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New General Synthesis of Mixed Phosphorus and Sulfonic Acids Anhydrides *via* Reaction of Phosphorus Acids Bromides and Iodides with Silver Salts of Sulfonic Acids: A Route to P-Chiral Anhydrides

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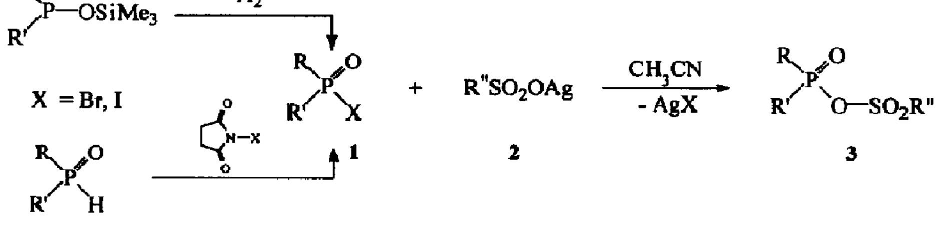
Abstract: Reaction of phosphorus acids bromides and iodides with silver salts of sulfonic acids leads to the formation of mixed phosphorus and sulfonic acids anhydrides3 in excellent yield. This method allowed the first synthesis of mixed anhydrides containing a P-chiral centre; they were subsequently separated into pure diastereoisomers.

Mixed anhydrides of phosphorus and sulfuric acids are of importance since the compounds such as adenosine-5'-phosphosulfate (APS) are known to take part in inorganic sulfur metabolism[1]. Mixed phosphorus and sulfonic acids anhydrides RR'P(O)OSO$_2$R" **3** are of interest as phosphorylating reagents and intermediates in biological oxidations of organothiophosphorus compounds. Our studies on the anhydrides **3** required us to find better methods of making them. Anhydrides **3** are normally prepared by the reaction of phosphorus acids azolides with sulfonic acids or their anhydrides.[2,3,4] They can be also prepared by the reaction of stannyl esters of phosphorus acids with sulfonic chlorides or anhydrides[5] and in special cases by the reaction of sulfonic acid azolides with phosphorus acids[2]. Although the azolides of phosphorus acids are relatively readily available, the pure anhydrous sulfonic acids and the sulfonic anhydrides require tedious preparative procedures.

In this communication we describe a new, general synthesis of mixed phosphorus and sulfonic acids anhydrides **3** by condensation of phosphorus acid bromides or iodides with sulfonic acids silver salts.



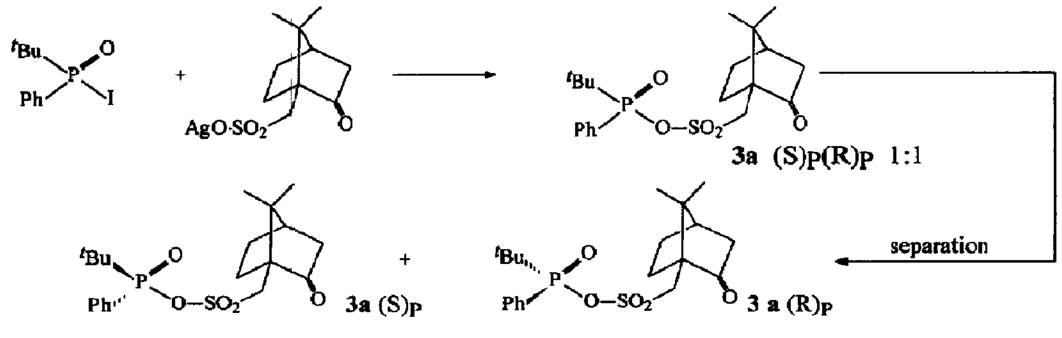
(1)

Table 1

	3a	3b	3c	3d	3e	3f	3g	3h
R	t-Bu	t-Bu	EtO	EtO	EtO	i-PrO	i-PrO	i-PrO
R'	Ph	Ph	EtO	EtO	EtO	i-PrO	i-PrO	i-PrO
R"	10-camphorsulfonyl	benzyl	p-tolyl	benzyl	2,4,6-trimethylphenyl	10-camphorsulfonyl	2,4,6-trimethylphenyl	ethyl

Phosphorus acids halides **1** are readily prepared by an Arbusov type reaction of the trimethylsilyl esters $RR'POSiMe_3$ with elemental halogens,[6] or by the reaction of hydrogen phosphonate type structures RR'P(O)H with N-halosuccinic imides.[7] Yield in these reactions are very high and the halides **1** can be used without further purification. In our experience, the presence of succinimide as side product does not interfere with the condensation reaction (1). Silver salts **2** are prepared from commercially available sulfonic acids.[8] Representative examples of anhydrides **3** are listed in Table 1. The reaction (1) proceeded smoothly and in very good yield. All the anhydrides **3** have chemical and spectroscopic properties consistent with the defined structure.[9] We noted that the reaction of chloroanhydrides **1** (X= Cl) with silver salts of sulfonic acids proceeds very slowly and leads to a spectrum of products. The failure of experiments with the chloroanhydrides **1** (X= Cl) seems to be connected with the strength of P^{IV}-Cl bond which is considerably higher than that of the corresponding bromo **1** (X= Br) and iodo **1** (X= I) anhydrides.

Particular advantages of the route (1) compared with previously described methods[2,3,4,5] are brevity, the mild conditions, procedure simplicity, ready availability of starting materials and the fact that there is built-in flexibility for the synthesis of the anhydrides **3** containing a P-chiral center and a chiral leaving group. Preparation of the P-chiral anhydride **3a** is exemplified in Scheme (2). The mixture of diastereoisomers **3a** was separated by chromatography on silica gel.



(2)

This new general synthesis of mixed phosphorus and sulfonic acid anhydrides is in our experience superior to those described earlier. In contrast to the chloroanhydrides **1** (X= Cl) their bromo **1** (X= Br) and iodo **1** (X= I) analogues were in past scarcely employed in synthetic procedures. These studies illustrate how they can be used advantageously.

Exemplified experimental procedures. *Protocol A*: (Synthesis of *tert*-butylphenylphosphinic 10-camphorsulfonic anhydride **3a**) To the stirred solution of 0.91 g (5 mM) of *tert*-butyl phenyl phosphine oxide in 5 mL of dry acetonitrile 1.12 g (5 mM) of N-iodosuccinimide in 5 mL of dry acetonitrile was added. After the reaction was completed the solution of 1.46 g (5.2 mM) of silver camphorsulfonate in 10 mL of dry acetonitrile was added. The reaction mixture was stirred overnight, evaporated to dryness and extracted with dry methylene chloride. Evaporation of extract leaves crude anhydride **3a** which was chromatographed on silica gel using carbon tetrachloride - diethyl ether (2:1) as eluent. Overall yield of separated products: 1.55g (75%). Isomer $(S)_P$ ('fast' $R_f = 0.3$ HR TLC CCl_4/Et_2O 1:2): mp. 119-120° C; $[\alpha]_D = +11.8$ ($c=12$ C_6H_6); $\delta^{31}P$ ($CDCl_3$): 56.98 ppm ; $\delta^{1}H$ ($CDCl_3$): 0.89 (s 3H), 1.05 (s 3H), 1.23 (d 9H $^3J_{HP} = 17.2$ Hz), 1.33-1.46 (m 1H), 1.65-1.74 (m 1H), 1.91-2.11 (m 3H), 2.33-2.44 (m 2H), 3.69 (AB 1H $^2J_{HH} = 10.6$ Hz), 3.93 (AB 1H $^2J_{HH} = 10.6$ Hz), 7.51-7.65 (m 3H), 7.83-7.90 (m 2H); $\delta^{13}C$ ($CDCl_3$):19.54 (d $^2J_{CP} = 6.83$ Hz), 23.58, 24.96, 26.78, 34.25 (d $^1J_{CP} = 93.6$ Hz), 42.34, 42.49, 47.94, 52.13, 58.21, 126.43 (d $^1J_{CP} = 116.76$ Hz), 128.34 (d $J_{CP} = 12.45$ Hz), 132.65 (d $J_{CP} = 10.16$ Hz), 133.08, 213.60; HR MS(CI): M+H 413.15394 (calculated for $C_{20}H_{30}O_5PS$: 413.155161). Isomer $(R)_P$ ('slow' $R_f = 0.26$ HR TLC CCl_4/Et_2O 1:2): mp. 140-142° C; $[\alpha]_D = -5.66$ ($c= 13$ C_6H_6); $\delta^{31}P$ ($CDCl_3$): 56.78 ppm ; $\delta^{1}H$ ($CDCl_3$): 0.9 (s 3H), 1.13 (s 3H), 1.22 (d 9H $^3J_{HP} = 17.3$ Hz), 1.38-1.46 (m 1H), 1.64-1.76 (m 1H), 1.90-2.12 (m 3H), 2.35-2.48 (m 2H), 3.54 (AB 1H $^1J_{HH} = 14.9$ Hz), 3.95 (AB 1H $^1J_{HH} = 14.9$ Hz), 7.49-7.65 (m 3H), 7.84-7.91 (m 2H); $\delta^{13}C$ ($CDCl_3$): 19.61 (d $^2J_{CP} = 7.62$ Hz), 23.74, 25.41, 26.68, 34.34 (d $^1J_{CP} = 92.39$ Hz), 42.28, 42.97, 47.70, 52.30, 58.32, 127.04 (d $^1J_{CP} = 114.25$ Hz), 128.34 (d $J_{CP} = 12.48$ Hz), 132.62 (d $J_{CP} = 9.94$ Hz), 133.04, 213.39; HR MS(CI): M+H 413.15406 (calculated for $C_{20}H_{30}O_5PS$: 413.155161). *Protocol B:* (Synthesis of O,O'-diethylphosphoric benzylsulfonic anhydride **3d**) To the stirred solution of 1.05 g (5 mM) of diethyl trimethylsilyl phosphite in dry methylene chloride the solution of an equivalent amount of bromine in dry methylene chloride was added at -60° C. The reaction mixture was allowed to warm up and evaporated to dryness avoiding heating. The residue was immediately dissolved in 10 mL of dry acetonitrile and was allowed to react with 1.45 g (5.2 mM) of silver benzylsulfonate according to protocol A. Anhydride **3d** was obtained as a colorless oil which did not need any purification in 95% yield (1.46 g,). $\delta^{31}P$ ($CDCl_3$): -12.5 ppm; $\delta^{1}H$ ($CDCl_3$): 1.27 (dt 6H $^4J_{HP} = 1.33$ Hz $^3J_{HH} = 7.09$ Hz), 4.09-4.27 (m 4H), 4.69 (s 2H), 7.25-7.50 (m 5H); $\delta^{13}C$ ($CDCl_3$): 15.76 (d $^3J_{CP} = 6.96$ Hz), 58.59, 66.27 (d $^2J_{CP} = 6.07$ Hz), 126.90, 128.88, 129.36, 130.90; HR MS(CI): M+H 309.0545 (calculated for $C_{11}H_{18}O_6PS$: 309.0562).

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8. Silver salts of sulfonic acids were prepared as follows: To the vigorously stirred suspension of 11 mM (2.3 g) of silver oxide in 10 mL of acetonitrile 5mM of sulfonic acid in 10 mL of acetonitrile was added dropwise. The reaction was complete within 10 min. Excess of silver oxide was filtered off and the solute evaporated to dryness. Solid silver salt was washed twice with 20 mL of methylene chloride, dried *in vaccuo* over phosphorus pentoxide and used directly in the reaction. Yields are quantitative.
9. **3b**: mp.: 87-88 °C; $\delta^{31}P$ ($CDCl_3$): 57.68; $\delta^{1}H$ ($CDCl_3$): 1.16 (d 9H $^3J_{HP}$= 17.32 Hz), 4.75 (s 2H), 7.21-7.85 (m 5H); $\delta^{13}C$ ($CDCl_3$): 23.81, 60.67, 126.9-133.19 (10 signals)
3c: oil; $\delta^{31}P$ ($CDCl_3$): -13.9; $\delta^{1}H$ ($CDCl_3$): 1.27 (dt 6H $^4J_{HP}$= 1.07 Hz $^3J_{HH}$= 7.21 Hz), 2.35 (s 3H), 4.08-4.31 (m 4H), 7.33 (d 1H $^3J_{HH}$=8.45 Hz), 7.85 (d 1H $^3J_{HH}$=8.45 Hz).; $\delta^{13}C$ ($CDCl_3$):15.60 (d $^3J_{CP}$= 6.46 Hz), 21.24, 66.48 (d $^2J_{CP}$= 8.07 Hz), 126.45, 129.15, 136.86, 143.01
3e: oil; $\delta^{31}P$ ($CDCl_3$): -12.9; $\delta^{1}H$ ($CDCl_3$): 1.28 (dt 6H $^4J_{HP}$= 1.29 Hz $^3J_{HH}$= 7.09 Hz), 2.28 (s 3H), 2.62 (s 6H), 4.06-4.29 (m 4H), 6.96 (s 2H); $\delta^{13}C$ ($CDCl_3$):15.66 (d $^3J_{CP}$= 3.28 Hz), 20.93, 22.39, 65.72 (d $^2J_{CP}$= 5.77 Hz), 131.68, 138.14, 139.9, 142.22
3f: oil; $\delta^{31}P$ ($CDCl_3$): -14.5; $\delta^{1}H$ ($CDCl_3$): 0.85 (s 1H), 1.07 (s 3H), 1.35 (d 12H $^3J_{HH}$= 6.16 Hz), 1.39-1.46 (m 1H), 1.64-1.73 (m 1H), 1.85-2.10 (m 3H), 2.29-2.42 (m 2H), 3.44 (AB 1H $^2J_{HH}$= 14.92 Hz), 3.84 (AB 1H $^2J_{HH}$= 14.92 Hz), 4.78 (dsept 2H $^3J_{HP}$= 6.96 Hz $^3J_{HH}$= 6.16 Hz); $\delta^{13}C$ ($CDCl_3$):19.57, 23.39 (d $^3J_{CP}$= 3.5 Hz), 24.95, 26.65, 42.24, 42.62, 48.99, 50.21, 57.98, 75.8 (d $^2J_{CP}$= 6.31 Hz), 213.41
3g: oil; $\delta^{31}P$ ($CDCl_3$): -14.9; $\delta^{1}H$ ($CDCl_3$): 1.29 (dd 12H $^4J_{HP}$= 0.5 Hz $^3J_{HH}$= 6.21 Hz), 2.29 (s 3H), 2.64 (s 6H), 4.71 (dsept 2H $^3J_{HP}$= 6.96 Hz $^3J_{HH}$= 6.21 Hz), 6.96 (s 2H); $\delta^{13}C$ ($CDCl_3$): 21.00, 22.50, 23.38 (d $^3J_{CP}$= 4.32 Hz), 75.45 (d $^2J_{CP}$= 7.17 Hz), 131.68, 139.97, 141.01, 144.07
3h: oil; $\delta^{31}P$ ($CDCl_3$): -14.7; $\delta^{1}H$ ($CDCl_3$): 1.37 (t 3H $^3J_{HH}$= 7,41 Hz), 1.38 (dd 12H $^4J_{HP}$= 0.8 Hz $^3J_{HH}$= 6.22 Hz), 3.46 (q 2H $^3J_{HH}$= 7,41 Hz), 4.83 (dsept 2H $^3J_{HP}$= 6.98 Hz $^3J_{HH}$= 6.22 Hz); $\delta^{13}C$ ($CDCl_3$): 7.96, 23.21 (d $^3J_{CP}$= 5.32 Hz), 47.65, 76.07 (d $^2J_{CP}$= 6.84 Hz)

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