SYNTHESIS AND CERTAIN PROPERTIES OF 2-SUBSTITUTED 4,5-BENZO-1,3,2-THIAZAPHOSPHOLANES

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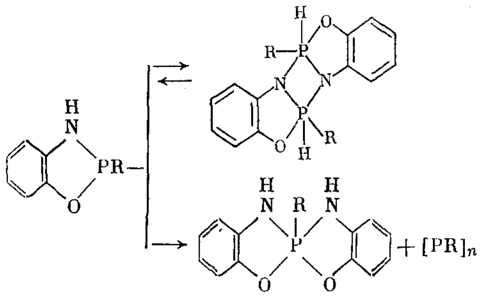
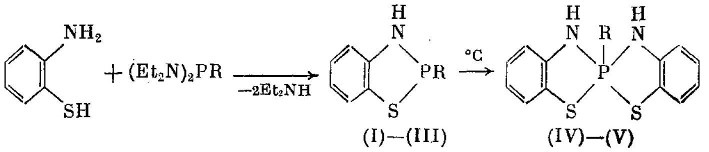
During the study of the properties of 4,5-benzo-1,3,2-oxazaphospholanes containing a P—C bond, it was found that these systems, while experiencing a considerable ring strain, are stabilized in two directions: with a proton transfer from the N to P atom and formation of dimers of oxazaphospholenes, and by a transformation into a spirophosphorane structure [1]



It was interesting to study the effect of substitution of the endocyclic O atom by a S atom on the properties of the heterocyclic system.

In [2], we have described the synthesis of certain N-methylated 4,5-benzo-1,3,2-thiazaphospholanes, containing alkoxy and dialkylamino groups attached to the P atom. In this investigation, we obtained a large number of 4,5-benzo-1,3,2-thiazaphospholanes containing a secondary or tertiary amino group in the ring and various substituents at the P atom, including alkyl groups.

The reactions of o-aminothiophenol (OATP) with tetraethyldiamides of methyl-, ethyl- and phenylphosphonous acids proceed exothermally, and after distillation of Et_2NH, lead to 2-alkyl-4,5-benzo-1,3,2-thiazaphospholanes (I)-(III)



R = CH_3 (I), (IV), C_2H_5 (II), (V), C_6H_5 (III).

The chemical shifts of the P atoms are −77 (I), −81 (II), and −65 ppm (III). It should be noted that when these reactions are carried out under mild conditions without heating, the formation of linear intermediate products phosphorylated at the mercapto group can be spectrally recorded. Thus, methylamidothiophosphonite has δP −99, and its ethyl analog −110 ppm. Moreover, in the reaction, a crystalline salt of OATP with Et_2NH is obtained, which further enters the reaction.

In contrast to oxazaphospholanes, compounds (I)-(III) are fairly stable and can be isolated in a pure state by distillation in vacuo. Their structure is confirmed by IR, ^1H, and ^{31}P NMR spectra. For example, in the PMR spectrum of thiazaphospholane (I), there is a doublet of protons of the CH_3 group at 1.15 ppm, J_{HP} = 9 Hz, a broadened singlet of the secondary amino group at 4.59 ppm, and a multiplet of protons of the

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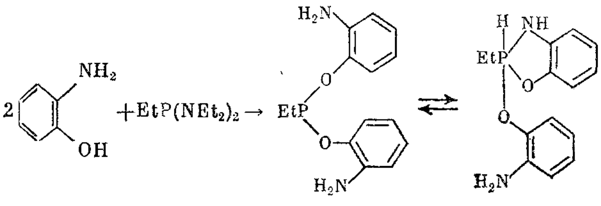
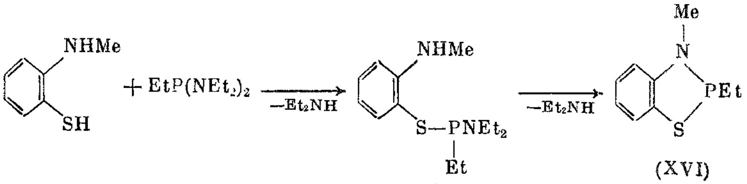
phenylene system at 6.73 ppm. Only after a prolonged standing of P-alkylated phospholanes (I) and (II), new signals of spirophosphoranes appear in the ^{31}P NMR spectra at 41 (IV) and 30 ppm (V), corresponding to the $P^{III} \rightarrow P^{V}$ transition. The transition is catalyzed by $AlCl_3$ and alkyldichlorophosphines.

Thus, substitution of the ring O atom by an S atom leads to increasing stability of the cyclic system with the P^{III} atom. This is, apparently, due to, most of all, the fact that the S atom in the five-membered ring exhibits a stronger electron-acceptor action than the O atom [3]. The result of this is a decrease in the basicity of the P atom, so that a proton transfer to it is inconvenient. Moreover, the data available in the literature, and our own data make it possible to conclude that pentacovalent structures which include sulfur, are thermodynamically less convenient than those of their oxygen analogs [4]. This conclusion is confirmed by the results of the reactions of tetraethyldiamide of ethylphosphonous acid with two equivalents of OATP and o-aminophenol (OAP). While in the first case only a product with a trivalent P atom is formed (δP −106 ppm), the ethylphosphonite (VI) (δP −142 ppm) obtained from OAP, exists at 20°C in an equilibrium with the pentacovalent form (VII), δP −28 ppm, J_{HP} = 720 Hz; ratio of (II):(III) ~60:40%

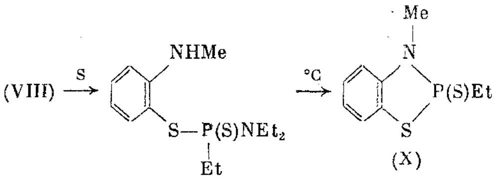

(VI) (VII)

In contrast to OATP, the reactions of N-methyl-o-aminothiophenol with diamides of alkyl(aryl)phosphonous acids lead mainly to the products with a linear and not cyclic structure


(VIII) (XVI)

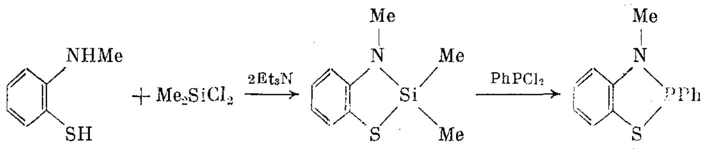
For example, as the result of the reaction of tetraethyldiamidoethylphosphonite with N-methyl-OATP, thiophosphonite (VIII) (δP −110 ppm) is mainly obtained, together with a smaller amount of thiazaphospholane (XVI); even after heating the reaction mixture at 160°C for 2 h, the acyclic product predominates. Thus, while the first stage of the phosphorylation of OATP and N-methyl-OATP in both cases proceeds readily and exothermally, the cyclization stage occurs much more readily in the case of OATP. It is possible that intramolecular transamidation is impeded when a CH_3 group is attached to the N atom, because of an increase in the steric hindrance, and a decrease in the acidic properties of the amino group. Considering the data on the transamidation mechanism in several derivatives of P^{III} [5], we can assume that the cyclization stage should take place much more readily under the conditions of acid catalysis. As catalysts, we tried $Et_3N \cdot HCl$ and AcOH, and the latter was found to be particularly suitable and effective: addition of a few drops of it at the beginning of the reaction ensures a quantitative formation of the corresponding thiazaphospholanes.

The addition of sulfur to thiophosphonite (VIII) leads to thionophosphonate (IX), which under the conditions of a distillation, partially cyclizes


(IX)

This is indicated by the fact that the PMR spectrum of the distilled product contains both a singlet of the NCH_3 group of compound (IX) at 2.80 ppm, and a doublet of the NCH_3 belonging to the cyclic system of phospholane (X) at 3.07 ppm, J_{HP} = 11 Hz.

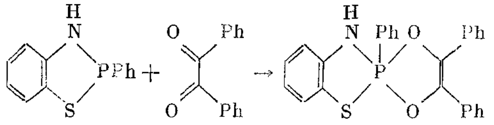
In [6], a reaction of OATP with methyldichlorophosphine is reported, but the constants characterizing the product obtained are not given. We should note that while the reaction of OATP with diamidoalkyl(aryl)-phosphonites proceed smoothly and give phospholanes (I)-(III) in high yields, a similar reaction with dichlorophosphines is accompanied by side processes. For example, in the ^{31}P NMR spectrum of the reaction mixture obtained in the reaction of OATP with $EtPCl_2$ in benzene in the presence of a base, carried out with cooling, there are four signals at −102, −92, −80, and −64 ppm. However, it instead of the OATP itself or N-methyl-OATP being used in the reaction, the silicon-containing heterocycle obtained from it, for example (XI), is used, the subsequent reaction with $PhPCl_2$ proceeds smoothly with the formation of the desired product



(XI) (XVII)

Compounds (XI) was not isolated in the pure state, but its structure was confirmed by the PMR spectrum; singlets at 2.77 and 0.49 ppm with the intensity ratio of 1:2 correspond to the protons of the CH_3 group attached to the N and Si atoms.

The reaction of thiazaphospholane (III) with benzil leads to the formation of one of the few spirophosphoranes containing the P–S bond known at the present time; for (XII) δP 11 ppm.



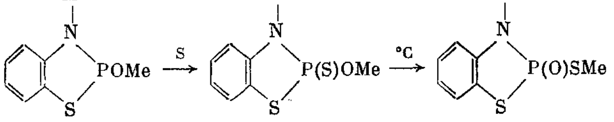
(III) (XII)

The reaction of other thiazaphospholanes containing the P–C bond with benzil proceeds similarly. However, the spirans obtained from (I) and (II) are undistillable vitreous compounds, and were not isolated in a pure state; their δP are 8 and 3 ppm, respectively.

Several 2-alkoxy derivatives [(XIII)-(XIV), (XVIII) and (XIX), see Table 1] were obtained by the reaction of tetraethyldiamides of alkylphosphorous acids with OATP or N-methyl-OATP. In the PMR spectrum of 2-methoxy-3-methyl-4,5-benzo-1,3,2-oxazaphospholane (XIII), two doublets of equal intensity at 3.23 ppm (J_{HP} = 12 Hz) and 2.84 ppm (J_{HP} = 9 Hz) correspond to the protons of the OCH_3 and NCH_3 groups. In the PMR spectrum of 2-isopropoxythiazaphospholane (XIX), the CH_3 groups are anisochronous (0.96; 0.82 ppm, J_{HP} = 7 Hz) owing to the presence of an asymmetric center at the P atom.

2-Substituted thiazaphospholanes add sulfur exothermally with formation of the corresponding thiono derivatives, and are readily oxidized by the action of DMSO in $CHCl_3$ in the presence of an iodine crystal, according to the method described in [7]. In the PMR spectrum of 2-dimethylamino-2-oxo-3-methyl-4,5-benzo-1,3,2-thiazaphospholane (XXI), there are two doublets at 2.97 (MeN, J_{HP} = 9.5 Hz) and 2.71 ppm (Me_2N, J_{HP} = 13 Hz) with the intensity ratio of the signals of 1:2.

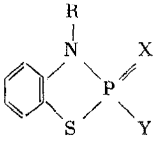
It is interesting to note that addition of sulfur to 2-methoxy-3-methyl-4,5-benzo-1,3,2-thiazaphospholane (XIII) is accompanied by a thione–thiol isomerization with the formation of 2-methylthio-2-oxo-3-methyl-4,5-benzo-1,3,2-thiazaphospholane (XX)



(XIII) (XX)

The structure of (XX) is confirmed by the ^{31}P NMR spectrum (δP −60 ppm) and PMR spectrum, in which doublets of the CH_3S group are present at 2.08 ppm (J_{HP} = 18 Hz) and CH_3N at 3.17 ppm (J_{HP} = 10 Hz).

TABLE 1. 2,3-Substituted 4,5-Benzo-1,3,2-thiazaphospholanes



Compound	X	Y	R	Yield, %	bp, °C (p, mm Hg)	d_4^{20}	n_D^{20}	Found, %				Empirical formula	Calculated, %				δP, ppm
								C	H	N	P		C	H	N	P	
(I)	–	Me	H	52	89 (0,03)	1,2619	1,6765	–	–	–	18,05	C_7H_8NPS	–	–	–	18,34	–77
(II)	–	Et	H	56	83 (0,06)	1,2161	1,6565	52,16	5,47	7,09	16,48	$C_8H_{15}NPS$	52,46	5,46	7,65	16,94	–81
(III)	–	Ph	H	61	148 (0,05)	–	–	62,04	–	6,50	–	$C_{12}H_{10}NPS$	62,34	–	6,06	–	–65
(VIII)	–	OMe	Me	68	77 (0,004)	1,2221	1,6131	–	–	7,04	15,58	$C_8H_{10}NOPS$	–	–	7,29	15,15	–126
(XIV)	–	OBu	Me	65	95 (0,004)	1,1452	1,5814	54,78	6,64	5,81	12,87	$C_{11}H_{16}NOPS$	55,31	6,84	6,04	12,74	–124
(XV)	–	Me	Me	79	78 (0,03)	1,1679	1,6341	–	–	7,65	16,94	$C_8H_{10}NPS$	–	–	7,62	17,01	–93
(XVI)	–	Et	Me	82	80 (0,04)	1,1524	1,6233	54,82	6,09	7,11	–	$C_9H_{12}NPS$	55,22	5,95	7,08	–	–102
(XVII)	–	Ph	Me	74	138 (0,04)	1,2174	1,6574	63,67	4,90	5,71	–	$C_{13}H_{12}NPS$	63,82	5,09	5,30	–	–81
(XVIII)	–	OEt	H	55	114 (0,01)	1,2462	1,6239	48,24	5,03	7,04	–	$C_8H_{10}NOPS$	48,20	5,07	6,96	–	–112
(XIX)	–	OPr-*i*	H	61	112 (0,08)	–	–	–	–	6,57	14,55	$C_9H_{12}NOPS$ *	–	–	6,60	14,56	–111
(XX)	O	SMe	Me	50	146 (0,004)	–	1,6480	–	–	6,06	13,42	$C_8H_{10}NOPS_2$	–	–	5,69	13,20	–60
(XXI)	O	NMe₂	Me	69	142 (0,001)	–	1,6089	–	–	12,28	13,60	$C_9H_{13}N_2OPS$	–	–	12,00	12,96	–44
(XXII)	S	OEt	Me	78	132 (0,001)	1,2727	1,6276	–	–	5,71	12,65	$C_9H_{12}NOPS_2$	–	–	5,89	12,40	–92
(XXIII)	S	OPr	Me	70	138 (0,001)	1,2406	1,6182	–	–	5,41	11,97	$C_{10}H_{14}NOPS_2$	–	–	5,33	11,69	–94
(XXIV)	S	OBu	Me	76	144 (0,001)	1,2177	1,6078	–	–	–	11,36	$C_{11}H_{16}NOPS_2$	–	–	–	11,44	–82

*Found: S 15.06%, Calculated: S 15.02%.

EXPERIMENTAL

The ^{31}P NMR spectra were taken on the NMR KGU-4 apparatus (10.2 MHz) with 85% H_3PO_4 serving as a standard. The PMR spectra were recorded on the Varian T-60 apparatus, with TMS as internal standard.

2-Substituted 4,5-Benzo-1,3,2-thiazaphospholanes (XIII)-(XIX). To a calculated amount of OATP or N-methyl-OATP, an equimolecular amount of tetraalkyldiamidophosphite or phosphonite and a few drops of AcOH were added. The mixture was heated for 1/2 to 1 h at 100-140°C, until no more Et_2NH evolved. The products were distilled in vacuo (see Table 1).

Reaction of 2-Phenyl-4,5-benzo-1,3,2-thiazaphospholane (III) with Benzil. A 2.1 g portion of benzil was added to 2.3 g of thiazaphospholane (III) in 15 ml of benzene, and the mixture was left to stand for 3 days. Thus, 3.0 g (68%) of the crystalline spirophospholane (XII), mp 123°C, was obtained. Found: C 70.83; H 4.85; N 2.94; P 6.64; S 7.38%. $C_{26}H_{20}NO_2PS$. Calculated: C 70.75; H 4.54; N 3.17; P 7.03; S 7.26%.

CONCLUSIONS

In the reaction of o-aminothiophenol and N-methyl-o-aminothiophenol with tetraalkyldiamidophosphites and phosphonites, 2-substituted 4,5-benzo-1,3,2-thiazaphospholanes were obtained in high yields. On heating, 2-alkyl-4,5-benzo-1,3,2-thiazaphospholanes can transform into spirophosphoranes with a P—C bond.

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