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Synthesis of New Organophosphorus-Substituted Derivatives of Ethanesulfonic Acid

Andrey A. Prishchenko, Mikhail V. Livantsov, Olga P. Novikova, Ludmila I. Livantsova, and Valery S. Petrosyan

Department of Chemistry, M. V. Lomonosov Moscow State University, Moscow 119991, Russia

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ABSTRACT: *Nucleophilic addition of trimethylsilyl esters of hypophosphorus acid to trimethylsilyl ester and diethylamide of vinylsulfonic acid is proposed as convenient methods for the synthesis of new 2-sulfonylethylphosphonites and their derivatives under mild conditions. Also the new functionalized derivatives of these phosphonites, including aminomethyl fragments as well as certain properties of these compounds as important precursors of new organophosphorus-substituted derivatives of ethanesulfonic acid, are presented.* © 2008 Wiley Periodicals, Inc. Heteroatom Chem 19:470–473, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20448

INTRODUCTION

Organophosphorus analogues of amino acids containing carboxy and amino groups are of great interest as promising ligands and biologically active compounds [1–4]. Also sulfur-containing amino acids such as cysteine, cysteine sulfonic acid, and taurine are important biologically active substances [5]. Recently, we have found that the new organophosphorus-substituted derivatives of functionalized propionates and including fragments of indan, γ-butyrolactone, furan, pyridine, proline, and sarcosine were obtained in high yields via addition of trimethylsilyl esters of trivalent organophosphorus acids to trimethylsilyl acrylate and its various functionalized or cyclic analogues [6]. In the present work, the results of the nucleophilic addition of bis(trimethylsiloxy)phosphine and trimethylsilyl hypophosphite to trimethylsilyl ester and diethylamide of vinylsulfonic acid are reported. The obtained phosphonites were easily transformed to aminomethyl phosphinates using various methods of aminomethylation thoroughly investigated by us (cf. [7,8]). These reactions provide a convenient synthetic route to new organophosphorus-substituted derivatives of ethanesulfonic acid as promising biometrics of taurine (2-aminoethanesulfonic acid).

Correspondence to: Andrey A. Prishchenko; e-mail: aprishchenko@yandex.ru.

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RESULTS AND DISCUSSION

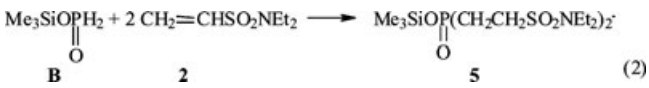
So in the present work, we showed that the reaction of bis(trimethylsiloxy)phosphine **A** also smoothly adds to trimethylsilyl vinylsulfonate **1** and *N*,*N*-diethylvinylsulfonamide **2** in methylene chloride at 5–10°C to form the corresponding phosphonites **3,4** in high yields (Eq. (1)).

$$\underset{\mathbf{A}}{(Me_3SiO)_2PH} + \underset{\mathbf{1,2}}{CH_2{=}CHSO_2X} \longrightarrow \underset{\mathbf{3,4}}{(Me_3SiO)_2PCH_2CH_2SO_2X} \quad (1)$$

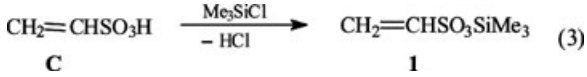
X = OSiMe$_3$ (**1,3**), NEt$_2$ (**2,4**)

It should be noted that this reaction also gives a by-product, phosphinate **5**, in 12% yield. Obviously, it arises from an in situ reaction of trimethylsilyl

hypophosphite **B** with two molecules of vinylsulfonamide **2** (Eq. (2)).

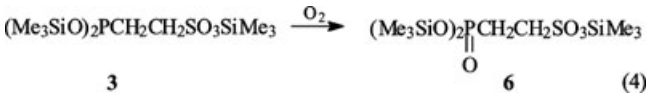


The new starting ester **1** was prepared in high yield by the reaction of the excess trimethylchlorosilane with vinylsulfonic acid **C** (Eq. (3), cf. [9]).

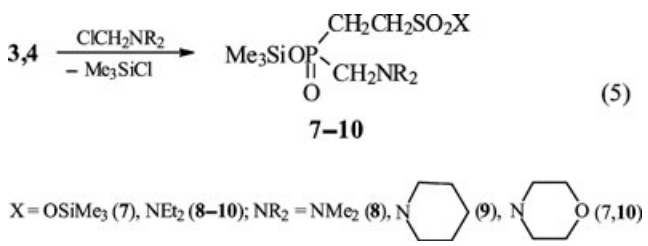


The synthesis of acid **C** and vinyl sulfonamide **2** was described previously [10,11].

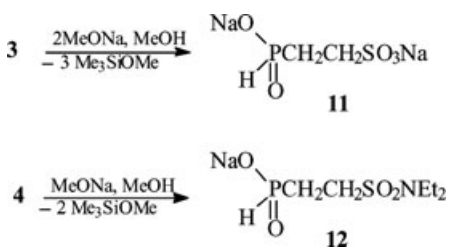
Phosphonites **3,4** are the convenient precursors for preparing various organophosphorus-substituted derivatives of ethanesulfonic acid. In particular, phosphonite **3** is readily oxidized with atmospheric oxygen to form phosphonate **6** in high yield (Eq. (4)).

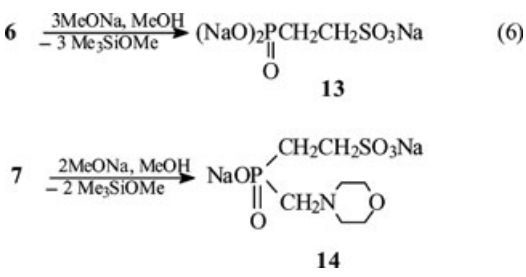


Phosphonites **3,4** readily react with chloromethyl amines under mild conditions to give aminomethyl-(2-sulfonylethyl)phosphinates **7–10** (Eq. (5)).



Treatment of **3,4,6,7** with dilute solutions of sodium methylate in methanol gives water-soluble sodium salts **11–14** as white hygroscopic crystals (Eq. (6)).





Also the trimethylsilyl groups of phosphinates **5,8–10** are easily removed with excess methanol to form free phosphinic acids **15–18**, which are of great interest as complexones, and biologically active compounds (Eq. (7)).

Synthesized acids **15–18** are white hygroscopic crystals (acid **16** is thick oil, see Table 1) and may be used as water-soluble ligands as well as biologically active compounds (cf. [3–5]). The elemental analysis data of some synthesized compounds are summarized in Table 2.

EXPERIMENTAL

The ^{1}H, ^{13}C, and ^{31}P NMR spectra were registered on the Varian VXR-400 and Bruker-Avance-400 spectrometers (400, 100, and 162 MHz, respectively) in $CDCl_3$ (**1–10**) or D_2O (**11–18**) against TMS (^{1}H, ^{13}C) and 85% H_3PO_4 in D_2O (^{31}P). All reactions were carried out under dry argon in anhydrous solvents.

*O-Trimethylsilyl vinylsulfonate(***1***).* A mixture of 32.4 g of vinylsulfonic acid was prepared according to the procedure of Athens and Dudley [10], and 110 g of trimethylchlorosilane was refluxed until the evolution of hydrogen chloride was complete, after which it was distilled to give 50.8 g (94%) of ester **1**, bp 70°C (1 mm), n_D^{20} 1.4355. ^{1}H NMR spectrum, δ, J, Hz: 5.47 and 6.00 m, *ABX* [$C^{1}H_AH_B$, $^{2}J(H_AH_B)$ 20, $^{3}J(H_AH_X)$ 10.4, $^{3}J(H_BH_X)$ 16.8], 6.34 dd [$C^{2}H_X$,

TABLE 1 Yields, Product Constants, and NMR spectral data for the $PC^1H_2C^2H_2S$ and PC^3H_2N fragments[a] (δ, ppm; J, Hz) of Compounds **3–18**[a]

No	*Yield (%)*	*Bp (°C) (p, mmHg) (mp, °C)*	*$\delta(C^1)$ d*	*$^1J_{PC}$*	*$\delta(C^2)$ s*	*$\delta(C^3)$ d*	*$^1J_{PC}$*	*$\delta(P)$ s[b]*
3	84	152 (2)	33.68	31.4	44.66[c]	–	–	149.60
4	78	162 (4)	33.31	30.8	44.16[c]	41.07[d]	–	151.07
5	12	265 (4)	24.88	92.9	45.15	41.92[d]	–	37.65
6	89	174 (2)	24.16	147.7	47.30	–	–	5.19
7	69	185 (1)	24.71	90.5	46.74	58.22	117.2	34.96
8	73	166 (1)	24.01	91.2	45.92	59.12	116.2	35.96
9	75	187 (1)	24.30	89.8	46.14	58.93	115.7	35.73
10	73	192 (1), (56)	24.19	90.0	45.97	58.37	115.2	35.06
11	98	[e]	27.08	86.5	44.25	–	–	23.08
12	97	[e]	26.26	85.7	44.08	40.98[d]	–	24.68
13	95	[e]	26.28	139.2	46.89	–	-	14.74
14	94	[e]	25.74	87.4	47.85	59.64	104.9	31.69
15	94	(113)	23.47	88.1	42.19	42.18[d]	–	38.99
16	93	oil	25.06	94.7	42.18	56.23	86.5	22.83
17	95	(97)	25.36	93.7	42.17	55.16	86.5	22.88
18	94	(133)	25.38	95.3	42.19	55.41	85.3	22.26

[a]All signals of alkyl, cycloalkyl, and trimethylsilyl groups are in the standard area. In the ^1H NMR spectra, the signals of protons of the methylene groups C^1H_2andC^2H_2 are multiplets in the ranges 1.3–2.2 and 2.6–3.2 ppm, respectively, which partially overlap with the signals of the protons of the PCH_2N and NCH_2 fragments. Fragments PH in ^1H NMR spectra, d, $^1J_{PH}$, **11**: 6.94, 518.2; **12**: 6.92, 522.1. n_D^{20} for compounds, **5**: 1.4810, **8**: 1.4670, **9**: 1.4775.
[b]Data of $^{31}P\{H\}$ spectra.
[c]d, $^2J_{PC}$: **3**, 8.6; **4**, 9.5.
[d]Fragments NCH_2, s.
[e]The salts **11–14** are very hygroscopic crystals; therefore, their melting points were not measured.

$^3J(H_AH_X)$ 10.4, $^3J(H_BH_X)$ 16.8], 0.18 s (Me_3Si). ^{13}C spectrum, δ_C, ppm: 126.47 s (C^1), 136.07 s (C^2), 0.18 s (CSi).

*O,O-Bis(trimethylsilyl)-2-(trimethylsiloxysulfonyl)ethylphosphonite (**3**).* To a solution of 42 g of bis(trimethylsiloxy)phosphine in 100 mL of diethyl ether, a solution of 18 g of **1** in 50 mL of diethyl ether was added dropwise with stirring at 5°C; the mixture was kept for 1 h at 20°C. The solvent was removed, and the residue was distilled in a vacuum to give 32.8 g of phosphonite **3**.

Phosphonite **4** was prepared similarly, but the high boiling fraction contained 1.8 g of phosphinate **5**.

*O,O-Bis(trimethylsilyl)-2-(trimethylsiloxysulfonyl)ethylphosphonate (**6**).* Dry air was slowly passed for 2 h at 10°C through a solution of 11.7 g of phosphonite **3** in 50 mL methylene chloride. The

TABLE 2 Elemental Analyses Data of Synthesized Compounds[a]

No	*Empirical Formula*	*Formula Weight*	*Calcd (%)*		*Found (%)*	
			C	*H*	*C*	*H*
5	$C_{15}H_{37}N_2O_6PS_2Si$	464.38	38.78	8.03	38.62	7.97
8	$C_{12}H_{31}N_2O_4PSSi$	358.67	40.20	8.71	40.03	8.59
9	$C_{15}H_{35}N_2O_4PSSi$	398.64	45.20	8.85	44.98	8.78
10	$C_{14}H_{33}N_2O_5PSSi$	400.72	41.98	8.30	41.81	8.12
11	$C_2H_5Na_2O_5PS$	218.08	11.01	2.31	10.94	2.39
12	$C_6H_{15}NNaO_4PS$	251.23	28.69	6.02	28.52	6.09
13	$C_2H_4Na_3O_6PS$	256.06	9.38	1.57	9.26	1.68
14	$C_7H_{14}Na_2O_6PS$	303.21	27.73	4.65	27.69	4.74
15	$C_{12}H_{29}N_2O_6PS_2$	392.35	36.72	7.45	36.65	7.31
16	$C_9H_{23}N_2O_4PS$	286.17	37.75	8.10	37.69	7.96
17	$C_{12}H_{27}N_2O_4PS$	326.26	44.16	8.34	43.90	8.23
18	$C_{11}H_{25}N_2O_5PS$	328.55	40.24	7.67	40.02	7.59

[a]The other compounds are unstable in the air atmosphere; therefore, these substances were analyzed as their sodium salts.

solvent was removed, and the residue was distilled under vacuum to obtain 10.8 g of phosphonate **6**.

*O-Trimethylsilyl N-morpholinomethyl-2-(trimethylsiloxysulfonyl)ethylphosphinate (**7**).* To a solution of 8 g of phosphonite **3** in 30 mL of methylene chloride, a solution of 2.8 g of *N*-(chloromethyl)-morpholine in 15 mL of methylene chloride was added dropwise with stirring at 10°C. The solvent was removed, and the residue was distilled to give 5.9 g of phosphinate **7**.

The phosphinates **8–10** were prepared similarly.

*Disodium 2-Sulfonylethylphosphonite (**11**).* To a solution of 2.5 g of sodium methylate in 30 mL of methanol, a solution of phosphonite **3** in 10 mL of diethyl ether was added with stirring at 10°C. The mixture was heated to reflux, the solvent was removed, and the residue was kept in a vacuum (1 mm) for 1 h to give 4.9 g of salt **11**.

The salts **12–14** were prepared similarly.

*Bis(2-diethylaminosulfonylethyl)phosphinic acid (**15**).* Methanol (10 mL), was added to a solution of 1.8 g of phosphinate **5** in 10 mL of methylene chloride. The mixture was refluxed for 0.5 h, the solvent was removed, and the residue was kept in a vacuum (1 mm) for 1 h to give 1.4 g of acid **15**.

The acids **16–18** were obtained analogously.

REFERENCES

[1] McKenna, C. E.; Kashemirov, B. A.; Li, Z.-M. Phosphorus Sulfur Silicon 1999, 144–146, 313–316.
[2] Esswein, A.; Bauss, F.; Muehlbauer, R.; Guenther, H.; Bosies, E. Phosphorus Sulfur Silicon 1999, 144–146, 13–16.
[3] Kukhar, V. P.; Hudson, H. R. Aminophosphonic and Aminophosphinic Acids. Chemistry and Biological Activity; Wiley: New York, 2000.
[4] Kolodiazhnyi, O. I. Usp Khim 2006, 75, 254–282 (in Russian).
[5] Dawson, R. M. C.; Elliot, D. C.; Elliot, W. H.; Jones, K. M. Data for Biochemical Research; Clarendon Press: Oxford, UK, 1986.
[6] Prishchenko, A. A.; Livantsov, M. V.; Novikova, O. P.; Livantsova, L. I.; Petrosyan, V. S. Heteroatom Chem 2008, 19, 418–428.
[7] Prishchenko, A. A.; Livantsov, M. V.; Novikova, O. P.; Livantsova, L. I.; Petrosyan, V. S. Heteroatom Chem 2008, 19, 345–351.
[8] Prishchenko, A. A.; Livantsov, M. V.; Petrosyan, V. S. Zh Obsh Khim 1994, 64, 1316–1330 (in Russian).
[9] Hergott, H. H.; Siminen, O. Synthesis 1980, 626.
[10] Athens, J. A.; Dudley, J. R. U.S. Patent 2597696, 1952; Chem Abstr 1953, 47, 2196a.
[11] Petrov, K. A.; Neymysheva, A. A. Zh Obsh Khim 1959, 29, 1494 (in Russian).