A Highly Efficient and Practical Synthesis of Cyclic Phosphinates Using Ring-Closing Metathesis

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Structural mimics of key intermediates and transition states have been extensively used to study and regulate important metabolic processes. Recently, cyclic phosphinic acids which are nonhydrolyzable and isoteric analogues of naturally occurring cyclic phosphodiesters have attracted much attention as mimics of adenosine monophosphate (cAMP), guanosine monophosphate (cGMP), or inositol-1,2-cyclic monophosphates.[1] In addition, these cyclic phosphodiesters mimics can be employed as transition states analogues for antibodies production or as potent enzyme inhibitors.[2]

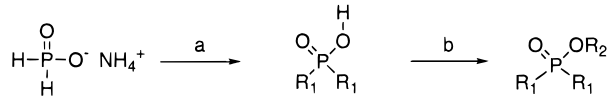
As part of our program aimed at synthesizing new transition state analogues for eliciting catalytic antibodies, we became interested in differently substituted cyclic phosphinic esters. A survey of the literature revealed that there were only a few methods for the synthesis of cyclic phosphinates,[3] and many of them suffered from either lack of generality or low yields and used conditions that were not compatible with the presence of various functional groups. In this paper, we report a novel and highly efficient procedure for preparing a number of diverse cyclic phosphinates using ring-closing metathesis (RCM), a methodology emerging as a new tool in synthetic organic chemistry.[4]

Results and Discussion

Substrate Synthesis. A series of symmetrical and unsymmetrical dienes having a phosphinate moiety was easily prepared in good yields from the corresponding phosphinic acids. The symmetrical phosphinic acids **1a**, **1c**, and **1d** (Scheme 1, method A) were prepared, according to a known procedure,[5] using a one-pot intermolecular Arbusov-type reaction between bis(trimethylsilyloxy)-phosphine (BTSP), generated in situ from ammonium phosphinate and hexamethyldisilazane (HMDS), and the corresponding alkyl or allyl halide. The conversion of the phosphinic acids **1a**, **1c**, and **1d** into the desired phosphinates **2a**, **2c**, and **2d** was achieved by esterification with the corresponding alcohol in the presence of triethylamine, after activation of the phosphinic acids with oxalyl chloride.[6] The preparation of unsymmetrical phosphinic acids (Scheme 1, method B) using the sequential addition of two different alkyl halides, as previously described in the literature,[5] proved problematic as mixtures of both unsymmetrical and the undesired symmetrical phosphinic acids were always obtained. However, these two products were easily separated by column chromatography following esterification with the desired alcohol to provide the analytically pure unsymmetrical phosphinates **2e**−**2g**. Dienes **2h** and **2i** were prepared by alkylation at low temperature of the corresponding phosphinates **2b** and **2a** (Scheme 2).[7]

Scheme 1. Preparation of Dienes 2a−2g

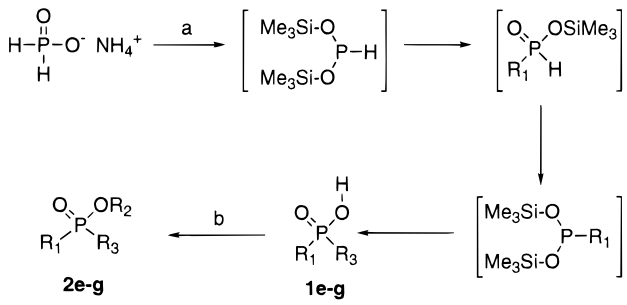
Method A: Symmetrical Phosphinates



R_1= $CH_2CH{=}CH_2$, R_2= Bn	**1a** yield: 62%	**2a** yield: 55%
R_1= $CH_2CH{=}CH_2$, R_2=Et	**1a** yield: 62%	**2b** yield: 51%
R_1= $CH_2CH_2CH{=}CH_2$, R_2= Bn	**1c** yield: 18%	**2c** yield: 55%
R_1= $CH_2C(CH_3){=}CH_2$, R_2= Bn	**1d** yield: 71%	**2d** yield: 70%

(a): 2eq HMDS, 4eq R_1X, toluene, reflux then HCl / MeOH; (b): $(COCl)_2$ then Et_3N, 1eq. R_2OH

Method B: Unsymmetrical Phosphinates



R_1= $CH_2CH_2CH{=}CH_2$, R_3= $CH_2CH{=}CH_2$, R_2= Bn	**2e** yield: 60%
R_1= $CH_2CH{=}CH_2$, R_3= $CH_2C(CH_3){=}CH_2$, R_2= Bn	**2f** yield: 17%
R_1= $CH_2CH{=}CH_2$, R_3= $CH_2C(Ph){=}CH_2$, R_2= Bn	**2g** yield: 58%

(a) 1eq HMDS, neat 110°C; then1eq. R_1X, 12h; then 0°C, 1eq. HMDS, 2h; then1eq R_3X, rt, 12h; then HCl/MeOH (b): $(COCl)_2$ thenEt_3N, 1eq. R_2OH

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(1) Montchamp, J.-L.; Frost, J. W. *J. Org. Chem.* **1994**, *59*, 7596. Richard, J. P. *J. Am. Chem. Soc.* **1984**, *106*, 4926. Periana, R. A.; Motiu-DeGrood, R.; Chiang, Y.; Hupe, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 3923.

(2) Campbell, M. M.; Carruthers, N. I.; Mickel, S. J.; Winton, P. M. *J. Chem. Soc., Chem. Commun.* **1984**, 200. Gibbs, R. A.; Taylor, S.; Benkovic, S. J. *Science* **1992**, *258*, 803. Currie, M.; Suckling, C. J.; Zhu, L.-M.; Irvine, J.; Stimson, W. H. *Tetrahedron* **1995**, *51*, 8915.

(3) Montchamp, J.-L.; Tian, F.; Frost, J. W. *J. Org. Chem.* **1995**, *60*, 6076 and references therein.

(4) For recent synthetic applications of RCM, see: (a) Crimmins, M. T.; King, B. W. *J. Org. Chem.* **1996**, *61*, 4192. (b) Yang, Z.; He, Y.; Vourloumis, D.; Vallberg, H.; Nicolaou, K. C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 166. (c) Meng, D.; Su, D.-S.; Balog, A.; Bertinato, P.; Sorensen, E. J.; Danishefsky, S. J.; Zheng, Y.-H.; Chou, T.-C.; He, L.; Horwitz, S. *J. Am. Chem. Soc.* **1997**, *119*, 2733.

(5) Boyd, E. A.; Regan, A. C. *Tetrahedron Lett.* **1994**, *35*, 4223. Majewski, P. *Phosphorus, Sulfur, Silicon* **1989**, *45*, 151.

(6) Froneman, M.; Modro, T. A. *Synthesis* **1991**, 201.

(7) Liotta, L. J.; Gibbs, R. A.; Taylor, S. D.; Benkovic, P.; Benkovic, S. J. *J. Am. Chem. Soc.* **1995**, *117*, 4729. Phillips, A. M.; Modro, T. A. *Phosphorus, Sulfur, Silicon* **1991**, *55*, 41.

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Scheme 2. Preparation of Dienes 2h and 2i

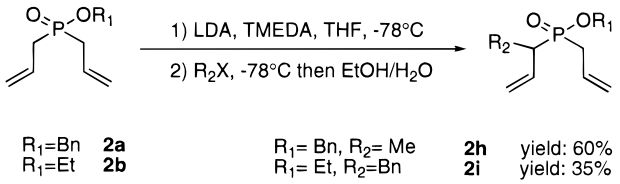
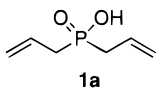
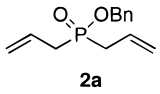
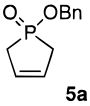
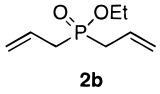
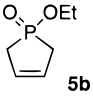
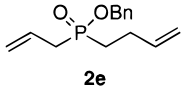
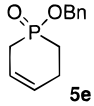
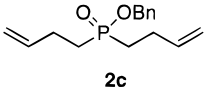
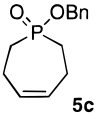
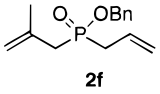
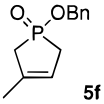
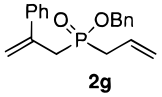
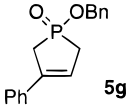
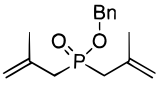
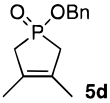
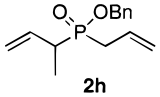
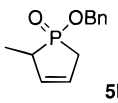
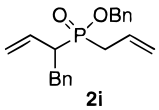
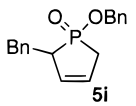


Table 1. Catalytic Ring-Closing Metathesis of Dienes 1a and 2a−2i with (2.5-3%) Alkylidene 3 (0.02 M CH_2Cl_2)

Entry	Substrate	Product	Yield [a]
1	 **1a**		No RCM[b] product
2	 **2a**	 **5a**	80%
3	 **2b**	 **5b**	80%
4	 **2e**	 **5e**	96%
5	 **2c**	 **5c**	97%
6	 **2f**	 **5f**	50%
7	 **2g**	 **5g**	No RCM[b] product
8	 **2d**	 **5d**	No RCM[b] product
9	 **2h**	 **5h**	77%
10	 **2i**	 **5i**	66%

[a] Isolated yield. [b] 100% recovered starting material.

RCM of Phosphinic Esters. The ring-closing metathesis of the acyclic dienes prepared above was achieved using catalytic ruthenium alkylidene **3** ($Cl_2(PCy_3)_2$-Ru=CHPh). [8] Table 1 summarizes the results.

Preliminary experiments showed that ruthenium alkylidene **3** was unable to catalyze the RCM of the diene **1a** which contains an unprotected phosphinic acid moiety (entry 1, Table 1). However, when a solution of the corresponding benzyl phosphinate **2a** in dichloromethane[9] (0.02 M) was heated at reflux in the presence of 2.5 mol % of **3**, the desired five-membered cyclic phosphinate **5a** was obtained in 80% isolated yield with no side products detected (entry 2, Table 1).[10] In addition, RCM was found to proceed with equal efficiency with the ethyl ester derivative **2b**, affording the ethyl phosphinate **5b** in an identical yield (80%) (entry 3, Table 1). Once it had been established that formation of a cyclic phosphinate with **3** was feasible, attention was turned toward the effect of ring size and the olefinic substituent.

Under the above metathesis conditions, the formation of both six- and seven-membered cyclic phosphinates **5e** and **5c** with alkylidene **3** was completed in very high yields and did not require extended reaction time compared to the formation of the five-membered product **5a** or **5b** (entries 4 and 5, Table 1).

The ring-closing metathesis can be extended to include both α- and *β*-substituted phosphinate dienes, however at the expense of reduced reactivity. Exposure of the methyl *β*-substituted diene **2f** to the alkylidene **3** yielded the expected five-membered cyclic phosphinate **5f** in only 50% yield (entry 6, Table 1). Similarly, alkylidene **3** showed no reaction with the phenyl-substituted diene **2g** or the *β*,*β*′-disubstituted diene **2d** over 5 days, supporting the hypothesis[11] that the combination of the steric effect of the substituent and the electron-withdrawing effect is unfavorable for promoting ring closure (entries 7 and 8, Table 1). Moreover, the data suggested that the steric influence on reactivity was less important for α-substituted phosphinates as exemplified with dienes **2h** and **2i**. Indeed, it was found that alkylidene **3** cyclized substrates **2h** and **2i** into the corresponding α-substituted heterocycles **5h** and **5i** in 77% and 66% yields, respectively (entries 9 and 10, Table 1).

The failure of ruthenium alkylidene **3** to promote the cyclization of the unprotected phosphinic acid **1a**, the hindered disubstituted diene **2d**, and the diene **2g** having the electron-withdrawing phenyl group at the *β*-position encouraged us to explore the use of the more reactive molybdenum alkylidene **4**[12] in an attempt to improve reactivity. Disappointingly, under a modified RCM condition of 0.02 M in toluene at 60 °C with 6−8 mol % of molybdenum catalyst **4**, there was no significant improvement in the reaction profile between the two catalysts as both afforded similar yields and reactivities for the substrates examined (Table 2).

However, the ruthenium alkylidene **3** is a much more convenient catalyst to use in the RCM since it does not require rigorous purification, drying, and degassing of substrates as seen with the more sensitive molybdenum alkylidene **4**.

(8) Schwab, P. E.; Grubbs, R. H.; Ziller, Z. W. *J. Am. Chem. Soc.* **1996**, *118*, 100.

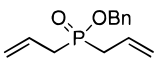
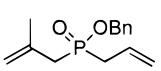
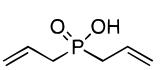
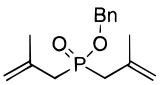
(9) CH_2Cl_2 was chosen as the optimal solvent for the reactions with **3** based on lower overall conversion obtained in benzene. When the reaction was carried out at room temperature, the RCM of substrate **2a** was slower and the overall conversion of **2a** into **5a** after 15 h did not go beyond 38%.

(10) The NMR analysis of the crude mixtures show only the desired cyclized product and the starting material with no side products. No trace of dimers was detected.

(11) Kirkland, T. A.; Grubbs, R. H. *J. Org. Chem.* **1997**, *62*, 7310.

(12) 2,6-Diisopropylphenyl**imidoneo**phylidene molybdenum(VI) bis-(hexafluoro-*tert*-butoxide) was used as the catalyst: Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O′ Regan, M.; Schrock, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 3875.

Table 2. Catalytic Ring-Closing Metathesis of Dienes 1a and 2a, 2d and 2f with 6−8% Alkylidene 4 (0.02 M Toluene)

Entry	Substrate	Product	Yield [a]
1	 **2a**	 **5a**	80%
2	 **2f**	 **5f**	50%
3	 **1a**		No RCM [b] product
4	 **2d**	 **5d**	No RCM [b] product

[a] Isolated yield. [b] 100% recovered starting material.

Conclusions

The efficiency of the catalytic ring-closing metathesis combined with the ease of preparation of the dienes makes this methodology an attractive alternative to the formation of differently substituted five-, six-, and seven-membered phosphinates. This is the first report related to the metathesis of dienes including a phosphinate function. During the course of our studies, RCM on a phosphonate template was described in the literature.[13] Further work is presently underway in our laboratory to extend this novel strategy to the synthesis of more functionalized and biologically active phosphorus containing heterocycles.

Experimental Section

General Methods. Mass spectra were performed by A. Valleix (CEA, Saclay) and the high-resolution mass spectra by P. Guenot (Université de Rennes I). ^{31}P NMR spectra were recorded using phosphoric acid (80%) as external reference. Ammonium phosphinate[14] was prepared as described in the literature. Alkylidenes **3** and **4** were purchased from Strem. The reactions with the air-sensitive Schrock's catalyst were carried out in a glovebox using dried and degassed substrates and solvents. Although the methodology presented here relies on in situ generation of BTSP, caution should still be exercised since neat BTSP is highly pyrophoric.

General Procedure for Preparation of Symmetrical Phosphinic Acids (Method A). A solution of 1 equiv of ammonium phosphinate, 2 equiv of HMDS, and 4 equiv of alkyl bromide (or triflate) in toluene was refluxed overnight. After cooling, the white precipitate (ammonium salt) was filtered over Celite and washed with CH_2Cl_2. The filtrate was concentrated and the residue treated with a 1:1 mixture of MeOH and CH_2Cl_2 for 15 min. The solution was evaporated, and the residual oil was dissolved in CH_2Cl_2 and washed with 4 N HCl. After concentration of the organic phase, the residual oil was used without further purification in the next step. However, it could be purified by column chromatography.

Diallylphosphinic acid (1a):[15] 12.6 mL (60 mmol) of HMDS, 2.5 g (30 mmol) of $H_2PO_2^-$ NH_4^+, 10.1 mL (120 mmol) of allyl bromide, 60 mL of toluene; yield 3.1 g (71%); pale yellow oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 6.48 (br s, 1H), 5.91−5.71 (m, 2H), 5.28−5.17 (m, 4H), 2.62 (d × d, J = 18.1, J = 7.8, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 127.6 (d, J = 8.7), 120.5 (d, J = 13.1), 33.9 (d, J = 90.1); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 51.6; IR (neat, cm^{-1}) 1638, 1232, 1160, 1058, 975, 919; MS (CI, NH_3) 147 (M + H^+), 164 (M + NH_4^+).

Dibut-3-enylphosphinic acid (1c): 4.9 mL (23.4 mmol) of HMDS, 0.97 g (11.7 mmol) of $H_2PO_2^-$ NH_4^+, 2.4 mL (23.4 mmol) of 4-bromo-but-1-ene, 20 mL of toluene; yield 0.35 g (18%); pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.87 (d × d × t, 2H, J = 16.9, J = 10.5, J = 6.2), 5.4 (br s, 1H), 5.09 (d × d, J = 16.9, J = 1.5, 2H), 5.03 (d × d, J = 10.3, J = 1.5, 2H), 2.37(m, 4H), 1.82(m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.3 (d, J = 16.0), 115.3, 28.3 (d, J = 91.5), 25.6 (d, J = 2.9); IR (neat, cm^{-1}) 1641, 1163, 988, 975, 913; MS (CI, NH_3) 175 (M + H^+).

Bis(2-methylallyl)phosphinic acid (1d): 4 mL (19 mmol) of HMDS, 0.8 g (9.6 mmol) of $H_2PO_2^-$ NH_4^+, 3.9 mL (38 mmol) of 3-bromo-2-methylpropene, 20 mL of toluene; yield 1.2 g (71%); colorless solid (mp 75−76 °C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.99−4.87 (m, 4H), 4.43 (br s, 1H), 2.60 (4H, d, J = 17.1 Hz), 1.91 (br s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.6 (d, J = 10.2), 115.7 (d, J = 11.6), 37.9 (d, J = 88.6), 24.0; ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 51.2; IR(neat, cm^{-1}) 2246, 1646, 1175, 1120, 956, 891; MS (CI, NH_3) 175 (M + H^+), 192 (M + NH_4^+).

General Procedure for Preparation of Unsymmetrical Phosphinic Acids (Method B). A mixture of 1.2 equiv of ammonium phosphinate and 1.2 equiv of HMDS was heated at 110 °C for 2 h. After the solution was cooled at 0 °C, CH_2Cl_2 was added all at once and then the less reactive alkyl halide was introduced. The reaction was allowed to warm to room temperature. After 12 h of stirring, the reaction was cooled at 0 °C and 1 equiv of HMDS was added at once. After stirring for 2 h at 0 °C, 1 equiv of the second alkyl halide was added at that temperature. After stirring for another 12 h at room temperature, the mixture was filtered on Celite. The filtrate was concentrated and the residual oil dissolved in CH_2Cl_2 and washed with 4 N HCl. After concentration of the organic phase, the residual oil was used without further purification for the esterification.

Allylbut-3-enylphosphinic acid (1e): 4.2 mL (20 mmol) of HMDS, 1.7 g (20 mmol) of $H_2PO_2^-$ NH_4^+; 2.5 g (12 mmol) of but-3-enyl triflate; then 2.5 mL (12 mmol) of HMDS, 1.7 mL (20 mmol) of allyl bromide; yield 2.1 g of a nonseparable mixture of **1a** and **1e** (ratio 3/7); ^{1}H NMR ($CDCl_3$, 300 MHz) (deduced from the mixture) δ 5.91−5.74 (m, 2H), 5.31−5.01 (m, 4H), 2.65 (d × d, J = 17.7, J = 7.53, 2H), 2.43−2.32 (m, 2H), 1.90−1.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) (deduced from the mixture) δ 137.1 (d, J = 14.5), 127.2 (d, J = 10.1), 120.8 (d, J = 13.1), 34.9 (d, J = 88.6), 26.8 (d, J = 93.0), 25.4 (d, J = 4.4).

Allyl(2-methylallyl)phosphinic acid (1f): 5.1 mL (24.1 mmol) of HMDS, 2.0 g (24.1 mmol) of $H_2PO_2^-$ NH_4^+; 2 mL (19.8 mmol) of 3-bromo-2-methylpropene; then 4.2 mL (19.8 mmol) of HMDS, 1.7 mL (19.8 mmol) of allyl bromide; yield 2.0 g of a nonseparable crude mixture of **1d** and **1f** (ratio 2/8); ^{1}H NMR ($CDCl_3$, 200 MHz) (deduced from the mixture) δ 5.83 (m, 1H), 5.25−5.11 (m, 2H), 4.96−4.86 (m, 2H), 2.55 (d, J = 17.5, 2H), 2.60 (d × d, 2H), 1.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) (deduced from the mixture) δ 136.9 (d), 128.3 (d, J = 8.7), 120.0 (d, J = 13.1), 115.4, 37.5 (d, J = 88.6), 34.5 (d, J = 90.1).

Allyl(2-phenylallyl)phosphinic acid (1g): 5.0 mL (24.0 mmol) of HMDS, 2.0 g (24.0 mmol) of $H_2PO_2^-$ NH_4^+; 0.48 g (2.4 mmol) of 1-bromo-2-phenylprop-2-ene; then 1 mL (5 mmol) of HMDS, 4 mL (48 mmol) of allyl bromide; yield 1.4 g of a nonseparable mixture of **1a** and **1g** (ratio 75/25); ^{1}H NMR ($CDCl_3$, 300 MHz) (deduced from the mixture) δ 7.48−7.30 (m, 5H), 5.82 (m, 1H), 5.53 (d, J = 4.9, 1H), 5.37 (d, J = 4.9, 1H), 5.12 (m, 2H), 3.05 (d, J = 17.3, 2H), 2.52 (d × d, J = 17.7, J = 7.5, 2H).

General Procedure for Preparation of Phosphinates 2a−2g. To a solution of 1 equiv of phosphinic acid and a catalytic amount of DMF (2 drops) in benzene or dichloromethane at 0 °C was added dropwise 3 equiv of oxalyl chloride. After addition, the mixture was allowed to warm to room temperature. After 1 h, the reaction was concentrated and the crude phosphinic acid chloride was used without further purification in the next step. To a solution of the crude phosphinic acid chloride, a catalytic

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amount of DMAP (2 mol %), and 1.1 equiv of Et_3N in CH_2Cl_2 at −78 °C was added dropwise 1.1 equiv of the alcohol. The mixture was allowed to warm to room temperature. After 4 h, the mixture was evaporated and the residue treated with pentane. After filtration of the salts, the residue was purified by column chromatography.

Diallylphosphinic acid benzyl ester (2a): 2 g (13.5 mmol) of **1a**, 3.5 mL (40.5 mmol) of $(COCl)_2$; 2.1 mL (14.9 mmol) of Et_3N, 1.55 mL (14.9 mmol) of benzylic alcohol; column chromatography (ether); yield 1.8 g (55%); $R_f = 0.3$ (ether); pale yellow oil; ^{1}H NMR($CDCl_3$, 200 MHz) δ 7.41−7.38 (m, 5H), 5.82 (m, 2H), 5.26−5.14 (m, 4H), 5.08 (d, $J = 7.8$, 2H), 2.64 (d × d, $J = 17.4$, $J = 7.5$, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.6 (d, $J = 5.8$), 128.6, 128.4, 127.9, 127.5 (d, $J = 8.7$), 120.6(d, $J = 13.1$), 66.1 (d, $J = 7.3$), 33.8 (d, $J = 88.6$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +50.7; IR (neat, cm^{-1}) 1636, 1245, 1187, 1036, 1001; HRMS calcd for $C_{13}H_{17}O_2P$ ($M^{+\bullet}$) 236.0966, found 236.0963.

Diallylphosphinic acid ethyl ester (2b):[16] 1.5 g (10.3 mmol) of **1a**, 1.8 mL (20.6 mmol) of $(COCl)_2$; 1.7 mL (12.4 mmol) of Et_3N, 0.73 mL (12.4 mmol) of ethanol; column chromatography (hexane/AcOEt:60/40); yield 0.92 g (51%); $R_f = 0.23$ (AcOEt); pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.9−5.74 (m, 2H), 5.26−5.18 (m, 4H), 4.11 (d × q, $J = 7.5$, $J = 7.2$, 2H), 2.63 (d × d, $J = 17.3$, $J = 7.5$, 4H), 1.33 (t, $J = 7.2$, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 127.6 (d, $J = 8.7$), 120.3 (d, $J = 13.1$), 60.7 (d, $J = 5.8$), 33.6 (d, $J = 88.6$), 16.6 (d, $J = 5.8$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +49.4; IR (neat, cm^{-1}) 1637, 1246, 1186, 1037; HRMS calcd for $C_8H_{15}O_2P$ ($M^{+\bullet}$) 174.0810, found 174.0813.

Bis(but-3-enyl)phosphinic acid benzyl ester (2c): 0.28 g (1.6 mmol) of **1c**, 0.42 mL (4.8 mmol) of $(COCl)_2$, 5 mL of benzene; 0.25 mL (1.8 mmol) of Et_3N, 0.19 mL (1.8 mmol) of benzylic alcohol; column chromatography (ether); yield 0.23 g (55%); $R_f = 0.28$ (ether); yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.34 (m, 5H), 5.82 (d × d × t, $J = 17.0$, $J = 10.2$, $J = 6.4$, 2H), 5.08−4.99 (m, 4H), 5.05 (d, 2H, $J = 7.9$), 2.38−2.28 (m, 4H), 1.94−1.75 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 137.1 (d, $J = 16.0$), 136.8 (d, $J = 5.8$), 128.6, 128.3, 127.8, 115.3, 65.6 (d, $J = 5.8$), 27.7 (d, $J = 88.6$), 25.9 (d, $J = 2.9$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +57.7; IR (neat, cm^{-1}) 1640, 1232, 1197, 1000, 915; HRMS calcd for $C_{15}H_{21}O_2P$ ($M^{+\bullet}$) 264.1279, found 264.1278.

Bis(2-methylallyl)phosphinic acid benzyl ester (2d): 1 g (5.7 mmol) of **1d**, 1.5 mL (17.1 mmol) of $(COCl)_2$, 10 mL of CH_2Cl_2; 0.65 mL (6.3 mmol) of Et_3N, 0.88 mL (6.3 mmol) of benzylic alcohol; column chromatography (ether); yield 0.75 g (70%); $R_f = 0.35$ (ether); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4−7.32 (m, 5H), 5.09 (d, $J = 7.3$, 2H), 4.97 (d, $J = 4.0$, 2H), 4.88 (d, $J = 4.0$, 2H), 2.64 (d, $J = 16.8$, 4H), 1.9 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.8, 136.6 (d, $J = 8.7$), 128.5, 128.3, 127.9, 115.8 (d, $J = 11.6$), 66.2 (d, $J = 5.8$), 38.0 (d, $J = 85.7$), 24.1; ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +51.0; IR (neat, cm^{-1}) 1645, 1228, 1195, 1009, 892; HRMS calcd for $C_{15}H_{21}O_2P$ ($M^{+\bullet}$) 264.1279, found 264.1278.

Allylbut-3-enylphosphinic acid benzyl ester (2e): 2 g of a mixture of both phosphinic acids **1a** and **1e** (30:70) was used; 3.9 mL (45 mmol) of $(COCl)_2$, 25 mL of benzene; 3.2 mL (23 mmol) of Et_3N, 2.4 mL (23 mmol) of benzylic alcohol; column chromatography (hexane/EtOAc 1/1); yield of **2e** from $H_2PO_2^-$ NH_4^+ 1.6 g (60%); $R_f = 0.54$ (AcOEt); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.36 (m, 5H), 5.82 (m, 2H), 5.23−5.16 (m, 2H), 5.09−4.99 (m, 4H), 2.63 (d × d, $J = 17.2$, $J = 7.7$, 2H), 2.34 (m, 2H), 1.85 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.1 (d, $J = 16.0$), 136.7 (d, $J = 5.8$), 128.6, 128.4, 127.9, 127.8, 127.7 (d, $J = 8.7$), 120.3 (d, $J = 13.1$), 115.3, 65.9 (d, $J = 5.8$), 34.8 (d, $J = 85.7$), 26.9 (d, $J = 91.6$), 25.7 (d, $J = 2.9$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +54.3; IR (neat, cm^{-1}) 1638, 1242, 1214, 1189, 1036, 1008, 919; HRMS calcd for $C_{14}H_{19}O_2P$ ($M^{+\bullet}$) 250.1123, found 250.1115.

Allyl(2-methylallyl)phosphinic acid benzyl ester (2f): 2.0 g of a mixture of both phosphinic acids **1f** and **1d** (20:80) was used; 3.5 mL (40 mmol) of $(COCl)_2$, 25 mL of CH_2Cl_2; 2.8 mL (19.8 mmol) of Et_3N, 2.0 mL (19.8 mmol) of benzylic alcohol; column chromatography (ether); yield of **2f** from $H_2PO_2^-$ NH_4^+ 0.8 g (17%); $R_f = 0.4$ (ether); colorless oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.36 (m, 5H), 5.8 (m, 1H), 5.22 (d × d, 1H, $J = 6.1$, $J = 3.1$), 5.19 (d × d, 1H, $J = 16.1$, $J = 3.0$), 5.08 (d, $J = 7.5$, 2H), 4.97 (d, $J = 4.0$, 1H), 4.87 (d, $J = 4.0$, 1H), 2.65 (d × d, $J = 17.0$, $J = 7.5$), 2.61 (d, $J = 17.3$), 1.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ136.7, 136.5(d), 128.6, 128.3, 127.8, 127.7, 120.4 (d, $J = 13.1$), 115.9 (d, $J = 11.6$), 66.1 (d, $J = 7.3$), 37.6 (d, $J = 87.2$), 34.0 (d, $J = 88.6$), 24.0; ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +51.1; IR (neat, cm^{-1}) 1636, 1242, 1214, 1036, 1000, 918; HRMS calcd for $C_{14}H_{19}O_2P$ ($M^{+\bullet}$) 250.1123, found 250.1115.

Allyl(2-phenylallyl)phosphinic acid benzyl ester (2g): 1.4 g of a mixture of both phosphinic acids **1a** and **1g** (75:25) was used; 2.2 mL (40 mmol) of $(COCl)_2$, 20 mL of benzene; 2.5 mL (15 mmol) of Et_3N, 1.9 mL (15 mmol) of benzylic alcohol; column chromatography (ether); yield of **2g** from $H_2PO_2^-$ NH_4^+ 0.44 g (58%); $R_f = 0.3$ (ether); colorless oil; ^{1}H NMR($CDCl_3$, 300 MHz) δ 7.47−7.20 (m, 10H), 5.8 (m, 1H), 5.74 (m, 1H), 5.52 (d, $J = 4.9$, 1H), 5.34 (d, $J = 4.2$, 1H), 5.17 (m, 1H), 5.07 (m, 1H), 5.02 (d × d, $J = 11.6$, $J = 10.8$, 1H), 4.85 (d × d, $J = 11.7$, $J = 9.0$, 1H), 3.11 (d, $J = 15.8$, 2H), 2.56 (d × d, $J = 17.0$, $J = 7.5$, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.7, 138.9 (d, $J = 8.7$), 136.6 (d, $J = 5.8$), 128.5, 128.2, 127.9, 127.8, 127.5 (d, $J = 8.7$), 126.4, 120.5 (d, $J = 13.1$), 117.8 (d, $J = 10.2$), 66.1 (d, $J = 7.3$), 35.4 (d, $J = 71.2$), 34.3 (d, $J = 74.1$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +50.32; IR (neat, cm^{-1}) 1245, 1010, 920, 840−701; HRMS calcd for $C_{19}H_{21}O_2P$ ($M^{+\bullet}$) 312.1279, found 312.1280.

Allyl-l(1-methylallyl)phosphinic Acid Benzyl Ester (2h). To a solution of 0.3 g (1.27 mmol) of **2a** and 0.96 mL (6.35 mmol) of TMEDA in 1.6 mL of THF at −78 °C was added dropwise 1.4 mmol of LDA (0.85 M). After stirring for 5 min, 0.12 mL (1.9 mmol) of iodomethane was added slowly at −78 °C. After stirring for 15 min, the reaction mixture was quenched with EtOH/H_2O (2/1) at −78 °C. The mixture was treated with saturated NH_4Cl and extracted with AcOEt. After the usual workup, compound **2h** was purified by column chromatography (hexane/EtOAc 4/6); yield 0.19 g (60%); $R_f = 0.53$ (AcOEt); colorless oil; mixture of two diastereomers (75:25) (minor diastereomer is indicated with *) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37−7.29 (m, 5H), 5.99−5.75 (m, 1H), 5.24−5.14 (m, 4H), 5.02 (d, $J = 7.9$, 2H), 2.78−2.59 (m, 3H), 1.32 (d × d, $J = 16.6$, $J = 7.0$, 3H) (1.30*(d × d, $J = 16.9$, $J = 7.2$)); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.9 (d, $J = 5.8$) (136.8 *(d, $J = 4.3$)), 134.7 (d, $J = 7.3$) (134.4* (d, $J = 7.3$)), 128.6, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 120.3 (d, $J = 13.1$), 117.93 (d, $J = 11.6$) (117.89* (d, $J = 11.6$)), 66.3 (d, $J = 7.3$) (65.5*(d, $J = 5.8$)), 38.5 (d, $J = 88.6$) (38.3* (d, $J = 88.6$)), 32.4 (d, $J = 84.3$) (32.4* (d, $J = 84.3$)), 12.5 (d, $J = 4.3$) (12.3* (d, $J = 4.3$)); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +53.4; IR (neat, cm^{-1}) 1242, 1214, 1036, 1000, 918; HRMS calcd for $C_{14}H_{19}O_2P$ ($M^{+\bullet}$) 250.1123, found 250.1115.

Allyl(1-benzylallyl)phosphinic Acid Ethyl Ester (2i). Compound **2i** was prepared in a manner similar to that of **2h** using 0.2 g (1.15 mmol) of **2b**, 0.87 mL (5.7 mmol) of TMEDA, 1.3 mmol of LDA (0.85 M), 1.5 mL of THF, and 0.2 mL (1.7 mmol) of benzyl bromide. Compound **2i** was purified by column chromatography (hexane/EtOAc 3/7); yield 0.1 g (35%); $R_f = 0.33$ (AcOEt); colorless oil; mixture of two diastereomers (70:30) (minor diastereomer is indicated with *) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28−7.13 (m, 5H), 5.98−5.60 (m, 2H), 5.28−4.91 (m, 4H), 4.16 (d × t, $J = 7.3$, 2H) (4.14* (d × t, $J = 7.3$, 2H), 3.37−3.17 (m, 1H), 2.93−2.58 (m, 4H), 1.34 (t, $J = 7.3$, 3H) (1.33* (t, $J = 7.3$, 3H)); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.9 (d, $J = 14.5$), 133.0 (d, $J = 8.7$) (132.5* (d, $J = 5.8$)), 129.07 (129.01*), 128.2, 127.7 (d, $J = 8.7$)126.3, 120.6, 120.4, 120.3, 120.2, 120.1, 120.0, 61.1 (d, $J = 7.3$) (60.69* (d, $J = 7.3$)), 46.5 (d, $J = 88.6$) (46.1* (d, $J = 90.1$)), 33.1, 33.0, 32.8 (d, $J = 87.2$) (32.7* (d, $J = 85.7$), 16.7 (d, $J = 5.8$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +50.79 (+50.88*); IR (neat, cm^{-1}) 1636, 1236, 1199, 1037, 952, 918−700; HRMS calcd for $C_{15}H_{21}O_2P$ ($M^{+\bullet}$) 264.1279, found 264.1278.

General Procedure of Ring-Closing Metathesis of Dienes 2a−2h Using Alkylidene 3. To a solution of the diene in dry CH_2Cl_2 was added catalyst **3**. The reaction mixture was refluxed, and the disappearance of the starting material was monitored by TLC. The reaction was concentrated and purified on silica gel.

General Procedure of Ring-Closing Metathesis of Dienes 2a−2h Using Alkylidene 4. To a solution of catalyst **4** in dry degassed benzene was added a solution of the diene in dry degassed benzene. After stirring at 60 °C until disappearance

(16) Lutsenko, I. F.; Prischenko, A. A.; Livantsov, M. V. *Phosphorus Sulfur* **1988**, *35*, 329.

of the starting material, the reaction was concentrated and purified on silica gel.

1-Benzyloxy-3-phospholene 1-Oxide (5a).[17] With **3**: 2.1 g (8.9 mmol) of **2a**, 0.15 g (2%) of **3**, 300 mL of CH_2Cl_2, 2 h; column chromatography (hexane/EtOAc 2/8); yield 1.5 g (80%). With **4**: 0.1 g (0.42 mmol), 0.025 g (8%) of **4**, 20 mL of toluene, yield 0.083 g (95%); R_f = 0.27 (AcOEt/hexane 80/20); pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42−7.33 (m, 5H), 5.91 (d, J = 33.5, 2H), 5.12 (d, J = 8.6, 2H), 2.52−2.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.2 (d, J = 5.8), 128.6, 128.5, 127.9, 126.9 (d, J = 16.0), 66.3 (d, J = 7.3), 29.4 (d, J = 90.1); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +75.7; IR (neat, cm^{-1}) 1251, 1204, 1008, 660; HRMS calcd for $C_{11}H_{13}O_2P$ ($M^{+\bullet}$) 208.0653, found 208.0643.

1-Ethoxy-3-phospholene 1-Oxide (5b).[18] With **3**: 0.15 g (0.86 mmol) of **2b**, 0.014 g (2%) of **3**, 40 mL of CH_2Cl_2, 2 h; column chromatography (hexane/EtOAc 1/9); yield 0.1 g (80%); R_f = 0.33 (AcOEt/hexane 90/10); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.92 (d, J = 33.2, 2H), 4.13 (d × q, J = 7.5, J = 7.2, 2H), 2.44 (d, J = 11.7, 4H), 1.37 (t, J = 7.1, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 127.0 (d, J = 16.0), 60.9 (d, J = 5.8), 29.3 (d, J = 91.7), 16.6 (d, J = 7.3); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +74.5; IR (neat, cm^{-1}) 2924, 1250, 1201, 1034, 960, 660; HRMS calcd for $C_6H_{11}O_2P$ ($M^{+\bullet}$) 146.0497, found 146.0494.

1-Benzyloxy-2,3,6,7-tetrahydrophosphepine 1-Oxide (5c). With **3**: 0.075 g (0.28 mmol) of **2c**, 0.006 g (2.5%) of **3**, 15 mL of CH_2Cl_2, 1.5 h; column chromatography (EtOAc); yield 0.064 g (97%); R_f = 0.26 (AcOEt); pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43−7.33 (m, 5H), 5.89 (m, 2H), 5.08 (d, J = 7.9, 2H), 2.33−2.23 (m, 4H), 1.96−1.72 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.8 (d, J = 5.8), 131.8, 128.6, 128.4, 127.9, 65.2 (d, J = 5.8), 28.5 (d, J = 87.2), 19.5 (d, J = 4.3); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +59.1; IR (neat, cm^{-1}) 1210, 1171, 1042, 1018, 1000, 961; HRMS calcd for $C_{13}H_{17}O_2P$ ($M^{+\bullet}$) 236.0966, found 236.0963.

1-Benzyloxy-5,6-dihydro-*2H* phosphorinane 1-Oxide (5e). With **3**: 0.15 g (0.6 mmol) of **2e**, 0.01 g (2.0%) of **3**, 30 mL of CH_2Cl_2, 30 min; column chromatography (EtOAc); yield 0.128 g (96%); R_f = 0.14 (AcOEt); pale yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39−7.33 (m, 5H), 5.88−5.55 (m, 2H), 5.09 (d, J = 8.7, 2H), 2.54−2.37 (m, 4H), 1.90 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.7 (d, J = 5.8), 128.6, 128.3, 128.2 (d, J = 17.4), 127.8, 121.3 (d, J = 5.8), 65.5 (d, J = 5.8), 26.3 (d, J = 88.6), 24.5 (d, J = 5.8), 23.4 (d, J = 87.2); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +48.1; IR (neat, cm^{-1}) 1680, 1290, 1230, 1193, 1040, 1009, 821; HRMS calcd for $C_{12}H_{15}O_2P$ ($M^{+\bullet}$) 222.0810, found 222.0823.

1-Benzyloxy-3-methyl-3-phospholene 1-Oxide (5f).[19] With **3**: 0.075 g (0.3 mmol) of **2a**, 0.012 g (2%) of **3**, 15 mL of CH_2Cl_2, 4 h; column chromatography (ether); yield 0.033 g (50%). With **4**: 0.1 g (0.4 mmol), 0.02 g (6.5%) of **4**, 20 mL toluene, yield 0.044 g (50%); yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.36 (m, 5H), 5.52 (d, J = 34.7, 1H), 5.10 (d, J = 9.0, 2H), 2.57−2.24 (m, 4H), 1.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 136.5, 136.4, 136.2, 128.7, 128.5, 127.9 120.4 (d, J = 11.6), 66.3 (d, J = 7.3), 33.7 (d, J = 91.5), 31.1 (d, J = 87.2), 20.8 (d, J = 13.1); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +76.1; IR (neat, cm^{-1}) 1295, 1236, 1189, 1033, 1002; HRMS calcd for $C_{12}H_{15}O_2P$ ($M^{+\bullet}$) 222.0810, found 222.0802.

1-Benzyloxy-2-methyl-3-phospholene 1-oxide (5h): 0.1 g (0.4 mmol) of **2h**, 0.011 g (3%) of **3**, 20 mL of CH_2Cl_2, 3.5 h; column chromatography (hexane/EtOAc 3/7); yield 0.068 g (77%) of two diastereomers; ratio 29/71. Minor diastereomer: 22 mg; R_f = 0.47 (AcOEt); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.35 (m, 5H), 5.86 (d, J = 32.4, 2H), 5.10 (d, J = 8.7, 2H), 2.51−2.31 (m, 3H), 1.25 (d × d, J = 16.6, J = 7.5, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.4 (d, J = 5.8), 134.5 (d, J = 20.3), 128.6, 128.5, 127.9, 124.9 (d, J = 16.0), 66.3 (d, J = 7.3), 33.7 (J = 91.5), 29.0 (J = 88.6), 13.6; ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ 75.8. Major diastereomer: 48 mg; R_f = 0.4 (AcOEt); colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.36 (m, 5H), 5.91−5.73 (m, 2H), 5.15 (m, 2H), 2.74 (m, 1H), 2.50−2.29 (m, 2H), 1.22 (d × d, J = 15.8, J = 7.2, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.5 (d, J = 5.8), 134.5 (d, J = 18.9), 128.6, 128.3, 127.7, 124.7 (d, J = 14.5), 66.2 (d, J = 7.3), 35.4 (d, J = 93.0), 29.5 (d, J = 85.7), 12.8 (d, J = 5.8); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +75.72; IR (neat, cm^{-1}) 1456, 1250, 1195, 1036, 1009; HRMS calcd for $C_{12}H_{15}O_2P$ ($M^{+\bullet}$) 222.0810, found 222.0823.

2-Benzyl-1-ethoxy-3-phospholene 1-oxide (5i): 0.06 g (0.23 mmol) of **2i**, 7 mg (3%) of **3**; 12 mL of CH_2Cl_2, 2 h; column chromatography (EtOAc); yield 0.035 g (66%); colorless oil; R_f = 0.37 (AcOEt); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.21 (m, 5H), 5.97−5.68 (m, 2H), 4.15 (m, 2H), 3.14 (m, 1H), 2.94 (m, 1H), 2.57 (m, 3H), 1.37 (t, J = 7.2, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 139.2 (d, J = 11.6), 132.2 (d, J = 20.3), 128.7, 128.5, 126.4, 125.3 (d, J = 13.1), 61.2 (d, J = 5.8), 42.2 (d, J = 91.5), 34.3 (d, J = 4.4), 29.9 (d, J = 85.7), 16.6 (d, J = 5.8); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ +72.59; IR (neat, cm^{-1}) 1245, 1035, 960; HRMS calcd for $C_{13}H_{17}O_2P$ ($M^{+\bullet}$) 236.0966, found 236.0963.

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Supporting Information Available: ^{1}H, ^{13}C, and ^{31}P spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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