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Synthesis of 2-(Thiophen-3-yl)vinylphosphonic Acid

Irma Linzaga-Elizalde,[1] Jaime Escalante,[1] María E. Nicho,[2] and Marisol Güizado-Rodríguez[2]

[1]Chemical Research Center, Morelos Autonomous State University, Morelos, Mexico

[2]Center of Research in Engineering and Applied Sciences, Morelos Autonomous State University, Morelos, Mexico

Abstract: A simple and efficient synthesis of 2-(thiophen-3-yl)vinylphosphonic acid has been developed. The title compound is obtained in 70% yield by addition of thiophene-3-carbaldehyde to lithium diethyl methylenephosphonate, followed by dehydration and hydrolysis. ^{1}H, ^{13}C, and ^{31}P NMR spectra are presented for each of the intermediates.

Keywords: Diethyl methylphosphonate, 2-(thiophen-3-yl)vinylphosphonic acid, thiophene-3-carbaldehyde

INTRODUCTION

There is a wide spectrum of applications for phosphonic acids, and because of their physical characteristics, they can be applied in polymer manufacture,[1] in the paper industry as additives,[2] as anticorrosion products,[3,4] as fire retardants, and as dental adhesives.[5] Polythiophenes have attracted attention as a result of their good electrical conductivities,[6] easy processability, high environmental stability, and amenity to a wide range of potential technological applications.[7] For these reasons,

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Address correspondence to Irma Linzaga-Elizalde, Centro de Investigaciones Químicas, Universidad Autónoma del Estado de Morelos, Av. Universidad 1001, Col. Chamilpa, C.P. 62209 Cuernavaca, Morelos, México. E-mail: linzaga@ciq.uaem.mx

we decided to develop a convenient methodology for the preparation of the thiophene derivative of phosphonic acid.

DISCUSSION

The addition reaction of thiophene-3-carbaldehyde to lithium diethyl methylenephosphonate,[8] which has been generated from *n*-BuLi and diethyl methylphosphonate under anhydrous conditions, affords the diethyl 2-hydroxy-2-(thiophen-3-yl)ethylphosphonate **1**, purified by column chromatography, in good yield.

The dehydration of phosphonate **1** was achieved by heating it to 90–100 °C in 3 N HCl in a sealed tube to afford the expected α,β,-unsaturated phosphonate compound **2** in good yield.

The final step of the conversion of thiophene-3-carbaldehyde to 2-(thiophen-3-yl)vinylphosphonic acid **3** was achieved by stirring a solution of **2** in bromotrimethylsilane at room temperature for 16 h, according to the method reported by Yuan et al.[9]

In conclusion, in this study we have prepared 2-(thiophen-3-yl)vinylphosphonic acid in good yield starting from diethyl methylphosphonate and thiophene-3-carbaldehyde.

EXPERIMENTAL

The diethyl methyl phosphonate was prepared according to a Michaelis–Arbuzov reaction.[10] Thiophene-3-carbaldehyde was purchased from Aldrich. Tetrahydrofuran was distilled from sodium/benzophenone ketyl prior to use. The melting points are uncorrected. The compounds were characterized by ^{1}H NMR (200 MHz), ^{13}C NMR (50 MHz), and ^{31}P NMR (80.98 MHz) spectroscopy. Mass spectrometry (MS) and high-resolution mass spectrometry (HRMS) were performed using the fast atom bombardment (FAB^{+}) mass spectra technique. The thiophene-3-carbaldehyde was distilled before use.

Diethyl Methylphosphonate

A mixture of triethyl phosphite (5.0 g, 30 mmol) and methyl iodide (4.69 g, 33 mmol) was refluxed for 5 h. Ethyl iodide was eliminated by distillation. Then, the diethyl methylphosphonate was distilled in a Kugel–Rohr apparatus, bp 55°C/2 mm Hg (54°C/1.5 mm Hg),[10b] 3.7 g, yield 80%.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.33 (t, $J = 7.2$ Hz, 6H), 1.47 (d, $J = 17.6$ Hz, 3H), 4.09 (m, 4H).

Diethyl 2-Hydroxy-2-(thiophen-3-yl)ethylphosphonate (1)

Diethyl methylphosphonate (3.12 g, 20 mmol) in anhydrous tetrahydrofuran (100 mL), was placed in a round-bottom flask, and a solution of *n*-buthyllithium (2.5 M in *n*-hexane, 9 mL, 22 mmol) was added at −78°C under a nitrogen atmosphere. After stirring the solution at this temperature for 20 min, thiophene-3-carbaldehyde (2.56 g, 22 mmol) was added. The mixture was stirred at −78°C for 45 min and then at room temperature for 20 min. A saturated solution of ammonium chloride was added, and the mixture was extracted with dichloromethane (3×50 mL). The combined organic phases were dried over anhydrous sodium sulfate and evaporated, and the residue was purified by column chromatography on silica gel using *n*-hexane–ethyl acetate (80:20→10:90) as eluent to give the product as a colorless oil (4.35 g, 83% yield).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.27 (t, $J = 7.0$ Hz, 3H), 1.30 (t, $J = 7.0$ Hz, 3H), 2.23 (m, 2H), 4.05 (m, 4H), 4.43 (s, OH), 5.17 (ddd, $J = 5.6$ Hz, 7.3, 12.3 Hz, 1H), 7.15 (m, 3H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 16.6 (d, $^3J_{CP} = 3.0$ Hz), 16.7 (d, $^3J_{CP} = 3.0$ Hz), 35.3 (d, $^1J_{CP} = 136.0$ Hz), 62.1 (d, $^2J_{CP} = 9.4$ Hz), 62.3 (d, $^2J_{CP} = 6.1$ Hz), 65.4 (d, $^2J_{CP} = 4.5$ Hz), 120.9, 125.5, 126.3, 145.0 (d, $^3J_{CP} = 15.9$ Hz). ^{31}P NMR ($CDCl_3$, 80.98 MHz): δ 29.9. EM: m/z: 264 (69%), 152 (71%), 125 (100%), 111 (30%), 97 (61%), 84 (8%). HRMS calcd for $C_{10}H_{17}O_4PS$:264.0585; found:264.0550.

Diethyl 2-(Thiophen-3-yl)vinylphosphonate (2)

A suspension of diethyl 2-hydroxy-2-(thiophen-3-yl)ethylphosphonate **1** (0.70 g, 2.65 mmol) in 10 mL of 3N HCl was heated in a sealed tube to 90–100°C for 1.5 h. The solution was then allowed to cool to ambient temperature and evaporated at reduced pressure to afford the crude product, which was purified by column chromatography on silica gel using *n*-hexane–ethyl acetate (80:20 → 0:100) as eluent to afford the product as a colorless oil (0.60 g, 91% yield).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.31 (t, $J = 7.1$ Hz, 6H), 4.08 (m, 4H), 6.01 (dd, $J = 17.8$ Hz, $^2J_{HP} = 35.6$ Hz, 1H), 7.39 (m, 4H), 7.46 (dd masked, $J = 17.6$ Hz, $^3J_{HP} = 22.8$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 16.6 (d, $^3J_{CP} = 6.45$ Hz), 61.9 (d, $^2J_{CP} = 5.3$ Hz), 113.2 (d, $^1J_{CP} = 190.95$ Hz),

124.9, 127.0, 127.7, 138.0, 138.5, 142.4 (d, $^{3}J_{CP} = 6.8$ Hz). ^{31}P NMR ($CDCl_3$, 80.98 MHz): δ 20.9. EM: m/z 246 (43%), 190 (23%), 173 (36%), 155 (44%), 137 (100%), 108 (5%), 97 (30%), 83 (8%), 82 (21%). HRMS calcd for $C_{10}H_{15}O_3PS$:246.0480; found:246.0501.

2-(Thiophen-3-yl)vinylphosphonic Acid (3)

In a round-bottom flask, trimethylsilylbromide (0.61 g, 0.52 mL, 4 mmol) was added to a cold solution of diethyl 2-(thiophen-3-yl)vinylphosphonate **2** (0.5 g, 2 mmol) in anhydrous dichlorometane. After stirring the mixture at room temperature for 16 h, the solvent was removed under reduced pressure, and water (5 mL) was added to the residue. The solid obtained was washed with *n*-hexane and ethyl acetate and then recrystallized from methanol–ethyl acetate (1:3) (mp = 149–151°C, (0.27 g, 70% yield).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.26 (dd, $J = 17.8$ Hz, $^{2}J_{HP} = 35.6$ Hz), 7.26 (br s, 1H), 7.40 (m, 3H), 7.60 (br s, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 117.8 (d, $^{1}J_{CP} = 186.8$ Hz), 126.0, 128.0, 128.2, 139.9, 140.5 (d, $^{3}J_{CP} = 6.1$ Hz). ^{31}P NMR ($CDCl_3$, 80.98 MHz): δ 18.0. EM: m/z 192 (14%), 191 (23%), 190 (22%), 111 (79%), 110 (100%), 109 (56%), 84 (21%), 81 (9%). HRMS calcd. for $C_6H_7O_3PS$:189.9854; found:189.9815.

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