

## Isomerization of 1,3-Diarylprop-2-yn-1-ols to Chalcones in the Presence of Potassium Hydroxide

Chan Sik Cho,<sup>†,\*</sup> Hyo Jin Seok, and Sang Chul Shim<sup>\*</sup>

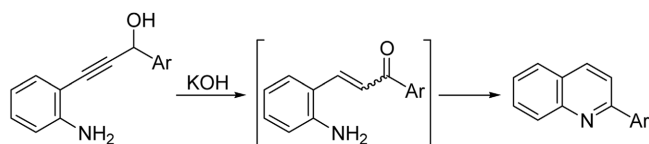
<sup>†</sup>Research Institute of Industrial Technology, Kyungpook National University, Daegu 702-701, Korea. \*E-mail: cscho@knu.ac.kr  
Department of Applied Chemistry, College of Engineering, Kyungpook National University, Daegu 702-701, Korea

\*E-mail: scshim@knu.ac.kr

Received April 6, 2005

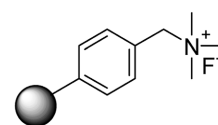
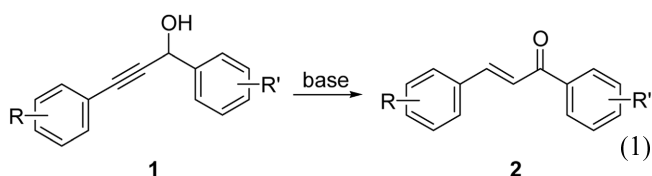
**Key Words :** Base, Chalcones, Isomerization, Polymer-supported fluoride, Propargylic alcohols

Many methods have been developed for the isomerization of propargylic alcohols to enones or enals. Besides the isomerization by transition metals such as Pd,<sup>1</sup> Ru,<sup>2</sup> Rh,<sup>3</sup> and Ir,<sup>4</sup> several organic bases such as tributylamine<sup>5</sup> and triton B<sup>6</sup> have been introduced for such an isomerization.<sup>7</sup> During the course of our ongoing studies on ruthenium-catalyzed synthesis of quinolines,<sup>8</sup> we found that 3-(2-aminophenyl)-1-arylprop-2-yn-1-ols undergo a consecutive isomerization and cyclization under treatment of KOH to afford 2-arylquinolines (Scheme 1).<sup>9</sup> This led us to investigate the isomerization of 1,3-diarylprop-2-yn-1-ols under similar conditions. Herein we describe the isomerization to chalcones in the presence of KOH.<sup>10</sup>



Scheme 1

The results of isomerization of 1,3-diphenylprop-2-yn-1-ol (**1a**, R = R' = H) to *trans*-chalcone (**2a**, R = R' = H) under various conditions are listed in Table 1 (Eq. 1). Treatment of **1a** with equimolar amount of KOH in toluene at 80 °C for 1 h afforded **2a** in 71% isolated yield with 89% conversion of **1a** (run 1). The yield of **2a** was not improved by a longer reaction time (run 2). Lower reaction temperature (25 °C) resulted in a similar yield of **2a** for prolonged reaction time (run 3). Lower reaction rate and yield were observed with tetrabutylammonium hydroxide (1.0 M aqueous solution) (run 4). Triethylamine was not effective for the present isomerization and **1a** was recovered mostly (run 5).<sup>7</sup> Similar treatment of **1a** with polymer-supported fluoride [(polystyrylmethyl)trimethylammonium fluoride] gave **2a** and *cis*-chalcone (**3**) in 81% yield as a mixture (**2a/3** = 6.9) (run 6).



Scheme 2

Table 1. Isomerization of **1a** to **2a** under various conditions<sup>a</sup>

Run	Base	Solvent	Temp (°C)	Time (h)	Yield (%) <sup>b</sup>
1	KOH	toluene	80	1	71 (89)
2	KOH	toluene	80	5	70 (85)
3	KOH	toluene	25	24	71 (85)
4	Bu <sub>4</sub> NOH	THF	25	24	16 (65)
5	Et <sub>3</sub> N	toluene	80	20	3 (9)
6	FPS <sup>c</sup>	dioxane	100	16	81 <sup>d</sup> (92)

<sup>a</sup>Reaction conditions: **1a** (0.3 mmol), base (0.3 mmol), solvent (2 mL).

<sup>b</sup>Isolated yield. Numbers in parenthesis indicate conversion of **1a**.

<sup>c</sup>Fluoride, polymer supported. <sup>d</sup>*trans*-Chalcone **2a**/*cis*-chalcone **3** = 6.9.

As shown in Scheme 2, when the polymer-supported fluoride was reused for the isomerization, the product yield and the ratio of *trans*- to *cis*-chalcone gradually decreased.<sup>12</sup>

Having established suitable reaction conditions, a series of 1,3-diarylprop-2-yn-1-ols **1** were screened in order to investigate the reaction scope, and the results are summarized in Table 2.<sup>11</sup> The isomerizations of 1,3-diarylprop-2-yn-1-ols (**1b-1h**), which have substituents on the aromatic ring attached to carbon bearing OH, also similarly proceed to afford the corresponding chalcones (**2b-2h**). The product yield is considerably affected by the position of the substituent, whereas its electronic nature of that has no relevance to the product yield. With *ortho*-substituted 1,3-diarylprop-2-yn-1-ols (**1d** and **1g**), the product yield is generally lower than those with 1,3-diarylprop-2-yn-1-ols having *meta*- and *para*-substituents. 1,3-Diarylprop-2-yn-1-ols (**1i-1m**), which have substituents on the aromatic ring

**Table 2.** Isomerization of **1** to **2** in the presence of KOH<sup>a</sup>

<b>1</b>		Product	Yield (%)
R =	R' =		
H	H ( <b>1a</b> )	<b>2a</b>	71
H	4-Me ( <b>1b</b> )	<b>2b</b>	67
H	3-Me ( <b>1c</b> )	<b>2c</b>	70
H	2-Me ( <b>1d</b> )	<b>2d</b>	19
H	4-OMe ( <b>1e</b> )	<b>2e</b>	37
H	3-OMe ( <b>1f</b> )	<b>2f</b>	54
H	2-OMe ( <b>1g</b> )	<b>2g</b>	32
H	4-F ( <b>1h</b> )	<b>2h</b>	51
4-Me	H ( <b>1i</b> )	<b>2i</b>	66
3-Me	H ( <b>1j</b> )	<b>2j</b>	67
2-Me	H ( <b>1k</b> )	<b>2k</b>	69
4-OMe	H ( <b>1l</b> )	<b>2l</b>	48
4-F	H ( <b>1m</b> )	<b>2m</b>	66

<sup>a</sup>Reaction conditions: **1** (0.3 mmol), KOH (0.3 mmol), toluene (2 mL), 80 °C, 1 h.

attached to acetylenic carbon, are also isomerized to the corresponding chalcones (**2i-2m**) in the range of 48-69% yields. However, in contrast to the isomerization with **1b-1h**, the product yield is not significantly affected by the electronic nature and position of the substituent on the aromatic ring attached to acetylenic carbon.

In summary, we have shown that 1,3-diarylprop-2-yn-1-ols are isomerized to chalcones in the presence of KOH. Further study on the synthetic applications for heterocycles using our observed isomerization is currently under investigation.

### Experimental Section

**Typical experimental procedure for the isomerization of **1** to **2**.** A mixture of **1a** (0.062 g, 0.3 mmol) and KOH (0.017 g, 0.3 mmol) in dry toluene (2 mL) was placed in a 5 mL screw-capped vial and allowed to react at 80 °C for 1 h. The reaction mixture was filtered through a short silica gel column (ethyl acetate-hexane mixture) to eliminate inorganic salts. Removal of the solvent left a crude mixture, which was separated by thin layer chromatography (silica gel, ethyl acetate/hexane = 1/5) to give **2a** (0.044 g, 71%). All products (**2b**,<sup>13</sup> **2c**,<sup>13</sup> **2d**,<sup>14</sup> **2e**,<sup>6</sup> **2f**,<sup>6</sup> **2g**,<sup>15</sup> **2h**,<sup>16</sup> **2i**,<sup>17</sup> **2j**,<sup>13</sup> **2k**,<sup>13</sup> **2l**,<sup>17</sup> and **2m**<sup>18</sup>) prepared by the above procedure are known compounds.

**Acknowledgment.** The present work was supported by BK-21 in 2003 and a Korea Research Foundation Grant (KRF-2002-070-C00055). C.S.C. gratefully acknowledges a Research Professor Grant of Kyungpook National University (2004).

### References

- Lu, X.; Ji, J.; Guo, C.; Shen, W. *J. Organomet. Chem.* **1992**, *428*, 259.
- (a) Shvo, Y.; Blum, Y.; Reshef, D. *J. Organomet. Chem.* **1982**, *238*, C79. (b) Tsuji, Y.; Yokoyama, Y.; Huh, K.-T.; Watanabe, Y. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3456. (c) Ma, D.; Lu, X. *J. Chem. Soc., Chem. Commun.* **1989**, 890. (d) Trost, B. M.; Livingston, R. C. *J. Am. Chem. Soc.* **1995**, *117*, 9586.
- Saiah, M. K. E.; Pellicciari, R. *Tetrahedron Lett.* **1995**, *36*, 4497.
- Ma, D.; Lu, X. *Tetrahedron Lett.* **1989**, *30*, 2109.
- Arcadi, A.; Cacchi, S.; Marinelli, F.; Misiti, D. *Tetrahedron Lett.* **1988**, *29*, 1457.
- Ishikawa, T.; Mizuta, T.; Hagiwara, K.; Aikawa, T.; Kudo, T.; Saito, S. *J. Org. Chem.* **2003**, *68*, 3702.
- It was also reported by several groups that limited halides such as 2-iodopyrimidines, 6-iodouracils, and (chloroarene)Cr(CO)<sub>3</sub> are coupled with propargylic alcohols to give coupled enones via isomerization of initial coupled propargylic alcohols under Sonogashira coupling conditions: (a) Minn, K. *Synlett* **1991**, 115. (b) Kundu, N. G.; Das, P. *J. Chem. Soc., Chem. Commun.* **1995**, 99. (c) Müller, T. J. J.; Ansorge, M.; Aktah, D. *Angew. Chem. Int. Ed.* **2000**, *39*, 1253.
- (a) Cho, C. S.; Oh, B. H.; Shim, S. C. *Tetrahedron Lett.* **1999**, *40*, 1499. (b) Cho, C. S.; Oh, B. H.; Shim, S. C. *J. Heterocyclic Chem.* **1999**, *36*, 1175. (c) Cho, C. S.; Kim, J. S.; Oh, B. H.; Kim, T.-J.; Shim, S. C. *Tetrahedron* **2000**, *56*, 7747. (d) Cho, C. S.; Oh, B. H.; Kim, J. S.; Kim, T.-J.; Shim, S. C. *Chem. Commun.* **2000**, 1885. (e) Cho, C. S.; Kim, B. T.; Kim, T.-J.; Shim, S. C. *Chem. Commun.* **2001**, 2576. (f) Cho, C. S.; Kim, T. K.; Kim, B. T.; Kim, T.-J.; Shim, S. C. *J. Organomet. Chem.* **2002**, *650*, 65. (g) Cho, C. S.; Kim, B. T.; Choi, H.-J.; Kim, T.-J.; Shim, S. C. *Tetrahedron* **2003**, *59*, 7997. (h) Cho, C. S.; Lee, N. Y.; Kim, T.-J.; Shim, S. C. *J. Heterocyclic Chem.* **2004**, *41*, 423.
- Cho, C. S.; Lee, N. Y.; Kim, T.-J.; Shim, S. C. *J. Heterocyclic Chem.* **2004**, *41*, 409.
- In ref. 9, we exemplified one case for the isomerization of 1,3-diphenylprop-2-yn-1-ol to *trans*-chalcone in the presence of KOH.
- All 1,3-diarylprop-2-yn-1-ols (**1a-1m**) are prepared by the reported methods such as Grignard reaction and Sonogashira coupling: (a) Bagley, M. C.; Bashford, K. E.; Hesketh, C. L.; Moody, C. J. *J. Am. Chem. Soc.* **2000**, *122*, 3301. (b) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46 and references cited therein.
- It is known that polymer-supported fluoride works as a recyclable catalyst for a N-heteroannulation: Yasuhara, A.; Suzuki, N.; Yoshino, T.; Takeda, Y.; Sakamoto, T. *Tetrahedron Lett.* **2002**, *43*, 6579.
- Arai, S.; Tsuge, H.; Oku, M.; Miura, M.; Shioiri, T. *Tetrahedron* **2002**, *58*, 1623.
- Chen, W.; Egar, A. L.; Hursthouse, M. B.; Malik, K. M. A.; Mathews, J. E.; Roberts, S. M. *Tetrahedron Lett.* **1998**, *39*, 8495.
- Kumaraswamy, G.; Sastry, M. N. V.; Jena, N.; Kumar, K. R.; Vairamani, M. *Tetrahedron: Asymmetry* **2003**, *14*, 3797.
- Timmons, C.; Chen, D.; Barney, C. E.; Kirtane, S.; Li, G. *Tetrahedron* **2004**, *60*, 12095.
- Bharadwaj, A. R.; Scheidt, K. A. *Org. Lett.* **2004**, *6*, 2465.
- Chan, P. W. H.; Kamijo, S.; Yamamoto, Y. *Synlett* **2001**, 910.