Reaction of ethyl *N,N*-(*p*-methoxybenzal)-*p*-aminobenzoate with dialkyl phosphonates

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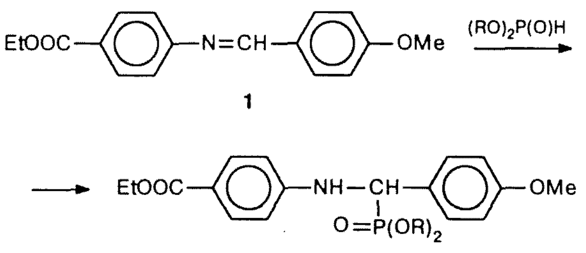
Interaction of ethyl *N,N*-(*p*-methoxybenzal)-*p*-aminobenzoate with dialkyl phosphonates results in dialkyl (*N*-*p*-ethoxycarbonylphenylamino)-*p*-methoxybenzyl phosphonates. In the resulting compounds hydrogen bonds are observed by IR spectroscopy.

Key words: ethyl *N,N*-(*p*-methoxybenzal)-*p*-aminobenzoate, dialkyl phosphonates, reaction; hydrogen bond; IR spectra.

We have found previously[1] that phosphorylated anesthesine derivatives increase radioresistance *in vivo*. The search for radioprotectors among the related compounds was shown to be promising. In this work ethyl *N,N*-(*p*-methoxybenzal)-*p*-aminobenzoate (**1**) was synthesized and its interaction with dialkyl esters of phosphonic acid was investigated.



1

2—5

R = Me (**2**), Et (**3**), Pr (**4**), Bu (**5**)

The reactions take place readily at room temperature, to give esters of (*N*-*p*-ethoxycarbonylphenylamino)-*p*-methoxybenzylphosphonic acid **2—5** in high yields (Table 1).

The structures of compounds obtained were confirmed by IR spectoscopy data (Table 2). The narrow and rather intense absorption band of secondary amino group ν(NH) in spectra of the crystalline compounds **3** and **4** is a doublet. In the case of the concentrated solutions of these esters in CCl_4 two bands of ν(NH) at 3290 and 3410 cm^{-1} are registered. When the solutions are diluted to ~10^{-3} mol L^{-1}, the low-frequency band disappears and only the high-frequency band remains (Fig. 1). Therefore the first band was assigned to NH groups that participate in intermolecular hydrogen bonds, and the second band is classified as "free" molecules. The relatively low (for this type of the phosphorus atom environment) absorption of the phosphoryl group[3] indicated to the possibility of its participation in hydrogen bonds as a proton acceptor.

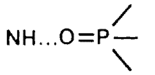


Table 1. The main physicochemical characteristics of esters of (*N*-*p*-ethoxycarbonylphenylamino)-*p*-methoxybenzylphosphonic acid

Compound	R	Yield (%)	M.p. /°C	Found / Calculated (%)				Molecular formula
				C	H	N	P	
2	Me	89.0	151	$\underline{57.85}$ 58.01	$\underline{6.22}$ 6.15	$\underline{3.42}$ 3.56	$\underline{7.46}$ 6.87	$C_{19}H_{24}NO_6P$
3	Et	86.0	114	$\underline{59.70}$ 59.56	$\underline{6.59}$ 6.65	$\underline{3.28}$ 3.33	$\underline{7.35}$ 7.40	$C_{21}H_{21}NO_6P$
4	Pr	86.0	106	$\underline{61.63}$ 61.46	$\underline{6.98}$ 7.17	$\underline{3.20}$ 3.20	$\underline{6.89}$ 6.72	$C_{23}H_{32}NO_6P$
5	Bu	92.1	101—102	$\underline{62.88}$ 62.68	$\underline{7.80}$ 7.60	$\underline{2.93}$ 3.00	$\underline{6.49}$ 6.55	$C_{25}H_{36}NO_6P$

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Table 2. Characteristic frequencies[2,3] in IR spectra and ^{31}P NMR spectral data of the compounds **2**—**5**

Compound	ν(NH)	ν(C=O)	ν(C⋯C)	ν(C—O—C)	ν(P=O)	ν(P—O—R)	γ(CH)	δ ^{31}P
				cm^{-1}				
2	3302 s	1712 vs	1607 vs, 1514 s	1272 vs, 1246 s, 1175 s	1233 s	1064 s, 1029 vs	844 m	22
3	3335 w, 3287 s (3410 m)	1702 s, 1691 s	1606 vs, 1510 vs	1277 vs, 1244 s	1232 s	1025 s, 968 s	847 m, 835 m	22
4	3343 m, 3286 s (3410 m)	1689 vs	1605 vs, 1512 s	1275 vs, 1245 s	1231 s	1008 vw	849 m, 831 m	21
5	3283 vs (3410 m)	1708 vs	1607 vs, 1513 s	1266 vs	1229 vs	1070 s, 1065 s, 976 s	849 m, 833 m	21

Note. In brackets the frequencies for the solution in CCl_4 are presented.

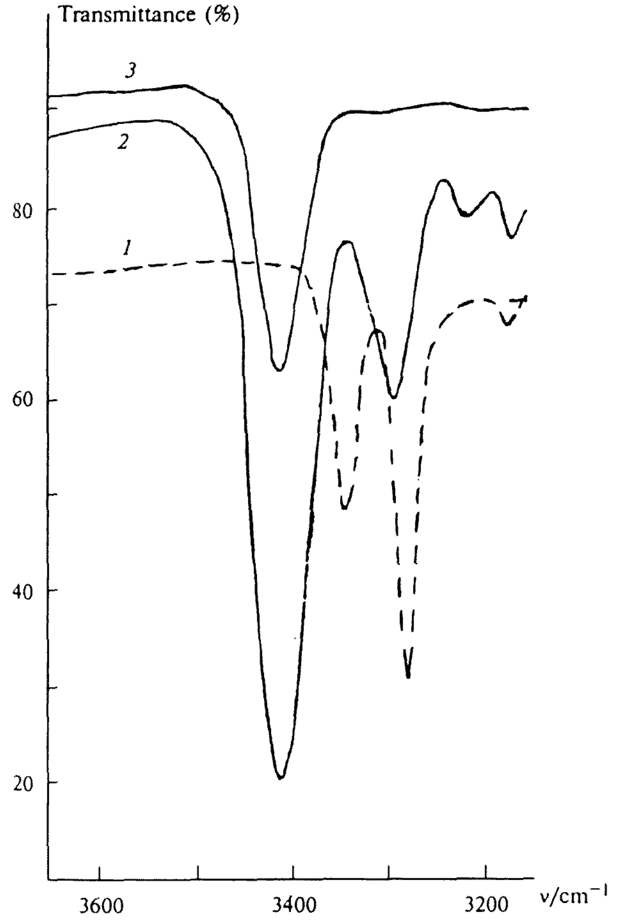
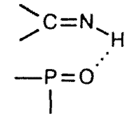


Fig. 1. IR spectra of dipropyl (*N*-*p*-ethoxycarbonylphenylamino)-*p*-methoxybenzylphosphonate (**4**): *1*, crystals of **4** in Vaseline oil; *2*, concentrated solutions of **4** in CCl_4; *3*, diluted solutions of **4** in CCl_4.

Taking this fact into account the doublet peak of ν(NH) in spectra of compounds **3** and **4** in the solid state could be explained by the existence of two different crystalline modifications of these esters. One of the peaks of the doublet is likely to belong to such a crystalline modification (**A**) in which compounds **3** and **4** form intramolecular hydrogen bonds along with intermolucular ones.



Experimental

^{31}P NMR spectra were obtained on a KGU-4 spectrometer (10.2 MHz, 85 % H_3PO_4 is an internal standard) in acetone. IR spectra were recorded on a IR-FT specrtometer Bruker IFS-113V. The samples of compounds for registration were prepared as pellets in KBr, or as solutions in CCl_4 (l = 5 cm).

Ethyl *N,N*-(*p*-methoxybenzal)-*p*-aminobenzoate (1). A mixture of anisaldehyde (24 g) and anesthesine (29 g) in benzene (300 mL) was refluxed in a flask connected with a Dean—Stark trap for 10 h. After cooling, benzene was removed, the crystalline residue was recrystallized from methanol to give compound **1** (33 g, 66 %), m.p. 76 °C. Found (%): C, 72.11; H, 6.00; N, 4.92. $C_{17}H_{17}NO_3$. Calculated (%): C, 72.20; H, 6.02; N, 4.98.

Esters of (*N*-*p*-ethoxycarbonylphenylamino)-*p*-methoxybenzylphosphonic acid. A mixture of an equmolar amounts of ethyl *N,N*-(*p*-methoxybenzal)-*p*-aminobenzoate **1** and dialkyl phosphonate was heated in a water bath for 3 h. The reaction with dimethyl ether results in the crystalline ester **2** immediately; in other cases syrup-like liquids were crystallized after standing for 1—2 days. Compounds **2**—**5** were washed on a glass filter with anhydrous ether. The main constants and spectral parameters of the esters obtained are presented in Table 1 and 2, respectively.

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Reactions of dialkyl phosphonates and phosphinates with bis(benzylideneimino)toluene

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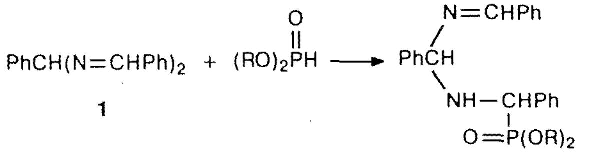
Dialkyl phosphonates bind to the C=N bond of bis(benzylideneimino)toluene, with formation of dialkyl (benzylideneimino)benzylaminobenzyl phosphonates. The complicated character of IR spectra of these compounds is connected with the possibility of formation of dimeric cyclic associates and intramolecular hydrogen bonding. Phosphinic acid reacts with bis(benzylidenimino)toluene in a 2 : 1 ratio to afford *N,N'*-benzylidenebis(α-aminobenzylphosphonic) acid.

Key words: dialkyl phosphonates; phosphinic acid; dialkyl (benzylideneimino)benzylaminobenzyl phosphonates, hydrogen bond.

Previously,[1] it was shown that dialkyl phosphonates attach to *N,N'*-dibenzylideneazine at one of the two C=N bonds at ~20 °C. For this reason, it was appropriate to introduce into this reaction the compounds containing two isolated C=N bonds.

Reactions of dialkyl phosphonates and phosphinates with bis(benzylidenimino)toluene (**1**) are described in this work.

Dialkyl phosphonates add only to one of the two C=N bonds of compound **1** at 20 °C to form dialkyl (benzylideneimino)benzylaminobenzyl phosphonates **2**—**4**.



1 **2—4**

R = Et (**2**), Pr (**3**), Bu (**4**)

The resulting amino phosphonates are transparent viscous liquids. They decompose into the initial compounds upon heating. Their main physicochemical parameters are presented in Table 1, and their spectral characteristics are shown in Table 2.

Table 2 does not contain the frequencies of NH bond stretching vibrations, whose identification is important to confirm the structures of the compounds obtained, but in fact it is a rather complicated task. IR spectra of the pure substances (films and pellets with KBr) contain only several very weak diffuse bands in the frequency range of ν(NH) higher than 3000 cm^{-1} (Fig. 1). At the same time, a well pronounced absorption maximum at 3393 cm^{-1} is registered in the IR spectra of the solutions of amino phosphonates in CCl_4. This absorption characterizes the stretching vibrations of the NH group. We assigned less intense low-frequency components manifesting themselves additionally at 3327 and 3267 cm^{-1} to ν(NH) of conformers with intramolecular hydrogen bond and an overtone of stretching vibrations of the C=N group, respectively.[2] The absence of pronounced absorption bands ν(NH) in the IR spectra of amines and their derivatives

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