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A simple and practical method for the stereoselective synthesis of (*Z*)-1-iodo-1-alkenes from 1,1-diiodo-1-alkenes

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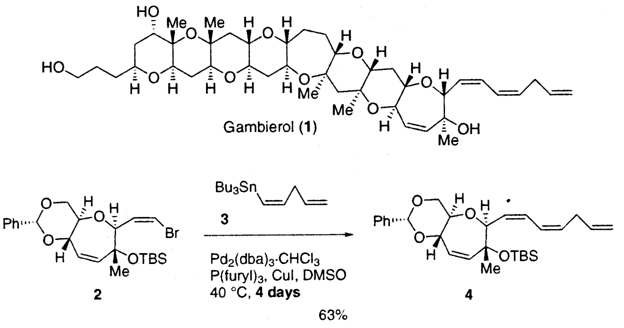
Abstract—Treatment of the 1,1-diiodo-1-alkenes **8**, prepared from the corresponding aldehydes with CI_4/PPh_3, with Zn–Cu/AcOH in THF–MeOH gave the (*Z*)-1-iodo-1-alkenes **9**, selectively, in good yields.

Transition metal catalyzed coupling of haloalkenes with organometallic reagents is well recognized as a powerful tool for C–C bond formation. Since most of the reactions proceed with retention of the olefin geometry, stereoselective synthesis of haloalkenes is very important. In the course of our total synthetic study of gambierol (**1**), the Stille coupling[1] was chosen as a promising candidate for the construction of the triene side chain. Thus, the (*Z*)-1-bromoalkene **2**, prepared from the corresponding dibromoalkene by the Uenishi procedure,[2] was subjected to the coupling with the (*Z*)-vinyl stannane **3** under the modified Stille conditions[3] to afford the triene **4** as a single stereoisomer in 63% yield (Scheme 1).[4] Although **4** was obtained selectively in an allowable yield, the reaction was very slow. A significant amount of the starting material **2** remained even after 4 days. To solve this problem, we examined the preparation of the iodoalkene counterpart which was expected to be more reactive than **2**.

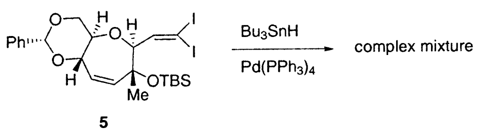
However, stereoselective synthesis of the desired (*Z*)-iodoalkene derivative by the known procedures was problematic. For example, hydrogenolysis of the diiodoalkene **5** with Bu_3SnH in the presence $Pd(PPh_3)_4$ gave a complex mixture, as reported by Uenishi (Scheme 2).[2c]

Although the Wittig reaction of the aldehyde **6** under the Stork conditions[5] gave the iodoalkene **7** in high yield, no stereoselectivity was observed in this reaction (Scheme 3).

After several unfruitful attempts, we found that the treatment of 1,1-diiodo-1-alkenes **8** with Zn–Cu/AcOH in THF–MeOH afforded the (*Z*)-1-alkenes **9** selectively (Scheme 4).[6] This methodology was successfully applied to the total synthesis of gambierol (**1**).[7] In this paper, we wish to describe the generality and stereoselectivity of this reaction.



Scheme 1.



Scheme 2.

Keywords: iodoalkenes; diiodoalkenes; stereoselective reduction; zinc.

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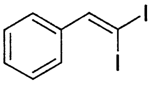
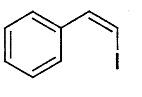
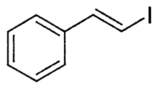
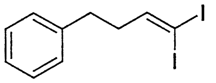
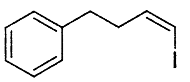
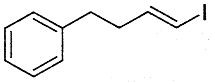
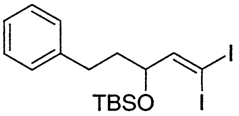
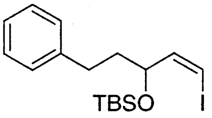
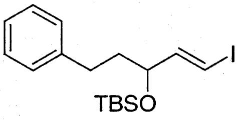
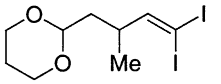
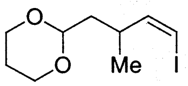
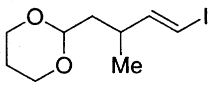
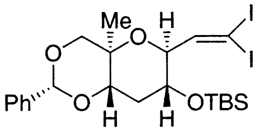
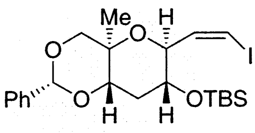
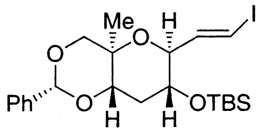
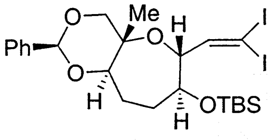
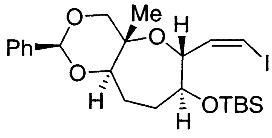
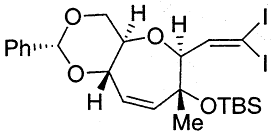
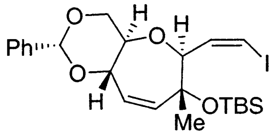
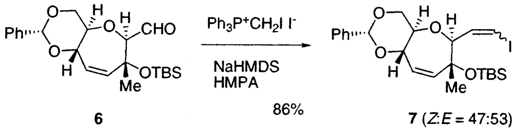
Results of the reduction of various diiodoalkenes, prepared from the corresponding aldehydes with CI_4/PPh_3,[8] are summarized in Table 1. Although the reaction of the conjugated diiodoalkene **8a** gave the (*E*)-iodoalkene **10a** as the major product (entry 1),[9] a wide variety of the aliphatic diiodoalkenes **8b**–**g** gave the (*Z*)-iodoalkenes **9b**–**g**, either predominantly or exclusively, in good yields (entries 2–7). None of the over-reduced product was detected in any case. Very high stereoselectivities were observed in the reactions of **8f** and **8g** which have a seven-membered ring (entries 6 and 7). The (*Z*)-iodoalkenes **9f** and **9g** were obtained as the sole products in both cases.

The reduction of **8e** is representative. To a stirred solution of **8e** (100 mg, 0.16 mmol) in THF (5 mL) and MeOH (3 mL) at 0°C were added AcOH (0.5 mL) and Zn–Cu[10] (200 mg). After stirring for 0.5 h at the same

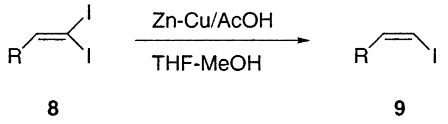
Table 1. Stereoselective reduction of 1,1-diiodo-1-alkenes **8a**–**g** with Zn–Cu/AcOH[a]

Entry	Substrate[b]	Products			Yield[c]
1	 **8a**	 **9a**	25:75	 **10a**	74%
2	 **8b**	 **9b**	83:17	 **10b**	74%
3	 **8c**	 **9c**	89:11	 **10c**	95%
4	 **8d**	 **9d**	90:10	 **10d**	80%
5	 **8e**	 **9e**	79:21	 **10e**	82%
6	 **8f**	 **9f**			86%
7	 **8g**	 **9g**			80%

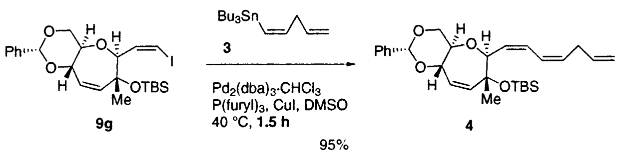
[a] Reactions were carried out with 30 equiv of Zn-Cu and 100 equiv of AcOH in THF-MeOH at 0 °C. [b] Substrates were prepared from the corresponding aldehydes with CI_4/PPh_3. [c] Combined isolated yields.



Scheme 3.



Scheme 4.



Scheme 5.

temperature, the insoluble material was filtered off. The filtrate was diluted with ether, then washed with satd. NaHCO$_3$ and brine. Concentration and chromatography (hexane/EtOAc, 20:1) gave **9e** (49 mg, 61%) and **10e** (17 mg, 21%).

The usefulness of this reaction was demonstrated by the modified Stille coupling of the (*Z*)-iodoalkene **9g** with the vinylstannane **3** as shown in Scheme 5. The reaction was finished within 1.5 h to afford **4** in 95% yield. None of the other olefinic isomer was detected in this reaction.

In conclusion, we have developed a simple and practical method for the stereoselective synthesis of (*Z*)-1-iodoalkenes. To the best of our knowledge, this is the first example of the stereoselective reduction of 1,1-diiodo-1-alkenes. It should be noted that the present methodology does not require the use of toxic tin compounds nor expensive metal reagents. We are now in a position to use (*Z*)-1-iodoalkenes as useful coupling partners for Stille and related coupling reactions.

Acknowledgements

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