SHORT COMMUNICATION

STRUCTURE OF SQUAMOLONE, A NOVEL DIAZEPINE FROM *ANONA SQUAMOSA L.*

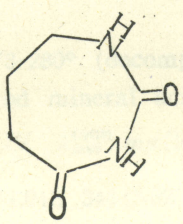
TSANG-HSIUNG YANG (楊藏雄) AND CHI-MING CHEN (陳繼明)

Department of Pharmaceutical Chemistry, Taipei Medical College
Taipei, Taiwan, CHINA.

(*Received July 12, 1972*)

The isolation and characterization of a number of alkaloids and diterpene from *Anona squamosa L.* (Anonaceae) was described in the previous papers[1,2]. These include anonaine, michelalbine, oxoushinsunine, anolobine, reticuline and (−)-kaur-16-en-19-oic acid. Oxoushinsunine (liriodenine) showed a significant tumor inhibitory activity against human carcinoma of the nasopharynx, reported recently by David Warthen et al[3]. And kaurenoic acid has proved to be a plant regulator activity[4] like gibberellins. The present communication deals with the isolation and structural elucidation of a new diazepine compound which we named squamolone. It was isolated from the acidic chloroform soluble fraction of the ethanol extract.

Squamolone, $C_5H_8N_2O_2$, is feebly acidic, soluble in water, chloroform, methanol, ethanol, acetone, crystallized from benzene as colorless prisms, mp. 145-146°, sublimable and is optical inactive. It forms white precipitates with Mayer's reagent in 6*N* sulfuric acid solution. The ultra-violet maximum absorption mealy at 209 *mu* (log ε 2.45) and infrared (KBr) bands at 1710 and 1735 cm^{-1} indicate the presence of a cyclic imide mojety[5,6]. The NMR spectrum of squamolone in deuterochloroform revealed two broad peaks of two imino or hydroxyl protons at 3.80 and 1.80τ, disappeared by deutero oxide. It resists to acetylation with acetic anhydride-pyridine and diazomethane methylation suggesting the existence of imino functions. The chemical shift of the three adjacent methylene protons exhibited six protons at 6.12τ (C—7, 2H, triplet, j=7 Hz), 7.35τ (C—5, 2H, quartet) and 7.70-8.20τ (C-6, 2H, multiplet).

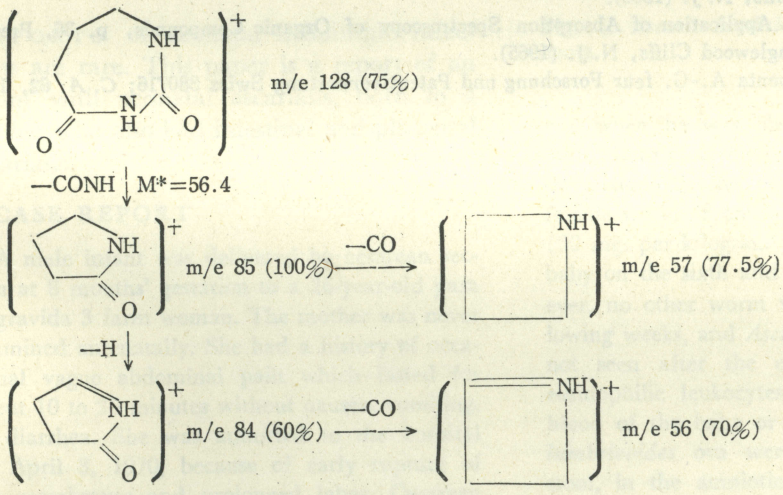


(I)

Squamolone was fused with sodium hydroxide pellet to liberate ammonia. Mild

J. Chinese Chem. Soc., 19, 149-151 (1972)

alkaline hydrolysis with 10% NaOH aq. solution and then acidified by conc.-HCl yielded a crystalline product from ethanol, mp. 175-176°, IR (nujol) cm^{-1}: 3200, 3350, 3400 (N—H stretching), 2500, 2650, 2750, 1700 (—COOH), 1650 (acyclic urea carbonyl)[6]. This cleavage product was found identical to the synthetic sample of gamma-ureidobutyric acid (literature mp. 175°)[7], prepared by fusing of gamma-aminobutyric acid and urea at 110-120°C. These evidences suggested the structure of squamolone to be the formula of I and this was supported by mass fragmentation. Its mass spectrum gave a molecular ion peak at m/e 128 corresponding to the molecular formula, $C_5H_8N_2O_2$. The metastable ion peak ($M^*=m_2^2/m_1$) at m/e 56.4 (M^*) indicated the fragment of m/e 85 (m_2) is formed in a one-step process from molecular ion m/e 128 (m_1), corresponding to the loss of one carboimino group. The principal mass fragmentation pattern is shown as follow.



The final proof of structure was carried out by chemical synthesis from gamma-aminobutyric acid (gammalon). Condensation of gammalon with urea at 110-120° and then cyclization in the presence of phosphorousoxychloride afforded a colorless prisms, mp. 145-146° (benzene) of I (36.7% yield). This synthetic specimen shows superimposable with the natural squamolone in IR ($CHCl_3$), NMR ($CDCl_3$) comparison and no depression of their mixed melting point.

$$\left.\begin{matrix} NH_2CH_2CH_2CH_2COOH \\ NH_2CONH_2 \end{matrix}\right\} \longrightarrow NH_2CONHCH_2CH_2CH_2COOH \longrightarrow I$$

These above spectral and chemical evidences definitely proved that the structure of squamolone is represented by the formula I, and it has a unique structure feature of diazepine skeleton occurring in nature.

We express our gratitude to Emeritous Professor M. Tomita, Koyto University for the microanalytical and NMR data, to Dr. T. J. Lin, Purdue University for the mass

spectrum and Mr. J. I. Liu, Chemical Research Center, National Taiwan University for the NMR spectrum. The authors also thank to Taiwan Daiichi Sheiyaku Kaisha Ltd., for the generous gift of sample, gammalon. This research was supported in part by the National Science Council of the Republic of China.

REFERENCES

(1) T. H. Yang and C. M. Chen, *J. Chinese Chem. Soc.*, **17**(4), 243 (1970).
(2) T. H. Yang, C. M. Chen, J. L. Chang and K. W. Chung, *J. Taiwan Pharm. Assoc.*, **23**(1), 8 (1971).
(3) David Warthen, Ernest L. Gooden and Martin Jacobson, *J. Pharm. Sci.*, **58**(5), 637 (1968).
(4) Yutaka Murakami, *Shokubutsugaku Zasshi*, 81, 100 (1968); *C. A.* **68**, 113533y (1968).
(5) Daniel J. Pasto and Carl R. Johnson, Organic Structure Determination, p. 92, Prentice-Hall Inc., Englewood Cliffs, N. J. (1969).
(6) John R. Dyer, Application of Absorption Spectroscopy of Organic Compounds, p. 36, Prentice-Hall Inc., Englewood Cliffs, N. J. (1965).
(7) Kurt Kahr, Inventa A.-G. feur Forschung und Patentiverwertung Swiss 380716; *C. A.* **62**, 16069g (1965).