Tetrahedron Letters, Vol.32, No.24, pp 2797-2798, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

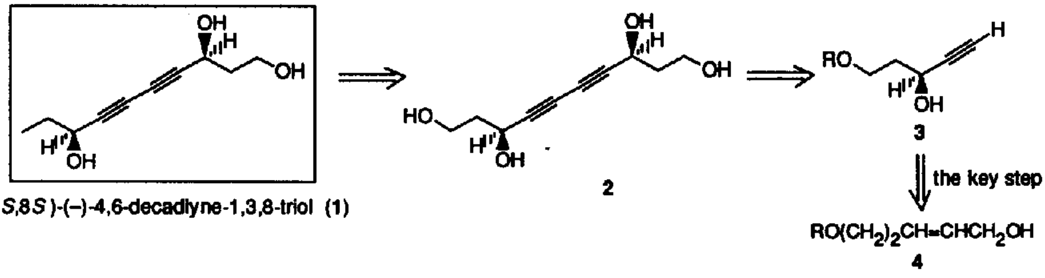
# THE FIRST ENANTIOCONTROLLED SYNTHESIS OF (3*S*,8*S*)-(−)-4,6-DECADIYNE-1,3,8-TRIOL ISOLATED FROM A TOXIC MUSHROOM *GYMNOPILUS SPECTABILIS*

Seiichi Takano,* Takumichi Sugihara, and Kunio Ogasawara
*Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan*

*Summary*: The first synthesis of (3*S*,8*S*)-(−)-4,6-decadiyne-1,3,8-triol, isolated from a toxic mushroom *Gymnopilus spectabilis*, has been achieved by employing the chiral 3-hydroxyalkyne formation reaction as the key step.

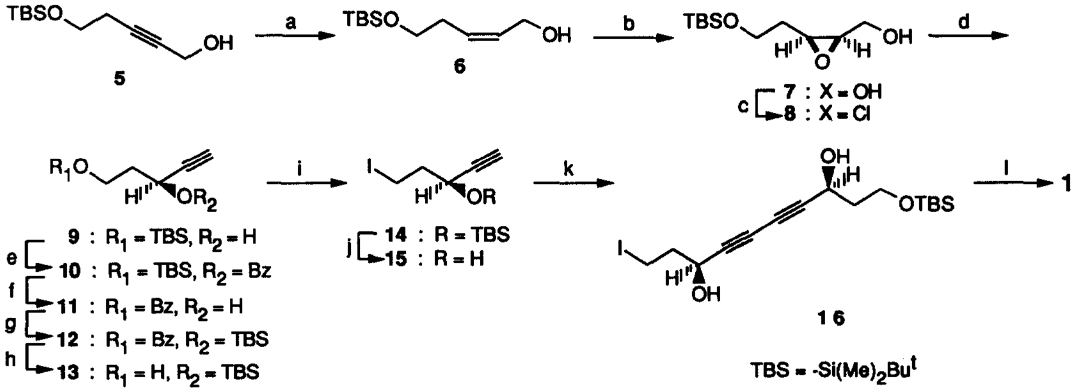
(3*S*,8*S*)-(−)-4,6-Decadiyne-1,3,8-triol (1) was first isolated in 1986 from a toxic mushroom "Ohwaraitake (Big laughter mushroom)", *Gymnopilus spectabilis*, by Nozoe and coworkers[1] who determined its planer structure. In 1989, Shirahama and coworkers[2] established its relative and absolute structure as 3*S*,8*S* by correlating its degradation products with (*S*)-(+)-2-aminobutyric acid and (*S*)-(−)-malic acid. Now we wish to describe the first synthesis of this unique natural product employing the chiral 3-hydroxyalkyne formation reaction[3] which we have developed recently.

Based on latent symmetry of the target molecule (1), we first planned to complete the synthesis by selective removal of one of the primary hydroxy groups in the symmetric diacetylene (2) starting from a prochiral allylic alcohol (4) by employing the chiral 3-hydroxyalkyne formation reaction to produce a key acetylene intermediate (3). However, difficulty in selective manipulation of the primary hydroxy groups of 2 made further execution of our initial plan impossible though we could actually have obtained 2 in an excellent overall yield (Scheme 1).



Scheme 1

Thus, we undertook a modified approach which successfully led to the first synthesis of the natural product (1). The Katsuki-Sharpless asymmetric epoxidation reaction[4] of the (*Z*)-allyl alcohol (6), prepared from 3-butynol in 3 steps (~90% overall yield) via 5, gave the (2*R*,3*S*)-epoxide (7), $[\alpha]_D^{29}$ −7.81° (*c* 1.04, $CHCl_3$), in 74% yield after purification via the acetate, $[\alpha]_D^{31}$ +10.40° (*c* 1.07, $CHCl_3$). Chlorination of 7 under neutral conditions followed by exposing the resulting chloride (8) to lithium diisopropylamide (LDA) afforded the α-hydroxyacetylene (9), $[\alpha]_D^{29}$ −12.93° (*c* 1.02, $CHCl_3$), in 92% overall yield. Optical purity of 9 was determined as ~80% ee by $^1$H-NMR analysis[5] of its MTPA (both enantiomers) esters. When the benzoate (10), $[\alpha]_D^{30}$ −30.30° (*c* 1.04, $CHCl_3$), derived from 9, was treated with tetrabutylammonium fluoride, desilylation



**Scheme 2**

***Reagents and conditions***: a) $H_2$, Lindlar catalyst, benzene, r.t., b) (D)-(–)-DIPT (1.06 equiv.), $Ti(O^iPr)_4$ (1.06 equiv), TBHP (1.6 equiv.), 4A molecular sieves, $CH_2Cl_2$, –30 °C, 64 h, c) $PPh_3$ (1.5 equiv.), $CCl_4$, reflux, d) LDA (7.2 equiv.), THF, –30 °C, 15 min, e) PhCOCl (1.5 equiv.), $Et_3N$ (2.4 equiv.), DMAP (10 mol%), $CH_2Cl_2$, r.t., f) $^nBu_4NF$ (1.6 equiv.), THF, 0 °C ~ r.t., g) TBS-Cl (1.5 equiv.), imidazole (2.2 equiv.), DMF-$CH_2Cl_2$ (10:3), r.t., h) $K_2CO_3$ (1.0 equiv.), MeOH, r.t., i) $I_2$ (2.0 equiv.), $PPh_3$ (2.0 equiv.), imidazole (2.0 equiv.), THF-MeCN (3:2), reflux, j) $^nBu_4NF$ (1.5 equiv.), THF, 0 °C, k) **9** (3.4 equiv.), $(Ph_3P)_2PdCl_2$ (1.4 mol%), CuI (3.5 mol%), $Et_3N$ (4.6 equiv.), $O_2$, DMF, r.t., 19 h, l) (i) $^tBuLi$ (3.9 equiv.), TMEDA (5.0 equiv.), THF, –75 °C, 80 min, –35 °C, 130 min, then aq. $NH_4Cl$, (ii) $^nBu_4NF$ (1.5 equiv.), THF, r.t.

occurred with clean rearrangement of the benzoyl group to give the primary benzoate (**11**), $[\alpha]_D^{30}$ +9.05° (*c* 1.03, $CHCl_3$), selectively, in 91% yield. Protection of the secondary hydroxy group followed by methanolysis **11** provided the primary alcohol (**13**), $[\alpha]_D^{28}$ –53.69° (*c* 1.02, $CHCl_3$), in 94% yield, which was transformed into the iodo-alcohol (**15**), $[\alpha]_D^{28}$ –0.90° (*c* 1.04, $CHCl_3$), in 75% overall yield on sequential iodination[6] and deprotection.

Upon treatment of the iodide (**15**) and 3.3 fold excess of the silyl ether (**9**) in the presence of a catalytic amount of dichlorobis(triphenylphosphine)palladium(II) and copper(I) iodide under oxygen,[7] a cross-coupling reaction occurred preferentially to afford the mixed diacetylene (**16**), $[\alpha]_D^{27}$ +5.14° (*c* 0.95, $CHCl_3$), in 54% yield from **15**, accompanied by minor amounts of two readily separable homocoupling products. Finally, **16** was dehalogenated with exposure to *tert* butyllithium[8] followed by aqueous ammonium chloride and desilylated to give the natural product[9] (**1**), $[\alpha]_D^{26}$ –5.69° (*c* 0.25, MeOH) [lit.[2]: $[\alpha]_D^{23}$ –5.8° (*c* 1.7, MeOH)].

## References and Notes

1. G. Kusano, Y. Koike, H. Inoue, and S. Nozoe, *Chem. Pharm. Bull.*, 1986, **34**, 3465.
2. M. Hashimoto, M. Yanagiya, T. Okuno, and H. Shirahama, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2751.
3. S. Takano, K. Samizu, T. Sugihara, and K. Ogasawara, *J. Chem. Soc., Chem. Commun.*, **1989**, 1344; S. Takano, T. Sugihara, K. Samizu, M. Akiyama, and K. Ogasawara, *Chem. Lett.*, **1989**, 1781; S. Takano, T. Sugihara, and K. Ogasawara, *Synlett*, **1990**, 451.
4. T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974.
5. Cf. S. Takano, M. Takahashi, M. Yanase, Y. Sekiguchi, Y. Iwabuchi, and K. Ogasawara, *Chem. Lett.*, **1988**, 1827.
6. P. J. Garegg and B. Samuelsson, *J. Chem. Soc., Chem. Commun.*, **1979**, 978.
7. Cf. S. Takano, T. Sugihara, and K. Ogasawara, *Synlett*, **1990**, 453.
8. Cf. W. F. Bailey and E. R. Punzalan, *J. Org. Chem.*, 1990, **55**, 5404; E. Negishi, D. R. Swanson, and C. J. Rousset, *ibid.*, 1990, **55**, 5406.
9. Spectral data (ir, $^1H$-nmr, mass) were identical with those of an authentic material.[1]

(Received in Japan 29 January 1991)