Tetrahedron Letters 51 (2010) 2274–2276

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

A simple and effective synthesis of activated vinylphosphonates from 3-methoxy-2-diethoxyphosphorylacrylate

Tomasz Janecki *, Anna Albrecht, Jacek F. Koszuk, Jakub Modranka, Dominika Słowak

Institute of Organic Chemistry, Technical University of Łódź, 90-924 Łódź, Żeromskiego 116, Poland

ARTICLE INFO

Article history:
Received 28 December 2009
Revised 10 February 2010
Accepted 19 February 2010
Available online 23 February 2010

ABSTRACT

A facile, efficient and general one-step procedure for the synthesis of 3-substituted 2-diethoxyphosphorylacrylates from 3-methoxy-2-diethoxyphosphorylacrylate **1b** and nitrogen, carbon and phosphorus nucleophiles is presented. Reaction of **1b** with 3,5-dimethoxyphenol in the presence of trifluoromethanesulfonic acid yields 3-diethoxyphosphoryl-5,7-dimethoxychromen-2-one.

Vinylphosphonates are a well known class of organophosphorus compounds which have proved to be very useful reagents in organic synthesis. They are frequently used as intermediates in the synthesis of many important acyclic, carbocyclic and especially heterocyclic compounds.[1–3] They are also excellent substrates for the synthesis of 1,2-epoxyalkylphosphonates—compounds of great synthetic and biological significance.[4] The presence of an electron-withdrawing substituent, such as an alkoxycarbonyl group at the α-position greatly enhances the synthetic utility of vinylphosphonates by both, facilitating Michael-type additions and enabling further functionalization of the adduct, for example, Horner–Wadsworth–Emmons olefination.[1,3] Many synthetic methods leading to vinylphosphonates have been described so far.[1–3] We envisioned that the reaction of 3-alkoxy or 3-dimethylamino-2-dialkoxyphosphorylacrylates **1** or **2** with nucleophiles, to yield substitution products **3** via an addition/elimination mechanism, would have great synthetic potential as a simple and general method for the synthesis of activated vinylphosphonates (Fig. 1). Acrylates **1** and **2** can be regarded as phosphonate analogs of alkoxymethylidenemalonates **4**[5] or dimethylaminomethylidenemalonates **5**,[6] respectively, a well known group of organic reagents which undergo substitution reactions with various nitrogen, sulfur, oxygen and carbon nucleophiles, and which have proved to be excellent starting materials for the synthesis of many biologically important classes of compounds, including 4-oxochromene-, 4-oxoquinoline- and 4-oxonaphthyridine-3-carboxylic acids.[5–7]

Surprisingly, in contrast to the wide synthetic applications of malonates **4** and **5**, only a few reactions of acrylates **1** or **2** with nucleophiles have been reported so far. Phosphonoacrylates **1a** and **2a** were employed in reactions with arylhydrazines to give intermediate substitution products which cyclized to 2-aryl-3-hydroxy-4-dimethoxyphosphorylpyrazoles.[8] Similar reaction of **2b** with hydrazine gave 3-hydroxy-4-diethoxyphosphorylpyrazole.[9] Finally, reaction of **2b** with guanidine hydrochloride yielded 2-amino-5-diethoxyphosphoryl-4-hydroxypyrimidine.[10] In this Letter, we report that the reaction of 3-methoxy-2-diethoxyphosphorylacrylate (**1b**) with various nucleophiles proved to be an efficient synthetic route to diverse activated vinylphosphonates.

Acrylate **1b** was efficiently synthesized from ethyl diethoxyphosphorylacetate, methyl formate and methyl iodide by modifying the method described for the synthesis of 3-methoxy-2-dimethoxyphosphorylacrylate (**1a**).[8] Phosphorylacrylate **1b** was then tested in reactions with various nitrogen and carbon nucleophiles. In all cases, the corresponding crude substitution products were purified by distillation or column chromatography to give pure **6a–p** in moderate to high yields (Table 1). Reactions with amines proceeded smoothly in methanol or ethanol as solvent according to the conditions given in Table 1 (entries 1–12).[11] Benzamide, *t*-butyl carbamate and carbon nucleophiles also reacted smoothly with **1b** in the presence of butyllithium or sodium hydride, to give products **6m–p** in moderate to high yields (entries

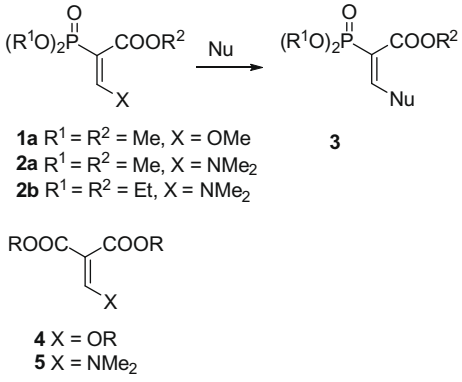
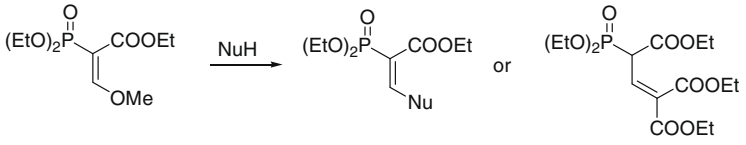


Figure 1. Synthesis of activated vinylphosphonates from 3-alkoxy or 3-dimethylamino-2-dialkoxyphosphorylacrylates and the structures of malonates **4** and **5**.

* Corresponding author. Tel.: +48 42 6313220; fax: +48 42 6365533.
E-mail address: tjanecki@p.lodz.pl (T. Janecki).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.02.108

Table 1
Scope of the reaction of **1b** with various nitrogen and carbon nucleophiles



1b **6a-o** **6p**

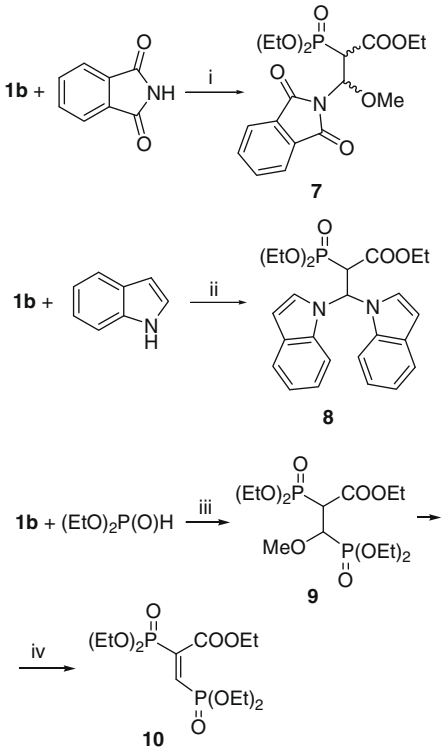
Entry	Product	NuH	Conditions	Yield[a] (%)	*E*/*Z*[b]	Purification method[c]
1	**6a**	NH_3	EtOH/H_2O, rt, 20 h	71	75/25	185–190 °C/0.04 Torr
2	**6b**	$PrNH_2$	EtOH, rt, 20 h	82	65/35	175 °C/0.5 Torr
3	**6c**	CyclohexylNH_2	EtOH, rt, 20 h	89	70/30	$CHCl_3$/acetone = 99/1
4	**6d**	$BnNH_2$	EtOH, rt, 20 h	73	60/40	225 °C/0.4 Torr
5	**6e**	PhCH(Me)NH_2	EtOH, rt, 20 h	72	70/30	225 °C/0.4 Torr
6	**6f**	Pyrrolidine	EtOH, rt, 20 h	74	>99/1	185–190 °C/0.5 Torr
7	**6g**	Piperidine	EtOH, rt, 20 h	70	>99/1	190–200 °C/0.6 Torr
8	**6h**	Morpholine	EtOH, rt, 20 h	80	>99/1	220–225 °C/0.6 Torr
9	**6i**	$PhNH_2$	EtOH, rt, 20 h	75	65/35	215–220 °C/0.4 Torr
10	**6j**	2-Aminopyridine	EtOH, rt, 2 h	90	60/40	$CHCl_3$
11	**6k**	$PhNHNH_2$	EtOH, rt, 20 h	76	70/30	$CHCl_3$/acetone = 98/2
12	**6l**	PhNHNHBoc	MeOH, reflux, 1 h	80	>99/1	$CHCl_3$/acetone = 98/2
13	**6m**	$Ph(CO)NH_2$	*n*-BuLi, THF, rt, 20 h	50	50/50	$CHCl_3$/acetone = 98/2
14	**6n**	$BocNH_2$	NaH, Et_2O, rt, 16 h	36/53[d]	40/60	$CHCl_3$
15	**6o**	$(EtO)_2P(O)CH_2COOEt$	NaH, THF, rt, 4 h	56	70/30	$CHCl_3$/acetone = 98/2
16	**6p**	$CH_2(COOEt)_2$	NaH, THF, rt, 4 h	88	—	$CHCl_3$/acetone = 98/2

[a] Yield of pure, isolated products based on **1b**.
[b] Determined from the ^{31}P NMR spectrum of the crude product.
[c] Distillation (bp/pressure) or column chromatography on silica gel (eluent).
[d] Yield of pure *E* and *Z* isomers respectively, separated by column chromatography.

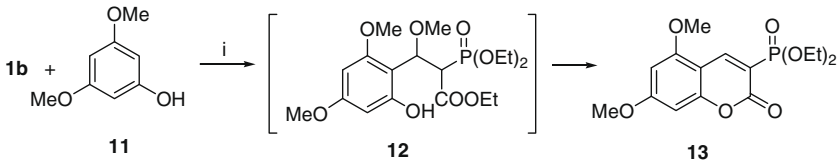
13–16).[12] Substitution products **6a–o** were obtained as pure *E* isomers or as mixtures of *E* and *Z* isomers in the ratios shown in Table 1. Reaction with ethyl malonate (entry 16) gave allylphosphonate **6p**. Vinylphosphonate **6n** was separated into individual *E* and *Z* isomers but no efforts were undertaken to separate the other isomeric mixtures.

To explore further the reactivity of **1b**, additional experiments were performed (Scheme 1). Reaction of **1b** with 2 equiv of phthalimide in the presence of NaH, gave adduct **7** in 75% yield, as a mixture of two diastereomers in a 95:5 ratio. No substitution product could be detected. Our efforts to eliminate methanol from this adduct by heating it in toluene or xylene in the presence of acidic catalysts (*p*-toluenesulfonic or trifluoromethanesulfonic acids) failed. Reaction of **1b** with indole (1 equiv) and NaH (1.1 equiv) afforded a mixture of 3-indolyl-3-methoxy- and 3,3-bis(indolyl)-2-diethoxyphosphorylpropanoates which were difficult to separate. Interestingly, the same reaction performed with two equivalents of indole and 2.1 equiv of NaH gave bis(indolyl)propanoate **8** in 68% yield as the only product. In turn, the reaction of **1b** with 1.2 equiv of diethyl phosphite and NaH gave adduct **9**. Pleasingly, when crude **9** was heated in toluene in the presence of *p*-toluenesulfonic acid, followed by low pressure (Kugelrohr) distillation of the solvent and volatile by-products, and further purification of the residue by column chromatography on silica gel ($CHCl_3$/acetone = 95:5), (*E*)-2,3-di(diethoxyphosphoryl)acrylate (**10**) was obtained in 56% overall yield.[13]

Finally, 3,5-dimethoxyphenol **11** proved to be an effective C-nucleophile in the reaction with **1b**. Initially, the reaction was performed in the presence of two equivalents of methanesulfonic acid as catalyst at room temperature. The progress of the reaction was monitored by ^{31}P NMR spectroscopy. Under these conditions the reaction was very slow and conversion of **1b** was only 24% after 18 days. However, we were pleased to observe that when trifluoromethanesulfonic acid was used as the catalyst[14] the reaction was complete in 6 days at room temperature. After purification of the crude product, 3-diethoxyphosphorylchromen-2-one **13** was obtained in 88% yield (Scheme 2).[15] Clearly, trifluoromethanesulfonic acid effectively promotes the Friedel–Crafts reaction of phenol **11** with acrylate **1b** yielding intermediate phosphonate **12**. Subsequent spontaneous lactonization and elimination of methanol gives the final chromenone **13**.



Scheme 1. Reagents and conditions: (i) phthalimide (2 equiv), NaH (2.1 equiv), THF, rt, 16 h, 75%; (ii) indole (2 equiv), NaH (2.1 equiv), THF, rt, 16 h, 68%; (iii) $(EtO)_2P(O)H$ (1.2 equiv), NaH (1.3 equiv), THF, −20 °C, 4 h; (iv) TsOH (0.5 equiv), toluene, reflux, 4 h, 56%.



11 12 13

Scheme 2. Reagents and conditions: (i) CF_3SO_3H (2 equiv), CH_2Cl_2, rt, 6 d, 88%.

The structures and stereochemistry of products **6a–p**, **7–10**, and **13** were confirmed by IR, ^1H, ^{13}C and ^{31}P NMR spectroscopy as well as by elemental analysis.

We also tested the reaction of ethyl 3-dimethylamino-2-diethoxyphosphorylacrylate (**2b**) with several nucleophiles or pronucleophiles, for example, simple amines, benzamide, phthalimide, indole and diethyl phosphite, but no advantage over the use of **1b** was found. Typically, these reactions were less effective or failed.

In conclusion, a simple, highly effective and general method for the synthesis of β-substituted vinylphosphonates from easily accessible 3-methoxy-2-diethoxyphosphorylacrylate (**1b**) and nitrogen, carbon and phosphorus nucleophiles, has been demonstrated. Currently we are studying the scope of this method with respect to other nucleophiles. Also, further studies directed towards the application of the obtained substitution products in the synthesis of phosphoryl substituted heterocycles are underway.

Acknowledgements

This work was financed by the Ministry of Science and Higher Education (Project No. NN204 005736).

References and notes

1. Minami, T.; Okauchi, T.; Kouno, R. *Synthesis* **2001**, 349.
2. Dembitsky, V. M.; Quntar, A. A. A.; Haj-Yehia, A.; Srebnik, M. *Mini-Rev. Org. Chem.* **2005**, *2*, 91.
3. Janecki, T.; Kędzia, J.; Wąsek, T. *Synthesis* **2009**, 1227.
4. Iorga, B.; Eymery, F.; Savignac, P. *Synthesis* **1999**, 207.
5. Milata, V. *Aldrichim. Acta* **2001**, *34*, 20.
6. Hermecz, I.; Kereszturi, G.; Vasvari-Debreczy, L. In *Aminomethylenemalonates and Their Use in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Academic Press Inc.: San Diego, 1992; Vol. 54.
7. Milata, V.; Claramunt, R. M.; Elguero, J.; Zalupsky, P. In *Targets in Heterocyclic Systems*; Attanasi, O. A., Spinelli, D., Eds.; Italian Society of Chemistry: Rome, 2000; Vol. 4, p 167.
8. Miller, P. C.; Molyneaux, J. M. *Org. Prep. Proced. Int.* **1999**, *31*, 295.
9. Aboujaoude, E. E.; Collignon, N.; Savignac, P. *Tetrahedron* **1985**, *41*, 427.
10. Aboujaoude, E. E.; Collignon, N.; Savignac, P. *Phosphorus, Sulfur Relat. Elem.* **1987**, *31*, 231.
11. General procedure for the reactions of **1b** with amines: a solution of **1b** (2 mmol, 532 mg) and the corresponding amine (2.2 mmol) in an appropriate solvent (5 ml) was stirred under the conditions given in Table 1. Evaporation of the solvent and purification (Table 1) gave **6a–l**. Sample data: (*E,Z*)-*Ethyl 3-(benzylamino)-2-(diethoxyphosphoryl)acrylate* (*E,Z*)-**6d**: (498 mg, 73%); oil; IR (film, cm^{-1}): 1656, 1609, 1213; ^1H NMR (250 MHz, $CDCl_3$):[16] δ = 1.28 (t, J = 7.1 Hz, 3H, C(O)OCH$_2$C*H*$_3$), 1.31 (t, J = 7.1 Hz, 6H, P(O)(OCH$_2$C*H*$_3$)$_2$), 3.96–4.11 (m, 4H, P(O)(OC*H*$_2$CH$_3$)$_2$), 4.19 (q, J = 7.1 Hz, 2H, C(O)OC*H*$_2$CH$_3$), 4.44 (d, J = 6.2 Hz, 0.4H, NHC*H*$_2$Ph (*Z*)-isomer), 4.47 (d, J = 6.2 Hz, 0.6H, NHC*H*$_2$Ph (*E*)-isomer), 7.20–7.40 (m, 5H, C^{Ar}-*H*), 7.81 (dd, J = 12.7 Hz, J = 13.9 Hz, 0.6H, =C*H*–NH (*E*)-isomer), 8.19 (dd, J = 14.3 Hz, J = 37.3 Hz, 0.4 H, =C*H*–NH (*Z*)-isomer), 9.10–9.36 (m, 1H, N*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$):[16] δ = 13.8 (s, C(O)CH$_2$*C*H$_3$ (*E*)-isomer), 13.9 (s, C(O)CH$_2$*C*H$_3$ (*Z*)-isomer), 15.6 (d, J = 6.6 Hz, P(O)(OCH$_2$*C*H$_3$)$_2$ (*Z*)-isomer), 15.7 (d, J = 6.9 Hz, P(O)(OCH$_2$*C*H$_3$)$_2$ (*E*)-isomer), 52.3 (s, NHC*H*$_2$Ph (*Z*)-isomer), 52.6 (s, NHC*H*$_2$Ph (*E*)-isomer), 58.9 (s, C(O)O*C*H$_2$CH$_3$), 60.9 (d, J = 5.2 Hz, P(O)(O*C*H$_2$CH$_3$)$_2$ (*E*)-isomer), 61.2 (d, J = 5.0 Hz, P(O)(O*C*H$_2$CH$_3$)$_2$ (*Z*)-isomer), 79.3 (d, J = 194.0 Hz, P(O)*C* = (*Z*)-isomer), 80.8 (d, J = 208.0 Hz, P(O)*C* = (*E*)-isomer), 126.5 (s, *C*2^{Ar} (*Z*)-isomer), 126.7 (s, *C*2^{Ar} (*E*)-isomer), 127.0 (s, *C*4^{Ar} (*Z*)-isomer), 127.2 (s, *C*4^{Ar} (*E*)-isomer), 127.4 (s, *C*3^{Ar} (*Z*)-isomer), 128.3 (s, *C*3^{Ar} (*E*)-isomer), 136.3 (s, *C*1^{Ar} (*E*)-isomer), 136.5 (s, *C*1^{Ar} (*Z*)-isomer), 161.5 (d, J = 18.2 Hz, =CH–N (*E*)-isomer), 161.9 (d, J = 8.6 Hz, =CH–N (*Z*)-isomer), 166.7 (d, J = 11.7 Hz, *C*O$_2$Et (*Z*)-isomer), 168.2 (d, J = 10.5 Hz, *C*O$_2$Et (*E*)-isomer); ^{31}P NMR (101 MHz, $CDCl_3$):[16] (*E*)-isomer δ = 22.04, (*Z*)-isomer δ = 22.87. Anal. Calcd for $C_{16}H_{24}NO_5P$: C, 56.30; H, 7.09. Found: C, 56.16; H, 7.18. (*E*)-*Ethyl 2-(diethoxyphosphoryl)-3-morpholinoacrylate* (*E*)-**6h**: (514 mg, 80%); oil; IR (film, cm^{-1}): 1679, 1586, 1273, 1020; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.21–1.50 (m, 9H, C*H*$_3$CH$_2$OC(O), (C*H*$_3$CH$_2$O)$_2$P(O)), 3.45–3.60 (m, 4H, 2 × *H*$_2$), 3.65–3.80 (m, 4H, 2 × *H*$_2$), 3.93–4.30 (m, 6H, CH$_3$C*H*$_2$OC(O), (CH$_3$C*H*$_2$O)$_2$P(O)), 7.43 (d, J = 15.4 Hz, 1H, *H*-3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 12.5 (s, *C*H$_3$CH$_2$OC(O)), 14.5 (d, J = 6.9 Hz, (*C*H$_3$CH$_2$O)$_2$P(O)), 21.1 (s, *C*H$_2$), 21.9 (s, *C*H$_2$), 27.1 (s, *C*H$_2$), 28.5 (s, *C*H$_2$), 57.9 (s, CH$_3$*C*H$_2$OC(O)), 59.7 (d, J = 5.1 Hz, (CH$_3$*C*H$_2$O)$_2$P(O)), 80.8 (d, J = 197.4 Hz, *C*-2), 154.0 (d, J = 18.8 Hz, *C*-3), 163.7 (d, J = 10.1 Hz, *C*-1); ^{31}P NMR (101 MHz, $CDCl_3$): δ = 24.21; Anal. Calcd for $C_{13}H_{24}NO_6P$: C, 48.60; H, 7.53. Found: C, 48.46; H, 7.59.
12. Typical procedure for the reactions with amides, indole, and carbon nucleophiles: to a solution of *tert*-butyl carbamate (0.825 mmol, 97 mg) in Et_2O (5 mL), NaH (0.825 mmol, 20 mg) was added in one portion, under an argon atmosphere, at 0 °C and the mixture was stirred for 1 h, at rt. After this time, a solution of **1b** (0.750 mmol, 200 mg) in Et_2O (5 mL) was added at 0 °C. The mixture was stirred for 16 h, at rt, then H_2O (20 mL) was added. Extraction with CH_2Cl_2 (3 × 10 mL), drying (Na_2SO_4) and evaporation of the solvent gave the crude product as a mixture of *E*/*Z* isomers in a 40/60 ratio, which was purified by column chromatography (eluent: $CHCl_3$) to yield pure (*E*)- and (*Z*)-**6n**. *Ethyl (E)-3-(tert-butoxycarbonylamino)-2-(diethoxyphosphoryl)acrylate* (*E*)-**6n**: (95 mg, 36%); oil; IR (film, cm^{-1}): 1745, 1603, 1231, 1020; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, J = 7.1 Hz, 9H, C*H*$_3$CH$_2$OC(O), (C*H*$_3$CH$_2$O)$_2$P(O)), 1.49 (s, 9H, C(C*H*$_3$)$_3$), 4.01–4.17 (m, 4H, (CH$_3$C*H*$_2$O)$_2$P(O)), 4.26 (q, J = 7.1 Hz, 2H, CH$_3$C*H*$_2$OC(O)), 8.16 (dd, J = 14.9 Hz, J = 12.5 Hz, 1H, =C*H*–NH), 10.21 (d, J = 12.5 Hz, 1H, N*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8 (s, C(O)CH$_2$*C*H$_3$), 16.1 (d, J = 6.4 Hz, P(O)(OCH$_2$*C*H$_3$)$_2$), 27.7 (s, C(*C*H$_3$)$_3$), 60.6 (s, C(O)O*C*H$_2$CH$_3$), 61.9 (d, J = 5.6 Hz, P(O)(O*C*H$_2$CH$_3$)$_2$), 83.8 (s, *C*(CH$_3$)$_3$), 94.0 (d, J = 202.6 Hz, P(O)*C*=), 150.7 (s, NH*C*(O)O), 152.0 (d, J = 18.2 Hz, =*C*H–N), 167.1 (d, J = 10.6 Hz, *C*O$_2$Et); ^{31}P NMR (101 MHz, $CDCl_3$): δ = 22.04; Anal. Calcd for $C_{14}H_{26}NO_7P$: C, 47.86; H, 7.46. Found: C, 47.71; H, 7.53. *Ethyl (Z)-3-(tert-butoxycarbonylamino)-2-(diethoxyphosphoryl)acrylate* (*Z*)-**6n**: (140 mg, 53%); oil; IR (film, cm^{-1}): 1745, 1603, 1231, 1020; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.1 Hz, 3H, C*H*$_3$CH$_2$OC(O)), 1.33 (t, J = 7.1 Hz, 6H, (C*H*$_3$CH$_2$O)$_2$P(O)), 1.50 (s, 9H, C(C*H*$_3$)$_3$), 4.01–4.20 (m, 4H, (CH$_3$C*H*$_2$O)$_2$P(O)), 4.22 (q, J = 7.1 Hz, 2H, CH$_3$C*H*$_2$OC(O)), 8.64 (dd, J = 39.5 Hz, J = 12.7 Hz, 1H, =C*H*–NH), 10.39 (d, J = 12.7 Hz, 1H, N*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.0 (s, C(O)CH$_2$*C*H$_3$), 15.9 (d, J = 6.5 Hz, P(O)(OCH$_2$*C*H$_3$)$_2$), 27.7 (s, C(*C*H$_3$)$_3$), 60.3 (s, C(O)O*C*H$_2$CH$_3$), 62.4 (d, J = 5.4 Hz, P(O)(O*C*H$_2$CH$_3$)$_2$), 82.7 (s, *C*(CH$_3$)$_3$), 93.0 (d, J = 187.2 Hz, P(O)*C*=), 151.0 (s, NH*C*(O)O), 153.0 (d, J = 4.6 Hz, =CH–N), 165.0 (d, J = 11.8 Hz, *C*O$_2$Et); ^{31}P NMR (101 MHz, $CDCl_3$): δ = 22.87; Anal. Calcd for $C_{14}H_{26}NO_7P$: C, 47.86; H, 7.46. Found: C, 47.98; H, 7.53.
13. Spectral data for *(E)-Ethyl 2,3-di(diethoxyphosphoryl)acrylate* (**10**): oil, IR (film, cm^{-1}): 1732, 1598, 1254, 1013; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.25–1.42 (m, 15H, C*H*$_3$CH$_2$OC(O), 2 × (C*H*$_3$CH$_2$O)$_2$P(O)); 4.05–4.25 (m, 8H, 2 × (CH$_3$C*H*$_2$O)$_2$P(O)); 4.34 (q, J = 7.1 Hz, 2H, CH$_3$C*H*$_2$OC(O)); 6.82 (dd, J = 18.4 Hz, J = 24.8 Hz, 1H, *H*-3); ^1H NMR{^{31}P} ($CDCl_3$): δ = 1.25–1.42 (m, 15H, C*H*$_3$CH$_2$OC(O), 2 × (C*H*$_3$CH$_2$O)$_2$P(O)), 4.05–4.25 (m, 8H, 2 × (CH$_3$C*H*$_2$O)$_2$P(O)), 4.34 (q, J = 7.1 Hz, 2H, CH$_3$C*H*$_2$OC(O)), 6.80 (s, 1H, *H*-3); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.9 (s, *C*H$_3$CH$_2$OC(O)), 14.1 (d, J = 7.3 Hz, (*C*H$_3$CH$_2$O)$_2$P(O)), 14.2 (d, J = 6.9 Hz, (*C*H$_3$CH$_2$O)$_2$P(O)), 60.2 (s, CH$_3$*C*H$_2$OC(O)), 60.6 (d, J = 4.5 Hz, (CH$_3$*C*H$_2$O)$_2$P(O)), 61.4 (d, J = 4.2 Hz, (CH$_3$*C*H$_2$O)$_2$P(O)), 133.2 (dd, J = 179.3 Hz, J = 38.8 Hz, *C*-2), 141.3 (dd, J = 168.5 Hz, J = 39.3 Hz, *C*-3), 162.3 (dd, J = 12.7 Hz, J = 2.2 Hz, *C*-1); ^{31}P NMR (101 MHz, $CDCl_3$): δ = 9.91 (d, $^3J_{P-P}$ = 10.3 Hz, *P*); 10.73 (d, $^3J_{P-P}$ = 10.3 Hz, *P*); Anal. Calcd for $C_{13}H_{26}O_8P_2$: C, 41.94; H, 7.04. Found: C, 41.87; H, 7.18.
14. Krawczyk, H.; Albrecht, Ł.; Wojciechowski, J.; Wolf, W. M. *Tetrahedron* **2007**, *63*, 12583.
15. *3-Diethoxyphosphoryl-5,7-dimethoxy-2H-chromen-2-one* (**13**): To a solution of **1b** (0.750 mmol, 20 mg) and 3,5-dimethoxyphenol (**11**) (0.820 mmol, 102 mg) in CH_2Cl_2 (5 mL), TfOH (0.750 mmol, 113 mg) was added in one portion. The mixture was stirred for 6 d at rt. Next, a saturated solution of $NaHCO_3$ (10 mL) was added. Extraction with CH_2Cl_2 (3 × 10 mL), drying (Na_2SO_4) and evaporation of the solvent gave a crude product, which was purified by crystallization from Et_2O to yield pure **13** (226 mg, 88%) as orange crystals, mp 97 °C (Et_2O); IR (film, cm^{-1}): 1732, 1600, 1256, 1136, 1032, 784; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.35–1.50 (m, 6H, (C*H*$_3$CH$_2$O)$_2$P(O)), 3.88 (s, 3H, C*H*$_3$O), 3.91 (s, 3H, C*H*$_3$O), 4.00–4.45 (m, 4H, (CH$_3$C*H*$_2$O)$_2$P(O)), 6.20–6.50 (m, 2H, 2 × C*H*-Ar), 8.77 (d, J = 17.4 Hz, 1H, *H*-3); ^{13}C NMR (62.9, MHz, $CDCl_3$): δ = 16.15 (d, J = 6.3 Hz, (CH$_3$CH$_2$O)$_2$P(O)), 55.83 (s, *C*H$_3$O), 55.90 (s, *C*H$_3$O), 62.77 (d, J = 5.8 Hz, (CH$_3$CH$_2$O)$_2$P(O)), 92.57 (s, 2 × *C*-Ar), 94.75 (s, 2 × *C*-Ar), 103.40 (d, J = 14.3 Hz, *C*-4), 110.05 (d, J = 200.8 Hz, *C*-3), 148.64 (d, J = 8.2 Hz, *C*-2), 158.15 (s, *C*-Ar), 165.97 (s, *C*-Ar); ^{31}P NMR (101 MHz, $CDCl_3$): δ = 13.39; Anal. Calcd for $C_{15}H_{19}O_7P$: C, 52.64; H, 5.60. Found: C, 52.32; H, 5.74.
16. Values for specific isomers were obtained from the spectra of the mixture of isomers.