A Novel Route to Olefins from Vicinal Diols

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A novel reagent system consisting of chlorodiphenylphosphine, imidazole, and iodine in an inert solvent converts vicinal diols to olefins. Reagents are, after completed reaction, removed by extractive procedures, which facilitates large-scale preparations. Vicinal diols consisting of either a primary and a secondary hydroxyl or two secondary hydroxyls are in this way converted to olefins in high yields.

Introduction

The conversion of vicinal diols into olefins has attracted considerable attention over the past years for modification of natural products and for refunctionalization of polyhydroxy compounds of the chiral pool.

There exist today a number of methods to generate the olefinic linkage from diols.[1] A majority of these procedures require a transformation of the vicinal hydroxyls into activated groups, which are subsequently converted into olefins in a futher step. Examples of activating groups are disulfonates,[1a,b] cylic phosphatamides,[1e] cyclic thiocarbonates,[1f,h,i] bis-*O,O'*-dithiocarbonates,[1j] ortho esters, or cyclic 1-(dimethylamino)methylene acetals.[1k]

A one-step conversion of vicinal diols has also been reported in which high yields of olefin were obtained for trans-disposed diol systems using triphenylphosphine and triiodoimidazole.[2] For diols involving one primary hydroxyl this system did not give useful results. A disadvantage of this reaction system is that triphenylphosphine and its oxide are difficult to remove in the product isolation step.

In connection with a study on the conversion of isolated hydroxyl groups to halogens (iodides, bromides),[3] it was found that vicinal diols are converted to olefins in high yields when reacted with commercially available chlorodiphenylphosphine (1) together with iodine and imidazole.

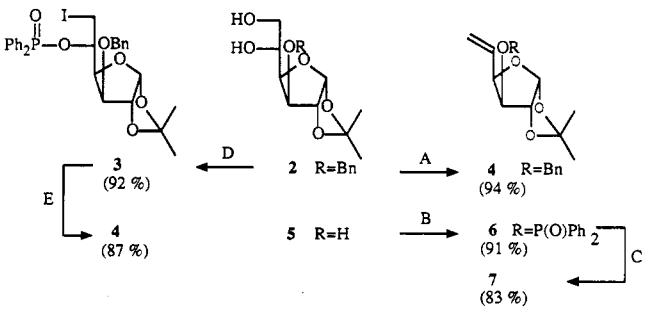
Ph_2P-Cl

1

Results and Discussion

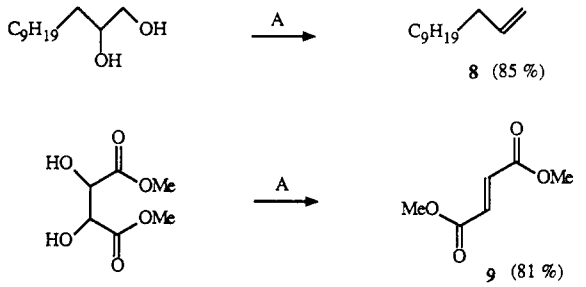
Reacting vicinal diols with chlorodiphenylphosphine (1) (2.2 equiv/diol), imidazole (4 equiv/diol), and iodine (2 equiv/diol) in an inert solvent, preferably toluene, results in the formation of the corresponding olefin generally in high yields (Schemes I and II and Table I). The phosphorus-containing byproducts derived from the reagents, mainly diphenylphosphinic acid, and imidazole are conveniently extracted from the organic phase into an aqueous potassium/sodium carbonate or sodium hydroxide phase,

Scheme I[a]



[a] Key: (A) imidazole (4 equiv), 1 (2.2 equiv), reflux, 30 min, zinc powder; (B) imidazole (12 equiv), 1 (5 equiv), I_2 (5 equiv), reflux, 2 h; (C) methanol, KOH, (2.2 equiv); (D) imidazole (4 equiv), 1 (2.2 equiv), I_2 (2.2 equiv), 100 °C, 30 min; (E) zinc powder (10 equiv), acetic acid (2 equiv), ethanol, 1 h.

Scheme II[a]



[a] Key: (A) imidazole (3.3 equiv), 1 (1.5 equiv), I_2 (1.5 equiv), room temperature, 30 min.

giving an essentially reagent-free organic phase. The reaction generally proceeds smoothly directly from diol to olefin, presumably via a vicinal iodo diphenylphosphinate that is reductively eliminated to olefin by iodide ions present in the reaction mixture. The vicinal iodo diphenylphosphinate can sometimes be detected (TLC) as an intermediate during the course of the reaction, or it may be isolated and characterized. Should the reaction fail to go to completion at the iodo diphenylphosphinate stage, zinc may be added. Thus, when 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (2) was reacted (Scheme I), the vicinal iodo diphenylphosphinate 3 was isolated in 92% yield. Compound 3 was then converted into the corresponding olefin 4 with use of zinc in ethanol containing acetic acid at room temperature.[4] This two-step procedure was preferably carried out in situ by adding zinc (10 equiv) directly to the reaction mixture vide supra after a 30-min reaction time. Olefin 4 was thus isolated in 94% yield (from 2). This olefination procedure was also applied

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(2) Garegg, P. J.; Samuelsson, B. *Synthesis* **1979**, 469; **1974**, 813.

(3) Classon, B.; Liu, Z.; Samuelsson, B. *J. Org. Chem.* **1988**, *53*, 6126.

(4) Classon, B.; Garegg, P. J.; Samuelsson, B. *Acta Chem. Scand.* **1982**, *B36*, 251.

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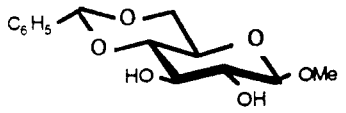
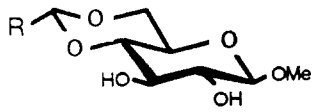
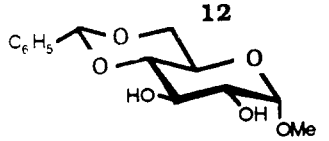
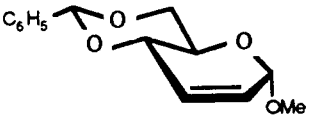
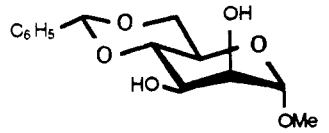
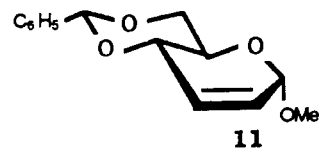
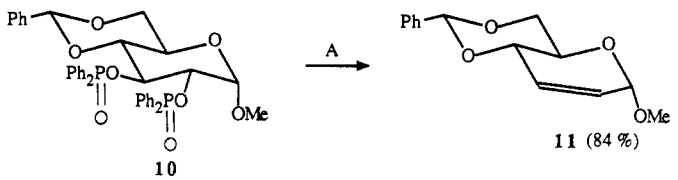
Table I[a]

substrate	product	yield, %	$[\alpha]^{22}_D$ ($CHCl_3$), deg found	$[\alpha]^{22}_D$ ($CHCl_3$), deg lit.	mp, °C found	mp, °C lit.
		75	+40	+43[9]	93–95	94–95
 R = *p*-$OCH_3C_6H_4$ **12**	 R = *p*-$OCH_3C_6H_4$ **13**	88	+46		101–104	
		89	+130	+126[10]	116–118	117–119
	 **11**	52	+131	+126	116–118	117–119

[a] Reaction conditions: chlorodiphenylphosphine (2.2 equiv/diol), imidazole (4 equiv/diol), and iodine (2 equiv/diol) in toluene at 90 °C for 2 h.

Scheme III[a]



[a] Key: (A) imidazole (2 equiv), I_2 (2 equiv), reflux, 1 h.

to 1,2-*O*-isopropylidene-α-D-glucofuranose (**5**), producing the corresponding 5,6-unsaturated derivative with a diphenylphosphinate ester at O-3 in 91% yield (without the use of zinc). The phosphinate ester **6** was saponified with use of potassium hydroxide in methanol, giving **7** in 83% yield.

When 1,2-dodecanediol or dimethyl tartrate (Scheme II) was reacted with the chlorodiphenylphosphine reagent system at room temperature, 1-dodecene (**8**) was obtained in 87% yield and dimethyl fumarate (**9**) was obtained in 81% yield.

To examine further routes to olefins from vicinal diols, methyl 2,3-bis-*O*-(diphenylphosphino)-4,6-*O*-benzylidene-α-D-glucopyranoside[5] (**10**), prepared from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside and chlorodiphenylphosphine, was reacted with iodine (2 equiv) and imidazole (2 equiv) in toluene for 1 h at 90 °C to afford the olefin **11** in 84% isolated yield (Scheme III). This two-step sequence could presumably in some instances be advantageous compared to the one-pot procedure.

Also, polymer-bound triphenylphosphine or [*p*-(dimethylamino)phenyl]diphenylphosphine[3] in combination with iodine and imidazole was studied as methods to produce olefins from methyl 4,6-O-benzylidenehexosides in analogy with the triphenylphosphine procedure.[2] These two procedures gave slightly lower yields than the chlorodiphenylphosphine method for both cis and trans vicinal diols. They suffer the same disadvantage as the triphenylphosphine system in that olefins, in useful yields, are not obtained from vicinal diols containing a primary and a secondary hydroxyl group as in **2** and **5**.

In conclusion, chlorodiphenylphosphine in combination with iodine and imidazole is a novel and versatile system for converting vicinal diols into olefins. Large-scale preparations are facilitated by the ease by which reagents are removed by extractive procedures.

Experimental Section

General Methods. Melting points are corrected. Concentrations were performed under diminished pressure (1–2 kPa) at a bath temperature not exceeding 40 °C. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. NMR spectra were recorded at 25 °C unless otherwise stated, with a Jeol GSX-270 instrument. Chemical shifts are given (ppm) downfield from tetramethylsilane. NMR spectra for all compounds were in accordance with the postulated structures. Thin-layer chromatography was carried out with use of precoated silica gel plates (F 250 Merck), and the spots were visualized by UV light and/or charring with 8% aqueous sulfuric acid. All reactions were monitored by TLC. Column chromatography was performed with aluminium oxide 90 (II–III) and toluene as eluent unless otherwise stated. The loadings were in the range 1/25–1/100. Organic phases were dried over anhydrous magnesium sulfate. The yields given below are for purified products. Chlorodiphenylphosphine, obtained from Aldrich Chemical Co., was distilled [bp 130 °C (0.5 Pa)] prior to use.

The following experimental conditions were used for all the reactions in Schemes I–III:

3-*O*-Benzyl-6-deoxy-6-iodo-1,2-*O*-isopropylidene-5-*O*-(diphenylphosphinyl)-α-D-glucofuranose (3). To a stirred mixture of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**2**) (0.40 g, 1.29 mmol), imidazole (0.35 g, 5.16 mmol), and chlorodiphenylphosphine (0.63 g, 2.84 mmol) in toluene (30 mL) was added iodine (0.72 g, 2.84 mmol) portionwise at 80 °C. The mixture was stirred for 30 min at 100 °C. The mixture was cooled to room temperature and washed with aqueous sodium thiosulfate, 1 M sodium hydroxide, and water. The organic phase was dried, concentrated, and subjected to silica gel column chromatography (toluene–ethyl acetate, 4:1) to render **3**: 0.72 g, 92%; $[\alpha]^{22}_D$ −22° (*c* 1.47, $CHCl_3$); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 11.2 (C-6), 26.5, 27.1 (2 CH_3), 68.9 (C-5), 71.5 (benzyl), 80.6, 81.5, 81.6, 105.0 (C-1), 112.3 [$C(CH_3)_2$].

(5) Culler, W. R.; Yoshihiro, S. *Tetrahderon Lett.* **1978**, *19*, 1635.

Anal. Calcd for $C_{28}H_{30}IO_6P$: C, 54.2; H, 4.87; O, 15.5; P, 5.0. Found: C, 54.0; H, 4.9; O, 15.8; P, 5.2.

3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (4). Method A. To a stirred solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**2**) (0.50 g, 1.61 mmol), imidazole (0.44 g, 6.45 mmol), and chlorodiphenylphosphine (0.78 g, 3.55 mmol) in toluene (30 mL) was added iodine (0.90 g, 3.55 mmol) portionwise at 80 °C. The mixture was stirred for 30 min at reflux temperature. Zinc powder (1.1 g, 16.1 mmol) was added, and stirring at reflux temperature was continued for another 30 min. The mixture was cooled to room temperature and washed with 1 M sodium hydroxide and water. The organic phase was dried, concentrated, and subjected to column chromatography to render **4**: 0.42 g, 94%; $[\alpha]^{22}_D$ −61° (*c* 2.13, ethanol) [lit.[6] [α] −66° (*c* 3, ethanol)], [lit.[7] bp 124–129 °C (0.2 Torr), $[\alpha]^{28}_D$ −56.4° ($CHCl_3$)]; ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 26.2, 26.8 (2 CH_3), 72.0 (benzyl), 81.6, 82.9, 83.5, 104.9 (C-1), 111.4, 118.9 (C-6), 127.5–129.0 (phenyl), 132.4 (C-5).

Method B. To a stirred solution of **3** (0.20 g, 0.32 mmol) in ethanol (20 mL) were added zinc powder (0.2 g, 3.22 mmol) and acetic acid (0.04 g, 0.65 mmol) at room temperature. After being stirred for 1 h, the mixture was filtered through Celite and partioned between ethyl acetate and 1 M aqueous sodium hydroxide. The organic layer was washed with water, dried, concentrated, and subjected to column chromatography to render **4**: 77 mg, 86%; data as above.

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(diphenylphosphinyl)-α-D-*xylo*-hex-5-enofuranose (6). To a stirred mixture of 1,2-*O*-isopropylidene-α-D-glucofuranose (**5**) (20 g, 91 mmol), imidazole (74.2 g, 1.09 mol), and chlorodiphenylphosphine (99.3 g, 0.45 mol) in toluene (750 mL) was added iodine (114 g, 0.45 mol) portionwise at 80 °C. The mixture was stirred for 2 h at reflux temperature. The mixture was cooled to room temperature and washed with aqueous sodium thiosulfate, 1 M sodium hydroxide, and water. The organic phase was dried, concentrated, and subjected to silica gel column chromatography (toluene–ethyl acetate, 2:1) to render **6**: 31.9 g, 91%; $[\alpha]^{22}D$ −94° (*c* 0.71, $CHCl_3$); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 26.2, 26.7 (2 CH_3), 79.2, 80.8, 84.2, 104.6 (C-1), 112.3 [$C(CH_3)_2$], 119.6 (C-6), 128.5–131.5 (phenyl), 132.5 (C-5).

Anal. Calcd for $C_{21}H_{23}O_5P$: C, 65.3; H, 6.0; O, 20.7; P, 8.02. Found: C, 65.3; H, 6.0; O, 21.3; P, 8.10.

5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (7). To a stirred solution of **6** (32.1 g, 83 mmol) in methanol (280 mL) was added potassium hydroxide (10.2 g, 0.18 mol) at room temperature. After 2 h the mixture was diluted with dichloromethane (400 mL) and washed with 1 M sodium hydroxide and water. The organic phase was dried, concentrated, and subjected to silica gel column chromatography (toluene–ethyl acetate, 2:1) to render **7**: 12.8 g, 83%; mp 61–63 °C; $[\alpha]^{22}_D$ −64° (*c* 1.83, $CHCl_3$); [lit.[6] mp 61–65 °C; [α] −60° (*c* 2, $CHCl_3$)], [lit.[8] mp 61–65 °C, $[\alpha]_D$ −51.5° (*c* 1.1, $CHCl_3$)].

1,2-Dodecene[11] (8). To a stirred solution of 1,2-dodecanediol (0.5 g, 2.47 mmol), imidazole (0.55 g, 8.08 mmol), and chlorodiphenylphosphine (0.82 g, 3.72 mmol) in toluene–acetonitrile 2:1 (15 mL) was added iodine (0.94 g, 3.72 mmol) at room temperature. After 16 h the reaction mixture was diluted with toluene and washed successively with aqueous sodium thiosulfate, 1 M sodium hydroxide, and then water. Silica gel column chromatography (*n*-hexane) yielded **8**, 353 mg, 85%.

Dimethyl Fumarate[12] (9). Dimethyl L-tartrate (0.5 g, 2.81 mol) was subjected to the same reaction conditions as for **8** but purified by distillation to yield **9**, 327 mg, 81%.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (11). To a stirred mixture of methyl 2,3-bis-*O*-(diphenylphosphino)-4,6-*O*-benzylidene-α-D-glucopyranoside[5] (**10**) (0.30 g, 0.41 mmol) and imidazole (56 mg, 0.82 mmol) in toluene (10 mL) was added iodine (0.21 g, 0.82 mmol) at 80 °C. The mixture was stirred for 1 h at reflux temperature. The mixture was cooled to room temperature and washed with aqueous sodium thiosulfate, 1 M sodium hydroxide, and water. The organic phase was dried, concentrated, and subjected to column chromatography to render **11**: 86 mg, 84%; mp 116–118 °C; $[\alpha]^{22}_D$ +126° (*c* 1.1, $CHCl_3$), [lit.[10] mp 117–119 °C; $[\alpha]^{22}_D$ +130° (*c* 1.1, $CHCl_3$)].

The following experimental conditions were used for all the reactions in Table I:

Methyl 2,3-Dideoxy-4,6-*O*-(4-methoxybenzylidene)-β-D-*erythro*-hex-2-enopyranoside (13). To a stirred mixture of methyl 4,6-*O*-(4-methoxybenzylidene)-β-D-glucopyranoside[7] (**12**) (0.50 g, 1.6 mmol), imidazole (0.65 g, 9.6 mmol), and chlorodiphenylphosphine (0.78 g, 3.52 mmol) in toluene (30 mL) was added iodine (0.81 g, 3.2 mmol) portionwise at room temperature. The mixture was stirred for 2 h at 90 °C. The mixture was cooled to room temperature and washed with aqueous sodium thiosulfate, 1 M sodium hydroxide, and water. The organic phase was dried, concentrated, and subjected to column chromatography to render the title compound: 0.39 g, 88%; mp 101–104 °C; $[\alpha]^{22}_D$ +46° (*c* 0.4, $CHCl_3$); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 55.0 (2 OCH_3), 69.0, 70.5, 74.9, 99.3 (benzylidene), 102.0 (C-1), 128.0, 131.6 (C-3, C-2).

Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.7; H, 6.52. Found: C, 64.7; H, 6.40.

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