PHOSPHORYLATED 1-(NITROPHENYL)-2-FORMYLPYRROLES

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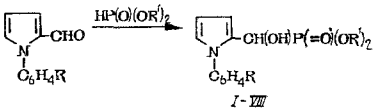
There have been no reports in the literature on the biological activity of phosphorylated pyrroles, although numerous organophosphorus compounds are used as drugs.

Available information on phosphorylated pyrroles is limited. The preparation of tripyrrolylphosphine and its thioxide has been reported [1]. Tris-(2-pyrrolyl)phosphine oxide has been described [2]. Using the pyrrole Grignard reagent, the same workers [3] synthesized 2-pyrrolylphosphonates and amidophosphonates. Information on amidophosphite esters containing pyrrole as the amide moiety has been given [4, 5]. The Abramov phosphorylation of 2-formylheterocycles has been described [7].

In this study, we limited ourselves to the phosphorylation of 1-(nitrophenyl)-2-formylpyrroles, in view of the fact that the presence of nitrophenyl substituents in phosphorylated compounds has a definite influence on the appearance of biological activity.

The starting 1-(nitrophenyl)-2-formylpyrroles were synthesized from furfural and the appropriate nitroanilines by the method described in [9]. Attempts to obtain a compound with a nitro-group in the o-position were unsuccessful.

Phosphorylation was effected with dialkyl phosphites as described in [7], using as catalysts the appropriate alkoxides or triethylamine.



I-VIII

I: R = NO_2-p, R′ = CH_3; II: R = NO_2-p, R′ = C_2H_5; III: R = NO_2-p, R′ = C_3H_7;
IV: R = NO_2-p, R′ = C_3H_7-iso; V: R = NO_2-p, R′ = CH_3; VI: R = NO_2-m
R′ = C_2H_5; VII: R = NO_2-m R′ = C_3H_7; VIII: R = NO_2-m, R′ = C_3H_7-iso

1-(Nitrophenyl)-2-[(O,O-dialkylphosphonyl)(hydroxymethyl)]pyrroles were obtained in high yields as colorless, crystalline solids. The compounds were purified by recrystallization from the appropriate alcohol.

EXPERIMENTAL CHEMICAL SECTION

IR spectra were obtained in Vaseline oil on a UR-20 instrument (East Germany), and PMR spectra on a Bruker WP-80 spectrometer, internal standard tetramethylsilane.

1[(p-Nitrophenyl(-2-(O,O-dimethylphosphonyl)(hydroxymethyl)]pyrrole (I). To a reaction mixture consisting of 5 g (0.02 mole) of finely ground 1-(p-nitrophenyl)-2-formylpyrrole, 2.4 g (0.02 mole) of dimethylphosphorous acid, and 10 ml of dry ether was added rapidly with vigorous stirring 1 ml of a saturated solution of sodium methoxide. The temperature of the reaction mixture rose by 20°C. The mixture was stirred for a further 30 min. After this time, the starting material had dissolved completely in the ether solution, and the product separated as a colorless solid. The solid was filtered off, washed with ether, and recrystallized from methanol. Compounds (II-VIII) were obtained similarly. The properties of the compounds are given in Table 1.

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TABLE 1. Chemical Properties of Phosphonylpyrroles (I-VIII)

Compound	Yield, %	mp, °C	Found, %				Molecular formula	Calculated, %			
			C	H	N	P		C	H	N	P
I	80	137	47,84	6,83	8,44	9,28	$C_{13}H_{22}N_2O_5P$	47,71	6,79	8,56	9,46
II	75	128	50,81	7,44	7,56	8,50	$C_{15}H_{26}N_2O_5P$	50,66	7,39	7,87	8,72
III	70	121	66,70	7,98	7,24	8,01	$C_{17}H_{30}N_2O_5P$	66,52	7,90	7,30	8,08
IV	80	167	66,56	7,77	7,30	8,08	$C_{17}H_{30}N_2O_5P$	66,52	7,90	7,30	8,08
V	75	165	47,90	6,90	8,48	9,37	$C_{13}H_{22}N_2O_5P$	47,71	6,79	8,56	9,46
VI	70	130	50,32	7,34	7,89	8,64	$C_{15}H_{26}N_2O_5P$	50,66	7,39	7,87	8,72
VII	70	108	66,44	7,87	7,27	8,18	$C_{17}H_{30}N_2O_5P$	66,52	7,90	7,30	8,08
VIII	75	166	66,71	7,64	7,33	8,20	$C_{17}H_{30}N_2O_5P$	66,52	7,90	7,30	8,08

TABLE 2. Antimicrobial Activity of Phosphonylpyrroles (III), (IV), and (VII)

Compound	N. meningitidis	Staphylococcus	Streptococcus
	minimum bactericidal concentration, g/ml		
III	0,001	0.0025	0,0025
IV	0,001	—	—
VII	0.0025		

EXPERIMENTAL BIOLOGICAL SECTION

The antimicrobial activity of the compounds was determined by serial dilution in a liquid nutrient medium [10] against three species of bacteria. Most of the compounds were inactive against Gram-positive and Gram-negative bacteria, and their 1-2% solutions failed to inhibit the growth of microorganisms. However, the compounds containing a propyl or an isopropyl group attached to phosphorus were biologically active (Table 2). A study of the biological activity of phosphorylated pyrroles therefore holds promise.

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