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REGIOSELECTIVE HYDROXYLATION OF β-MYRCENE USING Pd(II) COMPLEXES

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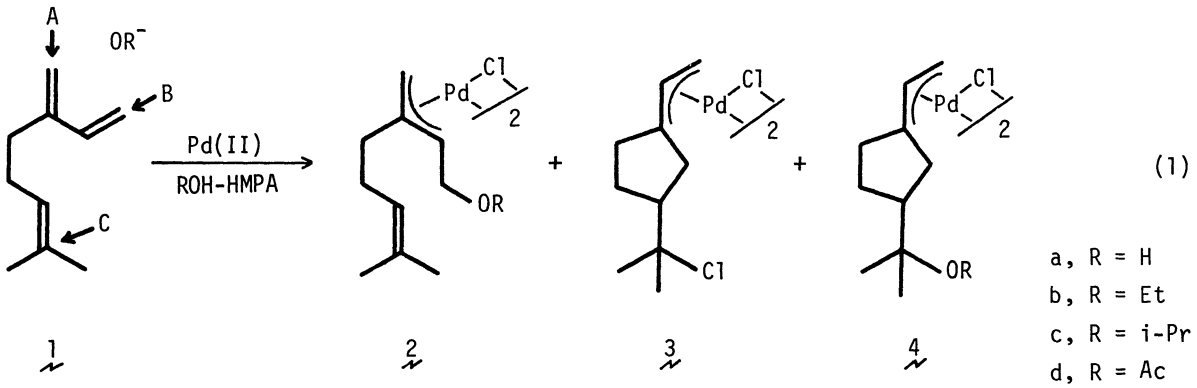
O-nucleophiles, RO^- (R = H, Et, i-Pr, and Ac) were introduced regioselectively into the terminal position of β-myrcene to form linear π-allylpalladium complexes, 2 using HMPA as solvent. Decomposition of 2a gave nerol and citral selectively.

Selective introduction of oxygen atom or hydroxyl group to the terminal position of 1,3-diene for myrcene or ocimene is the simplest method to prepare the corresponding alcohols and aldehydes, e.g., geraniol, nerol, citronellol and citral. The application of organometallics, especially palladium complexes has been challenged and π-allylpalladium complexes for myrcene and ocimene were prepared in the presence of nucleophiles.[1] However, attack of nucleophiles to β-myrcene (1) occurs preferentially from C-side in Eq. 1 causing intramolecular cyclization and the main π-allyl species were reported as 3 and 4. The only example for anti-Markovnikov 1,2-addition of nucleophiles to 1 was recently reported by Tamaru et al. in 1,2-hydrosulphonylation of 1 for C-C bond formation.[2] We wish to report here that RO^- (R = H, Et, i-Pr, and Ac) is introduced regioselectively into the terminal position of 1 to form π-allylpalladium complex 2



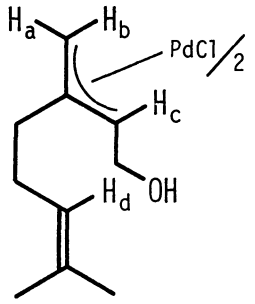
(1)

1 2 3 4

a, R = H
b, R = Et
c, R = i-Pr
d, R = Ac

using HMPA as solvent and the decomposition of 2a gives nerol (5) and citral (6) selectively.

In a typical reaction, β-myrcene (1) (2.2 mmol) and $(CH_3CN)_2PdCl_2$ (1.5 mmol) were stirred in a mixed solvent of HMPA and water (10 : 1) for 5 hr at room temperature. After extraction with benzene-HCl(1/2N), drying ($CaCl_2$) and removal of the solvent under reduced pressure, the yellow oily residue was separated by column chromatography (silica gel, benzene-ethyl acetate, 5:1) into three parts. Recrystallization of main product from CH_2Cl_2 gave 2a as yellow needles (75% yield based on $PdCl_2$). Two kinds of by-product were also purified and characterized as 3a (4%) and 4a[3] (4%) spectroscopically.



2a

2a; mp 86.5-88.5°C, IR(CCl_4), ν_{OH} 3640, 3550, $\nu_{(C-O)}$ 1050 cm^{-1}; (KBr), ν_{OH} 3250, $\nu_{(C-O)}$ 995 cm^{-1}. NMR($CDCl_3$); δ 1.63(3H,s,$-CH_3$), 1.70(3H,s,$-CH_3$), 2.35(4H,m,$-CH_2CH_2-$), 2.50(1H,s,OH, D_2O exchangeable), 2.78(1H,s,H_b), 3.65(3H,s, overlapping of H_c and $-CH_2OH$), 3.72(1H,s,H_a), 5.15(1H,m, H_d). Anal: Calcd for $C_{10}H_{17}OClPd$: C, 40.70; H, 5.81;

Table 1. Attack of O-Nucleophiles to β-Myrcene to Form π-Allylpalladium Complexes[a]

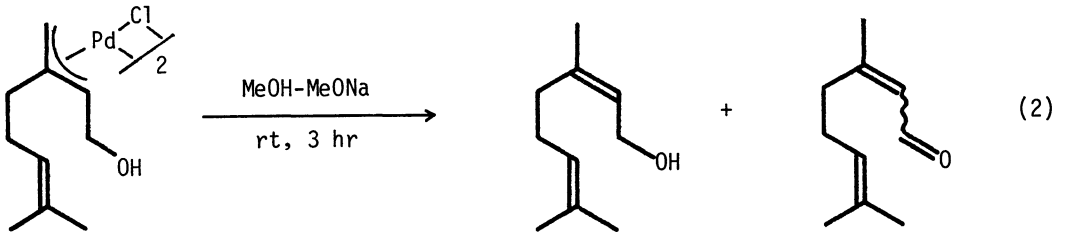
Nucleophile (ROH)	Solvent[b]	Base added	Time (hr)	Product yield (%)[c]		
				2	3	4
R = H	H_2O-HMPA	-	5	75	4	4
	H_2O-acetone	-	0.2	-	60	30
	H_2O-acetone	Li_2CO_3	3	25	6	30
	H_2O-DMF	Li_2CO_3	6	33	7	6
Et	EtOH	-	1	-	26	35
	EtOH-HMPA	-	4	57	5	-
i-Pr	i-Pr	-	4	-	48	43
	i-Pr-HMPA	-	24	44	15	-
Ac	AcOH	-	0.2	-	51	30
	AcOH-HMPA	LiOAc	24	64	-	-

a) The usual scale is as follows: 1 (2.25 mmol), $(CH_3CN)_2PdCl_2$ (1.5 mmol), base (5 mmol) in 20 ml of a solvent. Each run was terminated according to the TLC analysis. b) The ratio for the mixed solvent was nucleophile/solvent = 1/10. c) The isolated yield based on $(CH_3CN)_2PdCl_2$ used.

Cl, 12.01. Found: C, 40.88; H, 6.11; Cl, 11.54. 3a; mp 149-152°C, IR(KBr) ν(C-H) 3060, 3020, δ(C-H) 1494 cm^{-1}. NMR($CDCl_3$); δ 1.57(6H,s,2-CH_3), 1.5-3.0(7H, m), 3.05(1H,d,J=13Hz, allylic-anti), 3.95(1H,d,J=7Hz, allylic-syn), 5.25(1H,m, allylic-central). Anal: Calcd for $C_{10}H_{16}Cl_2Pd$: C, 38.31; H, 5.14; Cl, 22.61. Found: C, 38.64; H, 5.27; Cl, 21.98.

As described above, three allylic protons in 2a, H_a, H_b and H_c show singlet NMR peaks at 3.72, 2.79 and 3.65 ppm, respectively. This pattern is quite different from ABX for 3a and 4a. In addition, the three substituted olefinic proton in 1 (1H, δ5.15,m) remains unaltered after complexation to form 2a. These data indicate that hydroxyl group attacks regioselectively at the terminal carbon atom of diene from B-side in Eq. 1. The results for other nucleophiles are summarized in Table 1.[4)]

The present reaction is affected remarkably by the solvent used. It was found that acetone and alcohols gave only the mixture of cyclic products 3 and 4. Addition of base such as Li_2CO_3 afforded 2 in low yield. DMF also improved the yield of 2 but the reaction remained still non-selective. Regioselective introduction of nucleophiles at the terminal carbon atom from B-side of 1 was realized by using HMPA as solvent. Although the reaction rate was retarded, but π-allyl complex 2 was formed exclusively in the attack of every O-nucleophile examined.



(2)

2a

5 45(51)%

6 36(38)%

( ): GLC yield

The decomposition of 2a was completed at room temperature for 3 hr in MeOH in the presence of 2.5 equiv of MeONa giving the corresponding alcohol and aldehyde selectively.[5)] Purification by silica gel chromatography afforded nerol (5) and citral (6)[6)] in 45% and 36% isolated yields, respectively. Geraniol, the trans-isomer for 5 was not detected in the recovered products. This result further confirms the structure of 2a, especially syn-conformation of $-CH_2OH$. Works of decomposition of 2a under various conditions and catalytic recyclization of palladium are now in progress.

References and Notes

1) K. Dunne and F. J. McQuillin, J. Chem. Soc. (C), 2196, 2200, 2203 (1970); F. J. McQuillin and D. G. Parker, J. Chem. Soc. Perkin I, 809 (1974).
2) Y. Tamaru, M. Kagotani and Z. Yoshida, J. Chem. Soc. Chem. Comm., 367 (1978).
3) Spectroscopic data for 4a agreed with those reported in reference 1. The result of elemental analysis was also satisfactory.
4) The spectral, physical and analytical data of the new compounds obtained in this study are as follows:
2b; yellow needles, mp 114-115°C, IR(KBr), ν(C-H, π-allyl) 3060, δ(C-H, π-allyl) 1485, ν(C-O-C) 1090 cm^{-1}. NMR($CDCl_3$); δ 1.20(3H,t), 1.62(3H,s), 1.70(3H,s), 2.30(4H,m), 2.76(1H,s), 3.60(5H,m), 3.76(1H,s), 5.13(1H,m). Anal: Calcd for $C_{12}H_{21}OClPd$: C, 44.60; H, 6.55; Cl, 10.97. Found: C, 44.40; H, 6.71; Cl, 11.45.
2c; yellow needles, mp 100-103°C, IR(KBr), ν(C-H, π-allyl) 3060, ν(C-O-C) 1150, 1125, 1042 cm^{-1}. NMR($CDCl_3$); δ 1.15(6H,d,J=6Hz), 1.62(3H,s), 1.70(3H,s), 2.30(4H,m), 2.76(1H,s), 3.60(4H,m), 3.75(1H,s), 5.15(1H,m). Anal: Calcd for $C_{13}H_{23}OClPd$: C, 46.31; H, 6.88; Cl, 10.51. Found: C, 46.32; H, 6.91; Cl, 10.06.
2d; yellow needles, mp 121-122.5°C, IR(KBr), ν(C-H, π-allyl) 3050, ν(C=O) 1735, ν(C-O) 1230 cm^{-1}. NMR($CDCl_3$); δ 1.65(3H,s), 1.75(3H,s), 2.3-2.5(4H,m), 2.16(3H,s), 2.90(1H,s), 3.62(1H,dd,J=7,10Hz), 3.90(1H,s), 4.30(1H,dd,J=10, 13Hz), 4.49(1H,dd,J=7,13Hz), 5.25(1H,m). Anal: Calcd for $C_{12}H_{19}O_2ClPd$: C, 42.75; H, 5.68; Cl, 10.52. Found: C, 42.54; H, 5.72; Cl, 10.43.
5) No other products were detected by gas chromatography.
6) The observed ratio for cis- to trans-isomer, i.e., neral to geranial was 2 : 3.

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