

Facile Synthesis of 2,5-Disubstituted Furans *via* Palladium Complex and Perfluorinated Resinsulfonic Acid Catalysed Isomerization–Dehydration of Alkynediols

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2,5-Disubstituted furans have been synthesized *via* the isomerization–dehydration of alkynediols catalysed by $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$, Bu_3P and perfluorinated resinsulfonic acid at 130 °C in good yields; (H_4dba = dibenzylideneacetone).

Substituted furans, which not only occur widely in nature,¹ but also are versatile synthetic intermediates for the preparation of a wide range of cyclic and acyclic organic compounds,^{1d,2} enjoy wide application in a variety of commercially important products, such as pharmaceuticals, flavouring and aroma compounds, insect and fish antifeedants.^{1a,3} The synthesis of substituted furans, which is usually either by intramolecular reactions of 1,4-diketones or by the introduction of substituents to furan rings,^{2b,4} has received wide interest. Recently, we have reported that alkynediols could efficiently isomerize to 1,4-diketones under the catalysis of $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ **1** and Bu_3P at 80 °C in good yields.⁵ In this paper, we report the synthesis of 2,5-disubstituted furans *via* the isomerization–

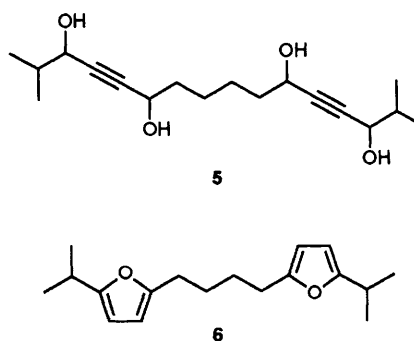
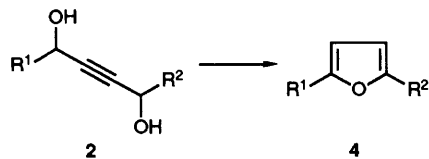




Table 1 Isomerization–dehydration of alkyne-1,4-diols catalysed by **1** and **3**^a


Entry	Compound 2		t/h	Product ^d 4	Isolated yield (%)
	R ¹	R ²			
1	Me	Me	a ^a	a	71
2	Et	Et	b ^a	b	84
3	Bu ⁿ	H	c ^a	c	45
4	Pr ⁱ	Pr ⁱ	d ^b	d	72
5		2d ^c		d	82
6	n-C ₁₆ H ₁₃	Me	e ^c	e	66
7	n-C ₇ H ₁₅	Et	f ^c	f	77
8			g ^c	g	45

^a A mixture of **1** (207 mg, 0.2 mmol), **2** (10 mmol), **3** (232 mg, 0.2 mequiv.) and Bu₃P (81 mg, 0.4 mmol) was heated at 130 °C under Ar. ^b Same as ^a except that the reaction was carried out under reduced pressure (20 mmHg) and the product was distilled during the reaction. ^c A mixture of **1** (21 mg, 0.02 mmol), **2** (1 mmol), **3** (23 mg, 0.02 mequiv.), Bu₃P (8 mg, 0.04 mmol) and xylene (10 ml) was stirred at 130 °C under Ar. ^d The products were confirmed by ¹H NMR, IR and mass spectral data.

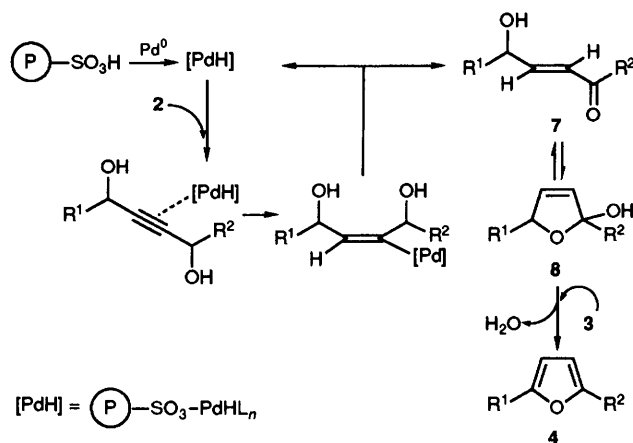
dehydration of alkyne-1,4-diols **2** catalysed by **1**, Bu₃P and perfluorinated resinsulfonic acid **3** (Nafion-H type, 0.86 mol equiv. Hg⁻¹).

Table 1 shows the results of the isomerization–dehydration of alkyne-1,4-diols catalysed by **1**, **3** and Bu₃P. For those furans with a boiling point lower than 120 °C (**4a–c**), the reaction was carried out in the absence of solvent, and the product was distilled during the reaction (entries 1–3). For those furans with a boiling point higher than 170 °C (**4d–g**), xylene was chosen as the best solvent for the reaction, and the crude product was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) (entries 5–8).

This reaction can be applied to the bis(alkyne-1,4-diol) **5** and bis(2,5-disubstituted furan) **6**[†] was obtained in 84% yield.

No reaction occurred when **2a** was heated either in the absence of **1** or in the absence of **3**. Pittman⁶ reported that hexane-2,5-dione can be transformed to **4a** by catalysis with Nafion-H under severe conditions for 12 h but only in low yield. So the initial formation of 1,4-diketone in this reaction can be ruled out. A possible isomerization–dehydration mechanism is shown in Scheme 1. Being a superacid, **3** may not only play a role in the formation of the active species [PdH] which catalyse the isomerization of the alkyne-1,4-diol **2** to γ -hydroxy- α,β -unsaturated ketone **7**^{5,7} followed by immediate formation of the lactol **8**, but also catalyses the dehydration of **8** to yield **4**.^{6,8}

[†] Spectral data for **6**: ¹H NMR (60 MHz, CCl₄) δ 5.70 (s, 2H), 2.90 (m, 1H), 2.50 (t, 2H, *J* 7 Hz), 1.60 (m, 2H), 1.15 (d, 6H, *J* 6 Hz); IR ν /cm⁻¹ (neat) 3100, 1610, 1560, 1460, 1380, 1360, 960, 780; MS *m/z* 274 (M⁺), 232, 190, 164, 150, 136, 123, 105, 79, 66, 57.

**Scheme 1**

This reaction combines the isomerization and dehydration in one pot and offers a convenient route for preparing 2,5-disubstituted furans from easily available alkyne-1,4-diols under mild conditions in good yields.

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