Synthesis of the substituted 3,9-bisphenoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5,5]undecanes and investigation of the effect of substituents on their resistance to hydrolysis

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The 3,9-bisphenoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5,5]undecanes substituted in positions 2; 4; 2,4; 2,6 of the phenyl groups were synthesized and the influence of substituents on hydrostability of these substances was investigated by the use of a developed titrimetric method.

It has been found that different alkyl or aralkyl substituents in position 2 or 4 have not any significant influence on hydrostability. The resistance to hydrolysis of the 2,4-disubstituted derivatives in the phenyl group depends on character of the substituent in position 2 and electronic effect of the substituent in position 4. A convenient alkyl or aralkyl substitution in position 2 or 4 enables us to obtain hydrolytically very stable cyclic phosphites.

Были синтезированы 3,9-бисфенокси-2,4,8,10-тетраокса-3,9-дифосфаспиро[5,5]ундеканы, замещенные в положениях 2; 4; 2,4 или 2,6 фенильных групп, и исследовалось влияние строения на их гидростабильность с помощью специально разработанного метода титрования.

Обнаружено, что различные алкильные или аралкильные заместители в положениях 2 или 4 не оказывают существенного влияния на гидростабильность. Устойчивость по отношению к гидролизу 2,4-дизамещенных по фенильной группе производных зависит от характера заместителя в положении 2 и электронного эффекта заместителя в положении 4. Подбором подходящего алкильного или аралкильного заместителя в положениях 2 и 4 можно получить чрезвычайно устойчивые по отношению к гидролизу циклические фосфиты.

Cyclic phosphites represent a group of antioxidants which are used as thermal stabilizers of polymers, especially in their treatment and simultaneously have favourable influence on the colour of polymers or raise their resistance to atmospheric effects [1—6]. Many of these compounds are subjected to hydrolysis even by the effect of air humidity though the rate of their hydrolysis may be very different. At present, the literature gives only poor information about these problems and in most cases there are no real data but only statement that these substances are instable [7]. In order to prepare an antioxidant of the type of cyclic phosphite resistant to hydrolysis, we synthesized a series of these compounds for which the influence of substitution on their resistance to hydrolysis was investigated.

Experimental

The course of reaction was investigated by the method of TLC on Silufol plates. Benzene was used as an eluant.

Silica gel L 40/100 and aluminium oxide H neutral (Lachema, Brno) were employed in column chromatography. Benzene or n-heptane was used as an eluant.

The infrared spectra were taken on an instrument UR 20 (Zeiss, Jena), carbon tetrachloride being used as a solvent. The infrared spectra of cyclic phosphites with a P—O—aryl bond exhibited strong absorption bands corresponding to stretching vibration at $\tilde{\nu} = 1150$—$1250\ \mathrm{cm}^{-1}$

The ^{1}H, ^{13}C, and ^{31}P NMR spectra of the analyzed substances were measured on an instrument Jeol PX 100 at laboratory temperature by using $CDCl_3$ as solvent, TMS as internal standard, and 85 % H_3PO_4 as external standard.

The substituted 3,9-bisphenoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5,5]undecanes I—XVII

3,9-Dichloro-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5,5]undecane (2.64 g; 0.01 mol) dissolved in anhydrous benzene (100 cm^3) was put in a flask equipped with a stirrer, reflux, and calcium chloride closure. Triethylamine (2.02 g; 0.02 mol) was added. Then the substituted phenol (0.02 mol) was dropwise added under constant stirring at 25—40 °C. The reaction temperature was held at 25—40 °C. The course of reaction (2—6 h) was investigated by the method of TLC on Silufol plates. The separated precipitate of triethylammonium chloride was filtered off and benzene was evaporated. For products *XV—XVII* the reaction temperature had to be raised to 60—70 °C. The yields of crude products were 85—97 %.

The crude products were purified by column chromatography and crystallization. The prepared derivatives *I—XVII* were identified by determining the content of phosphorus and measuring the infrared and ^{1}H, ^{13}C, ^{31}P NMR spectra.

Hydrolytic stability [8]

100 cm^3 of distilled water were put into a 250 cm^3 flask equipped with a stirrer, reflux, and thermometer. After heating to 70 °C, 1 g of the pertinent cyclic phosphite was added. The mixture was stirred for 60 min at 70 °C. After cooling, 100 cm^3 of ethanol were added. The samples were titrated with 0.1 M-KOH by using bromphenol blue as indicator.

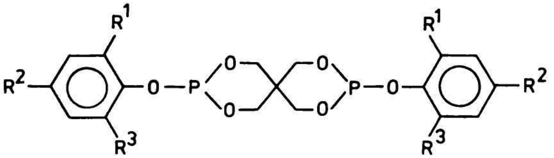
The hydrostability was expressed by the degree of hydrolysis α (%) according to the formula

$$\alpha = \frac{V_a}{V_t} 100$$

where V_a is the real and V_t is the theoretical consumption (cm^3) of 0.1 M-KOH for titration of a sample. The obtained values of α are given in Table 1.

Results and discussion

The influence of substituents R^1, R^2, and R^3 on the degree of hydrolysis was investigated for a series of compounds of the type



According to present view, compounds of the type of cyclic phosphites are prone to hydrolysis on the P—O bond which is outside the ring [9]. It is obvious on the basis of this view that substituents R^1, R^2, and R^3 are able to affect the degree of hydrolysis significantly by their *I* effects and as for substituents R^1 and R^3 we must take into consideration a possible steric effect which brings about a turning of the benzene ring.

A comparison of the degrees of hydrolysis of compounds *I—IV* shows that the influence of substitution in position 2 manifests itself only little and some of the differences found in measurements are in the range of error of the method of determination of the degree of hydrolysis (± 1 %). This statement is also valid for substitution in position 4 (compounds *I, V—VIII*).

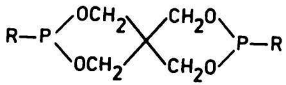
A low degree of hydrolysis was found for some derivatives in which phenyl was substituted by voluminous groups in positions 2 and 4. That is why we investigated the influence of substitution in position 4 at constant substitution by *tert*-butyl in position 2 and the influence of substitution in position 2 at constant substitution by α,α-dimethylbenzyl in position 4 on the degree of hydrolysis.

Provided *tert*-butyl is in position 2 (*IV*), it is remarkable that a significant decrease in the degree of hydrolysis is to be achieved even by introducing methyl (*IX*), isopropyl (*X*) or *tert*-butyl (*XI*) in position 4. The most conspicuous decrease appears if α,α-dimethylbenzyl is used as substituent (*XII*).

If there is an α,α-dimethylbenzyl substituent in position 4, the methyl or

Table 1

Analytical data of substances of the type



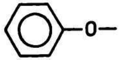
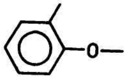
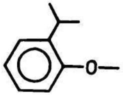
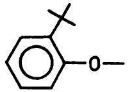
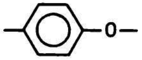
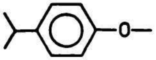
Compound	Substituent R	Formula	M_r	w_P(calc.)/% w_P(found)/%	M.p./°C	α/%
I		$C_{17}H_{18}O_6P_2$	379.26	16.36 16.29	120—121	57.6
II		$C_{19}H_{22}O_6P_2$	408.34	15.15 14.86	88—91	53.8
III		$C_{23}H_{30}O_6P_2$	464.44	13.30 12.96	100—101	53.5
IV		$C_{25}H_{34}O_6P_2$	492.47	12.60 12.06	120—125	53.1
V		$C_{19}H_{32}O_6P_2$	408.34	15.15 14.95	152—155	57.2
VI		$C_{23}H_{30}O_6P_2$	464.44	13.30 12.90	182—184	56.2

Table 1 (Continued)

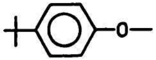
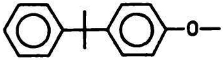
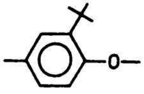
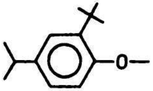
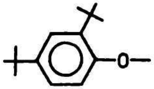
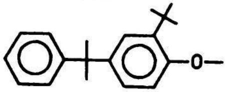
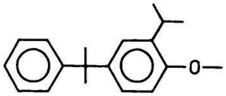
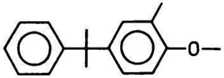
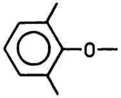
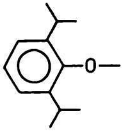
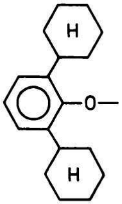
Compound	Substituent R	Formula	M_r	w_P(calc.)/% w_P(found)/%	M.p./°C	α/%
VII		$C_{25}H_{34}O_6P_2$	492.47	12.60 12.25	137—139	55.4
VIII		$C_{35}H_{38}O_6P_2$	616.60	10.05 9.55	124—126	49.1
IX		$C_{27}H_{38}O_6P_2$	520.55	11.75 11.61	181—189	18.0
X		$C_{31}H_{46}O_6P_2$	575.63	10.70 10.23	175—176	18.2
XI		$C_{33}H_{44}O_6P_2$	604.68	10.25 10.15	172—173	17.6
XII		$C_{43}H_{54}O_6P_2$	728.23	8.46 8.26	160—162	0.0

Table 1 (Continued)

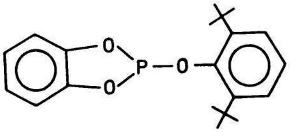
Compound	Substituent R	Formula	M_r	w_P(calc.)/% w_P(found)/%	M.p./°C	α/%
XIII		$C_{41}H_{50}O_6P_2$	700.86	8.80 8.60	178—181	49.1
XIV		$C_{37}H_{42}O_6P_2$	644.67	9.45 9.25	144—146	49.2
XV		$C_{21}H_{26}O_6P_2$	436.37	14.10 13.95	166—167	52.5
XVI		$C_{29}H_{42}O_6P_2$	548.25	11.29 10.95	160—161	52.3
XVII		$C_{41}H_{58}O_6P_2$	708.85	8.75 8.52	215—217	49.6

isopropyl substituent in position 2 has practically no influence on decrease in the degree of hydrolysis (compounds *VIII*, *XIII*, *XIV*). A considerable decrease sets in only by introducing the *tert*-butyl substituent in position 2 (*XII*).

However, there is the question to what extent the steric effect in position 2 and the electronic effect of both groups in positions 2 and 4 contribute to the increase in resistance to hydrolysis.

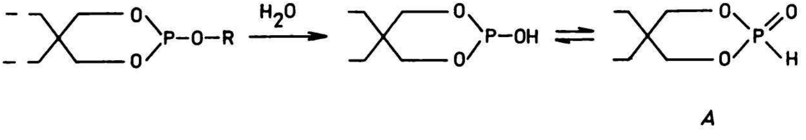
The evidence that only the steric shielding of the P—O—C bond by voluminous groups is not able to reduce the resistance to hydrolysis of cyclic phosphites is given by the results of hydrolysis of some derivatives in which the phenolic component was 2,6-dimethylphenol (*XV*), 2,6-diisopropylphenol (*XVI*), and 2,6-dicyclohexylphenol (*XVII*). The measured degrees of hydrolysis are only a little lower than the degrees of hydrolysis of the corresponding 2-substituted derivatives (*II*, *III*).

Our attempts to prepare the substituted 2,4,8,10-tetraoxa-3,9-diphosphaspiro[5,5]undecane from 2,6-di-*tert*-butyl-4-methylphenol failed. The preparation of cyclic phosphite has been described in literature [10] but we did not succeed in preparing the required compound even if equal conditions were used. Variable results obtained by using equal method may be due to unequal angles of bonds to phosphorus.



The substituents of the investigated derivatives were selected in the main with respect to their practical availability. The described investigations of hydrolyzability of phosphites by the titrimetric method fulfil for a wide series of phosphites prone to hydrolysis though the determination by means of ^{31}P NMR spectra is more sensitive to every change involving phosphorus.

According to literature [11], the first stage of hydrolysis gives rise to the phosphonate form (*A*) which does not manifest itself in titration though phenol has already yielded to hydrolysis



A

In the subsequent stage the phosphorinane ring is opened and the grouping (*B*) on phosphorus comes into existence. This grouping can be titrated and thus a change in the degree of hydrolysis may be revealed.

Table 2

^{1}H NMR chemical shifts (δ/ppm) of the investigated compounds

Compound	$O(CH_2)_4C^a$	C_6H_5 ; C_6H_4	CH_3	$(CH_3)_2CH$	CH	$(CH_3)_3C$	$(CH_3)_2C$
I	3.35—4.59	6.77—7.40 (m, 10H)	—	—	—	—	—
II	3.30—4.60	6.85—7.35 (m, 8H)	2.30 (s, 6H)	—	—	—	—
III	3.50—4.60	6.90—7.40 (m, 8H)	—	1.23, 1.30 (d, 12H)	3.40 (m, 2H)	—	—
IV	3.80—4.60	6.80—7.30 (m, 8H)	—	—	—	1.45 (s, 18H)	—
V	3.30—4.60	6.90—7.20 (m, 8H)	2.30 (s, 6H)	—	—	—	—
VI	3.35—4.58	6.70—7.30 (m, 8H)	—	1.20, 1.27 (d, 12H)	2.89 (m, 2H)	—	—
VII	3.25—4.60	6.90—7.35 (m, 8H)	—	—	—	1.43 (s, 18H)	—
VIII	3.33—4.61	6.90—7.25 (m, 18H)	—	—	—	—	1.67 (s, 12H)
IX	4.10—4.60	6.94—7.23 (m, 6H)	2.31 (s, 6H)	—		1.42 (s, 18H)	—
X	3.30—4.80	6.90—7.30 (m, 6H)	—	1.10, 1.17 (d, 12H)	2.68 (m, 2H)	1.26 (s, 18H)	—
XI	3.40—4.80	6.90—7.40 (m, 6H)	—	—	—	1.31 (s, 18H) 1.43 (s, 18H)	—
XII	3.37—4.74	6.80—7.23 (m, 16H)	—	—	—	1.37 (s, 18H)	1.67 (s, 12H)
XIII	3.25—4.80	6.80—7.35 (m, 16H)	—	1.16, 1.19 (d, 12H)	2.96—3.60 (m, 2H)	—	1.62 (s, 12H)
XIV	3.30—4.80	6.80—7.30 (m, 16H)	2.30 (s, 6H)	—	—		1.65 (s, 12H)
XV	3.40—3.60	6.80—7.40 (m, 6H)	2.31 (s, 12H)	—	—	—	—
XVI	3.48—4.75	6.90—7.20 (m, 6H)	—	1.20, 1.28 (d, 24H)	3.30 (m, 4H)	—	—
XVII	3.50—4.80	6.60—7.40 (m, 8H)	1.02—2.25 (m, 44H; CH_2 cyclohexyl)				

a) Multiplex 8H.

Table 3

^{13}C and ^{31}P NMR chemical shifts (δ/ppm) of the investigated compounds

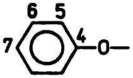
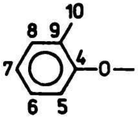
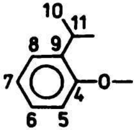
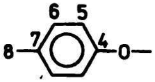
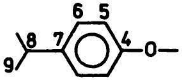
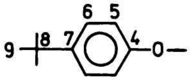
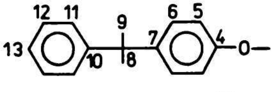
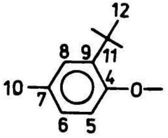
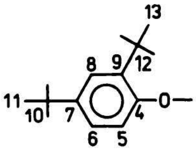
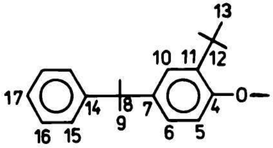
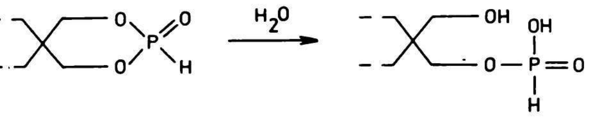
Compound	Substituent R	^{31}P	^{13}C										
			C-1	C-2,3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12
I		−117.2	37.2	62.2	152.3	119.8	129.8	123.7					
II		−117.3	37.1	62.1	150.7	118.9	123.6	123.6	131.2	129.2	16.6		
III		−117.2	37.1	62.9	149.8	118.9	126.7	123.9	126.7	139.4	20.3	22.8	
V		−117.5	37.2	62.1	149.9	119.7	130.3	133.2	20.7				
VI		−117.3	37.1	62.2	150.2	119.6	127.7	144.3	33.5	24.1			

Table 3 (Continued)

Compound	Substituent R	^{31}P	^{13}C										
			C-1	C-2,3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12
VII		−117.1	37.2	62.2	149.9	119.2	126.7	146.6	34.3	31.5			
VIII		−117.5	37.1	62.1	150.0	119.1	146.1	42.5	30.8	150.5	126.7	128.0	125.6
IX		−116.4	37.0	62.6	149.2	119.1	128.1	132.6	127.4	139.7	20.9	34.6	30.1
XI		−116.2	37.0	62.5	149.1	118.5	124.4	145.8	123.8	139.1	34.5	30.1	34.9[a]
XII		−116.2	37.0	62.5	149.2	118.5	125.6	145.4	125.4	139.1	34.8	30.1	42.5[b]

a) C-13 31.5; *b*) C-13 30.9, C-14 150.6, C-15 126.7, C-16 127.9, C-17 125.8.



B

The degree of hydrolysis depends on the rate of hydrolysis of the substituted phenol because the rate of hydrolysis of the formed phosphonate (*A*) is then in all cases equal. The titrimetric method of determination of the degree of hydrolysis under above conditions does not enable us to distinguish the fine differences due to substitution on the benzene ring, especially for derivatives which are liable to hydrolysis. If the time of hydrolysis is shortened (10 min) and the temperature reduced (20 °C), some differences in substitutions appear, but these conditions are not of practical importance for characterizing the hydrolyzability of some phosphites that are resistant to hydrolysis, *i.e.* those which can with profit be used as antioxidants.

The evidence of these facts results from the investigations of hydrolyzability by means of the ^{31}P NMR spectra of two compounds the phenolic component of which is the nonsubstituted phenol (*I*) and 2-methylphenol (*II*). As for compound *II*, the hydrolysis of 2-methylphenol is retarded, but in the subsequent stage the rate of hydrolysis is unchanged. These detailed investigations of hydrolysis of cyclic phosphites will be the topic of further study.

The measurement of the degree of hydrolysis of this series of phosphites has shown that the monosubstitution itself by alkyl or aralkyl either in position 2 or 4 has no significant influence on hydrolytic stability and even a voluminous substituent in position 2 does not bring about an appreciable decrease in hydrolyzability. Considerable differences manifest themselves with 2,4-disubstituted derivatives for which it holds that the lowest degree of hydrolysis is exhibited by the compounds having a voluminous group in position 2 which simultaneously shows $+I$ effect (*e.g.* *tert*-butyl) and position 4 is occupied by a group with significant positive electronic effect.

The basic chemical shifts giving evidence of the identity of the prepared substances are presented in this paper (Tables 2 and 3). A more detailed study of the ^{13}C, ^{1}H, and ^{31}P NMR spectra is the topic of separate papers [12, 13].

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