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Preparation of 2-(trimethylsilyl)methyl-2-propen-1-ol derivatives by cobalt catalyzed sp2-sp3 coupling

M. Tariq Riaz, Ivanna Pohorilets, Jackson J. Hernandez, Jeovanna Rios, Nancy I. Totah *

Department of Chemistry, Syracuse University, Syracuse, NY 13244, USA

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ABSTRACT

A practical, operationally simple preparation of 2-(trimethylsilyl)methyl-2-propen-1-ol derivatives is described. The cobalt catalyzed coupling of a protected vinyl halide with trimethylsilylmethylmagnesium chloride shows excellent functional group tolerance and provides these synthetically useful allyl silanes in good overall yield. By this method, the use of highly concentrated organolithium reagents, complex reaction protocols, and expensive starting materials is avoided.

Introduction

Protected 2-(trimethylsilyl)methyl-2-propen-1-ols **1** have found widespread application in organic synthesis. These versatile reagents are able to function as nucleophiles [1], as electrophiles [2] (depending on the nature of the oxygen protecting group), and as all-carbon 1,3-dipole equivalents in transition metal catalyzed processes [3]. As such, these compounds participate in 1,2- and 1,4-addition reactions [4], ene reactions [5], C-glycosylation [6] and Ferrier-type processes [7], and oxidative radical additions [8], to name a few. Compounds **1** in which the oxygen atom bears an ester functionality are particularly useful in ring forming reactions. Such processes include [3 + 2] cycloadditions for the preparation of cyclopentanes (**2**, **3**) [9], dihydrofurans (**4**) [10], and pyrrolidines (**5**) [11], [3 + 3] cycloadditions for the preparation of piperidines (**6**) [12] and other heterocycles (**7**) [13] and [3 + 4] cycloadditions for the preparation of fused seven-membered carbocyclic ring systems (**8**) [14]. The preparation of bridged 9-membered carbocycles (**9**) by [3 + 6] cycloaddition reactions with tropones is also known [15]. Examples shown in Scheme 1 are representative. Reagents of these types (**1**) have also found application in the preparation of natural products and other complex molecular frameworks [16].

The synthesis of these reagents **1** is typically achieved by manipulation of the corresponding alcohol, itself prepared in two steps from 2-methyl-2-propen-1-ol through the intermediacy of the corresponding dianion [17]. Though direct, this process is technically demanding, and requires the use of highly concentrated *n*-butyllithium and carefully controlled reaction conditions. Over the years a number of other protocols have been reported for the synthesis of 2-(trimethylsilyl)methyl-2-propen-1-ol, but these preparations often require the use of specially prepared reagents, labyrinthine reaction protocols, and superfluous protection and/or deprotection steps [18]. In most cases, the requisite starting material is also quite expensive.

Results and discussion

Our interest in the development of tandem reaction processes using functionalized allylsilanes led us to consider an alternative preparation of protected 2-(trimethylsilyl)methyl-2-propen-1-ols **1** that was operationally simple and made use of relatively inexpensive starting materials. Toward this end, we anticipated that the desired substrates would be accessible through a cobalt catalyzed sp^2-sp^3 coupling reaction between trimethylsilyl-methylmagnesium chloride [19] and a functionalized vinyl halide **10** in which a variety of protected alcohols are available by manipulation of 2-iodo-2-propen-1-ol **11** (Scheme 2). This latter is readily available on large scale from inexpensive propargyl alcohol [20]. This strategy differs from prior methods of preparation in that functionalization of the hydroxyl group occurs prior to C—C bond formation and thus avoids superfluous protecting group manipulations.

In the forward sense, the requisite vinyl iodide was readily prepared by the method of Nicolaou [20] whereby addition of the

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* Corresponding author.
E-mail address: ntotah@syr.edu (N.I. Totah).

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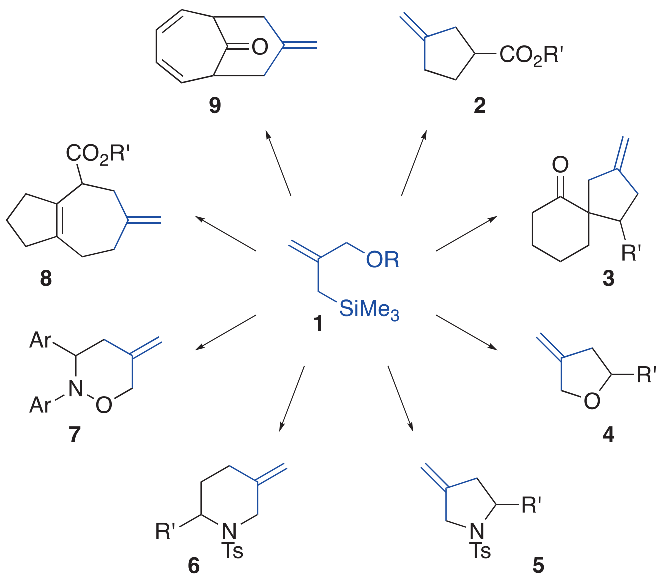
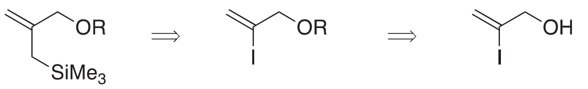


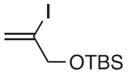
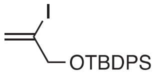
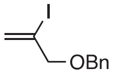
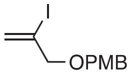
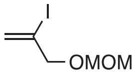
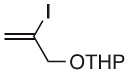
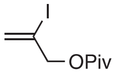
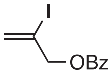
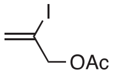
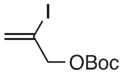
Scheme 1. Some accessible frameworks.



1 10 11

Scheme 2. Approach to the synthesis of 2-(trimethylsilyl)methyl-2-propen-1-ol derivatives.

Table 1
Protection of Vinyl Iodide **11**.

entry	vinyl iodide		yield
1	 OTBS	**12**	72%
2	 OTBDPS	**13**	83%
3	 OBn	**14**	98%
4	 OPMB	**15**	63%
5	 OMOM	**16**	83%
6	 OTHP	**17**	82%
7	 OPiv	**18**	85%
8	 OBz	**19**	85%
9	 OAc	**20**	76%
10	 OBoc	**21**	98%

alkyne to a mixture of NaI and TMSCl in wet acetonitrile provided the desired product **11** as a single regioisomer in 60% yield. Purification can be effected by either column chromatography or vacuum distillation, depending on reaction scale. This product can be stored over copper wire in the freezer for several months without significant decomposition.

With the vinyl halide **11** in hand, a variety of ethers, esters and carbonates were prepared for evaluation in the cobalt catalyzed coupling reaction. The choice of protecting groups was influenced by differences in steric bulk, stability to acidic and/or basic reaction conditions, reactivity toward Grignard reagents, and variation in deprotection regimens. Protecting groups were introduced under standard conditions to give the desired products in good to excellent yields (Table 1). Attempts to prepare the benzyl ethers **14** and **15** under basic conditions were unsatisfactory, though the desired compounds could be readily obtained under acidic conditions using the corresponding benzyl-or p-methyoxybenzyl trichloroacetimidates respectively (entries 3 and 4). Additional details on the preparation of protected vinyl iodides **12**–**21** are provided in the experimental section.

These protected vinyl halides were then subjected to the cobalt-catalyzed cross coupling reaction with trimethylsilylmethylmagnesium chloride (Table 2) [21]. Initial experiments focused on the use of substrates in which the alcohol **11** was protected as an ether functionality. Both TBS **12** and TBDPS **13** ethers performed well in this transformation providing the coupled products **22** and **23** in 74 and 81% yields respectively (entries 1 and 2). Benzyl **14** and p-methoxybenzyl **15** ethers (entries 3 and 4) were also compatible with the reaction conditions, as were acetals with MOM **16** and THP groups **17** (entries 5 and 6). Yields of the corresponding allyl silanes **24**–**27** ranged from 66 to 79%.

A more challenging test of this methodology was anticipated to be the use of vinyl halides **1** that contained ester functionality. As the corresponding allyl silanes are commonly used as precursors to trimethylenemethane metal complexes, we were interested to see if this method could be utilized for the preparation of substrates of this type. A series of carbonyl compounds **18**–**21** were thus prepared, and their compatibility for use with a Grignard coupling partner evaluated. As shown, not only were hindered and less reactive substrates with pivalate **18** and Boc **21** protecting groups tolerant of the reaction conditions (entries 7 and 10), but benzoate **19** and acetate **20** protected substrates could be utilized as well (entries 8 and 9). In these cases, yields ranged from 70 to 76%. Examination of the crude proton NMRs of the coupling reactions of ester protected substrates showed little if any products resulting from cleavage of the protecting group.

Conclusion

In summary, a practical protocol for the synthesis of protected 2-(trimethylsilyl)methyl-2-propen-1-ols has been developed. Preparation of these synthetically useful allyl silanes via the cobalt-catalyzed sp^2-sp^3 coupling reaction of a protected 2-iodo-2-propen-1-ol **11** and (trimethylsilylmethyl)magnesium chloride provides an attractive alternative to existing methodologies. The sequence is operationally simple, makes use of inexpensive, readily available starting materials, and is characterized by short reaction times. All reactions in the sequence proceed at room temperature. Intricate reagent preparations are not required, and the use of concentrated organolithiums is avoided. Further, the procedure is compatible with a wide variety of functionality, facilitating the direct preparation of different oxygen derivatives without extraneous protection/deprotection steps.