SYNTHESIS OF ESTERS OF PHOSPHONIC ACIDS, CONTAINING HETEROCYCLIC RADICALS

COMMUNICATION 9. REACTION OF BENZYLIDENERHODANINES WITH TRIALKYL PHOSPHITES AND DIALKYLPHOSPHOROUS ACIDS

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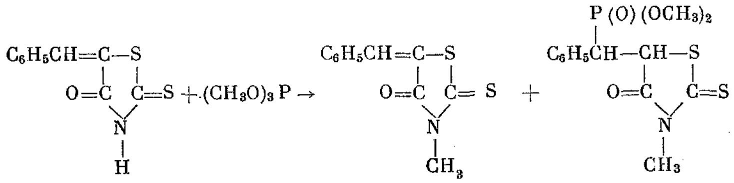
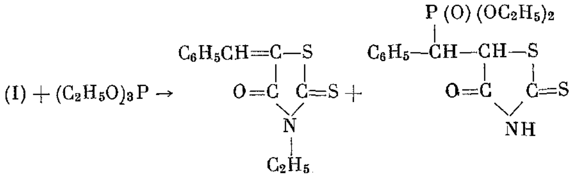
UDC 542.91+547.7+661.718.1

In studying the reaction of trialkyl phosphites and dialkylphosphorous acids with compounds, containing the C=C−C=C group [1-4], we included within the scope of our studies heterocyclic compounds, containing the benzylidene grouping, conjugated with the carbonyl group of the heterocyclic ring [5, 6]. In order to ascertain the possibility of the carbonyl group of the idene derivatives of heterocycles taking part in the addition reactions of trialkyl phosphites and dialkylphosphorous acids we selected the idene derivatives of rhodanines (benzylidene, ethylidene- and α-picolylidenerhodanines). As a result of the performed experiments it was shown that trimethyl phosphite reacts with benzylidenerhodanine (I) to give a phosphorus-free product, proving to be N-methylbenzylidenerhodanine (II), and the product of the addition of dimethylphosphorous acid, formed during the N-alkylation reaction, to N-methylbenzylidenerhodanine (III) (dimethyl ester of N-methyl-5-rhodanilylbenzylphosphonic acid).



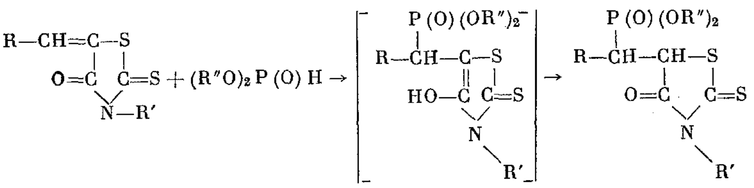
(I) (II) (III)

Benzylidene-N-ethylrhodanine (IV), and the product of the addition of diethylphosphorous acid to the starting benzylidenerhodanine (V), were isolated in the analogous reaction with triethyl phosphite.



(IV) (V)

The structure of products (II) and (IV) was proved by their respective counter syntheses [5]. As a result, trialkyl phosphites initially alkylate the N-unsubstituted benzylidenerhodanine with the formation of dialkylphosphorous acids, and the latter then add to either N-alkylated or unalkylated benzylidenerhodanines at the conjugated bond.



R=C_6H_5, C_5H_4N; R′=H, CH_3, C_2H_5, C_3H_5, C_4H_9; R″=CH_3, C_2H_5

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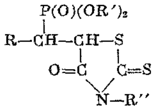
TABLE 1.



Cpd. No.	R	R′	R″	mp, °C	Yield,* %
1	C_6H_5	CH_3	CH_3	140.5—141	11.7(59.3)
2	C_6H_5	C_2H_5	H	162—164	17.14
3	C_6H_5	C_2H_5	C_2H_5	92.5—93	64.5(30.7)
4	C_6H_5	C_2H_5	CH_3	89—89.5	62.5
5	C_6H_5	CH_3	C_2H_5	115—116.5	17.2
6	C_6H_5	CH_3	C_4H_9	97—99	52.6
7	C_5H_4N	CH_3	C_2H_5	145—146	63.6
8	C_5H_4N	CH_3	C_3H_5	110—111	—

*The yields obtained in the reactions of benzylidenerhodanine with excess dialkyl phosphite are given in parentheses.

In support of the above-adopted course for the reactions, it was shown by means of separate experiments that dialkylphosphorous acids easily add to N-alkylbenzylidene- and α-picolylidenerhodanines. When dialkyl phosphites are reacted with an N-unsubstituted benzylidenerhodanine there can occur N-alkylation of the benzylidenerhodanine and the addition of dialkylphosphorous acids to alkylated and unalkylated benzylidenerhodanines. When a 3-fold excess of dialkyl phosphites is used only the products of the addition of dialkylphosphorous acids to N-alkylated benzylidenerhodanines are obtained. As a result, dialkylphosphorous acids are also capable of N-alkylation reactions.

In harmony with the above said, trialkyl phosphites do not react with N-alkylbenzylidenerhodanines either under the conditions described for the cases of the N-unsubstituted benzylidene- and α-picolylidenerhodanines, or under more drastic conditions.

In Table 1 are given the melting points and yields of various ester derivatives of 5-rhodanilylbenzyl- and α-picolylphosphonic acids, obtained by the reaction of trialkyl phosphites and dialkylphosphorous acids with the appropriate idene derivatives of rhodanines. Not included in Table 1 are the data on the reaction products of trimethyl phosphite, dimethyl phosphite and diethyl phosphite with ethylidenerhodanine, since here viscous noncrystallizing liquids are obtained that cannot be distilled in a high vacuum.

The structure of the compounds described in the present paper was also confirmed by the data of the infrared spectra. The absorption bands: ν(P=O) 1240-1260 cm^{-1}; ν(P—O—C) 980, 1020-1030 cm^{-1}; ν(C=O) 1732-1740 cm^{-1}, are present in the infrared spectra of all of the obtained compounds. The absorption band ν(C=C) is absent.

It should be mentioned that the absorption band ν(C=O) in the infrared spectra of the reaction products is of higher frequency than in the starting idene rhodanine derivatives [ν(C=O) 1700 cm^{-1}], which indicates that conjugation of the C=O group with the double bond is absent in them. The infrared spectrum of product 2 (see Table 1) has a broad diffuse absorption band of the NH group (2400-2800 cm^{-1}). The absorption band ν(P=O) is very intense and is shifted toward lower frequencies (1230 cm^{-1}), which indicates possible association of the P=O group with the NH group.

EXPERIMENTAL

Rhodanine was obtained as described in [7], based on the method that was developed in [8].

Reaction of Benzylidenerhodanine with Trimethyl Phosphite. A mixture of 7.1 g of benzylidenerhodanine and 3.9 g of trimethyl phosphite in 150 ml of methylene chloride was heated under reflux, with stirring, in a dry nitrogen stream, for 5 h. Since the reaction failed to go to completion, the methylene chloride was replaced by benzene and the reaction mixture was heated up to the boiling point. At the end of reaction the benzene was removed in vacuo. The residue was a slurry of crystals and a viscous liquid, which was treated with 30 ml of cold methanol. The insoluble material was filtered; weight 0.7 g; mp 168-169° (from methanol). The compound is N-methylbenzylidenerhodanine. Found %: C 56.02; H 4.01; S 27.09. $C_{11}H_9S_2ON$. Calculated %: C 56.13; H 3.85; S 27.25.

The methanol filtrate was evaporated and the honeylike residue gradually crystallized. The dimethyl ester of N-methyl-5-rhodanilylbenzylphosphonic acid was obtained; weight of crude product 1.3 g (11.7%); mp 140.5-141° (from ethanol). Found %: C 45.11, 45.17; H 4.70, 4.73; P 8.93, 8.90; S 18.41, 18.44. $C_{13}H_{16} \cdot PO_4S_2N$. Calculated %: C 45.20; H 4.66; P 8.97; S 18.56.

Reaction of Benzylidenerhodanine with Triethyl Phosphite. With stirring, a mixture of 7.8 g of benzylidenerhodanine and 5.1 g of triethyl phosphite in 175 ml of methylene chloride was heated under reflux, in a dry nitrogen stream, for 4 h. At the end of reaction the solvent was distilled off. The residue, a slurry composed of crystals and a viscous liquid, was treated 3 times with benzene (to remove the unreacted phosphite) and cold methanol. The insoluble material was filtered. We obtained 0.5 g (5.6%) of N-ethylbenzylidenerhodanine with mp 148-149° (from methanol). The mixed melting point with the product obtained by counter synthesis was not depressed. Found %: C 57.21, 57.10; H 4.83, 4.72; S 26.09, 26.01. $C_{12}H_{11}ONS_2$. Calculated %: C 57.77; H 4.84; S 25.70.

Evaporation of the methanol solution gave 11 g of a honeylike liquid as residue, which crystallized after standing for 15-20 days. The diethyl ester of 5-rhodanilylbenzylphosphonic acid was obtained as tiny transparent prisms with mp 162-164° (from ethanol); yield 17.14%. Found %: C 46.61; H 5.01; P 8.60; S 18.01. $C_{14}H_{18}O_4S_2NP$. Calculated %: C 46.75; H 5.04; P 8.62; S 18.12.

Reaction of Benzylidenerhodanine with Dimethyl Phosphite. a) A mixture of 3 g of benzylidenerhodanine, 1.5 g of dimethyl phosphite and 0.5 ml of triethylamine, sealed in an ampule, was heated: at 100° for 1 h, and at 120° for 4 h. At the end of reaction the mixture was treated with cold ethanol. We obtained 0.25 g (7.8%) of N-methylbenzylidenerhodanine with mp 168-169° (from methanol). The mixed melting point with the product obtained in the reaction of trimethyl phosphite with benzylidenerhodanine was not depressed.

b) A mixture of 3 g of benzylidenerhodanine, 4.5 g (3-fold excess) of dimethyl phosphite and 2 ml of triethylamine was heated in a sealed ampule. A precipitate of N-methylbenzylidenerhodanine was obtained after heating at 80° for 15 min, which dissolved completely when heated at 98° for 1 h. The reaction mixture was treated with alcohol and then diluted with an equal volume of water. We obtained 1.9 g (59.3%) of the dimethyl ester of N-methyl-5-rhodanilylbenzylphosphonic acid with mp 140.5-141° (from aqueous alcohol). The mixed melting point with the product obtained in the reaction of benzylidenerhodanine with trimethyl phosphite was not depressed.

Reaction of Benzylidenerhodanine with Diethyl Phosphite. a) A mixture of 3g of benzylidenerhodanine, 1.8 g of diethyl phosphite and 0.5 ml of triethylamine was heated in a sealed ampule under the same conditions as described in the preceding experiment (a). On working up the reaction mixture we obtained 1.8 g of the starting benzylidenerhodanine and 0.2 g (5.30%) of pale yellow crystals; mp 146-147° (from methanol). The mixed melting point with the product obtained in the reaction of triethyl phosphite with benzylidenerhodanine was not depressed.

Several crystals with mp 157° were obtained from the ethanol filtrate. The mixed melting point with the product obtained in the reaction of triethyl phosphite with benzylidenerhodanine was not depressed (159°).

b) A mixture of 3 g of benzylidenerhodanine, 4.5 g (3-fold excess) of diethyl phosphite and 2.5 ml of triethylamine was heated in a sealed ampule on the steam bath for 3 h. The reaction mixture was dissolved in ethanol and then diluted with an equal volume of water. We obtained 1.6 g (30.7%) of the diethyl ester of N-ethyl-5-rhodanilylbenzylphosphonic acid as pale yellow platelets; mp 92.5-93° (from aqueous alcohol). Found %: C 49.62, 49.65; H 5.63, 5.68; P 8.00, 7.93; S 16.39, 16.42. $C_{16}H_{22}O_4S_2NP$. Calculated: C 49.59; H 5.72; P 8.00; S 16.55.

Reaction of N-Methylbenzylidenerhodanine with Diethyl Phosphite. A mixture of 0.2 g of N-methylbenzylidenerhodanine, 0.1 g of dimethyl phosphite and 3 drops of triethylamine was heated in an ampule at 75° for 30 min. The ampule contents were dissolved in alcohol and the product was precipitated with water. We obtained 0.1 g (34.4%) of substance with mp 138-139° (from aqueous alcohol). The mixed melting point with the product obtained in the reaction of benzylidenerhodanine with trimethyl phosphite was not depressed.

Reaction of N-Methylbenzylidenerhodanine with Diethyl Phosphite. A mixture of 0.2 g of N-methylbenzylidenerhodanine, 0.1 g of diethyl phosphite and 3 drops of triethylamine was heated in an ampule at 100° for 30 min. We obtained 0.2 g (62.5%) of the diethyl ester of N-methyl-5-rhodanilylbenzylphosphonic acid with mp 89-89.5° (from aqueous alcohol). Found %: C 48.09, 48.11; H 5.30, 5.32; P 8.19, 8.21; S 17.01, 17.08. $C_{15}H_{20}O_4S_2NP$. Calculated %: C 48.23; H 5.39; P 8.30; S 17.17.

Reaction of N-Ethylbenzylidenerhodanine with Dimethyl Phosphite. A mixture of 0.2 g of N-ethylbenzylidenerhodanine, 0.1 g of dimethyl phosphite and 3 drops of triethylamine was heated in an ampule at 90° for 30 min. We obtained 0.05 g (17.2%) of the dimethyl ester of N-ethyl-5-rhodanilylbenzylphosphonic acid with mp 115-116.5° (from aqueous alcohol). Found %: C 46.48; H 5.02; P 8.86; S 17.99. $C_{14}H_{18}O_4S_2NP$. Calculated %: C 46.75; H 5.04; P 8.62; S 18.12.

Reaction of N-Ethylbenzylidenerhodanine with Diethyl Phosphite. A mixture of 0.2 g of N-ethylbenzylidenerhodanine, 0.1 g of dimethyl phosphite and 3 drops of ethylamine was heated in an ampule at 100° for 30 min. We obtained 0.2 g (64.5%) of white platelets with mp 92.5-93° (from aqueous alcohol). The mixed melting point with the product obtained in the reaction of benzylidenerhodanine with diethyl phosphite was not depressed.

Reaction of N-Butylbenzylidenerhodanine with Dimethyl Phosphite. A mixture of 0.3 g of N-butylbenzylidenerhodanine [5], 0.2 g of dimethyl phosphite and several drops of triethylamine in absolute benzene solution was heated in an ampule at 100° for 45 min. We obtained 0.2 g (52.6%) of the dimethyl ester of N-butyl-5-rhodanilylbenzylphosphonic acid with mp 97-99° (from aqueous alcohol). Found %: C 49.40, 49.50; H 5.58, 5.63; P 7.76, 8.01; S 16.38, 16.30. $C_{16}H_{22}O_4NS_2P$. Calculated %: C 49.59; H 5.72; P 8.00; S 16.55.

Reaction of 2-Pyridinylidene-5-(N-ethyl)rhodanine with Dimethyl Phosphite. A mixture of 0.8 g of 2-pyridinylidene-5-(N-ethyl)rhodanine [6], 0.4 g of dimethyl phosphite and several drops of triethylamine was heated in an ampule at 100° for 35 min. We obtained 0.7 g (63.6%) of the dimethyl ester of N-ethyl-5-rhodanilylpicolylphosphonic acid with mp 145-146° (from methanol). Found %: C 43.42; H 4.75; P 8.60; S 17.79. $C_{13}H_{17}O_4N_2S_2P$. Calculated %: C 43.32; H 4.72; P 8.60; S 17.79.

Reaction of 2-Pyridinylidene-5-(N-allyl)rhodanine with Dimethyl Phosphite. A mixture of 0.1 g of 2-pyridinylidene-5-(N-allyl)rhodanine [6] and 0.1 g of dimethyl phosphite, in the presence of triethylamine, was heated in an ampule at 75-76° for 10 min. The dimethyl ester of N-allyl-5-rhodanilylpicolylphosphonic acid was obtained; mp 110-111° (from benzene—hexane). Found %: C 45.23, 45.11; H 4.70, 4.54; P 8.11, 8.20; S 17.01, 17.10. $C_{14}H_{17}O_4N_2S_2P$. Calculated %: C 45.14; H 4.60; P 8.32; S 17.22.

We wish to thank V. S. Vinogradova for her assistance in deciphering the infrared spectra of the synthesized compounds.

CONCLUSIONS

1. Trialkyl phosphites react with benzylidenerhodanine to give N-alkylbenzylidenerhodanines and dialkyl phosphites.

2. Dialkyl phosphites also alkylate benzylidenerhodanines and form addition products at the idene bond of both N-alkylated and unalkylated benzylidenerhodanines.

3. Trialkyl phosphites do not react with N-alkylbenzylidenerhodanines, either under the reaction conditions of trialkyl phosphites with unsubstituted benzylidenerhodanines or under more drastic conditions.

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