BENZOXAZOLINONES.

II. SYNTHESIS OF 3-VINYLBENZOXAZOLINONES AND 3-VINYLBENZOXAZOLINETHIONE

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A method has been developed for obtaining 3-vinylbenzoxazolinones and 3-vinylbenzoxazolinethione. It has been shown that it is also possible to obtain 3-methylbenzoxazolinethione by this method in good yield (76%).

Continuing a systematic investigation [1] of the chemical and pesticidal properties of benzoxazolinone (BN) and benzoxazoline-2-thione (BT) we set ourselves the aim of synthesizing their 3-substituted derivatives since the reaction of BT with various alkylating agents [2-4] leads to 2-substituted products in the majority of cases.

According to available information in the literature [2, 5], such vinylazoles can be synthesized with the aid of acetylene. However, this requires special catalysts and severe conditions (temperatures of 160-175°C, pressure).

We have performed the reaction of 3-chloromethylbenzoxazolinones (Ia-c) with triphenylphosphine in dioxane solution. After 8-10 h of boiling this gave a good yield (Table 1) of (2-oxobenzoxazolin-3-ylmethyl)triphenylphosphonium chlorides (IIIa-c). Treatment of the latter with aqueous solutions of sodium carbonate and formaldehyde and separation on a column gave the 3-vinylbenzoxazolinones (IVa-c) with yields of 41-76%.

In contrast to Popov et al. [6], we also isolated the 3-methylbenzoxazolinones (Va-c) as reaction products. Below we give the properties of the compounds synthesized:

Compound	Yield, %	mp, °C	R_f	Empirical formula
IIIa	94	234-236	0.10	$C_{26}H_{21}NO_2PCl$
IIIb	92	260-261	0.10	$C_{26}H_{20}NO_2PCl_2$
IIIc	90	253-255	0.10	$C_{26}H_{20}NO_2PClBr$
IIId	95	231-233	0.10	$C_{26}H_{21}NOSPCl$
IVa	76	49-51	0.83	$C_9H_7NO_2$
IVb	41.2	79-80	0.82	$C_9H_6NO_2Br$
IVc	45	77-78	0.85	$C_9H_6NO_2Br$
IVd	30.2	100-102	0.86	C_9H_7NOS
Va	19	83-84	0.61	$C_8H_7NO_2$
Vb	44	102-103	0.62	$C_8H_6NO_2Cl$
Vc	55.5	143-144	0.60	$C_8H_6NO_2Br$
Vd	76	127-129	0.76	C_8H_7NOS

Similarly, starting from 3-chloromethylbenzoxazolinethione (1 g) we synthesized 3-vinylbenzoxazoline-2-thione (IVd) with mp 100-102°C and 3-methylbenzoxazoline-2-thione (Vd), mp 126-127°C (according to the literature, mp 126°C [1]). The yields of (IV) and (V) are given above. When compounds (IIIa-d) were treated with water or an aqueous solution of formaldehyde (30%) no reaction products (IV and V) were formed according to thin-layer chromatography (TLC). The addition of equimolecular amounts of aqueous solutions of Na_2CO_3, NaOH, or C_2H_5ONa led to compounds (Va-d).

The treatment of chloroform solutions of (IIIa-d) with aqueous solutions of formaldehyde and Na_2CO_3 formed mixtures of products (IVa-d).

The structures of the compounds synthesized were confirmed by the results of IR and mass spectroscopy. The elementary analyses coincided with the calculated figures.

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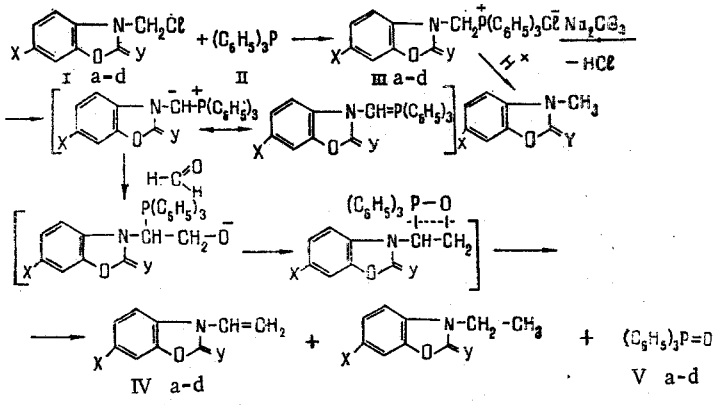

a X=H, Y=O; b X=Cl, Y=O; c X=Bz, Y=O; d X=H, Y=S

The introduction of electronegative groups (Cl, Br) into position 6 of benzoxazolinone led to a fall in the yield of vinylated products, with a simultaneous increase in the yield of 3-methylated products (Vb, c).

Thus, a method has been developed for obtaining 3-vinylbenzoxazolinones and 3-vinylbenzoxazolinethione. By this method it is also possible to obtain 3-methylbenzoxazolinethione in good yield (76%).

The compounds synthesizedhave been studied as fungicides against the causative agent of *Verticillium dahliae* and *Fusarium oxysporium*. The phosphonium salts were slightly active. Among the 6-substituted compounds (Cl, Br, NO_2), the most active against the organisms mentioned proved to be 3-methyl-6-nitrobenzoxazolinone, and the fungicidal activity of 3-vinylbenzoxazolinethione was higher than that of the 3-vinylbenzoxazolinones.

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer in tablets molded with KBr, and mass spectra on a MKh-1303 instrument with direct introduction at an ionizing voltage of 40 eV. 3-Chloromethylbenzoxazolinone, 3-chloromethylbenzoxazolinethione, and triphenylphosphine were synthesized by known methods.

Preparation of 3-Vinylbenzoxazolinone (IVa). A mixture of 1.86 g (10 mmole) of 3-chloromethylbenzoxazolinone (Ia), 2.62 g (10 mmole) of triphenylphosphine (II), and 25 ml of dioxane was boiled under reflux for 8 h, and then the dioxane was distilled off and the residue was washed with acetone. This gave 4.2 g (94%) of (2-oxobenzoxazolin-3-ylmethyl)triphenylphosphonium chloride (IIIa), mp 234-236°C, R_f 0.10 in the benzene—ethanol (10:1) system. The qualitative reaction for phosphorus was positive.

A solution of 2.33 g (5 mmole) of IIIa) in 30 ml of chloroform was treated at room temperature with 1 ml of aqueous formaldehyde solution (30%) and 5 ml of aqueous sodium carbonate solution (10%) and the mixture was stirred for 1 h. Then the chloroform layer was separated off and it was washed with water and dried over $CaCl_2$, and the solvent was distilled off. The residue, according to TLC, consisted of three products. They were separated on a column (50 × 2 cm) filled with silica gel (0.1-0.25 μ). Separation of the products was monitored by the TLC method. Revealing agent: $KMnO_4$ + 48 ml H_2O + 2 ml H_2SO_4.

Elution with benzene gave 1.4 g (76%) of 3-vinylbenzoxazolinone (IVa) with mp 49-51°C, R_f 0.83; according to the literature [4]: mp 52°C. The mass spectrum of (IVa) contained the peaks of ions with m/e 161 (M^+), 133, 118, 90, and 92. The characteristics of its IR spectrum also confirm the structure of (IVa) (absorption bands in the 925, 985, 1428, and 1652 cm^{-1} region of a terminal $-CH-CH_2$ group).

We also isolated 0.25 g (19%) of 3-methylbenzoxazolinone (Va) with mp 81-82°C, R_f 0.61. The product gave no depression of the melting point with authentic 3-methylbenzoxazolinone [1]. In addition to the compounds mentioned above, on further elution with benzene—ethanol 2.34 g (90%) of triphenylphosphine oxide was obtained with mp 152-153°C, R_f 0.30; according to the literature: mp 151-153°C.

Under similar conditions, (IIIb and c) led to 6-chloro-3-vinylbenzoxazolinone (IVb), yield 41.2%, mp 79-80°C, R_f 0.82; and led to 3-vinylbenzoxazolinethione (IVd), yield

30.2% mp 100-102°C, R_f 0.86, and also 3-methylbenzoxazolinethione, yield 76%, mp 126-127°C; according to the literature [1]: mp 127-129°C.

SUMMARY

1. A method has been developed for obtaining 3-vinylbenzoxazolinones and 3-vinylbenzoxazolinethione.

2. It has been shown that by this method it is also possible to obtain 3-methylbenzoxazolinethione in good yield (76%).

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ISOLATION AND PURIFICATION OF BIOPOLYMERS BY AFFINITY CHROMATOGRAPHY. VI.* PREPARATION AND PROPERTIES OF AN AFFINITY ADSORBENT WITH A POLYSACCHARIDE SPACER FOR THE PURIFICATION OF PROTEOLYTIC ENZYMES

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A new affinity sorbent has been synthesized — soybean trypsin inhibitor (STI)-amylopectin-hydrazidosuccinyl-Sepharose — and its properties have been studied in comparison with those of an analogous adsorbent without the spacer STI-Sepharose. The STI-amylopectin-hydrazidosuccinyl-Sepharose adsorbent has been used for the purification of trypsin from porcine pancreas and of callicrein from human blood plasma.

Affinity chromatography (AFC) on immobilized soybean trypsin inhibitor (STI) is widely used to purify proteolytic enzymes [2]. Thus, highly purified preparations of trypsin [3, 4] and of callicrein from human blood plasma [5, 6] has been obtained by AFC on STI-Sepharose.

As a rule, the STI is attached to the Sepharose by the cyanogen bromide method [4, 7]. The direct attachment of a high-molecular-weight ligand to a solid support can create substantial steric hindrance for the subsequent interaction of the immobilized ligand with the active center of the enzyme to be isolated which, in the final account, will lead to a decrease in the capacity of the affinity adsorbent. In this connection the use of a spacer separating the ligand from the surface of the solid support could lead to an improvement in the quality of the adsorbent. One of the recent examples of the immobilization of STI on Sepharose through a spacer is the work of Karube et al. [8], who used the activation of Sepharose containing amino groups with the aid of glutaraldehyde and the subsequent attachment of the STI.

*For Communication V, see [1].

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