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REGIOSELECTIVE C-C BOND FORMATION OF O-LINALYL-N,N-DIMETHYLHYDROXYLAMINE VIA CARBOPALLADATION

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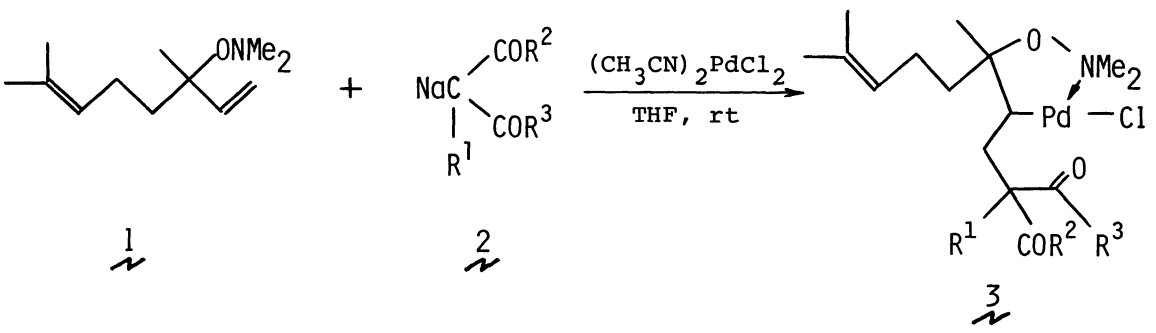
Stable carbopalladation complexes were prepared by regioselective addition of active methylene compounds to O-linalyl-N,N-dimethylhydroxylamine (1) in the presence of Pd(II) complexes, and degradated selectively to the corresponding alkene derivatives by treatment with trimethylsilyl chloride.

O-Linalylhydroxylamine (1) is industrially produced by dimerization of isoprene in the presence of amine followed by the oxidation and the rearrangement. We wish to report here that the application of carbopalladation[1] to 1 mediated by the intramolecular chelation of nitrogen to palladium to form five membered ring[2] results in the regioselective C-C bond formation to the terminal carbon to give the stable carbopalladation products and their demetalation by trimethylsilyl chloride affords geranyl and neryl derivatives selectively.

First, 1 was treated with active methylene compounds in the presence of a stoichiometric amount of $(CH_3CN)_2PdCl_2$. Carbopalladation of 1 with stabilized enolates such as dimethyl malonate and methyl acetoacetate in THF proceeded regio- and chemoselectively. The coordination of the nitrogen atom to palladium



1 2 3

gave the carbopalladation products which were sufficiently stable for the isolation and characterization.

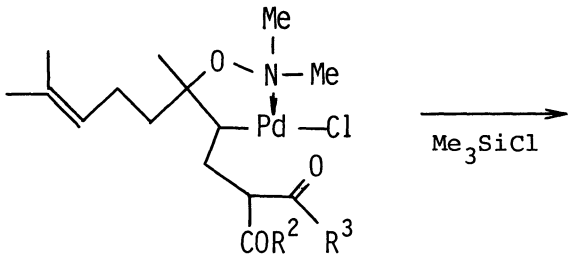
In a typical preparation, the addition of 1 (1.53 mmol) to a suspension of $(CH_3CN)_2PdCl_2$ (1.51 mmol) in 15 ml of THF produced a homogeneous yellowish brown solution, to which dimethyl sodiomalonate (2a, 1.51 mmol) in 15 ml of THF was added at -30°C. The reaction mixture was allowed to warm slowly to room temperature with stirring and then react for 9 hr at 30°C. The color of the solution turned into yellowish green gradually on addition of sodiomalonate. After the prescribed time, the reaction mixture was diluted by aqueous HCl. The reaction product was extracted with ethyl ether and dried on $MgSO_4$. After removal of solvent, a residual yellow oil was purified by column chromatography (SiO_2, 10 cm × 1.7 cmϕ, benzene-ether; 20 : 1 v/v) to give 3a as a yellow oil (82% isolated yield based on $(CH_3CN)_2PdCl_2$); IR(CCl_4), ν_{CO} 1740s, 1725s, ν_{COO} 1260s cm^{-1}. NMR($CDCl_3$); δ 0.7-1.4(3H,m), 1.60(3H,s), 1.68(3H,s), 1.7-2.6(6H,m), 2.86(1H,m), 3.08(6H,s), 3.63(3H,s), 3.76(3H,s), 4.13(1H,m), 5.07(1H,m). Anal: Calcd for $C_{17}H_{30}NO_5ClPd$: C, 43.42; H, 6.43; N, 2.98. Found: C, 43.65; H, 6.55; N, 2.94%. Cryoscopy in benzene showed that 3a was a monomeric complex; Mw: Calcd 470.3, Found 475.6.[3] Several metalation complexes of Pd(II) were prepared similarly[4] and the results are summarized in Table 1. It was found that the isolated yields of 3 depended seriously on the steric factor of the enolates

Table 1. Carbopalladation of O-Linalylhydroxylamine with Stabilized Enolates[a]

	Enolate[b]				1	Pd(II)[c]	Reaction time	Isolated[d] yield
	R^1	R^2	R^3	(mmol)	(mmol)	(mmol)	(hr)	(%)
2a	H	MeO	MeO	1.51	1.53	1.51	9	82
2b	Me	MeO	MeO	1.67	2.04	1.53	24	29
2c	Bu	MeO	MeO	2.36	2.88	1.56	12	24
2d	H	Me	MeO	2.18	1.79	1.64	24	90
2e	H	Me	EtO	3.04	2.98	1.94	24	79
2f	H	Et	MeO	7.20	8.73	4.28	3	77

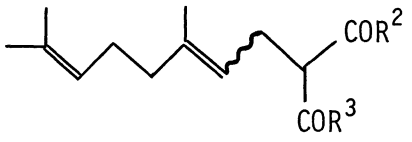
a) The usual conditions are as follows: Solvent, THF 30 ml (70 ml for 2f); Reaction temp, 30°C. Each run was followed by the TLC analysis.
b) Enolate; $NaCR^1(COR^2)(COR^3)$. c) $(CH_3CN)_2PdCl_2$. d) Based on Pd(II) used.

used. When R^1 in 2 was hydrogen (2a, 2d, 2e, and 2f), the reaction proceeded almost quantitatively. Introduction of the alkyl group in R^1 (2b and 2c) resulted in the deposition of palladium metal during the reaction and reduced the yield of 3 considerably. However, it is noteworthy that C-C bond formation by the former enolate (R^1 = H, R^2 = alkyl, and R^3 = alkoxy group) suffices for the synthetic route for target molecules such as sesquiterpenes.



3

Me_3SiCl

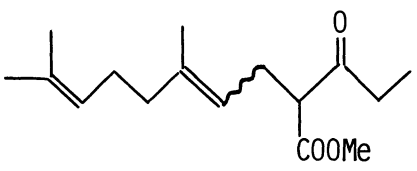


4

		R^2	R^3	Isolated yield (%)	Isomer[5] ratio (E/Z)
3a	4a	MeO	MeO	56 (61)	1
3d	4b	Me	MeO	56 (61)	0.1 >
3e	4c	Me	EtO	58 (76)	0.1
3f	4d	Et	MeO	73	0.1

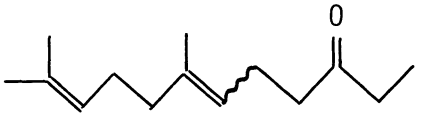
( ); Conversion yield

The degradation of complexes 3 with trimethylsilyl chloride occurred selectively to give the regioselective addition products of C-nucleophiles to O-allyl compound. Typically, 3d (1.97 mmol) was treated with trimethylsilyl chloride (5.0 ml) in 15 ml of benzene at 90°C in a sealed tube for 4 hr. Filtration of deposited palladium dichloride followed by column chromatography led to the isolation of 4b in a 56% yield. Similarly the reactions of 3a, 3e, and 3f with trimethylsilyl chloride proceeded to give the alkene derivatives, 4a, 4c, and 4d in 56, 58, and 73% isolated yields, respectively.[6] Finally, demetalated products 4 were easily converted to the intermediates to sesquiterpenes by the usual method, hydrolysis and decarboxylation.



4d

$Ba(OH)_2$
H_2O-MeOH
rfx, 2 day
72.4%



References and Notes

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3) Intramolecular coordination of the carbonyl group to palladium or coordinative unsaturation of palladium atom is considered for the monomeric structure of the complex 3. CPK-model and ir spectra of carbonyl groups support the coordinative unsaturation.

4) The spectral, physical and analytical data of the complexes 3 are as follows:
3c; yellow powder, mp(dec) 151-152°C, IR(KBr), ν(C=O) 1740, 1717, ν(C-O) 1260 cm^{-1}. NMR($CDCl_3$); δ 0.92(3H,t), 1.59 and 1.67(each 3H,s), 1.2-2.4(15H,m), 2.77(1H,m), 3.06 and 3.13(each 3H,s), 3.64(3H,s), 3.94(3H,s), 5.08(1H,m). Anal: Calcd for $C_{21}H_{38}O_5NClPd$: C, 47.92; H, 7.28; N, 2.66. Found: C, 47.49; H, 7.59; N, 2.84%.
3d; yellow oil, IR(neat), ν(C=O) 1740, 1714, ν(C-O) 1250 cm^{-1}. NMR($CDCl_3$); δ 0.57-1.47(3H,m), 1.63 and 1.72(each 3H,s), 1.73-2.23(6H,m), 2.30 and 2.43 (3H, each s), 2.75(1H,m), 3.12(6H,s), 3.72 and 3.82(3H, each s), 4.00-4.83 (1H,m), 5.17(1H,m). Anal: Calcd for $C_{17}H_{30}O_4NClPd$: C, 44.95; H, 6.60; N, 3.08. Found: C, 44.84; H, 7.09; N, 3.12.
3e; yellow oil, IR(neat), ν(C=O) 1743, 1714, ν(C-O) 1264 cm^{-1}. NMR(CCl_4); δ 1.23(3H,m), 1.27 and 1.35(3H, each t), 1.63 and 1.67(each 3H,s), 1.70-2.33 (6H,m), 2.20 and 2.37(3H, each s), 2.82(1H,m), 3.08(6H,s), 4.10 and 4.23(2H, each q), 3.83-4.50(1H,m), 5.07(1H,m). Anal: Calcd for $C_{18}H_{32}O_4NClPd$: C, 46.17; H, 6.89; N, 2.99. Found: C, 46.34; H, 7.28; N, 2.98%.
3f; yellow oil, IR(CCl_4), ν(C=O) 1737, 1728, ν(C-O) 1244 cm^{-1}. NMR(CCl_4); δ 1.15(3H,t), 1.18(6H,t), 1.2-1.6(3H,m), 1.68 and 1.75(each 3H,s), 2.10(4H,m), 2.2-2.8(3H,m), 2.58(2H,q), 2.72(4H,q), 3.74(3H,s), 4.15(1H,m), 5.15(1H,m). Anal: Calcd for $C_{20}H_{36}O_4NClPd$: C, 48.40; H, 7.31; N, 2.82. Found: C, 48.58; H, 8.75; N, 2.52%.

5) E- and Z-isomers of 4 were roughly separated by liquid chromatography and determined from ^{13}C-nmr spectra.

6) Spectral and analytical data for these compounds were satisfactory.

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