Tetrahedron Letters,Vol.25,No.5,pp 565-568,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

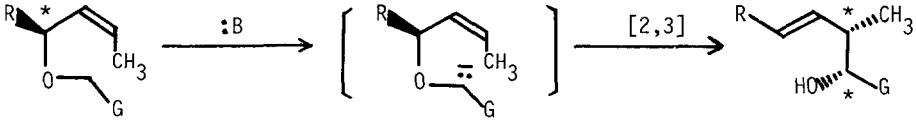
ACYCLIC STEREOCONTROL VIA ASYMMETRIC [2,3]-WITTIG REARRANGEMENT WITH HIGH ENANTIO- AND ERYTHRO-SELECTIVITY AND ITS USE IN THE CHIRAL SYNTHESIS OF INSECT PHEROMONES

Noboru SAYO, Ken-ichi AZUMA, Kōichi MIKAMI, and Takeshi NAKAI*

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

SUMMARY: Such an asymmetric [2,3]-Wittig variant that is both highly enantio- and erythro-selective is described within the context of the chiral synthesis of the insect pheromones, (3S, 4S)-4-methyl-3- heptanol and (S)-4-methyl-3-heptanone.

The control of both diastereo- and enantioselection during carbon-carbon bond formations is of great importance in synthesis. Recently several asymmetric aldol-type reactions have reached impressive levels of success.[1] As part of a program designed to develop the [2,3]-Wittig sigmatropic rearrangement into a new, basic strategy for acyclic stereocontrol,[2] we have now investigated the feasibility of an asymmetric version as illustrated by eq 1, where the substrate chirality could specifically be transmitted to the two newly created chiral centers.



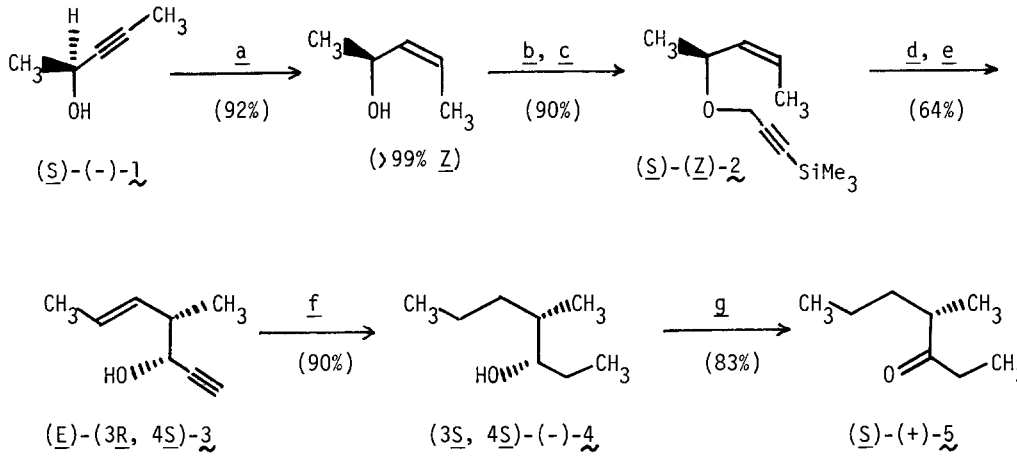
(1)

In order to take complete advantage of the stereochemical features inherent in this strategy, the proper choice of the substituent G is essential since the steric factor of G exerts a great influence in dictating the level of diastereoselection.[3] Herein we report for the first time such a [2,3]-Wittig variant of an enantiomerically-enriched allylic ether that is both highly enantio- and erythro-selective, and illustrate its potential through the chiral synthesis of insect pheromones.

In the context of this project, we selected trimethylsilylethynyl ($C\equiv C\text{-}SiMe_3$) as the key G based on our previous observation that the use of this group provides an exceptionally high erythro-selectivity in the [2,3]-Wittig process of the achiral (Z)-crotyl ether (R=H).[3c]

Thus, we examined the diastereo- and enantioselection in the [2,3]-Wittig rearrangement of the optically-active propargyl ether (S)-(Z)-2 within the context of the chiral synthesis of (3S, 4S)-(-)-4-methyl-3-heptanol (4), an aggregation pheromone of the smaller European elm bark beetle (*Scolytus multistriatus*),[4] and (S)-(+)-4-methyl-3-heptanone (5), an alarm pheromone of the leaf-cutting ant (*Atta texana*)[5] (Scheme I).

Scheme I



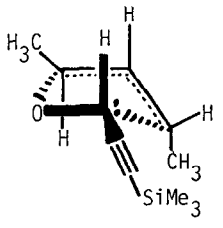
(S)-(-)-1 (S)-(Z)-2 (E)-(3R, 4S)-3 (3S, 4S)-(-)-4 (S)-(+)-5

(a) H_2, Lindlar cat., pentane; (b) HC≡C-CH_2Br, n-Bu_4NI (cat.), 75% aqueous NaOH; (c) EtMgBr, Me_3SiCl, THF; (d) n-BuLi, THF, -85°C, 6 h; (e) CsF (cat.), aqueous MeOH, 50°C; (f) H_2, Raney Ni cat.; (g) CrO_3, H_2SO_4

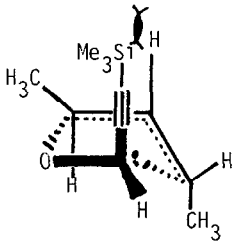
The requisite chiral ether, (S)-(Z)-2 (>99% Z), was prepared from the optically-resolved[6] propargylic alcohol (S)-1 with 95-98% ee[7] ($[\alpha]_D^{15}$ -47.6° (c 1.00, dioxane)) via the conventional sequence. The carbanion rearrangement followed by protodesilylation afforded the alcohol 3 in a high geometric (>99% E) and diastereomeric purity (>99% erythro).[8] Hydrogenation of 3 furnished the desired pheromone (3S, 4S)-4[9] with 98% ee ($[\alpha]_D^{18}$ -21.4° (c 1.02, hexane)), as judged from the highest $[\alpha]_D$-value (-21.7°) reported for this pheromone.[4c] Jones oxidation of 4 provided the other pheromone (S)-5[9] with 91% ee ($[\alpha]_D^{19}$ +20.2° (c 1.09, hexane)), as compared to the literature value (+22.1°).

The most notable feature in the chiral synthesis outlined here is that the enantiomeric purity of the final product is essentially the same as the enantiomeric purity of the starting

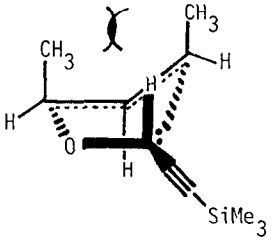
propargylic alcohol. Thus, the substrate chirality is specifically transmitted to the two new chiral centers with nearly 100% efficiency by virtue of the combination of the high (E)- and erythro-selectivity with complete transfer (suprafacial) of chirality along the allylic array. On the basis of our own transition-state model,[10] this high stereospecificity can be visualized by the transition state A depicted below; the conformation A is sterically less constrained than any other possible conformations which place the ethynyl group at the pseudo-axial position and/or the methyl group at the endo-orientation, since the conformations B and C, for instance, suffer the pseudo-1,3-diaxial repulsion as indicated in the formula.



A → (E)-(3R, 4S)-3



B → (E)-(3S, 4S)-3



C → (Z)-(3R, 4R)-3

In summary, this work convincingly demonstrates that the [2,3]-Wittig rearrangement of an enantiomerically-enriched allylic ether, when properly designed, provides an efficient method (starting from chiral propargylic alcohols) for the highly enantiospecific synthesis of erythro β-methyl homoallylic alcohols. The simplicity of the procedure, coupled with the relatively easy availability of chiral propargylic alcohols,[11] makes the present strategy potentially useful for acyclic stereocontrol. We are now investigating different sets of asymmetric [2,3]-Wittig variants and their applications in natural product synthesis.

Acknowledgment. This research was generously supported in part by the Kurata Foundation and the Grant-in-Aid for Special Project Research (No. 57218008) from the Ministry of Education, Science and Culture, Japan.

References and Notes

1. Recent reviews: D. A. Evans, J. V. Nelsen, and T. R. Taber, *Top. Stereochem.*, 13, 1 (1982); S. Masamune, "Organic Synthesis: Today and Tomorrow", B. M. Trost and C. R. Huchinson, Ed., Pergamon, Oxford, 1981, p.197. For more recent examples, see: D. S. Matteson and K. M. Sadhu, *J. Am. Chem. Soc.*, 105, 2077 (1983); M. M. Midland and S. B. Preston, *ibid.*, 104, 2330 (1982); T. Hayashi, M. Konishi, and M. Kumada, *ibid.*, 104, 4963 (1982); N. Iwasawa and T. Mukaiyama, *Chem. Lett.*, 1441 (1982), and references cited therein.

2. For a preceding paper on this series, see: K. Mikami, K. Fujimoto, and T. Nakai, *Tetrahedron Lett.*, 24, 513 (1983). For a review on acyclic stereocontrol via [2,3]-sigmatropic rearrangements, see: T. Nakai, K. Mikami, and N. Sayo, *J. Synth. Org. Chem., Jpn.*, 41, 100 (1983).

3. (a) T. Nakai, K. Mikami, S. Taya, and Y. Fujita, *J. Am. Chem. Soc.*, 103, 6492 (1981); (b) K. Mikami, Y. Kimura, N. Kishi, and T. Nakai, *J. Org. Chem.*, 48, 279 (1983); (c) K. Mikami, K. Azuma, and T. Nakai, *Chem. Lett.*, 1379 (1983).

4. (a) G. T. Pearce, W. E. Gore, R. M. Silverstein, J. W. Peacock, R. A. Cuthbert, G. N. Lanier, and J. B. Simeone, *J. Chem. Ecol.*, 1, 115 (1975); (b) K. Mori, *Tetrahedron*, 33, 289 (1977); (c) K. Mori and H. Iwasawa, *ibid.*, 36, 2209 (1980); (d) J.-R. Pougny and P. Sinay, *J. Chem. Res. (M)*, 186 (1982).

5. (a) J. C. Moser, R. G. Brownlee, and R. M. Silverstein, *J. Insect. Physiol.*, 14, 529 (1968); (b) R. G. Riley, R. M. Silverstein, and J. C. Moser, *Science*, 183, 760 (1974); (c) R. G. Riley and R. M. Silverstein, *Tetrahedron*, 30, 1171 (1974).

6. K. Koosha, J. Berlan, M.-L. Capmau, and W. Chodkiewicz, *Bull. Soc. Chim. Fr.*, 1291 (1975).

7. Since the maximum rotation value for 1 is not available, we determined the optical purity by NMR assay using a solution of (+)-Eu(DPPM)$_3$ in $CF_2ClCFCl_2$ as the chiral shift reagent which was kindly provided by Professor N. Ishikawa of this Institute: H. Kawa, F. Yamaguchi, and N. Ishikawa, *Chem. Lett.*, 153 (1982).

8. Bp 60-65°C/10 mmHg; IR (film) 3400 and 980 cm^{-1}. The (E)-geometry was confirmed by ^{13}C-NMR spectrum which shows only one signal (δ 18.03 ppm) due to the methyl bonded to the olefinic carbon. The erythro-configuration was verified by GLC comparison (PEG 20M, 150°C) with an authentic threo-rich mixture: t_R 19.4 min (erythro) and 21.8 min (threo).

9. The physical properties (bp, IR and NMR) of this compound are in agreement with the literature values.

10. For a detailed discussion of the transition-state geometry for [2,3]-Wittig rearrangement, see: ref 3b.

11. Although we adopted the resolution method for obtaining (S)-1 in this work, it should be noted here that this type of chiral alcohols are now obtainable in a particularly high enantiomeric excess via asymmetric reduction of the corresponding α,β-ynone. For efficient reducing reagents, see: R. S. Brinkmeyer and V. M. Kapoor, *J. Am. Chem. Soc.*, 99, 8339 (1977); M. M. Midland, D. C. McDowell, R. L. Hatch, and A. Tramontano, *ibid.*, 102, 867 (1980); R. Noyori, *Pure Appl. Chem.*, 53, 2315 (1981); W. S. Johnson, R. Elliott, and J. D. Elliott, *J. Am. Chem. Soc.*, 105, 2904 (1983).

(Received in Japan 2 November 1983)