Pergamon

Tetrahedron Letters, Vol. 37, No. 8, pp. 1173-1176, 1996

0040-4039/96 $15.00 + 0.00

0040-4039(95)02403-4

INTERMOLECULAR COPPER(I) CHLORIDE-MEDIATED COUPLING OF ALKENYLTRIALKYLSTANNANE FUNCTIONS: A CONVENIENT SYNTHESIS OF CONJUGATED DIENE SYSTEMS

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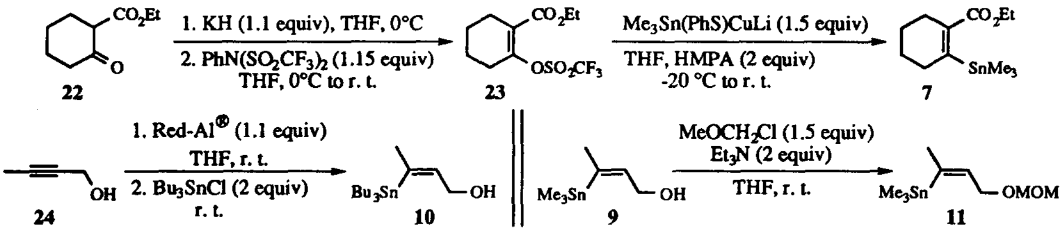
Abstract: *A novel copper(I)-mediated coupling of alkenyltrialkylstannane functions is reported. Thus, treatment of the functionalized stannanes **1-11** with 2.5 equivalents of CuCl in* N,N-*dimethylformamide (DMF) at room temperature provides good-to-excellent yields of the dienes **12-21**.*

The palladium(0)-catalyzed intermolecular cross couplings of alkenyl triflates, iodides, or bromides with alkenyltrialkylstannane functions (the Stille coupling) represent very important processes for the construction of carbon-carbon single bonds and, concomitantly, for the stereospecific synthesis of conjugated diene systems.[1-3] Recent work carried out in this laboratory led to the discovery that *intra*molecular coupling of alkenyltrimethylstannyl groups with vinyl halide (Br, I) functions can also be performed efficiently by treatment of a mixture of the requisite substrates with copper(I) chloride (~2-3 equiv) in DMF.[4] We report herein the novel finding that the copper(I) chloride-mediated *inter*molecular coupling of two alkenyltrialkylstannyl functions constitutes an efficient, potentially valuable method for the assembly of structurally diverse conjugated diene systems. In this connection, the reports[5,6] describing the *copper(II) nitrate*-mediated intermolecular coupling of alkenyltributylstannanes should be noted. However, in the earlier paper,[5] only four examples are given and in all the substrates employed in Quayle's work,[6] the carbon atom bearing the Bu_3Sn function was also attached to a heteroatom (oxygen or sulfur) and, therefore, the products possess vinyl ether or vinyl sulfide linkages.[7]

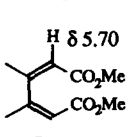
Of the substrates **1-11** (see Table) employed in the present study, compounds **1**,[8] **2**,[9] **3**,[10] **4-6**,[11] **8**,[12] and **9**[13] have been reported previously in connection with our continuing investigations into the preparation and synthetic uses of alkenyltrialkylstannanes. Compound **7** was prepared from the keto ester **22** via a method modified from that described for the corresponding methyl ester.[12] Thus, sequential treatment of **22** with KH and $PhN(SO_2CF_3)_2$ gave the corresponding vinyl triflate **23**,[14] which, upon reaction with lithium (phenylthio)(trimethylstannyl)cuprate[15] provided the ester stannane **7** (85% from **22**). Hydroalumination of 2-butyn-1-ol (**24**) with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al®), followed by reaction of the resultant intermediate with tributylstannyl chloride,[16] afforded the substrate **10**, while treatment of the alcohol **9**[13] with methoxymethyl chloride in the presence of triethylamine produced the ether stannane **11**.



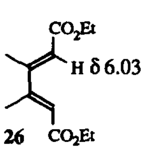
Addition of copper(I) chloride (2.5 equivalents) to a solution of ethyl (*Z*)-5-methyl-3-trimethylstannyl-2-hexenoate (**1**) in DMF, followed by stirring of the resultant mixture for 1 h at room temperature, provided the (*Z,Z*)-diene **12** in high yield (Table, entry 1).[17] In very similar fashion, the β-trialkylstannyl α,β-unsaturated esters **2-8** were transformed cleanly and efficiently into functionalized dienes **13-19**, respectively (entries 2-8). On the other hand, couplings involving the stannane alcohols **9** and **10** and the stannane ether **11**, although successful, were somewhat less efficient (entries 9-11). Although most of the reactions carried out thus far have involved the use of tri*methyl*stannyl substrates, the couplings summarized in entries 3 and 10 of the Table show that tri*butyl*stannanes are also suitable participants in these processes.

The results outlined in the Table demonstrate that the new coupling method tolerates the presence of a variety of functional groups. Furthermore, from a synthetic viewpoint, it is important that the process occurs without loss of stereochemical integrity. The reactions proceed cleanly with retention of configuration at the alkenyl centers that are being coupled and, as shown by the conversion of the geometrically isomeric substrates **5** and **6** into the corresponding dienes **16** and **17** (entries 5 and 6), the coupling process is stereospecific.

Of the products listed in the Table, substances **18**[18] and **20**[19] have been reported previously. The geometric configurations of the products **12-17** were established by use of ^{1}H NMR spectroscopy. The olefinic protons of the known diesters **25**[20] and **26**[21] resonate ($CDCl_3$) at δ 5.70 and 6.03, respectively. In the same solvent, the signals due to the olefinic hydrogens of compounds **12** and **14-16** appear at δ 5.63, 5.61, 5.68, and 5.70, respectively, while corresponding resonances in the spectra of **13** and **17** are found at δ 5.85 and 5.93, respectively. These data provide strong evidence for the stereochemical assignments. It should also be noted that, as expected, the protons of the allylic CH_2 groups in the (*Z,Z*)-diene **16** resonate at higher field than the corresponding protons of the (*E,E*)-diene **17**. Similar chemical shift patterns can be observed in the ^{1}H NMR spectra of substances **12-15**.



25



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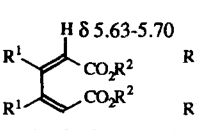
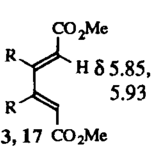
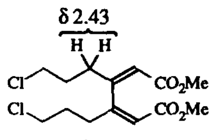


12, 14-16



13, 17



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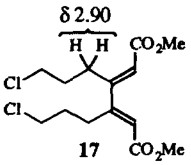

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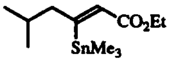
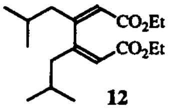
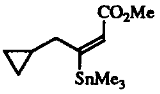
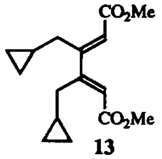
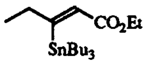
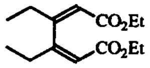
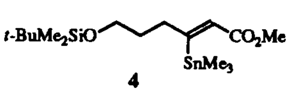
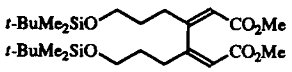
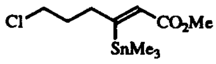
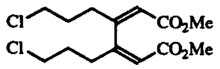
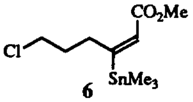
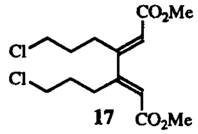
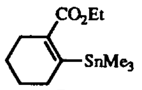
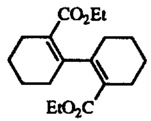
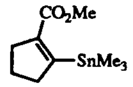
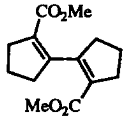
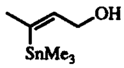
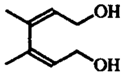
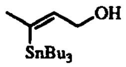
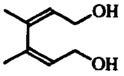
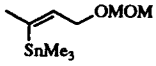
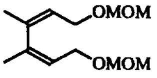
The mechanistic details of the new coupling process remain unclear. Nevertheless, on the basis of results of other recent studies,[13,22] it is likely that the reaction is initiated by transmetallation of the alkenyltrialkylstannane function with copper(I) chloride to produce the corresponding trialkylstannyl chloride and an alkenylcopper(I) intermediate. Further mechanistic discussion is deferred to a full account of this work.

From a synthetic viewpoint, the results presented above show clearly that the copper(I) chloride-mediated coupling of alkenyltrialkylstannane functions represents a potentially valuable method for preparing

Table. Intermolecular Coupling of Alkenyltrimethylstannane Functions

Entry	Starting Material	Reaction Conditions	Product	Yield (%)
1	 1	CuCl (2.5 equiv) DMF, r. t., 1 h	 12	96
2	 2	CuCl (2.5 equiv) DMF, r. t., 2 h	 13	92
3	 3	CuCl (2.5 equiv) DMF, r. t., 1 h	 14	97
4	 4	CuCl (2.5 equiv) DMF, r. t., 1 h	 15	86
5	 5	CuCl (2.5 equiv) DMF, r. t., 1 h	 16	90
6	 6	CuCl (2.5 equiv) DMF, r. t., 1 h	 17	82
7	 7	CuCl (2.5 equiv) DMF, r. t., 1 h	 18	80
8	 8	CuCl (2.5 equiv) DMF, r. t., 1 h	 19	99
9	 9	CuCl (2.5 equiv) DMF, r. t., 1 h	 20	63
10	 10	CuCl (2.5 equiv) DMF, r. t., 1 h	 20	51
11	 11	CuCl (2.5 equiv) DMF, r. t., 1 h	 21	53

usefully functionalized conjugated diene systems. Since, in terms of carbon framework and functionality, a wide variety of alkenyltrialkylstannanes are readily prepared,[4,8-13,15,23] a number of extensions to this work can be envisaged. Furthermore, the structurally novel diene products (e.g. **12-21**) would appear to be worthy intermediates for future investigations in organic synthesis. We are actively pursuing a number of possibilities.

Acknowledgments. We thank NSERC of Canada and Merck Frosst Canada Inc. for financial support. A NSERC of Canada Postgraduate Scholarship (to E.J.M.) is gratefully acknowledged.

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(*Received in USA* 20 *November* 1995; *revised* 7 *December* 1995; *accepted* 11 *December* 1995)