Structure Elucidation of MM 17880, a New Fused β-Lactam Antibiotic isolated from *Streptomyces olivaceus*; a Mild β-Lactam Degradation Reaction

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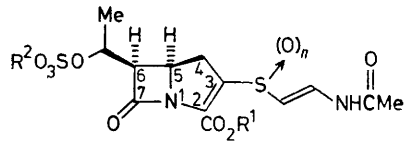
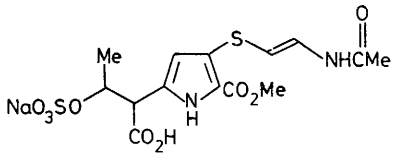
Summary The structure of the olivanic acid derivative (**1**) has been confirmed by a novel β-lactam degradation in dimethyl sulphoxide; application of this reaction has resulted in the structure elucidation of a new antibiotic, MM 17880.

IN an earlier communication[1] we described the spectroscopic data to support structures (**1**) and (**2**) for two new, β-lactam antibiotics isolated from *Streptomyces olivaceus*. We now report a novel transformation which confirms structure (**1**) and which enabled us to elucidate the structure (**12**) of a closely related, co-occurring metabolite, MM 17880.[2]



(1) $R^1 = R^2 = H$; $n = 0$
(2) $R^1 = R^2 = H$; $n = 1$
(3) $R^1 = Me$; $R^2 = Na$; $n = 0$



(4)

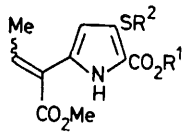
Alkylation of the disodium salt of (**1**) with methyl iodide in dimethylformamide gave the monomethyl ester (**3**; 65%).† When (**3**) was heated in dimethyl sulphoxide (70 °C, 2 h) an essentially quantitative transformation occurred‡ to give a product which, on the basis of ^{13}C (Table) and ^1H n.m.r. spectra, was assigned structure (**4**). Confirmation of this structure was obtained by successive treatment with diazomethane and 1,5-diazabicyclo[5.4.0]-undec-5-ene (DBU) to yield the less-polar pyrrole (**5**) [25% from (**3**)],† M^+ 338·0934 ($C_{15}H_{18}N_2O_5S$).§ The mass spectral fragmentation pattern was particularly informative and gave, *inter alia*, ions at *m/e* 255 and 84, formally corresponding to (**7**) and (**9**).

TABLE. ^{13}C N.m.r. spectra of (**3**) and (**4**).[a]

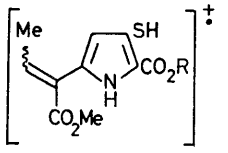
(3)		(4)	
Chemical shift	Assignment	Chemical shift	Assignment
176 (s)	C=O	171 (s)	C=O
167 (s)	C=O	167 (s)	C=O
161 (s)	C=O	160 (s)	C=O
152 (s)	>C=	133 (s)	Pyrrole-C
133 (d)	=CH.NH–	130 (d)	=CH.NH–
121 (s)	>C=	126 (s)	Pyrrole-C
97 (d)	=CH.S–	115 (s)	Pyrrole-C
68 (d)	$-CHOSO_3^-$	108 (d)	Pyrrole-CH
58 (d)	5(6)-CH	101 (d)	=CH.S–
53 (d)	6(5)-CH	72 (d)	$-CHOSO_3^-$
52 (q)	$-OCH_3$	50·8 (q)	–OMe
37 (t)	4-CH_2	50·5 (d)	$-CH(CO_2H)$
23 (q)	–CO.*Me*	23 (q)	–CO.*Me*
20 (q)	O–CH.*Me*	19 (q)	OCH–*Me*

[a] In $(CD_3)_2SO$, rel. to dioxan internal standard.

The utility of the above reaction was demonstrated by the structure elucidation of a new antibiotic, MM 17880, which was also isolated from *Streptomyces olivaceus* as the disodium salt; ν_{max} 1750 (β-lactam CO), 1590—1650 (amide CO, CO_2^-), and 1220—1270 cm^{-1} (OSO_3^-); λ_{max} (H_2O) 298 nm (ε 8410). The ^1H n.m.r. spectrum (D_2O) revealed two methyl groups similar to those in both (**1**) and (**2**), but the *trans*-disubstituted double bond was absent. The region δ 2·8—3·75 was complex but appeared to contain four protons in excess of those observed in the spectra of (**1**) and (**2**). These data, together with the absence of a short wavelength absorption in the u.v. spectrum, suggested that MM 17880 was the dihydro-derivative of either (**1**) or (**2**).

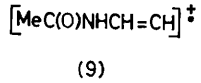


(5) R^1 = Me
R^2 = –CH^t=CHNHC(O)Me

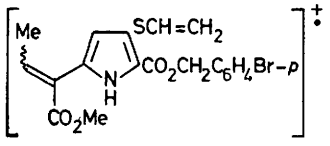


(7) R = Me
(8) R = $CH_2C_6H_4Br$-*p*

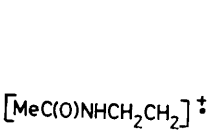
(6) $R^1 = CH_2C_6H_4Br$-*p*
$R^2 = -CH_2CH_2NHC(O)Me$



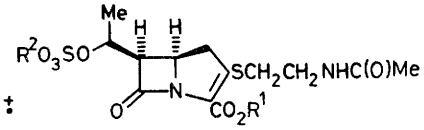
(9)



(10)



(11)



(12) $R^1 = R^2 = H$
(13) $R^1 = -CH_2C_6H_4Br$-*p*
R^2 = Na

Alkylation of the disodium salt of MM 17880 with *p*-bromobenzyl bromide gave the mono-ester (**13**)† which, after (a) heating in dimethyl sulphoxide (70 °C, 2 h), (b) esterification with diazomethane, and (c) treatment with DBU, gave the pyrrole (**6**),† M^+ 494·0515 ($C_{21}H_{23}BrN_2O_5S$).§ The mass spectrum of (**6**) contained ions formally corresponding to (**8**), (**10**), and (**11**), and on the basis of this evidence, MM 17880 was assigned structure (**12**). The *cis* arrangement of the protons on the β-lactam ring was inferred from the appearance (dd, *J* 9·5 and 6·0 Hz) of the C-6 proton. Both coupling constants are incompatible with a *trans*-substituted β-lactam, whereas the 6·0 Hz coupling was similar to that observed in the n.m.r. spectra of (**1**) and (**2**).

MM 17880, like (**1**) and (**2**), inhibits a wide range of β-lactamases and also possesses potent antibacterial properties.

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† Spectral properties were in accord with the structure.

‡ When the reaction was monitored by both ^1H and ^{13}C n.m.r. spectroscopy, formation of (**4**) alone was observed as a single stereoisomer.

§ This product was obtained as an inseparable mixture of *E*- and *Z*-isomers.

[1] A. G. Brown, D. F. Corbett, A. J. Eglington, and T. T. Howarth, *J.C.S. Chem. Comm.*, 1977, 523.
[2] S. Box and J. D. Hood, Belgian P. 839–324.