JOC*Note*

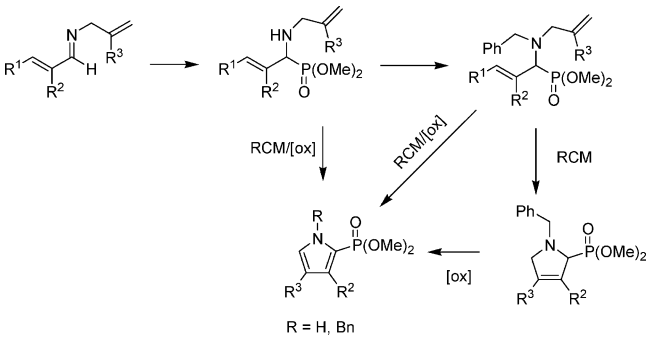
Synthesis of 2-Phosphonopyrroles via a One-Pot RCM/Oxidation Sequence

Kristof Moonen, Nicolai Dieltiens, and Christian V. Stevens*

Research Group SynBioC, Department of Organic Chemistry, Faculty of Bioscience Engineering, Ghent University, Coupure links 653, B-9000 Ghent, Belgium

chris.stevens@ugent.be

Received January 24, 2006



A four-step synthesis of 2-phosphonopyrroles is presented starting from suitable aldehydes. The key step in the synthesis involves a one-pot ring-closing metathesis/oxidation sequence of a functionalized α-aminoalkenyl phosphonate. Notwithstanding the presence of a nucleophilic nitrogen atom and high substitution patterns in the substrate, the results of the RCM reaction are excellent using mild reaction conditions. Furthermore, a synergism is observed between the RCM catalyst and the oxidizing agent, causing higher oxidation rates and allowing reaction for substrates that normally fail to ring close under standard RCM conditions.

Phosphonylated azaheterocycles are an important class of compounds with high biological potential as conformationally restricted bioisosteres of amino acids.[1] During our research[2] in this area, we became interested in phosphonopyrroles as the well-known biological properties of pyrroles[3] may be enhanced by the presence of a phosphonate group. Only a limited amount of research on the synthesis of these compounds has been performed. 2-Phosphonopyrroles can be obtained through direct phosphorylation of a pyrrole nucleus, but only in low to moderate yields.[4] Nitrile ylides containing an electron-withdrawing phosphonate group have been reacted with alkynes[5] or alkenes containing a suitable leaving group[6] to yield 2-phosphonopyrroles via a 1,3-dipolar cycloaddition. One example was presented in which a BOC-protected 3-oxo-2-phosphonopyrrolidine was converted to the corresponding 3-hydroxy-2-phosphonopyrrole by treatment with trifluoroacetic acid.[7] On the other hand, addition of enolates and enamines to phosphonoazoalkenes[8] or addition of cyano methylphosphonate anion to azoalkenes[9] was shown to lead to 3-phosphonopyrroles. Finally, only one example of a meta-mediated ring closure between an alkyne and a C−N double bond using Pd has been reported.[10] However, since the discovery and development of practical useful ruthenium-based metathesis catalysts in the past decennium,[11] ring-closing metathesis (RCM) has found wide application in the synthesis of complex (hetero)cyclic compounds.[12] Furthermore, an increasing interest exists in combining ring-closing metathesis with a second reaction step in order to obtain complex, highly functionalized molecules in a one-pot reaction.[13] The use of RCM to form heteroaromatic compounds, however, has only recently appeared in the literature.[14] In this paper, we present the synthesis of *N*-benzyl-2-phosphono-3-pyrrolines via RCM starting from functionalized α-aminoalkenyl phosphonates and their in situ conversion to the corresponding 2-phosphonopyrroles by tetrachloroquinone (TCQ).

α,β-Unsaturated *N*-allylaldimines **1** are phosphonylated with complete regioselectivity[15] using a modified Pudovik reaction

(1) The topic of nonaromatic phosphonylated azaheterocycles has been reviewed recently: Moonen, K.; Laureyn, I.; Stevens, C. V. *Chem. Rev.* **2004**, *104*, 6177.

(2) (a) Moonen, K.; Stevens, C. V. *Synthesis* **2005**, 3603. (b) Vanderhoydonck, B.; Stevens, C. V. *J. Org. Chem.* **2005**, *70*, 191.

(3) *The Synthesis, Reactivity, and Physical Properties of Substituted Pyrroles*; Alan Jones, R., Ed.; Pyrroles; John Wiley & Sons:New York, 1992; Vol. 48, Part 2, p 640.

(4) (a) Ivonin, S. P.; Tolmachev, A. A.; Terikovska, T. E.; Anischchenko, A. A.; Chaikovskaya, A. A., Pinchuk, A. M. *Heteroatom Chem.* **2003**, *14*, 258. (b) Quin, L. D.; Marsi, B. G. *J. Am. Chem. Soc.* **1985**, *107*, 3389. (c) Griffin, C. E.; Peller, R. P.; Peters, J. A. *J. Org. Chem.* **1965**, *30*, 91.

(5) (a) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 9263. (b) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *Tetrahedron Lett.* **2005**, *46*, 2563. (c) Berrée, F.; Marchand, E. Morel, G. *Tetrahedron Lett.* **1992**, *33*, 6155.

(6) (a) Huang, W.-S.; Zhang, Y.-X.; Yuan, C. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1893. (b) Ngwe, H.; Kinoshita, H.; Inomata, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3320. (c) Yuan, C.; Huang, W. *Synthesis* **1993**, 473.

(7) Davis, F. A.; Wu, Y.; Xu, H.; Zhang, J. *Org. Lett.* **2004**, *6*, 4523.

(8) (a) Palacios, F.; Aparicio, D.; de los Santos, J. *Tetrahedron* **1999**, *55*, 13767. (b) Haelters, J.-P.; Corbel, B.; Sturtz, G. *Phosphorus, Sulfur, Silicon Relat. Elem.* **1989**, *44*, 53.

(9) Attanasi, O. A.; De Crescentini, L.; Foresti, E.; Gatti, G.; Giorgi, R.; Perrulli, F. R.; Santeusanio, S. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1829.

(10) Palacios, F.; Aparicio, D.; de los Santos, J. M.; Vicario, J. *Tetrahedron* **2001**, *57*, 1961.

(11) For reviews concerning recent developments in design of ruthenium metathesis catalysts, see: (a) Dragutan, I.; Dragutan, V.; Filip, P. *Arkivoc*, **2005**, *x*, 105. (b) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3013.

(12) (a) Nicolau, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490. (b) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (c) Phillips, A. J.; Abell, A. D. *Aldrichim. Acta* **1999**, *32*, 75. (d) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. For a recent review on the use of RCM for the synthesis of nitrogen-containing heterocycles, see: (e) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199.

(13) (a) van Otterlo, W. A. L.; Coyanis, E.; Mabel, E.; Panayides, J.-L.; de Koning, C. B.; Fernandes, M. A. *Synlett* **2005**, 501. (b) van Otterlo, W. A. L.; Morgans, G. L.; Madeley, L. G.; Kuzvidza, S.; Moleele, S. S.; Thornton, N.; de Koning, C. B. *Tetrahedron* **2005**, *61*, 7746. (c) Schmidt, B. *J. Org. Chem.* **2004**, *69*, 7672. (d) Lee, H.-Y.; Kim, H. Y.; Tae, H.; Kim, B. G.; Lee, J. *Org. Lett.* **2003**, *5*, 3439. (e) Grigg, R.; Hodgson, A.; Morris, J.; Sridharan, V. *Tetrahedron Lett.* **2003**, *44*, 1023. (f) Kinderman, S. S.; Van Maarseven, J. H.; Schoenmaker, H. E.; Hiemstra, H.; Rutjes, F. P. J. T. *Org. Lett.* **2001,** *3*, 2045. (g) Evans, P.; Grigg, R.; Ramzan, M. I.; Sridharan, V.; York, M. *Tetrahedron Lett.* **1999**, *40*, 3021.

(14) (a) Donohoe, T. J.; Orr, A. J.; Gosby, K.; Bingham, M. *Eur. J. Org. Chem.* **2005**, 1969 (and references therein). (b) Evanno, L.; Nay, B.; Bodo, B. *Synth. Commun.* **2005**, *35*, 1559.

(15) We reported recently that regioselectivity in phosphite additions to α,β-unsaturated imines is very dependent on the type of reagent used: Moonen, K.; Van Meenen, E.; Verwée, A.; Stevens, C. V. *Angew. Chem., Int. Ed.* **2005**, *44*, 7407.

10.1021/jo060160e CCC: $33.50
Published on Web 04/11/2006

SCHEME 1

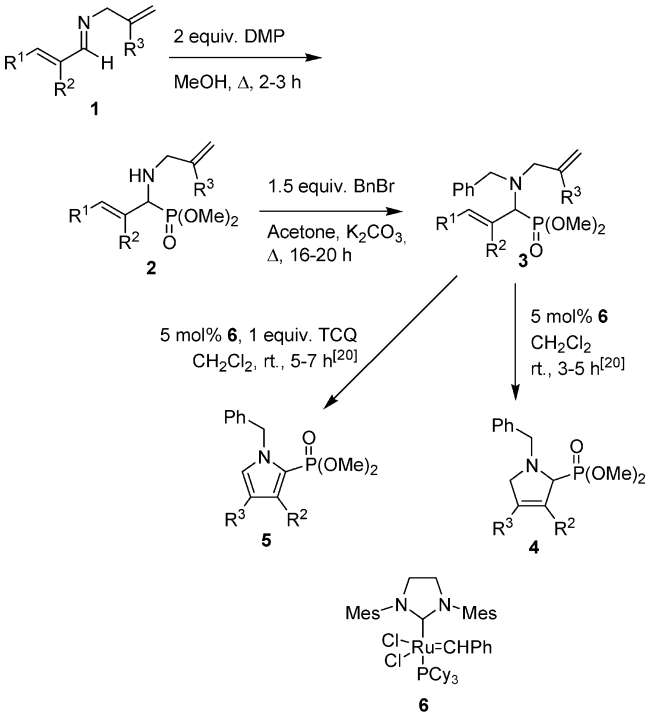


TABLE 1. Synthesis of Phosphonates 2−5

	R^1	R^2	R^3	**2**[a] (%)	**3**[b] (%)	**4**[a] **(%)**	**5**[b] (%)
a	Ph	H	H	95	61	44	75
b	Ph	Me	H	90	50	58	84
c	Me	Bn	H	27	50	62	72
d	Ph	isoamyl	H	88[c]	54[c]	70	70
e	Me	Ph	H	80[c]	35[c]	54[d]	75
f	Me	CH_2CH_2Ph	H	44	92		71
g	Ph	H	Me	74	86		

[a] Yield after acid/base extraction. [b] Yield after column chromatography. [c] Mixture of *E* and *Z* isomers. [d] Spontaneous oxidation to pyrrole **5e** using air was observed during workup.

(Scheme 1).[16] The α-aminoalkenyl phosphonates are obtained in high yield and purity after a simple acid/base extraction (Table 1). Benzylation was performed using 1.5 equiv of benzyl bromide in acetone and an excess of K_2CO_3 as a base. Complete conversion usually occurs in 16−20 h at reflux temperature, giving clean mixtures of *N*-benzylated phosphonates **3** and benzyl bromide. The reaction speed can be increased by adding catalytic amounts of sodium iodide (5−10 h) or by using microwave heating. Opposite to phosphonates **2**, *N*-benzylaminoalkenyl phosphonates **3** could not be isolated using an acid/base extraction, probably indicating decreased base characteristics of the substrate. The phosphonates **3** could be obtained in pure form via column chromatography; however, considerable product losses resulted.

The obtained aminoalkenyl phosphonates **3** were treated with Grubbs' second-generation catalyst **6**, and the reaction was easily monitored using ^{31}P NMR. Pyrrolines **4** were formed very smoothly at room temperature in dichloromethane as a single reaction product ($\delta^{31}P$ = 24.58−24.91 ppm). Most examples of azaheterocyclic ring formation via RCM presented in the literature deal with non-nucleophilic nitrogen groups (e.g., amides, carbamates, sulfonamides...).[12b,c,e] Failure of RCM reactions with substrates containing a nucleophilic nitrogen atom adjacent to the metathesized alkene is often attributed to poisoning of the catalyst or to disfavored conformation of the substrate.[17] The poisoning of the catalyst was possibly avoided in our case because of the presence of the electron-withdrawing phosphonate group, which reduced the nucleophilic properties of the amine.

Furthermore, in case of R^1 phenyl, styrene is formed during the ring-closing reaction, which unlike ethene does not boil off from the reaction mixture. Liberation of ethene from the reaction mixture is often indicated as the driving force in RCM reactions. A closer look to the crude ^1H NMR spectrum revealed, however, the presence of stilbene, which could also be obtained as colorless crystals from the reaction mixture. Stilbene is probably formed together with ethene via cross-metathesis of styrene in a second catalytic cycle (Scheme 2) and is easily removed during the subsequent chromatographic purification. It should be noted that two active species of the catalyst are present in the reaction mixture: carbene **9**, which is presented as the propagating species in the general Chauvin mechanism,[18] and Grubbs' carbene **8**, which is regenerated during the catalytic cycle in this case. While substituted double bounds are often not well tolerated by ruthenium-based catalysts,[19] R^1 (Ph or Me) and R^2 groups are very well tolerated in our case, even under very mild conditions. However, when phosphonate **3g** (R^3 = Me) was selected as a substrate in the RCM reaction, no reaction occurred at all and the starting material was recovered, even under reflux in CH_2Cl_2 or benzene. When switching to refluxing in chlorobenzene as a solvent, ^{31}P NMR showed the disappearance of the starting material and the simultaneous appearance of a signal at 10.4 ppm. Upon workup, this signal proved to be the corresponding enaminophosphonate resulting from the migration of the double bond toward the phosphonate. These observations indicated that the RCM reaction is most likely initiated via the least hindered double bond and that the following intramolecular conversions are less dependent on the steric bulk of the olefin. When two substituted double bonds are present in the molecule, the initiation seems to be delayed to such a large extent that no reaction is possible anymore.[19]

After complete conversion of the starting amino phosphonates **3** (3−5 h at room temperature),[20] the phosphonopyrrolines **4** could be obtained in pure form as a colorless oil via an acid/base extraction of the reaction mixture, which illustrated the basic properties of the pyrroline. Pyrroline **4f** could not be isolated. Instead, 1-benzyl-3-(2-phenylethyl)-1*H*-pyrrole was formed due to aromatization through elimination of the phosphonate group during workup. This side reaction was not observed in any of the other cases.

To obtain phosphonopyrroles **5**, the use of tetrachloroquinone (TCQ) has already proven effective in combination with catalyst

(16) Van Meenen, E.; Moonen, K.; Acke, D.; Stevens, C. V. *Arkivoc* **2006**, *i*, 31.

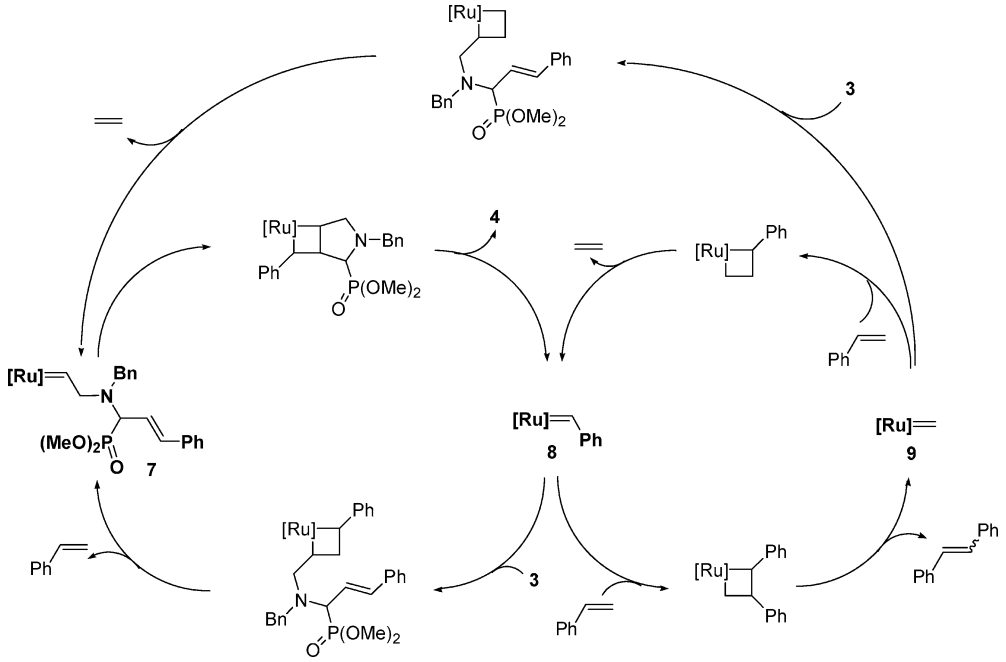
(17) (a) Yang, Q.; Xiao, W.-J.; Yu, Z. *Org. Lett.* **2005**, *7*, 871. (b) Le Flohic, A.; Meyer, C.; Cossy, J.; Desmurs, J.-R. *Tetrahedron Lett.* **2003**, *44*, 8577. (c) Briot, A.; Bujard, M.; Gouverneur, V.; Nolan, S. P.; Mioskowski, C. *Org. Lett.* **2000**, *2*, 1517. (d) Fürstner, A.; Thiel, O. R.; Ackermann, L.; Schanz, H.-J.; Nolan, S. P. *J. Org. Chem.* **2000**, *65*, 2204. (e) Campagne, J.-M.; Ghosez, L. *Tetrahedron Lett.* **1998**, *39*, 6175. (f) Rutjes, F. P.; Schoemaker, H. E. *Tetrahedron Lett.* **1997**, *38*, 677. (g) Shon, Y.-S.; Lee, T. R. *Tetrahedron Lett.* **1997**, *38*, 1283.

(18) Hérisson, J.-L.; Chauvin, Y. *Macromol. Chem.* **1971**, *141*, 161.

(19) Wallace, D. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 1912 and references therein.

(20) In case of phosphonate **3e**, complete conversion to pyrroline **4e** needed 3 h at reflux temperature. Complete conversion to pyrrole **5e** was obtained after 5 h at reflux followed by 12 h at room temperature.

SCHEME 2

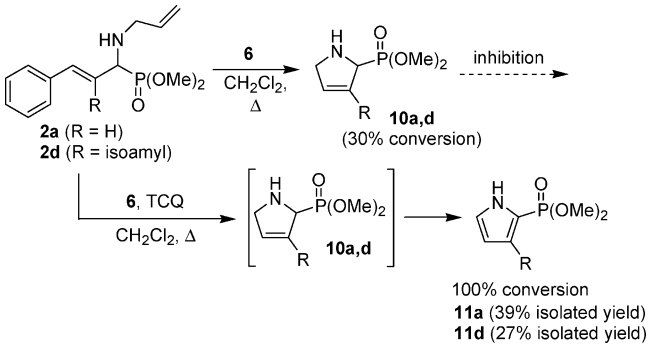


6.[21] When phosphonates **3** are treated with catalyst **6** and 1 equiv of TCQ, the expected pyrroles **5** are formed as a single reaction product ($\delta^{31}P = 13-15$ ppm) after stirring for up to 16 h at room temperature. By monitoring the reaction using ^{31}P NMR, a minor decrease of the RCM reaction rate was observed by the action of TCQ. When catalyst **6** was allowed to react for 2 h with the substrate (giving approximately 60% conversion to the pyrroline) before the addition of TCQ, the pyrroles were obtained after 5−7 h at room temperature.[20]

A mechanism for this ring-closing metathesis with in situ oxidative aromatization has already been proposed before.[21] No ruthenium is really required for the oxidation,[22] as pure **4b** and **4c** are also converted to the corresponding pyrroles **5b**,**c** by stirring with TCQ at room temperature for 22 h. However, this is considerably slower than in the presence of catalyst **6**. Two reaction pathways may be considered to explain these results: (a) hydrogen atoms are transferred in the process of oxidative addition and reductive elimination which involves hydride complexes or (b) hydrogen donor and acceptor are brought together by simultaneous coordination to the central metal of the catalyst, followed by direct transfer of the hydrogen atoms from the pyrroline to the TCQ.[23] In light of the mild reaction conditions in combination with the fact that no pyrrole formation is observed in the absence of TCQ, the assumption that hydrogens are transferred via pathway (b) seems to be reasonable.

With these excellent RCM results in hand, we tried to ring close phosphonates **3a** and **3d** possessing a free NH group.

SCHEME 3



When the reaction was monitored using ^{31}P NMR, decreasing reaction rates were observed in connection to reaction time, and a maximum conversion of only 30% was reached. This kind of behavior suggests catalyst inhibition by the pyrroline **10a**,**d** rather than by the starting material **2a**,**d** (Scheme 3). When TCQ was added together with catalyst **6**, the formed pyrroline was oxidized immediately in the reaction mixture, and 100% conversion to the pyrrole **11a**,**d** took place at reflux temperature in dichloromethane in 23 h or in benzene in 7 h. The reaction mixture was much less clean than in the case of the *N*-benzyl substrates **3**, and pyrroles **11** could only be obtained in low yields after a laborious chromatographic purification. Nevertheless, the reaction sequence clearly illustrates the synergism between ruthenium mediated ring-closing metathesis and oxidation by TCQ. Furthermore, the failure of RCM reactions with substrates containing a NH functionality should be attributed to its nucleophilic properties rather than to the need of a proper conformation for ring closure.

In conclusion, we have presented an interesting pathway toward functionalized 2-phosphonopyrroles and pyrrolines. Phenyl-substituted alkenes can be used in the RCM reaction, giving rise to the formation of styrene and stilbene as side products. The nucleophilic nitrogen atom in the substrates **3** is very well tolerated by the catalyst. Furthermore, an opportunistic

(21) Dieltiens, N.; Stevens, C. V.; Allaert, B.; Verpoort, F. *Arkivoc* **2005**, *i*, 92.

(22) (a) Dieltiens, N.; Stevens, C. V.; De Vos, D.; Allaert, B.; Drozdzak, R.; Verpoort, F. *Tetrahedron Lett.* **2004**, *45*, 8995. (b) Cren, S.; Wilson, C.; Thomas, N. R. *Org. Lett.* **2005**, *7*, 3521.

(23) Nishiguchi, T.; Kurooka, A.; Fukuzumi, K. *J. Org. Chem.* **1974**, *39*, 2403.

(24) % conversion to the pyrrole was observed using ^{31}P NMR. Yields reported are isolated yields (after column chromatography). Pyrrole **10d** could only be obtained in 90% purity.

(25) Takabe, K.; Fujiwara, H.; Katagiri, T.; Tanaka, J. *Tetrahedron Lett.* **1975**, 1237.

synergism exists between catalyst **6** and oxidant TCQ, which allows the conversion of NH containing substrates to the corresponding pyrroles. To the best of our knowledge, this is the first example of RCM using the second-generation Grubbs' catalyst on secondary free amines without the need to convert them to a hydrochloride salt. We are currently planning to broaden the scope of this reaction to include substrates suitable for enyne metathesis.

Experimental Section

Synthesis *N*-Benzyl α-Aminoalkenyl Phosphonates 3. To a round-bottom flask was added 3.1 mmol of α-aminoalkenyl phosphonate **2** together with 3 g of K_2CO_3, 0.23 g (1.5 mmol) of NaI, and 4 mL of acetone. Then, 0.79 g (4.65 mmol) of benzyl bromide was added, and the mixture was refluxed for 5−10 h. The course of the reaction was conveniently monitored via ^{31}P NMR spectra directly from the reaction mixture. After complete conversion of the starting material, the solids were removed by filtration and the solvent by evaporation under reduced pressure. The corresponding *N*-benzyl α-aminoalkenyl phosphonate **3** was obtained in pure form as a pale yellow oil after column chromatography over silica gel using a hexane/ethyl acetate mixture as a mobile phase.

Dimethyl (2*E*)-1-(Allyl(benzyl)amino)-3-phenylprop-2-enylphosphonate (3a). ^{1}H NMR δ (300 MHz, ppm): 3.10 (1H, dd, J_{AB} = 14.0 Hz, J = 7.7 Hz); 3.51 (1H, d, J_{AB} = 13.8 Hz); 3.63−3.68 (1H, multiplet); 3.68 (3H, d, J_{H-P} = 10.5 Hz); 3.85 (3H, d, J_{H-P} = 10.7 Hz); 3.85 (1H, dd, J_{H-P} = 24.2 Hz, J = 9.1 Hz); 4.22 (dd, J_{AB} = 13.8 Hz, J = 1.9 Hz); 5.19−5.29 (2H, multiplet); 5.79−5.93 (1H, multiplet); 6.37 (1H, ddd, J_{trans} = 16.7 Hz, J = 9.1 Hz, J_{H-P} = 6.3 Hz); 6.60 (1H, J_{trans} = 15.7 Hz, J_{H-P} = 3.03 Hz); 7.20−7.45 (10H, multiplet). ^{13}C NMR δ (75 MHz, ppm): 52.7 (d, J_{C-P} = 6.9 Hz); 53.7 (d, J_{C-P} = 6.9 Hz); 54.3 (d, J_{C-P} = 6.9 Hz); 55.2 (d, J_{C-P} = 8.4 Hz); 59.5 (d, J_{C-P} = 160.4 Hz); 117.7; 119.8; 126.7; 127.1; 128.1; 128.3; 128.5; 128.7; 128.8; 129.0; 136.3; 136.4; 137.0 (d, J_{C-P} = 6.9 Hz); 139.4. ^{31}P NMR δ (121 MHz, ppm): 27.11. IR ν_{max} (cm^{-1}): 1642, 1601 (C═C); 1243 (P═O); 1039 (br, P−O). MS *m*/*z*: 262 (13); 372 ([M + H]$^+$, 100). Chromatography: Hex/EtOAc (3/4) R_f = 0.26. Yield: 61%.

Synthesis of 2-Phosphono-3-pyrrolines 4. To an oven-dried round-bottom flask was added 0.34 mmol of aminoalkenyl phosphonate **3** together with 4 mL of dry dichloromethane. The solution was stirred under a nitrogen atmosphere, and 14.4 mg (5 mol %) of Grubbs' second-generation catalyst **6** was added. The reaction mixture was then stirred for 3−5 h at room temperature, depending on the derivative used. The course of the reaction was conveniently monitored via ^{31}P NMR spectra of samples directly from the reaction mixture. Only in the case of phosphonate **3e** did complete conversion to pyrroline **4e** require 3 h at reflux temperature. The reaction mixture was then poured into a separatory funnel containing 5 mL of 1 N $HCl_{(aq)}$. After vigorous shaking and phase separation, the organic layer was removed from the funnel. The remaining aqueous layer was washed twice with 2 mL of dichloromethane, neutralized until slightly alkaline, and extracted twice with 4 mL of dichloromethane. The combined organic phases were dried using $MgSO_4$. The corresponding pyrrolines **4** were obtained as clear, colorless oils after filtration and evaporation of the solvent.

Dimethyl 1-Benzyl-2,5-dihydro-1*H*-pyrrol-2-ylphosphonate (4a). ^{1}H NMR δ (300 MHz, ppm): 3.29−3.43 (1H, multiplet); 3.65 (1H, d, J_{AB} = 13.5 Hz); 3.71−3.80 (1H, multiplet); 3.80 (3H, d, J_{H-P} = 10.2 Hz); 3.83 (3H, d, J_{H-P} = 10.2 Hz); 4.09−4.16 (1H, multiplet); 5.74−5.92 (1H, multiplet); 5.87−5.92 (1H, multiplet); 7.22−7.38 (5H, multiplet). ^{13}C NMR δ (75 MHz, ppm): 53.1 (d, J_{C-P} = 8.1 Hz); 53.7 (d, J_{C-P} = 6.9 Hz); 60.1 (d, J_{C-P} = 5.8 Hz); 60.53 (d, J_{C-P} = 8.1 Hz); 68.4 (d, J_{C-P} = 176.5 Hz); 124.0 (d, J_{C-P} = 5.8 Hz); 127.0; 128.3; 128.6; 130.2 (d, J_{C-P} = 12.7 Hz); 139.2. ^{31}P NMR δ (121 MHz, ppm): 24.58. IR ν_{max} (cm^{-1}): 1246 (P═O); 1058, 1031 (P−O). MS *m*/*z*: 268 (100, [M + H]$^+$, 158 (18, [M + H − PO(OMe)$_2$]$^+$). Yield: 44%.

Synthesis of 2-Phosphonopyrroles 5. To an oven-dried round-bottom flask was added 0.39 mmol of aminoalkenyl phosphonate **3** together with 4 mL of dry dichloromethane. The solution was stirred under a nitrogen atmosphere, and 16.4 mg (5 mol %) of Grubbs' second-generation catalyst **6** was added. The reaction mixture was then stirred for 2 h at room temperature, giving approximately 60% conversion to the pyrroline. Then 94.8 mg (0.39 mmol) of TCQ was added, and stirring was continued for 3−5 h at room temperature. The course of the reaction was conveniently monitored via ^{31}P NMR spectra of samples directly from the reaction mixture. In case of phosphonate **3e**, complete conversion to pyrrole **5e** was only obtained after 5 h at reflux. When complete conversion was obtained, the solvent was removed under reduced pressure. The pyrroles **5** were obtained in pure form as brownish oils using column chromatography on silica gel with a hexane/ethyl acetate mixture as a mobile phase.

Dimethyl 1-Benzyl-1*H*-pyrrol-2-ylphosphonate (5a). ^{1}H NMR δ (300 MHz, ppm): 3.60 (6H, d, J_{H-P} = 11.6 Hz); 5.36 (2H, s); 6.22−6.26 (1H, multiplet); 6.86−6.89 (1H, multiplet); 6.90−6.94 (1H, multiplet); 7.10−7.34 (5H, multiplet). ^{13}C NMR δ (75 MHz, ppm): 52.4; 52.8 (d, J_{C-P} = 4.6 Hz); 109.1 (d, J_{C-P} = 13.8 Hz); 117.6 (d, J_{C-P} = 227.3 Hz); 122.5 (d, J_{C-P} = 17.3 Hz); 127.2; 127.7; 128.7; 129.0 (d, J_{C-P} = 11.5 Hz); 137.9. ^{31}P NMR δ (121 MHz, ppm): 13.63. IR ν_{max} (cm^{-1}): 1250 (P═O); 1029 (br, P−O). MS *m*/*z*: 266 (100, [M + H]$^+$). Chromatography: Hex/EtOAc (2/3) R_f = 0.26. Yield: 75%.

Acknowledgment. We thank the Fund for Scientific Research Flanders (FWO Vlaanderen) and Ghent University (BOF) for financial support.

Supporting Information Available: Spectral data of compounds **2b**−**g**, **3b**−**g**, **4b**−**e**, **5b**−**f**, and **11a**,**d** are reported together with copies of their ^{13}C spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060160E