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A Novel Stereoselective Synthesis of (*Z*)-3-Iodo-3-alken-1-one from 2-Alkyn-1-one

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Abstract: A one-pot reaction of 2-alkyn-1-one with sodium iodide/acetonitrile/trimethylsilyl chloride/water or trimethylsilyl iodide/acetonitrile at 25°C gave almost exclusively (*Z*)-3-iodo-3-alken-1-one in good yields.

The synthesis of stereoselective 3-halo-3-alken-1-ones is still a synthetic challenge. Recently, we reported that a one-pot reaction of terminal alkynes with *in situ* generated hydrogen iodide and organozinc compounds in the presence of palladium catalyst could provide a simple and useful method for the preparation of *gem*-disubstituted-alkenes.¹ We now report that using sodium iodide/acetonitrile/trimethylsilyl chloride/water (Method A) or trimethylsilyl iodide/acetonitrile (Method B) at 25°C 2-alkyn-1-one could give good yields of (*Z*)-3-iodo-3-alken-1-one² with stereoselectivities $\geq 95\%$ as judged by both ¹H- and ¹H-2D NOESY NMR spectral analysis. The results are summarized in Table I.³ In a typical procedure, CH₃CN (5 mL), TMSI (0.55 g, 5 mmol), water (0.05 g, 2.5 mmol), and 3-decyn-2-one **1** (0.76 g, 5 mmol) were sequentially added into a dry flask containing NaI (0.75 g, 5 mmol) under nitrogen atmosphere at room temperature. After 2h, the reaction mixture was quenched with water, extracted with ether, concentrated, and chromatographed (silica gel, n-hexane/ether = 4/1) to give (*Z*)-4-iodo-4-decen-2-one **2**⁴ in 85% yield. No great changes in the product yields were observed when we treated **1** with 1 equiv of 1,4-benzoquinone prior to run the reactions under either Method A or B conditions. Besides, using hexane instead of CH₃CN in the reaction, no reaction occurred. These results may rule out the possibility that both reactions involved a radical process. TMSI was essential to this reaction. Without adding TMSI to the reaction, only starting material **1** was recovered under the NaI/CH₃CN/H₂O system. Water also played an important role in the NaI/CH₃CN/TMSI/H₂O system. In the absence of water, **1** was recovered in 76-83% after 3h in the reaction conditions of TMSI/NaI/CH₃CN. Using excess of water in the TMSI/NaI/CH₃CN system, the products (*E*)-4-iodo-3-decen-2-one **3** and (*Z*)-4-iodo-3-decen-2-one **4** become increased (entries 2, 3, 4, and 5). When we treated heptadeca-7,10-diyn-9-one with 2 equiv of NaI/TMSI/H₂O in CH₃CN, only (*Z,Z*)-7,11-diiodoheptadeca-6,11-dien-9-one can be isolated in good yield (78%).

Treatment of **1** with TMSI/CH₃CN at -25°C followed by the addition of benzaldehyde gave (*Z*)-3-(hydroxy-phenyl-methyl)-4-iodo-4-decen-2-one with 85% diastereoselectivity in 46% yield.⁵ These results indicate that the first step in the mechanism (Scheme I) would be the formation of an iodo allenol silane **5**⁶ by the 1,4-addition of iodide on to the silicon activated electrophilic oxygen. Acid catalyzed double bond migration in the intermediate **5** by the protonation of the central carbon of the allene and simultaneous deprotonation of the γ -carbon by an intermolecular base would give rise to the more stable dienyl silane **6**. Hydrolysis of **6** would result in the observed product **2**.

Acknowledgment

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Table I. One-Pot Conversion of 2-Alkyn-1-one into (Z)-3-Iodo-3-alken-1-one.

$$n\text{-C}_6\text{-C}\equiv\text{C}-\overset{\text{O}}{\parallel}\text{C}-\text{R} \xrightarrow{\text{Method A or B}} n\text{-C}_5\text{-CH=CH(I)-CH}_2\text{-C(=O)-R}$$

Method A: TMSCl/NaI/H₂O/CH₃CN, B: TMSI/CH₃CN.

Entry	R =	Method	Iso. Yield (%)
1	Me-	A	85
2	Me-	A ^a	86 ^b
3	Me-	A ^c	23 ^d
4	Me-	A ^e	43 ^f
5	Me-	A ^g	<1 ^h
6	n-C ₅ -	A	81
7	Ph-	A	78
8	Me-	B	86
9	n-C ₅ -	B	83
10	Ph-	B	76
11	H-	A	75
12	H-	B	80

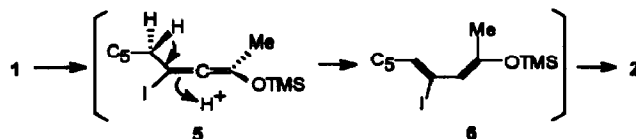
^a Used 1 equiv of H₂O in this reaction. ^b By-product is 4 (4%). ^c Used 5 equiv of H₂O in this reaction.

^d By-products are 3 (17%) and 4 (40%). ^e Used 5 equiv of H₂O and 5 equiv of TMSCl in this reaction.

^f The other major product is (Z)-4-chloro-4-decen-2-one (43%). ^g Used 20 equiv of H₂O in this reaction.

^h Other compounds are 3 (26%), 4 (31%), (Z)-4-chloro-3-decen-2-one (14%), and (E)-4-chloro-3-decen-2-one (29%).

Scheme 1. The Proposed Mechanism for the Formation of (Z)-4-Iodo-4-decen-2-one 2.



References and Notes

- Luo, F. T.; Fwu, S. L.; Hwang, W. S. *Tetrahedron Lett.* **1992**, 33, 6839.
- The reaction of 1-phenyl-2-propynone with metal halides in acetic acid at room temperature gave *E/Z* mixture of 3-halo-2-alken-1-ones: Ma, S.; Lu, X.; Li, Z. *J. Org. Chem.* **1992**, 57, 709.
- All new compounds have been fully characterized by ¹H- and ¹³C-NMR, MS or IR spectroscopy, and either elemental analysis or high resolution mass spectroscopy.
- (Z)-4-Iodo-4-decen-2-one 2. ¹H NMR (CDCl₃, TMS) δ 0.90 (t, *J* = 6.7 Hz, 3 H), 1.28-1.45 (m, 6 H), 2.14 (q with one singlet at δ 2.18, *J* = 6.8 Hz, 5 H), 3.70 (s, 2 H), 5.67 (t, *J* = 6.8 Hz, 1 H) ppm; ¹³C-NMR (CDCl₃, TMS) δ 13.93, 22.34, 27.71, 29.26, 31.18, 36.51, 59.08, 95.89, 140.75, 204.89 ppm; IR (neat) 2959 (m), 2930 (m), 1708 (s), 1630 (w), 1580 (w), 1455 (w), 1410 (w), 1353 (m), 1205 (m), 1150 (m) cm⁻¹; MS *m/z* 280 (*M*⁺) 209, 170, 153, 135, 109; HRMS calcd for C₁₀H₁₇IO 280.0325, found 280.0328; Anal. Calcd for C₁₀H₁₇IO: C, 42.87; H, 6.11. Found: C, 42.92; H, 6.13.
- The aldol reaction of allenates with benzaldehyde has been shown in the literature: Taniguchi, M.; Hino, T.; Kishi, Y. *Tetrahedron Lett.* **1986**, 27, 4767.
- Spectroscopically detectable TMS-allenoate has been reported in the literature: Taniguchi, M.; Kobayashi, S.; Nakagawa, M.; Hino, T.; Kishi, Y. *Tetrahedron Lett.* **1986**, 27, 4763.

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