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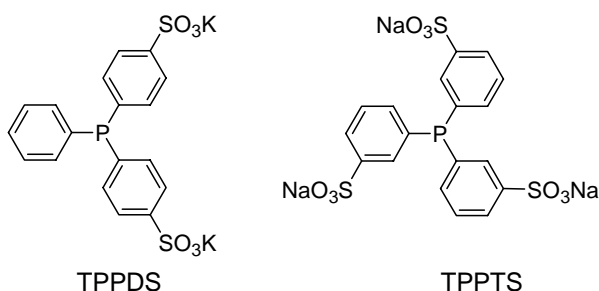
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PALLADIUM-CATALYZED INSERTION-CYCLIZATION REACTION OF 2,3-DIENYL ALCOHOLS WITH ARYL IODIDES IN WATER: SYNTHESIS OF 1-ARYLVINYL-SUBSTITUTED EPOXIDES[§]**Masahiro Yoshida,* Takayuki Ishii, Takahiro Gotou, and Masataka Ihara***

Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Aobayama, Sendai, 980-8578, Japan

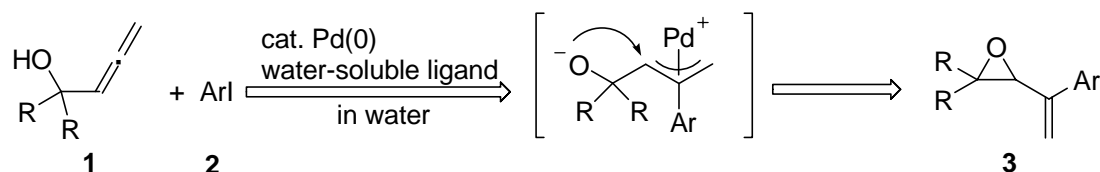
Abstract – A methodology for the synthesis of substituted epoxides in water has been described. The reactions of 2,3-dienyl alcohols with aryl iodides in the presence of palladium catalyst in water afford the 1-arylvinyl-substituted epoxides. It is clear that water-soluble ligand TPPDS is suitable for the reaction, and various epoxides are produced in moderate to good yields.

Organic reactions in aqueous medium have been received significant attention as a result of environmental and economic considerations. The formation of carbon–carbon bonds using a transition metal catalyst in water represents one of the most attractive tactic in this area.¹ Transition metal catalysts generally have poor reactivity in water because of low solubility in aqueous medium. To solve these problems, various water-soluble ligands have been developed.² TPPDS and TPPTS are the most popular water-soluble ligands,³ which are utilized in a variety of transition metal-catalyzed reactions.^{1,2}



Palladium-catalyzed reaction of 2,3-dienylalcohols with aryl iodides is the useful method to construct 1-arylvinyl-substituted epoxides.⁴ In the reaction, an epoxide ring is effectively produced in accordance with the formation of carbon–carbon bond *via* the π -allylpalladium intermediate. We were interested in the reaction carrying out in aqueous media. Herein, we describe a preliminary result concerning the palladium-catalyzed reaction of 2,3-dienylalcohols with aryl iodides in water (Scheme 1).

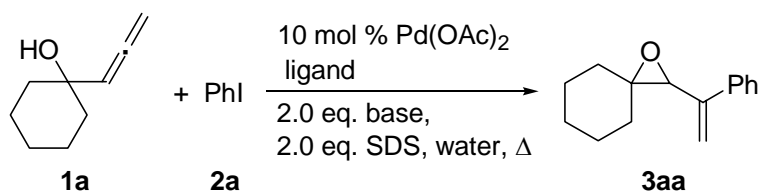
[§]Dedicated to Dr. Pierre Potier on the occasion of his 70th birthday



Scheme 1. Synthesis of 1-arylvinyl-substituted epoxides in water.

Initial experiments focused on finding a catalyst system that would promote the reaction in water (Table 1).⁵ When the reaction of 1-(1,2-propadienyl)cyclohexanol (**1a**)⁶ with iodobenzene (**2b**) was carried out in the presence of 10 mol % Pd(OAc)₂, 10 mol % dppe, 2.0 eq. of *i*-Pr₂NH and sodium dodecyl sulfate (SDS) in water at 80 °C for 96 h, the corresponding epoxide (**3aa**) was produced in 51% yield (Entry 1). Although the attempts using other bidentate ligands dppb and dppf were failed (Entries 2 and 3), **3aa** was provided in 62% yield in case of monodentate PPh₃ (Entry 4). Furthermore, it was clear that the yield was improved by using water-soluble ligands (Entries 5 and 6). The epoxide was obtained in 66% yield when 20 mol % TPPTS was used as a ligand (Entry 5). The reaction in the presence of TPPDS completed within 12 h to afford **3aa** in 83% yield (Entry 6). Studies using other bases at various temperature did not improve the yield (Entries 7–10).

Table 1. Reactions of 2,3-dienyl alcohol (**1a**) with iodobenzene (**2a**) in water.



Entry	Ligand	Base	Temp. (°C)	Time (h)	Yield (%)
1	10 mol % dppe	<i>i</i> -Pr ₂ NH	80	96	51
2	10 mol % dppb	<i>i</i> -Pr ₂ NH	80	96	trace
3	10 mol % dppf	<i>i</i> -Pr ₂ NH	80	96	23
4	20 mol % PPh ₃	<i>i</i> -Pr ₂ NH	80	36	62
5	20 mol % TPPTS	<i>i</i> -Pr ₂ NH	80	74	66
6	20 mol % TPPDS	<i>i</i> -Pr ₂ NH	80	12	83
7	20 mol % TPPDS	Et ₃ N	80	12	59
8	20 mol % TPPDS	K ₂ CO ₃	80	12	53
9	20 mol % TPPDS	<i>i</i> -Pr ₂ NH	60	18	54
10	20 mol % TPPDS	<i>i</i> -Pr ₂ NH	100	10	61

A series of substituted aryl iodides (**2a–f**) were subjected to the reaction with **1a** to further define the reaction scope (Table 2). When **1a** was treated with the electron donating group-substituted aryl iodides (**2b** and **2c**), the corresponding epoxides (**3ab** and **3ac**) were obtained in 33% and 32% yields, respectively (Entries 2 and 3). The reaction with 1-iodonaphthalene (**2d**) also afforded the

naphthyl-substituted product (**3ad**) in 51% yield (Entry 3). On the other hand, the nitro- and 4-acetylphenyl-substituted products (**3ae** and **3af**) were provided in 86% and 69% yields within 5 h from electron deficient aryl iodides (**2e** and **2f**) (Entries 5 and 6).

Table 2. Reactions of 2,3-dienyl alcohol (**1a**) with aryl iodides (**2a–f**) in water.

Entry	Ar	Time (h)	Product	Yield (%)
1	2a : phenyl	12	3aa	83
2	2b : 4-methylphenyl	96	3ab	33
3	2c : 4-methoxyphenyl	96	3ac	32
4	2d : 1-naphthyl	36	3ad	51
5	2e : 4-nitrophenyl	2.5	3ae	86
6	2f : 4-acetylphenyl	5	3af	69

We next examined the reactions of various 2,3-dienylalcohols (**1a–e**) with iodobenzene (**2a**) (Table 3). When the substrates (**1b** and **1c**) containing alkyl side chains were used, the corresponding products (**3ba** and **3ca**) were successfully yielded in 74% and 54% yields, respectively (Entries 2 and 3). The reaction of diphenyl-substituted substrate (**1d**)⁷ also afforded **3da** in 72% yield (Entry 4). We also studied the reaction using an unsymmetric substrate. The substrate (**1e**),⁷ having a methyl and phenyl groups, reacted with **2a** to afford a mixture of products (*trans*- and *cis*-**3ea**) in 70% yield with *trans*-selectivity (*trans* : *cis* = 10 : 3).

Table 3. Reactions of various 2,3-dienyl alcohols (**1a–e**) with iodobenzene (**2a**) in water.

Entry	Substrate	Time (h)	Product	Yield (%)
1	1a : R ¹ + R ² = cyclohexyl	12	3aa	83
2	1b : R ¹ , R ² = propyl	80	3ba	74
3	1c : R ¹ , R ² = pentyl	96	3ca	54
4	1d : R ¹ , R ² = phenyl	9	3da	72
5	1e : R ¹ = Me, R ² = Ph	11	<i>trans</i> - and <i>cis</i> - 3ea	70 (<i>trans</i> : <i>cis</i> =10:3) ^a

^a The ratio of diastereomer was determined by ¹H-NMR spectral integration of olefinic methylene signals (δ 5.71 and 5.41 for *trans*-**3ea**, δ 5.27 and 5.10 for *cis*-**3ea**), and the stereochemistry was determined by NOESY spectra of *trans*-**3ea**.

In conclusion, we have developed a methodology for the synthesis of 1-arylvinyl-substituted epoxides in water. A variety of 2,3-dienyl alcohols and aryl iodides were transformed to the corresponding products by palladium catalyst in combination with water-soluble ligand TPPDS, and the methodology is a useful in view of environmental concerns. Applications to the other kinds of palladium-catalyzed carbon-carbon bonds-formation reactions in water are now in progress.

ACKNOWLEDGEMENTS

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5. **General procedure for the palladium-catalyzed reaction of 2,3-dienyl alcohols with aryl iodides (Entry 6 in Table 1).** To a stirred solution of **1a** (49.1 mg, 0.36 mmol) in H₂O (3.5 mL) was added iodobenzene (**1b**) (60 μ L, 0.53 mmol), Pd(OAc)₂ (8.1 mg, 0.036 mmol), TPPDS (35.4 mg, 0.071 mmol), *i*-Pr₂NH (0.100 mL, 0.710 mmol), and SDS (216 mg, 0.710 mmol) at rt, and stirring was continued for 12 h at 80 °C. After extraction of the reaction mixture with AcOEt followed by evaporation of the elute, the residue was chromatographed on silica gel with hexane-AcOEt (96 : 4) as eluent to give **3aa** (63.3 mg, 83%) as a yellow oil: R_f = 0.49 (10 % AcOEt in hexane); IR (neat) 2932, 2856, 1630 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.45 (2H, d, *J* = 7.2 Hz), 7.36 (2H, t, *J* = 7.2 Hz), 7.31 (1H, t, *J* = 7.2 Hz), 5.62 (1H, s), 5.25 (1H, s), 3.58 (1H, s), 1.82–1.42 (10H, m); ¹³C-NMR (100 MHz, CDCl₃) δ 141.6, 138.2, 128.4, 127.8, 125.6, 112.7, 65.2, 64.8, 35.5, 27.7, 25.7, 25.1, 24.7; MS *m/z* 214 (M⁺); HRMS *m/z* calcd for C₁₅H₁₈O 214.1357 (M⁺), found 214.1331.
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