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Structural Revision of Isoconcinndiol by Its Synthesis[1)]

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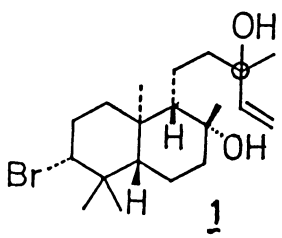
The originally proposed formula of isoconcinndiol was revised to ($3R^*$,$8S^*$,$13R^*$)-enantio-labd-14-ene-8,13-diol by its synthesis.

Isoconcinndiol isolated from Laurencia species is a typical bromine containing labdane type diterpene. Mainly on the basis of NMR spectra and mass fragmentation patterns, the original formula (1) was proposed leaving the C_{13}-stereochemistry unclarified.[2)] Recently, however, Masamune's group[3)] revealed by synthesis that the formula (1) does not represent the correct structure of isoconcinndiol. As far as we are aware, no report has been published on the correct structure after Masamune's demonstration. In this communication, we describe the evidence indicating that the structure of isoconcinndiol should be revised to the formula (2b).



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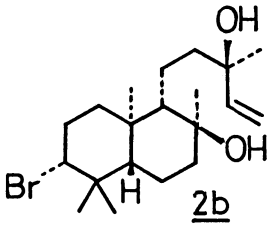
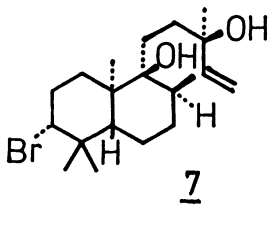


2b



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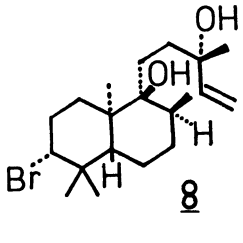

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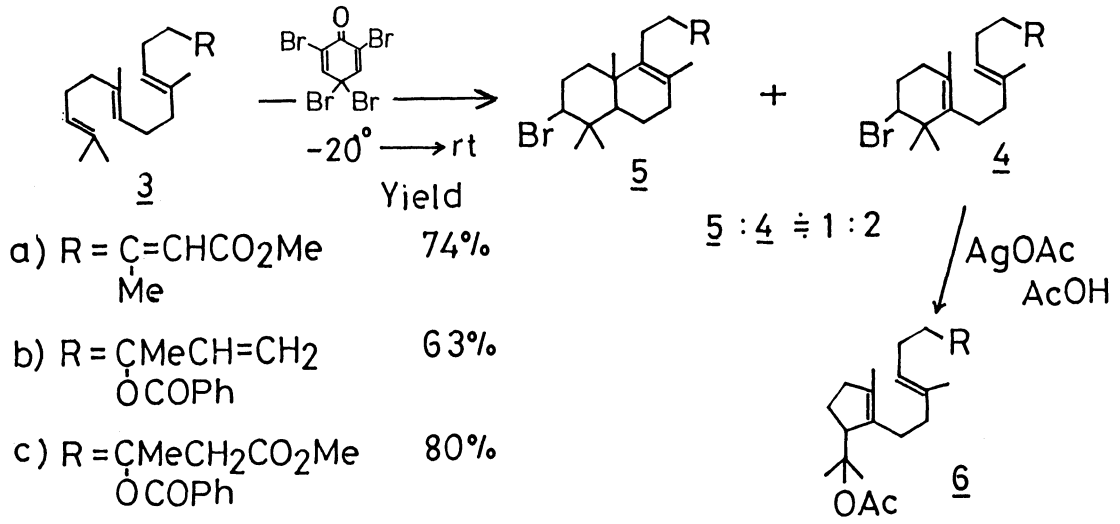
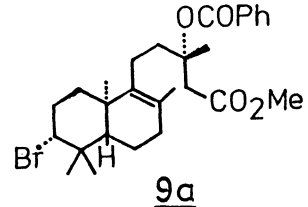
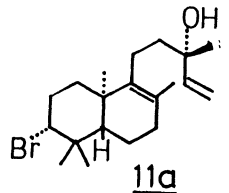
In the previous paper, we have demonstrated that 2,4,4,6-tetrabromocyclohexadienone (TBCO) is an effective reagent for the brominative cyclization of polyenes.[4)] For an instance, polyenes (3a and b) were converted to mono (4a or b) and bicyclic (5a or b) bromides in moderate yields by treatment with TBCO in CH_3CN.[5)] The latter bicyclic bromide (5a) has been efficiently[1)] transformed into the representative bromine containing labdanoid, concinndiol (7) and its 13-epimer (8), structurally related to isoconcinndiol.



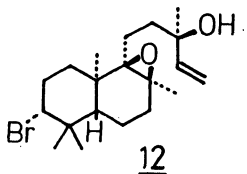
The straightforward application of TBCO to the polyene (3c) afforded the corresponding bromides [4c in 50% and 5c in 30% yields]. The resulting bicyclic bromide (5c) is a 1:1 diastereomeric mixture, which is separable to each component (9a and b) by repeated silica gel high pressure liquid chromatography.[6] The stereochemistry at 13-position was determined as follows. Each diastereomer (9a and b) was independently converted quantitatively to diol (10a and b) by $LiAlH_4$ reduction. Successive treatments of each diol with o-nitrophenyl selenocyanate and tributyl phosphine in THF followed by $NaIO_4$ oxidation furnished the allyl alcohol (11a and b) in 59% yield. One diastereomer (11a) corresponds to (±)-pinnatol D isolated recently by Masamune's group[7] from a Laurencia species. While 90 MHz ^1H NMR spectra of 11a can not be differentiated with that of 11b and both are identical with that of pinnatol D, chemical shifts of a few carbons are different within 0.1 ppm in the ^{13}C NMR spectra of each diastereomer. Unfortunately, however, ^{13}C NMR spectra of



9a



11a



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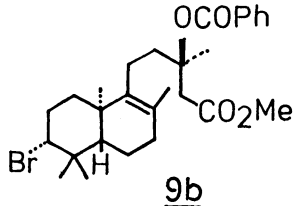
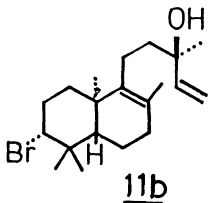
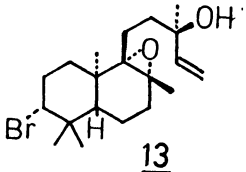


9b



11b



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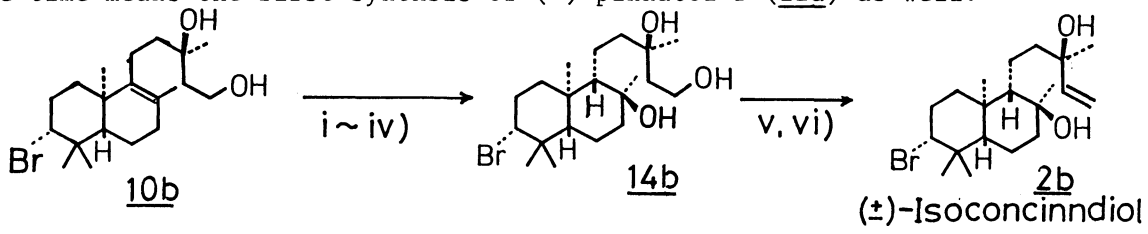
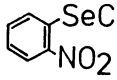
pinnatol D is not available due to its limitted amounts from nature and hence stereochemistry at 13-position remained undetermined at this stage.[8)]

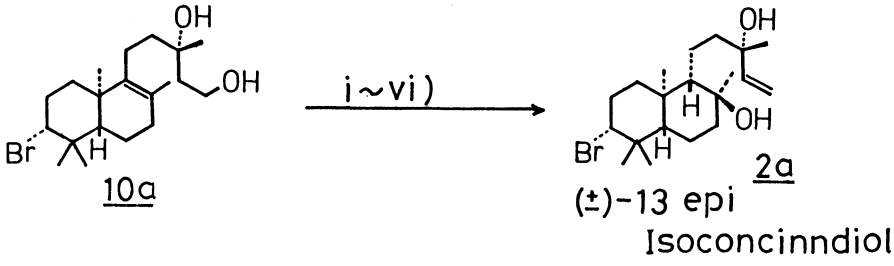
The allyl alcohol (11b)(13-epi-pinnatol D) furnished a 2:1 mixture of epoxides (12 and 13) by mCPBA oxidation. The major epoxide (12) was reduced with AlH_3 at 0°C to afford (±)-concinndiol (7) selectively. The same treatments of the other diastereomer (11a)(pinnatol D) gave the 13-epi-concinndiol (8). Since stereochemistry of concinndiol was determined unequivocally by an X ray crystallographic analysis,[9)] the above transformation reactions establishes the stereochemistry at 13-position of 9a and 9b, respectively.

Upon treatment with $Me_2C(OMe)_2$/pTsOH, the diol (10b) was converted to acetonide, which was submitted to hydroboration reaction with $BH_3.Me_2S$ in CH_2Cl_2 followed by H_2O_2/NaOH oxidation to give triol (14b) in 30% yield[10)] after hydrolysis of the acetonide group by pTsOH treatment. The allyl alcohol (2b) was obtained from the triol (14b) by converting the hydroxyethylene moiety to the vinyl group by the sequential reactions described in the scheme. Similarly, 13 epimer (2a) was provided from the isomeric diol (10a) by the same successive treatments. ^1H and ^{13}C NMR spectra of the former allyl alcohol (2b) was identical with those reported for isoconcinndiol.

The present study establishes the structure of isoconcinndiol and at the same time means the first synthsis of (±)-pinnatol D (11a) as well.



i) $Me_2C(OMe)_2$. ppTs
ii) $BH_3 \cdot Me_2S$/ CH_2Cl_2 (Y: 50%)
iii) NaOH, H_2O_2
iv) ppTs/MeOH
v)  , Bu_3P
vi) $NaIO_4$



References

1) This constitutes part 45 of the series of cyclization of polyenes. Part 44: Y. Yamaguchi, T. Uyehara, and T. Kato, Tetrahedron Lett., 26, 343 (1985).

2) B. M. Howard and W. Fenical, Phytochemistry, 19, 2774 (1980).

3) A. Murai, A. Abiko, and T. Masamune, Tetrahedron Lett., 25, 4955 (1984).

4) T. Kato, M. Mochizuki, T. Hirano, S. Fujiwara, and T. Uyehara, Chem. Commun., 1984, 1077. See also Ref. 1.

5) It is difficult to separate 4 and 5 by the conventional column chromatography in a large scale preparation. When the mixture is treated with AgOAc in AcOH, 4 rearranges to cyclopentene derivative (6), which is separated from the unchanged bicyclic bromide (5).

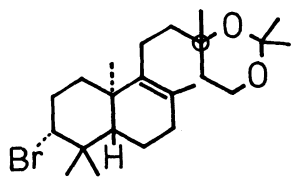
6) Only one stereoisomer of dl-form is described.

7) A. Fukuzawa, M. Miyamoto, Y. Kumagai, A. Abiko, Y. Takaya, and T. Masamune, Chem. Lett., 1985, 1259.

8) Physical data of pinnatol A and D were kindly provided by professor T. Masamune, whom we appreciate.

9) J. J. Sims, G. H. Y. Lin, R. M. Wing, and W. Fenical, Chem. Commun., 1973, 470.

10) In our model experiment using 13-epimeric mixture (10a and b), the acetonide (15) afforded three isomeric triols 16, 17, and 14(a and b) in 22, 5, and 30% yields, respectively by the reactions (ii-iv) in the scheme. Conversion of 10a to pinnatol A (18)[7] is now in progress.



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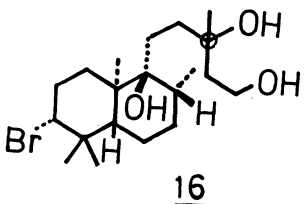

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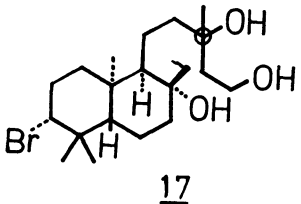

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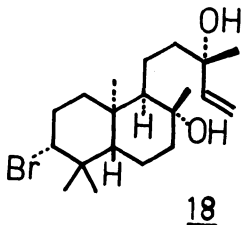

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