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Intramolecular Dehydration of β-Hydroxyalkylphosphonic Acid Monoesters. A Novel Type of Olefin Formation

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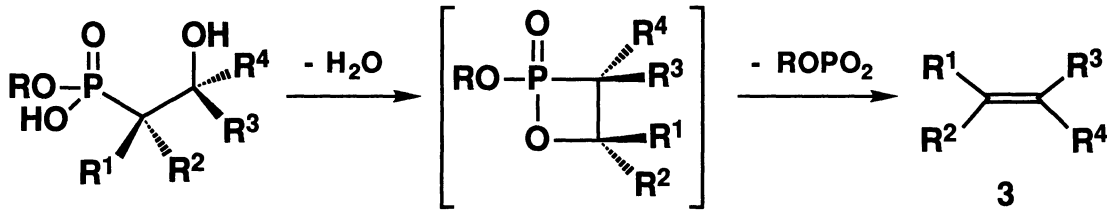
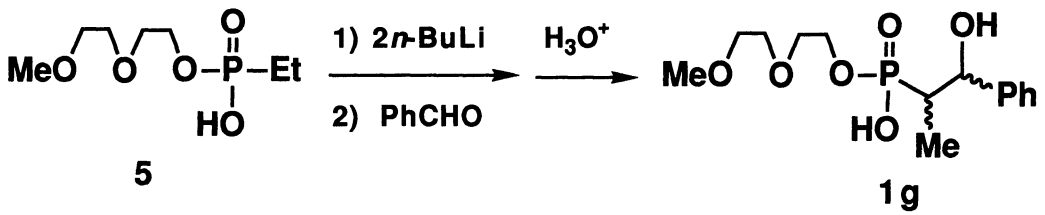
The title reaction using dicyclohexylcarbodiimide (DCC) gave stereospecifically the corresponding olefins in good yields via tetracoordinate 1,2-oxaphosphetanes. Use of more than one equivalent of DCC afforded better yields of the olefin.

β-Lactones and β-sultines have been known as strained molecules to give olefins on thermolysis.[1] On the other hand, tetracoordinate 1,2-oxaphosphetanes, their phosphorus analogue, have been synthesized as stable compounds,[2] but most of them have not been characterized unambiguously in contrast to pentacoordinate species.[3] In fact, revised structures have been proposed for some compounds.[2b,2c,4] In this paper we wish to report the title reaction as a novel mode of olefin formation via a tetracoordinate 1,2-oxaphosphetane.



1 2 3

β-Hydroxyalkylphosphinic acid monoesters **1**[5] were prepared in moderate to good yields by treatment of the corresponding diester **4** with NaI in boiling acetonitrile. A direct method for the preparation of **1 g** was also developed as shown in the following scheme. The polyether moiety of alkylphosphonic acid monoester **5** is necessary for effective dilithiation, otherwise no carbonyl adduct was obtained.



5 1g

Table 1. Synthesis of β-Hydroxyalkylphosphonic Acid Monoesters **1** and Olefins **3**

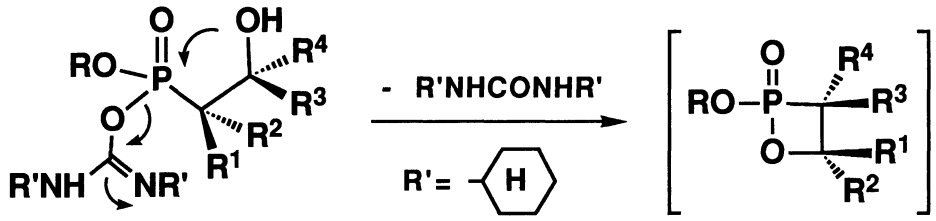
Run		R	R^1	R^2	R^3	R^4	Yields[a]/% **1**	Yields[a]/% **3**
1	**a**:	Me	H	H	CH_2Ph	CH_2Ph	98	91[b]
2	**b**:	Me	H	H	H	*n*-$C_{11}H_{23}$	89	71
3	**c**:	Me	H	H	H	*p*-$NO_2C_6H_4$	34	76
4	**d**:	Me	Me	Me	H	Ph	46	82[c]
5	**e**:	Me	H	Me	H	Ph	62[d]	72[c,e]
6	**f**:	Me	H	Me	H	*n*-C_6H_{13}	76[f]	77[c,g]
7	**g**:	$Me(OCH_2CH_2)_2$	H	Me	H	Ph	49[h]	91[c,i]

a) Isolated yields based on **4** and **1** for **1** and **3**, respectively. b) When 0.6, 1.0, 1.5, and 2 equivalents of DCC were used, yields of **3a** were 55-56, 60-66, 91, and 90%, respectively. c) Determined by ^{1}H NMR spectroscopy. d) *erythro*:*threo*=78:22. e) (*Z*): (*E*)= 77:23. f) *erythro*:*threo* =76:24. g) (*Z*): (*E*)=72:28. h) Isolated yield based on **5**. *erythro*: *threo*=60:40. i) (*Z*): (*E*)=58:42.

Treatment of β-hydroxyalkylphosphonic acid monoesters **1** with dicyclohexylcarbodiimide (DCC) in CH_2Cl_2 at 0 °C then at room temperature for 1 h gave the corresponding olefins **3** along with dicyclohexylurea after chromatography on silica gel. The results using 2 equivalents of DCC are shown in Table 1. The reaction was monitored by ^{31}P NMR spectroscopy and showed that the signal due to the starting material (δ_P 33.4) disappeared rapidly to give a new signal (δ_P 24.3), which decreased gradually over -30 °C to afford finally complex signals. The value of δ_P and nonequivalency of two protons of α-methylene group (^{1}H NMR) and that of two benzyl groups (^{1}H and ^{13}C NMR) are consistent with a structure of intermediate **2a**.[5] As shown in the footnote of Table 1 use of more than one equivalent of DCC gave better yields of **3a**, indicating that DCC probably plays an important role at the stage of olefin formation from the intermediate.[6]

Table 1 shows that the present method can be used for the preparation of mono-, di-, and tri-substituted olefins, and is applicable also to **1c** and **1d**, the methyl ester of which (**4c** and **4d**) did not give the olefin under reported basic conditions.[8] As shown in Runs 5, 6, and 7 the reaction using an *erythro*-enriched diastereomeric mixture gave a (*Z*)-enriched olefin mixture. In each reaction the *erythro*/*threo* ratio is almost same as the (*Z*)/(*E*) ratio, indicating that the present reaction proceeds stereospecifically via syn elimination. Taking into account the above results and the fact that use of the sodium salt of **1a** or diester **4a** gave no olefin, it is most likely that the

reaction is initiated by acid-catalyzed addition of the acid monoester to the imino group of the carbodiimide, followed by back-side attack of the hydroxyl group to give intermediate **2** and dicyclohexylurea, the former of which undergoes a Wittig-like reaction to afford the olefin together with readily oligomerized metaphosphate.[7)]



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These tetracoordinate 1,2-oxaphosphetanes, which are intermediates of a novel type of olefin formation, are highly reactive in marked contrast to the previously reported ones.[2a,d,e,h)] Also, it is very interesting that the present olefin formation proceeds under milder reaction conditions compared with usual Horner-Emmons reaction from β-hydroxyalkylphosphonates[8)] or -phosphine oxides[9)] without any carbanion-stabilizing group at the α-position.

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5) Physical and spectral data of **1a** and **2a** are shown as typical examples: **1a**: mp 100.9-102.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ= 2.00 (2H, d, J_{HP}=19.1 Hz, $PC\underline{H}_2$), 2.83 (2H, d, J_{HH}=13.6 Hz, $PCH_2(C\underline{H}H'Ph)_2$), 2.97 (2H, dd, J_{HH}=13.6 Hz, J_{HP}=3.1 Hz, $PCH_2(CH\underline{H}'Ph)_2$), 3.68 (3H, d, J_{HP}=11.4 Hz, $POC\underline{H}_3$), and 7.21-7.38 (12H, m, 2×OH, $2\times C_6\underline{H}_5$). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 32.99 (d, J_{CP}=140.5 Hz, $P\underline{C}H_2$), 46.32 (d, J_{CP}=9.2 Hz, $\underline{C}H_2Ph$), 51.40 (d, J_{CP}=7.0 Hz, $PO\underline{C}H_3$), 72.57 (d, J_{CP}=4.1 Hz, $\underline{C}OH(CH_2Ph)_2$), 126.53 (s), 128.12 (s), 130.74 (s), and 136.33 (s). ^{31}P NMR (36.3 MHz, $CDCl_3$): δ =33.4. Found: C, 63.56; H, 6.31%. Calcd for $C_{17}H_{21}O_4P$: C, 63.74; H, 6.61%. **2a**: ^{1}H NMR (500 MHz, $CDCl_3$, -33 °C): δ = 2.92 (1H, dd, J_{HH}=14.7 Hz, J_{HP}= 19.2 Hz, $PC\underline{H}H'$), 2.96 (1H, dd, J_{HH}=14.7 Hz, J_{HP}=18.6 Hz, $PCH\underline{H}'$), 3.07 (1H, d, J_{HH}=14.1 Hz, $C\underline{H}H'Ph$), 3.12 (1H, d, J_{HH}=14.2 Hz, $C\underline{H}H'Ph'$), 3.13 (1H, d, J_{HH}=14.1 Hz, $CH\underline{H}'Ph$), 3.16 (1H, d, J_{HH}=14.2 Hz, $CH\underline{H}'Ph'$), 3.73 (3H, d, J_{HP}=11.6 Hz, $POC\underline{H}_3$), and 7.25-7.45 (10H, m). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$, -33 °C): δ = 39.76 (d, J_{CP}=97.6 Hz, $P\underline{C}H_2$), 43.91 (d, J_{CP}=5.9 Hz, $\underline{C}H_2Ph$), 44.74 (d, J_{CP}=7.6 Hz, $\underline{C}H_2Ph'$), 53.33 (d, J_{CP}=6.5 Hz, $PO\underline{C}H_3$), 76.91 (d, J_{CP}=20.0 Hz, $PO\underline{C}(CH_2Ph)_2$), 127.04 (s), 127.19 (s), 128.23 (s), 128.30 (s), 130.50 (s), 130.55 (s), 134.53 (s), and 134.77 (s). ^{31}P NMR (36.3 MHz, $CDCl_3$, -38 °C): δ = 24.3.

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