CHEMISTRY LETTERS, pp. 1293-1294, 1973. Published by the Chemical Society of Japan

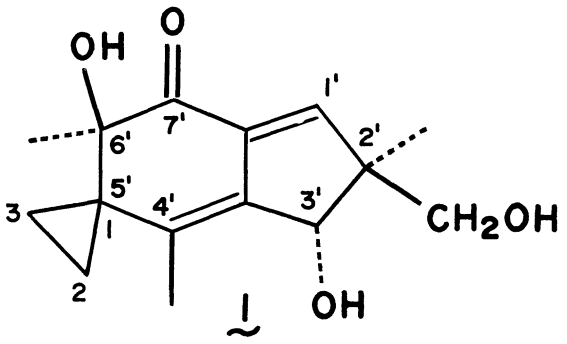
DETERMINATION OF THE CHIRALITY OF ILLUDIN S BY THE BIJVOET X-RAY METHOD

Akio FURUSAKI, Haruhisa SHIRAHAMA, and Takeshi MATSUMOTO
Chemistry Department, Faculty of Science
Hokkaido University, Sapporo 060

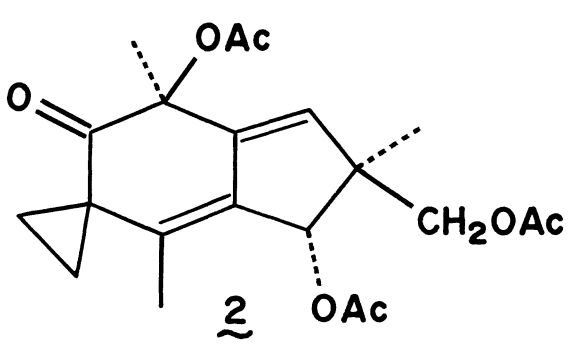
The chirality of illudin S has been unambiguously determined as 1 (2'S, 3'R, 6'R) by applying the anomalous dispersion method to isoilludin S triacetate 2.

The absolute configuration 1 has been suggested[1] for the antitumor antibiotic illudin S[2] by means of Horeau's method and this has been supported by the exciton chirality method[3]. However, the exciton analysis of the c. d. spectra is based on a number of assumptions[4] and recently examples[5] of an anomalous class, for which the opposite conclusion was drawn from the approximate chiroptical theoretical analysis, have been reported. On the other hand, determination of the absolute configurations deduced by the Bijvoet X-ray method[6] is accepted as entirely reliable. The present paper describes studies of the chirality of isoilludin S triacetate[2a, c] by the Bijvoet technique.

The crystals are orthorhombic, with four molecules in a unit cell of the dimensions, a = 13.463 ± 0.003, b = 17.161 ± 0.003, and c = 9.112 ± 0.002 Å. The space group is $P2_12_12_1$. Intensities of 2180 unique reflections with 2θ values up to 140° were collected on a Rigaku automatic four-circle diffractometer using Cu Kα radiation monochromatized with a LiF crystal. The structure was solved by the direct method, and refined by the block-diagonal-matrix least-squares method with anisotropic temperature factors for all the non-hydrogen atoms. From a difference Fourier map, the locations of 26 hydrogen atoms were also found. Further least-squares refinement including these hydrogen atoms yielded R = 4.8%.[7] The absolute configuration was determined by taking account of the anomalous dispersion effect of oxygen atoms for Cu Kα radiation ($\Delta f'' = 0.1$). The intensity measurement was made on 97 pairs of hkl and $\bar{h}kl$ reflections with the largest



1



2

values of $D = ||F_c(hkl)| - |F_c(\bar{h}\bar{k}\bar{l})|| / \sigma(F_o)$. The observed and calculated inequalities for 20 pairs of reflections having the largest D values are given in Table 1. This clearly indicates that the actual absolute configuration of isoilludin S triacetate corresponds to that shown in formula 2. This conclusion was supported also by the comparison of R values for all the 97 pairs of reflections; the R values were 3.71 and 3.85% for the structure shown in formula 2 and its antipode respectively.

Since the configurational correlation between illudin S and isoilludin S is beyond doubt, the above result unambiguously defines the chirality of illudin S as 1 (2'S, 3'R, 6'R).

Table 1. Bijvoet inequalities

h	k	l	$\|F_o\|$ [a]	ΔF_o [b]	$\|F_c\|$	ΔF_c [c]	h	k	l	$\|F_o\|$	ΔF_o	$\|F_c\|$	ΔF_c
2	6	2	24.43	-0.14(7)	23.00	-1.41	2	5	3	30.17	0.41(8)	28.83	0.89
1	2	2	12.08	-0.20(4)	10.45	-1.17	1	1	2	48.82	0.66(9)	48.57	0.52
2	2	1	62.03	0.52(14)	71.07	1.26	4	4	4	13.49	0.48(7)	13.12	0.89
5	3	2	29.16	-0.03(8)	27.13	-1.15	4	1	3	20.21	-0.06(7)	20.77	-0.69
7	1	1	24.85	-0.23(9)	22.33	-1.20	3	4	1	47.33	0.35(10)	47.98	0.58
6	1	3	26.92	0.01(8)	25.86	-1.21	2	10	2	15.75	-0.18(7)	14.65	-0.85
1	3	2	42.92	0.61(13)	43.50	0.80	4	4	1	23.13	-0.11(4)	22.65	-0.63
2	2	5	19.67	0.39(6)	20.56	1.18	4	4	2	14.81	-0.07(7)	14.03	-0.67
5	1	1	25.88	-0.12(5)	24.11	-0.83	2	1	3	54.71	0.92(7)	56.39	0.57
5	5	5	19.53	-0.24(7)	19.01	-1.19	4	3	1	12.78	0.16(3)	11.39	0.62

a) For each pair, intensities were measured five times. The average of the five $|F_o|$ values was used. The e.s.d.'s for ΔF_o's are given in parentheses.

b) $\Delta F_o = |F_o(hkl)| - |F_o(\bar{h}\bar{k}\bar{l})|$ c) $\Delta F_c = |F_c(hkl)| - |F_c(\bar{h}\bar{k}\bar{l})|$

References and Notes

1) T. Matsumoto, Y. Fukuoka, A. Ichihara, Y. Mori, H. Shirahama, Y. Takahashi, and M. Watanabe, Bull. Chem. Soc. Jap., 37, 1716 (1964).

2) a) T. Matsumoto, H. Shirahama, A. Ichihara, Y. Fukuoka, Y. Takahashi, Y. Mori, and M. Watanabe, Tetrahedron, 21, 2671 (1965). b) T. C. McMorris and M. Anchel, J. Amer. Chem. Soc., 87, 1594 (1965). c) K. Nakanishi, M. Ohashi, M. Toda, and Y. Yamada, Tetrahedron, 21, 1231 (1965).

3) N. Harada and K. Nakanishi, Chem. Commun., 1970, 310.

4) N. Harada and K. Nakanishi, Acc. Chem. Res., 5, 257 (1972).

5) a) J. Tanaka, Ch. Katayama, F. Ogura, H. Tatemitsu, and M. Nakagawa, Chem. Commun., 1973, 21. b) S. F. Mason, ibid., 1973, 239.

6) J. M. Bijvoet, A. F. Feerdeman, and A. J. Van Bommel, Nature, 168, 271 (1951).

7) The atomic coordinates of the triacetate will be reported in a full paper.

We thank the Computing Center of Hokkaido University for calculations.

(Received October 4, 1973)