Pergamon

Tetrahedron Letters 39 (1998) 471–474

TETRAHEDRON
LETTERS

Lewis Acid Promoted Highly Diastereoselective Desymmetric Intramolecular Cyclization of Allylstannane with a Diketone

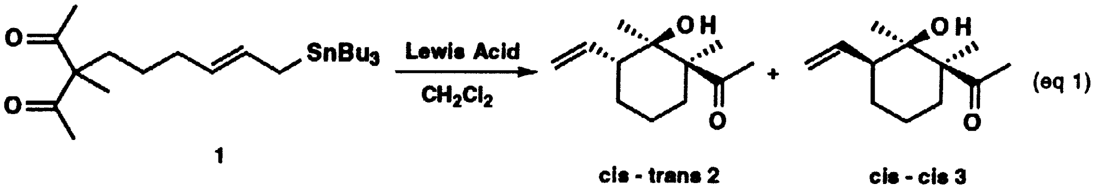
Takashi Shimada and Yoshinori Yamamoto*

Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-77, Japan

Received 23 September 1997; revised 3 November 1997; accepted 7 November 1997

Abstract: The Lewis acid mediated desymmetric intramolecular cyclization of prochiral allylstannyl diketone **1** gave a mixture of two diastereomers **2** and **3**. Highly diastereoselective synthesis of each diastereoisomer was accomplished by proper choice of the Lewis acids.

The condensation of allylstannane with aldehydes and ketones is one of the most important synthetic methods for C-C bond formation.[1] The utility of this reaction derives from the high yield, excellent regio- and stereoselectivity, and mild conditions under which the reaction can be performed. While a number of methods for inter- and intramolecular condensation with aldehydes and ketones have been studied during last decade,[2] to the best of our knowledge, there is no report on the desymmetric condensation of allylstannanes with ketones.[3] We wish to report a highly diastereoselective desymmetric intramolecular cyclization of allylstannane with a 1,3-diketone; the Lewis acid mediated desymmetric intramolecular cyclization of prochiral allylstannyl diketone **1** gave a mixture of two diastereomers **2** and **3**, and highly diastereoselective synthesis of each diastereoisomer was accomplished by proper choice of the Lewis acids (eq 1). The use of $TiCl_4$ and $TiCl_2(OiPr)_2$ afforded *cis-trans* **2** with high diastereoselectivity, while the use of $InCl_3$, $SnCl_4$, and $Yb(OiPr)_3$ gave *cis-cis* **3** exclusively or predominantly.



The preparation of **1** is shown in Scheme 1. The reaction of 1,4-butanediol **4** with TBDMSCl/imidazole in DMF gave the monosilylated alcohol **5** in 86% yield. Swern oxidation of **5** followed by the treatment with methyl (triphenylphosphoranylidene)acetate gave the corresponding α,β-unsaturated ester **6** in 70% yield. The ester group of **6** was reduced by DIBAL, and the resulting alcohol was acetylated with acetic anhydride in pyridine. Subsequent treatment with acetic acid in $THF-H_2O$ gave **7** in 94% yield. The bromination of **7** was

0040-4039/98/$19.00 © 1997 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(97)10579-2

Scheme 1

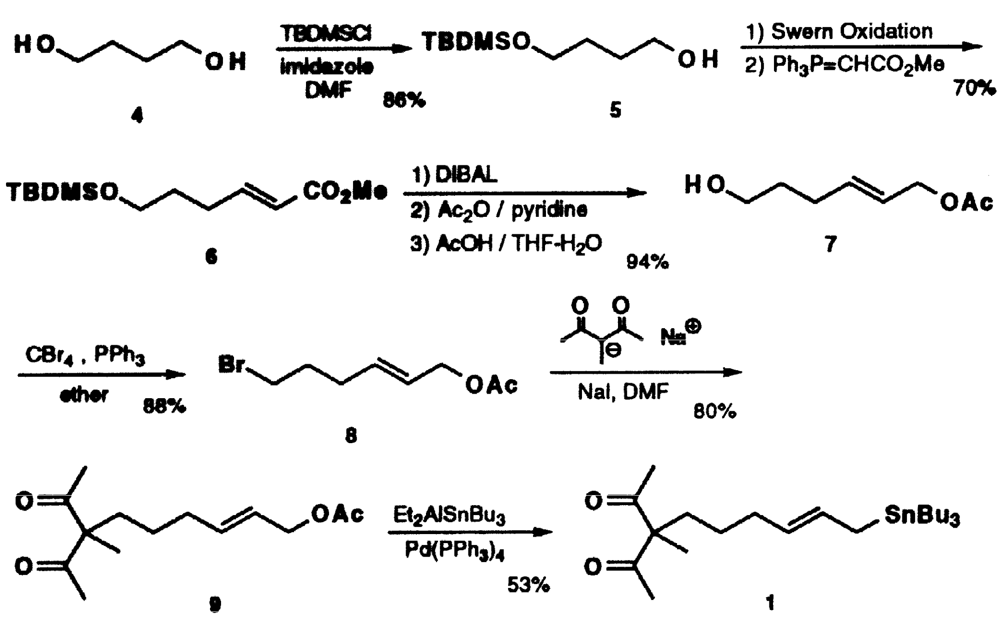


Table 1. Cyclization of 1[a]

entry	Lewis Acid (equiv)	temp/°C	time/h	ratio (2 : 3)[b]	yield/%[c]
1	$TiCl_4$ (1.0)	-78	1	92 : 8	83 (87[e])
2	$TiCl_2(OiPr)_2$ (1.5)	-35	12	95 : 5	67[d]
3	$AlCl_3$ (1.0)	-78	2	73 : 27	61
4	$EtAlCl_2$ (2.0)	-10	2	77 : 23	66
5	Et_2AlCl (2.0)	rt	50	-	0[f]
6	$SnCl_4$ (1.0)	-78	1	1 : >99	62 (66[e])
7	$ZnBr_2$ (1.0)	rt	96	21 : 79	60
8	$InCl_3$ (1.0)	-20	13	3 : 97	55
9	$Yb(OiPr)_3$ (1.0)	rt	1.3	8 : 92	76
10	$BF_3{\bullet}OEt_2$ (2.0)	-10	2	32 : 68	29[d]

[a] The reactions were carried out with 0.1M substrate in CH_2Cl_2 under the conditions indicated in the table, and quenched with saturated aqueous $NaHCO_3$ solution at the reaction temperature. [b] Ratios were determined by ^{1}H-NMR. [c] Yields were determined by ^{1}H-NMR (*p*-xylene was used as an internal standard). [d] The reduced product 10 was obtained as a by-product (entry 2: 26%, entry 10: 10%, see reference 6). [e] Overall yield of isolated mixture of diastereomers. [f] No reaction took place.

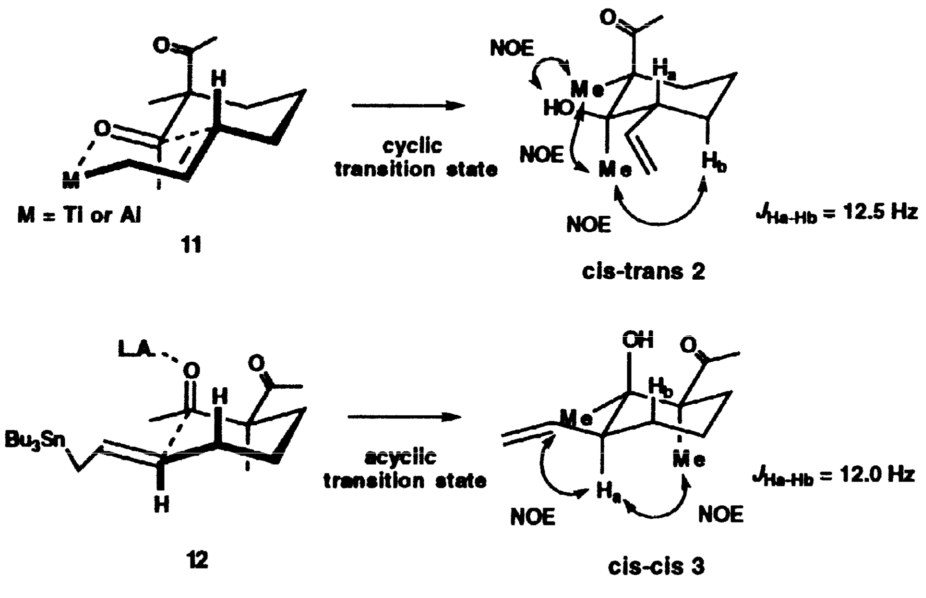
performed by CBr_4/PPh_3 to give **8** in 88% yield. Alkylation of **8** with 3-methyl-2,4-pentanedione/NaH in DMF produced **9** in 80% yield. The palladium catalyzed reaction of **9** with $Et_2AlSnBu_3$[4] gave **1** in 53% yield.

The results of the Lewis acid mediated cyclization of **1** are summarized in Table 1.[5] In all cases, only two diastereoisomers, *cis-trans* **2** and *cis-cis* **3**, were obtained among four possible stereoisomeric cyclization products. The use of $TiCl_4$ gave a 92:8 mixture of *cis-trans* **2** and *cis-cis* **3** in 87% isolated yield (entry 1).

Although the diastereoselectivity of **2** increased up to 95:5 in the presence of $TiCl_2(OiPr)_2$, the chemical yield decreased to 67% and the reduced product **10** was obtained in 26% yield (entry 2). The reactions mediated by $AlCl_3$ and $EtAlCl_2$ also afforded *cis-trans* isomer **2** as a major product, but in both cases, the chemical yield and the diastereoselectivity were lower than those via the $TiCl_4$ mediated reaction (entries 3 and 4). The cyclization of **1** did not proceed in the presence of a weaker Lewis acid such as Et_2AlCl (entry 5). Interestingly, the reactions mediated by $ZnBr_2$ (entry 7), $InCl_3$ (entry 8), and $Yb(OiPr)_3$ (entry 9) afforded *cis-cis* **3** as a major product in moderate yields. The use of $SnCl_4$ gave only *cis-cis* isomer **3** in 66% isolated yield (entry 6). The $BF_3{\bullet}OEt_2$ mediated cyclization of **1** gave a mixture of **2** and **3** in low diastereoselectivity and low chemical yield (entry 10).

The stereostructures of the two products were assigned by ^1H-NMR decoupling and NOE experiments. The coupling constants between Ha and Hb of **2** and **3** were J = 12.5 Hz and J = 12.0 Hz, respectively, indicating that the stereochemical relation between Ha and Hb were axial-axial in both compounds. Therefore, the vinyl substituent of both isomers could be assigned to be equatorial. In *cis-trans* isomer **2**, NOE effects were observed between a hydroxyl proton and the neighboring methyl group, between Hb and the methyl group attached to the carbon of COH, and between these two methyl groups, indicating that the methyl group at COH was in the 1,3-diaxial position from Hb. It is clear that the stereochemical relation between the vinyl and hydroxyl group is trans, and that of hydroxyl and acetyl group is cis. In *cis-cis* isomer **3**, NOE effects were observed between Ha and the neighboring methyl group, and between Ha and the methyl group attached to the carbon of $C(CO)CH_3$. It is clear that the stereochemical relation between the vinyl and hydroxyl group is cis, and that of hydroxyl and acetyl group is cis.

The mechanism for the present dramatic diastereoselectivity difference between the $TiCl_4$ mediated and $SnCl_4$ (also $InCl_3$ and $Yb(OiPr)_3$) mediated reactions has not been unambiguously established. A possible explanation is as follows. When $TiCl_4$ was used as a Lewis acid, the transmetalation between stannane of **1** and $TiCl_4$ would take place very rapidly and the resulting allyltitanium compound would undergo cyclization via a cyclic transition state **11**. Perhaps the ethylaluminium dichloride mediated reaction would proceed also via **11**. On the other hand, the transmetalation reaction between stannane of **1** and $SnCl_4$ ($InCl_3$ and $Yb(OiPr)_3$) would be slower, and thus the cyclization would take place via an acyclic transition state **12**, in which the Lewis acid would coordinate to carbonyl oxygen and facilitate the cyclization.



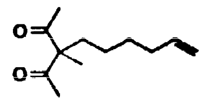
Irrespective of the precise mechanism, we are now in a position to carry out desymmetric intramolecular cyclization of prochiral allylstannyl diketone **1** by proper choice of Lewis acids, and to control the stereochemistries of three contiguous chiral centers of **2** and **3**. Application of this methodology to the asymmetric desymmetric cyclization is under investigation.

References

1. For reviews see: (a) Roush, W. R. In *Comprehensive Organic Synthesis*, Vol. 2, Trost, ed., *Pergamon Press*: Oxford, **1991**, 1. (b) Fleming, I. *ibid.* 563. (c) Marshall, J. A. *Chemtracts*, **1992**, *5*, 75. (d) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (e) Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395.
2. (a) Yamamoto, Y.; Komatsu, T,; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1983**, 191. (b) Krämer, T.; Schwark, J. R.; Hoppe, D. *Tetrahedron Lett.* **1989**, *30*, 7037. (c) Takuwa, A.; Nishigaichi, Y.; Yamashita, K.; Iwamoto, H. *Chem. Lett.* **1990**, 1761. (d) Zhou, J. Y.; Chen, Z. G.; Wu, S. H. *J. Chem. Soc., Chem. Commun.* **1994**, 2783. (e) Denmark, S. E.; Hosoi, S. *J. Org. Chem.* **1994**, *59*, 5133. (f) Keck, G. E.; Dougherty, S. M.; Savin, K. A. *J. Am. Chem. Soc.* **1995**, *117*, 6210. (g) Li, C. J.; Lu, Y. Q. *Tetrahedron Lett.* **1995**, *36*, 2721. (h) Yasuda, M.; Sugawa, Y.; Yamamoto, A.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1996**, *37*, 5951. (i) Kadota, I.; Kawada, M.; Saya, S.; Yamamoto, Y. *Tetrahedron Lett.* **1996**, *37*, 2109, and references cited therein.
3. Intramolecular cyclization of allylsilane with diketones: Schinzer, D.; Panke, G. *J. Org. Chem.* **1996**, *61*, 4496.
4. Trost, B. M.; Herndon, J. W. *J. Am. Chem. Soc.* **1984**, *106*, 6835.
5. Typical procedure: To a stirred solution of **1** (48.5 mg, 0.1mmol) in 1 mL of dry CH_2Cl_2 under Ar at -78 °C was added $TiCl_4$ (1.0 M solution in CH_2Cl_2, 0.1 mL, 0.1 mmol), and the mixture was stirred for 1 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution, extracted with ether, washed with brine, and dried over $MgSO_4$. The solvents were removed in vacuo, and the residue was purified by silica gel column chromatography. The diastereomer ratio was determined by ^{1}H-NMR; a 92:8 mixture of **2** and **3** was obtained in 87% (17.1 mg).

   2: ^{1}H-NMR (500 MH$_Z$, $CDCl_3$) δ 6.13 (ddd, J = 17.5, 10.5, 6.0 Hz, 1H), 5.09 (ddd, J = 10.5, 2.0, 2.0 Hz, 1H), 5.00 (ddd, J = 17.5, 2.0, 2.0 Hz, 1H), 4.55 (q, J = 1.2 Hz, 1H), 2.52 (ddd, J = 6.0, 6.0, 12.5 Hz, 1H), 2.23 (s, 3H), 2.07 (m, 1H), 1.77-1.70 (m, 2H), 1.57 (ddd, J = 3.8, 14.5, 14.5 Hz, 1H), 1.36 (dddd, J = 4.2, 12.0, 12.5, 12.5 Hz, 1H), 1.22 (s, 3H), 1.20 (m, 1H), 1.03 (d, J = 1.2 Hz, 3H); HRMS calcd for $C_{12}H_{20}O_2$ (196.1463), found 196.1473.

   3: ^{1}H-NMR (500 MH$_Z$, $CDCl_3$) δ 5.92 (ddd, J = 17.0, 10.0, 8.5 Hz, 1H), 5.03 (ddd, J = 10.0, 2.2, 0.4 Hz, 1H), 4.99 (ddd, J = 17.0, 2.2, 0.8 Hz, 1H), 4.32 (s, 1H), 2.20 (s, 3H), 2.15 (ddd, J = 4.0, 8.5, 12.0 Hz, 1H), 2.05 (ddd, J = 4.5, 13.0, 13.0, 1H), 1.75 (dddd, J = 4.5, 12.0, 12.5, 12.5 Hz, 1H), 1.65-1.58 (m, 2H), 1.45-1.38 (m, 2H), 1.30 (s, 3H), 1.13 (s, 3H); HRMS calcd for $C_{12}H_{20}O_2$ (196.1463), found 196.1460.
6. Destannylated diketone **10** was obtained as a by-product.


10