SYNTHESES OF FLUOPSINS

Sir:

In a recent report we described the isolation and structural elucidation of new antibacterial substances, fluopsins C and F[1]. This communication reports the syntheses of fluopsin F and its analogous compounds.

A solution of 2.3 g of potassium dithioformate in 20 ml of methanol was added dropwise to a solution of 835 mg of N-methylhydroxylamine hydrochloride in 10 ml of methanol and 10 ml of chloroform. During the reaction 4 N hydrochloric acid was also added to keep the mixture acidic. After stirring for 10 minutes, nitrogen was bubbled into the solution to remove hydrogen sulfide. To the resulting solution without isolation of fluopsin (N-methyl-N-thioformylhydroxylamine) was added 120 ml of chloroform and 1.5 g of nickel sulfate heptahydrate dissolved in 20 ml of water. After the mixture was shaken for 5 minutes, the chloroform layer was separated, washed, and dried. Evaporation of the solvent afforded 504 mg of red purple crystals, which were crystallized from ethanol to give 418 mg of needles. Its infrared and NMR spectra were identical with those of authentic fluopsin N[1].

Fuopsin, 20.9 mmol in 1.25 liter of chloroform, and ferric chloride hexahydrate, 20.7 g in 0.5 liter of water, were shaken vigorously for 5 minutes. The aqueous layer, which was acidic and purple blue, was extracted with chloroform. After the resulting aqueous layer was diluted with 0.5 liter of water and neutralized with saturated aqueous sodium bicarbonate under ice-cooling, the blue-colored material was extracted with chloroform (200×3 and 150×4 ml). The chloroform extract (1.2 liter) was washed with small amount of water and evaporated to

Table 1.

Fluopsins	Formulae*	Decomposition point (°C)	Color	ν_{max} in KBr (cm^{-1})	Reagents
Fluopsin A	$C_2H_4NOSAg \cdot H_2O$	>300°	gray	1554, 1380, 1150, 927, 871, 576	$AgNO_3$
〃 C	$C_4H_8N_2O_2S_2Cu$	182°	dark brown	1580, 1458, 1152, 1090, 908, 888, 875, 683	$CuSO_4 \cdot 5H_2O$
〃 CA	$C_4H_8N_2O_2S_2Ca$	>300°	white	1576, 1568, 1159, 1016, 1003, 928, 887, 597	$Ca(OH)_2$
〃 CD	$C_4H_8N_2O_2S_2Cd$	>300°	white	1560, 1356, 1149, 1110, 928, 877, 866, 586	$Cd(OAc)_2 \cdot 2H_2O$
〃 CO	$C_6H_{12}N_3O_3S_3Co$	>300°	black	1581, 1142, 1093, 890, 888, 828, 621	$CoCl_2 \cdot 6H_2O$
〃 CR	$C_6H_{12}N_3O_3S_3Cr$	>300°	greenish black	1595, 1144, 900, 886, 644	$CrCl_3 \cdot 6H_2O$
〃 F	$C_6H_{12}N_3O_3S_3Fe$**	218°	dark purple	1561, 1456, 1155, 916, 893, 868, 610, 601	$FeCl_3 \cdot 6H_2O$
〃 H	$C_4H_8N_2O_2S_2Hg$	>300°	yellow	1595, 1445, 1142, 904, 868, 548	$HgCl_2$
〃 N	$C_4H_8N_2O_2S_2Ni$	212°	purple red	1592, 1442, 1153, 904, 880, 810, 698, 643	$NiSO_4 \cdot 7H_2O$
〃 P	$C_6H_{12}N_3O_3S_3Pt$	>300°	brown	1585, 1445, 1128, 885, 875, 655	$H_2PtCl_6 \cdot 6H_2O$
〃 PD	$C_4H_8N_2O_2S_2Pd$	>300°	dark brown	1593, 1440, 1133, 901, 893, 685, 632	$PdCl_2$
〃 H	$C_6H_{12}N_3O_3S_3Rh$	>300°	orange	1590, 1425, 1126, 907, 871, 659	$RhCl_3 \cdot 3H_2O$
〃 S	$C_2H_4NOSSnCl$	173°	pale yellow	1587, 1443, 1146, 906, 882, 837, 616	$SnCl_2 \cdot 2H_2O$
〃 Z	$C_4H_8N_2O_2S_2Zn$	>300°	colorless	1565, 1450, 1146, 918, 880, 854, 605	$Zn(OAc)_2 \cdot 2H_2O$

* All the fluopsins except fluopsins C, F and N are insoluble in ordinary solvents and can not be recrystallized. These formulae, although they have not given satisfactory analytical values, are estimated on the basis of their elementary analyses and infrared spectra which show no ν_{OH} except fluopsin A.

** In the previous paper[1] we made an error in analytical value of Fe. By atomic absorption analysis, 20% of Fe were found. The calculated value is 17.1%.

give a dark purple residue, which was treated with acetonitrile and insoluble material was removed by filtration. The filtrate was stood overnight after chloroform was added. Thus 1.12 g of dark purple prisms, fluopsin F, were obtained. Its infrared spectrum was identical with that of the fermentation product.

By the similar procedure more 12 fluopsin complexes were prepared, the infrared absorptions and color of which were shown in Table 1.

KUNIKATSU SHIRAHATA
TADATOSHI HAYASHI
ISAO MATSUBARA

Tokyo Research Laboratory,
Kyowa Hakko Kogyo Co. Ltd.,
Machida, Tokyo, Japan

(Received November 25, 1970)

Reference

1) SHIRAHATA, K.; T. DEGUCHI, T. HAYASHI, I. MATSUBARA & T. SUZUKI: The structures of fluopsins C and F. J. Antibiotics 23: 546~550, 1970