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## Reaction of Stannyl Esters of Phosphorus Acids with Sulfonic Acids Chlorides and Carboxylic Acids Anhydrides. A Novel Synthesis of Phosphoric-Sulfonic and Phosphoric-Carboxylic Anhydrides

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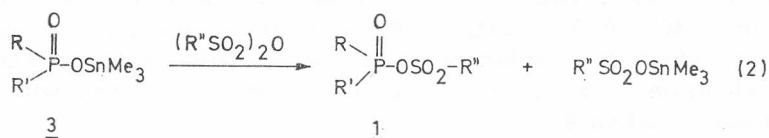
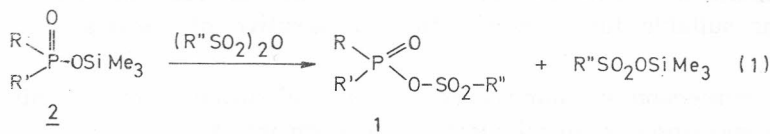
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New methods employing stannyl phosphates for the synthesis of phosphorus-sulfonic anhydrides and acylphosphates are presented.

Mixed anhydrides of phosphorus sulfonic acids  $RR'P(O)OSO_2R''$  **1** are of interest in the biological transfer of sulfates<sup>1</sup>. In the chemical synthesis of oligonucleotides, phosphoric sulfonic anhydrides **1** ( $R', R =$  nucleoside) are postulated as important and reactive intermediates<sup>2,3,3a</sup>. Anhydrides **1** were also suggested as intermediates in biooxidation of thiophosphates<sup>4</sup>. Structural analogues of anhydride **1**, derived from phosphorus monothioacids, were successfully used as models for studying the mechanism and stereochemistry of nucleophilic displacement reactions at the tetra-coordinate phosphorus centre<sup>5,6,7</sup>.

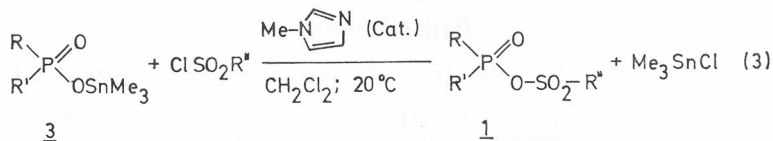
Satisfactory syntheses of phosphorus-sulfonic anhydrides **1** have been reported only recently<sup>8,9</sup>. From the point of view of the nucleotide and medicinal chemistry it has become interesting to explore the scope of previously described methods for the preparation of **1** and to discover new routes of potential applicability to the chemistry of reactive phosphorus compounds of biological interest<sup>10</sup>.

Our recent approach<sup>9</sup> to the synthesis of mixed anhydrides **1** was based on the phosphorus silyl and stannyl esters (reactions 1 and 2).



Both classes of phosphorus esters have been found to react with sulfonic anhydrides to yield mixed anhydrides *1* under mild conditions. The yield and purity of the reaction products were high. However, in the case of reaction 2, some inconvenient features arose related to the separation of sulfonic acid stannyl esters due to their low volatility.

In this communication we report a convenient procedure for the synthesis of phosphoric-sulfonic anhydrides *1* employing stannic phosphates and sulfonic acid chlorides (reaction 3). Trialkylstannyl phosphates are readily available and have been already employed for the synthesis of phosphate derivatives of biological interest<sup>11</sup>.



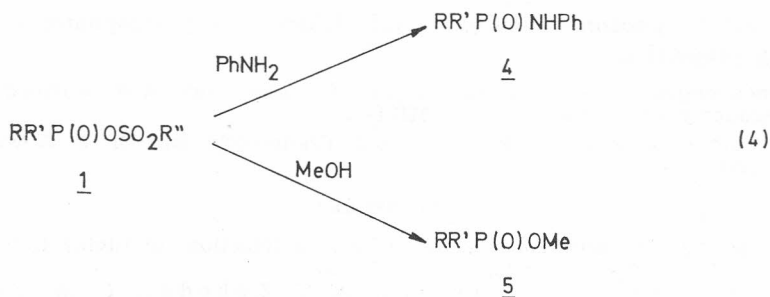
We have found that freshly prepared stannyl<sup>12</sup> phosphates react smoothly and stoichiometrically with sulphonic acid chlorides at ambient temperature in the presence of a catalytic amount of *N*-methylimidazole (Table I).

TABLE I

R	R'	R''	Yield	<sup>31</sup> P ppm
EtO	H	Me	100%	— 3.8
EtO	EtO	Me	100%	—13.1
EtO	EtO	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	100%	—14.1
PhO	PhO	Me	100%	—24.1
PhO	PhO	C <sub>6</sub> H <sub>5</sub>	100%	—25.0
PhO	PhO	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	100%	—25.0
PhO	PhO	2,3,5-tri-C <sub>3</sub> H <sub>7</sub> <sup>1</sup> -C <sub>6</sub> H <sub>2</sub>	100%	—26.0

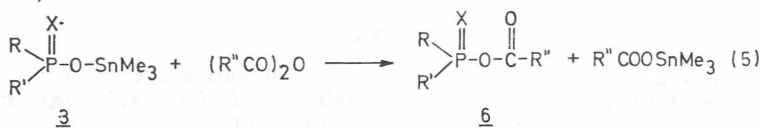
It is interesting to note that the analogous reaction of trimethylsilyl phosphates with sulfonic acid chlorides failed to give the desired anhydride *1* under conditions suitable for transformation of sensitive phosphates of biological interest.

The conversion of stannyl esters into anhydride *1* was monitored by <sup>31</sup>P NMR spectroscopy. In all cases the reaction was found to be completed in less than two hours. After removal of the solvent and trimethylstannyl chloride (b. p. 40 °C/0.15 mmHg) by evaporation in vacuo, the residue was almost pure anhydride *1* contaminated only by *N*-methylimidazole. The structure of anhydride *1* was additionally confirmed by the reaction with aniline and methanol (reaction 4).



The reaction products, anilide 4 and methyl ester 5, were identical with the authentic specimens.<sup>9</sup> The presented method of synthesis of anhydrides 1 seems to be applicable to all classes of sulfonic acid chlorides including those containing bulky groups attached to the sulfonic residue.

The following is the typical procedure: To a solution of sulfonic acid chloride (10 mmol) in dry  $\text{CH}_2\text{Cl}_2$ , 20 ml, a solution of *N*-methylimidazole (1 mmol) in dry  $\text{CH}_2\text{Cl}_2$  5 ml, was added at 15 °C. Then, to the resulting mixture, a solution of trimethylstannylphosphate (10 mmol) in dry  $\text{CH}_2\text{Cl}_2$  20 ml was added at room temperature. The reaction mixture was stirred for 1 h at r. t., then methylene chloride and trimethylstannylchloride and *N*-methylimidazole were removed by evaporation under reduced pressure (30 °C/0.01 Torr). The purity of the formed anhydrides 1 was estimated on the basis of <sup>31</sup>P NMR spectra. It was also proved that stannyl phosphates react smoothly with carboxylic acid anhydrides yielding dialkylacylphosphates (reaction 5).



This reaction is relevant to the method described by Hata et al.<sup>11</sup> in which acetyl phosphates were synthesized from stannyl phosphates and acetyl chloride.

The synthetic procedure and reaction conditions of the synthesis of dialkylacylphosphates correspond to those given for the synthesis of phosphorus-sulfonic anhydrides. The yields and purity of the reaction products were monitored by <sup>31</sup>P NMR spectroscopy (Table II).

TABLE II

R	R'	R''	X	Yield	<sup>31</sup> P NMR
EtO	EtO	CH <sub>3</sub>	O	100%	— 10.1
EtO	EtO	CF <sub>3</sub>	O	100%	— 9.8
EtO	EtO	CH <sub>3</sub>	S	100%	+ 58.0
EtO	EtO	CF <sub>3</sub>	S	100%	+ 56.0
Ph	But	CF <sub>3</sub>	S	100%	+111.8
Ph	But	CH <sub>3</sub>	S	100%	+100.3

In contrast to phosphorus-sulfonic anhydrides 1, acylphosphates 6 exhibit acylating properties.

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#### POVZETEK

**Reakcije stanilnih estrov fosforne kisline s kloridi sulfonskih kislin in anhidridi karboksilnih kislin. Nove sinteze anhidridov fosforne-sulfonske in fosforne-karboksilnih kislin**

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Opisan je nov način sinteze anhidridov fosforne-sulfonske kisline in acilfosfatov s pomočjo stanilfosfatov.