PYRROLOPHENOXATHIIN DIOXIDES. 1. SYNTHESIS OF 3*H*-PYRROLO[2,3-*c*]PHENOXATHIIN 11,11-DIOXIDE AND 1*H*-PYRROLO[3,2-*b*]PHENOXATHIIN 10,10-DIOXIDE BY THE FISCHER REACTION

T. E. Khoshtariya, M. G. Maisuradze, L. M. Tevzadze, L. N. Kurkovskaya, and N. N. Suvorov

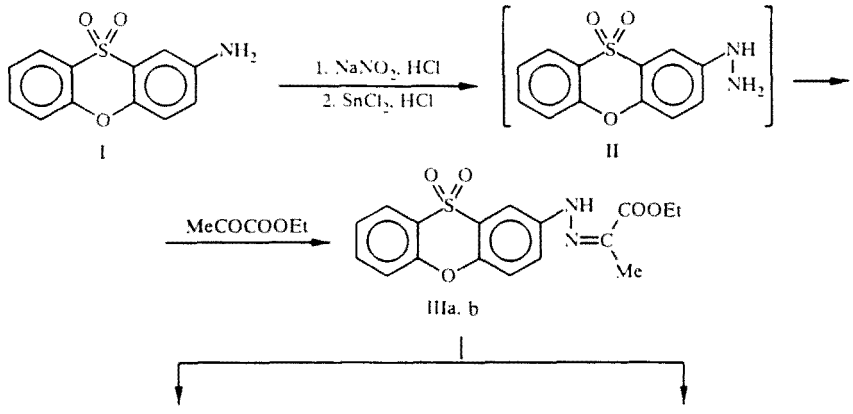
Cyclization of the 2-phenoxathiin 10,10-dioxide hydrazone of ethyl pyruvate in ethyl polyphosphate results in the concurrent formation of the respective cyclic esters of both angular and linear structures. The parent compounds of a new condensed heterocyclic system of pyrrolophenoxathiin dioxides are synthesized from the latter.

As a continuation of studies into the chemistry of condensed tetracyclic pyrrole-containing compounds, we have carried out the synthesis of the so-far unreported 3*H*-pyrrolo[2,3-*c*]phenoxathiin 11,11-dioxide and 1*H*-pyrrolo[3,2-*b*]phenoxathiin 10,10-dioxide from 2-aminophenoxathiin 10,10-dioxide (I) by the Fischer reaction.

Hydrazone III was obtained as a mixture of *syn* and *anti* isomers that were separated by column chromatography. The PMR spectra of the solutions of stereoisomers of hydrazone III differ considerably (Table 1). In the *syn* form of the hydrazone there is a considerable downfield shift (to 12.2 ppm) of the signal due to the NH proton compared to the *anti* form (8 ppm), resulting from the participation of the NH group proton in strong intramolecular hydrogen bonding. Corresponding changes caused by the formation of an intramolecular hydrogen bond are also noted in the IR and UV spectra of compound III.

Cyclization under Fischer reaction conditions [1] by treatment of the mixture of isomers with ethyl polyphosphate resulted in the isolation of two isomeric tetracyclic pyrrole-containing esters — ethyl 3*H*-pyrrolo[2,3-*c*]phenoxathiin-2-carboxylate 11,11-dioxide (IV) and ethyl 1*H*-pyrrolo[3,2-*b*]phenoxathiin-2-carboxylate 10,10-dioxide (VII). Although the linear isomer (VII) was formed in trace amounts, we succeeded in isolating and characterizing both isomers.

Saponification of cyclic esters IV and VII followed by decarboxylation of the respective acids V and VIII (for the reason mentioned above, decarboxylation of acid VIII was carried out without it being isolated in a pure form) afforded the unsubstituted compounds VI and IX.



Georgian Technical University, Tbilisi 380075. D. I. Mendeleev Russian Chemical Engineering University, Moscow 125047. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 409-412, March, 1996. Original article submitted July 1, 1995.

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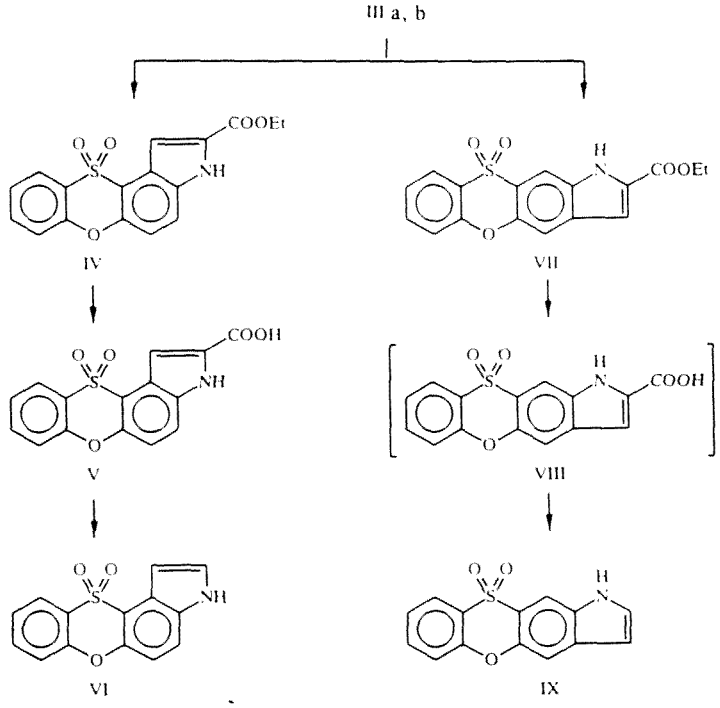
TABLE 1. PMR Spectra of Hydrazones III (in $CDCl_3$)

Compound	Chemical shifts, δ, ppm				
	CH_3	CH_2 CH_3	CH_2–CH_3	NH	$J_{CH_2CH_3}$, Hz
syn-III	2.18	4.27	1.35	12.2	6.8
anti-III	2.13	4.24	1.31	8.0	7.3



The IR, UV, and PMR spectroscopic data confirmed the structures of all the compounds that we synthesized (Tables 1 and 2).

EXPERIMENTAL

The course of the reactions and purity of compounds were monitored on Silufol UV-254 plates, with benzene–acetone (8:1) as eluent. The UV spectra were recorded on a LOMO SF-26 spectrometer (in ethanol) and the IR spectra were recorded on a UR-10W instrument with NaCl and LiF prisms (in Vaseline oil). The PMR spectra were recorded on a Bruker WP-200 SY spectrometer, and the chemical shifts were measured relative to TMS as the internal standard.

2-Phenoxathiin 10,10-Dioxide Ethyl Pyruvate Hydrazone (III). To 5 g (0.02 mole) of 2-aminophenoxathiin 10,10-dioxide [2] and 1.4 g (0.02 mole) of sodium nitrite in 30 ml of water was added dropwise 1.9 g (0.027 mole) of HCl in 8 ml of water at 0°C over a period of 15 min. The mixture was agitated for 30 min at the same temperature. To the resulting solution of diazonium salt was added a solution of 13.5 g (0.06 mole) of $SnCl_2 \cdot H_2O$ in 67.7 ml of concentrated HCl at −2°C, and the mixture was agitated for 3 h. The precipitate of hydrazine hydrochloride II that separated was filtered off, dissolved in hot water, and rapidly filtered again. A saturated solution of sodium acetate was then added until pH 3 was reached, and a solution of 2.21 g (0.02 mole) of ethyl pyruvate in 13 ml of ethanol was slowly added with agitation. The colorless precipitate of hydrazone (III) was filtered off, washed with water, and dried; yield 4.2 g (57%). The stereoisomeric forms were separated on a 100/250 μ silica gel column (benzene–acetone, 8:1, as eluent); ratio of *syn* to *anti* forms of hydrazone = 1:9. For the *syn* isomer: mp 190-193°C, R_f 0.4. IR spectrum: 3370 (NH), 1690 cm^{-1} (C=O). UV spectra, λ_{max} (log ε): 219 (4.07), 255 (3.36), 328 (3.43), 360 nm (3.34). Found, %: C 56.5; H 4.5; N 7.8; S 8.5. $C_{17}H_{16}N_2O_5S$. Calculated, %: C 56.7; H 4.4; N 7.8; S 8.9. For the *anti* isomer: mp 175-178°C, R_f 0.78. IR spectrum: 3320 (NH), 1720 cm^{-1} (C=O). UV spectrum, λ_{max},

TABLE 2. PMR Spectral Parameters of Compounds IV-VII and IX [in $(CD_3)_2CO$]

Compound	Chemical shifts, δ, ppm									
	NH	2-R	1-H	4-H	5-H	7-H	8-H	9-H	10-H	J, Hz
IV	11.65	4.43, 1.41	7.64	7.95	7.43	7.55	7.82	7.56	8.11	J_{CH2CH3} = 6.94, J_{14} = 0.73, $J_{NH,1}$ = 2.19, J_{45} = 9.14
V	11.59	—	7.67	7.95	7.44	7.57	7.82	7.56	8.11	J_{14} = 0.73, J_{45} = 9.14
VI	10.95	7.65	7.05	7.84	7.23	7.51	7.78	7.51	8.08	J_{21} = 2.92, $J_{NH,2}$ = 2.56, $J_{NH,1}$ = 2.19, J_{14} = 0.74, J_{45} = 8.77
	NH	2-R	3-H	4-H	6-H	7-H	8-H	9-H	11-H	
VII	11.55	4.79, 1.40	7.33	7.87	~7.5	~7.8	~7.5	8.05	8.23	J_{CH2CH3} = 7.31
IX	10.88	7.75	6.68	7.73	7.53	7.77	7.49	8.04	8.15	$J_{NH,2}$ = 2.56, $J_{NH,3}$ = 2.20, J_{23} = 2.92, $J_{4,15} \sim J_{3,11} \sim J_{NH,3}$ = 0.4

(log ε): 208 (4.05), 220 (4.16), 321 (4.20), 340 nm (3.86). Found, %: C 56.4; H 4.6; N 7.8; S 8.7. $C_{17}H_{16}N_2O_5S$. Calculated, %: C 56.7; H 4.4; N 7.8; S 8.9.

Ethyl 3*H*-Pyrrolo[2,3-*c*]phenoxathiin-2-carboxylate 11,11-Dioxide (IV) and Ethyl 1*H*-Pyrrolo[3,2-*b*]phenoxathiin-2-carboxylate 10,10-Dioxide (VII). To 40 g of ethyl polyphosphate was added 4 g of a mixture of isomers III with constant agitation, and the mixture was heated to 100-110°C for 1 h, cooled, and poured into an ice bath. The precipitate was filtered off, washed with water, and dried. The resulting mixture of compounds IV and VII was separated on a 100/250 μ silica gel column (benzene–acetone, 8:1, as eluent). Yield of compound IV was 3 g (75%), mp 220-223°C, R_f 0.28. IR spectrum: 3590 (NH), 1710 cm^{-1} (C=O). UV spectrum, λ_{max}, (log ε): 209 (4.15), 220 (4.18), 240 (3.92), 320 nm (3.87). Found, %: C 59.3; H 3.9; N 4.2; S 9.1. $C_{17}H_{13}NO_5S$. Calculated, %: C 59.5; H 3.8; N 4.1; S 9.3. Compound VII was obtained in trace amounts, mp 216-219°C, R_f 0.54. IR spectrum: 3590 (NH), 1710 cm^{-1} (C=O). UV spectrum, λ_{max}, (log ε): 209 (4.34), 220 (4.37), 248 (4.03), 320 nm (3.99). Found, %: C 59.2; H 3.7; N 4.2; S 9.4. $C_{17}H_{13}NO_5S$. Calculated, %: C 59.5; H 3.8; N 4.0; S 9.3.

3*H*-Pyrrolo[2,3-*c*]phenoxathiin-2-carboxylic Acid 11,11-Dioxide (V). A mixture of 0.3 g (0.0008 mole) of ester IV, 0.18 g (0.003 mole) of KOH, and 4.5 g (0.09 mole) of ethanol was refluxed with constant agitation for 1 h. The solution was cooled, filtered off, and the filtrate was brought to pH 1 with a dilute solution of HCl. The crystals that separated were washed with water and dried. Yield of compound VI was quantitative, mp 300°C (decomp.). IR spectrum: 3570 (NH), 1700 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 217 (4.50), 240 (4.35), 265 (4.60), 340 nm (4.32). Found, %: C 57.3; H 2.5; N 4.4; S 10.5. $C_{15}H_9NO_5S$. Calculated, %: C 57.1; H 2.9; N 4.4; S 10.1.

3*H*-Pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxide (VI). Cyclic acid V (0.2 g, 0.0005 mole) was decarboxylated at 290-300°C. After cooling, the product was purified on a 100/250 μ silica gel column (benzene–acetone, 8:1, as eluent). Yield of compound VII was 0.13 g (59%), mp 314-316°C, R_f 0.24. IR spectrum: 3590 cm^{-1} (NH). UV spectrum, λ_{max}, (log ε): 209 (4.16), 220 (4.30), 242 (4.04), 250 nm (3.91). Found, %: C 62.3; H 3.3; N 5.2; S 12.0. $C_{14}H_9NO_3S$. Calculated: C 62.0; H 3.3; N 5.2; S 12.0.

1*H*-Pyrrolo[3,2-*b*]phenoxathiin 10,10-Dioxide (IX). This was obtained in a similar manner to compound VI from acid VIII (the latter not being isolated in a pure form); mp 321-323°C, R_f 0.42. IR spectrum: 3580 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 212 (4.30), 250 (4.40), 268 (4.05), 340 nm (4.15). Found, %: C 62.3; H 3.2; N 5.3; S 12.0. $C_{14}H_9NO_3S$. Calculated, %: C 62.0; H 3.3; N 5.2; S 12.0.

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