

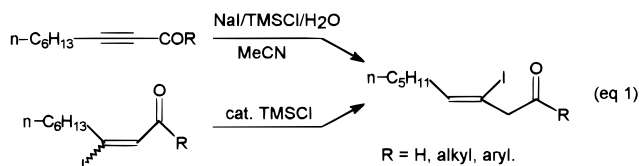
Mechanistic Study of the Transformation from 3-Decyn-2-one to (Z)-4-Iodo-4-decen-2-one†

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Received January 28, 1998

Recently, we have reported a stereoselective synthesis of (Z)-3-iodo-3-alken-1-one either from 2-alkyn-1-one by treating it with NaI, and TMSCl in aqueous MeCN or from (E)- and (Z)-3-iodo-2-alken-1-one using a catalytic amount of TMSCl in MeCN at room temperature as shown in eq 1.^{1,2} The stereoselectivities of both reactions

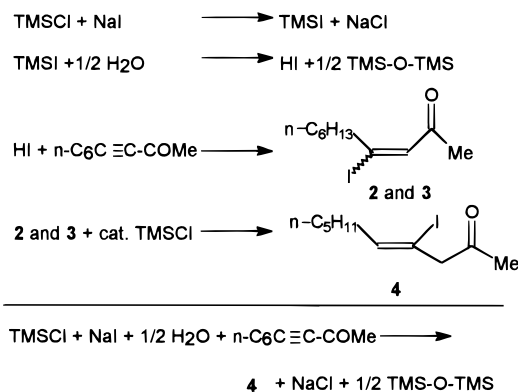


were $\geq 95\%$ as judged by ¹H NMR spectral analysis. The potential utility of (Z)-3-iodo-3-alken-1-one as an intermediate in organic synthesis was enhanced by the reduction with NaBH₄ in MeOH at 0 °C to give (Z)-3-iodo-3-alken-1-ol in high yield. Corey has demonstrated the synthetic utility of 2-haloallyl carbinols by a number of transformations.³ Suzuki also reported the asymmetric synthesis of 2-bromohomoallylic alcohols and their application in organic synthesis of using the tartrate ester of (2-bromoallyl)boronic acid.⁴ Normant and co-workers used 2-iodohomoallylic alcohols in their study to prepare stereoselective cyclopropane derivatives via metallacyclopropane rearrangement.⁵ Furthermore, this one-pot reaction could generate three useful functional groups for further transformations. For example, an application of this reaction to the preparation of (Z)- α -alkylidene- γ -butyrolactone,⁶ a potential plant growth regulator,⁷ has been reported. Although the transformation from conjugated alkynone to deconjugated (Z)-iodoenone seems to be a useful reaction in organic synthesis, its reaction mechanism is still unclear. The proposed intermediate disclosed in our previous work¹ has not been detected so far. Herein, we present a reaction mechanism for this reaction based on some new observations.

When 1 equiv of 3-decyn-2-one (**1**) was treated with anhydrous HI, generated in situ by the addition of TMSCl (1 equiv) to NaI (1 equiv) in MeCN (1 M solution) followed by the addition of H₂O (0.5 equiv), (E)-4-iodo-3-decen-2-one (**2**) and (Z)-4-iodo-3-decen-2-one (**3**) could be generated in 2–4 h in 54% and 37% yields, respectively. Only

trace amount (<5%) of deconjugated (Z)-4-iodo-4-decen-2-one (**4**) was detected by ¹H NMR of its crude. The products ratio did not change despite prolonging the reaction time to 72 h. Without the addition of TMSCl in the reaction, only starting material was recovered. No great changes in the yield of the product were observed even when 1 equiv of 1,4-benzoquinone was added. No reaction was observed when hexane was used in place of MeCN. These results rule out the possibility that the reaction involves a radical process. Water also played an important role in the reaction. In the absence of H₂O, the starting material was recovered in 80% yield after 3 h at room temperature. Use of excess H₂O (2 equiv) resulted in **2** and **3** being the major products while **4** was obtained in trace amount (<5%). However, when 1.1 equiv of TMSCl was used instead of 1 equiv, **4** was isolated in 76% yield in 4 h at room temperature along with only trace amount of **2** and **3** as detected by ¹H NMR. Thus, a little bit of excess TMSCl plays an important role in the reaction. Therefore, it is suggested that **2** and **3** are the real intermediates in the reaction, and they are formed by direct regioselective hydroiodination of the carbon–carbon triple bond.

The TMSCl-catalyzed deconjugation gave **4** stereoselectively as we reported previously.² We attempted deconjugation by treating **2** and **3** with TMSCl (1.1 equiv) and NaI (1 equiv) and H₂O (0.5 equiv) in MeCN; however, starting materials were recovered in 90–94% yields, and trace amount of **4** was detected as revealed by ¹H NMR. This result can be rationalized by assuming that first the oxygen of the carbonyl group gets protonated by the in situ generated HI, and then coordination of the carbonyl group by the TMS group becomes difficult. As a result no further deconjugation process takes place.² When excess water was added, the deconjugation process is terminated, since both TMSI and TMSCl form HI and HCl very quickly on addition of water. The heats of formation for **2**, **3**, and **4** were found to be –48.19, –46.92, and –49.62 kcal/mol, respectively, using AM1 calculation with PC Spartan computer program. Thus, the relative stability order is **4** > **2** > **3**. This may also support the fact that the deconjugation process may be dominated by the thermostability of the iodoenone isomers. The proposed mechanism for this reaction is as follows:



(8) The stereochemistry of the two isomers was determined by their 2D NOESY ¹H NMR spectral analysis.

† Dedicated to Prof. Ei-ichi Negishi on the occasion of his 63rd birthday.

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Experimental Section

(Z)-4-Iodo-4-decen-2-one. To a flask was added NaI (0.68 g, 4.5 mmol, 1.5 equiv); it was then flame-dried under high vacuum (1 mmHg) for 5 min. After cooling to room temperature, the flask was flushed with dry nitrogen with high purity. Dry MeCN was added into the flask, and stirring was started.⁹ TMSCl (0.46 mL, 3.6 mmol, 1.2 equiv) was added to the flask, and stirring was continued for another 20 min at room temperature. Water (27 μ L, 1.5 mmol, 0.5 equiv) was added into the flask, and the mixture stirred for another 10 min at room temperature. 3-Decyn-2-one (0.46 g, 3 mmol, 1 equiv) was added quickly into the flask. After stirring for another 4 h, the reaction mixture was quenched with saturated sodium thiosulfate and extracted with ether three times. The organic layer was dried over MgSO₄ followed by filtration, concentration, and chromatography (silica gel, ethyl acetate/hexanes = 8/1) to give (Z)-4-iodo-4-decen-2-one (0.64 g, 76% yield) as a colorless oil (R_f = 0.53 on Si60 F254, ethyl acetate/hexanes = 4/1): ¹H NMR (CDCl₃, TMS) δ 0.90 (t, J = 7 Hz, 3 H), 1.28–1.45 (m, 6 H), 2.14 (q with one singlet at δ 2.18, J = 7 Hz, 5 H), 3.70 (s, 2 H), 5.67 (t, J = 7 Hz, 1 H); ¹³C NMR (CDCl₃, TMS) δ 13.93, 22.34, 27.71, 29.26,

(9) Normally, 1 mmol of NaI with 1 mL of MeCN to form about 1 M solution is good enough to dissolve NaI completely. Be sure to completely dissolve NaI at this stage for further steps.

31.18, 36.51, 59.08, 95.89, 140.75, 204.89; 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, 95, 81, 71, 67, 54; 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.

(E)-4-Iodo-3-decen-2-one: ¹H NMR (CDCl₃, TMS) δ 0.90 (t, J = 7 Hz, 3 H), 1.2–1.6 (m, 8 H), 2.15 (s, 3 H), 3.05 (t, J = 7 Hz, 2 H), 7.02 (s, 1 H); ¹³C NMR (CDCl₃, TMS) δ 14.00, 22.48, 28.08, 29.73, 31.15, 31.51, 41.53, 130.83, 138.52, 195.22; IR (neat) 1691 (s), 1577 (s), 1350 (m), 1109 (m), 906 (s), 713 (m) cm⁻¹; MS m/z 280 (M⁺), 153, 128, 111, 95.

(Z)-4-Iodo-3-decen-2-one: ¹H NMR (CDCl₃, TMS) δ 0.90 (t, J = 7 Hz, 3 H), 1.2–1.6 (m, 8 H), 2.28 (s, 3 H), 2.67 (t, J = 7 Hz, 2 H), 6.66 (s, 1 H); ¹³C NMR (CDCl₃, TMS) δ 13.44, 22.48, 27.94, 29.32, 31.47 (2 C's), 48.02, 117.75, 131.22, 196.06; IR (neat) 1692 (s), 1587 (s), 1355 (m), 1108 (m), 906 (s), 745 (m) cm⁻¹; MS m/z 280 (M⁺), 153, 128, 111, 95; HRMS calcd for C₁₀H₁₇IO 280.0325, found 280.0326.

Acknowledgment. The author thanks the National Science Council of the Republic of China and Academia Sinica for financial support.

JO980154L