Communications to the Editor

[Chem. Pharm. Bull. 33(7)3062—3064(1985)]

THE CRYSTAL STRUCTURE OF 3,7,11,15-TETRAMETHYL-2,4,6,10,14-ALL TRANS-HEXADECAPENTAENOIC ACID (E-5166)

Kazuhide Ashizawa,[a] Yoshiyuki Kawakami,*,[a] Tadashi Sato,[a] Isao Yamatsu,[a] Toshihiko Hori[b] and Yasutoshi Muto[c]

Tsukuba Research Laboratories, Eisai Co., Ltd.,[a] Tokodai 5-1-3, Toyosato-machi, Tsukuba-gun, Ibaraki 300-26, Japan, Rigaku Denki Co., Ltd.,[b] Matsubara-cho, Akishima, Tokyo 196, Japan, and First Department of Internal Medicine, Gifu University School of Medicine,[c] 40 Tsukasa-machi, Gifu City 500, Japan

The crystal structure of 3,7,11,15-tetramethyl-2,4,6,10,14-all trans-hexadecapentaenoic acid (E-5166) was determined by the X-ray method. The compound crystallized in a space group $P\bar{1}$, with unit cell dimensions a=11.674(3), b=11.375(3), c=7.367(2) Å, α=106.57(2)°, β=81.75(2)°, γ=93.95(2)°. The final R-value was 0.062 for 2270 reflections.

KEYWORDS —— polyprenoic acid; X-ray analysis; crystal structure; molecular geometry; cellular retinoic acid-binding protein; vitamin A acid

3,7,11,15-Tetramethyl-2,4,6,10,14-all trans-hexadecapentaenoic acid, E-5166, is a newly synthesized polyprenoic acid derivative with potent cancer chemopreventive activity.[1] It has been found to have a strong binding affinity to the cellular retinoic acid-binding protein (CRABP) from rat testis.[2] This led us to investigate the stereochemistry of E-5166 compared with Vitamin A acid.[3] The present X-ray study was performed to determine the crystal structure and to establish the molecular geometry.

A single crystal of E-5166 was obtained by recrystallization from acetonitrile. Lattice parameters and reflection intensities were measured on a RIGAKU AFC-5R diffractometer with graphite-monochromated Mo Kα radiation. The intensities of 2270 independent reflections with $2\theta<55°$ were measured. The structure was solved by the direct method using MULTAN-82[4] and refined by the block-diagonal least-squares method with anisotropic temperature factors to an R-value of

0.062. Crystal data were as follows:

$C_{20}H_{30}O_2$, M.W. 302.46, triclinic, space group $P\bar{1}$, Z=2,
a=11.674(3), b=11.375(3), c=7.367(2) Å, α=106.57(2)°,
β=81.75(2)°, γ=93.95(2)°, V=927.5 $Å^3$, D=1.08 $g.cm^{-3}$.

A stereoscopic view of E-5166 is shown in Fig. 1. The interatomic distances are shown in Fig. 2. Fig. 3 shows the planarity of the molecule. The numbers in Fig. 3 give the deviations of the atoms (Å) above or below the least-squares plane formed by the ten atoms (C1-C10). The two molecules are associated in a dimer through intermolecular hydrogen-bonds between the two carboxyl groups. The conformation of E-5166 was an extended form with ca. 20 Å length. The detailed structure of E-5166 will be reported elsewhere.

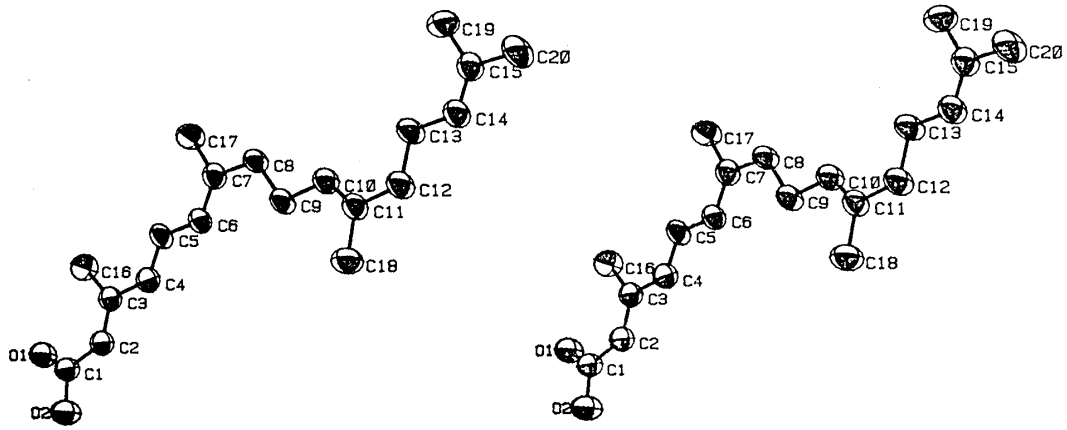

Fig. 1. Stereoscopic View of E-5166

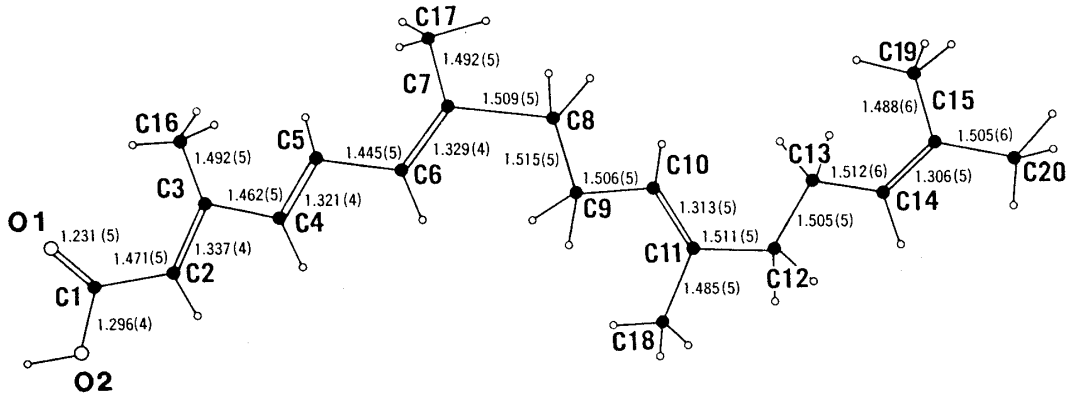

Fig. 2. Bond Lengths (Å) of E-5166

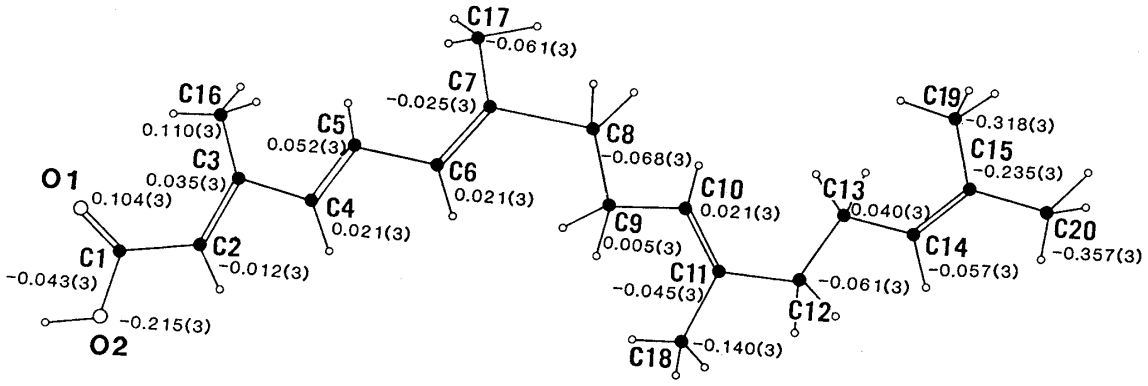

Fig. 3. Deviations of the Atom (Å) above (Plus) or below (Minus) the Least-Squares Plane Formed by the Ten Atoms (C1-C10) in E-5166

The authors are grateful to Professor Y. Iitaka of the University of Tokyo, for many helpful discussions and suggestions in this work. Thanks are also due to Dr. M. Goto of National Chemical Laboratory for Industry, for helpful discussion.

REFERENCES

1) Y. Muto, H. Moriwaki and M. Omori, Gann, 72, 974 (1981).

2) Y. Muto and H. Moriwaki, J. Natl. Cancer Inst., 73, 1389 (1984).

3) C. H. Stam, Acta Cryst., B28, 2936 (1972).

4) P. Main, " A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data," Univ. of York, England. (1982).

(Received May 23, 1985)