Tetrahedron Letters, Vol.32, No.35, pp 4509-4512, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

PREPARATION OF RACEMIC AND CHIRAL ALKYL(1,3-BUTADIEN-2-YL)METHANOL DERIVATIVES UTILIZING 1-TRIMETHYLSILYL-2,3-BUTADIENE AS A DIENE SOURCE

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Summary: Ti(IV) chloride mediated reaction of 1-trimethylsilyl-2,3-butadiene with various aldehydes and acetals has been examined establishing an efficient method for the preparation of alkyl(1,3-butadien-2-yl)methanols. Application of this method to chiral acetals prepared from (*R*,*R*)-2,4-pentanediol led to chiral alkyl(1,3-butadien-2-yl)methanol derivatives with high optical purity which were alternatively synthesized by the Sharpless kinetic resolution of racemic alkyl(1,3-butadien-2-yl)methanols.

While allylsilanes have been widely utilized in organic synthesis,[1] their congeners 1-trimethylsilyl-2,3-butadienes have not received so much attention from a synthetic point of view[2] in spite of their ready availability[2b,3] and potential utility for the preparation of substituted 1,3-butadienes. Goré and co-workers[3a] reported a pioneer work on Lewis acid mediated addition of a 1-trimethylsilyl-2,3-butadiene derivative to an aldehyde. However, they have demonstrated the only one successful result and this reaction has not been fully examined thereafter. We now wish to report our results of Lewis acid mediated reaction of 1-trimethylsilyl-2,3-butadiene (**1**) with various aldehydes and acetals and also to report two methods for the preparation of chiral alkyl(1,3-butadien-2-yl)methanol derivatives.

Table 1 summarizes the Ti(IV) chloride mediated addition of **1** to a variety of aldehydes and their acetals.[4] It can be seen that this reaction has broad applicability even though in the cases of aldehydes the yields were moderate. It is worthy of note that benzaldehyde, geranial, and their acetals gave no successful results because of extremely high instability of the products. It is also noteworthy that in some cases of acetals (entries 5, 8, 13) the production of *rac*-**3** (R'=OMe) was diminished by the formation of **4** at –78 °C. This side reaction, however, could be suppressed by carrying out the reaction at –95 °C.

It is well documented[5] that the Lewis acid mediated addition of an allylsilane to a homochiral 2,4-pentanediol acetal proceeds with high diastereoselectivity. According to this methodology, we then examined the reaction of **1** with chiral acetals **5** in order to develop a new method for the preparation of chiral alkyl(1,3-butadien-2-yl)methanols **3** which can be expected as a new type of chiral building block.[6] Table 2 shows several examples of the preparation of chiral alcohols **3**. The typical

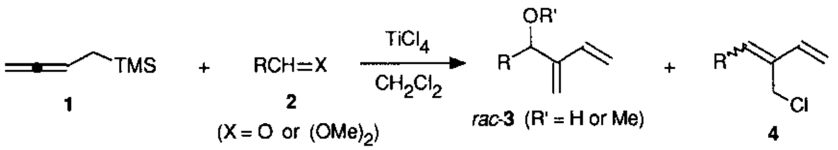
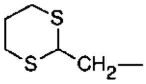
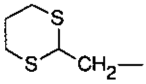
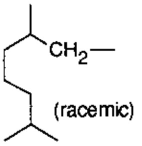
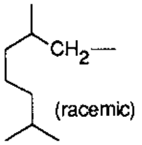
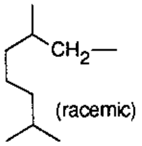


Table 1. Ti(IV) chloride mediated reaction[a] of 1-trimethylsilylmethyl-2,3-butadiene (**1**) with aldehydes and acetals

			conditions			
Entry	R	X	temp. (°C)	time (min.)	yield[b] of **3** (%)	yield[b] of **4** (%)
1	$ph(CH_2)_2$–	O	–95	45	57	
2	$ph(CH_2)_2$–	$(OMe)_2$	–78	30	97	
3	$phCH_2$–	O	–95	25	68	
4	$phCH_2$–	$(OMe)_2$	–95	30	97	
5	$phCH_2$–	$(OMe)_2$	–78	30	75	10
6	c-C_6H_{11}	O	–95	25	60	
7	c-C_6H_{11}	$(OMe)_2$	–95	30	70	
8	c-C_6H_{11}	$(OMe)_2$	–78	10	trace	72
9		O	–30	30	72	
10		$(OMe)_2$	–30	180	56[c]	
11		O	–95	40	47[d]	
12		$(OMe)_2$	–95	30	76[d]	
13		$(OMe)_2$	–78	20	none	65

a) the typical reaction was performed employing **1** (10 mmol), **2** (5 mmol), and $TiCl_4$ (6 mmol) in CH_2Cl_2 (30 ml). b) isolated yield. c) hydrolysis of the acetal moiety partially took place. d) 1:1 epimeric mixture.

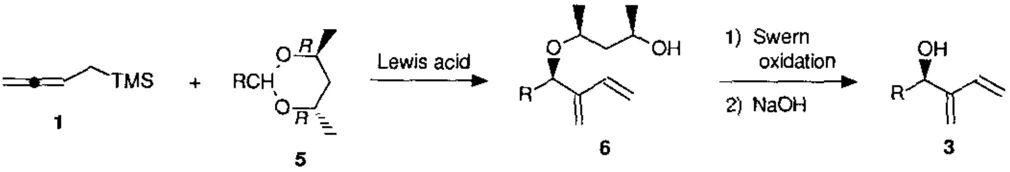
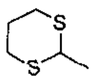


Table 2. Preparation of chiral alkyl(1,3-butadien-2-yl)methanols via chiral acetals

		cond.^{a} of addition		overall		
Entry	R	Lewis acid	temp (°C)	yield of 3 (%)	ee^c (%)	$[\alpha]_D^{29d}$
1	ph$(CH_2)_2$–	$TiCl_4$	–78	19^b	0	
2	ph$(CH_2)_2$–	$TiCl_4$	–98	63	77	+36.4°
3	ph$(CH_2)_2$–	$6TiCl_4 \cdot 5Ti(O^iPr)_4$	–78	80	94	+48.6°
4	phCH_2–	$6TiCl_4 \cdot 5Ti(O^iPr)_4$	–78	77	96	+42.6°
5	c-C_6H_{11}	$6TiCl_4 \cdot 5Ti(O^iPr)_4$	–78	74	88	–5.8°
6		$6TiCl_4 \cdot 5Ti(O^iPr)_4$	–78	no reaction		

a) $TiCl_4$ was added via a syringe in one portion, while a mixed titanium reagent was added via a motorized syringe over 12 h. b) the corresponding chloride 4 was formed as a major product in the initial reaction. c) determined by ^1H NMR (500 MHz) analysis of the corresponding *R*- and *S*-MTPA esters. d) measured in $CHCl_3$.

reaction of **1** with **5** was executed by adding a mixed titanium catalyst prepared from $Ti(OiPr)_4$ (40 mmol) and $TiCl_4$ (48 mmol) in methylene chloride (140 ml) to a solution of **5** (8 mmol) and **1** (64 mmol) in methylene chloride (40 ml) at –78 °C using a motorized syringe over 12 h. Removal of the chiral auxiliary *via* a two step sequence according to the established method[7] afforded **3** in high optical purity. It should be pointed out that the mixed titanium reagent is the catalyst of choice (entries 3, 4, 5). It turned out that this enantio-selective process proceeds in the same predictable manner as established in the reaction of allylsilanes.[5] The absolute configurations of the alcohols **3** were determined by mechanistic considerations and ^1H NMR (500 MHz) analysis of *R* and *S*-MTPA ester derivatives on the basis of the empirical rule.[8] Furthermore, kinetic resolution[9,10] of racemic alcohols *rac*-**3** (R'=H) under the Sharpless asymmetric epoxidation conditions led to valid determination of the absolute configurations. Table 3 summarizes the results of the kinetic resolution suggesting that this method also can be an alternative way to construct chiral alkyl(1,3-butadien-2-yl)methanols **3**.

In conclusion, we have demonstrated in the present work that 1-trimethylsilylmethyl-2,3-butadiene (**1**) can serve as an methylenated allylsilane with broad applicability in the Lewis acid mediated reaction.

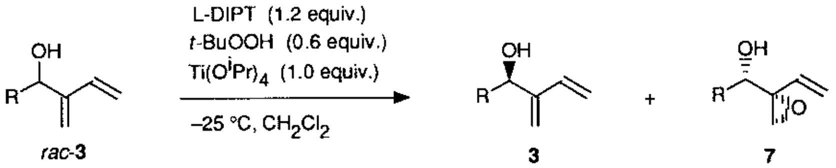


Table 3. Kinetic resolution of racemic alkyl(1,3-butadien-2-yl)methanols

Entry	R	time (h)	diene 3			epoxide 7		
			yield[a] (%)	ee[b] (%)	$[\alpha]_D^{29}$[c]	yield[a] (%)	ee[b] (%)	$[\alpha]_D^{29}$[c]
1	ph$(CH_2)_2$–	11	37	94	+48.2°	33	82	–45.2°
2	phCH_2–	14	35	97	+42.4°	33	83	–69.5°
3	phCH_2–	3	45	61	+26.5°	34	89	–74.0°
4	c-C_6H_{11}	15	34	87	–5.8°	36	75	–24.7°

a) isolated yield. b) determined by ^{1}H NMR (500 MHz) analysis of the corresponding *R*- and *S*-MTPA esters. c) measured in $CHCl_3$.

References and Notes

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2. There are a few examples showing the synthetic utility of 1-trimethylsilyl-2,3-butadienes: (a) Liu, C.; Wang, K. K. *J. Org. Chem.* **1986**, *51*, 4733. (b) Imai, T.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 4849. (c) Chaptal, N.; Colovray-Gotteland, V.; Grandjean, C.; Cazes, B.; Goré, J. *Tetrahedron Lett.* **1991**, *32*, 1795.
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10. To the best of our knowledge, the Sharpless kinetic resolution of this type of dienols is unprecedented, see: Johnson, R. A.; Sharpless, K. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 7, Chapter 3.2.

(Received in Japan 25 April 1991)