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# Structure and Absolute Stereochemistry of Bisconicasterone from the Marine Sponge *Theonella swinhoei*

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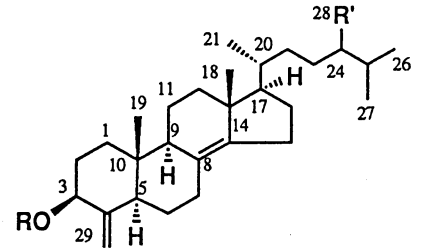
Bisconicasterone was isolated from the marine sponge *Theonella swinhoei*, and its structure was established by spectroscopic analysis as well as chemical correlation with its monomeric component, conicasterone, the absolute stereochemistry of which was confirmed by modified Mosher's method, chemical conversion, and by X ray crystallography.

Chromatographic separation of the ethanol extract of the marine sponge *Theonella swinhoei* collected off the Hachijo-jima island afforded conicasterol (**1**)[1] together with a new compound bisconicasterone (**5**).

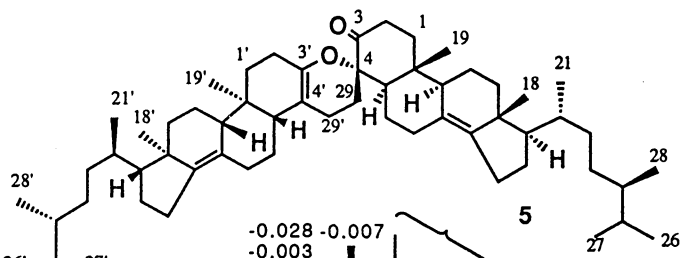
The physical properties of **1**, mp 139-143 °C (MeOH) and $^{13}$C-NMR signals, are identical with those reported for conicasterol previously isolated by Djerassi.[1] The chiroptical property, $[\alpha]_D^{25}$ +57.7° (c 1.028, $CHCl_3$), of the present compound, however, is significantly different from the reported value, $[\alpha]_D^{25}$ +97° ($CHCl_3$, no specification on concentration). The planar structure of **1** was verified by extensive analysis of the homo and heteronuclear 2D-NMR spectra, which resulted in correction of the previous assignment of the carbon signals.[2] The stereochemical features of conicasterol including the configuration of the side-chain methyl at 24 carbon had been deduced by the chemical-shift comparison with other steroids.[1] To exclude the ambiguity, the full stereochemistry of conicasterol was unequivocally established by X-ray crystallography (see **2a**) worked on its *p*-bromophenylurethane derivative (**2**).[3] Because of the poor crystalline character, the absolute configuration was not determined by this experiment. Finally, the absolute configuration of **1** was confirmed by the modified Mosher's method,[4] which gave $\Delta\delta$ values of the protons on A and B-rings as shown in **1a**.

The new compound (**5**), bisconicasterone,[5] exhibited more than fifty carbon signals including the ones assignable to a carbonyl carbon [$^{13}$C; $\delta$ 207.53 (s)] and an enol ether olefin [$^{13}$C; $\delta$ 147.32 (s) , 103.18 (s)], which suggested that this compound is a Diels-Alder type dimer of conicasterone (**4**), as exemplified by bistheonellasterone (**6**).[6] When solid conicasterone (**4**), obtained by oxidation of **1**, was allowed to stand at room temperature, it gradually changed into the dimer that was identical with bisconicasterone in all respects. The structure of the dimer was determined to be **5** by 2D-spectral analysis. The stereochemistry around the dihydropyrane ring was deduced from the endo rule of the Diels-Alder reaction.

It is worth mentioning that no trace of theonellasterol (**3**) has been isolated from the present *Theonella* sponge, the same species collected at Okinawa and investigated by Kitagawa *et al*, who reported **3** as a major component.[6] Such site-dependence of the ingredients of marine organisms is quite interesting and will stimulate further investigation on the same sponge collected at other places.



1; R = H, R' = β-Me
2; R = *p*-Br-Ph-NHCO, R'=β-Me
3; R = H, R' = α-Et
4; 3-keto, R' = β-Me



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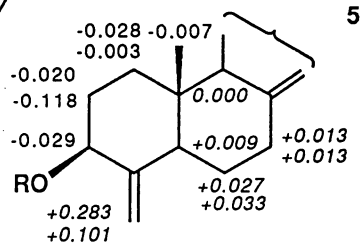
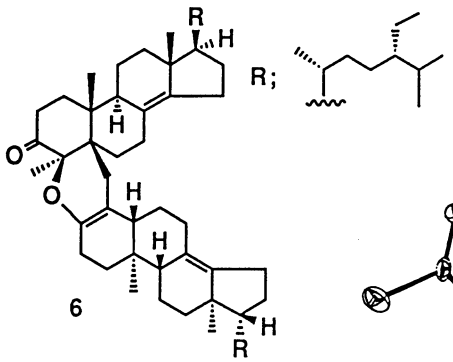


1a; R = MTPA, R'=β-Me



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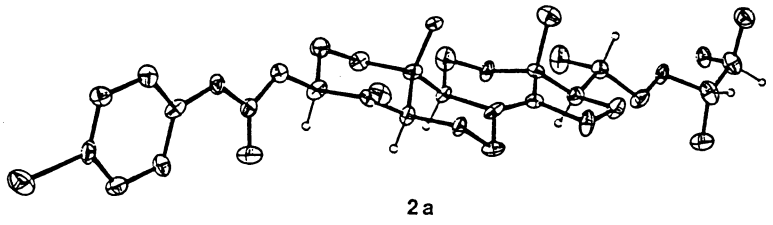

2a

References

1) E. Kho, D. K. Imagawa, M. Rohmer, Y. Kashman, and C. Djerassi, *J. Org. Chem.*, **46**, 1836 (1981).
2) $^{13}$C-NMR (corrected assignment, 125 MHz, $CDCl_3$): δ 153.24 (4), 143.02 (14), 125.76 (8), 102.86 (29), 73.47 (3), 56.95 (17), 49.55 (5), 49.34 (9), 42.83 (13), 40.08 (10), 39.02 (24), 37.44 (12), 36.82 (1), 34.63 (20), 33.62 (22), 33.28 (2), 32.47 (25), 30.26 (23), 29.45 (7), 27.13 (16), 25.88 (15), 24.75 (6), 20.51 (11), 20.29 (26), 19.16 (21), 18.30 (18), 18.28 (27), 15.46 (28), 13.28 (19).
3) Mp 162–164 °C (dec), $C_{36}H_{52}BrNO_2$, FW 610.69, orthorhombic, $P2_12_12_1$, a = 13.547 (3), b = 43.049 (3), c = 11.298 (1) Å, V = 6588 (1) Å$^3$, Z = 8, R = 0.093 for non-hydrogen atoms.
4) I. Ohtani, T. Kusumi, Y. Kashman, and H. Kakisawa, *J. Am. Chem. Soc.*, **113**, 4092 (1991).
5) Mp 213-216 °C; IR: 1721, 1682 cm$^{-1}$ ($CCl_4$); $^1$H-NMR (500 MHz, $C_6D_6$): δ 1.069. 1.050 (each 3H, d, *J* = 6.5 Hz, Me-21, 21'), 0.985 (3H, s, Me-18'), 0.969 (3H, s, Me-18), 0.953 (6H, d, *J* = 6.5 Hz, Me-26, 26'), 0.905 (3H, s, Me-19'), 0.899 (3H, s, Me-19), 0.906 (12H, d, *J* = 6.5 Hz, Me-27, 27', 28, 28'); $^{13}$C-NMR (125 MHz, $C_6D_6$): δ 207.53 (3), 147.32 (3'), 143.67 (14), 142.71 (14'), 127.23 (8'), 126.16 (8), 103.18 (4'), 84.33 (4), 57.67 (17), 57.57 (17'), 57.55 (5), 51.75 (9), 48.92 (9'), 46.95 (5'), 43.53 (13'), 43.40 (13), 39.97 (1), 39.77 (24 and 24'), 38.77 (10), 38.30 (12'), 37.92 (12), 37.65 (10'), 35.37 (20 or 20'), 35.28 (20 or 20'), 35.28 (2), 34.53 (1'), 34.38 (22 or 22'), 34.34 (22 or 22'), 33.13 (25 and 25'), 31.12 (23 and 23'), 30.62 (7'), 30.36 (7), 27.89 (16), 27.72 (16'), 26.56 (15), 26.53 (15'), 26.47 (29), 25.86 (2' and 6'), 22.62 (6), 20.94 (11'), 20.80 (26 and 26'), 20.41 (11), 19.77 (21 or 21'), 19.75 (21 or 21'), 19.61(29'), 19.15 (18'), 18.95 (18), 18.80 (27 and 27'), 16.03 (28 and 28'), 15.10 (19), 13.67 (19').
6) M. Kobayashi, K. Kawazoe, T. Katori, and I. Kitagawa, *Chem. Pharm. Bull.*, **40**, 1773 (1992).

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