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Palladium(0)-Catalyzed Coupling Reaction of Isoprene Bromohydrin with Aromatic Organolithium Reagents

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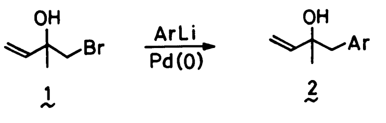
Synopsis. Palladium(0)-catalyzed reaction of isoprene bromohydrin with aromatic organolithium reagents selectively gave good yields of coupling products without rearrangement.

In our continuous study on the reaction of isoprene bromohydrin (1-bromo-2-methyl-3-buten-2-ol) (**1**) with organometallic reagents, we have recently reported the coupling reaction of **1** with Grignard reagents in the presence of a palladium(0) catalyst which gives exclusively vinyl-group-migrated products. With phenylmagnesium bromide, for example, **1** selectively gave 2-phenyl-4-penten-2-ol in 85% yield.[1] It is interesting to examine the palladium(0)-catalyzed coupling of **1** with organometallics other than Grignard reagent, because isoprene bromohydrin (**1**) shows diverse reaction behavior in the transition-metal-catalyzed coupling with various types of organometallic reagents.[2] We now report the palladium(0)-catalyzed reaction of **1** with aryllithium reagents which yields, in contrast with the reaction of Grignard reagents,[1] non-rearranged coupling products (**2**) with high selectivity (Eq. 1).



(1)

When the reaction of 1 with phenyllithium was conducted in the presence of a catalytic amount (0.1 mol%) of tetrakis(triphenylphosphine)palladium, 2-methyl-1-phenyl-3-buten-2-ol (**2a**) was obtained selectively in 53% isolated yield. No other coupling products could be found in the reaction mixture. In the absence of the catalyst, a mixture of **2a** and 2-methyl-4-phenyl-2-buten-1-ol (*E*/*Z* 52/48) was formed in the ratio 76:24 in 85% combined yield.

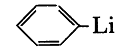
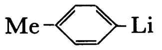
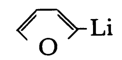
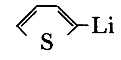
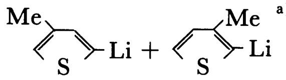
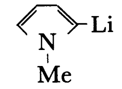
Results for other aryllithium reagents are summarized in Table 1, which shows that a variety of aryllithiums (phenyl, *p*-tolyl, 2-furyl, 2-thienyl, and 2-pyrrolyl) all give coupling products (**2a—f**) without rearrangement. However, the reactions of **1** with alkyl- and allyllithium reagents such as butyl- and prenyllithium in the presence of the Pd(0) catalyst gave complex product mixtures. For example, the coupling of **1** with prenyllithium under the similar reaction conditions described above gave complex mixture of products in which no trace of linalool could be found.

The present procedure provides a facile and synthetically useful method for introducing a 2-hydroxy-2-methyl-3-butenyl group, an isoprenoid C_5 synthon, to an aromatic nucleus.

Experimental

General. Infrared spectra were recorded on a JASCO IRA-1 spectrophotometer. ^{1}H NMR spectra were recorded on a Hitachi R-24A spectrometer (60 MHz) or on a Varian XL-200 spectrometer (200 MHz) with Me_4Si as internal standard. Mass spectra were determined using a Hitachi M-52 instrument at 20 eV. GLC analyses were performed on a Yanaco G1800 gas chromatograph equipped with a column packed with Apiezon grease L on Uniport B (15%). Elemental analyses were performed at the Elemental Analysis Center of Kyoto University. For Kugelrohr distillation, a Shibata GTO-250R glass tube oven was used.

Table 1. Pd(0)-Catalyzed Reaction of **1** with Aryllithiums

Aryllithium	Product	Yield/%
	**2a**	53
	**2b**	86
	**2c**	60
	**2d**	78
 [a]	**2e**[b]	92
	**2f**	70

a) Prepared by the lithiation of 3-methylthiophene.[4]
b) Mixture of the products coupled at the 5- and 2-positions of 3-methylthiophene (7 : 3).

Palladium(0)-Catalyzed Coupling Reaction of Isoprene Bromohydrin (1) with Aryllithium Reagents. The following reaction with 2-furyllithium represents the general procedure. Tetrakis(triphenylphosphine)palladium (12 mg, 0.01 mmol) was added to a solution of 2-furyllithium, prepared from furan (680 mg, 10 mmol) and a hexane solution of butyllithium (1.6 M, 6.3 cm^3, 10 mmol (1 M=1 mol dm^{-3})) in ether (10 cm^3) according to the literature method,[3] and the mixture was stirred at 0 °C for 10 min. A solution of **1** (330 mg, 2 mmol) in ether (2 cm^3) was then added at 0 °C and the mixture was left overnight at room temperature. The reaction was quenched by the addition of saturated aqueous ammonium chloride and the product was extracted with ether. The extracts were dried (Na_2SO_4) and the solvent was evaporated. The residue was distilled (Kugelrohr) (bp 115 °C/ 18 Torr; 1 Torr≈133.322 Pa) to give a colorless oil (182 mg, 60%), which was found pure 2c by glc and ^{1}H NMR analyses.

The reactions with other aryllithium reagents were similarly carried out. Lithiation of thiophene,[4] 3-methylthiophene,[5] and 1-methylpyrrole[6] was performed according to literature. The structures of the coupling products (**2a—f**) were deduced by their spectral and analytical data, except for **2a** which was confirmed by the direct comparison with an authentic sample.[1]

2-Methyl-1-(*p*-tolyl)-3-buten-2-ol (2b): Bp 110 °C/3 Torr;

IR (neat) 3420, 2980, 1644, 1516, 1110, 920, and 812 cm^{-1}; ^{1}H NMR (CDCl$_3$) 1.29 (s, 3H, CH$_3$), 1.64 (bs, 1H, OH), 2.34 (s, 3H, CH$_3$), 2.80 (AB q, J=14 Hz, 2H, CH$_2$), 5.07 (dd, J=10, 2 Hz, 1H olefin), 5.14 (dd, J=17, 2 Hz, 1H, olefin), 6.00 (dd, J=17, 10 Hz, 1H, olefin), 7.13 (m, 5H, Ph); MS *m/z* 176 (M$^+$); Found: C, 81.47; H, 9.24%. Calcd for C$_{12}$H$_{16}$O: C, 81.77; H, 9.15%.

1-(2-Furyl)-2-methyl-3-buten-2-ol (2c): Bp 115 °C/18 Torr; IR (neat) 3430, 2980, 1642, 1594, 1504, 1146, 1010, 926, and 728 cm^{-1}; ^{1}H NMR (CCl$_4$) 1.22 (s, 3H, CH$_3$), 1.76 (bs, 1H, OH), 2.81 (s, 2H, CH$_2$), 5.00 (dd, J=10, 2 Hz, 1H, olefin), 5.21 (dd, J=17, 2 Hz, 1H, olefin), 5.92 (dd, J=17, 10 Hz, 1H, olefin), 6.08 (m, 1H, furan H-3), 6.27 (m, 1H, furan H-4), 7.32 (m, 1H, furan H-5); MS *m/z* 152 (M$^+$); Found: C, 70.96; H, 8.04%. Calcd for C$_9$H$_{12}$O$_2$: C, 71.02; H, 7.95%.

2-Methyl-1-(2-thienyl)-3-buten-2-ol (2d): Bp 120 °C/5 Torr; IR (neat) 3450, 2980, 1642, 1372, 1223, 1150, 994, 922, and 692 cm^{-1}; ^{1}H NMR (CDCl$_3$) 1.34 (s, 3H, CH$_3$), 1.73 (bs, 1H, OH), 3.06 (s, 2H, CH$_2$), 5.15 (dd, J=10, 2 Hz, 1H, olefin), 5.22 (dd, J=17, 2 Hz, 1H, olefin), 6.03 (dd, J=17, 10 Hz, 1H, olefin), 6.90 (m, 1H, thiophene H-3), 7.00 (m, 1H, thiophene H-4), 7.22 (m, 1H, thiophene H-5); MS *m/z* 168 (M$^+$); Found: C, 64.67; H, 7.37%. Calcd for C$_9$H$_{12}$OS: C, 64.25; H, 7.19%.

2-Methyl-1-(4-methyl-2-thienyl)-3-buten-2-ol and 2-Methyl-1-(3-methyl-2-thienyl)-3-buten-2-ol (2e) (7:3 Mixture): Bp 110 °C/ 3 Torr; IR (neat) 3450, 2980, 1642, 1370, 1120, 992, 920, 850, and 700 cm^{-1}; ^{1}H NMR (CDCl$_3$) 1.32 (s, 2.1H, CH$_3$), 1.33 (s, 0.9H, CH$_3$), 1.73 (bs, 1H, OH), 2.19 (s, 0.9H, CH$_3$), 2.22 (s, 2.1H, CH$_3$), 2.99 (s, 2H, CH$_2$), 5.12 (dd, J=10, 2 Hz, 1H, olefin), 5.21 (dd, J=17, 2 Hz, 1H, olefin), 6.01 (dd, J=17, 10 Hz, 1H, olefin), 6.69 (bs, 0.7H, thiophene H-3), 6.76 (bs, 0.7H, thiophene H-5), 6.85 (d, J=5 Hz, 0.3H, thiophene H-4), 7.12 (d, J=5 Hz, 0.3H, thiophene H-5); MS *m/z* 182 (M$^+$); Found: C, 65.78; H, 7.88%. Calcd for C$_{10}$H$_{14}$OS: C, 65.89; H, 7.74%.

2-Methyl-1-(1-methyl-2-pyrrolyl)-3-buten-2-ol (2f): Bp 130 °C/ 5 Torr; IR (neat) 3500, 2980, 1642, 1490, 1298, 1088, 1018, 920, and 704 cm^{-1}; ^{1}H NMR (CDCl$_3$) 1.32 (s, 3H, CH$_3$), 1.92 (bs, 1H, OH), 2.81 (AB q, J=15 Hz, 2H, CH$_2$), 3.57 (s, 3H, NCH$_3$), 5.11 (dd, J=10, 2 Hz, 1H, olefin), 5.18 (dd, J=17, 2 Hz, 1H, olefin), 5.99 (dd, J=17, 10 Hz, 1H, olefin), 6.04 (m, 1H, pyrrole H-3 or H-4), 6.11 (m, 1H, pyrrole H-4 or H-3), 6.60 (m, 1H, pyrrole H-5); MS *m/z* 165 (M$^+$); Found: C, 72.52; H, 9.21%. Calcd for C$_{10}$H$_{15}$NO: C, 72.69; H, 9.15%.

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