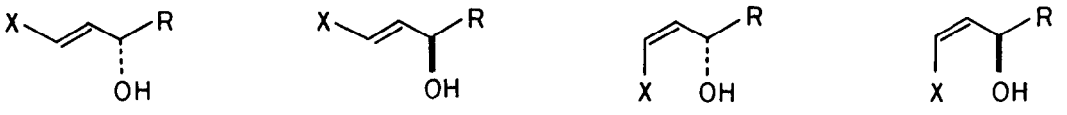
Tetrahedron Letters,Vol.28,No.18,pp 2033-2036,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

A HIGHLY EFFICIENT SYNTHESIS OF γ-HALO ALLYLIC ALCOHOLS AND PROPARGYLIC ALCOHOLS WITH HIGH OPTICAL PURITY. PRACTICAL METHOD FOR SYNTHESIS OF THE PROSTAGLANDIN ω-CHAIN

Sentaro Okamoto, Toshiyuki Shimazaki, Yuichi Kobayashi, and Fumie Sato*
Department of Chemical Engineering, Tokyo Institute of Technology
Meguro, Tokyo 152, Japan

Summary: Kinetic resolution of γ-trimethylsilyl allylic alcohols 5 by the Sharpless process combined with the reactivity of epoxysilyl or vinylsilyl compounds affords a highly efficient method for preparation of optically pure γ-halo secondary allylic alcohols of type 1-4 and propargylic alcohols 14, thus providing a practical route to the prostaglandin ω-chain.

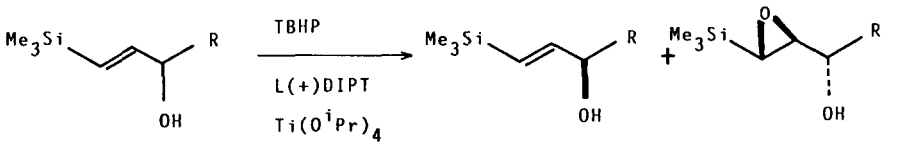
Enantioselective preparation of secondary allylic alcohols having halo substituent at γ-position with E- or Z-configuration, 1-4, has been attracted much interest in recent years especially in relation to the synthesis of metabolites of arachidonic acid such as cyclooxygenase products (prostaglandin (PG))[1] and lipoxygenase products,[2] and also their analogs.



1 2 3 4

X : halogen

Recently we have found that the kinetic resolution of γ-trimethylsilyl allylic alcohols by the Sharpless asymmetric epoxidation reaction[3] proceeds with very large variation in rate for the two enantiomers in comparison with usual secondary allylic alcohols to afford both the epoxy alcohols and the allylic alcohols with more than 99% optical purity, simultaneously (eq 1).[4]



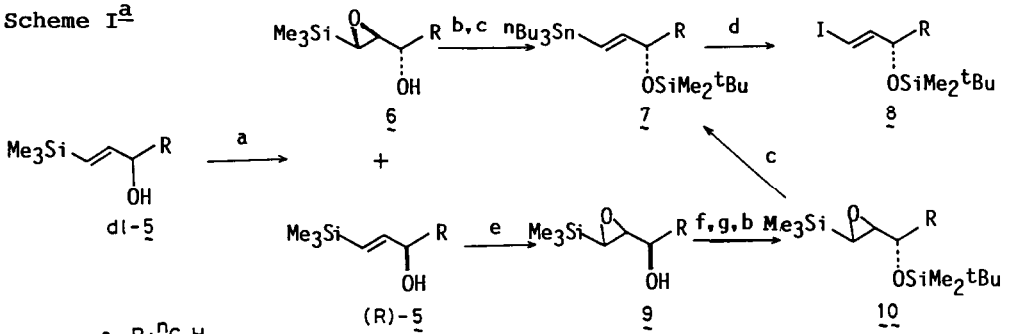
(1)

Since both epoxysilanes and vinylsilanes are useful precursors of vinyl halides,[5] the reaction of eq 1 promises to provide a convenient and general method for preparation of 1-4, and this communication demonstrates the successful realization of such an approach.

The derivative of the alcohol of type 1, 8a, used for the synthesis of

naturally occurring PG such as PGE_1 or PGE_2 in the conjugate addition approach,[1,6] lipoxin A,[7] and Di-HETE,[8] has been prepared as shown in Scheme I. After the kinetic resolution of 5a, the resulting epoxy alcohol 6a (>99% ee) and the allylic alcohol (R)-5a (>99% ee) were separated by column chromatography on silica gel. Reaction of the silyl ether of 6a with $^{n}Bu_3SnLi$ prepared in situ from $^{n}Bu_3SnH$ and LDA in THF[9] resulted in regiospecific ring opening and successive Peterson olefination reaction[10] to afford 7a as the sole product in 93% yield. Although the alcohol 7a can be used as the PGE_1 or PGE_2 ω-chain in itself,[11] it was converted quantitatively into 8a, $[\alpha]_D^{23}$ -38.8° (c 0.985, MeOH), (lit.[12] $[\alpha]_D^{23}$ -37.5° (c 0.97, MeOH)), by treatment with I_2 in ether.[13] The optical purity of 8a was estimated to be more than 99% on the basis of $[\alpha]_D$ value and also ^1H NMR analysis of the corresponding MTPA ester.[14] The allylic alcohol (R)-5a was also readily changed to 8a with more than 99% ee in 61% overall yield after converting into the epoxy compound 10a (threo:erythro = 3:1) by epoxidation using TBHP/$VO(acac)_2$ followed by inversion of hydroxy group by the Mitsunobu procedure.[15]

Scheme I[a]



[a](a) TBHP (1.5 equiv), L(+)DIPT (1.2 equiv), $Ti(O^iPr)_4$ (1.0 equiv), CH_2Cl_2, -20 °C; (b) $^tBuMe_2SiCl$, Imidazole, DMF; (c) $^nBu_3SnH$ (1.5 equiv), LDA (1.8 equiv), THF, 0 °C; (d) I_2, Et_2O, 0 °C; (e) TBHP, $VO(acac)_2$ or $Ti(O^iPr)_4$, CH_2Cl_2; (f) p-NO_2-C_6H_4COOH, $EtO_2CN{=}NCO_2Et$, PPh_3, THF; (g) 1N NaOH aq, THF, MeOH.

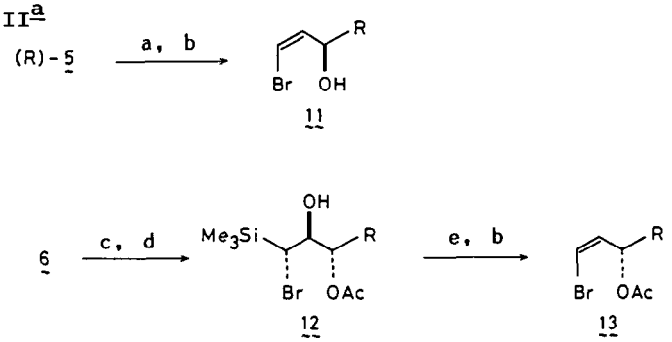
Similarly, the alcohol 8b, $[\alpha]_D^{25}$ -8.4° (c 1.00, $CHCl_3$), which can be used for the synthesis of PG analogs such as 16-phenoxy-17,18,19,20-tetranor-prostaglandin E_2[16] and sulprostone (Pfizer-Schering),[17] was obtained in 75% overall yield from the racemic alcohol 5b (Scheme I). In the kinetic resolution reaction of 5b, both (R)-5b and 6b with >99% optical purity were obtained simultaneously after 13 h at -20 °C. The optical purity of 8b thus obtained was found to be >99% by ^1H NMR analysis after coverting into the corresponding MTPA ester.

It is clear that the enantiomer of 8 (the derivative of the allylic alcohol of type 2) which is corresponded to the 15-epi PG ω-chain[1] can be similarly prepared from 9 and 6 (after the Mitsunobu inversion).

Hitherto PG ω-chain 8a has been prepared by the asymmetric reduction of (E)-1-iodo-1-octen-3-one microbiologically (80% ee)[18] or by using (S)-BINAL-H (BINAL = 2,2'-dihydroxy-1,1'-binaphthyl) (97% ee).[19] Asymmetric reduction of 1-octyn-3-one with B-3-pinanyl-9-BBN followed by hydrostannation with $^{n}Bu_3SnH$ and treatment with Br_2 also affords an efficient route to the PG 1-chain, (S)-1-bromo-1-octen-3-ol,(92% ee).[8] In comparison with these methods, the present method provides 8a with higher optical purity.[20,22] Moreover, the present method appears to have wider applicability to prepare various kinds of the PG ω-chain including those of analogs of naturally occurring PG, since the efficiency of asymmetric reductions of β-halo-α,β-olefinic ketones or α,β-acetylenic ketones is highly dependent on the substrate, and therefore is unreliable.[19,23]

The optically active allylic alcohols of type 3 and 4 can also be readily prepared by the procedure shown in Scheme II. Thus, the reaction of (R)-5a with Br_2 followed by treatment of the resulting adduct with $^{n}Bu_4NF$ afforded 11a, $[\alpha]_D^{25}$ +40.8° (c 1.79, $CHCl_3$), in 99% yield[24] which can be also used as the PG ω-chain.[25] While, treatment of the acetate of 6a with $MgBr_2$ in ether resulted in regiospecific epoxide ring opening[26] to afford 12a which was converted into 13a (the acetate of the enantiomer of 11a) by mesylation followed by treatment with $^{n}Bu_4NF$ (79% overall yield from 6a). Optical purity of 11a and 13a thus prepared checked by ^{1}H NMR analysis after converting into the corresponding MTPA esters was found to be more than 99% ee, respectively. It should be noted that the epoxy alcohol 6a can also be converted into 11a by carrying out the inversion of the hydroxy group before

Scheme II[a]

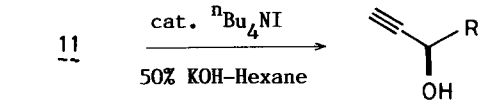


[a](a) Br_2, CH_2Cl_2; (b) $^{n}Bu_4NF$, THF, 0 °C; (c) Ac_2O, C_5H_5N; (d) $MgBr_2 \cdot OEt_2$ (2 equiv), Et_2O, 0 °C; (e) MsCl, Et_3N, hexane.

the reaction with $MgBr_2$. The present preparation of the alcohols of type 3 and 4 appears to be much more effective than the existing method which includes optical resolution of propargylic alcohols followed by halogenation and reduction.[25]

Since the allylic alcohols 8, 11, and 13 thus prepared are useful precursors of the corresponding propargylic alcohols, the present reaction should provide very efficient method for preparation of optically pure propargylic alcohols which are recognized as important synthetic

intermediates.[27] Actually, the alcohols 11a was converted quantitatively into the propargylic alcohol 14a, $[\alpha]_D^{21}$ +22.3° (c 1.38, ether), (lit.[25] $[\alpha]_D$ +20° (c 1.0, ether)), with more than 99% optical purity (checked by HPLC analysis of its MTPA ester) by treatment with KOH in the presence of a catalytic amount of $^nBu_4NI$ in H_2O-hexane (50 °C, 3 h) (eq 2).



11 → 14 (2)

In conclusion, the method described above is remarkably general and should in many cases provide the best, if not only, route to the optically pure allylic alcohols 1-4 and propargylic alcohol.

Acknowledgement: A part of this work was supported by the Grant-in-Aid for Special Project Research from the Ministry of Education, Science and Culture (No. 61125005).

References and Notes

(1) S. M. Roberts and F. Scheinmann, "New Synthetic Routes to Prostaglandins and Thromboxanes" Academic Press: New York, 1982; R. Noyori and M. Suzuki, Angew. Chem., Int. Ed. Engl., 23, 847 (1984). (2) R. H. Green and P. F. Lambeth, Tetrahedron, 39, 1687 (1983); J. Rokach and J. Adams, J. Acc. Chem. Res., 18, 87 (1985). (3) V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda, and K. B. Sharpless, J. Am. Chem. Soc., 103, 6237 (1981). (4) Y. Kitano, T. Matsumoto, and F. Sato, J. Chem. Soc., Chem. Commun., 1323 (1986). (5) E. W. Colvin, "Silicon in Organic Synthesis" Butterworths: London, 1981; W. P. Weber, "Silicon Reagents for Organic Synthesis" Springer-Verlag: New York, 1983. (6) M. Suzuki, A. Yanagisawa, and R. Noyori, J. Am. Chem. Soc. 107, 3348 (1985). (7) K. C. Nicolaou, C. A. Veale, S. E. Webber, and H. Katerinopoulos, ibid., 107, 7515 (1985). (8) K. C. Nicolaou and S. E. Webber, ibid., 106, 5734 (1984). (9) W. C. Still, ibid., 100, 1481 (1978). (10) P. F. Hudrlik, D. Peterson, and R. J. Rona, J. Org. Chem., 40, 2263 (1975). (11) S.-M. L. Chen, R. E. Schaub, and C. V. Grudzinskas, ibid., 43, 3450 (1978). (12) M. Suzuki, T. Kawagishi, and R. Noyori, Tetrahedron Lett., 23, 5563 (1982). (13) J. Davies, S. M. Roberts, D. P. Reynolds, and R. F. Newton, J. Chem. Soc., Perkin Trans. 1, 1317 (1981). (14) J. A. Dale, D. L. Dull, H. S. Mosher, J. Org. Chem., 34, 2543 (1969). (15) O. Mitsunobu, Synthesis, 1 (1981). (16) N. S. Crossley, Prostaglandins, 10, 5 (1975). (17) H.-J. Hess, J. S. Bindra, J. W. Constantine, W. Elger, O. Loge, E. Schillinger, and W. Losert, Experientia, 33, 1076 (1977). (18) C. J. Sih, J. B. Heather, R. Sood, P. Price, G. Peruzzotti, L.-F. H. Lee, and S. S. Lee, J. Am. Chem. Soc., 97, 865 (1975). (19) R. Noyori, I. Tomino, M. Yamada, and M. Nishizawa, ibid., 106, 6717 (1984). (20) By using the optical resolution of 1-iodo-1-octen-3-ol or its precursor, optically pure 8a has been prepared,[21] however, it is tedious and not so effective. (21) A. F. Kluge, K. G. Untch, and J. H. Fried, J. Am. Chem. Soc., 94, 7827 (1972). (22) It should be noted that if the relative rate difference of the two enantiomers in eq 1 is more than 20, though not so great as almost infinity, optically pure allylic alcohol (R)-5 (thus optically pure PG ω-chain) can be obtained in reasonable yield.[3] (23) M. M. Midland, D. C. McDowell, R. L. Hatch, and A. Tramontano, J. Am. Chem. Soc., 102, 867 (1980); R. S. Brinkmeyer, and V. M. Kapoor, ibid., 99, 8339 (1977); M. M. Midland, and A. Kazubski, J. Org. Chem., 47, 2814 (1982). (24) T. H. Chan, Acc. Chem. Res., 10, 442 (1977); R. F. Cunico, E. M. Dexheimer, J. Am. Chem. Soc., 94, 2868 (1972). (25) A. F. Kluge, K. G. Untch, and J. H. Fried, ibid., 94, 9256 (1972). (26) P. F. Hudrlik, R. N. Misra, G. P. Withers, A. M. Hudrlik, R. J. Rona, and J. P. Arcoleo, Tetrahedron Lett., 1453 (1976). (27) For preparation of optically active propargylic alcohols: see ref. 19 and 23. See also: J. Fried, C. Lin, M. Mehra, W. Kao, and P. Dalven, Ann. N. Y. Acad. Sci., 180, 38 (1971).

(Received in Japan 12 February 1987)