

X-Ray Analysis of Two Steroids from Sponges of Family Halichondriidae: Sokotrasterol and 24,24,26,26-Tetramethylcholesta-5,22(E),25(27)-trien-3#-ol Acetate

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**X-RAY ANALYSIS OF TWO STEROIDS FROM SPONGES OF
FAMILY HALICHONDRIIDAE: SOKOTRASTEROL AND
24,24,26,26-TETRAMETHYLCHOLESTA-
5,22(E),25(27)-TRIEN-3 β -OL ACETATE**

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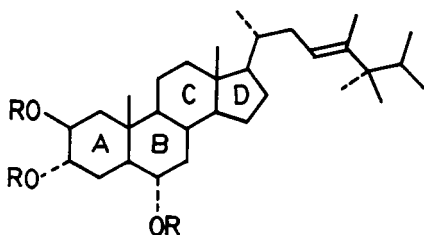
ABSTRACT.—The crystal and molecular structures of uncommon marine steroids **1** and **2** possessing two methyl substituents at C-26 have been determined by X-ray measurements.

Sponges have proved to be a rich source of uncommon sterols possessing additional alkylation patterns in side chains (1–3). Recently a new and growing group of such sponge metabolites characterized by the presence of two methyl substituents at C-26 has been reported (4–7). Stereochemical peculiarities of such compounds were not studied although the stereochemistry is important for the understanding of their biosynthesis pathway. Sokotrasterol sulfate [**1**] (4,5) and 24,24,26,26-tetramethylcholesta-5,22(*E*),25(27)-trien-3 β -ol [**2**] (7) were isolated from sponges of the family Halichondriidae and structurally studied by spectral methods as two unique steroids of this series.

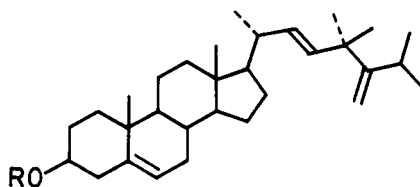
In order to confirm proposed formulae and establish the stereochemistry of these steroids we now report crystal and molecular structures of triol **3** obtained from **1** after acid hydrolysis, and of sterol acetate **4**.

Spatial models of the molecules are given in Figures 1 and 2. Six-membered rings A, B, and C of the molecule **3** have chair conformations, and the conformation of the five-membered ring D is 13 β -envelope. In compound **4**, the A ring is in a chair conformation, the B ring in 8 β ,9 α half-chair, the C ring chair, and the D ring 13 β ,14 α half chair, deviated to 13 β -envelope. Ring junction configurations for A/B, B/C, and C/D in **3** are trans. The molecule **4** has similar B/C and C/D ring junction configuration, but the A/B junction is quasi-trans. The side chain conformations in accordance with the definitions of Klyne and Prelog (8) in molecules **3** and **4** are antiperiplanar (the torsion angles C-13–C-17–C-20–C-22 are -174° and -179° , respectively).

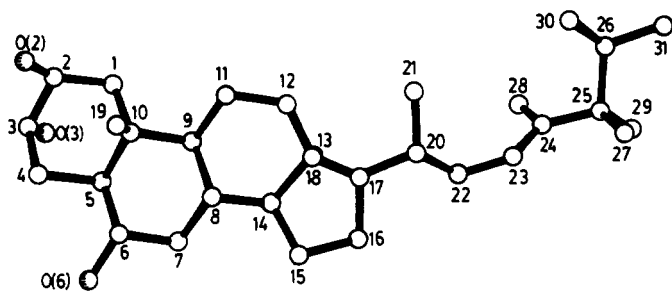
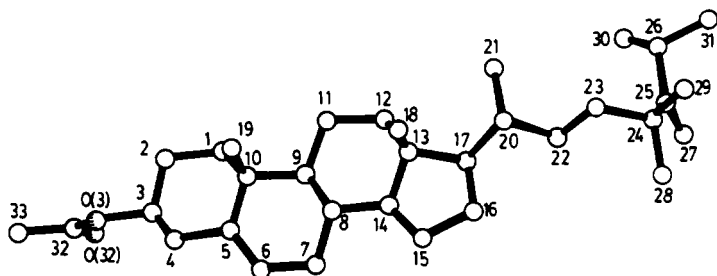
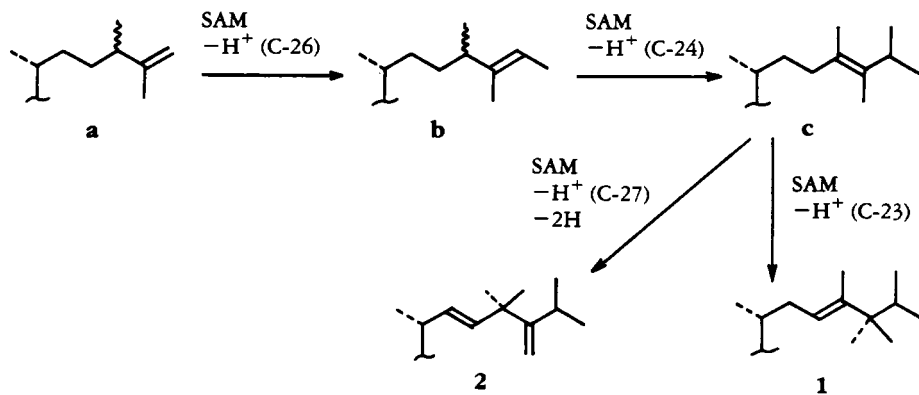
The crystal structure of the pyridine solvate **3** contains intermolecular hydrogen bonds O-2 . . . O-6', 2.66 Å; O-3 . . . O-2'', 2.75 Å; and O-6 . . . N



1 R=SO₃Na
3 R=H



2 R=H
4 R=Ac

FIGURE 1. The molecular structure of **3** with atom numbering.FIGURE 2. The molecular structure of **4** with atom numbering.

SCHEME 1

(pyridine), 2.75 Å, in which the first atoms are donors.

As suggested by Djerassi (3), marine sterols with 25-unsaturated side chains are possible precursors of highly alkylated steroids in sponges. In accordance with this suggestion a scheme of biosynthesis of side chains of **1** and **2** from a sterol with the side chain **a** through common intermediates of type **c** could be proposed (Scheme 1).

The studied compounds possess the same 17*R*,20*S* configuration as majority

of marine sterols, for example codisterol and epicodisterol, and these substances could be biosynthetic precursors of **1** and **2**.

EXPERIMENTAL

Compound **3** was crystallized from pyridine-hexane (1:1) as a solvate complex. Crystal data¹ for

¹Atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, UK.

TABLE 1. Fractional Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($\text{\AA}^2 \times 10^3$), with Estimated Standard Deviations in Parentheses, for Compound 3.

Atom	x	y	z	U_{eq}^a
N-1'	8923 (8)	6299	-899 (4)	104 (4)
C-2'	9588 (12)	4790 (18)	-915 (6)	128 (6)
C-3'	10901 (15)	4657 (25)	-783 (8)	152 (7)
C-4'	11581 (12)	6202 (38)	-637 (8)	174 (9)
C-5'	10936 (15)	7746 (29)	-632 (8)	169 (9)
C-6'	9624 (13)	7728 (20)	-772 (6)	135 (6)
C-1	4234 (6)	2348 (11)	-1505 (2)	46 (2)
C-2	4645 (6)	2622 (11)	-830 (2)	45 (2)
C-3	4931 (6)	873 (11)	-489 (3)	46 (2)
C-4	5842 (6)	-329 (11)	-784 (3)	44 (2)
C-5	5279 (6)	-670 (11)	-1454 (3)	40 (2)
C-6	6044 (6)	-2032 (10)	-1750 (3)	43 (2)
C-7	5280 (6)	-2530 (11)	-2367 (3)	43 (2)
C-8	5045 (6)	-849 (10)	-2770 (3)	39 (2)
C-9	4362 (6)	643 (10)	-2461 (3)	39 (2)
C-10	5091 (6)	1102 (11)	-1820 (2)	38 (2)
C-11	4093 (7)	2270 (11)	-2881 (3)	49 (2)
C-12	3320 (7)	1800 (11)	-3507 (3)	49 (2)
C-13	3999 (7)	321 (11)	-3818 (3)	42 (2)
C-14	4201 (6)	-1284 (11)	-3379 (3)	40 (2)
C-15	4625 (7)	-2806 (12)	-3763 (3)	55 (3)
C-16	3814 (7)	-2443 (12)	-4396 (3)	54 (3)
C-17	3156 (6)	-605 (11)	-4365 (3)	49 (2)
C-18	5281 (7)	1037 (12)	-3990 (3)	55 (3)
C-19	6414 (6)	2012 (10)	-1862 (3)	44 (2)
C-20	2909 (7)	339 (12)	-4991 (3)	54 (3)
C-21	2400 (9)	2236 (13)	-4967 (3)	73 (3)
C-22	1924 (7)	-804 (12)	-5433 (3)	57 (3)
C-23	1640 (7)	-73 (12)	-6062 (3)	57 (3)
C-24	510 (6)	608 (12)	-6340 (3)	55 (3)
C-25	284 (6)	1287 (14)	-6993 (3)	62 (3)
C-26	-120 (8)	3302 (15)	-7023 (4)	82 (3)
C-27	1500 (8)	1045 (18)	-7287 (3)	100 (4)
C-28	-659 (7)	769 (14)	-6021 (4)	83 (3)
C-29	-833 (9)	150 (17)	-7355 (4)	95 (4)
C-30	-383 (10)	4077 (20)	-7663 (5)	122 (5)
C-31	885 (12)	4482 (17)	-6631 (5)	128 (5)
O-2	5830 (5)	3670 (9)	-683 (2)	53 (2)
O-3	3701 (4)	7 (10)	-475 (2)	60 (2)
O-6	6299 (4)	-3625 (9)	-1391 (2)	50 (2)

^aEquivalent isotropic U are defined as $1/3 (U_{11} + U_{22} + U_{33})$.

compound 3: $C_{31}H_{54}O_3 \cdot C_5H_5N$, $M_r = 553.87$, monoclinic space group $P2_1$, $Z = 2$, $a = 10.350$ (5), $b = 7.447$ (3), $c = 22.46$ (1) \AA , $\beta = 99.56$ (3) $^\circ$, $V = 1707$ \AA^3 , $D_c = 1.08$ $\text{g} \cdot \text{cm}^{-3}$. Crystals of 4 were obtained from ErOAc . Crystal data for compound 4: $C_{33}H_{54}O_2$, $M_r = 482.79$, monoclinic, space group $P2_1$, $Z = 2$, $a = 19.093$ (3), $b = 9.935$ (1), $c = 8.115$ (1) \AA , $\beta = 96.40$ (1) $^\circ$, $V = 1530$ \AA^3 , $D_c = 1.05$ $\text{g} \cdot \text{cm}^{-3}$, λ (MoK α) = 0.71069 \AA .

Intensities of 1940 and 1957 symmetry-inde-

pendent reflections at 2θ limits up to 42° and 44° were measured on Syntex P1 diffractometer (MoK α radiation, graphite monochromator, θ - 2θ scanning technique) for 3 and 4, respectively, at room temperature. The Lorentz and polarization corrections were applied. The structures were solved by direct methods (9,10) and refined by full matrix least-squares procedure of SHELX-76 (11) programs. All non-hydrogen atoms were included with anisotropic temperature factors. Hydrogen atoms were included in the structure

TABLE 2. Fractional Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($\text{\AA}^2 \times 10^3$), with Estimated Standard Deviations in Parentheses, for Compound 4.

Atom	x	y	z	U_{eq}^a
C-1	-1987 (2)	-738	588 (5)	54 (2)
C-2	-2704 (2)	-819 (7)	1277 (6)	65 (2)
C-3	-3289 (2)	-613 (7)	-89 (6)	65 (2)
C-4	-3264 (2)	-1640 (7)	-1462 (6)	62 (2)
C-5	-2546 (2)	-1654 (7)	-2127 (6)	51 (2)
C-6	-2500 (2)	-1558 (7)	-3736 (6)	57 (2)
C-7	-1831 (2)	-1644 (7)	-4521 (5)	55 (2)
C-8	-1203 (2)	-2120 (6)	-3307 (5)	44 (2)
C-9	-1225 (2)	-1423 (6)	-1620 (5)	46 (2)
C-10	-1902 (2)	-1777 (6)	-824 (5)	47 (2)
C-11	-546 (2)	-1661 (7)	-453 (5)	53 (2)
C-12	133 (2)	-1346 (6)	-1246 (5)	51 (2)
C-13	162 (2)	-2174 (6)	-2835 (5)	42 (2)
C-14	-503 (2)	-1808 (6)	-3984 (5)	45 (2)
C-15	-380 (2)	-2406 (6)	-5662 (5)	57 (2)
C-16	422 (2)	-2249 (7)	-5710 (5)	57 (2)
C-17	738 (2)	-1779 (6)	-3952 (5)	48 (2)
C-18	200 (2)	-3698 (7)	-2446 (6)	55 (2)
C-19	-1874 (3)	-3219 (7)	-114 (6)	58 (2)
C-20	1498 (2)	-2301 (6)	-3504 (5)	53 (2)
C-21	1801 (2)	-1908 (7)	-1735 (6)	68 (2)
C-22	1982 (2)	-1791 (7)	-4761 (6)	57 (2)
C-23	2660 (2)	-2617 (6)	-4745 (6)	59 (2)
C-24	3199 (3)	-2099 (7)	-5844 (6)	58 (2)
C-25	3508 (3)	-754 (8)	-5213 (7)	67 (2)
C-26	3876 (3)	-721 (8)	-3452 (7)	86 (3)
C-27	3470 (3)	331 (8)	-6157 (8)	102 (3)
C-28	2869 (3)	-2031 (8)	-7653 (6)	89 (3)
C-29	3808 (3)	-3145 (7)	-5787 (7)	82 (3)
C-30	3553 (3)	350 (10)	-2388 (9)	151 (4)
C-31	4667 (3)	-509 (11)	-3429 (8)	133 (3)
C-32	-4296 (4)	264 (13)	982 (10)	116 (4)
C-33	-4967 (3)	-82 (12)	1664 (7)	177 (6)
O-3	-3960 (2)	-813 (7)	573 (5)	90 (2)
O-32	-4094 (4)	1395 (8)	821 (10)	177 (4)

^aEquivalent isotropic U are defined as $1/3 (U_{11} + U_{22} + U_{33})$.

factor calculations with fixed positional and thermal parameters. Final R values were reduced to 0.042 [1774 reflections with $|F| \geq 3\sigma(|F|)$] and to 0.048 [1908 reflections with $|F| \geq 3\sigma(|F|)$] for 3 and 4, respectively. Atomic coordinates of non-hydrogen atoms are given in Tables 1 and 2.

ACKNOWLEDGMENTS

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ERRATUM

For the paper by Sady and Seiber entitled "Field Test for Screening Milkweed Latex for Cardenolides," *J. Nat. Prod.*, **54**, 1105 (1991) entries in Table 1 should be corrected as follows:

- 13 *Asclepias eastwoodiana* Barneby, ++;
- 15 *Asclepias cordifolia* (Benth.) Jepson, +++;
- 16 *Asclepias cryptoceras* S. Wats., +.