Palladium-Catalyzed C-Allylation of Naphthols by Direct Use of Allylic Alcohols under Neutral Conditions

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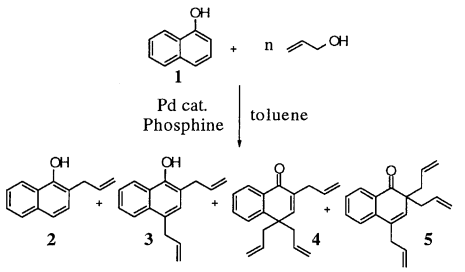
C-Allylation of 1- or 2-naphthols to give mono-, di-, and triallylnaphthols selectively using allylic alcohols directly under neutral conditions has been realized by employing palladium catalysts in the presence of molecular sieve 4A. This method is also applicable for the multiple allylation of 2,6-dihydroxynaphthalene.

Phenolic compounds with propenyl or prenyl substituents constitute an important class of naturally occurring compounds of biological activities.[1] Various substitution processes of aromatic compounds to synthesize these compounds are now known.[2] However, most of the processes require allylic halides in combination with stoichiometric amounts of metals and bases with eventual removal of metal halide salts.[3] Thus, development of a direct method utilizing allylic alcohols in the presence of catalytic amounts of metals is more desirable. In our previous study seeking the direct use of allylic alcohols, we found a remarkable rate enhancement effect of carbon dioxide in the palladium-catalyzed allylation of active methylene compounds and amines.[4] We report here that allylation of naphthols with allylic alcohols proceeds smoothly in the presence of molecular sieve 4A (MS-4A) without carbon dioxide.



Scheme 1.

Table 1. Palladium-catalyzed C-allylation of 1-naphthol with allyl alcohol

Run	Conditions	Yields (%) 2	3	4	5	1
1	A	24	—	—	—	74
2	B	10	63	—	—	—
3	C	—	78	—	—	—
4	D	—	12	31	12	—

A : $Pd_2(dba)_3CHCl_3$ (2.5 mol%), PPh_3 (10 mol%), 150 °C, 16 h, n = 1.5
B : $Pd_2(dba)_3CHCl_3$ (2.5 mol%), PPh_3 (20 mol%), MS-4A, 150 °C, 37.5 h, n = 1.5
C : $Pd_2(dba)_3CHCl_3$ (2.5 mol%), dppf (10 mol%), MS-4A, 100 °C, 48 h, n = 1.6
D : $Pd(OAc)_2$ (5 mol%), dppf (10 mol%), MS-4A, 100 °C, 24 h, n = 3

Our preliminary studies showed that 1-naphthol can be allylated directly with allyl alcohol at 150 °C when catalyzed by a palladium(0) catalyst albeit in a low conversion (Run 1 in Table 1). Addition of MS-4A to the same system resulted in complete conversion of 1-naphthol into mono- and diallylnaphthols **2** and **3** (Run 2). Employment of 1,1'-bis(diphenylphosphino)ferrocene (dppf) in combination with $Pd_2(dba)_3CHCl_3$ (dba = dibenzilideneacetone) and MS-4A caused selective diallylation to give **3** in high yield (Run 3). Furthermore, when $Pd(OAc)_2$ was used instead of $Pd_2(dba)_3CHCl_3$,[5] triallylation was achieved to give **4** and **5** (Run 4).

Table 2. The reaction of 1- and 2-naphthol with various allylic alcohols

Run	Allylic Alcohols	Yields
1[a]	3 h, n = 1.5	**6** 84%
2[b, c]	1 h, n = 1.5	**7** 76% **8** 0% **9** 0%
3[b]	6 h, n = 5	**7** 21% **8** 62% **9** 7%
4[b]	1.5 h, n = 1.5	**10** 80% **11** 13%
5[b]	24 h, n = 1.5	**12** 31% (Z:E = 1 : 5) **13** 5% 2-Naphthol 48% recovered
6[b]	1 h, n = 1.5	**12** 68% (Z:E = 1 : 4) **13** 17%
7[b]	24 h, n = 1.5	**14** 21% **15** 3% 2-Naphthol 41% recovered
8[b]	19 h, n = 1.5	**14** 21% **15** 8% 2-Naphthol 29% recovered
9[b]	6 h, n = 1.5	**16** 73% **17** 23%

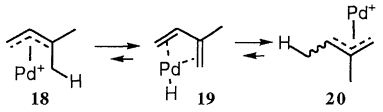
Reaction conditions: Naphthol (1 mmol), Allylic Alcohol (n mmol), $Pd(OAc)_2$ (0.05 mmol), dppf (0.10 mmol), MS-4A, toluene, 100 °C
[a] 1-Naphthol was used as a substrate.
[b] 2-Naphthol was used as a substrate.
[c] $Pd_2(dba)_3CHCl_3$ (0.025 mmol) and PPh_3 (0.20 mmol) were used instead of $Pd(OAc)_2$ and dppf.

The presence of the hydroxy group in naphthols seems to be essential in the allylation process since use of 1-methoxynaphthalene instead of 1-naphthol gave no allylation product.

Other results of the direct allylation of 1- and 2-naphthol with various allylic alcohols are shown in Table 2. When 1-naphthol was used (Run 1), allylic groups were introduced at the C-2 and C-4 positions of 1-naphthol. On the other hand, in the case of allylation of 2-naphthol (Runs 2-9), allylic groups were

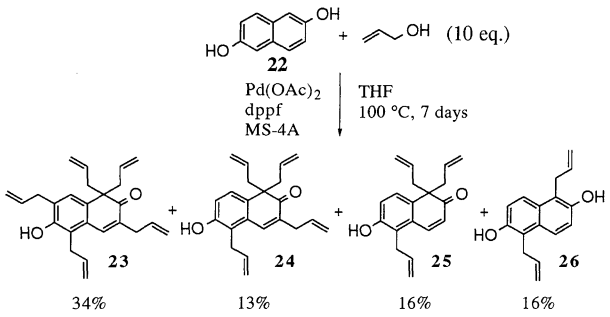
introduced only at C-1 position. Since both 2-buten-1-ol and 3-buten-2-ol gave mixtures of the regio isomers **12** and **13** in similar ratios (Runs 5 and 6), the reaction is considered to proceed via η^3-allylpalladium intermediates.

When 3-methyl-2-buten-1-ol and 2-methyl-3-buten-2-ol were used as allylic alcohols, the allylated products **14** and **15** were obtained predominantly, and prenylated naphthols were not isolated (Runs 7 and 8). In these reactions, the η^3-allylpalladium intermediate **18** is considered to be isomerized to **20** prior to the nucleophilic attack of 2-naphthol to **18** (eq. 1).[6]



(eq. 1)

Application of this palladium-catalyzed C-allylation process to 2,6-dihydroxynaphthalene (**22**) has enabled the multiple allylation of **22**. Thus, reaction of **22** with allyl alcohol (10 eq.) in THF[7] in the presence of $Pd(OAc)_2$, dppf, and MS-4A gave polyallylated naphthol derivatives **23**, **24**, **25**, and **26** in 34%, 13%, 16% and 16% yields, respectively (Scheme 2).



Scheme 2.

The present method enables the direct palladium-catalyzed allylation of naphthols under neutral conditions. It offers an environmentally favorable and halide-free process of potential use.

A typical procedure is as follows: A mixture of $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), dppf (55.4 mg, 0.1 mmol), 1-naphthol (144.2 mg, 1.0 mmol), allyl alcohol (0.1 mL, 1.5 mmol), and MS-4A (500 mg) in toluene (5 mL) was heated at 100 °C. After heating for several hours, the resulting mixture was filtered with Celite® and concentrated. The products were isolated by flash column chromatography (Wakogel C-300) or preparative TLC (Merck Kieselgel $60F_{254}$).

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7 Dihydroxynaphthalene **22** is insoluble in toluene.

8 Spectroscopic data for **4**: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 8.18 (dd, 1H, J = 7.9, 1.6 Hz), 7.56 (ddd, 1H, J = 7.5, 7.5, 1.3 Hz), 7.47 (d, 1H, J = 7.0 Hz), 7.37 (ddd, 1H, J = 7.5, 7.5, 1.3 Hz), 6.60 (s, 1H), 5.89 (ddt, 1H, J = 16.9, 10.4, 6.6 Hz), 5.26 (ddt, 2H, J = 17.2, 9.9, 7.3 Hz), 5.17-5.04 (m, 2H), 4.92-4.74 (m, 4H), 3.20 (dd, 2H, J = 6.6, 1.0 Hz), 2.73 (dd, 2H, J = 13.7, 7.1 Hz), 2.56 (dd, 2H, J = 13.7, 7.4 Hz). ^{13}C-NMR ($CDCl_3$, MHz) δ 184.8, 150.2, 146.0, 137.9, 135.7, 132.6, 132.2, 127.0, 126.8, 125.8, 118.3, 116.5, 46.1, 45.0, 33.5.
5: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 8.06 (d, 1H, J = 7.9 Hz), 7.57 (ddd, 1H, J = 7.9, 7.9, 1.0 Hz), 7.41 (d, 1H, J = 7.9 Hz), 7.35 (dd, 1H, J = 7.9, 7.9 Hz), 5.97 (ddt, 1H, J = 17.2, 10.6, 6.3 Hz), 5.92 (s, 1H), 5.54 (ddt, 2H, J = 16.8, 9.9, 7.3 Hz), 5.20-5.05 (m, 2H), 5.00 (dd, 2H, J = 16.8, 1.0 Hz), 4.90 (dd, 2H, J = 10.2, 1.0 Hz), 3.31 (d, 2H, J = 5.9 Hz), 2.66 (dd, 2H, J = 13.1, 7.5 Hz), 2.30 (dd, 2H, J = 13.1, 7.2 Hz). ^{13}C-NMR ($CDCl_3$, MHz) δ 202.4, 138.3, 135.8, 135.5, 134.1, 133.0, 131.8, 130.0, 127.5, 127.1, 124.4, 118.1, 116.8, 52.8, 43.7, 36.7.
23: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 7.40 (s, 1H), 7.04 (s, 1H), 6.19-5.77 (m, 3H), 5.33-5.02 (m, 9H), 4.91 (dd, 1H, J = 17.2, 2.0 Hz), 4.85-4.72 (m, 3H), 3.60 (ddd, 2H, J = 5.7, 1.6, 1.6 Hz), 3.46 (d, 2H, J = 4.6 Hz), 3.12 (dd, 2H, J = 6.8, 1.2 Hz), 2.86 (dd, 2H, J = 13.4, 7.4 Hz), 2.52 (dd, 2H, J = 13.4, 7.4 Hz). ^{13}C-NMR ($CDCl_3$, 67.9 MHz) δ 202.2, 150.9, 137.7, 136.0, 135.8, 135.5, 134.8, 133.0, 129.0, 126.8, 126.4, 123.4, 117.6, 117.0, 116.6, 115.8, 55.1, 46.5, 35.8, 33.5, 29.2.
24: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 7.45 (s, 1H), 7.16 (d, 1H, J = 8.4 Hz), 6.90 (d, 1H, J = 8.4 Hz), 6.20-5.78 (m, 2H), 5.53 (s, 1H), 5.34-5.00 (m, 6H), 4.97-4.72 (m, 4H), 3.66-3.56 (m, 2H), 3.13 (dd, 2H, J = 6.8, 1.0 Hz), 2.86 (dd, 2H, J = 13.5, 7.6 Hz), 2.53 (dd, 2H, J = 13.5, 7.0 Hz).
25: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ 7.64 (d, 1H, J = 10.3 Hz), 7.20 (d, 1H, J = 8.6 Hz), 6.95 (d, 1H, J = 8.6 Hz), 6.17 (d, 1H, J = 10.3 Hz), 6.03 (ddt, 1H, J = 17.1, 10.2, 5.4 Hz), 5.59-5.42 (br, 1H), 5.27 (ddt, 2H, J = 17.2, 10.2, 7.3 Hz), 5.09 (dd, 1H, J = 10.3, 1.7 Hz), 4.94-4.74 (m, 5H), 3.62 (ddd, 2H, J = 5.4, 1.8, 1.8 Hz), 2.87 (dd, 2H, J = 13.6, 7.3 Hz), 2.55 (dd, 2H, J = 13.6, 6.8 Hz). ^{13}C-NMR ($CDCl_3$, 67.9 MHz) δ 203.5, 152.4, 141.3, 136.7, 135.8, 132.7, 130.3, 126.1, 126.0, 123.7, 117.9, 117.4, 116.0, 55.6, 46.5, 28.9.