Tetrahedron Letters Vol. 21, pp 2811 - 2812
©Pergamon Press Ltd. 1980. Printed in Great Britain

0040-4039/80/0715-2811$02.00/0

STEREOSELECTIVE TOTAL SYNTHESIS OF BAZZANENE

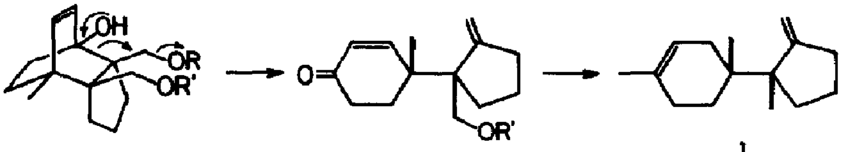
Mitsuaki Kodama, Toshiya Takahashi, Toshio Kurihara and Shô Itô

Department of Chemistry, Tohoku University

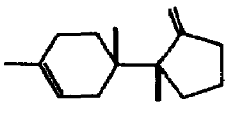
Sendai 980, Japan

Abstract Bazzanene, the stereoisomer of trichodiene, isolated from a liverwort was synthesized with complete stereoselectivity in 8 steps (12% yield) starting from a known bicyclo[2.2.2]octane derivati

Bazzanene 1 is a bicyclic sesquiterpene isolated from a liverwort, Bazzania pompeana[1], and is the biogenetic precursor of the tricyclic barbatane (gymnomitrane) carbon skeleton. The first structure[1] propc was revised to the presently accepted structure 1[2] on the basis of NMR and CD spectra and the chemicc correlation with trichodiene, 2, a fungal metabolite[3]. This paper describes a stereoselective total synthe of bazzanene 1.



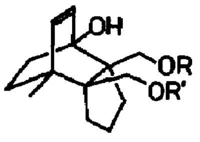
A B 1



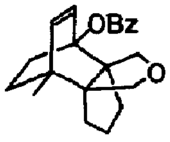
2

Our strategy involves the C-C bond cleavage (arrow) of a properly substituted tricyclo[5.2.2.$0^{2,6}$]undecane A with better leaving group OR than OR'. This single process (A→B) would not only create a exocyclic double bond on 5-membered ring, but also forms a cyclohexenone moiety in the product B, allowing the discrimination of α and α' positions of the carbonyl group, and leading stereoselectively to ,

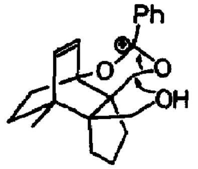
We have started the synthesis from the triol 3 which was one of the intermediates in our recent tot synthesis of barbatane sesquiterpenes[4]. Benzoylation of 3 afforded the monobenzoate 4, m.p. 132-133°, and the dibenzoate 5, viscous oil, in 25% and 59% yields, respectively. Although attempted protection primary hydroxyl group in 4 as tetrahydropyranyl ether furnished only the ether benzoate 6, m.p. 138.5-139° (probably via 7), mild hydrolysis of 5 with catalytic amount of NaOH in MeOH at room temperatur afforded another benzoate 8, m.p. 111-111.5°, in 45% yield together with 3 (35%) and the recovered 5 (14%). Only a trace of 4 was detected[5]. The 1,3-glycol structure in 8 was confirmed by the formatio of an acetonide, m.p. 118-119.5° ($CuSO_4$/Acetone).



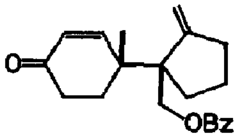
3: R=R'=H
4: R=Bz, R'=H
5: R=R'=Bz
8: R=H, R'=Bz



6



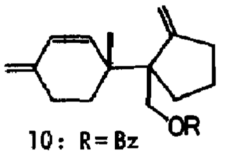
7



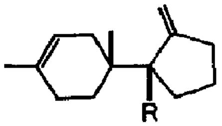
9

When the mesylate obtained from 8 by MsCl in pyridine was treated with KOtBu in THF at room temperature, the crucial bond cleavage took place cleanly and the expected cyclohexenone 9 was obtaine in 75% yield from 8. 9: m/e 324 (M^+), 105 (b.p.), ν 1712, 1670, 885 cm^{-1}, δ ($CDCl_3$) 1.25 (3H, s 4.38 (2H, s), 4.97 (1H, br.s), 5.21 (1H, br.s), 5.91 (1H, d, J=10), 6.88 (1H, dd, J=10, 1.5).

For the regioselective construction of methylcyclohexene moiety in 1, 9 was subjected to Wittig reaction (CH_2=PPh_3 in THF) by which two products, the triene benzoate 10, oil, and the triene alcohol 11, oil, were obtained in 52% and 36% yields, respectively. Bouveault-Blanc reduction (Na/nBuOH, 8 of both 10 and 11 afforded the desired 1,4-reduction product 12 in 93-94% yield. The conversion of th hydroxymethyl group in 12 to a methyl group was achieved by CrO_3 oxidation to the aldehyde 13 and th subsequent Huang-Minlon reduction (70% overall yield). The hydrocarbon obtained exhibited the identic



10: R=Bz
11: R=H



12: R=CH_2OH
13: R=CHO

MS, IR and NMR spectra with natural bazzanene(6). Thus, total synthesis of 1 was achieved with comple stereoselectivity.

References and Notes

1) S. Hayashi A. Matsuo and T. Matsuura, Experientia, 25, 1139 (1969); A. Matsuo, Tetrahedron, 27, 2757 (1971).

2) A. Matsuo and S. Hayashi, J.C.S. Chem. Comm., 566 (1977).

3) S. Nozoe and Y. Machida, Tetrahedron Letters, 2761 (1970). Idem, Tetrahedron, 28, 5105 (1972). Y. Machida and S. Nozoe, ibid., 28, 5113 (1972).

4) M. Kodama, T. Kurihara, J. Sasaki and S. Itô, Can. J. Chem., 57, 3343 (1979).

5) This selectivity in hydrolysis is apparently due to the participation of the neighboring tert-OH group [C S.M. Kupchan, et al., J. Am. Chem. Soc., 85, 350 (1963), 88, 343, 347 (1966)]. Once a benzo group was liberated, the hydrolysis of the second benzoxyl group took place rather rapidly (again by t similar participation), so that the change of the hydrolytic condition had little effect on the yield of

6) The authors are deeply indebted to Professor S. Hayashi and Dr. A. Matsuo, Hiroshima University, for the spectra of bazzanene and to Professor S. Nozoe, Tohoku University, for the spectra of trichodien

(Received in Japan 9 April 1980)