ORGANIC LETTERS

2001
Vol. 3, No. 2
241−242

Catalytic Ethenylation Reaction of Phenol Using $SnCl_4$

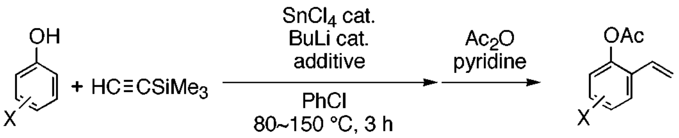
Katsumi Kobayashi and Masahiko Yamaguchi*

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

yama@mail.pharm.tohoku.ac.jp

Received November 18, 2000

ABSTRACT

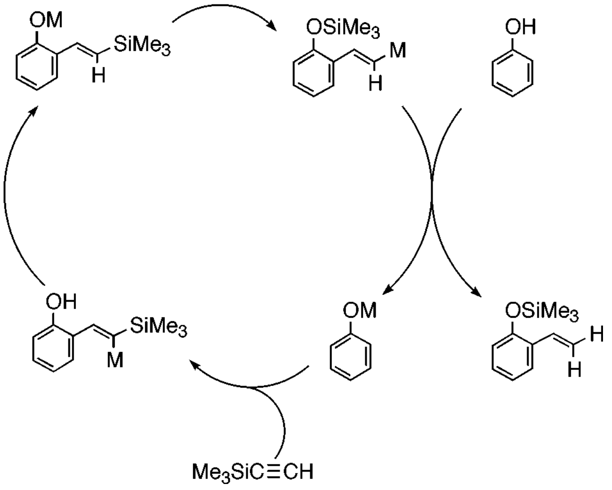


Ethenylation reaction of phenol with silylethyne at the *o*-position is catalyzed by the $SnCl_4$–BuLi reagent. While turn over numbers (TONs) in the reactions of *m*- or *p*-substituted phenols are 3 to 4, those for *o*-substituted phenols are 8 to 9.

Previously, we reported the ethenylation reaction of phenol using the $SnCl_4-Bu_3N$ reagent system.[1] Although this reaction can directly introduce the ethenyl group to the *o*-position of the phenol hydroxy group, it has a drawback of employing the $SnCl_4-Bu_3N$ reagent the amount of 2 molar equiv. We now describe the catalytic version of the reaction using silylethyne (Scheme 1).

Butyllithium (50 mol %) and $SnCl_4$ (25 mol %) were added successively to phenol in chlorobenzene, and after addition of silylethyne the mixture was heated at 105 °C for 3 h. β-Silylethenylation of phenol first takes place at the *o*-position, which is followed by C−O migration of the trimethylsilyl group. The reaction is quenched by treatment with aqueous potassium fluoride in methanol, and the *o*-ethenylphenol is isolated after acetylation in 90% yield (Table 1). The use of butyllithium for the base is essential, and Bu_3N is not effective in the catalytic reaction. More economically, lithium phenoxide prepared from LiOH and phenol in methanol can be used provided that the salt is sufficiently dried at 80 °C (3 Torr) for 3 h. A 1:2 ratio of $SnCl_4$ and butyllithium is critical. The reaction temperature of 100 to 105 °C is also important, and the yield decreases either at higher or at lower temperatures. The reaction can be applied to various *p*- and *m*-substituted phenols, giving the products in high yields. As was the case in the stoichiometric reaction, *m*-substituted phenols give comparable amounts of the regioisomers even in the case of *m*-(*tert*-butyl)phenol. The turn over number (TON) based on $SnCl_4$ is between 3 and 4, which implies that the amount of $SnCl_4$ can be reduced to approximately 1/10 of that of the original stoichiometric procedures.[1] Although the reason is not clear, employment of larger amounts of phenol results in the drastic

Scheme 1

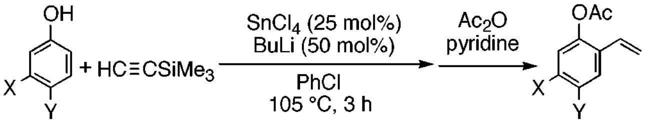


---

(1) (a)Yamaguchi, M.; Hayashi, A.; Hirama, M. *J. Am. Chem. Soc.* **1995**, *117*, 1151. (b) Yamaguchi, M.; Arisawa, M.; Kido, Y.; Hirama, M. *J. Chem. Soc., Chem. Commun.* **1997**, 1663. (c)Yamaguchi, M.; Arisawa, M.; Omata, K.; Kabuto, K.; Hirama, M.; Uchimaru, T. *J. Org. Chem.* **1998**, *63*, 7298. (d)Yamaguchi, M. *Pure Appl. Chem.* **1998**, *70*, 1091.

10.1021/ol006888d CCC: \$20.00

Table 1. Catalytic Ethenylation of Phenol



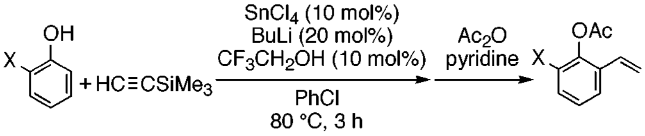
substituent	yield/%[a]
H	90
4-Me	87
4-(*t*-Bu)	85
4-MeO	91
4-Cl	51
3-(*t*-Bu)	85[b]
3-(*t*-$BuMe_2SiO$)	95[c]

[a] Yields of isolated products are shown. [b] Ratio of 3-(*tert*-butyl)-2-ethenylphenol:3-(*tert*-butyl)-6-ethenylphenol = 1:2. [c] Ratio of 2-ethenyl-3-(silyloxy)phenol:6-ethenyl-3-(silyloxy)phenol = 1:3.

decrease in the yield. It might be suspected that a TON of less than 4 does not mean catalysis but is the result of the involvement of four Sn−Cl bonds in $SnCl_4$. This may be unlikely since $BuSnCl_3$ and Bu_2SnCl_2 are not effective for the present reaction. In addition, the reaction of the *o*-substituted phenols (vide infra) demonstrates the catalytic nature of this reaction.

The ethenylation of *o*-substituted phenol is conducted under modified reaction conditions (Table 2). *O*-Cresol is reacted with silylethyne using 10 mol % of $SnCl_4$, 20 mol % of butyllithium, and 10 mol % of CF_3CH_2OH in chlorobenzene at 80 °C for 3 h, and 2-ethenyl-6-methylphenol is obtained in 85% yield (TON 8.5 based on $SnCl_4$). Again, the C−O silicon migration takes place in the reaction mixture. The presence of CF_3CH_2OH is essential, and the yield decreases to 35% in its absence. Small amounts of ethanol, methanol, and even water are also effective for improving the yield, while acetic acid, benzoic acid, ammonium chloride, or triethylamine hydrochloride inhibits the reaction. Probably, the acidic compounds participate in the protodestannylation of the organotin intermediate formed.[2] A reaction temperature of 80 °C is essential in this reaction. This method is applicable to other *o*-methylated phenols as well as 1-naphthol under similar reaction conditions. Higher reaction temperatures give better results in the cases of *o*-ethylphenol and *o*-isopropylphenol. The ethenylation of *o*-(*tert*-butyl)phenol is effectively conducted at 150 °C in the presence of 10 mol % of *p*-$CF_3C_6H_4COOH$ in place of CF_3CH_2OH. The origin of the higher TON in the ethenylation of *o*-substituted phenol is not known at present. Some part of the mechanism might be different, since addition of CF_3CH_2OH inhibits the reaction of phenol.

Table 2. Catalytic Ethenylation of *o*-Substituted Phenol



substituent	yield/%[a]
2-Me	85
2-Me-4-Cl	81
2-Me-4-I	84
1-naphthol	80
2-Et	83[b]
2-(*i*-Pr)	81[c]
2-(*t*-Bu)	92[d]

[a] Yields of isolated products are shown. [b] Reaction conducted at 95 °C. [c] Reaction conducted at 105 °C. [d] Reaction conducted at 150 °C in the presence of *p*-$CF_3C_6H_4COOH$ (10 mol %).

The mechanism of this catalytic ethenylation most likely involves carbostannylation of phenoxytin with silylethyne, resulting in the β-silylethenylation as was the case in the stoichiometric reaction.[2] In addition, protodestannylation of the carbostannylated intermediate and silicon migration take place, and two protons at the terminal carbon atom of the ethenylphenol are transferred from the phenolic hydroxy group and the *o*-position of phenol. Although the actual metal species responsible for these two processes are unclear, a schematic presentation of the mechanism can be summarized as shown in the Scheme 1.[3]

Acknowledgment. This work was supported by grants from JSPS. A fellowship to K.K. from JSPS for young Japanese scientists is also gratefully acknowledged.

Supporting Information Available: Experimental details and spectra data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL006888D

---

(2) Yamaguchi, M.; Kobayashi, K.; Arisawa, M. *Synlett* **1998**, 1317.

(3) **Typical procedures for the ethenylation of *o*-substituted phenol.** Under an argon atmosphere, to *o*-cresol (1.08 g, 10.0 mmol) in chlorobenzene (30 mL) were added 1.6 M butyllithium in hexane (1.25 mL, 2.0 mmol) and $SnCl_4$ (0.12 mL, 1.0 mmol) at 0 °C. The mixture was stirred for 10 min at room temperature, and 2,2,2-trifluoroethanol (0.073 mL, 1.0 mmol) and trimethylsilylethyne (1.56 mL, 11.0 mmol) were added. Then, the mixture was heated at 80 °C for 3 h. Methanol (20 mL), THF (20 mL), and potassium fluoride (580 mg, 10.0 mmol) were added, and the mixture was stirred for 30 min. Then water was added, and the organic materials were extracted with ethyl acetate. The organic layer was dried over $MgSO_4$, filtered, and concentrated to a small volume under reduced pressure (concentration to dryness caused the decomposition of the product). Flash chromatography (hexane:ethyl acetate = 50:1) over silica gel separated the product from a small amount of the unreacted starting material. The product was acetylated with pyridine (3.24 mL) and acetic anhydride (1.92 mL) at room temperature for 12 h. After pouring the mixture into water, the organic materials were extracted with ethyl acetate, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (hexane:ethyl acetate = 10:1) over silica gel gave 2-ethenyl-6-methylphenyl acetate (1.50 g, 85%).