BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 49(4), 1153—1154 (1976)

# The Crystal Structures of Sterigmatocystin and *O*-Methylsterigmatocystin, Metabolites of the Genus *Aspergillus*

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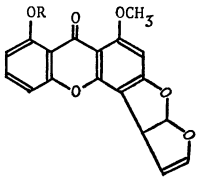
(Received December 27, 1975)

**Synopsis.** The crystal and molecular structures of sterigmatocystin and *O*-methylsterigmatocystin have been studied by the X-ray diffraction method. Both compounds crystallized in the space group $P2_1$ with $Z=2$. The cell dimensions are $a=16.068$, $b=4.293$, $c=11.243$ Å, and $\beta=113.23°$ for sterigmatocystin, and $a=8.835$, $b=16.769$, $c=5.403$ Å, and $\beta=109.21°$ for *O*-methylsterigmatocystin.

Sterigmatocystin (I) was isolated as a metabolite of *Aspergillus versicolor* (Vuillemin) Tiraboschi.[1] The structure and absolute configuration have been determined by chemical and X-ray methods.[2,3] *O*-Methylsterigmatocystin (II) was isolated by Burkhardt *et al.* from *Aspergillus flavus* Link ex Fries, and was synthesized by the methylation of sterigmatocystin.[4] In the series of studies of the structures of the metabolites of the genus *Aspergillus*,[5] X-ray structure analyses of the title compounds have been undertaken.




(I) R:H
(II) R:$CH_3$

Sterigmatocystin crystallized from aqueous acetone solution in the form of pale yellow needles elongated along the b axis. *O*-Methylsterigmatocystin crystallized from acetone solution in the form of colorless prisms elongated along the c axis. The crystal data for each compound are listed in Table 1. The intensities of each compound were measured up to $\sin\theta/\lambda=0.53$ on a Toshiba four-circle diffractometer with Ni-filtered Cu $K\alpha$ radiation. The approximate size of specimen used in the intensity measurement was $0.10\times0.35\times0.12$ mm for sterigmatocystin and $0.11\times0.14\times0.31$ mm for *O*-methylsterigmatocystin. The stationary-crystal stationary-counter method was used, with a counting time of 30 s. The background for each reflection was taken from plots of background as a function of $2\theta$. The intensities were corrected only for Lorentz and polarization factors.

TABLE 1. CRYSTAL DATA

| | Sterigmatocystin | *O*-Methylsterigmatocystin |
|---|---|---|
| Molecular formula | $C_{18}H_{12}O_6$ | $C_{19}H_{14}O_6$ |
| Molecular weight | 324.3 | 338.3 |
| Crystal system | Monoclinic | Monoclinic |
| Space group | $P2_1$ | $P2_1$ |
| $a$ | 16.068(5) Å | 8.835(4) Å |
| $b$ | 4.293(2) | 16.769(6) |
| $c$ | 11.243(3) | 5.403(3) |
| $\beta$ | 113.23(8)° | 109.21(8)° |
| $Z$ | 2 | 2 |
| $D_x$ | 1.51 g/cm³ | 1.49 g/cm³ |
| $D_0$ | 1.50 | 1.50 |
| $\mu$(for Cu$K\alpha$) | 9.7 cm$^{-1}$ | 9.6 cm$^{-1}$ |

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*Sterigmatocystin.* The structure was solved by interpretation of Patterson function followed by successive Fourier syntheses. The structure was refined to $R=0.08$ by a block-diagonal least-squares method with anisotropic temperature factors for non-hydrogen atoms. The positions of all the hydrogen atoms were determined from difference synthesis. Including positional parameters and isotropic temperature factors of hydrogen atoms, the refinement reduced the $R$ value to 0.074 for 1018 independent reflections ($R=0.060$ for non-zero reflections). The weighting scheme adopted in the final calculations was; $w=0.3$ for $F_o=0$, $w=1.0$ for $0<F_o\leqq20$, and $w=1.0/(1.0+0.75(F_o-20))$ for $20<F_o$. The final atomic parameters are given in Tables 2(a) and 3(a).

*O-Methylsterigmatocystin.* The structure was solved by application of the convolution molecule method[6] followed by Fourier syntheses. The refinement was carried out in the same way as that of sterigmatocystin. The final $R$ value is 0.060 for 973 independent reflections ($R=0.055$ for non-zero reflections). The weighting scheme adopted in the final calculations was; $w=0.2$ for $F_o=0$, $w=1.0$ for $0<F_o\leqq15$, and $w=1.0/(1.0+0.83(F_o-15))$ for $15<F_o$. The final atomic parameters are given in Tables 2(b) and 3(b). The atomic scattering factors were taken from the International Tables for X-ray Crystallography.[7]

The bond lengths and angles with their estimated standard deviations are shown in Fig. 1. The difference Fourier synthesis indicates that sterigmatocystin molecule has a intramolecular hydrogen bond, O(3)–H(O3)···O(2). The methoxy groups of both compounds are nearly coplanar with xanthone skeleton; the torsion angle of C(1)–C(2)–O(1)–C(18) in sterigmatocystin is −8.0°, and the angles of C(1)–C(2)–O(1)–C(18) and C(7)–C(6)–O(3)–C(19) in *O*-methylsterigmatocystin are 0.3° and 1.2° respectively. The dihedral angle between the xanthone skeleton and the terminal five-membered ring in sterigmatocystin is 64.9°, and that in *O*-methylsterigmatocystin is 61.0°.

The crystal structure for each compound is shown in Fig. 2. The molecules of sterigmatocystin are stacked with the interplanar distance of xanthone skeleton of 3.4 Å along the b axis to form a column. In *O*-

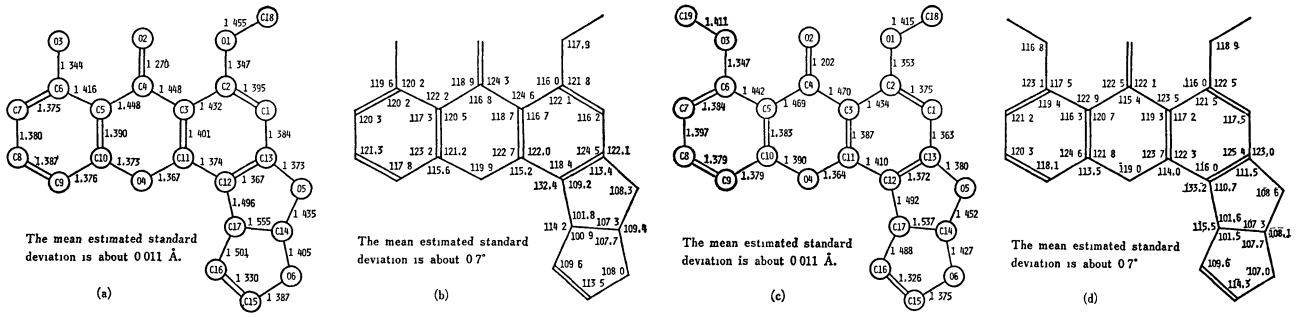


Fig. 1. Bond lengths and angles. (a) and (b) are those in sterigmatocystin, and (c) and (d) are in *O*-methylsterigmatocysten.

Table 2. Final atomic parameters and e.s.d.'s ($\times 10^4$) for non-hydrogen atoms

The anisotropic temperature factors are of the form; $\exp(-\beta_{11}h^2-\beta_{22}k^2-\beta_{33}l^2-\beta_{12}hk-\beta_{13}hl-\beta_{23}kl)$.

(a) Sterigmatocystin

| | x | y | z | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{12}$ | $\beta_{13}$ | $\beta_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| C(1) | 4396(4) | 886(18) | 2598(5) | 46(3) | 613(47) | 95(6) | 13(23) | 40(7) | -33(34) |
| C(2) | 3989(4) | 1957(18) | 1326(6) | 50(3) | 598(47) | 103(6) | -10(22) | 61(8) | -32(33) |
| C(3) | 3084(4) | 1102(17) | 491(5) | 40(3) | 545(43) | 86(6) | 9(21) | 35(7) | -77(31) |
| C(4) | 2628(4) | 2126(19) | -837(5) | 43(3) | 675(49) | 103(6) | 50(22) | 45(7) | -48(32) |
| C(5) | 1725(4) | 925(18) | -1549(5) | 43(3) | 534(43) | 88(6) | 54(21) | 30(7) | -65(31) |
| C(6) | 1218(4) | 1698(19) | -2863(6) | 54(3) | 740(56) | 101(7) | 76(26) | 48(8) | -46(37) |
| C(7) | 353(5) | 571(20) | -3492(6) | 71(4) | 565(48) | 105(7) | 79(27) | 18(9) | -66(34) |
| C(8) | -22(4) | -1361(20) | -2855(6) | 56(4) | 630(52) | 112(7) | 20(26) | -3(8) | 14(38) |
| C(9) | 447(4) | -2132(20) | -1563(6) | 46(3) | 750(60) | 130(7) | -36(26) | 24(8) | -37(40) |
| C(10) | 1312(4) | -987(18) | -946(5) | 47(3) | 610(49) | 100(6) | 29(24) | 34(7) | -94(35) |
| C(11) | 2626(4) | -908(18) | 1008(5) | 46(3) | 603(47) | 87(6) | 4(23) | 43(7) | -2(33) |
| C(12) | 3012(4) | -1966(17) | 2262(5) | 51(3) | 495(43) | 90(6) | 20(21) | 49(7) | -9(30) |
| C(13) | 3880(4) | -1090(19) | 3006(5) | 50(3) | 746(53) | 75(6) | 70(26) | 33(7) | 4(34) |
| C(14) | 3494(4) | -4153(20) | 4359(6) | 68(4) | 666(52) | 95(6) | 8(21) | 47(8) | 59(36) |
| C(15) | 2376(5) | -1723(23) | 4739(7) | 82(5) | 855(65) | 160(9) | 14(33) | 131(11) | 15(47) |
| C(16) | 1992(5) | -2297(20) | 3475(6) | 72(4) | 596(51) | 128(8) | 31(27) | 93(9) | 109(38) |
| C(17) | 2656(4) | -3933(18) | 3054(6) | 55(3) | 633(49) | 91(6) | -8(25) | 41(7) | 21(34) |
| C(18) | 5375(4) | 4522(21) | 1572(7) | 46(3) | 882(66) | 142(8) | -36(27) | 41(9) | 120(43) |
| O(1) | 4421(2) | 3889(13) | 816(4) | 47(2) | 712(35) | 114(5) | -27(17) | 49(5) | 16(24) |
| O(2) | 2970(3) | 3976(14) | -1403(4) | 53(2) | 834(40) | 114(5) | -37(18) | 49(5) | 76(26) |
| O(3) | 1579(3) | 3532(14) | -3503(4) | 64(2) | 839(39) | 103(4) | 51(19) | 47(5) | 80(26) |
| O(4) | 1754(2) | -1859(12) | 325(3) | 44(2) | 690(34) | 90(4) | -32(15) | 19(4) | 39(22) |
| O(5) | 4192(3) | -2252(12) | 4243(4) | 58(2) | 646(34) | 92(4) | -47(17) | 22(5) | 32(23) |
| O(6) | 3244(3) | -2930(16) | 5330(4) | 87(3) | 1078(48) | 99(5) | -1(22) | 78(6) | -55(28) |

(b) O-Methylsterigmatocystin

| | x | y | z | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ | $\beta_{12}$ | $\beta_{13}$ | $\beta_{23}$ |
|---|---|---|---|---|---|---|---|---|---|
| C(1) | 2662(9) | -1503(5) | -634(15) | 154(12) | 44(3) | 484(34) | 38(11) | 313(34) | -9(18) |
| C(2) | 1427(8) | -1781(5) | 152(14) | 142(12) | 35(3) | 479(33) | 6(11) | 210(32) | 3(18) |
| C(3) | 772(8) | -1310(4) | 1768(14) | 115(10) | 31(3) | 408(31) | -11(9) | 180(29) | -4(15) |
| C(4) | -597(9) | -1564(5) | 2555(16) | 180(13) | 36(3) | 525(36) | -22(11) | 314(37) | -34(18) |
| C(5) | -1105(8) | -994(5) | 4190(14) | 128(11) | 40(3) | 414(32) | -8(10) | 206(30) | 16(16) |
| C(6) | -2416(9) | -1147(5) | 5158(14) | 137(12) | 43(3) | 433(33) | 3(10) | 240(32) | 21(17) |
| C(7) | -2799(9) | -585(5) | 6735(14) | 143(12) | 58(4) | 414(32) | 34(12) | 222(33) | 39(20) |
| C(8) | -1977(9) | 139(5) | 7324(15) | 158(12) | 39(3) | 492(37) | 18(11) | 282(35) | -12(19) |
| C(9) | -739(9) | 303(5) | 6378(15) | 144(11) | 45(3) | 419(34) | -9(11) | 230(33) | -18(19) |
| C(10) | -344(8) | -266(5) | 4853(13) | 136(12) | 43(3) | 350(28) | 19(10) | 198(31) | 9(17) |
| C(11) | 1453(8) | -566(4) | 2544(13) | 122(11) | 33(3) | 376(28) | 15(9) | 181(29) | 19(15) |
| C(12) | 2741(8) | -277(5) | 1805(13) | 116(11) | 45(3) | 359(28) | 9(10) | 169(29) | 1(17) |
| C(13) | 3256(8) | -764(5) | 205(14) | 134(12) | 39(3) | 418(32) | 14(10) | 229(32) | 11(17) |
| C(14) | 4918(9) | 329(5) | 966(15) | 145(12) | 43(3) | 469(36) | 20(11) | 234(34) | 41(19) |
| C(15) | 3460(10) | 1405(6) | -894(17) | 191(14) | 51(4) | 501(38) | 12(13) | 314(39) | -10(20) |
| C(16) | 2832(9) | 1196(5) | 926(17) | 145(13) | 37(3) | 633(41) | -39(11) | 287(37) | -65(19) |
| C(17) | 3680(9) | 481(5) | 2352(15) | 158(11) | 43(3) | 445(34) | -29(10) | 271(33) | -39(17) |
| C(18) | 1381(13) | -3012(6) | -2081(21) | 262(19) | 43(4) | 822(58) | 2(14) | 502(56) | -74(25) |
| C(19) | -4395(10) | -2012(6) | 5628(18) | 174(14) | 57(4) | 672(44) | -32(13) | 401(43) | 49(24) |
| O(1) | 776(7) | -2513(3) | -511(12) | 222(11) | 40(2) | 719(33) | -30(9) | 432(32) | -94(15) |
| O(2) | -1223(9) | -2204(4) | 1957(17) | 348(16) | 58(3) | 1272(54) | -114(12) | 1017(51) | -235(22) |
| O(3) | -3177(6) | -1852(3) | 4541(11) | 165(9) | 46(2) | 680(29) | -23(8) | 383(27) | -14(15) |
| O(4) | 936(6) | -48(3) | 4040(10) | 160(8) | 37(2) | 472(23) | -20(7) | 337(22) | -38(11) |
| O(5) | 4521(6) | -429(3) | -388(11) | 170(9) | 47(3) | 599(26) | -31(8) | 413(26) | -60(14) |
| O(6) | 4729(6) | 940(4) | -953(10) | 189(9) | 46(2) | 550(27) | 7(8) | 367(27) | 29(14) |

Table 3. Final positional parameters ($\times 10^3$) and isotropic temperature factors ($\times$Å$^{-2}$) for hydrogen atoms

(a) Sterigmatocystin

| | x | y | z | B |
|---|---|---|---|---|
| H(C1) | 506(4) | 128(19) | 314(5) | 4.0(16) |
| H(O3) | 217(4) | 345(21) | -313(6) | 4 8(17) |
| H(C7) | 1(4) | 128(19) | -445(5) | 4.3(17) |
| H(C8) | -68(4) | -241(21) | -333(6) | 4 2(16) |
| H(C9) | 10(4) | -350(20) | -131(6) | 4 4(17) |
| H(C14) | 380(4) | -613(19) | 464(6) | 3 8(16) |
| H(C15) | 210(4) | -81(21) | 533(6) | 4 6(18) |
| H(C16) | 139(4) | -145(22) | 282(6) | 5 6(19) |
| H(C17) | 242(4) | -626(19) | 265(5) | 3.5(15) |
| H(C18) | 571(4) | 278(22) | 179(6) | 5.4(18) |
| H(C18) | 552(4) | 516(24) | 260(6) | 6.0(19) |
| H(C18) | 555(4) | 607(22) | 120(6) | 5 4(19) |

(b) O-Methylsterigmatocystin

| | x | y | z | B |
|---|---|---|---|---|
| H(C1) | 323(8) | -188(5) | -151(14) | 2.6(16) |
| H(C7) | -378(9) | -69(5) | 733(15) | 3.5(18) |
| H(C8) | -215(8) | 59(4) | 852(15) | 2.4(16) |
| H(C9) | -11(8) | 86(5) | 696(14) | 2.3(16) |
| H(C14) | 624(9) | 23(5) | 717(15) | 3.0(17) |
| H(C15) | 312(9) | 189(5) | -221(14) | 2.4(16) |
| H(C16) | 186(9) | 143(5) | 119(16) | 3.7(19) |
| H(C17) | 425(8) | 55(5) | 442(14) | 2 3(17) |
| H(C18) | 251(11) | -308(6) | -173(19) | 6 1(25) |
| H(C18) | 95(12) | -280(7) | -399(21) | 6 7(26) |
| H(C18) | 77(10) | -357(5) | -223(16) | 4 5(21) |
| H(C19) | -493(12) | -252(5) | 496(19) | 4 1(20) |
| H(C19) | -382(10) | -203(6) | 766(16) | 4 1(20) |
| H(C19) | -525(9) | -151(5) | 504(16) | 2 5(16) |

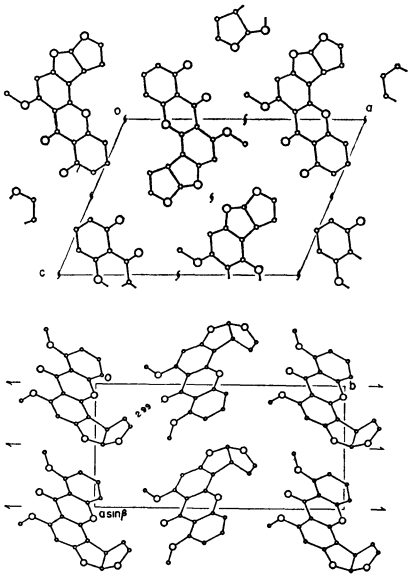


Fig. 2. Projections of the crystal structures of (a) sterigmatocystin and (b) *O*-methylsterigmatocystin.

methylsterigmatocystin the interplanar distance of the xanthone skeletons related by unit translation along the c axis is 3.5Å. The xanthone planes related by screw axis make an angle of 76° in sterigmatocystin, while the angle is 48° in *O*-methylsterigmatocystin. The closest intermolecular contact in the crystal of *O*-methylsterigmatocystin is observed between the terminal of the dihydrofuranofuran moiety and carbonyl oxygen atom. The distances between the C(15) and O(2) atoms and between the H(C15) and O(2) atoms are 2.99 Å and 2.3Å respectively. No intermolecular hydrogen bond is observed in both crystals.

The authors wish to thank Mr. Isao Tanaka and Professor Tamaichi Ashida of Nagoya University for computer programs. They are also indebted to Mr. Fumiyoshi Nishimura for the assistance in this work.

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