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ACYCLIC STEREOSELECTION USING RELATIVE 1,2-ASYMMETRIC INDUCTION. SELECTIVE SYNTHESIS OF (+)-BLASTMYCINONE

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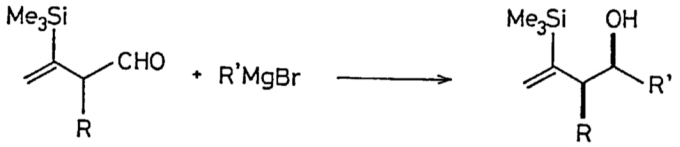
(+)-Blastmycinone has been synthesized based on the stereoselective addition reaction of 1-trimethylsilylvinylmagnesium bromide with (-)-(R)-2-butyl-3-trimethylsilylbut-3-enal.

(+)-Blastmycinone (1) is a degradation product of antimycin A_3, an antifungal antibiotic[1] and has been synthesized in both racemic and optically active forms by several groups.[2] Herein, we report the synthesis of (+)-1 by a method of the stereocontrolled construction of acyclic systems.[3,4]

Recently, we have shown that 2-methyl-3-trimethylsilylbut-3-enal (2) (R = Me) reacts with Grignard reagents highly selectively affording syn addition products with more than 99% diastereoselectivity (Eq. 1).[5] We also reported the convenient method for preparation of both (R)- and (S)-2 (R = Me), which was based



(1)

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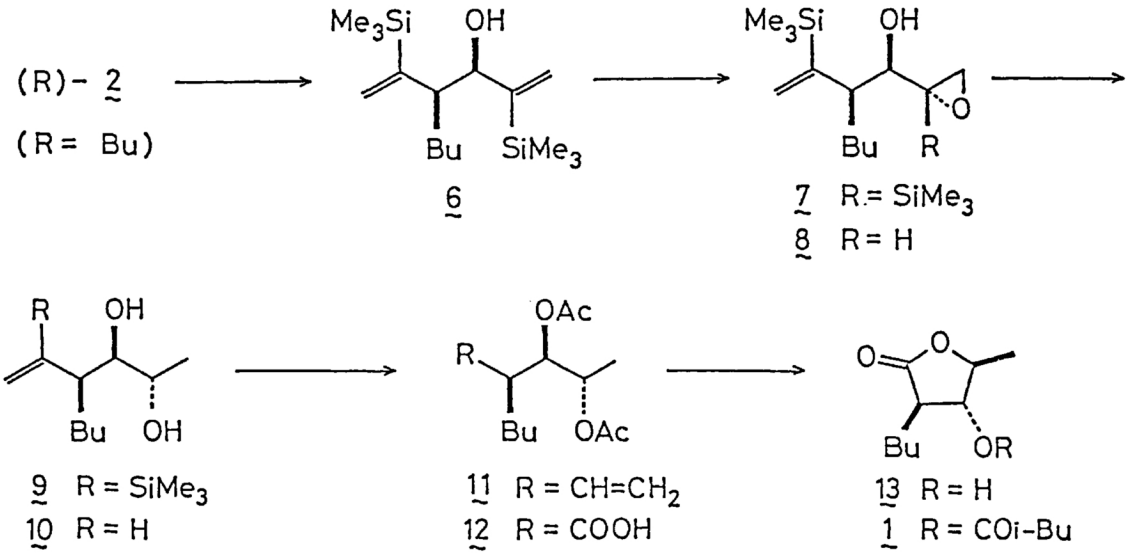
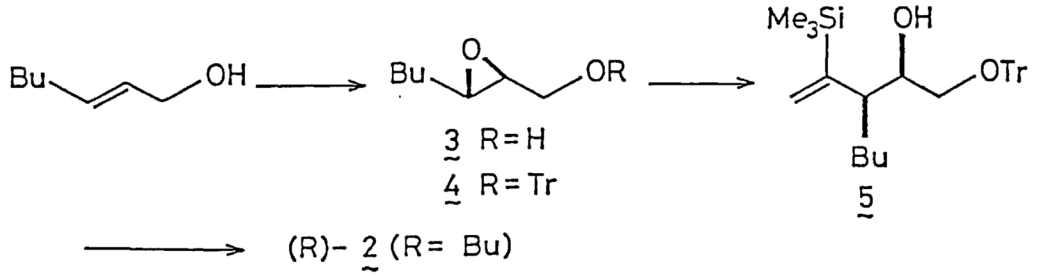
on the regiospecific ring opening of the epoxide obtained by Sharpless asymmetric epoxidation of trans-crotyl alcohol.[6] Based on these findings, we have prepared (+)-1 starting with the optically active aldehyde (R)-2 (R = Bu). Our method is shown in Scheme 1.

The aldehyde (R)-2 (R = Bu) was prepared according to Eq. 2 as described in the previous paper.[6] Thus, (E)-2-hexen-1-ol, prepared from propargyl alcohol and butyl bromide,[7] was epoxidized to 3[8] in 70% yield using (L)-(+)-diisopropyl tartrate and TBHP.[9] After protection of 3 as trityl ether (TrCl, Et_3N,



Scheme 1.

DMAP, CH_2Cl_2), the resulting 4 was treated with 1-trimethylsilylvinylmagnesium bromide in THF in the presence of CuI to afford the alcohol 5.[10] Deprotection of crude 5 ($Cl_2CHCOOH$, H_2O), purification by column chromatography on silica gel, and subsequent treatment with $NaIO_4$ afforded (R)-2 (R = Bu), $[\alpha]_D^{25}$ -16.7° (c 1.04, $CHCl_3$). The yield of (R)-2 from 3 was 68%.



(2)

Reaction of (R)-2 (R = Bu) thus prepared with 1-trimethylsilylvinylmagnesium bromide in THF (-78 °C→r.t.) yielded 6 exclusively in 91% yield.[5] Epoxidation of 6 with TBHP and $Ti(Oi\text{-}Pr)_4$ in CH_2Cl_2 gave 7 (73%) and its regioisomer (3%) which could be separated by column chromatography on silica gel.[9,11] Noteworthy is the fact that V^{5+}-catalyzed epoxidation of 6 resulted in low yield (10-30%) of 7.[12] Treatment of 7 with t-BuOK and then with Bu_4NF in THF resulted in regiospecific protodesilylation[13] yielding 8 (96%), which was changed to the diol 9 (92%) by treatment with $LiAlH_4$ in ether (0 °C→r.t.). Protodesilylation of 9 with KH-HMPA (r.t., 10 h)[14] and acetylation with Ac_2O-pyridine afforded 11 (75%). Ozonolysis of 11 in MeOH (-78 °C, 30 min), treatment with Me_2S and oxidation (CrO_3-H_2SO_4) gave 12 in 70% yield. The compound 12 was converted to blast-

mycinolactol (13) (95%), mp 49.0-49.5 °C (lit[2d] mp 50-51 °C), $[\alpha]_D^{22}$ -18.7° (c 1.55, MeOH) (lit[2d] -18° (c 1.61, MeOH), by treatment with K_2CO_3 in MeOH-H_2O (4:1) followed by addition of aqueous HCl. Finally, treatment of 13 with isovaleryl chloride afforded (+)-blastmycinone (1) (80%), $[\alpha]_D^{23}$ +11.0° (c 1.16, $CHCl_3$) (lit[2d] +10° (c 1.50, $CHCl_3$)). ^1H NMR spectral data were in accord with values reported in the literature.[2e,15]

In conclusion, we succeeded in a highly stereoselective synthesis of (+)-1. The present method can be effectively used for controlling three consecutive asymmetric centers of α,β-dihydroxy-γ-methyl compounds.

References

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3) Part of this report was presented at the 31st Symposium on Organometallic Chemistry, Tsukuba, October 1984, Abstr., B123.

4) Recently, Fujisawa et al. reported preparation of (+)-1 using the ester enolate Claisen rearrangement as a key step. See ref. 2h.

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6) Y. Kobayashi, Y. Kitano, and F. Sato, J. Chem. Soc., Chem. Commun., 1984, 1329.

7) D. E. Ames, A. N. Covell, and T. G. Goodburn, J. Chem. Soc., 1963, 5889.

8) Since asymmetric epoxidation of this type of trans-allyl alcohols is known to proceed with high enantiomeric excess (over 95%), the optical purities of 3 and other intermediates used here were not confirmed.

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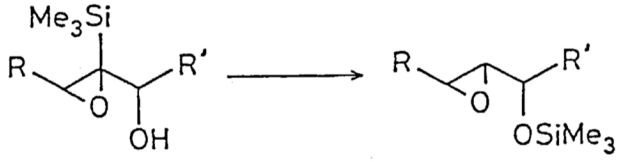
10) To a solution of CuI (2.5 mmol) in THF (2 ml) and Me_2S (0.4 ml) was added a THF solution of 1-trimethylsilylvinylmagnesium bromide (46 ml, 0.55 M, 25 mmol) and then 3 (15 mmol) dissolved in THF (20 ml) at 0 °C. The reaction mixture was stirred for 24 h at 0 °C and usual work up afforded 5, which was used for the next step without purification.

11) To a solution of 6 (4.7 mmol) in CH_2Cl_2 (45 ml) was added $Ti(Oi\text{-}Pr)_4$ (4.7 mmol) and the mixture was stirred for 20 min at 0 °C. Anhydrous TBHP (7.1 mmol) in CH_2Cl_2 (2.5 ml) was added to the reaction mixture. After 12 h at 0 °C, usual work up gave 7, which was purified by column chromatography on silica gel.

12) For the V^{5+}-catalyzed stereoselective epoxidation of allylic alcohols having trimethylsilyl group on the double bonds, see the following reports: H. Tomioka, T. Suzuki, K. Oshima, and H. Nozaki, Tetrahedron Lett., 23, 3387 (1982); A. S. Narula, ibid., 23, 5579 (1982).

13) NaH in HMPA or t-BuOK in THF was found to be effective for facile shift of the 1,3-trimethylsilyl group in β'-hydroxy-α,β-epoxysilanes giving silyloxy epoxides at room temperature (unpublished results).



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15) The ^{13}C NMR ($CDCl_3$) spectra of 1 and 13 are as follows: 1, δ 13.5, 19.1, 22.1, 25.4, 28.7, 42.9, 46.2, 78.2, 78.9, 172.0, 175.3; 13, δ 13.8, 18.2, 22.5, 28.1, 28.7, 48.5, 78.6, 80.6, 177.2.

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