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In Turn or in Reverse Palladium-Catalyzed Carbonyl Allylation and Diels-Alder Reaction by 2-Methylene-3-buten-1-ol

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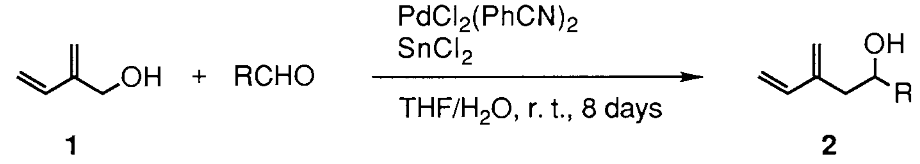
Using $PdCl_2(PhCN)_2$-$SnCl_2$, 2-methylene-3-buten-1-ol causes carbonyl allylation of various aldehydes to afford 1-substituted-3-methylene-4-penten-1-ols; the Diels-Alder reaction of those with dienophiles produces 1-(2-hydroxyethyl)cyclohexenes. Diels-Alder reaction of 2-methylene-3-buten-1-ol with dienophiles followed by carbonyl allylation produces structurally isomeric 1-methylene-2-(hydroxymethyl)cyclohexanes.

Carbonyl allylation by isoprenylmetal compounds is one of the most reliable methods for introduction of 1,3-diene skeleton, and can be applied to the synthesis of ipsenol and ipsdienol.1-3) One starting material, 2-bromomethyl-1,3-butadiene is unstable and is usually prepared from 2-methylene-3-buten-1-ol (**1**).1) Other starting materials, 2-(trimethylsilyl)methyl-1,3-butadiene2) and 2-(trimethylstannyl)methyl-1,3-butadiene3) are somewhat troublesome to prepare. We report here palladium-catalyzed carbonyl allylation by 2-methylene-3-buten-1-ol (**1**), easily derived from 3,4-epoxy-3-methyl-1-butene with lithium diisopropylamide,1) with $SnCl_2$4) and construction of structurally isomeric six-membered cyclic systems by A) carbonyl allylation/Diels-Alder reaction and B) Diels-Alder reaction/carbonyl allylation.5)

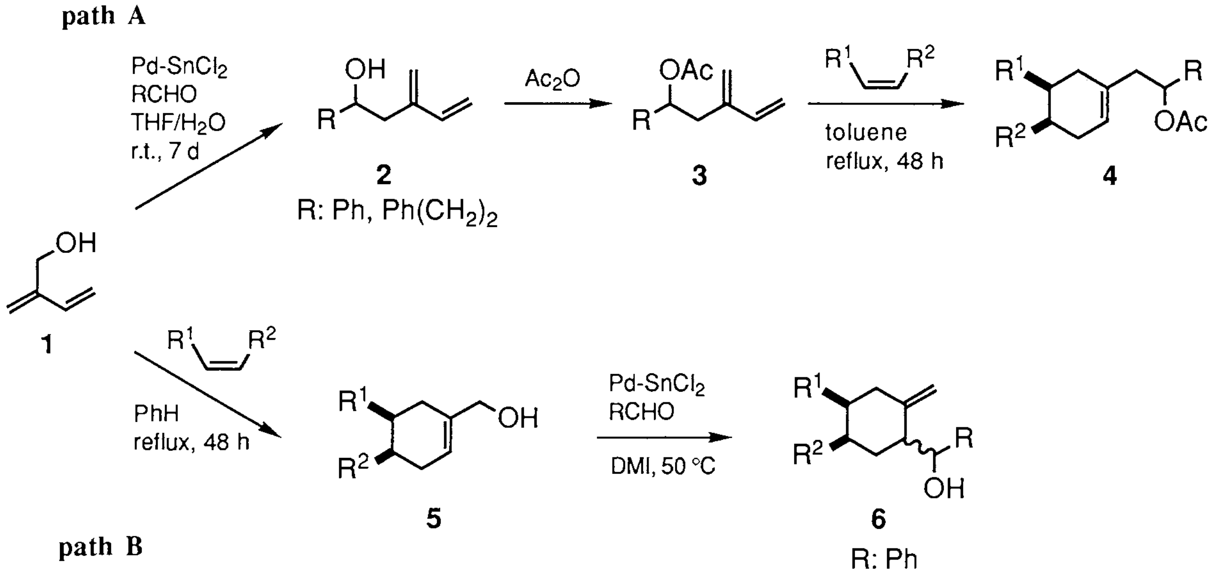
Carbonyl allylation by **1** was carried out in the presence of $PdCl_2(PhCN)_2$6) with $SnCl_2$ at ambient temperature7) in THF-H_2O8) to produce the corresponding 3-methylene-4-penten-1-ols.9) The results are summarized in Table 1. The carbonyl allylation is very slow, but both aromatic and aliphatic aldehydes can be employed. Aldehyde chemoselectively reacted in the presence of ester or aryl halide under those conditions. The preparation of ipsenol (**2e**) was achieved by the reaction of 3-methylbutanal with **1**.

Table 1. Palladium-Catalyzed Carbonyl Allylation by **1** with $SnCl_2$[a)]



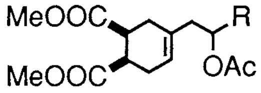
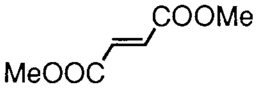
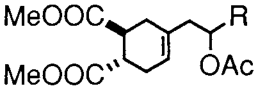
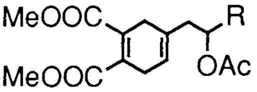
Entry	R	Product	Yield/%[b)]
1	C_6H_5	**2a**	78
2	$4\text{-}CH_3OOCC_6H_4$	**2b**	83
3	$3,4\text{-}(CH_2O_2)C_6H_3$	**2c**	76
4	$2\text{-}BrC_6H_4$	**2d**	76
5	$(CH_3)_2CHCH_2$	**2e**	56
6	$c\text{-}C_6H_{11}$	**2f**	58
7	$C_6H_5(CH_2)_2$	**2g**	68
8	$C_6H_5CH(CH_3)$	**2h**	74[c)]
9	$CH_2{=}CH(CH_2)_8$	**2i**	79

a) The reaction of 2-methylene-3-buten-1-ol (**1**, 0.13 g, 1.5 mmol) and aldehydes (1 mmol) was carried out with $PdCl_2(PhCN)_2$ (8 mg, 0.02 mmol) and $SnCl_2$ (0.57 g, 3 mmol) in THF/H_2O (3/1, 4 mL) at room temperature under a nitrogen atmosphere. b) Isolated yields. c) *syn:anti*=72:28.



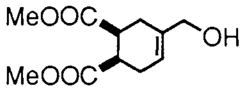
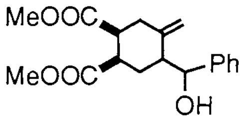
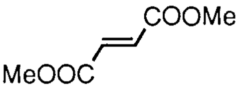
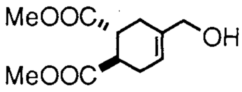
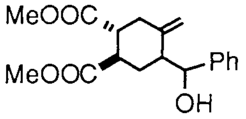
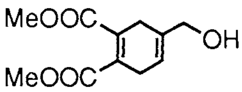
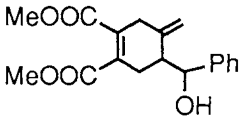
Scheme 1.

Table 2. Diels-Alder Reaction of **3** with Dienophiles a)

Entry	Diene	Dienophile	Product	Yield/% b)
1	**3a**		 **4a**; $R=C_6H_5$	88 c)
2	**3g**		**4b**; $R=C_6H_5(CH_2)_2$	70 c)
3	**3a**		 **4c**; $R=C_6H_5$	73 c)
4	**3g**		**4d**; $R=C_6H_5(CH_2)_2$	77 c)
5	**3a**	MeOOC—≡—COOMe	 **4e**; $R=C_6H_5$	75 d)
6	**3g**		**4f**; $R=C_6H_5(CH_2)_2$	73 d)

a) The reaction of **3** (1 mmol) with dienophiles (1.5 mmol) was carried out in refluxing toluene (5 ml) for 48 h. b) Isolated yields. c) The structure and ratio of diastereomers were not confirmed. d) **4e** and **4f** contain dehydrogenated aromatic compounds in 17% and 43% yields, respectively.

Table 3. Diels-Alder Reaction of **1** with Dienophiles and Carbonyl Allylation by **5**

Entry	Diels-Alder Reaction a)			Carbonyl Allylation b)	
	Dienophile	Product	Yield/% c)	Product	Yield/% c)
1		 **5a**	75	 **6a**	88 d)
2		 **5b**	85	 **6b**	71 d)
3	MeOOC—≡—COOMe	 **5c**	72	 **6c**	79 e)

a) The reaction of **1** (84 mg, 1 mmol) with dienophiles (1.5 mmol) was carried out in refluxing benzene (5 ml) for 48 h. b) The allylation of benzaldehyde (0.16 g, 1.5 mmol) by **5** (1 mmol) was carried out with $PdCl_2(PhCN)_2$ (8 mg, 0.02 mmol) and $SnCl_2$ (0.38 g, 2 mmol) in DMI (3 ml) at 50 °C for 5-7 days. c) Isolated yields. d) The structure and ratio of diastereomers were not confirmed. e) The diastereomer ratio is 85:15.

Formation of structurally isomeric six-membered cyclic compounds was carried out with **1**, benzaldehyde, and a few dienophiles via A) carbonyl allylation followed by Diels-Alder reaction or B) Diels-Alder reaction followed by carbonyl allylation.9) The reactions are illustrated in Scheme 1. 3-Methylene-1-phenyl-4-penten-1-ol (**2a**), prepared by the carbonyl allylation of benzaldehyde with **1**, was not applied to Diels-Alder reaction with dienophiles, because **2a** caused polymerization. 3-Methylene-1-phenyl-4-pentenyl acetate (**3a**), derived from 3-

methylene-1-phenyl-4-penten-1-ol (**2a**) with acetic anhydride, caused Diels-Alder reaction with dienophiles to produce 1-(2-hydroxyalkyl)cyclohexene derivatives **4** (Table 2). 3-Methylene-1-(2-phenylethyl)-4-pentenyl acetate (**3g**) can be also employed in the Diels-Alder reaction (Table 2). Diels-Alder reaction of **1** with dienophiles in refluxing benzene afforded 1-(hydroxymethyl)cyclohexene derivatives **5**, which reacted with benzaldehyde in the presence of $PdCl_2(PhCN)_2$-$SnCl_2$ to produce 1-(1-hydroxy-1-phenylmethyl)-2-methylenecyclohexane derivatives **6** regioselectively (Table 3). These results show that order of those reactions controls regiochemistry in the connection of three components, namely **1**, benzaldehyde, and dienophiles.

References

1) J. A. Katzenellenbogen and R. S. Lenox, *J. Org. Chem.*, **38**, 326 (1973); R. G. Riley, R. M. Silverstein, J. A. Katzenellenbogen, and R. S. Lenox, *ibid.*, **39**, 1957 (1974).
2) A. Hosomi, M. Saito, and H. Sakurai, *Tetrahedron Lett.*, **1979**, 429.
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4) J. P. Takahara, Y. Masuyama, and Y. Kurusu, *J. Am. Chem. Soc.*, **114**, 2577 (1992); Y. Masuyama, in "Advances in Metal-Organic Chemistry," ed by L. S. Liebeskind, JAI Press Inc., Greenwich, Connecticut, in press.
5) A. Hosomi, M. Saito, and H. Sakurai, *Tetrahedron Lett.*, **21**, 355 (1980).
6) Palladium catalysts such as $Pd(PPh_3)_4$ and $PdCl_2(PPh_3)_2$ were also employed.
7) The reaction with 4-(methoxycarbonyl)benzaldehyde at 50 °C caused many side-reactions and failed to produce any significant amounts of carbonyl isoprenylated product.
8) THF-H_2O was a better solvent than DMI, DMF, DMSO, or alcohol with H_2O or without H_2O.
9) All new compounds obtained here exhibited satisfactory spectral and physical properties. Typical ^1H NMR ($CDCl_3$) spectra of compounds **2**, **4**, **5**, and **6** are as follows. **2a**: δ 2.11 (br, 1H), 2.56 (dd, *J*=14.3, 8.9 Hz, 1H), 2.70 (dd, *J*=14.3, 4.0 Hz, 1H), 4.84 (dd, *J*=8.9, 4.0 Hz, 1H), 5.10 (s, 1H), 5.15 (d, *J*=10.4 Hz, 1H), 5.17 (s, 1H), 5.33 (d, *J*=17.3 Hz, 1H), 6.41 (dd, *J*=17.3, 10.4 Hz, 1H), 7.37 (br, 5H). **4c**: δ 2.05 (s, 3H), 2.08-2.25 (m, 2H), 2.26-2.44 (m, 3H), 2.50-2.63 (m, 1H), 2.69-2.91 (m, 2H), 3.68 (s, 3H), 3.69 (s, 3H), 5.40 (br, 1H), 5.81-5.91 (m, 1H), 7.31 (br, 5H). **5b**: δ 1.88 (br, 1H), 2.12-2.30 (m, 2H), 2.38-2.54 (m, 2H), 2.79-2.97 (m, 2H), 3.70 (s, 6H), 4.02 (s, 2H), 5.70 (br, 1H). **6b**: δ 1.44-1.73 (m, 1H), 2.10-2.58 (m, 5H), 2.62-2.83 (m, 1H), 2.86-3.07 (m, 1H), 3.57, 3.61, 3.68, 3.70, 3.71, 3.72 (6s, 6H), 4.68-4.85 (m, 1H), 5.07, 5.12, 5.18, 5.54 (4br.s, 2H), 7.31-7.43 (m, 5H).

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