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PYRROLOPHENOXATHIIN DIOXIDES.
2.* SOME DERIVATIVES OF 3H-PYRROLO[2,3-*c*]-PHENOXATHIIN 11,11-DIOXIDE

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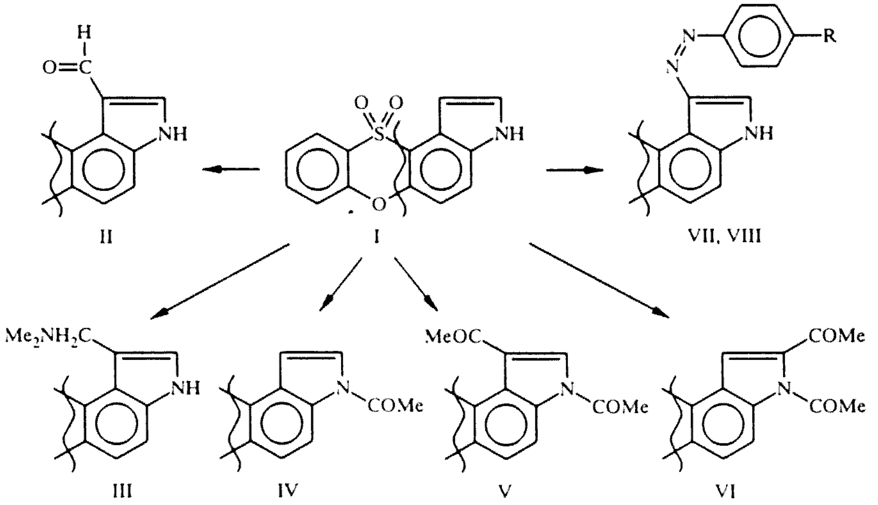
The behavior of 3H-pyrrolo[2,3-c]phenoxathiin 11,11-dioxide in electrophilic substitution reactions is similar to that of other indole derivatives. The corresponding 1-substituted compounds of pyrrolophenoxathiin dioxides have been obtained.

With the aim of studying the reactivity of the tetracyclic pyrrole-containing condensed system 3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-dioxide previously synthesized by us, we have investigated some electrophilic substitution reactions that are typical of indole compounds (Vilsmeier, Mannich, acylation, and azo coupling reactions). In view of the definite structural similarity between pyrrolophenoxathiin dioxide and indole, the above reactions were, with some changes, carried out under the conditions reported for indole itself [2-4].



VII R = H, VIII R = Cl

It was found that compound I is formylated fairly readily with a Vilsmeier system to give 1-formyl-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-dioxide (II). IR spectrum of compound II, in addition to a band at 3330 cm^{-1} corresponding to the NH group, there is a band at 1640 cm^{-1} due to stretching vibrations of a conjugated carbonyl group. In the PMR spectrum of compound II there is a signal that is characteristic of an aldehyde proton — a sharp singlet at 10.1 ppm (Table 1). The absence

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*For Communication 1, see [1].

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TABLE 1. PMR Spectroscopic Parameters for Compounds II-VIII in $(CD_3)_2CO$

Compound	1-R	2-R	3-R	Chemical shift, δ, ppm									J, Hz
				1-R	2-R	3-R	4-H	5-H	7-H	8-H	9-H	10-H	
II	CHO	H	H	10,11	8,34	10,85	8,02	7,40	7,55	7,83	7,65	8,29	J_{45} = 9,40
III	$(CH_3)_2NCH_2$	H	H	4,00, 2,38	7,65	11,00	7,82	7,19	7,51	7,78	7,51	8,05	J_{45} = 9,18
IV	H	H	$COCH_3$	7,19	8,10	2,78	8,72	7,45	~7,5	7,83	~7,5	8,09	J_{12} = 3,66, J_{45} = 9,14
V	$COCH_3$	H	$COCH_3$	2,63	8,44	2,85	8,82	7,58	7,57	7,80	7,54	8,01	J_{45} = 9,51
VI	H	$COCH_3$	$COCH_3$	8,11	2,59	2,85	7,91*	7,39	7,51	7,75	7,50	8,00	J_{45} = 9,60
VII	$C_6H_5N{=}N$	H	H	~7,5, 8,09†	~8,1	11,6	7,93	7,33	~7,5	7,76	~7,5	8,14	J_{45} = 8,77
VIII	p-$ClC_6H_4N{=}N$	H	H	~ 7,53, 8,10	~8,1	11,7	7,93	7,33	~7,5	7,77	~7,5	8,12	J_{45} = 9,14, J_{om} = 8,0

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*Free rotation and anisotropic effect from the C=O group of the 3-R substituent are absent because of steric interaction with 2-R.

†Overall shift of *meta*- and *para*-protons of the substituent.

of a signal from the 1-H proton and the significant downfield shift of the signals from the 2-H, 3-H and 10-H protons compared to the unsubstituted ring of I as a result of the deshielding effect of the aldehyde group indicate that formylation has occurred on the β-carbon atom of the pyrrole ring. The deshielding effect of the formyl group also gives rise to changes in the chemical shifts of the 4-H and 5-H protons.

Compound I undergoes a Mannich reaction to form 1-(N,N-dimethylaminomethyl)-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-dioxide (III). The PMR spectrum of compound III provides confirmation that the aminomethyl group occurs on the C-1 carbon atom of the pyrrole ring. In the IR spectrum of this compound a band due to the NH group stretching vibrations is retained at 3280 cm^{-1}.

Acylation was carried out using acetic anhydride or a mixture of acetic anhydride and acetic acid under more severe conditions than for indole. In the first case — in contrast to indole, which forms a mixture of 3-acetyl- and 1-acetylindoles together with 1,3-diacetylindole as the principal reaction product [5] — 3-acetyl-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-dioxide (IV) was obtained as the sole reaction product. The absence of a signal from an NH proton demonstrates that the acetyl group does not occur at the 3-position of the pyrrole ring. Acylation with a mixture of anhydride and acid yields a mixture of products consisting of 1,3-diacetyl and 2,3-diacetyl derivatives (V) and (VI), which is supported by the PMR spectroscopic data.

Azo coupling was carried out in a 1:1 mixture of dioxane and water in neutral media with diazonium salts obtained from aniline and *p*-chloroaniline by the established method. The PMR spectroscopic data for the azo compounds provide confirmation of their structure. The absence of a signal from the 1-H proton indicates that hydrogen has been replaced at the 1-position of the pyrrole ring.

EXPERIMENTAL

The course of the reactions and purity of the compounds were monitored on Silufol UV-254 plates in an ethyl acetate–hexane (1:1) solvent system. The UV spectra were recorded on a LOMO SF-26 spectrometer (in ethanol) while 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. The chemical shifts were recorded relative to TMS as the internal standard.

1-Formyl-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxide (II). To 1.72 ml (0.018 mole) of freshly distilled DMF at 0°C was slowly added 0.5 ml of phosphorus oxychloride. The reaction mixture was allowed to stand for 1 h at room temperature and 0.5 g (0.002 mole) of a solution of compound I in 3 ml of DMF was added. The mixture was heated to 60°C for 4 h, cooled, 10 g of crushed ice was added, and the solution was made alkaline with the addition of a 0.1 N solution of NaOH. The precipitate was filtered off, washed with water, and dried. The product was purified on a silica gel column (ethyl acetate–hexane, 1:1, as eluent), yield 0.35 g (60.3%), mp 302-304°C. IR spectrum (cm^{-1}): 3330 (NH), 1640 (C=O). UV spectrum (nm), λ_{max} (log ε): 238 (4.34), 241 (4.32), 247 (4.24) (4.24). Found, %: C 60.1; H 3.3; N 4.5; S 10.5. $C_{15}H_9NO_4S$. Calculated, %: C 60.2; H 3.0; N 4.6; S 10.7.

1-(N,N)-Dimethylaminomethyl)-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxide (III). To 4 ml (0.004 mole) of a 33% aqueous solution of dimethylamine was slowly added 4 ml of glacial acetic acid with cooling, followed by the addition of 25 ml of 40% formalin and 0.5 g (0.002 mole) of compound I. The mixture was left to stand for 3 h at 40°C, poured into water, and made alkaline with a 10% solution of NaOH. The precipitate that formed was filtered off, washed with water, and dried over KOH in a vacuum desiccator. Yield 0.52 g (85%), mp 152-154°C. IR spectrum (cm^{-1}): 3280 (NH), 1470 (C–N). UV spectrum (nm), λ_{max} (log ε): 232 (3.39), 241 (4.37), 247 (4.30). Found, %: C 62.2; H 4.6; N 8.4; S 10.0. $C_{17}H_{16}N_2O_4S$. Calculated, %: C 62.1; H 4.8; N 8.5; S 9.7.

3-Acetyl-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxide (IV). A mixture of 0.2 g (0.0007 mole) of compound I and 40 ml of acetic anhydride was refluxed for 10 h. The reaction mixture was poured into water and allowed to stand overnight. The reaction product was extracted with ethyl acetate, thoroughly washed with a solution of $NaHCO_3$ and water, and dried over Na_2SO_4. After removal of the solvent, the product was purified on a silica gel column (ethyl acetate–hexane, 1:1, as eluent). Yield 0.1 g (45%), mp 238-240°C. IR spectrum (cm^{-1}): 3320 (NH), 1700 (C=O). UV spectrum (nm), λ_{max} (log ε): 236 (4.13), 239 (4.37), 247 (4.24). Found, %: C 61.1; H 3.4; N 4.0; S 10.0. $C_{16}H_{11}NO_4S$. Calculated, %: C 61.3; H 3.5; N 4.4; S 10.2.

1,3-Diacetyl- and 2,3-Diacetyl-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxides (V) and (VI). A mixture of 0.2 g (0.0007 mole) of compound I, 6 ml (0.0066 mole) of freshly distilled acetic anhydride, and 4 ml (0.05 ml) of glacial acetic acid was refluxed for 25 h. The reaction mixture was poured into water and allowed to stand for 12 h. The product was extracted with ethyl acetate, thoroughly washed with a solution of $NaHCO_3$ and water, and dried over Na_2SO_4. Yield of mixture 0.1 g (43%). The mixture was separated on a silica gel column (ethyl acetate–hexane, 1:1, as eluent). Compound V: mp 266-268°C. IR spectrum (cm^{-1}): 3300 (NH), 1700, 1590 (C=O). UV spectrum (nm), λ_{max} (log ε): 241 (4.88), 246 (4.71). Found, %: C 60.7; H 3.6; N 3.7; S 8.9. $C_{18}H_{13}NO_5S$. Calculated, %: C 60.8; H 3.6; N 3.9; S 9.0. Compound VI: mp 182-184°C. IR spectrum (cm^{-1}): 3280 (NH), 1710, 1590 (C=O). UV spectrum (nm), λ_{max} (log ε): 233 (4.21), 239 (4.40), 246 (4.39). Found, %: C 60.6; H 3.5; N 4.1; S 9.2. $C_{18}H_{13}NO_5S$. Calculated, %: C 60.8; H 3.5; N 3.9; S 9.0.

1-Phenylazo-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxide (VII). To a solution of 0.5 g (0.002 mole) of compound I in 20 ml of dioxane and 20 ml of water in the presence of 1 g of CH_3COONa at 0°C was added a solution (0.002 mole) of phenyldiazonium chloride obtained by the usual method. The coupling reaction was carried out at pH 6-7 over a period of 2 h. The reaction product was extracted with ether and chromatographed on a silica gel column (ether–hexane, 1:1, as eluent), yield 0.3 g (41%), mp 196-198°C. IR spectrum (cm^{-1}): 3240 (NH), 1460 (N=N). UV spectrum (nm), λ_{max}, (log ε): 233 (3.98), 241 (4.23), 247 (4.21). Found, %: C 64.1; H 3.4; N 11.1; S 8.8. $C_{20}H_{13}N_3O_3S$. Calculated, %: C 64.0; H 3.4; N 11.2; S 8.5.

1-(4-Chlorophenylazo)-3H-pyrrolo[2,3-*c*]phenoxathiin 11,11-Dioxide (IX). This was obtained by the method described above from 0.5 g (0.002 mole) of compound I and an equimolar quantity of *p*-chlorophenyldiazonium chloride. Yield 0.35 g (43%), mp 224-225°C. IR spectrum (cm^{-1}): 3250 (NH), 1460 (N=N). UV spectrum (nm), λ_{max} (log ε): 238 (4.34), 241 (4.32), 247 (4.28). Found, %: C 58.3; H 2.8; Cl 8.9; N 10.0; S 7.9. $C_{20}H_{12}ClN_3O_3S$. Calculated, %: C 58.6; H 2.9; Cl 8.7; N 10.2; S 7.8.

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