crystals of **20** (0.28 g, 75%): mp 142 °C dec; mass spectrum, *m/e* 186 (M^+, 60.8). Anal. Calcd for $C_{11}H_6OS$: C, 70.96; H, 3.22; S, 17.2. Found: C, 70.84; H, 3.29; S, 17.13.

Dithiolactone 24. A mixture of thioloactone **23b**[14] (1.2 g) and Lawesson's reagent (1.4 g) in chlorobenzene (15 mL) was heated for 4 h at 120 °C. The solvent was removed in vacuo, and the residue was chromatographed on silica gel, eluting with ethyl acetate–hexane (1:8) to give 1.1 g (85%) of dark reddish crystalline dithiolactone **24**: mp 98 °C dec (lit.[14] mp 96–97 °C); mass spectrum, *m/e* 202 (M^+, 100), 158 (M^+ – 44, 35.2).

Adduct 25 from 24 and Norbornylene. A mixture of dithiolactone **24** (0.5 g) and norbornylene (0.69 g) in benzene (14 mL) was refluxed for 10 h under N_2. The solvent was removed, and the residue was chromatographed on silica with benzene–hexane (1:4) to give 0.45 g (61%) of adduct **24**: mp 114 °C; NMR δ 7.56 (d, 1 H, *J* = 8.06), 7.25 (m, 1 H), 7.04 (d, 1 H, *J* = 7.3), 6.7 (d, 1 H, *J* = 9.82), 6.27 (d, 1 H, *J* = 9.81), 3.16 (m, 1 H), 2.83 (m, 1 H), 2.64 (br, 1 H), 2.34 (m, 1 H), 2.23 (m, 1 H), 1.9–1.7 (m, 3 H), 1.2–1.4 (m, 3 H); mass spectrum, *m/e* 296 (M^+, 4.2), 202 (M^+ – 94, 100). Anal. Calcd for $C_{18}H_{16}S_2$: C, 72.97; H, 5.4; S, 21.62. Found: C, 72.94; H, 5.46; S, 21.55.

Thermal Isomerization of Adduct 24 to 25. A solution of cycloadduct **24** (0.32 g) in chlorobenzene (10 mL) was heated for 3 h at 130 °C under N_2. The residue, after removal of chlorobenzene, was chromatographed on silica, employing methylene chloride–hexane (1:4) to give a white solid. Crystallization from methylene chloride–hexane gave white crystals of **25** (0.19 g, 60%): mp 185 °C; NMR δ 7.64 (d, 1 H, *J* = 8.48), 7.52 (d, 1 H, *J* = 8.42), 7.43 (m, 1 H), 7.34 (m, 1 H), 7.20 (m, 1 H), 5.78 (s, 1 H), 3.65 (m, 1 H), 2.94 (br, 1 H), 2.75 (m, 1 H), 2.35 (m, 1 H), 1.9–1.7 (m, 2 H), 1.6–1.3 (m, 3 H), 1.15 (m, 1 H); mass spectrum, *m/e* 296 (M^+, 26.3), 202 (M^+ – 94, 100). Anal. Calcd for $C_{18}H_{16}S_2$: C, 72.97; H, 5.4; S, 21.62. Found: C, 72.40; H, 5.41; S, 21.40.

Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE 8607458).

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Synthesis of α-Phosphono Lactones and Esters through a Vinyl Phosphate–Phosphonate Rearrangement

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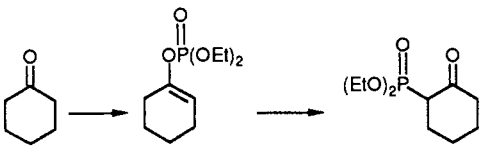
Upon treatment with base, the diethyl vinyl phosphate derivatives of five-, six-, and seven-membered-ring lactones undergo rearrangement to α-phosphono lactones in very good yields. Because the vinyl phosphates can be prepared in situ, these α-phosphono lactones can be obtained from the parent lactones in a one-flask protocol, making this methodology a convenient alternative to the traditional Arbuzov synthesis. An analogous reaction sequence can be used to prepare some α-phosphono esters, but yields are generally lower and the rearrangement becomes minimal with esters hindered at the β-position.

We recently introduced a new and general route to cyclic β-keto phosphonates, which is based upon the rearrangement of a vinyl phosphate anion to a β-keto phosphonate anion (Scheme I).[2] To continue probing the limits of this rearrangement, and to extend its utility, we turned our attention to its potential application in the synthesis of α-phosphono lactones.[3] While some α-phosphono lactones have been prepared from the analogous α-bromo compounds through the Arbuzov approach,[4] few α-bromo lactones are commercially available. Accordingly, preparation of α-phosphono lactones by a route based on a vinyl phosphate to phosphonate rearrangement would be attractive, particularly if a one-flask protocol from the lactone to its phosphonate derivative could be established. In this report, the results of this approach to α-phosphono lactones are presented, along with our efforts to prepare α-phosphono esters by an analogous reaction sequence.

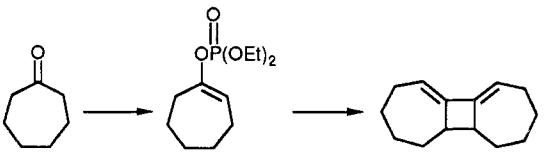
Results and Discussion

Because dialkyl vinyl phosphate derivatives of cyclic ketones rearrange readily to β-keto phosphonates upon

Scheme I



Scheme II



treatment with LDA,[2] the vinyl phosphate derivatives of lactones might be expected to react under similar conditions. The required vinyl phosphates can be obtained by sequential treatment of a lactone with LDA and a dialkyl phosphorochloridate. However, ^{31}P analysis of these reactions indicated mixtures more complex than expected. When HMPA was added to the reaction mixture, the desired vinyl phosphates were obtained cleanly,[5a] and either *N,N'*-dimethyl-*N,N'*-propyleneurea (DMPU)[5b] or 12-

(1) Fellow of the Alfred P. Sloan Foundation, 1985–1989.

(2) (a) Hammond, G. B.; Calogeropoulou, T.; Wiemer, D. F. *Tetrahedron Lett.* **1986**, *27*, 4265. (b) Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185.

(3) Portions of this work were reported at the 196th American Chemical Society Meeting, Los Angeles, CA, Sept 1988.

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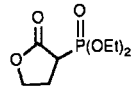
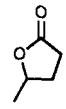
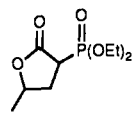
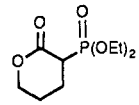
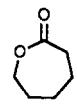
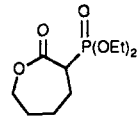
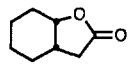
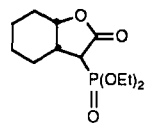
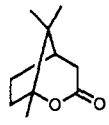
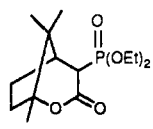
0022-3263/89/1954-4750$01.50/0

Table I. Synthesis of α-Phosphono Lactones

		% yield[a]
 1	 2	68
 3	 4	73[b]
 5	 6	78
 7	 8	73
 9	 10	77[c]
 11	 12	74[c]

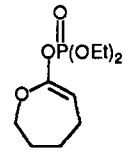
[a] Isolated yield from lactone to α-phosphono lactone. [b] Obtained as a mixture of diastereomers (^{31}P and ^{1}H NMR). [c] Obtained as a single diastereomer.

crown-4 could be used in place of HMPA with little decrease in yield.

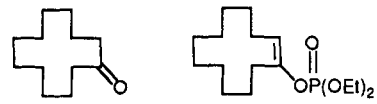
Once conditions were established for the smooth formation of the vinyl phosphates, we turned directly to exploration of a one-flask approach to α-phosphono lactones. Accordingly, the vinyl phosphates were prepared in situ and immediately treated with LDA to induce rearrangement. As shown in Table I, the results were generally favorable. The simple five-, six-, and seven-membered-ring lactones (**1**, **3**, **5**, and **7**) gave the desired phosphono lactones (**2**, **4**, **6**, and **8**) in isolated yields of approximately 70% based on the starting lactone. The bicyclic lactone **9**, which approximates the type of synthetic intermediate required for preparation of many sesquiterpene lactones, was converted to its phosphonate derivative **10** in 77% yield. Finally, the camphor-derived lactone **11** gave the expected phosphono lactone **12** in good yield, analogous to earlier results obtained with camphor itself.[2]

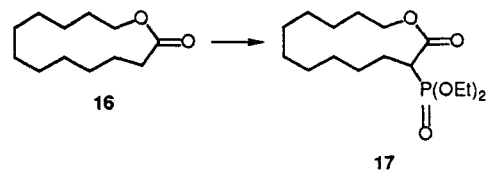
While there are many parallels between the rearrangements observed with these lactones and those previously reported for the vinyl phosphate derivatives of cyclic ketones, there are also significant differences. For example, when treated with LDA, the vinyl phosphate of cycloheptanone undergoes a phosphate elimination,[2b,6] ultimately yielding a hydrocarbon dimer (Scheme II).[7] This dimer may result from abstraction of a C-7 proton of the vinyl phosphate to form an allyl anion, followed by phosphate elimination and cycloaddition of the resulting, highly strained allene.[8] In contrast to the cycloheptanone case, with ε-caprolactone (**7**), where the placement of the ring oxygen prevents formation of an analogous allyl anion, rearrangement of the vinyl phosphate to its phosphono derivative **8** takes place smoothly.

More detail on the vinyl phosphate to phosphono lactone rearrangement was provided by a variable-temperature ^{31}P NMR study. For this experiment, a solution of the vinyl phosphate **13** in THF was cooled to −100 °C in an NMR tube and LDA was added. Spectra were taken periodically, at gradually increasing probe temperatures. At very low temperatures, only the resonance of the vinyl phosphate (ca. −6.5 ppm) could be detected. At intermediate temperatures of −50 to −40 °C, the resonance of the vinyl phosphate declined, while the resonance of the phosphono lactone anion (36.5 ppm) grew proportionally. By the time the probe temperature had reached 0 °C, only this latter resonance was observed. No resonance that could be attributed to a vinyl phosphate anion was detected. Thus, it appears that abstraction of a proton from the vinyl phosphate is the slow step in this rearrangement and that, once this anion is formed, rearrangement to the phosphono lactone is facile.


13

The successful preparation of the ε-caprolactone phosphonate **8** prompted comparison of a large-ring ketone with a macrocyclic lactone. The vinyl phosphate **15** was prepared in situ from cyclododecanone (**14**). Upon treatment with LDA, this vinyl phosphate undergoes elimination to afford a mixture of hydrocarbons. Analysis of the product mixture by GC FTIR and GC-MS suggests the presence of both acetylene and allene.[8] With the 13-membered-ring lactone **16**,[9] the same reaction sequence results in formation of the phosphono lactone **17**, albeit in low yield.


14 15


16 17

Even though attempted preparation of acyclic keto phosphonates through rearrangement of their vinyl phosphates has given only elimination products,[2b] the possibility that this approach might be useful for preparation of α-phosphono esters was attractive. In general, the α-phosphono derivatives of small esters are available via the Arbuzov reaction;[10] some are even commercially

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(7) Bottini, A. T.; Frost, K. A., II; Anderson, B. R.; Dev, V. *Tetrahedron* **1973**, *29*, 1975.
(8) Price, J. D.; Johnson, R. P. *Tetrahedron Lett.* **1986**, *27*, 4679 and references cited therein.
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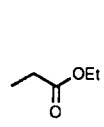
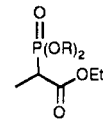
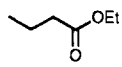
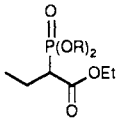
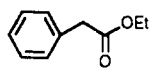
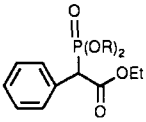
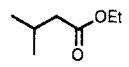
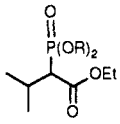
(10) Arbuzov, B. A. *Pure Appl. Chem.* **1964**, *9*, 307. Bhattacharya, A. K.; Thyagarajan, G. *Chem. Rev.* **1981**, *81*, 415.

Table II. Synthesis of α-Phosphono Esters

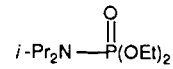
		% yield[a]
		
18	**19a**, R = Et	26
	b, R = *i*-Pr	41
		
20	**21a**, R = Et	14
	b, R = *i*-Pr	36
		
22	**23a**, R = Et	12
	b, R = *i*-Pr	9
		
24	**25a**, R = Et	–
	b, R = *i*-Pr	–

[a] Isolated yield from ester to α-phosphono ester.

available. With larger or uncommon esters, a rearrangement approach might prove competitive, especially if the α-halo ester required for an Arbuzov approach is not readily available or is sterically hindered. For example, the reaction of methyl 2-bromoisovalerate with triethyl phosphite affords phosphonate in only ~20% yield.[11]

An initial experiment applying this methodology with ethyl propionate (**18**, Table II) proved moderately encouraging. As monitored by ^{31}P NMR, reaction of the ethyl propionate enolate with diethyl phosphorochloridate under standard conditions results in smooth formation of the desired vinyl phosphate. When additional LDA is added to the reaction mixture, rearrangement to the α-phosphono ester **19a** takes place, although in low yield. The effect of additional β-substituents was tested by attempting preparations of phosphonates from ethyl butyrate (**20**), ethyl phenylacetate (**22**), and ethyl isovalerate (**24**). With the butyrate and the phenylacetate, the desired phosphono esters **21a** and **23a** were formed. However, when attempted rearrangement of the more hindered ester **24** was monitored by ^{31}P NMR, the vinyl phosphate was consumed but no phosphonate was detected.

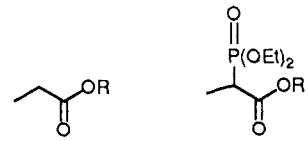
In the above cases, major reaction byproducts include the parent esters, their corresponding amides, and the phosphonamide **26**. The diisopropyl vinyl phosphates of



26

esters **18**, **20**, **22**, and **24** were prepared to establish if increasing steric hindrance near the phosphorus would diminish formation of these undesired products. When the vinyl phosphates of esters **18** and **20** were treated with LDA, the desired phosphonates **19b** and **21b** were formed, and isolated yields were much improved relative to those obtained with the diethyl phosphates. With the more hindered ester **22**, use of diisopropyl phosphorochloridate made little difference in yield. Finally, although the diisopropyl vinyl phosphate of ester **24** was clearly formed, its subsequent reaction with LDA under the standard conditions gave only the parent ester and its diisopropyl amide.

To explore the impact of steric effects in the carboxylic acid ester, both isopropyl and *tert*-butyl propionate (**27** and **29**) were examined. While the expected α-phosphono esters were obtained in both cases (i.e., **28** and **30**), there was no significant difference in yields over that observed with ethyl propionate.



27, R = *i*-Pr **28**, R = *i*-Pr
29, R = *t*-Bu **30**, R = *t*-Bu

In conclusion, a variety of lactones, and some esters, have been converted to their α-phosphono derivatives through rearrangement of their vinyl phosphate derivatives. Given the simplicity of this method and the generally high yields, it should become the method of choice for the preparation of phosphono lactones. Although yields with esters are lower, this approach may be a viable alternative to the Arbuzov reaction for the synthesis of some phosphono esters.

Experimental Section

Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use, and all reactions in this solvent were conducted under a positive pressure of an inert gas. Hexamethylphosphoramide (HMPA) was distilled from calcium hydride. Column chromatography was done on Merck grade 62 silica gel (60–200 mesh), while radial chromatography was performed with a Chromatotron apparatus and Merck PF254 silica gel with $CaSO_4 \cdot 0.5H_2O$. NMR spectra (^1H and ^{31}P) were recorded on either a JEOL FX-90Q or a Brucker WM-360 spectrometer, with deuteriochloroform as the solvent. The ^1H chemical shifts are reported in parts per million downfield from $(CH_3)_4Si$, while the ^{31}P chemical shifts are reported in parts per million relative to H_3PO_4 (external standard). Low-resolution electron-impact (EI) mass spectra were recorded with a Hewlett-Packard 5985B instrument operating at 70 eV; only selected ions are reported here. High-resolution mass spectra were recorded on a VG Instruments ZAB-HF spectrometer at the University of Iowa Mass Spectrometry Facility. Microanalyses were conducted by Galbraith Laboratories, Knoxville, TN, or by Desert Analytics, Tuscon, AZ.

α-(Diethoxyphosphinyl)-γ-butyrolactone (2). General Procedure for the Preparation of α-Phosphono Lactones. To a solution of LDA [5.5 mmol, prepared in situ from diisopropylamine (0.77 mL) and *n*-BuLi (3.75 mL, 1.6 M in hexane)] in anhydrous THF (15 mL) at −78 °C was added dropwise via syringe γ-butyrolactone (**1**, 0.38 mL, 5.0 mmol). After 30 min, a solution of diethyl phosphorochloridate (0.83 mL, 5.7 mmol) in HMPA (0.99 mL, 5.7 mmol) was added to the lactone enolate, and the resulting mixture was allowed to warm to room temperature over the course of 30 min. After cooling of the reaction mixture to −78 °C, a solution of LDA (2.2 equiv in 15 mL of THF) was added via syringe, and the reaction mixture was allowed to warm to room temperature over 2 h. The reaction was quenched by slow addition of a solution of acetic acid in diethyl ether (1 M, 4.4 equiv), and the resulting mixture was filtered through a 1-cm layer of Florisil (60–120 mesh). Final purification by column chromatography (silica gel, 50% EtOAc, 50% hexane, followed by 50% CH_3CN, 50% EtOAc) produced compound **2**[4] (602 mg, 68%): ^1H NMR δ 4.50–4.07 (m, 6), 3.23–2.45 (m, 3), 1.36 (t, 6, J = 7.0 Hz); ^{31}P NMR +21.1; EIMS, m/z (relative intensity) 222

(11) Wuts, P. G. M.; Putt, S. R.; Ritter, A. R. *J. Org. Chem.* 1988, *53*, 4503.

(M+, 2), 195 (38), 179 (20), 167 (67), 165 (53), 149 (44), 138 (65), 123 (40), 109 (63), 91 (30), 86 (100), 81 (63), 65 (48), 55 (50).

α-(Diethoxyphosphinyl)-γ-valerolactone (4). γ-Valerolactone (**3**, 500 mg, 5.0 mmol) was added to a solution of LDA in THF (1.1 equiv in 15 mL), and the resulting lactone enolate was treated sequentially with HMPA (1.0 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography produced the phosphono lactone **4** (861 mg, 73%).[4,12] Both ^{1}H NMR and EIMS data were consistent with published data;[12] ^{31}P NMR +21.37, 21.21.

α-(Diethoxyphosphinyl)-δ-valerolactone (6). To a solution of LDA (1.1 equiv) in THF (15 mL) was added δ-valerolactone (**5**, 500 mg, 5.0 mmol). The resulting enolate was treated sequentially with HMPA (1.0 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the expected phosphono lactone **6** (920 mg, 78%): ^{1}H NMR δ 4.49–4.30 (m, 2), 4.27–4.11 (m, 4), 3.18 (ddd, 1, J_{HP} = 27.2 Hz, J = 8.1, 6.8 Hz), 2.29–2.21 (m, 2), 2.17–2.02 (m, 1), 1.90–1.80 (m, 1), 1.36 (dt, 6, J_{HP} = 2.9 Hz, J = 7.0 Hz); ^{31}P NMR: +22.6; EIMS, m/z (relative intensity) 236 (M+, 2), 209 (6), 180 (16), 155 (18), 138 (44), 109 (69), 99 (69), 81 (100), 55 (82). Anal. Calcd for $C_9H_{17}O_5P$: C, 45.77; H, 7.25. Found: C, 45.67; H, 7.21.

α-(Diethoxyphosphinyl)-ε-caprolactone (8). After addition of ε-caprolactone (**7**, 570 mg, 5.5 mmol) to a solution of LDA in THF (1.1 equiv in 15 mL), the resulting enolate was treated sequentially with HMPA (1.0 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the desired phosphono lactone **8** (915 mg, 73%): ^{1}H NMR δ 4.39–4.06 (m, 6), 2.96 (ddd, 1, J_{HP} = 22.4 Hz, J = 10.1, 3.0 Hz), 2.01 (m, 1), 1.85 (m, 1), 1.65 (m, 2), 1.44 (m, 2), 1.33 (dt, 6, J_{HP} = 2.0 Hz, J = 7.5 Hz); ^{31}P NMR +23.0; EIMS, m/z (relative intensity) 250 (M+, 2), 205 (11), 194 (20), 178 (28), 165 (100), 155 (25), 137 (44), 109 (92), 99 (23), 91 (31), 81 (39), 55 (42). Anal. Calcd for $C_{10}H_{19}O_5P$: C, 48.00; H, 7.65. Found: C, 47.97; H, 7.78.

Phosphono Lactone 10. To a solution of LDA (1.1 equiv) in THF (10 mL) was added lactone **9**[13] (140 mg, 1.0 mmol), and the resulting enolate was treated sequentially with HMPA (1.2 mmol), diethyl phosphorochloridate (0.173 mL, 1.2 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the desired product **10** (213 mg, 77%): ^{1}H NMR δ 4.87–4.78 (m, 1), 4.38–4.03 (m, 4), 2.90 (dd, 1, J_{HP} = 23.8 Hz, J = 2.5 Hz), 2.2–1.5 (m, 9), 1.35 (dt, 6, J_{HP} = 1.5 Hz, J = 7.0 Hz); ^{31}P NMR +20.0; EIMS, m/z (relative intensity) 276 (M+, 2), 248 (28), 220 (12), 179 (77), 151 (23), 143 (27), 123 (29), 111 (16), 87 (80), 74 (100). Anal. Calcd for $C_{12}H_{21}O_5P$: C, 52.17; H, 7.66. Found: C, 52.31; H, 7.92.

α-(Diethoxyphosphinyl)camphorlactone (12). After addition of lactone **11** (350 mg, 2.1 mmol)[14] to a solution of LDA in THF (1.1 equiv in 10 mL), the resulting enolate was treated sequentially with HMPA (1.2 equiv), diethyl phosphorochloridate (0.34 mL, 2.3 mmol), and LDA (2.2 equiv) according to the general procedure. Final purification by column chromatography produced the desired product **12** (634 mg, 74%): ^{1}H NMR δ 4.35–4.08 (m, 4), 3.35 (dd, 1, J_{HP} = 30.0 Hz, J = 3.7 Hz), 2.3–1.8 (m, 5), 1.35 (t, 6, J = 7.0 Hz), 1.28 (s, 3), 1.05 (s, 6); ^{31}P NMR +21.7; EIMS, m/z (relative intensity) 304 (M+, 1), 219 (8), 179 (100), 151 (23), 123 (35), 109 (27), 108 (21), 105 (22), 91 (25), 81 (52), 55 (24); HRMS calcd for $C_{14}H_{25}O_5P$ 304.1434, found 304.1478. Anal. Calcd for $C_{14}H_{25}O_5P \cdot 0.5H_2O$: C, 53.67; H, 8.36. Found: C, 53.61; H, 8.36.

α-(Diethoxyphosphinyl)-1-oxacyclotridecan-2-one (17). Lactone **16** (990 mg, 5.0 mmol) was added to a solution of LDA in THF (1.1 equiv in 10 mL), and the resulting enolate was treated sequentially with HMPA (6 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the desired product **17** (135 mg, 8%): ^{1}H NMR δ 4.35–3.90 (m, 6), 2.94 (ddd, 1, J_{HP} = 21.7 Hz, J = 10.8, 3.9 Hz), 1.76–1.58 (m, 2), 1.34–1.01 (m, 22); ^{31}P NMR +23.6; EIMS, m/z (relative intensity) 334 (M+, 3), 209 (12), 197 (38), 191 (16), 179 (32), 165 (28), 152 (22), 138 (24), 123 (25), 109 (80), 91 (35), 81 (78), 55 (100); HRMS calcd for $C_{16}H_{31}O_5P$ 334.1903, found 334.1915. Anal. Calcd for $C_{16}H_{31}O_5P \cdot H_2O$: C, 54.53; H, 9.44. Found: C, 54.46; H, 9.39.

Ethyl α-(Diethoxyphosphinyl)propionate (19a). General Procedure for the Preparation of α-Phosphono Esters. To a solution of LDA [1.1 equiv, prepared in situ from diisopropylamine (0.77 mL) and *n*-BuLi (3.75 mL, 1.6 M in hexane)] in anhydrous THF (15 mL) at −78 °C was added dropwise via syringe ethyl propionate (**18**, 0.57 mL, 5 mmol). After 30 min, a solution of diethyl phosphorochloridate (0.83 mL, 5.7 mmol) in HMPA (0.99 mL, 5.7 mmol) was added to the ester enolate, and the resulting mixture was allowed to warm to room temperature over the course of 30 min. After cooling of the reaction mixture to −78 °C, a solution of LDA (2.2 equiv in 15 mL of THF) was added via syringe, and the reaction mixture was allowed to warm to room temperature over 2 h. The reaction was quenched by slow addition of a solution of acetic acid in diethyl ether (1 M, 3.3 equiv), and the resulting mixture was filtered through a Florisil pad (60–120 mesh). Final purification by column chromatography (silica gel, 50% EtOAc, 50% hexane, followed by 25% hexane, 25% CH_3CN, 50% EtOAc) produced pure compound **19a**[15] (315 mg, 26%): ^{1}H NMR[16] and EIMS[17] data were identical with those previously reported; ^{31}P NMR +23.4.

Ethyl α-(Diisopropoxyphosphinyl)propionate (19b). To a solution of LDA (1.1 equiv) in THF (15 mL) was added ethyl propionate (**18**), 510 mg, 5.0 mmol). The ester enolate was treated sequentially with HMPA (1.0 mL, 5.7 mmol), diisopropyl phosphorochloridate[18] (1.0 mL, 5.5 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the desired product[19] (545 mg, 41%): ^{1}H NMR δ 4.78–4.69 (m, 2), 4.19 (q, 2, J = 7.0 Hz), 2.96 (dq, 1, J_{HP} = 23.7 Hz, J = 7.0 Hz), 1.51–1.26 (m, 6), 1.33 (d, 12, J = 6.2 Hz); ^{31}P NMR +21.6; EIMS, m/z (relative intensity) 266 (M+, 1), 207 (13), 183 (88), 179 (14), 165 (53), 137 (100), 109 (27), 99 (17), 91 (9), 81 (14).

Ethyl α-(Diethoxyphosphinyl)butyrate (21a). Ethyl butyrate (**20**, 581 mg, 5.0 mmol) was treated sequentially with LDA (1.1 equiv in 15 mL of THF), HMPA (1.0 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the desired product **21a** (176 mg, 14%): ^{1}H NMR δ 4.34–3.98 (m, 6), 2.87 (ddd, 1, J_{HP} = 22.3 Hz, J = 8.7, 6.1 Hz), 2.11–1.82 (m, 2), 1.42–1.81 (m, 9), 0.98 (t, 3, J = 7.3 Hz); ^{31}P NMR +22.1; EIMS, identical with previous data.[17]

Ethyl α-(Diisopropoxyphosphinyl)butyrate (21b). Ethyl butyrate (**20**, 581 mg, 5.0 mmol) was treated sequentially with LDA (1.1 equiv in 15 mL of THF), HMPA (1.0 mL, 5.7 mmol), diisopropyl phosphorochloridate (1.00 mL, 5.5 mmol), and LDA (2.2 equiv) according to the general procedure. Standard workup and purification by column chromatography gave the desired product (510 mg, 36%): ^{1}H NMR δ 4.93–4.89 (m, 2), 4.21 (q, 2, J = 7.2 Hz), 2.79 (ddd, 1, J_{HP} = 22.1 Hz, J = 8.8, 6.0 Hz), 1.90 (m, 2), 1.32 (d, 12, J = 6.2 Hz), 1.29 (m, 3), 0.97 (t, 3, J = 7.5 Hz); ^{31}P NMR +20.8; EIMS, m/z (relative intensity) 280 (M+, 1), 221 (10), 197 (62), 179 (47), 151 (100), 123 (54), 109 (10), 99 (15), 69 (13), 43 (21). Anal. Calcd for $C_{12}H_{25}O_5P$: C, 51.42; H, 8.99. Found: C, 51.78; H, 9.28.

Ethyl α-(Diethoxyphosphinyl)phenylacetate (23a). Ethyl phenylacetate (**22**, 821 mg, 5.0 mmol) was treated sequentially with LDA (1.1 equiv in 15 mL of THF), HMPA (1.0 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) according to the general procedure. The desired phosphono ester **23a** was obtained as a colorless oil (180 mg, 12%) following purification by radical chromatography (silica, gradient

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from 30% to 50% EtOAc in hexane): ^{1}H NMR δ 7.55–7.27 (m, 5), 4.30–3.94 (m, 6), 3.57–3.51 (m, 1), 1.35–1.13 (m, 9); ^{31}P NMR +19.4; EIMS, *m/z* (relative intensity) 300 (M^+, 4), 254 (6), 199 (10), 196 (22), 172 (15), 118 (100), 109 (25), 91 (78), 79 (27); HRMS, calcd for $C_{14}H_{21}O_5P$ 300.1126, found 300.1122.

Ethyl α-(Diisopropoxyphosphinyl)phenylacetate (23b). Ethyl phenylacetate (**22**, 821 mg, 5.0 mmol) was treated sequentially with LDA (1.1 equiv in 15 mL of THF), HMPA (1.0 mL, 5.7 mmol), diisopropyl phosphorochloridate (1.00 mL, 5.5 mmol), and LDA (2.2 equiv) according to the general procedure. Purification by gradient radial chromatography (silica, 10% to 50% EtOAc in hexane) gave compound **23b** (154 mg, 9.4%): ^{1}H NMR δ 7.53 (d, 2, *J* = 7.8 Hz), 7.35–7.26 (m, 3), 4.70–4.56 (m, 2), 4.26–4.15 (m, 3), 1.30–1.24 (m, 15); ^{31}P NMR +17.5; EIMS, *m/z* (relative intensity) 328 (M^+, 5), 286 (5), 244 (7), 199 (12), 164 (22), 118 (100), 107 (25), 91 (34), 90 (34), 79 (28). Anal. Calcd for $C_{16}H_{25}O_5P$: C, 58.53; H, 7.67. Found: C, 58.26; H, 7.66.

Isopropyl α-(Diethoxyphosphinyl)propionate (28). In accordance with the general procedure, isopropyl propionate (**27**, 580 mg, 5.0 mmol) was added to a solution of LDA (1.2 equiv) in THF (15 mL) at −78 °C. The resulting enolate was treated sequentially with HMPA (0.99 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv). Standard workup and purification by column chromatography gave compound **28** (252 mg, 29%): ^{1}H NMR δ 5.19–4.92 (m, 1), 4.32–3.99 (m, 4), 3.01 (dq, 1, J_{HP} = 23.4 Hz, *J* = 7.3 Hz), 1.57–1.11 (m, 15): ^{31}P NMR +24.6; EIMS, *m/z* (relative abundance) 252 (M^+, 2), 210 (30), 193 (100), 165 (70), 137 (49), 109 (51), 99 (18), 81 (36). Anal. Calcd for $C_{10}H_{21}O_5P$: C, 47.62; H, 8.39. Found: C, 47.80; H, 8.54.

***tert*-Butyl α-(Diethoxyphosphinyl)propionate (30).** *tert*-Butyl propionate (**29**, 650 mg, 5.0 mmol) was added to a solution of LDA in THF (5.5 mmol in 15 mL) at −78 °C, and the resulting enolate was treated sequentially with HMPA (1.0 mL, 5.7 mmol), diethyl phosphorochloridate (0.83 mL, 5.7 mmol), and LDA (2.2 equiv) as in the general procedure. Standard workup and purification by column chromatography gave compound **30** (359 mg, 27%): ^{1}H NMR and EIMS data identical with previous data;[20] ^{31}P NMR +24.9.

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[4 + 2] Cycloadditions between 2*H*-Phospholes and Alkenes. Synthesis and Properties of 1-Phosphanorbornenes

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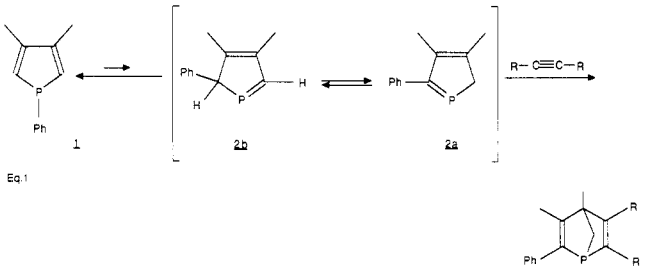
2*H*-Phospholes, obtained by isomerization of 1*H*-phospholes at ca. 150 °C, achieve [4 + 2] cycloadditions with disubstituted alkenes to yield 1-phosphanorbornenes. In the case of symmetrical (*E*)-alkenes, α-exo,β-endo compounds are formed predominantly or even exclusively. Spectral assignments of these compounds are checked by an X-ray structure determination. The 1-phosphanorbornenes formed by reacting 2*H*-phospholes and (*Z*)-alkenes undergo an epimerization and then give the same products as (*E*)-alkenes do. The study of the evolution of the reaction mixture shows that the [4 + 2] cycloaddition should proceed via a concerted mechanism followed by a cleavage of the newly formed P–C single bond. Regioselectivity of nonsymmetrical alkenes is controlled by the steric hindrance of the phosphole moiety. The transient phosphadiene exhibits a rather high reactivity toward dienophiles and the presence of an alcoholic function does not disturb the cycloaddition.

Introduction

Bicyclic systems with phosphorus at the bridgehead have been known for a long time[1-3] but their synthesis is so long and tedious and the overall yields are so low that the study of their properties has remained limited. In such a context, the discovery in our laboratory of a very simple one-step synthesis of 1-phosphanorbornadienes from phospholes and alkynes[4,5] opens interesting new perspectives. The key feature underlying this synthesis is the appearance, above ca. 150 °C, of an equilibrium between 1-phenyl-1*H*-phospholes such as **1** and 2-phenyl-2*H*- or -5*H*-phospholes such as **2a,b** via the superimposition of [1,5] phenyl and hydrogen sigmatropic shifts (eq 1).



Since this initial discovery, Regitz has been able to synthesize stable 2*H*-phospholes[6] but no further extension of the chemistry of these species has yet appeared in the literature. We report here on the reaction of the transient 2*H*-phospholes with alkenes with some emphasis on the stereochemistry of these [4 + 2] cycloadditions.

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