Tetrahedron Letters,Vol.25,No.45,pp 5151-5154,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

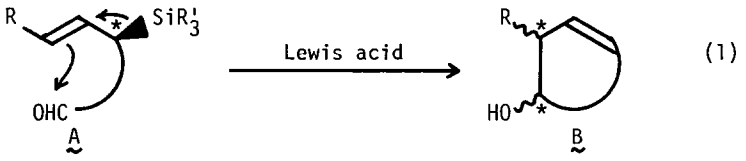
ASYMMETRIC ALLYLSILANE-MEDIATED CARBOCYCLIZATION: A HIGHLY ENANTIOSPECIFIC SYNTHESIS OF (1S, 2S)-(+)-2-METHYL-3-CYCLOPENTEN-1-OL

Kōichi Mikami, Toshihiko Maeda, Naoyuki Kishi, and Takeshi Nakai*

Department of Chemical Technology, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

SUMMARY: An enantiospecific synthesis of the title compound is described which involves the $TiCl_4$-promoted cyclization of the chiral allylic silane having formyl group, which was obtained via the Claisen rearrangement of (R, E)-1-trimethylsilyl-1-buten-3-ol.

In view of the well-defined stereochemistry of the S_E2' reaction of chiral allylic silanes with aldehydes,[1] the *intramolecular* version generalized by eq. 1 is conceptually feasible, wherein the silyl-chirality could specifically be transmitted to the two newly created chiral centers. Thus, this type of asymmetric endo-cyclization, if successful, would result in the direct formation of cycloalkenols B with both a high diastereo- and enantioselectivity.

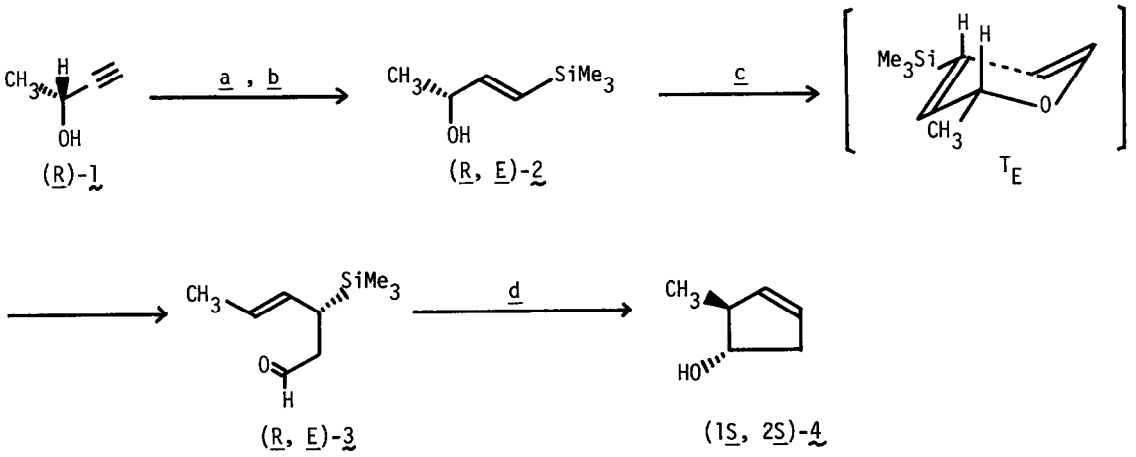


(1)

However, such strategy has never been explored, while its *racemic* version leading to the cyclopentenols has been precedented.[2] The major problem confronting the implementation of this strategy is, of course, associated with the difficulty encountered in the preparation of optically-active allylic silanes having formyl group.[3] Herein we wish to report the first success in this strategy within the context of a highly enantiospecific synthesis of (1S, 2S)-(+)-2-methyl-3-cyclopenten-1-ol,[4] an important intermediate for natural product syntheses.[4,5] The key to the success is the relatively easy availability of the stereochemically-defined allylic silane having formyl group via the Claisen rearrangement of an enantiomerically-enriched γ-(trimethylsilyl)allylic alcohol.

The overall transformation is depicted in Scheme I. The requisite chiral alcohol, (R, E)-2 (100% E by GLC assay),[6] was prepared in 73% yield from the optically-resolved[7] alcohol (R)-(+)-1 (100% e.e.) via the silylation followed by the highly (E)-selective hydride reduction of the triple bond.[8] The enol ether Claisen rearrangement[9] afforded 71% yield of a geometric mixture of the allylic silane 3 with moderate (E)-selectivity (E/Z = 83 : 17).[10] Although no attempt was made to assign the absolute configuration of 3, the configuration of (E)-3 might reasonably be assigned to (R) on the basis of the well-established chair-like transition state (T_E) for the

Scheme I

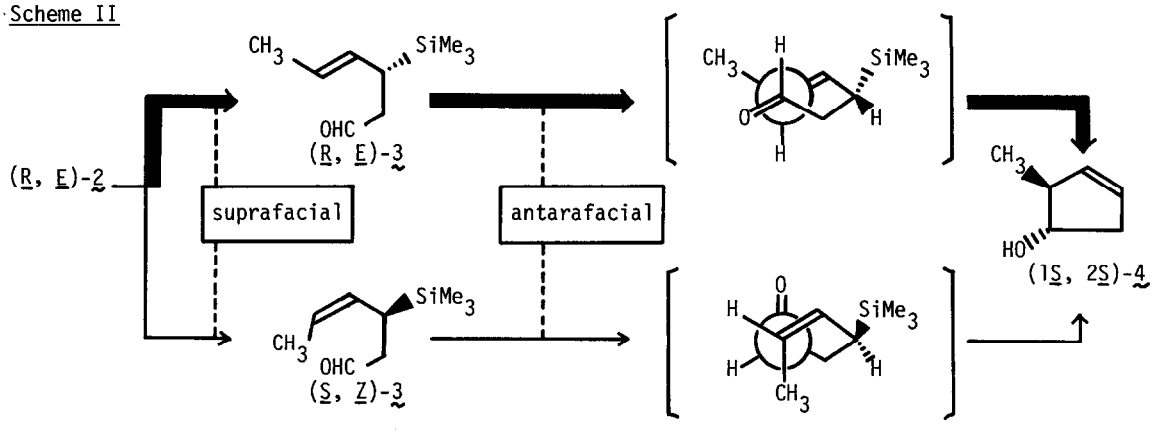


(a) $EtMgBr/Me_3SiCl$, THF; (b) $NaAlH(OCH_2CH_2OCH_3)_2$, toluene-Et_2O; (c) CH_2=CHOEt (excess)/$Hg(OAc)_2$, 100°C; (d) $TiCl_4$ (1.1 equiv), CH_2Cl_2, -78°C.

Claisen process.[11] The stereoisomeric mixture of 3 was then subjected to the cyclization process in the presence of titanium(IV) chloride[12] to provide seemingly quantitative[13] yield of the cyclopentenol 4 with a high diastereopurity (>98% trans by NMR assay).[14] Unfortunately, however, the isolated yield after preparative TLC was 59% because of its great instability.[4] The absolute configuration of (+)-trans-4 thus obtained was assigned to (1S, 2S) based on the reported configuration of (+)-(1S, 2S).[4] The enantiomeric purity was >98% e.e. as determined by NMR (300 MHz) comparison of the (-)-α-methoxy-α-trifluoromethylphenylacetate of 4 with the racemic counterpart independently prepared.

The most striking feature in the asymmetric synthesis outlined here is that the enantiomeric purity of the final product (4) is essentially the same as that of the starting alcohol (1). This means that the chirality transfer proceeds with nearly 100% efficiency throughout the Claisen-cyclization sequence, although the Claisen process provides only 83% of (E)-selectivity. This somewhat surprising outcome is reasonably rationalized in terms of a combination of the completely *suprafacial* transfer of chirality in the Claisen process with the completely *antarafacial* transfer in the cyclization process (Scheme II). In other words, the (R)-configuration in 2 is suprafacially transmitted to yield (R, E)- and (S, Z)-3 as described above, both of which undergo the diastereoselective S_E2'-type cyclization exclusively via the anti-attack by the formyl group as previously reported for the *intermolecular* versions,[1] ultimately leading to trans-4 with the identical configuration (1S, 2S).

Scheme II



In summary, this work convincingly demonstrates that the silicon-mediated asymmetric Claisen-cyclization sequence provides a new, efficient method for the enantiospecific synthesis of trans-2-alkyl-3-cyclopenten-1-ols. While only one example is presented here, the wide applicability established for both the Claisen process and the allylsilane chemistry, coupled with the simplicity of the procedure, makes the present strategy potentially useful for asymmetric carbocyclization. Further synthetic applications of our strategy are in progress.

Acknowledgment. Financial support of this research was made in part by the Kurata Foundation. We are indebted to Mr. K. Kushida of Analytica Corp. for the measurement of 300 MHz NMR spectra.

References and Notes

1. T. Hayashi, M. Konishi, and M. Kumada, *J. Am. Chem. Soc.*, 104, 4963 (1982); T. Hayashi, M. Konishi, and M. Kumada, *J. Org. Chem.*, 48, 281 (1983); cf. I. Fleming and N. K. Terrett, *Pure Appl. Chem.*, 55, 1707 (1983).

2. I. Kuwajima, T. Tanaka, and K. Atsumi, *Chem. Lett.*, 1979, 779. For the exo-cyclization of racemic allylic silanes having carbonyl group, see: T. K. Sarker and N. H. Andersen, *Tetrahedron Lett.*, 1978, 3513; A. Itoh, K. Oshima, and H. Nozaki, *ibid.*, 1979, 1783; B. M. Trost and J. E. Vincent, *J. Am. Chem. Soc.*, 102, 5683 (1980).

3. For preparation of optically-active allylic silanes without functionality, see T. Hayashi, M. Konishi, H. Ito, and M. Kumada, *J. Am. Chem. Soc.*, 104, 4962 (1982).

4. For the synthesis (via asymmetric hydroboration) and the stereochemical assignment, see: J. J. Partridge, N. K. Chadha, and M. R. Uskokovič, *J. Am. Chem. Soc.*, 95, 532 (1973).

5. G. Stork, I. Peterson, and F. K. C. Lee, *J. Am. Chem. Soc.*, 104, 4686 (1982).

6. Bp 80-82 °C/26 mmHg; $[\alpha]_D^{18}$ -5.23°(c 1.01, $CHCl_3$)(>98% e.e. as determined by NMR assay using a chiral shift reagent).

7. R. Weidman, A. Schoofs, and A. Horeau, *Bull. Soc. Chim. Fr.*, 1976, 645; L.-I. Olsson and A. Claeson, *Acta Chem. Scand.*, B31, 614 (1973).

8. S. E. Denmark and T. K. Jones, *J. Org. Chem.*, 47, 4595 (1982).

9. G. Saucy and R. Marbet, *Helv. Chim. Acta*, 50, 1158, 2091 (1967).

10. Bp 84-86 °C/16 mmHg; $[\alpha]_D^{15}$ +30.3°(c 1.03, $CHCl_3$). The geometrical purity was determined by GLC analysis (PEG 20M, 120 °C).

11. Likewise, (Z)-3 might be assigned to (S). Reviews on stereochemistry of the Claisen process: F. E. Ziegler, *Acc. Chem. Res.*, 10, 227 (1977); T. Nakai, K. Mikami, and N. Sayo, *J. Synth. Org. Chem., Jpn.*, 41, 100 (1983).

12. Use of BF_3OEt_2 as the promoter that gives the good result in the Kuwajima's cyclization (ref 2) led to a complex mixture. Use of $TfOSiMe_3$ provided a lower yield (27%).

13. No spots due to organic compounds other than trans-4 were observed on TLC of the reaction mixture.

14. NMR($CDCl_3$): δ 0.93 (d, J=7.8 Hz, CH_3), 3.92 (d,t, J=6.6 and 3.3 Hz, CH-OH) and 5.56 (s, olefinic protons); no signals due to the cis-isomer were detected. For the NMR of cis-4, see ref 4.

(Received in Japan 19 July 1984)