 3060, 1705, 1650, 1605 cm^{-1}; uv: λ max (log ε) 208 (4.129), 258 nm (4.003); ^1H nmr ($CDCl_3$): δ 8.83 (broad s, 1 H), 7.42 (s, 5 H), 7.30 (s, 1 H), 6.03 (d, 1 H, J = 2 Hz), 3.73 (s, 3 H); ms: m/z 233 (M^+).

Anal. Calcd. for $C_{12}H_{11}NO_4$ (233.23): C, 61.80; H, 4.75; N, 6.01. Found: C, 61.69; H, 4.85; N, 6.10.

6-Acetoxy-4-methoxy-2,5-dioxo-6-phenyl-1,2,5,6-tetrahydropyridine-3-carboxylic Acid Methyl Ester (**27a**).

A solution of 0.30 g (1 mmol) of compound **26a** and 0.12 g (1.5 mmol) of pyridine in acetic anhydride (10 ml) was stirred at room temperature for 1 hour. The solvent was removed completely *in vacuo* at 45° by repeating the evaporation several times after addition of small amounts of benzene. The solution of the reddish residue in diethyl ether (5 ml) containing two drops of acetic acid was kept in the refrigerator for crystallization. Yield 0.25 g (73%), colorless crystals (diisopropyl ether/methanol 1:1), mp 120° (dec, with red color); ir: ν 3180, 3060, 2930, 1745, 1720, 1165 cm^{-1}; uv: λ max (log ε) 267 nm (4.218); ^1H nmr ($CDCl_3$): δ 9.00 (s, 1 H), 7.73-7.27 (m, 5 H), 3.90 (s, 6 H), 2.20 (s, 3 H); ms: m/z 333 (M^+).

Anal. Calcd. for $C_{16}H_{15}NO_7$ (333.30): C, 57.66; H, 4.54; N, 4.20. Found: C, 57.44; H, 4.67; N, 4.20.

Acetic Acid 4-Methoxy-3,6-dioxo-2-phenyl-1,2,3,6-tetrahydropyridin-2-yl Ester (**27b**).

This compound was prepared analogously to **27a** from 0.30 g (1.3 mmol) of compound **26b**. Yield 0.21 g (58 %), colorless crystals (diisopropyl ether/methanol 1:1), mp 145° (dec, with red color); ir: ν 3170, 3040, 2930, 2890, 1730, 1710, 1650, 1605 cm^{-1}; uv: λ max (log ε) 264 nm (4.216); ^1H nmr ($CDCl_3$): δ 8.50 (broad s, 1H), 7.83-730 (m, 5 H), 6.00 (d, 1 H, J = 2 Hz), 3.80 (s, 3 H), 2.20 (s, 3 H); ms: m/z 275 (M^+).

Anal. Calcd. for $C_{14}H_{13}NO_5$ (275.26): C, 61.09; H, 4.76; N, 5.09. Found: C, 60.62; H, 4.81; N, 5.31.

4-Methoxy-2,5-dioxo-6-phenyl-2,5-dihydropyridine-3-carboxylic Acid Methyl Ester (**28a**).

Compound **27a** (0.1 g, 0.4 mmol) was heated to 120° *in vacuo* for 48 hours. Quantitative yield, light red powder, mp 149°; uv (CH_2Cl_2): λ max (log ε) 233 (4.188), 337 (3.971), 512 nm (3.002); ^1H nmr ($CDCl_3$): δ 8.33–8.10 (m, 2 H), 7.76-7.30 (m, 3 H), 4.13 (s, 3 H), 3.98 (s, 3 H).

4-Methoxy-6-phenylpyridine-2,5-dione (**28b**).

Compound **27b** (0.1 g, 0.5 mmol) was heated to 140° *in vacuo* for 5 hours and then held at 120° for 40 hours. Yield quantitative, dark red powder, mp 146°; uv (CH_2Cl_2): λ max (log ε) 232 (4.206), 328 (3.982), 515 nm (2.968); ^1H nmr ($CDCl_3$): δ 8.21-7.97 (m, 2 H), 7.63-7.25 (m, 3 H), 6.27 (s, 1 H), 3.88 (s, 3 H).

(4-Methoxy-5-methoxycarbonyl-3,6-dioxo-2-phenyl-1,2,3,6-tetrahydro-yridin-2-yl)-malonic Acid Dimethyl Ester (**29**).

A solution of 0.83 g (2.5 mmol) of compound **27a**, 0.35 g (2.6 mmol) of dimethyl malonate and 0.5 ml of pyridine in toluene (10 ml) was heated to 80° for one hour. From the now colorless

solution the volatile components were removed *in vacuo* and the residue crystallized from diisopropyl ether/methanol 1:1. Yield 0.66 g (65%), colorless crystals, mp 110°; ir: ν 3360, 3010, 2960, 1745, 1705, 1675, 1630 cm^{-1}; uv: λ max (log ε) 212 (3.861), 260 nm (3.874); ^1H nmr ($CDCl_3$): δ 7.43 (s, 5 H), 5.05 (s, 1 H), 3.97 (s, 3 H), 3.93 (s, 3 H), 3.83 (s, 3 H), 3.60 (s, 3 H); ms: m/z 405 (M^+).

Anal. Calcd. for $C_{19}H_{19}NO_9$ (405.36): C, 56.30; H, 4.72; N, 3.46. Found: C, 56.28; H, 4.83; N, 3.25.

8-Methoxy-4-methyl-6,9-dioxo-9a-phenyl-9,9a-dihydro-*4H,6H*-pyrido[2,1-b][1,3]oxazine-7-carboxylic Acid Methyl Ester (**30**).

A solution of 0.41 g (1.5 mmol) of compound **28a** (freshly prepared by thermolysis of 0.5 g of compound **27a**) and 0.14 g (0.2 mmol) of 2-butenal in toluene (5 ml) was heated to 80° under nitrogen until the red colour disappeared. The volatile components were removed *in vacuo* and the residue was purified by column chromatography using chloroform/ethyl acetate as eluent. Yield 0.25 g (45%), yellow crystals (diisopropyl ether/methanol 1:1), mp 125-129° (dec, with red color); ir: ν 3100, 3060, 2980, 1745, 1720, 1670, 1650, 1630 cm^{-1}; uv: λ max (log ε); 212 (3.794), 260 nm (3.880); ^1H nmr ($CDCl_3$): δ 7.40 (s, 5 H), 6.36 (d, 1 H, J = 8.1 Hz), 5.00 (dd**,** 1 H, J = 8.1 Hz, J = 2.4 Hz), 4.33 (mc, 1 H), 3.90 (s, 3 H), 3.80 (s, 3 H), 1.52 (d, 3 H, J = 6.1 Hz); ms: m/z 243 (M^+).

Anal. Calcd. for $C_{18}H_{17}NO_6$ (343.33): C, 62.97; H, 4.99; N, 4.08. Found: C, 63.16; H, 5.20; N, 4.00.

REFERENCES AND NOTES

[1] W. Steglich, H. Besl and A. Prax, *Tetrahedron Letters*, **13**, 4895 (1972); H.-J Lohrisch, L. Kopanski, R. Herrmann, H. Schmidt and W. Steglich, *Liebigs Ann. Chem.*, 177 (1986).

[2] R. L. Edwards and M. Gill, *J. Chem. Soc., Perkin Trans. I*, 1921 (1973); M. Gill, M. J. Kiefel, D. A. Lally and A. Ten, *Aust. J. Chem.*, **43**, 1497 (1990).

[3] G. Pattenden, N. A. Pegg and R. W. Kenyon, *Tetrahedron Letters*, **28**, 4779 (1987); G. Pattenden, N. A. Pegg and R. W. Kenyon, *J. Chem. Soc., Perkin Trans. I*, 2363 (1991).

[4] H. Poschenrieder, E. Eckl, H.-D. Stachel, A. Windt and K. Polborn, *J. Heterocyclic Chem.*, **37**, 839 (2000).

[5] H. Poschenrieder, G. Höfner and H.-D. Stachel, *Arch. Pharm. Pharm. Med. Chem.*, **333**, 211 (2000).

[6] H.-J. Knackmuss, *Chem. Ber.*, **101**, 1148 (1968); H.-J. Knackmuss, *Chem. Ber.*, **101**, 2679 (1968).

[7] H.-J. Knackmuss, *Angew. Chem.*, **95**, 163 (1973); P. Ashworth, *Tetrahedron*, **32**, 261 (1976).

[8] J. H. Boyer and S. Kruger, *J. Am. Chem. Soc.*, **79**, 3552 (1957).

[9] S. Radl, in: Advances in Heterocyclic Chemistry, Vol. **61**, ed. A. R. Katritzky, Academic Press, San Diego/ New York 1994, p 141.

[10] J. Backhaus, Ph. D. Dissertation, Universität Bonn, Germany, 1979.

[11] M. Gill and, W. Steglich, in: Progress in the Chemistry of Organic Natural Products, Vol. **51**, W. Herz, H. Grisebach, G. W. Kirby, C. Tamm, ed., Springer Verlag, Wien/ New York, 1987, p 231 – 235.

[12] K. C. Nicolaou, S. Sugita, P. S. Baran and Y.-L. Zhong, *Angew. Chem., Int. Ed. Engl.*, **40**, 207 (2001); Nicolaou, Y.-L. Zhong, P. S. Baran and K. Sugita, *Angew. Chem., Int. Ed. Engl.*, **40**, 2145 (2001).

[13] T. Billert, R. Beckert, P. Feeling, M. Döring and H. Görls, *Tetrahedron*, **53**, 5455 (1997).

[14] M. Ozaki, Y. Ezure, T. Okubo, K. Yamane and S. Matsumura, *Heterocycles* **11**, 191 (1978).

[15] P. S. Bailey and W. Trahanovsky, in: Organic Chemistry, Vol. **39**, ed. A. T. Blomquist, H. H. Wasserman, Academic Press, New York 1978, p 197 – 219.

[16] H. Poschenrieder and H.-D. Stachel, *Arch. Pharm.* (Weinheim, Germany), **322**, 301 (1989).

[17] G. A. Swan, *J. Chem. Soc. Perkin Trans. I*, 1757 (1985); P. Ashwood, *Tetrahedron*, **32**, 261 (1976).

[18] R. Kuhn, H. Bauer and H.-J. Knackmuss., *Chem. Ber.*, **98**, 2139 (1965); A. J. Shand and R. H. Thomson, *Tetrahedron*, **19**, 1919 (1963).

[19] H.-D. Stachel, B. Wiesend and C. Kreiner, *J. Heterocyclic Chem.*, **22**, 1413 (1985).

[20] H. Poschenrieder, G. Höfner and H.-D. Stachel, *Arch. Pharm. Pharm. Med. Chem.*, **332**, 309 (1999).

[21] M. Mawr, J. J. Kulagowski, P. D. Leeson, S. Grimwood and G. R. Marshall, *Bioorg. Med. Chem. Lett.*, **5**, 2643 (1995).

[22] G. L. Closs and R. A. Moss, *J. Am. Chem. Soc.*, **86**, 4042 (1964).

[23] G. M. Sheldrick, SHELXS-86, Universität Göttingen, Germany, 1990.

[24] G. M. Sheldrick, SHELXL-93, Universität Göttingen, Germany, 1993.

[25] L. Zolnay, G. Huttner, XPMA, ZORTEP, Universität Heidelberg, Germany, 1994.

[26] Copies of the data can be obtained free of charge on request to The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, Great Britain [fax: (+44) 1223-336-033; email: deposit@ccdc.cam.ac.uk].