LETTERS
TO THE EDITOR

Reaction between Pyrocatechol and *N,N,N',N'*-Tetraethylphenylphosphonous Diamide

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Abstract—The reaction between pyrocatechol and *N,N,N',N'*-tetraethylphenylphosphonous diamide was studied. It was found that the main reaction products are bisphosphorylated pyrocatehol and and the product of intramolecular cyclization, ester of pyrocatechol and phenylphosphonic acid.

Keywords: phosphorus amides, phosphonites, pyrocatechol, phosphorylation

Many phosphorus-containing pyrocatechol derivatives are prone to disproportionation due to the fact that their phosphorus-containing groups are spatially proximate to each other, and 3,5- and 3,6-*tert*-butylpyrocatechols react with hexaethylphosphorous triamide $P(NEt_2)_3$ to form cyclic products [1]. Some other information on the phosphorylation of pyrocatechol is available [2], but the synthesis of macrocyclic esters of phosphorus acids, derived from pyrocatechol, has never been reported [3].

Previously we studied the reaction of pyrocatechol **1** with hexaethylphosphorous triamide in a 1 : 2 ratio [4, 5]. The expected bisphosphorylated product was planned to be further used for macrocycization with resorcinol or hydroquinone. However, again, the only product that could be detected was formed by intramolecular cyclization: a five-membered ring with δ_P 148.94 ppm.
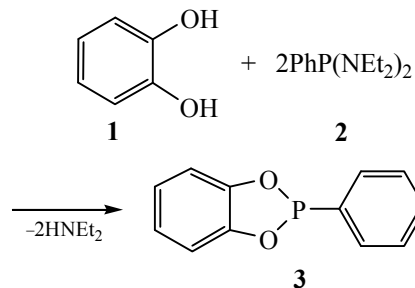
It was found bisphosphorylated pyrocatechol was impossible to prepare because of the through-space interaction between the tetraethylamido groups located ortho to each other in the benzene ring.
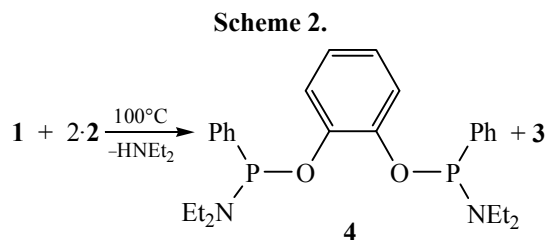
The bisphosphorylation of pyrocatechol with phosphonous amide **2** has been scarcely studied, and the available information is controversial. We suggested in [6] that the reaction involves intramolecular cyclization to form product **3** (Scheme 1).

By contrast, Blokhin et al. [7] stated that the reaction, depending on conditions, can produce both compound **3** and bisphosphorylated pyrocatechol **4**. According to [7], the ^{31}P NMR signal of compound **4** appears at 132.89 ppm. Pyrocatechol **4** is formed at a 1 : 2 reagent ratio under solvent-free conditions at 100°C with distilling off diethylamine in a water-jet-pump vacuum. Bisphosphorylated pyrocatechol **4** was used to synthesize a sulfurized product (δ_P 77.26 ppm). Compound **3** had δ_P 179.09 ppm, and it formed at different component ratios (1 : 1 or 1 : 2) under heating both under solvent-free conditions and in a solvent. However, it remained unclear how to synthesize specifically compound **3** or compound **4**, whether these two products can be separated from each other, and whether pyrocatechol **4** can be obtained individual for further use in the synthesis of macrocycles. Thus, by the start of our research the reaction of pyrocatechol **1** and *N,N,N',N'*-tetraethylphenylphosphonous diamide **2** called for further detailed study, and the reaction products had to be isolated pure and characterized by physicochemical methods.

Scheme 1.

Scheme 2.

$$1 + 2 \cdot 2 \xrightarrow[-HNEt_2]{100°C} \text{Ph} \quad \text{(structure 4)} \quad \text{Ph} + 3$$

Scheme 3.

$$4 \xrightarrow{2S} \text{(structure 5)}$$

As known, phosphonous amide **2** contains only two diethylamido groups which can be substituted, and, therefore, is it a weaker phosphorylating agent than P(NEt₂)₃ [8]. In this connection we first of all reacted pyrocatechol **1** with phosphonous amide **2** in a 1 : 2 ratio under the mild bisphosphorylation conditions developed earlier and used to success for bisphosphorylation of other simplest bisphenols such as resorcinol and hydroquinone [9].

The ³¹P NMR spectrum of the reaction mixture after a 24-h reaction of pyrocatechol **1** and phosphonous amide **2** in ethyl acetate, like in [7], displayed two signals: at 179 and 133 ppm in a 2.74 : 1 ratio. Even though the synthesis was performed in an argon atmosphere, in the ³¹P NR spectrum we also observed signals in the range 0–35 ppm with the total integral intensity of 1.5, which is characteristic of oxidation products. Among these signals we also identified that of an oxidized compound **3** (35 ppm [8]).

The spectrum of the reaction mixture after a 4-h reaction at 100°C under solvent-free conditions with simultaneous distillation of diethylamine underwent radical changes: the intensity ratio of the same signals became 0.64 : 1. The integral intensity of the signals of oxidation products was now 0.6, with 0.21 contributed by an oxidized product **4**. The reaction without a solvent was found to give less by-products than the reaction in ethyl acetate. The postreaction mixture, a light yellow thick thermoplastic glassy material, was dissolved in benzene under heating and subjected to sulfurization. The ³¹P NMR spectrum of the benzene solution after the separation of oxidation products showed only one signal characteristic of thione phosphonates (δ_P 77 ppm), as well as a few signals in the range 0–16 ppm, assignable to oxidation products remaining in the solution. The composition of the organophosphorus compounds in the benzene solution was studied by MALDI mass spectrometry. Pyrocatechol bis(thione phosphonate) **5** detected as the [M + H]⁺ ion at *m/z* 533.15 proved to be the main product. No derivatives of the cyclic product **3** were
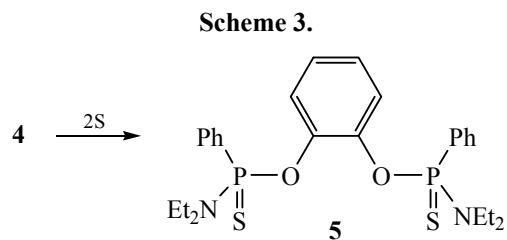
detected. Compound **5** was isolated pure by column chromatography.

Obviously, the reaction of pyrocatechol **1** with phosphonous amide **2** under solvent-free conditions initially forms both bisphosphorylated pyrocatechol **4** and the cyclic product **2** (Scheme 2).

Compound **3** could not be separated from pyrocatechol **4**. Both products decomposed on attempted distillation even in a high vacuum (10⁻⁴ mmHg) to form a tarry residue, like other similar P(III) derivatives of dihydric phenols [3, 9].

Under the sulfurization conditions, compound **3** either decomposed or precipitated from the benzene solution together with other oxidation products. Therewith, the sulfurization of bisphosphorylated pyrocatechol **4** resulted in a facile formation of thione phosphonate **5** as a light yellow solid amorphous material, which could be separated from other reaction products, even though in a very low yield (Scheme 3).

The mixture of compounds **3** and **4**, obtained under solvent-free conditions, was also oxidized by our earlier developed procedure [9]. Recrystallization gave bisphosphorylated phosphonate **6** as a white powder (Scheme 4). The reaction also gave the oxidation product of compound **3.** This product did not dissolve on heating in hexane, due to which it could be separated from phosphonate **6**.

Thus, we identified bisphosphorylated pyrocatechol **4** among the products of the reaction between pyrocatechol **1** and *N,N,N',N'*-tetraethylphenylphosphonous diamide **2** but have to admit that this product was impossible to isolate pure. Therefore, compound **4**

Scheme 4.

$$4 \xrightarrow[CH_3COOEt]{O_2} \text{(structure 6)}$$
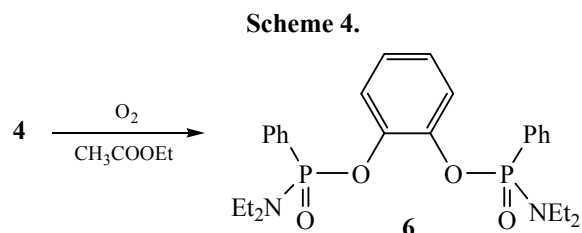
cannot be prepared in this way for further use in the synthesis of macrocycles.

All syntheses involving P(III) compounds were performed under dry argon. Thin-layer chromatography was performed using Silufol plates in 3 : 1 hexane–dioxane (A) or 5 : 1 chloroform–ethanol systems (B); the spots were visualized in UV light or by calcination at 200–250°C. Column chromatography was performed on silica gel L 100/250.

***O,O'*-(Benzene-1,2-diyl) bis(*N*,*N*-diethylphenylphosphonothioamidate) (5).** Phenylphosphonous amide **2**, 1.52 g (6 mmol), was added with stirring to 0.33 g (3 mmol) of pyrocatechol **1**. The reaction mixture was heated at 100°C in a vacuum (10 mmHg) for 4 h and then let to cool down to obtain a light yellow thick thermoplastic glassy material, the ^{31}P NMR spectrum of which showed two major (179.09 and 132.89 ppm) and a few minor signals (0–35 ppm) characteristic of oxidation products. The material was then dissolved under heating in 20 mL of benzene, and 0.19 g (6 mmol) of crystalline sulfur was added to it. The mixture was stirred until sulfur dissolved completely and left to stand for 24 h. The precipitate that formed was separated. The ^{31}P NMR spectrum of the filtrate showed a major signal at 77.26 ppm and a few minor signals in the range 0–16 ppm (intensity ratio 1 : 0.27). Thione phosphonate **5** was isolated by column chromatography, eluent benzene, and then dried for 2 h at 50°C in a vacuum (10 mmHg). Compound **5** was a light yellow solid paste liquefied at 55°C. Yield 0.38 g (24%), R_f 0.70 (A). ^{1}H NMR spectrum, δ, ppm: 0.99 t (12H, CH$_3$, $^3J_{HH}$ = 7.1 Hz), 3.32 m (8H, CH$_2$, $^3J_{PH}$ = 10.4 Hz), 7.36 m (2H, *p*-CH, Ph), 7.48 d (2H, *o*-CH, pyrocatechol, $^3J_{HH}$ = 6.0 Hz), 7.52 m (2H, *m*-CH, pyrocatechol), 7.78 m (4H, *o*-CH, Ph, $^3J_{PH}$ = 12.0, $^3J_{HH}$ = 8.0 Hz), 7.96 m (4H, *m*-CH, Ph). ^{31}P NMR spectrum: δ$_P$ 77.26 ppm. Mass spectrum, *m/z*: 533.15 [*M* + H]$^+$. Found P, %: 11.64. C$_{26}$H$_{34}$N$_2$O$_2$P$_2$S$_2$. Calculated P, %: 11.65.

***O,O'*-(Benzene-1,2-diyl) bis(*N*,*N*-diethylphenylphosphonamidate) (6).** The reaction mixture after the reaction of 3 mmol of pyrocatechol **1** and 6 mmol of phosphonous amide **4** was dissolved in ethyl acetate and stirred in air for 4 h. The solvent was removed in a vacuum. The residue was heated in hexane under reflux, and the undissolved substances were separated. The filtrate was let to cool down, and the resulting thick material was dried in a vacuum for 2 h at 50°C in a vacuum (10 mmHg) to obtain compound **8** as a light yellow powder, mp 50°C. Yield 0.42 g (27%), R_f 0.80

(B). ^{1}H NMR spectrum, δ, ppm: 0.98 t (12H, CH$_3$, $^3J_{HH}$ = 7.1 Hz), 3.30 m (8H, CH$_2$, $^3J_{PH}$ = 10.4 Hz), 7.34 m (2H, *p*-CH, Ph), 7.50 d (2H, *o*-CH, pyrocatechol, $^3J_{HH}$ = 5.8 Hz), 7.52 m (2H, *m*-CH, pyrocatechol), 7.78 m (4H, *o*-CH, Ph, $^3J_{PH}$ = 12.60, $^3J_{HH}$ = 8 Hz), 7.96 m (4H, *m*-CH, Ph). ^{31}P NMR spectrum: δ$_P$ 9.27 ppm. Mass spectrum, *m/z*: 501.19 [*M* + H]$^+$. Found P, %: 12.43. C$_{26}$H$_{34}$N$_2$O$_4$P$_2$. Calculated P, %: 12.40.

The ^{31}P NMR spectra were measured on a Bruker WP-80SY spectrometer at 32.4 MHz against 85% phosphoric acid. The ^{1}H NMR spectra were obtained on a Bruker AM-400 spectrometer at 400 MHz for CDCl$_3$ solutions. The MALDI mass spectra were measured on a Bruker Daltonics Autoflex II MALDI-ToF instrument with a nitrogen laser source (λ 337 nm), operated in the positive ion mode.

CONFLICT OF INTERESTS

No conflict of interest was declared by the authors.

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