Tetrahedron Letters No. 27, pp. 1881-1885, 1963. Pergamon Press Ltd.
Printed in Great Britain.

THE STRUCTURE OF ALBONOURSIN

A.S. Khokhlov, G.B. Lokshin
Institute for Chemistry of Natural Products,
Academy of Sciences of the USSR and Institute
of Antibiotics, Ministry of Health of the USSR

(Received 13 September 1963)

ALBONOURSIN was discovered during isolation and purification of the antifungal antibiotics albofungin (1) and nystatin (2) produced by two actinomycetes, Streptomyces albus var. fungatus and Streptomyces noursei. The identity of the substance obtained from the two different sources was established by direct comparison and it is to them that it owes its name (3).

Also Brown and Kelley isolated from a Streptomyces noursei mutant, producer of the antibiotic phalamycin, "component 2", similar to albonoursin (4-9). Careful comparison of a sample of "component 2", kindly sent to us by Dr. Brown, with albonoursin left no doubt as to their identity.

While studying the antitumor antibiotic B-73 produced by Streptomyces albulus, Rao and Cullen isolated the substance B-73, which also turned out to be identical with albonoursin (10, 11).

On the basis of elementary analysis and Rast mo-

lecular weight determination albonoursin had been tentatively ascribed the molecular formula $C_{23}H_{25}N_3O_3$, (3), but potentiometric titration with tetrabutylammonium hydroxide in pyridine showed the molecular weight to be less by a factor of 1.5 and as a result the formulas first of $C_{15}H_{16}N_2O_2$ and then $C_{16}H_{18}N_2O_2$ were proposed for this compound (8, 9).

Careful molecular weight determination by mass spectroscopy unequivocally showed it to be 256 and hence that the correct formula was $C_{15}H_{16}N_2O_2$.

Albonoursin does not react with phenylhydrazine, on heating does not undergo acylation and is not methylated by dimethyl sulfate. It is comparatively easily brominated.

In the alkaline hydrolyzate of albonoursin were identified benzaldehyde, isobutyraldehyde and ammonia. The same aldehydes are formed on degradation of its dibromo derivative $C_{15}H_{14}Br_2N_2O_2$ /which on the basis of the formerly accepted molecular weight had been described the formula $C_{23}H_{22}Br_3N_3O_3$ (12)/.

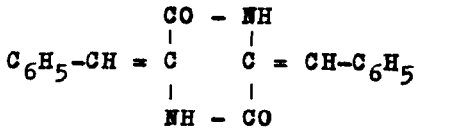
On acid hydrolysis (glacial acetic acid + HCl, 24 hrs., 105°) there were isolated 2 moles of ammonia, phenylpyruvic acid, isovalerylformic acid (identified as the 2,4-dinitrophenylhydrazone) and acetone, probably arising from further degradation of the latter compound. The degradation therefore evidently proceeds according to the equation:

$$C_{15}H_{16}N_2O_2 + 4\ H_2O = C_9H_8O_3 + C_6H_{10}O_3 + 2\ NH_3$$

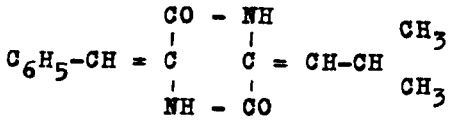
From the crude albonoursin preparation there was isolated a substance $C_{18}H_{14}N_2O_2$ (ca 15% from St. albus and ca 30% from St. noursei), which closely resembled albonoursin in a number of properties.

This substance gives 2 moles of ammonia and 2 moles of phenylpyruvic acid on acid hydrolysis. Hence it was assumed to be 3,6-dibenzylidene-2,5-diketopiperazine/I/ and this was confirmed by direct comparison with a synthetic specimen prepared according to Sasaki (13).

The close similarity between albonoursin and substance /I/ and a consideration of the degradation products of the former allows one to ascribe it the structure of 3-benzylidene-6-isobutylene-2,5-diketopiperazine /II/.



/I/



/II/

REFERENCES:

1. A.S. Khokhlov, G.S. Rosenfel'd, V.M. Baikina, B.Z. Cherches, N.O. Blinov, I.V. Borisenko. Tesisy dokladov Vtoroĭ Nauchnoĭ Konferentsii Leningradsko-

go Nauchno-issledovatel'skogo Instituta Antibiotikov. Leningrad, 11 (1960).

2. D.M. Trakhtenberg, E.I. Rodionovskaya, Z.V. Gordina, L.I. Rostovtseva, G.I. Kleiner, A.M. Nagle. Antibiotiki 5 No.5 (1960).
3. G.S. Rosenfel'd, L.I. Rostovtseva, V.M. Baikina, D.M. Trakhtenberg, A.S. Khokhlov. Antibiotiki 7 No.3 (1963).
4. R. Brown, Ch. Kelley. Annual Report of the New York State Department of Health. Albany, 10 (1957).
5. R. Brown, Ch. Kelley. Annual Report of the New York State Department of Health. Albany, 47 (1958).
6. R. Brown, Ch. Kelley. Annual Report of the New York State Department of Health. Albany, 52 (1959).
7. R. Brown, Ch. Kelley. Annual Report of the New York State Department of Health. Albany, 50 (1960).
8. R. Brown, Ch. Kelley. Annual Report of the New York State Department of Health. Albany, 40 (1961).
9. Ch. Kelley. Abstract of a Thesis Submitted to the Faculty of Department of Chemistry in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy. New York (1960).

10. K.V. Rao, W.P. Cullen. J. Amer. Chem. Soc. 82 1127 (1960).

11. R. Brown. Private Communication.

12. A.S. Khokhlov, G.B. Lokshin. Doklady Akad. Nauk USSR 148 1320 (1963).

13. T. Sasaki. Ber. 54 I 164 (1921)