Addition of $MeMgSnBu^n_3$ to Terminal Enyne; Preparation of Geometrically Pure 2-Substituted 1-Iodo-1,3-Dienes

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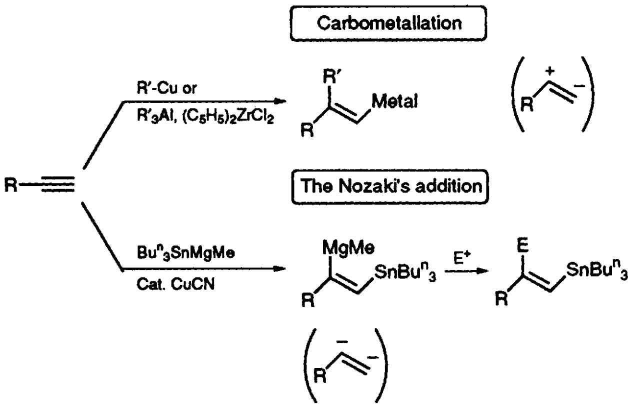
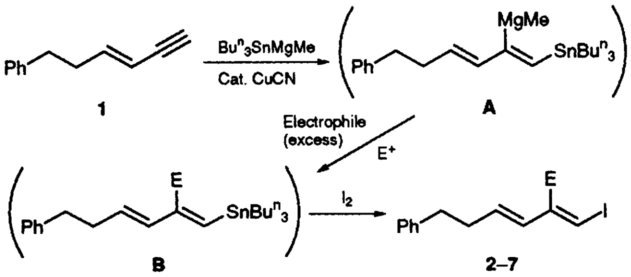
The title iododienes have been prepared from 6-phenylhex-3-en-yne by the addition of methylmagnesiumtributyltin, followed by reactions of stannylmagnesium intermediate **A** with appropriate electrophiles and of the resulting alkylated stannylidiene **B** with iodine.

Palladium catalysed cross-coupling reaction of an iodoalkene with an appropriate alkenylstannane or alkenylborane is one of the common methods to prepare polyenes.[1] For construction of polyene units in terpenoid syntheses, we require 2-alkyl substituted 1-iodo-1,3-diene derivatives. Carbometallation reactions of 1-alkynes developed by Normant and Alexakis,[2] Negishi[3] and others[4] have been adopted for a preparation of 2-alkyl substitued 1-iodoalkenes. In this type of reaction, a terminal acetylene is regarded as a di-positively charged 1-alkene equivalent. However, introduction of an alkyl group at the 2-position is limited to simple alkyl or allyl groups, because of the non-availability of other organocopper or organoaluminium species. If a terminal acetylene could act as a di-negatively charged 1-alkene equivalent,[5] a variety of electrophiles could be introduced on the 2-position; the Nozaki addition reaction of methylmagnesiumtributylstannane to terminal acetylenes[6] can be used for this purpose. After the *syn* addition of the reagent to 1-alkyne, trapping by alkyl halides or aldehydes gives 2-alkyl substituted 1-stannylalkenes.[7] However, this reaction has not been used for the synthesis of 2-alkyl substituted 1,3-dienes to the best of our knowledge.† We have now applied the Nozaki addition to terminal enynes and to the formation of geometrically pure 1-iodo-2-alkyl-1,3-dienes. In particular, this reaction allows a novel preparation of cyclic β-[2-(1-iodo-1,3-dienyl)]ketones.



Scheme 1

Methylmagnesiumtributylstannane was generated by the Nozaki's procedure which on exposure to enyne **1** (Scheme 2), in the presence of a catalytic amount of CuCN at −20 °C, produced 2-methylmagnesium-1-tributylstannyldiene intermediate **A**. Treatment of **A** with a large excess of iodomethane formed 2-methyl-1-stannyldiene **B** (E = Me). Although non-substituted tributylstannyldienes have been used in syntheses,[9] an attempt to isolate the stannyldiene **B** in pure form failed.‡ Acidic work up of **B** (E = Me) gave exclusively 2-methyl-1,3-diene in 93% yield. Quenching **B** with iodine



Scheme 2

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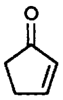
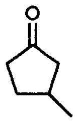
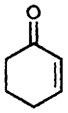
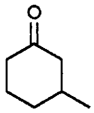
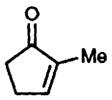
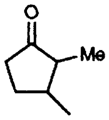
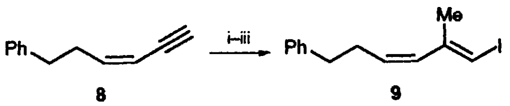
† Addition of $Bu^n_3SnMgMe$ to enyne substrates followed by protonation gave (*E*) and (*Z*) mixtures of 1,3-diene. See examples in ref. 8.

‡ 2-Substituted-1-tributylstannyl-1,3-dienes **B** are unstable and easily hydrolysed to give 2-substituted-1,3-dienes, they were always obtained as unseparable mixtures along with hydrolysed products.

Table 1 Reaction of **1** with electrophiles[a]

Entry	Electrophile	Compound (E)[a]	Yield (%)[b]
1	Me-I	Me **2**	91
2	$PhCH_2OCH_2$-Cl	$PhCH_2OCH_2$ **3**	65
3		$HOCH_2CH_2$ **4**	71
4		 **5**	67
5		 **6**	61
6		 **7**[c]	53

[a] All the products exhibited satisfactory spectral data. [b] Isolated yields. [c] Single diastereoisomer.



Scheme 3 *Reagents and conditions*: i, $Bu^n{}_3SnMgMe$, CuCN (cat.); ii, MeI; iii, I_2

after careful extraction by anhydrous hexane from the reaction mixture afforded the desired (*E,E*)-1-iodo-2-methyl-1,3-diene **2** in 91% yield. The stereochemistry of the original olefin was maintained without isomerization. Regioselectivity of the addition was exclusively *syn* and showed much more selectivity than the case of simple 1-alkynes.[7] Reactions with other electrophiles such as benzyloxymethyl chloride, ethylene oxide gave the corresponding 2-substituted 1-iodo-1,3-dienes **3** and **4** in 65 and 71% yields, respectively. These results are summarized in Table 1. More interestingly the reactions with cyclopentenone and cyclohexenone gave the corresponding β-substituted cyclic ketones **5** and **6** in medium yields, but acyclic enones did not react with **A**. In the cases of substituted cyclic enones, 2-methylcyclopentenone reacted to give dienyl ketone **7** in 53% yield, while 3-methylcyclopentenone and 3-methylcyclohexenone were inactive. The reaction of (*Z*)-enyne **8** proceeded stereospecifically and presented (*E,Z*)-1-iodo-2-methyl-1,3-diene **9** in 84% yield. No olefin isomerization occurred in the reaction process as long as the temperature was maintained at −20 °C in all the cases.§ This reaction offers versatile preparation of 2-substituted 1-iodo-1,3-dienes from terminal enynes, which will be useful synthetic pieces for polyene synthesis and for Diels–Alder ring construction reactions.

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§ Isomerization occurred at a higher temperature and the details will be discussed in a full account.