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Isomerization of alkynemono-ols catalyzed by palladium(0) complex and diols *

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Abstract

Isomerization of alkynemono-ols occurred by the catalysis of $Pd_2(dba)_3 \cdot CHCl_3$ (1)+$^iPr_3P$+ $HOCH_2CH_2OH$. Palladium hydride active species were supposed to be formed *in situ* by the oxidative addition of diols to 1 as determined by ^1H NMR spectra.

Introduction

Recently, isomerization of allylic alcohols catalyzed by transition metal complexes has attracted much attention [1–3], but the isomerization reaction of alkynols by transition metal complexes are rare [4,5]. We have reported that alkyne-1,4-diols could chemoselectively isomerize to the corresponding 1,4-diketones by the catalysis of **1**, and the *in situ* formation of the catalytically active [Pd–H] species by the reaction of alkyne-1,4-diols and **1** was speculated [6]. Unfortunately, alkynemono-ols failed to isomerize to the corresponding α,β-unsaturated ketones or aldehydes in the same conditions, although this reaction occurred under more severe conditions, *e.g.* at toluene reflux temperature [4–6]. We found that by adding a catalytic amount of diols, the isomerization of alkynemono-ols occurred smoothly under the milder reaction conditions (acetonitrile reflux temperature). We wish to report the details of these isomerization reactions by the catalysis of **1** promoted by diols in acetonitrile.

Results and discussion

Effect of acetic acid

While the isomerization of alkynemono-ols occurred in toluene at 110°C, the reaction did not take place in acetonitrile at 80°C. Trost reported that the

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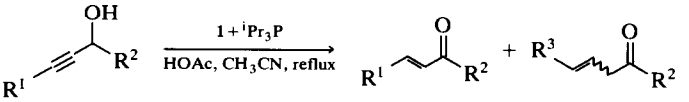
* Dedicated to Professor Akio Yamamoto upon his retirement from Tokyo Institute of Technology and in honor of his contributions to organometallic chemistry.

Table 1

Isomerization of alkynemono-ols effected by $Pd_2(dba)_3 \cdot CHCl_3$ and acetic acid [a]



$R^1 = R^3CH_2$

(2) (3) (4)

Compound				Reaction time (h)	Yield (%) [b]	Product [c]
R^1	R^2		R^3			3:4 [d]
n-C_4H_9	C_2H_5	(2a)	n-C_3H_7	40	79	80:20
n-C_4H_9	CH_3	(2b)	n-C_3H_7	65	82	78:22
n-C_5H_{11}	CH_3	(2c)	n-C_4H_9	65	82	77:23
n-C_6H_{13}	CH_3	(2d)	n-C_5H_{11}	65	84	76:24
n-C_4H_9	p-$CH_3C_6H_4$	(2e)	n-C_3H_7	35	90	78:22
C_6H_5	C_2H_5	(2f)	–	30	89	–
C_6H_5	H	(2g)	–	35	85	–

[a] Reaction conditions: a mixture of **2** (2 mmol), **1** (0.1 mmol), $^iPr_3P$ (0.2 mmol), HOAc (0.2 mmol) and CH_3CN (5 mL) was refluxed under argon. [b] Isolated yield. [c] All products were fully characterized spectrally. [d] Determined by ^1H NMR spectra.

isomerization of alkynones catalyzed by **1** was promoted by adding acetic acid [7]. We found that the isomerization of alkynemono-ols (**2**) could occur by the catalysis of **1** and acetic acid under milder condition. ^1H NMR spectra showed the formation of two isomers, (*E*)-α,β-enones (**3**) and β,γ-enones (**4**), in the ratio of about 4 to 1 (Table 1).

Effect of diols

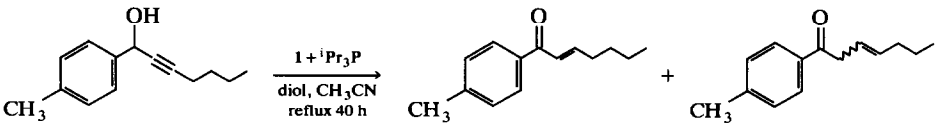
The success of the isomerization of alkynediols catalyzed by **1** in milder conditions [6] made us interested in the use of other diols as promoters. It was found that adding 10 mol% of diol, such as 1,2-ethanediol, 1,3-propanediol, 1,4-butanediol, 1,5-pentanediol or *cis*-2-butene-1,4-diol, compound **2e** isomerized to the corresponding α,β-enone (**3e**) and β,γ-enone (**4e**) in the ratio of about 4 to 1 by the catalysis of **1** even in acetonitrile (Table 2).

The isomerization of various alkynemono-ols (**2**) was studied by using **1** + $^iPr_3P$ + $HOCH_2CH_2OH$ as a catalyst in acetonitrile. The results are shown in Table 3. Here, ^1H NMR spectra also showed the formation of two isomers, (*E*)-α,β-enones (**3**) and β,γ-enones (**4**) in the ratio of about 4 to 1. This ratio is consistent with our previous work [4] and Hine's results [8].

It is generally suggested that the possible mechanism of the isomerization of alkyne derivatives catalyzed by transition metal complexes is through the repeated addition and elimination of metal hydride species [4–7,9,10]. By hydropalladation and dehydropalladation of alkynemono-ol (**2**) (Scheme 1), 1,2-dienol (**6**) or 2,3-dienol (**8**) intermediate was formed. Then **6** might further tautomerize to the corresponding conjugated enone **3**. By hydropalladation and dehydropalladation again, **8** could isomerize to 1,3-dienol (**10**) which tautomerize to the corresponding unconjugated enone **4**. There exists a thermodynamical equilibrium between **3** and **4**.

Table 2

Isomerization of 1-(*p*-tolyl)-2-heptyne-1-ol (**2e**) catalyzed by $Pd_2(dba)_3 \cdot CHCl_3$ and diols [a]



(**2e**) (**3e**) (**4e**)

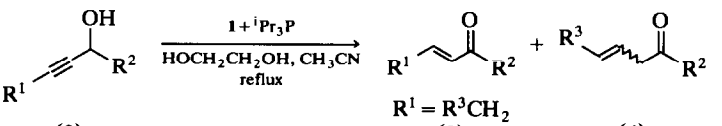
Diol	Yield (%) [b]	3:4 [c]
$HO(CH_2)_2OH$	90	78:22
$HO(CH_2)_3OH$	93	76:24
$HO(CH_2)_4OH$	86	75:25
$HO(CH_2)_5OH$	89	78:22
(*Z*)-$HOCH_2CH{=}CHCH_2OH$	88	77:23

[a] Reaction conditions: under argon, a mixture of **2e** (1 mmol), **1** (0.05 mmol), $^iPr_3P$ (0.1 mmol), diol (0.2 mmol) and CH_3CN (5 mL) was refluxed for 40 h. [b] Isolated yield. [c] The products were fully characterized spectrally and the ratio determined by ^1H NMR spectra.

Here, the [PdH] active species is formed *in situ* from the oxidative addition of a hydrogen donor to the zero valent palladium complex. The oxidative addition of acetic acid to Pd^0 is well known in the literature [11], but the oxidative addition of hydroxy group of alcohols to Pd^0 is rarely reported. Recently, Pasquali reported the oxidative addition of phenol with Pd^0 only because of the weak acidity of phenol [12]. Yamamoto also found that only those alcohols of sufficient acidity could react with an alkyl palladium complex [13]. The difficulty of the isomerization of alkynemono-ols in acetonitrile is consistent with both Pasquali's and Yamamoto's results that no reaction occurred when aliphatic alcohols were employed.

Table 3

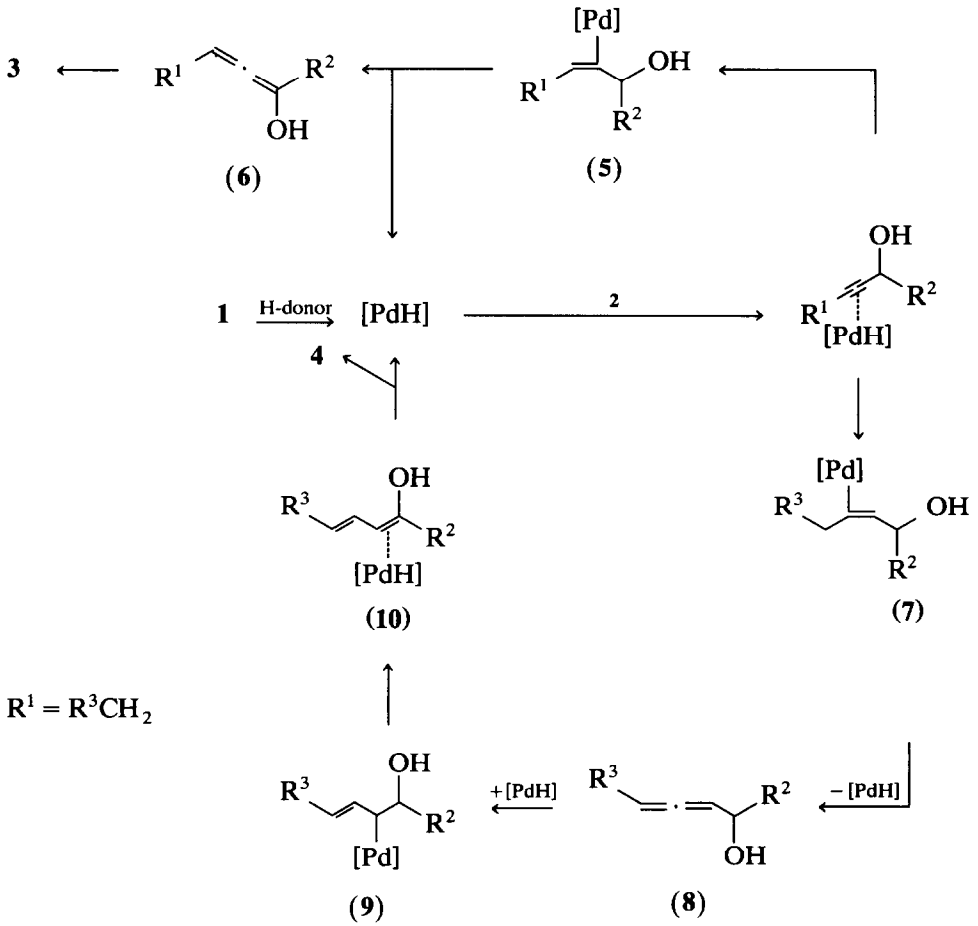
Isomerization of alkynemono-ols catalyzed by $Pd_2(dba)_3 \cdot CHCl_3$ and 1,2-ethanediol [a]



(**2**) (**3**) (**4**)

Compound	Time (h)	Yield (%) [b]	Product 3:4 [d]
2b	65	85	77:23
2c	65	82	84:16
2d	65	88	79:21
2e	40	90	78:22
2f	40	89	–

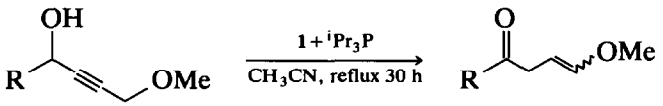
[a] Reaction conditions: a mixture of **2** (2 mmol), **1** (0.1 mmol), $^iPr_3P$ (0.2 mmol), $HOCH_2CH_2OH$ (0.2 mmol) and CH_3CN (5 ml) was refluxed under argon. [b] Isolated yield. [c] The products were determined by ^1H NMR, IR and MS spectra. [d] Determined by ^1H NMR.



Scheme 1. [PdH] = L_mPdH which represents the active species containing a Pd–H bond. It is still not certain whether L represents dba, $^iPr_3P$, solvent, or alkoxy group from the reaction of Pd^0 with alkynemono-ol or alkanediol.

We have speculated that the isomerization of alkynediols in milder conditions may be related to the easy formation of [PdH] species, which was supported by the high field signals that appeared on monitoring the reaction with ^1H NMR by the oxidative addition of alkynediols with Pd^0 [6]. Bennett reported the change of some properties of an *sp* carbon atom to that of an sp^2 carbon atom when the carbon–carbon triple bond coordinated to a transition metal complex [14]. This change will make the chelation of alkynediols with palladium possible, which may assist the oxidative addition of an O–H bond to Pd^0. Minn reported that only those propargylic alcohols of heterocycle compounds containing nitrogen atoms could isomerize to the corresponding α,β-unsaturated ketones by the catalysis of Pd^0 [15]. These results imply that the chelation between the substrate and Pd^0 is important in the oxidative addition reaction to generate the [PdH] catalytically active species.

In order to investigate the role of the possible chelation in assisting the oxidative addition in forming [PdH] species, an ether substituted alkynemono-ol (**11**), which may possibly chelate with Pd^0, was used. On refluxing **11** with **1** and $^iPr_3P$ in acetonitrile for 30 h, **11** was completely isomerized to the corresponding product, γ-methoxy-β,γ-unsaturated ketones (**12**) in high yield. The formation of the β,γ-unsaturated ketones as the main products may be due to the conjugation between the lone pair electrons of the oxygen atom of the methoxyl group with the carbon–carbon double bond [16].



(**11**) (**12**)

		Yield (%)
(**a**)	R = n-C_3H_7	77
(**b**)	n-C_4H_9	80
(**c**)	n-C_5H_{11}	81
(**d**)	n-C_6H_{13}	82

The oxidative addition of HCl and CF_3CO_2H to Pd^0 has been reported [17]. Although the oxidative addition of acetic acid to Pd^0 can occur [7–11], neither isolation of the oxidative addition product nor any special evidence has been given in the literature. Evidence for the formation of a [PdH] species by oxidative addition of hydrogen-donors with Pd^0 was obtained by monitoring the reaction with ^1H NMR spectroscopy. Table 4 shows that acetic acid, 3-hexyne-2,5-diol, 1-methoxy-2-octyne-4-ol (entries 1–3) and **1** give characteristic ^1H NMR signals at high field, which is in the range of characteristic signals of [PdH] (−3.0 to −19.0 ppm) [18]. While we failed to observe the characteristic signals of [PdH] species in relation to alkynemono-ol **2e** (entry 4), the characteristic signal of [PdH] species at high field appear when a catalytic amount of 1,2-ethanediol is added into the NMR tube (entry 5) which implies that the diols do play an important role in the formation of [PdH] species.

Table 4

^1H NMR study of the reaction of hydrogen donors with $Pd_2(dba)_3 \cdot CHCl_3$ [a]

Entry	Hydrogen donor	Solvent	^1H NMR (δ ppm)
1	CH_3CO_2H	CD_3CN	−14.25
2	$CH_3CH(OH)C{\equiv}CCH(OH)CH_3$	CD_3CN	−9.2, −16.2, −18.7
3	n-$C_4H_9CH(OH)C{\equiv}CCH_2OCH_3$	$CDCl_3$	−15.78
4	p-$CH_3C_6H_4CH(OH)C{\equiv}C$(n-$C_4H_9$) (**2e**)	$CDCl_3$	None
5	**2e** + $HO(CH_2)_2OH$ [b]	$CDCl_3$	−10.10

[a] Reaction conditions: a mixture of hydrogen donor (0.1 mmol), **1** (0.02 mmol), $^iPr_3P$ (0.04 mmol) and the solvent (0.5 mL) was sealed into a NMR tube under argon and allowed to stand at room temperature for 8 h. [b] The conditions were the same as above, except using **2e** (0.1 mmol), **1** (0.02 mmol), $^iPr_3P$ (0.04 mmol) and 1,2-ethanediol (0.04 mmol).

In conclusion, the addition of a catalytic amount of diols could promote the isomerization of alkynemono-ols to α,β-unsaturated ketones. This provides a neutral, mild, convenient method to prepare enones from the isomerization of easily available alkynemono-ols.

Experimental section

All reactions were carried out under a prepurified argon atmosphere. Acetonitrile was distilled from phosphorus pentoxide under a nitrogen atmosphere. ^{1}H NMR were recorded on an EM-360, Varian XL-200, or AMX-600 spectrometer. Chemical shifts are reported as δ values in parts per million with Me_4Si as an internal standard. Infrared spectra were taken as liquid film with an IR-440 instrument. Mass spectral data were obtained with electron ionization on a Finnigan 4021 spectrometer.

Preparation of alkynemono-ols

The alkynemono-ols, 4-nonyn-3-ol (**2a**) [19], 3-octyn-2-ol (**2b**) [20], 3-nonyn-2-ol (**2c**) [21], 3-undecyn-2-ol (**2d**) [22], 1-(4-methylphenyl)-2-heptyn-1-ol (**2e**), 1-phenyl-1-pentyn-3-ol (**2f**) [19], and 3-phenyl-propynol (**2g**) [23] were prepared by the reaction of acetylenic Grignard derivatives or lithium alkynylides with the corresponding aldehyde as reported [24].

Isomerization of alkynemono-ols effected by 1 and acetic acid

General procedure: under argon, a mixture of alkynemono-ol (2 mmol), **1** (0.1 mmol), $^i Pr_3P$ (0.2 mmol), HOAc (0.2 mmol) and CH_3CN (5 ml) was heated under reflux. After cooling and removal of the solvent, the residue was distilled under reduced pressure to obtain the products (Table 1).

Isomerization of alkynemono-ols effected by 1 and diols

General procedure: under argon, a mixture of alkynemono-ol (2 mmol), **1** (0.1 mmol), $^i Pr_3P$ (0.2 mmol), diol (0.2 mmol) and CH_3CN (5 ml) was heated under reflux. After cooling and removal of the solvent, the residue was distilled under reduced pressure to give the products (Tables 2 and 3).

*(E)-4-Nonen-3-one (**3a**) + 5-nonen-3-one (**4a**)*

B.p. 70–80°C (bath temperature)/5 mmHg [25]. IR (neat): 3050, 1720, 1680, 1640, 1620 cm^{-1}; MS: *m/e* 140 (M^+), 125, 111, 98, 97, 83, 57, 43. ^{1}H NMR (CCl_4/60 MHz): **3a**: 6.7 (dm, $J = 16$ Hz, 1H), 5.8 (d, $J = 16$ Hz, 1H), 2.4–1.9 (m, 4H), 1.4–0.9 (m, 10H) ppm; **4a**: 5.3 (m, 2H), 3.0 (d, $J = 5$ Hz, 2H), 2.4–1.9 (m, 4H), 1.4–0.9 (m, 8H) ppm.

*(E)-3-Octen-2-one (**3b**) and 4-octen-2-one (**4b**)*

B.p. 75–80°C (bath temperature)/6 mmHg (lit. [26] b.p. 75°C/15 mmHg). IR (neat): 3030, 1720, 1680, 1640, 1620 cm^{-1}. MS: *m/e* 126 (M^+), 111, 97, 83, 81, 71, 69, 55, 43. ^{1}H NMR (CCl_4/60 MHz): **3b**: 6.9 (dt, $J = 16$ Hz, 6 Hz, 1H), 6.0 (d, $J = 16$ Hz, 1H), 2.2 (m, 5H), 1.5–1.0 (m, 7H) ppm; **4b**: 5.4 (m, 2H), 3.0 (m, 2H), 2.2 (m, 5H), 1.5–1.0 (m, 5H) ppm.

(E)-3-Nonen-2-one (3c) and 4-nonen-2-one (4c)

B.p. 70–80°C (bath temperature)/10 mmHg (lit. [26] b.p. 92°C/19 mmHg). IR (neat): 3030, 1720, 1680, 1640, 1620 cm^{-1}. MS: *m/e* 140 (M^+), 125, 111, 97, 83, 82, 71, 69, 55, 43. ^1H NMR (CCl_4/60 MHz): **3c**: 6.9 (dt, $J = 16$ Hz, 6 Hz, 1H), 6.0 (d, $J = 16$ Hz, 1H), 2.3 (m, 5H), 1.5–0.9 (m, 9H) ppm; **4c**: 5.4 (m, 2H), 3.0 (d, $J = 5$ Hz, 2H), 2.3 (m, 5H), 1.5–0.9 (m, 7H) ppm.

(E)-3-Undecen-2-one (3d) and 4-undecen-2-one (4d)

B.p. 90–100°C (bath temperature)/1 mmHg [27]. IR (neat): 3040, 1720, 1680, 1630, 1640 cm^{-1}. MS: *m/e* 168 (M^+), 153, 139, 125, 115, 97, 85, 83, 71, 69, 57, 43. ^1H NMR (CCl_4/60 MHz): **3d**: 6.8 (dt, $J = 16$ Hz, 6 Hz, 1H), 5.9 (d, $J = 16$ Hz, 1H), 2.3–2.0 (m, 5H), 1.5–0.9 (m, 13H) ppm; **4d**: 5.4 (m, 2H), 3.0 (d, $J = 5$ Hz, 2H), 2.3 (m, 5H), 1.5–0.9 (m, 11H) ppm.

(E)-1-(p-Tolyl)-2-hepten-1-one (3e) and 1-(p-tolyl)-3-hepten-1-one (4e)

B.p. 120–130°C (bath temperature)/1 mmHg [28]. IR (neat): 3030, 1690, 1670, 1620, 1600, 1580, 1500 cm^{-1}. MS: *m/e* 202 (M^+), 187, 173, 159, 147, 145, 119, 91, 77, 57, 55, 43. ^1H NMR (CCl_4/60 MHz): **3e**: 7.8 (d, $J = 8$ Hz, 2H), 7.1 (d, $J = 8$ Hz, 2H), 6.9 (dt, $J = 16$ Hz, 5 Hz, 1H), 6.1 (d, $J = 16$ Hz, 1H), 2.3–2.1 (m, 5H), 1.5–1.3 (m, 4H), 1.0 (t, $J = 2$ Hz, 3H) ppm; **4e**: 7.8 (d, $J = 8$ Hz, 2H), 7.1 (d, $J = 8$ Hz, 2H), 5.4 (m, 2H), 3.0 (d, $J = 5$ Hz, 2H), 2.3–2.1 (m, 5H), 1.3 (m, 2H), 1.0 (t, $J = 2$ Hz, 3H) ppm.

(E)-1-Phenyl-1-penten-3-one (3f)

B.p. 110–115°C (bath temperature)/1 mmHg (lit. [26] b.p. 97°C/0.3 mmHg). IR (neat): 3010, 1690, 1660, 1620, 1580, 1500, 980 cm^{-1}. MS: *m/e* 160 (M^+), 144, 131, 103, 77, 57, 55. ^1H NMR (CCl_4/60 MHz): 7.5 (d, $J = 16$ Hz, 1H), 7.3–7.0 (m, 5H), 6.5 (d, $J = 16$ Hz, 1H), 2.4 (q, 2H), 1.1 (t, $J = 2$ Hz, 3H) ppm.

(E)-1-Phenyl-propen-3-al (3g)

B.p. 80°C (bath temperature)/5 mmHg (lit. [29] b.p. 220–225°C). IR (neat): 3010, 2700, 1680, 1620, 1600, 1580, 1500, 980 cm^{-1}. MS: *m/e* 130 (M^+), 129, 105, 91, 77, 51. ^1H NMR (CCl_4/60 MHz): 9.4 (d, $J = 8$ Hz, 1H), 7.4 (m, 5H), 7.1 (d, $J = 16$ Hz, 1H), 6.4 (dd, $J = 16$ Hz, 8 Hz, 1H) ppm.

Isomerization of 1-methoxy-alkyn-4-ols (11) catalyzed by $Pd_2(dba)_3 \cdot CHCl_3$ (1)

General procedure: a mixture of **11** (2 mmol), **1** (0.1 mmol) and $^iPr_3P$ (0.2 mmol) in acetonitrile (10 ml) was heated under reflux for about 30 h until the reaction was complete as monitored by TLC. After cooling the mixture and removal of the solvent, the red residue was distilled under reduced pressure to give 1-methoxy-1-alken-4-one (**12**). The spectral data of the products (**12a–12d**) were identical with the reported data [16].

^1H NMR study of the reaction of 1 and hydrogen donors

General procedure: under argon, a mixture of hydrogen donor (0.1 mmol), **1** (0.02 mmol), $^iPr_3P$ (0.04 mmol) and CD_3CN or $CDCl_3$ (0.5 mL) was sealed in a NMR tube and allowed to stand at room temperature for 8 h. The determination was carried out using a Varian XL-200 (entries 1–4) or AMX-600 spectrometer (entry 5). The results are shown in Table 4.

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