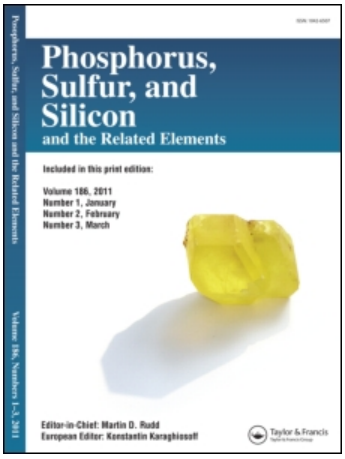

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Simple Method for the Preparation of Dialkyl (2,3-Dihydro-1,3-thiazol-2-YL)-phosphonates

Karolina Janikowska[a]; Sławomir Makowiec[a]
[a] Department of Organic Chemistry, Faculty of Chemistry, Gdansk University of Technology, Gdańsk, Poland

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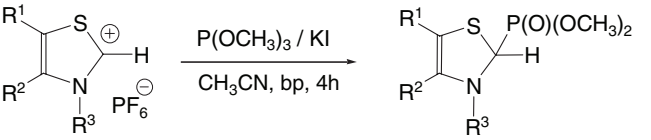
SIMPLE METHOD FOR THE PREPARATION OF DIALKYL (2,3-DIHYDRO-1,3-THIAZOL-2-YL)-PHOSPHONATES

Karolina Janikowska and Sławomir Makowiec
Department of Organic Chemistry, Faculty of Chemistry, Gdansk University of Technology, Gdańsk, Poland

GRAPHICAL ABSTRACT



Abstract *A simple synthesis of dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates from thiazolium salts and trialkyl phosphites is described. The series of dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates with various substituents in positions 3, 4, and 5 of the thiazole ring were prepared. However, only phosphonates with an aryl on the nitrogen atom were stable enough for chromatographic purification, although all the new phosphonates are very sensitive to oxidation. We made efforts to apply dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates in a Horner–Wadsworth–Emmons reaction, but the generated antiaromatic anion of phosphonate decomposed quickly, even at −70°C.*

Keywords Dithiadiazafulvalenes; organic metals; phosphonates

INTRODUCTION

The tetraheterofulvalenes belong to a class compounds that are in the circle of interest of many laboratories, from physics to organic chemistry. Their popularity is due to the great variety of applications of these compounds.

Most of the applications of tetraheterofulvalenes are as a result of their high electron-donating properties; this group of compounds is usually an integral part of synthetic metals,[1] semiconductors, and other advanced materials.[2] The majority of applied tetraheterofulvalenes contain four sulfur atoms or sulfur and selenium atoms due to their availability, relative oxidation stability, and easy modification in side chain, and also due to the possibility of preparing unsymmetrical tetrathiafulvalenes (TTF).[3]

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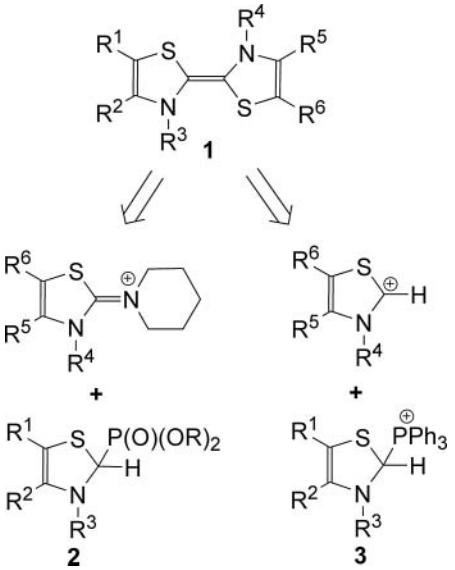
Address correspondence to Dr. Sławomir Makowiec, Department of Organic Chemistry, Faculty of Chemistry, Gdansk University of Technology, Narutowicza 11/12, Gdańsk 80-952, Poland. E-mail: mak@chem.pg.gda.pl

The Horner–Wadsworth–Emmons reaction is successfully used for the preparation of unsymmetrical tetrathiafulvalenes with high selectivity.[4–7] The Wittig reaction may also be used for the preparation of unsymmetrical tetrathiafulvalenes, however, with lower selectivity.[8–10] The aforementioned methods use 1,3-dithio-2-yl phosphonates esters or 1,3-dithio-2-yl phosphonium salts, respectively, as key intermediates.

However in recent years, there has been an interest in dithiadiazafulvalenes (DTDAFs)[11] as donor materials, but research in this area is limited due to the low stability of DTDAFs and the lack of methods for modification of already prepared DTDAFs, as well as a lack of a method for selective preparation of unsymmetrical dithiadiazafulvalenes.[12]

It is not difficult to deduce the hypothesis that unsymmetrical dithiadiazafulvalenes **1** could be prepared by the route similar to the strategy used for the preparation of unsymmetrical TTF[4–10] (Scheme 1) by the coupling of dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates **2** and 2-piperidin-1,3-thiazolium salts or (2,3-dihydro-1,3-thiazol-2-yl)-phosphonium salts **3** and 1,3-thiazolium salts.



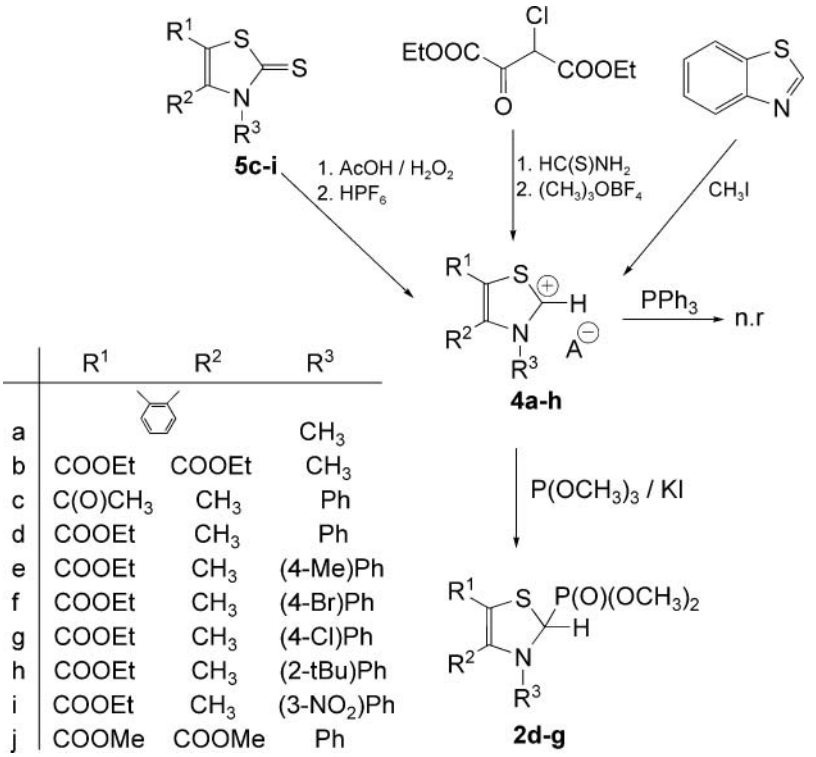
Scheme 1 Possible routes of synthesis of unsymmetrical dithiadiazafulvalenes.

However it must be pointed out that required key intermediates dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates **2** or (2,3-dihydro-1,3-thiazol-2-yl)-phosphonium salts **3** are not common compounds, with only three examples of these phosphonates described in the chemical literature. The first was published in 1967; Razumow et al.[13] prepared (2,3-dihydro-benzothiazol-2-yl)-phosphonate in the reaction of *o*-aminothiophenol with dialkyl (dimethoxy)methylphosphonate. Takamizawa et al. obtained a phosphonate derivative of thiamine[14] in a multistep reaction. One example of (3-methyl-2,3-dihydro-benzothiazol-2-yl)-phosphonate was also prepared in the cleavage of bis(3-methylthiazolidyn-2-ylidene) with diethyl phosphite.[15]

Therefore we made an attempt to find an easy and efficient method for the preparation of dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates **2**.

RESULTS AND DISCUSSION

It is well known that dithiadiazafulvalenes are very susceptible to oxidation by air oxygen.[11] Therefore, for our research, we needed models of thiazolium salts and phosphonates with an electron-withdrawing group to ensure the stability of possible unsymmetrical DTDAF.[12e] 3H-Thiazole-2-thiones **5** with one electron-withdrawing group were prepared from ethyl 2-chloroacetylacetate or 3-chloroacetylacetone and dithiocarbamate salts. They were subsequently oxidized to thiazolium salts **4**, based on adopted literature methods[16] (Scheme 2). 3-Phenyl-4,5-dimethoxycarbonyl-3H-thiazole-2-thione **5j** was prepared by the cycloaddition of 2-phenylimino-1,3-dithiolane with dimethyl acetylenedicarboxylate.[12e] We also attempted to obtain 3-methyl-4,5-diethoxycarbonyl-1,3-thiazolium tetrafluoroborate **4b** in a very inefficient process of condensation of 3-chloro-2-oxo-butanedioic acid with thioformamide followed by alkylation with trimethyloxonium tetrafluoroborate (Scheme 2).



	R^1	R^2	R^3
a			CH_3
b	COOEt	COOEt	CH_3
c	$C(O)CH_3$	CH_3	Ph
d	COOEt	CH_3	Ph
e	COOEt	CH_3	(4-Me)Ph
f	COOEt	CH_3	(4-Br)Ph
g	COOEt	CH_3	(4-Cl)Ph
h	COOEt	CH_3	(2-tBu)Ph
i	COOEt	CH_3	(3-NO_2)Ph
j	COOMe	COOMe	Ph

Scheme 2 Synthesis of dialkyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates.

The first experiments were performed by treating a solution of **4b** in acetonitrile with trimethyl phosphite in the presence of potassium iodide (Scheme 2). Even though we observed the formation of the new compound, any attempts to isolate it failed, as the compounds decompose during chromatography. Next we tried to obtain (3-methyl-2,3-dihydro-benzothiazol-2-yl)-phosphonate **2a** from easily available N-methyl benzothiazolium iodide[19] and trimethyl phosphite; we again observed the formation of a new product, which decomposed during chromatography isolation.

It should be pointed out that Kucukbay et al.[15] had prepared **2a** from bis(3-methylthiazolidyn-2-ylidene).[17]

We therefore repeated the experiment as described in the literature[15] and compared this reaction mixture with the crude reaction mixture composed of N-methyl benzothiazolium iodide and trimethyl phosphite in the ^{31}P NMR experiment. We observed a signal at 17,32 ppm, which increased after addition of an authentic sample.

The failure of the first experiments and the fact that 1,3-dithio-2-yl phosphonates[4–7] and 1,3,4-thiadiazol-2-yl phosphonate[18] are stable and easily isolable led us to the supposition that the instability may be related to the higher electron-donating properties of nitrogen.

In the next experiments, we used a series of thiazolium salts with aryl on nitrogen atom and ethoxycarbonyl, or acetyl in the 5 position of the ring. Reactions of thiazolium salts with trimethyl phosphite in the presence of potassium iodide allowed us to produce the desired phosphonates, which were stable enough in the cases of **2d–g** for chromatography purification under argon. However, we observed that any contact of the sample with air, for example, during preparation of the NMR sample caused rapid decomposition of the purified product to a complicated mixture of compounds. As we could only measure ^{13}C and ^{1}H NMR spectra, our attempts to obtain good elemental analysis failed.

Surprisingly, in the case of salt **4c** with an acetyl group, the obtained phosphonate **2c** was not stable enough to isolate as a clean product. On the other hand, the instability of phosphonate **2h**, having the bulky 2-tert-butylphenyl group, seems to confirm our supposition that electron-donating properties of nitrogen have an influence on the stability of (2,3-dihydro-1,3-thiazol-2-yl)-phosphonates.

In order to increase the stability of the produced phosphonates, we tried to obtain a model with two electron-withdrawing groups at positions 4 and 5. Unfortunately 3-phenyl-4,5-dimethoxycarbonyl-3H-thiazole-2-thione **5j** was completely resistant to oxidation, and we were not able to prepare thiazolium salt in this manner. We also tried to introduce a 3-nitrophenyl substitutent on a nitrogen atom to enhance the stability of the prepared phosphonate, but the obtained thione **5i** was also resistant to oxidation to the thiazolium salt.

As we indicate in our hypothesis, an alternative way to synthesize unsymmetrical DTDAF can be led through (2,3-dihydro-1,3-thiazol-2-yl)-phosphonium salts. However, we observed that thiazolium salts do not react with triphenylphosphine. From the reaction mixtures of 3-methyl-4,5-diethoxycarbonyl-1,3-thiazolium tetrafluoroborate or 3-phenyl-4-methyl-5-ethoxycarbonyl-1,3-thiazolium hexafluorphosphate with triphenylphosphine in boiling acetonitrile, after 3 hours we recovered quantitatively unreacted substrates (Scheme 2).

Despite the fact that only part of the prepared phosphonates showed moderate stability, we tried to perform Horner–Wadsworth–Emmons reactions between the prepared phosphonate and benzaldehyde as the simplest model. We treated freshly prepared and purified **2d** in the THF with tBuOK or LDA at $-70^{\circ}C$ followed by the addition of benzaldehyde. We obtained a complex mixture of products; we therefore tried another experiment where we generated the anion from **2d** at $-70^{\circ}C$ with LDA, and after 0.5 hours quenched it with D_2O. Surprisingly we did not recover deutered starting material, but instead again obtained a complex mixture of products. These results suggest that the antiaromatic anion of the phosphonate decomposes after generation, similar to the decomposition of 1,3-dithiol-2-yl-phophonate anion observed by Fourmigue et al.[4]

EXPERIMENTAL

Reagents were purchased from Sigma-Aldrich. Acetonitrile was distilled from CaH_2 under argon. Analytical TLC was performed on aluminum sheets of silica gel UV-254 from Merck. Flash chromatography was carried out using 40–63 microns silica gel from Zeochem. The ^{1}H, ^{13}C, and ^{31}P spectra were recorded on a Varian Gemini 200 and a Varian Unity Plus 500.

Commercially unavailable reagents were prepared by the procedures in the literature as follows: bis(3-methylthiazolidyn-2-ylidene),[17] N-methyl benzothiazolium iodide **4a**,[19] 2-phenylimino-1,3-dithiolane,[20] and 3-phenyl-4,5-dimethoxycarbonyl-1,3-thiazol-2(3H)-thion **5j**.[12e]

4,5-Diethoxycarbonyl-1,3-thiazol

To the cooled to $-10^{\circ}C$ suspension of diethyl oxalacetate sodium salt (10.5 g, 50 mmol) in dry ether (100 mL), SO_2Cl_2 (7.42 g, 55 mmol) was added over 0.5 h. Then, the reaction was stirred for 3 h, filtered, and solvent was removed under reduced pressure. The residue was dissolved in EtOH (100 mL), cooled to $-10^{\circ}C$, and a suspension of $HC(S)NH_2$ in EtOH (100 mL) that was freshly prepared from $HC(O)NH_2$ (4.5 g, 100 mmol) and P_2S_5 (4.44 g, 20 mmol) was added dropwise. The reaction was stirred 24 h at rt. EtOH was removed under reduced pressure, and the oil was dissolved in 100 mL of AcOEt, washed off with 1 M NaOH (3×25 mL), and dried with $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel using CH_2Cl_2 as eluent.

Oily liquid. Yield: 1.61 g, 14%, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.86 (s, 1H), 4.47 (q, 2H, $J = 7.32$ Hz), 4.40 (q, 2H, $J = 7.32$ Hz), 1.43 (t, 3H, $J = 7.32$ Hz), 1.39 (t, 2H, $J = 7.32$ Hz).

3-Methyl-4,5-diethoxycarbonyl-1,3-thiazolium Tetrafluoroborate 4b

4,5-Diethoxycarbonyl-1,3-thiazol (1.6 g, 7 mmol) was dissolved in CH_2Cl_2, and trimethyloxonium tetrafluoroborate (1.47 g, 10 mmol) was added. The solution was stirred for 24 h. Methanol (1 mL) was added, the solvent was removed under reduced pressure, and the residue was crystallized from CH_2Cl_2/Et_2O.

White solid. Yield: 1.85 g, 79%, mp: 110–111°C, ^{1}H NMR (500 MHz, acetone-d_6) δ: 10.38 (s, 1H), 4.61 (q, 2H, $J = 7.3$ Hz), 4.51 (q, 2H, $J = 6.8$ Hz), 4.49 (s, 2H), 1.43 (m, 6H) ^{13}C NMR (125 MHz, acetone-d_6) δ: 164.0, 157.5, 157.1, 141.7, 134.2, 64.7, 64.2, 42.5, 13.5, 13.3.

General Procedure for the Preparation of 3H-Thiazole-2-thiones 5c–i

3H-Thiazole-2-thiones **5c–i** were obtained by the adopted method described in literature for analogous compounds.[16] To a solution of derivative of aniline (100 mmol) in DMSO (50 mL), 20 M NaOH (5 mL) was added. The mixture was cooled to 0°C, and CS_2 (100 mmol, 7.61 g, 6 mL) was added. The reaction was stirred for 1 h at rt, cooled again to 0°C, and ethyl 2-chloroacetylacetate (100 mmol, 16.45 g), or in the case of **5c**, 3-chloroacetylacetone (100 mmol, 13.45 g), was added. The reaction mixture was stirred for an additional 1 h at rt, and ice (100 g) was added. The solidified product was filtered,

suspended in EtOH (100 mL), treated with conc. HCl (5 mL), and heated to reflux for 1 h. After cooling to rt, the crude precipitated product was filtered and crystallized from EtOH.

3-Phenyl-4-methyl-5-acetyl-3H-thiazole-2-thione 5c. Yellow solid. Yield: 13.44 g, 54%, mp: 171–174°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.62–7.54 (m, 3H), 7.28–7.23 (m, 2H), 2.43 (s, 3H), 2.33 (s, 3H) ^{13}C NMR (125 MHz, $CDCl_3$) δ: 189.7, 188.5, 147.6, 137.4, 130.5, 130.4, 128.4, 121.3, 30.6, 16.5.

3-Phenyl-4-methyl-5-ethoxycarbonyl-3H-thiazole-2-thione 5d. White solid. Yield: 20.64 g, 74%, mp: 158–160°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.61–7.54 (m, 3H), 7.28–7.23 (m, 2H), 4.34 (q, 2H, $J = 7.3$ Hz), 2.34 (s, 3H, Me), 1.37 (t, 3H, $J = 7.3$ Hz) ^{13}C NMR (125 MHz, $CDCl_3$) δ: 190.7, 160.4, 148.8, 137.6, 130.4, 130.3, 128.4, 112.6, 61.9, 15.8, 14.5.

3-(4-Methylphenyl)-4-methyl-5-ethoxycarbonyl-3H-thiazole-2-thione 5e. White solid. Yield: 19.04 g, 65%, mp: 143–145°C, ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.37 (d, 2H, $J = 8.4$ Hz), 7.10 (d, 2H, $J = 8.4$ Hz), 4.32 (q, 2H, $J = 7.2$ Hz), 2.44 (s, 3H), 2.32 (s, 3H), 1.36 (t, 3H, $J = 7.2$ Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 190.8, 160.4, 148.9, 140.6, 134.9, 131.1, 128.1, 112.5, 61.9, 21.7, 15.8, 14.5.

3-(4-Bromophenyl)-4-methyl-5-ethoxycarbonyl-3H-thiazole-2-thione 5f. White solid. Yield: 22.19 g, 62%, mp: 145–148°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.72 (d, 2H, $J = 8.3$ Hz), 7.14 (d, 2H, $J = 8.3$ Hz), 4.33 (q, 2H, $J = 6.8$ Hz), 2.34 (s, 3H), 1.37 (t, 3H, $J = 6.8$ Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 190.2, 159.9, 147.9, 136.1, 133.4, 129.8, 124.3, 112.6, 61.6, 15.4, 14.2.

3-(4-Chlorophenyl)-4-methyl-5-ethoxycarbonyl-3H-thiazole-2-thione 5g. White solid. Yield: 19.43 g, 62%, mp: 136–138°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.57 (d, 2H, $J = 8.3$ Hz), 7.20 (d, 2H, $J = 8.3$ Hz), 4.34 (q, 2H, $J = 7.3$ Hz), 2.34 (s, 3H), 1.37 (t, 3H, $J = 7.3$ Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 190.6, 160.2, 148.3, 136.5, 135.9, 130.8, 129.9, 112.9, 62.0, 15.8, 14.5.

3-(2-Tert-butylphenyl)-4-methyl-5-ethoxycarbonyl-3H-thiazole-2-thione 5h. White solid. Yield: 8.71 g, 26%, mp: 107–109°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.70 (d, 1H, $J = 8.3$ Hz), 7.50 (t, 1H, $J = 7.3$ Hz), 7.36 (t, 1H, $J = 7.3$ Hz), 6.88 (d, 1H, $J = 8.3$ Hz), 4.33 (q, 2H, $J = 7.3$ Hz), 2.32 (s, 3H), 1.39 (t, 3H, $J = 7.3$ Hz), 1.30 (s, 9H), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 191.2, 160.48, 149.6, 147.4, 134.4, 131.4, 130.5, 130.4, 128.0, 112.6, 61.9, 36.7, 32.0, 16.3, 14.5.

3-(3-Nitrophenyl)-4-methyl-5-ethoxycarbonyl-3H-thiazole-2-thione 5i. White solid. Yield: 11.98 g, 37%, mp: 175–177°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.44 (dd, 1H, $J = 8.3$ Hz, $J = 1.5$ Hz), 8.17 (t, 1H, $J = 1.5$ Hz), 7.83 (t, 1H, $J = 7.3$ Hz), 7.64 (dd, 1H, $J = 8.3$ Hz, $J = 1.5$ Hz), 4.36 (q, 2H, $J = 7.3$ Hz), 2.38 (s, 3H), 1.39 (t, 3H, $J = 7.3$ Hz).

General Procedure for the Preparation of 1,3-Thiazolium Hexafluorophosphates 4c–h

1,3-Thiazolium hexafluorophosphates **4c–h** were obtained by the adopted method described in literature for analogous compounds.[16] Compounds **5c–h** (2 mmol) were dissolved in acetic acid (5 mL), and 30% H_2O_2 (0.67 mL) was added. The solution was stirred at rt for 1 h for **4c–e** or 2.5 h for **4f–g**. Acetic acid was removed under reduced pressure. To the oily residue, 60% HPF_6 solution in water (0.29 mL) and water (20 mL) were added. The precipitate was filtered, washed with water, dissolved in CH_2Cl_2, and dried with $MgSO_4$.

The solvent was removed under reduced pressure, and the residue was crystallized from CH_2Cl_2/Et_2O.

3-Phenyl-4-methyl-5-acetyl-1,3-thiazolium hexafluorophosphate 4c. White solid. Yield: 0.465 g, 64%, mp: 87–90°C, ^{1}H NMR (500 MHz, acetone-d_6) δ: 10.49 (s, 1H), 7.85- 7.81 (m, 5H), 2.84 (s, 3H), 2.76 (s, 3H), ^{13}C NMR (125 MHz, acetone-d_6) δ = 189.3, 161.5, 150.6, 136.9, 136.7, 132.3, 130.7, 126.7, 29.7, 14.2.

3-Phenyl-4-methyl-5-ethoxycarbonyl-1,3-thiazolium hexafluorophosphate 4d. White solid. Yield: 0.621 g, 79%, mp: 157–158°C, ^{1}H NMR (500 MHz, acetone-d_6) δ: 10.53 (s, 1H), 7.86- 7.79 (m, 5H), 4.55 (q, 2H, J = 7.3 Hz), 2.75 (s, 3H), 1.44 (t, 3H, J = 7.3 Hz), ^{13}C NMR (125 MHz, acetone-d_6) δ = 162.0 159.0, 152.9, 136.8, 132.4, 130.7, 127.5, 126.7, 63.6, 13.7, 13.6.

3-(4-Methylphenyl)-4-methyl-5-ethoxycarbonyl-1,3-thiazolium hexafluorophosphate 4e. White solid. Yield: 0.651 g, 80%, mp: 130–132°C, ^{1}H NMR (200 MHz, acetone-d_6) δ: 9.63 (s, 1H), 7.45–7.38 (m, 4H), 4.46 (q, 2H, J = 7.2 Hz), 2.62 (s, 3H), 2.48 (s, 3H), 1.42 (t, 3H, J = 7.2 Hz) ^{13}C NMR (125 MHz, acetone-d_6) 160.1, 158.6, 152.2, 143.2, 133.6, 131.4, 127.9, 125.8, 63.8, 21.6, 14.3, 14.1.

3-(4-Bromophenyl)-4-methyl-5-ethoxycarbonyl-1,3-thiazolium hexafluorophosphate 4f. White solid. Yield: 0.585 g, 62%, mp: 132–134°C, ^{1}H NMR (500 MHz, acetone-d_6) δ: 10.5 (s, 1H), 7.97 (dd, 2H, J = 9.1 Hz, J = 2.5 Hz), 7.80 (dd, 2H, J = 9.1 Hz, J = 2.5 Hz), 4.52 (q, 2H, J = 7.3 Hz), 2.75 (s, 3H), 1.42 (t, 3H, J = 7.3 Hz), ^{13}C NMR (125 MHz, acetone-d_6) δ: 162.2, 158.9, 152.9, 135.9, 133.8, 128.8, 127.5, 126.1, 63.6, 13.7, 13.6.

3-(4-Chlorophenyl)-4-methyl-5-ethoxycarbonyl-1,3-thiazolium hexafluorophosphate 4g. White solid. Yield: 0.469 g, 55%, mp: 96–98°C, ^{1}H NMR (500 MHz, acetone-d_6) δ: 10.55 (s, 1H), 7.90 (dd, 2H, J = 8.8 Hz, J = 2.5 Hz), 7.85 (dd, 2H, J = 8.8 Hz, J = 2.5 Hz), 4.55 (q, 2H, J = 7.3 Hz), 2.78 (s, 3H), 1.45 (t, 3H, J = 7.3 Hz), ^{13}C NMR (125 MHz, acetone-d_6) δ: 162.4, 158.9, 152.9, 137.9, 135.4, 130.7, 128.7, 127.5, 63.6, 13.7, 13.6.

3-(2-Tert-butylphenyl)-4-methyl-5-ethoxycarbonyl-1,3-thiazolium hexafluorophosphate 4h. White solid. Yield: 0.666 g, 74%, mp: 138–143°C, ^{1}H NMR (500 MHz, acetone-d_6) δ: 10.75 (s, 1H), 7.97 (d, 1H, J = 8.3 Hz), 7.77 (t, 1H, J = 8.3 Hz), 7.55 (m, 2H, J = 7.3 Hz), 4.55 (q, 2H, J = 7.3 Hz), 2.70 (s, 3H), 1.45 (t, 3H, J = 7.3 Hz), 1.26 (s, 9H), ^{13}C NMR (125 MHz, acetone-d_6) δ: 163.8, 159.5, 154.2, 146.4, 134.6, 133.2, 131.5, 129.9, 129.0, 128.8, 64.2, 36.9, 31.9, 14.7, 14.2.

General Procedure for the Preparation Dimethyl (2,3-Dihydro-1,3-thiazol-2-yl)-phosphonates 2d–g

To the solution of thiazolium salt **4d–g** in acetonitrile (20 mL) under argon, KI (0.5 mmol, 83 mg) and trimethyl phosphite (0.5 mmol, 59 μL) were added. The reaction mixture was stirred and heated to reflux for 4 h. After removing the solvent under reduced pressure, the residue was purified by flash chromatography. All operations must be done under an argon atmosphere.

Dimethyl 3-phenyl-4-methyl-5-ethoxycarbonyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonate 2d. Eluent AcOEt/hexane (3:1). Oil. Yield: 0.144 g, 80%, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40 (m, 2H), 7.28 (m, 3H), 5.48 (d, 1H, $^2J_{PH}$ = 5.8 Hz), 4.20 (q, 2H, J = 7.3 Hz), 3.78 (d, 3H, $^3J_{PH}$ = 2.9 Hz), 3.76 (d, 3H, $^3J_{PH}$ = 3.4 Hz), 2.09 (s, 3H), 1.30 (t, 3H, J = 7.3 Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 164.0, 151.7, 142.24 (d, $^3J_{PC}$ =

2.2 Hz), 129.8, 127.6, 127.3, 100.06 (d, $^3J_{PC} = 2.2$ Hz), 65.6 (d, $^1J_{PC} = 178$ Hz), 60.6, 54.5 (d, $^2J_{PC} = 6.8$ Hz), 15.3, 14.6. ^{31}P NMR (200 MHz, $CDCl_3$) δ: 17.36.

Dimethyl 3-(4-methylphenyl)-4-methyl-5-ethoxycarbonyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonate 2e. Eluent AcOEt/hexane (3:1). Oil. Yield: 0.139 g, 75%, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.20 (s, 4H), 5.47 (d, 1H, $^2J_{PH} = 6.3$ Hz), 4.21 (q, 2H, J = 7.3 Hz), 3.78 (d, 3H, $^3J_{PH} = 4.8$ Hz), 3.76 (d, 3H, $^3J_{PH} = 4.3$ Hz), 2.37 (s, 3H), 2.09 (s, 3H), 1.30 (t, 3H, J = 7.3 Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 163.7, 151.9, 139.12 (d, $^3J_{PC} = 1.5$ Hz), 137.5, 130.0, 127.1, 98.5, 65.2 (d, $^1J_{PC} = 177$ Hz), 60.1, 54.1 (d, $^2J_{PC} = 7.6$ Hz), 20.9, 14.8, 14.3, ^{31}P NMR (200 MHz, $CDCl_3$) δ: 17.37.

Dimethyl 3-(4-bromophenyl)-4-methyl-5-ethoxycarbonyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonate 2f. Eluent AcOEt/hexane (3:1). Oil. Yield: 0.168 g, 77%, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.48 (d, 2H, J = 8.3 Hz), 7.17 (d, 2H, J = 8.3 Hz), 5.37 (d, 1H, $^2J_{PH} = 5.3$ Hz), 4.19 (q, 2H, J = 7.3 Hz), 3.78 (d, 3H, $^3J_{PH} = 10.0$ Hz), 3.76 (d, 3H, $^3J_{PH} = 10.0$ Hz), 2.37 (s, 3H), 2.07 (s, 3H), 1.27 (t, 3H, J = 7.3 Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 163.8, 150.6, 141.5 (d, $^3J_{PC} = 2.5$ Hz), 132.9, 128.6, 121.0, 101.7, 65.51 (d, $^1J_{PC} = 179$ Hz), 60.7, 54.7 (d, $^2J_{PC} = 7.1$ Hz), 54.5 (d, $^2J_{PC} = 6.1$ Hz), 15.2, 14.6, ^{31}P NMR (200 MHz, $CDCl_3$) δ: 17.11.

Dimethyl 3-(4-chlorophenyl)-4-methyl-5-ethoxycarbonyl (2,3-dihydro-1,3-thiazol-2-yl)-phosphonate 2g. Eluent AcOEt/hexane (5:2). Oil. Yield: 0.137 g, 70%, ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34 (d, 2H, J = 8.3 Hz), 7.23 (d, 2H, J = 8.3 Hz), 5.37 (d, 1H, $^2J_{PH} = 5.4$ Hz), 4.18 (q, 2H, J = 7.1 Hz), 3.78 (d, 3H, $^3J_{PH} = 10.7$ Hz), 3.76 (d, 3H, $^3J_{PH} = 10.2$ Hz), 2.37 (s, 3H), 2.06 (s, 3H), 1.27 (t, 3H, J = 7.1 Hz), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 163.9, 150.8, 140.9, 133.2, 129.9, 128.4, 101.3, 65.55 (d, $^1J_{PC} =$ 179 Hz), 60.7, 54.7 (d, $^2J_{PC} = 7.6$ Hz), 54.5 (d, $^2J_{PC} = 7.6$ Hz), 15.2, 14.6, ^{31}P NMR (200 MHz, $CDCl_3$) δ: 17.13.

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