Regio- and Stereoselective Conversion of Allylic Alcohols to Halides via Allylic Phosphates

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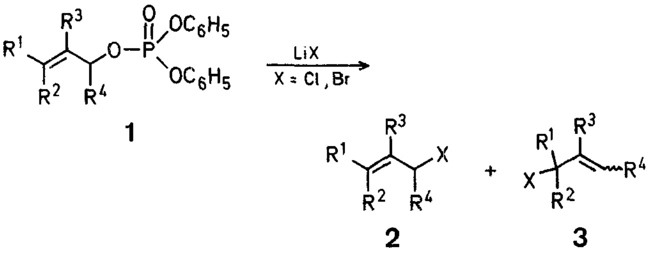
Regio- and stereoselective conversion of allylic alcohols to allylic halides is an important process in synthetic chemistry[1]. Several methods for this purpose have been developed, some of which are of satisfactory selectivity: treatment with thionyl chloride[2] or phosphorus tribromide[3], formation of a sulfonate ester[4] or dithiocarbamate[5] followed by the reaction with halide ion, reaction with triphenylphosphine/tetrachloromethane[6] or hexachloroacetone[7], reaction with dimethyl sulfide/*N*-halosuccinimide[8], reaction with titanium(IV) chloride/*N*-methylaniline[9], and treatment with chlorotrimethylsilane[10]. Here we describe a new method for the regio- and stereoselective transformation of allylic alcohols to halides which involves the reaction of allylic phosphates with lithium halides.

The reaction of allylic diphenyl phosphates **1**[11] with lithium chloride or bromide in dimethylformamide at room temperature gave 50–76 % yields of allylic chlorides or bromides **2** as summarized in the Table. All reactions proceeded with preservation of the stereochemistry, e.g., no detectable *cis*/*trans* isomerization of allylic double bond was observed. Small amounts (6–9 %) of the allylic rearrangement products **3** (S_N2' reaction) were observed for the reactions of 2-butenyl (**1c**), 1-methyl-2-propenyl (**1d**), and cinnamyl phosphates (**1e**), whereas geranyl (**1f**) and neryl phosphates (**1g**) gave the respective chlorides regiospecifically. Geranyl (**2h**) and neryl bromides (**2i**) were also obtained regio- and stereospecifically.



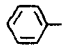
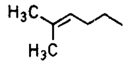
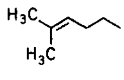
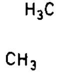
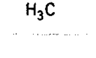
2, 3	R¹	R²	R³	R⁴	X
a	H	H	H	H	Cl
b	H	H	CH_3	H	Cl
c	CH_3	H	H	H	Cl
d	H	H	H	CH_3	Cl
e		H	H	H	Cl
f		CH_3	H	H	Cl
g	CH_3		H	H	Cl
h		CH_3	H	H	Br
i	CH_3		H	H	Br

Table. Compounds **2** (and **3**) prepared

Product **2**/**3**	Yield [%]	Ratio of **2**/**3**	b.p. [°C]/torr (b.p. reported)	^{1}H-N.M.R. (CCl_4) of **2** δ [ppm]	^{13}C-N.M.R. ($CDCl_3$) of **2** δ [ppm]
a	75	–	46–48°/760 (45°/760)[12]	6.25–5.55 (m, 1H, olefin); 5.46–4.95 (m, 2H, olefin); 3.93 (d, 2H, CH_2, $J = 6$ Hz)	133.9 (d), 118.5 (t), 45.2 (t)
b	64	–	71–76°/760 (71–72°/760)[13]	4.91 (m, 2H, olefin); 3.49 (s, 2H, CH_2); 1.80 (s, 3H, CH_3)	141.4 (s), 115.1 (t), 49.5 (t), 19.8 (q)
c	50	94/6[a]	82–88°/760[b] (84.8°/752)[14]	5.60 (m, 2H, olefin); 3.90 (d, 2H, CH_2, $J = 6$ Hz); 1.70 (m, 3H, CH_3)	131.2 (d), 128.0 (d), 45.8 (t), 18.0 (q)
d	70	93/7[a]	77–80°/760[b], (63.7°/748)[14]	6.10–5.50 (m, 1H, olefin); 5.25–4.83 (m, 2H, olefin); 4.34 (quin, 1H, CH, $J = 6$ Hz); 1.53 (d, 3H, CH_3, $J = 6$ Hz)	140.4 (d), 115.7 (t), 58.1 (d), 25.2 (q)
e	65	91/9[c]	57–70°/2[b] (125–126°/22)[15]	7.14 (s, 5H, C_6H_5); 6.60–5.80 (m, 2H, olefin); 4.09 (d, 2H, CH_2, $J = 6$ Hz)	136.2 (s), 134.3 (d), 128.9 (d), 128.6 (d), 127.0 (d), 125.2 (d), 45.8 (t)
f	76	100/0[d]	41–46°/2 (46–48°/0.5)[16]	5.34 (br. t, 1H, olefin, $J = 8$ Hz); 5.00 (br. s, 1H, olefin); 3.97 (d, 2H, CH_2, $J = 8$ Hz); 2.00 (m, 4H, CH_2), 1.65 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 1.54 (s, 3H, CH_3)	142.8 (s), 132.2 (s), 124.1 (d), 121.0 (d), 41.3 (t), 39.9 (t), 26.8 (t), 26.0 (q), 18.1 (q), 16.4 (q)
g	61	100/0[d]	48–50°/2.5 (44–46°/0.5)[16]	5.30 (br. t, 1H, olefin, $J = 8$ Hz); 4.98 (br. s, 1H, olefin); 3.91 (d, 2H, CH_2, $J = 8$ Hz); 2.05 (m, 4H, CH_2); 1.72 (s, 3H, CH_3); 1.63 (s, 3H, CH_3); 1.58 (s, 3H, CH_3)	142.7 (s), 132.6 (s), 124.1 (d), 121.9 (d), 41.1 (t), 32.4 (t), 27.1 (t), 26.1 (q), 23.9 (q), 18.1 (q)
h	64	100/0[d]	110°/3 (73–75°/1.5)[17]	5.46 (br. t, 1H, olefin, $J = 8$ Hz); 5.02 (br. s, 1H, olefin); 3.95 (d, 2H, CH_2, $J = 8$ Hz); 2.05 (m, 4H, CH_2); 1.70 (s, 3H, CH_3); 1.65 (s, 3H, CH_3); 1.58 (s, 3H, CH_3)	143.5 (s), 131.9 (s), 123.6 (d), 120.6 (d), 39.6 (t), 29.5 (t), 26.3 (t), 25.7 (q), 17.7 (q), 15.9 (q)
i	54	100/0[d]	105°/3 (63–64°/0.6)[17]	5.45 (br. t, 1H, olefin, $J = 8$ Hz); 5.03 (br. s, 1H, olefin); 3.86 (d, 2H, CH_2, $J = 8$ Hz); 2.08 (m, 4H, CH_2); 1.75 (s, 3H, CH_3); 1.65 (s, 3H, CH_3); 1.58 (s, 3H, CH_3)	143.2 (s), 132.3 (s), 123.5 (d), 121.5 (d), 31.8 (t), 29.2 (t), 26.3 (t), 25.7 (q), 23.5 (q), 17.7 (q)

[a] Determined by G.L.C. analysis at 50 °C on a 3,3′-oxydipropionitrile column (1 m).

[b] B.p. of **2**/**3** mixture.

[c] Determined by G.L.C. analysis at 130 °C on a Silicon SE-30 column (1 m).

[d] Determined by ^{1}H- and ^{13}C-N.M.R. spectrometry.

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The advantages of the present method are: (1) regio- and stereoselectivity are generally high, (2) reaction conditions are very mild, (3) experimental operations are simple, and (4) starting phosphates can be readily prepared from the corresponding alcohols[11]. Therefore, this method provides a convenient route for the regio- and stereoselective synthesis of allylic halides.

Geranyl Chloride (2f); Typical Procedure:

A mixture of geranyl diphenyl phosphate (**1f**; 3.23 g, 8.7 mmol) and lithium chloride (0.64 g, 15.1 mmol) in dimethylformamide (15 ml) is stirred at room temperature. After ~ 10 min, a white precipitate of lithium diphenyl phosphate is deposited, and the mixture is left overnight. The mixture is poured into water (100 ml) and the product extracted with ether (3 × 30 ml). The extracts are dried with anhydrous sodium sulfate and concentrated. The residue is distilled to give geranyl chloride (**2f**) as a colorless oil; yield: 1.14 g (76%); b.p. 41–46°C/2 torr.

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