NOVEL CYTOCIDAL COMPOUNDS, OXOPROPALINES FROM *Streptomyces sp.* G324 PRODUCING LAVENDAMYCIN

II. PHYSICO-CHEMICAL PROPERTIES AND STRUCTURE ELUCIDATIONS

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Novel cytocidal compounds designated oxopropalines A, B, D, E and G were isolated from the fermentation of an actinomycete named *Streptomyces* sp. G324, a strain that also produced an antitumor antibiotic, lavendamycin. All these compounds possessed a β-carboline chromophore. The structures of the oxopropalines were elucidated by several NMR spectral analyses and other spectroscopic experiments.

Oxopropalines, consisting of 5 components, A (**1**), B (**2**), D (**3**), E (**4**) and G (**5**) (Fig. 1), are novel cytocidal compounds with a β-carboline chromophore. These compounds were isolated from the culture of an actinomycete strain G324. The strain was found to produce an antitumor antibiotic, lavendamycin[1], also having a β-carboline moiety. The taxonomic studies of the producing organism, fermentation, isolation and biological activities have been described in a previous paper[2]. In the present report, we describe the physico-chemical properties and structure elucidation of the oxopropalines.

Physico-chemical Properties

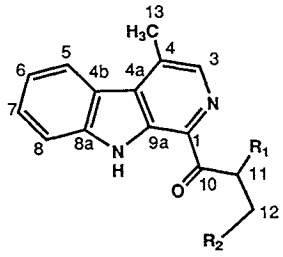
The physico-chemical properties of oxopropalines (Fig. 1) are summarized in Table 1. All oxopropalines were obtained as pale yellow powders. They are soluble in methanol and acetonitrile and insoluble in *n*-hexane and water. The UV absorption spectra of the oxopropalines in methanol revealed the characteristic common chromophore as a conjugated β-carboline, found also in lavendamycin (Fig. 2) and other β-carboline compounds[3~5]. The IR spectra of these compounds showed the expected absorption of a hydroxy group (3380~3450 cm^{-1}) and an α,β-unsaturated ketone group (1665~1680 cm^{-1}).

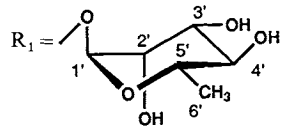
Structure Elucidation

Oxopropaline A (**1**) has the molecular formula $C_{21}H_{24}N_2O_7$ on the basis of the HRFAB-MS [*m/z* 417.1671 $(M+H)^+$; calcd. 417.1662] and NMR spectral analyses. The UV spectrum of **1** showed the presence of a conjugated β-carboline chromophore (λ_{max} 220, 265, 288 and 381 nm in CH_3OH), directly comparable with that of harman, a simple β-carboline compound, which was a commercially available authentic sample from Aldrich Chem. Co. In the IR spectrum (Fig. 3), the broad absorption band at 3380 cm^{-1} and the strong absorption band at 1675 cm^{-1} suggested the existence of a polyhydroxyl group and an α,β-unsaturated ketone group, respectively.

The ^{13}C NMR spectrum of **1** in CD_3OD (Table 2) and the DEPT experiment revealed the presence of twenty-one carbons as one carbonyl carbon, eleven sp^2 hybridized carbons, six oxygenated methines,

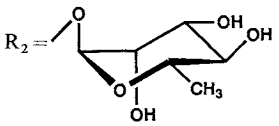
Fig. 1. Structures of oxopropalines A, B, D, E and G, and lavendamycin.





R_2 = –OH — Oxopropaline A (**1**)

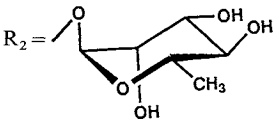
R_1 = –OH



Oxopropaline B (**2**)

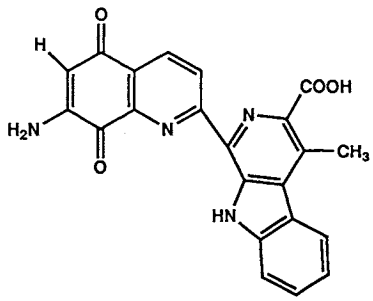
R_1 = –OH; R_2 = –OH — Oxopropaline D (**3**)

R_1 = H



Oxopropaline E (**4**)

R_1 = H; R_2 = –OH — Oxopropaline G (**5**)



Lavendamycin (**6**)

one oxygenated methylene and two methyl carbons. In addition, the ^{1}H NMR spectrum (Fig. 4 and Table 3), ^{1}H-^{1}H COSY and ^{13}C-^{1}H HETCOR spectra established the partial structures shown in Fig. 5. The sp^2 hybridized carbons (C-1 ~ C-9a) and the related five aromatic protons (δ 8.32, δ 8.27, δ 7.75, δ 7.60 and δ 7.35) revealed the presence of a disubstituted C-ring in the β-carboline skeleton. One substituent included three intercoupled protons (δ 5.97, δ 4.03 and δ 3.90) on oxygenated carbons, suggesting that an oxygenated methine (δ_C 80.5, C-11)–oxygenated methylene (δ_C 63.9, C-12) group was linked to the chromophore through the carbonyl carbon (δ_C 200.6, C-10). Hence, the methyl group (δ_C 18.0, δ_H 2.94) was directly substituted for a proton on the C-ring. The remaining six carbons (δ 103.6, δ 73.8, δ 72.5, δ 72.2, δ 70.3 and δ 17.6) formed a sugar moiety. The ^{1}H-^{1}H coupling constants of the sugar moiety in the ^{1}H NMR spectrum and assignments of the chemical shifts in the ^{13}C NMR spectrum suggested that the sugar was α-rhamnose.

The position of each partial structure and the full assignments of ^{13}C and ^{1}H NMR spectra were

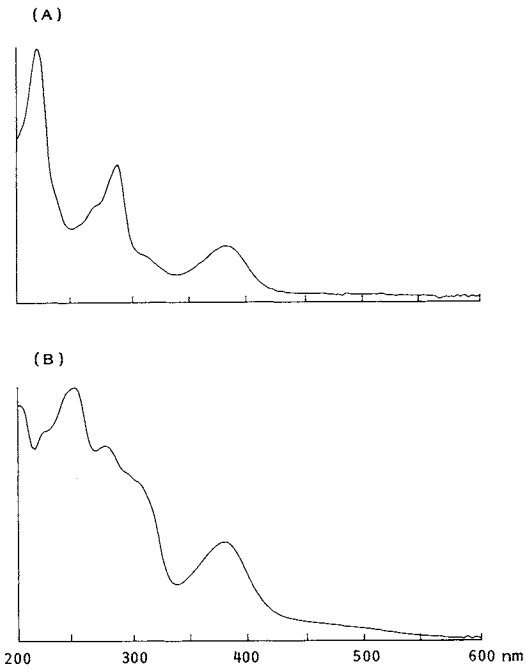
Table 1. Physico-chemical properties of oxopropalines A, B, D, E and G.

	A	B	D	E	G
Appearance	Pale yellow powder	Pale yellow powder	Pale yellow powder	Pale yellow powder	Pale yellow powder
$[\alpha]_D^{20}$ (CH_3OH)	+56° (*c* 0.05)	−39° (*c* 0.02)	+30° (*c* 0.1)	−39° (*c* 0.02)	Optically inactive
Molecular formula	$C_{21}H_{24}N_2O_7$	$C_{21}H_{24}N_2O_7$	$C_{15}H_{14}N_2O_3$	$C_{21}H_{24}N_2O_6$	$C_{15}H_{14}N_2O_2$
HRFAB-MS (*m/z*) $(M+H)^+$					
Calcd:	417.1662	417.1662	271.1082	401.1713	255.1133
Found:	417.1671	417.1674	271.1086	401.1713	255.1141
UV (CH_3OH) λ_{max} nm (ε)	220 (43,800), 265 (15,500), 288 (22,800), 381 (9,600)	218 (44,900), 265 (15,100), 287 (22,300), 378 (8,000)	219 (31,000), 264 (10,600), 287 (16,300), 381 (6,200)	218 (32,800), 262 (11,000), 284 (16,800), 377 (6,300)	218 (33,700), 263 (12,500), 284 (18,900), 375 (7,200)
IR (KBr) cm^{-1}	3380, 1675	3450, 1680	3430, 1680	3430, 1675	3540, 3340, 1665
TLC[a] Rf value[b]	0.06	0.13	0.53	0.24	0.74
Rf value[c]	0.10	0.22	0.57	0.33	0.76

[a] Kieselgel 60 F_{254} Art. No. 5715.
[b] TLC solvent system ($CHCl_3$ - MeOH, 9 : 1).
[c] TLC solvent system (CH_2Cl_2 - MeOH, 9 : 1).

Fig. 2. UV spectra of oxopropaline D and lavendamycin in CH_3OH.

(A) Oxopropaline D, (B) lavendamycin.



deduced from the ^1H-detected multiple-bond heteronuclear multiple quantum coherence (HMBC) spectrum, as summarized in Fig. 6. The long range couplings from 5-H (δ 8.27) to C-4a (δ 131.1), C-7 (δ 129.6) and C-8a (δ 143.2), from 6-H (δ 7.35) to C-4b (δ 122.2) and C-8 (δ 113.5), from 7-H (δ 7.60) to C-5 (δ 124.5) and C-8a (δ 143.2) and from 8-H (δ 7.75) to C-6 (δ 121.8) and C-4b (δ 122.2) supported the structure of the A- and B-ring moieties. The next long range couplings from 13-H_3 (δ 2.94) to C-4a (δ 131.1), C-4 (δ 134.6) and C-3 (δ 140.1) and from H-3 (δ 8.32) to C-4a (δ 131.1) and C-1 (δ 134.2) proved that the methyl group was substituted at C-4 and another substituent was linked at C-1. The HMBC spectrum of the remaining part showed long range couplings from 11-H (δ 5.97) to C-12 (δ 63.9), C-10 (δ 200.6) and C-1′ (δ 103.6), from 12-Ha (δ 3.90) to C-11 (δ 80.5), from 1′-H (δ 4.96) to C-11 (δ 80.5), C-3′ (δ 72.5) and C-5′ (δ 70.3), from 2′-H (δ 4.04) to C-3′ (δ 72.5) and C-4′ (δ 73.8), from 3′-H (δ 3.80) to C-4′ (δ 73.8), from 4′-H (δ 3.33) to C-3′ (δ 72.5), C-5′ (δ 70.3) and C-6′ (δ 17.6) and from 6′-H_3 (δ 0.85) to C-4′ (δ 73.8) and C-5′ (δ 70.3). The results of the HMBC experiment on the remaining part indicated that α-rhamnose was bound by a glycosidic linkage to the substituent at C-11, and the rhamnosyl substituent was connected to the β-carboline skeleton through the carbonyl carbon (C-10) at C-1.

The products of **1** treated with 1 N HCl at 100°C for 1.5 hours supported the above investigation.

Fig. 3. IR spectrum of oxopropaline A in KBr.

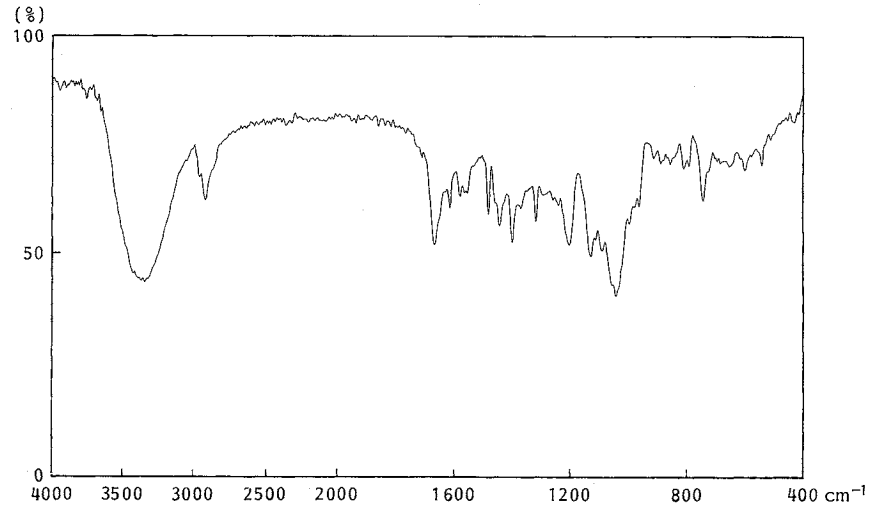


Table 2. ^{13}C NMR data of oxopropalines A, B, D, E and G.

Position	A	B	D	E	G
1	134.2 s	133.4 s	133.8 s	135.3 s	135.3 s
3	140.1 d	139.7 d	140.1 d	139.7 d	139.7 d
4	134.6 s	134.5 s	134.9 s	134.1 s	134.1 s
4a	131.1 s	131.0 s	131.5 s	131.1 s	131.1 s
4b	122.2 s	122.0 s	122.4 s	122.2 s	122.1 s
5	124.5 d	124.4 d	124.8 d	124.5 d	124.5 d
6	121.8 d	121.6 d	122.0 d	121.6 d	121.7 d
7	129.6 d	129.5 d	129.9 d	129.6 d	129.6 d
8	113.5 d	113.3 d	113.6 d	113.4 d	113.3 d
8a	143.2 s	143.1 s	143.5 s	143.2 s	143.2 s
9a	136.3 s	136.1 s	136.6 s	136.0 s	136.0 s
10	200.6 s	201.2 s	202.2 s	202.4 s	203.1 s
11	80.5 d	74.3 d	76.6 d	38.7 t	41.8 t
12	63.9 t	69.7 t	66.5 t	64.1 t	58.8 t
13	18.0 q	17.8 q	18.2 q	17.9 q	17.9 q
1′	103.6 d	101.7 d		101.8 d	
2′	72.2 d	71.8 d		72.3 d	
3′	72.5 d	72.0 d		72.3 d	
4′	73.8 d	73.7 d		73.9 d	
5′	70.3 d	71.3 d		69.8 d	
6′	17.6 q	17.8 q		17.9 q	

Measured at 100 MHz in CD_3OD; ppm from TMS.

The Rf value of the sugar moiety from **1** was identified as that of the authentic rhamnose on TLC. Acidic methanolysis of **1** followed by per-*p*-bromobenzoylation was performed to determine the absolute configuration of rhamnose from **1**, as shown in Scheme[6]. The derived 2,3,4-tri-*O*-(*p*-bromobenzoyl)-1-α-*O*-methyl-rhamnose was characterized by CD spectroscopy (Fig. 7). The CD spectrum of the rhamnose derivative was identical to that of the same derivative from authentic L-(+)-rhamnose. The structure of oxopropaline A (**1**) is shown in Fig. 1.

Oxopropaline B (**2**) has the molecular formula $C_{21}H_{24}N_2O_7$, which is the same as that of oxoplopaline

Fig. 4. ^1H NMR spectra of oxopropalines A and D in CD_3OD.

(A) Oxopropaline A, (B) oxopropaline D.

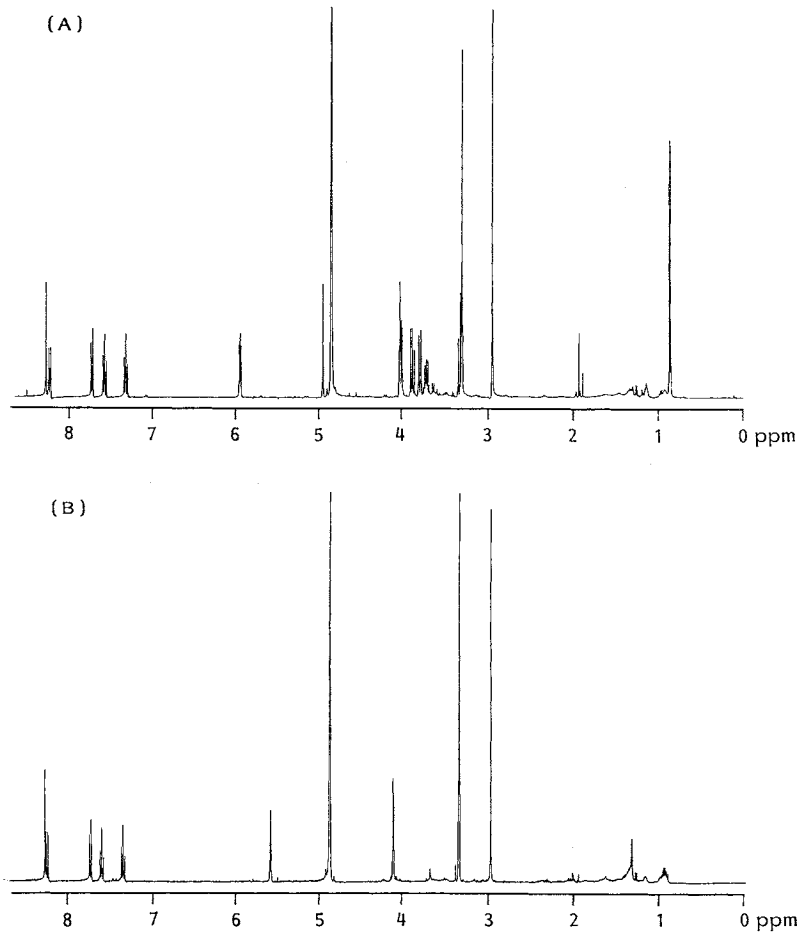


Table 3. ^1H NMR data for oxopropalines A, B, D, E and G.

Position	A	B	D	E	G
3-H	8.32 (s)	8.31 (s)	8.30 (s)	8.26 (s)	8.27 (s)
5-H	8.27 (d, 8.0)	8.27 (d, 8.0)	8.27 (d, 8.0)	8.24 (d, 7.9)	8.25 (d, 8.1)
6-H	7.35 (dd, 8.0, 7.2)	7.36 (dd, 8.0, 7.2)	7.35 (dd, 8.0, 7.2)	7.33 (dd, 7.9, 7.3)	7.34 (dd, 8.1, 7.1)
7-H	7.60 (dd, 8.3, 7.2)	7.61 (dd, 8.2, 7.2)	7.61 (dd, 8.2, 7.2)	7.59 (dd, 8.2, 7.3)	7.59 (dd, 7.1, 7.1)
8-H	7.75 (d, 8.3)	7.74 (d, 8.2)	7.74 (d, 8.2)	7.72 (d, 8.2)	7.72 (d, 7.1)
11-Ha	5.97 (dd, 7.0, 3.9)	5.72 (dd, 5.2, 3.3)	5.59 (t, 4.1)	3.61 (m)	3.54 (t, 6.2)[a]
11-Hb	—	—	—	3.94 (m)	—
12-Ha	3.90 (dd, 11.8, 7.0)	4.01 (dd, 10.4, 5.2)	4.10 (d, 4.1)[a]	3.92 (ddd, 9.8, 6.4, 5.3)	4.08 (t, 6.2)[a]
12-Hb	4.03 (dd, 11.8, 3.9)	4.21 (dd, 10.4, 3.3)	—	4.24 (ddd, 9.8, 7.2, 5.5)	—
13-H_3	2.94 (s)	2.95 (s)	2.94 (s)	2.92 (s)	2.92 (s)
1′-H	4.96 (d, 1.5)	4.56 (d, 1.5)	—	4.76 (d, 1.6)	—
2′-H	4.04 (dd, 3.4, 1.5)	3.61 (dd, 3.5, 1.5)	—	3.73 (dd, 3.4, 1.6)	—
3′-H	3.80 (dd, 10.0, 3.4)	3.58 (dd, 9.1, 3.5)	—	3.55 (dd, 9.5, 3.4)	—
4′-H	3.33 (dd, 10.0, 9.5)	3.30 (dd, 9.5, 9.1)	—	3.32 (dd, 9.5, 9.5)	—
5′-H	3.73 (dq, 9.5, 6.2)	3.72 (dq, 9.5, 6.2)	—	3.64 (dq, 9.5, 6.3)	—
6′-H_3	0.85 (d, 6.2)	1.24 (d, 6.2)	—	1.20 (d, 6.3)	—

Measured at 400 MHz, in CD_3OD; ppm from TMS.

[a] Two protons as methylene signal.

Fig. 5. Partial structures and chemical shifts δ_H (δ_C) in CD_3OD of oxopropaline A.

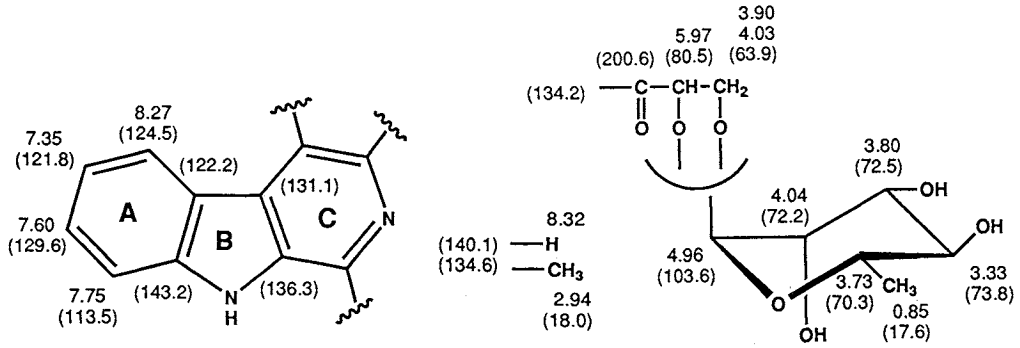
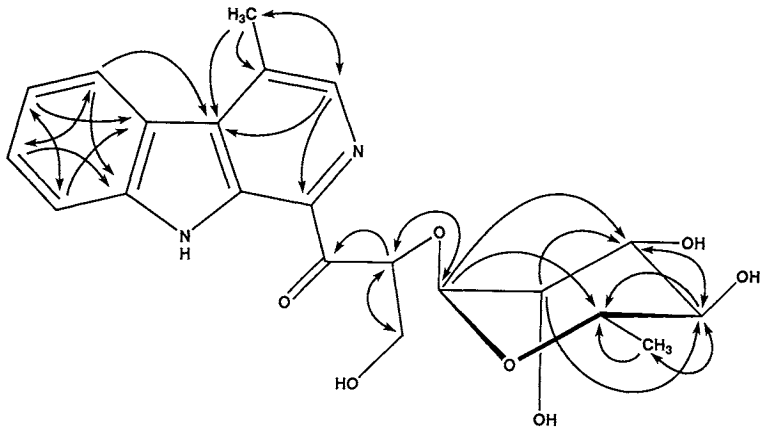


Fig. 6. Summary of HMBC experiment of oxopropaline A.

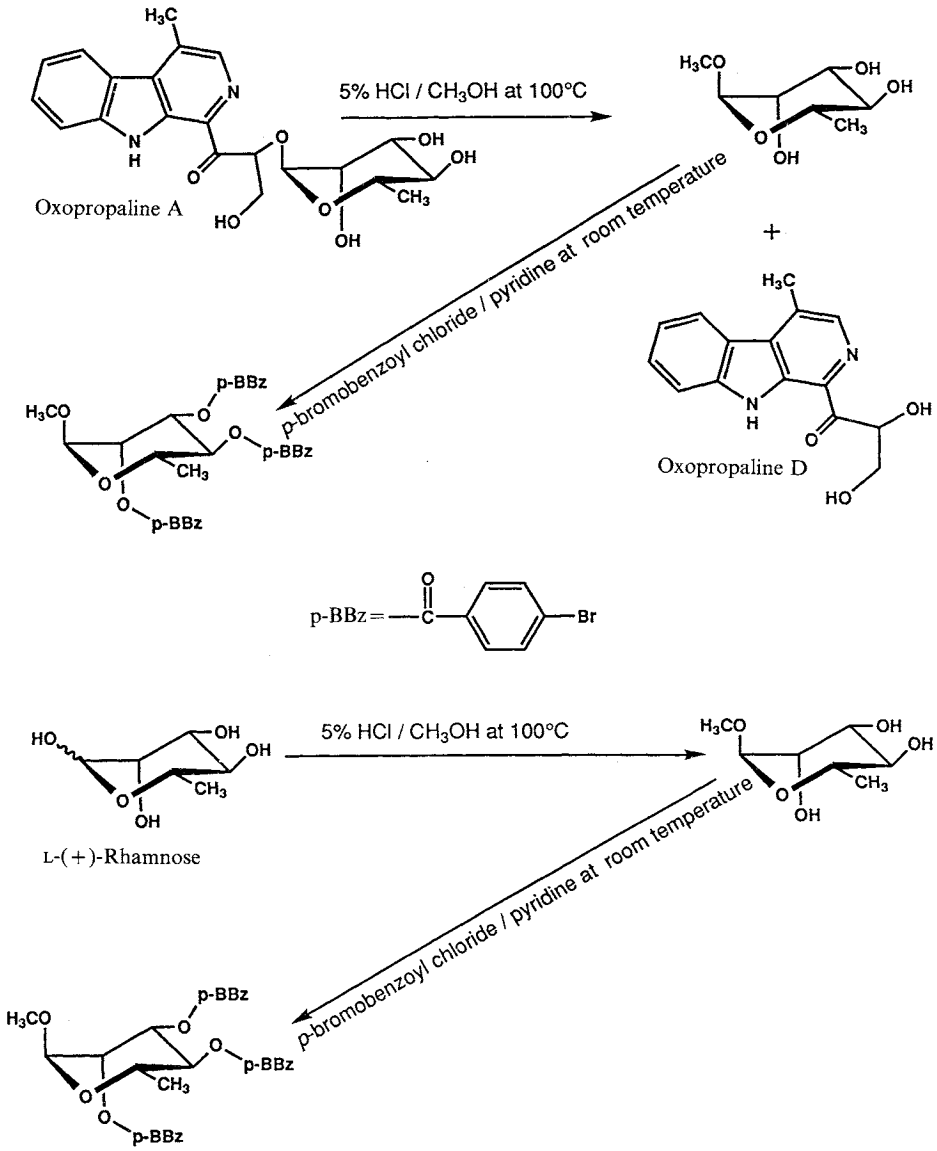


A (**1**), on the basis of the HRFAB-MS [*m/z* 417.1674 $(M+H)^+$; calcd. 417.1662]. The UV and IR spectra of **2** also revealed a profile similar to that of oxopropaline A. ^{13}C and ^1H NMR spectra of **1** and **2** differed in the C-1 side chain and rhamnosyl moiety. The chemical shifts in the ^{13}C and ^1H NMR spectra at C-11 of **1** (δ_C 80.5/δ_H 5.97) were at higher magnetic field in **2** (δ_C 74.3/δ_H 5.72), while the chemical shifts at C-12 of **1** (δ_C 63.9/δ_H 3.90 and 4.03) were at lower magnetic field in **2** (δ_C 69.7/δ_H 4.01 and 4.21). This behavior suggested that **2** has the rhamnosyl moiety linked at C-12. Furthermore, acidic hydrolysis, with 1 N HCl at 100°C for 1.5 hours, and acidic methanolysis followed by per-*p*-bromobenzylation gave the same results that were obtained with **1**. Thus, the structure of **2** was determined as that depicted in Fig. 1.

Oxopropaline D (**3**) was formulated as $C_{15}H_{14}N_2O_3$. The UV and IR spectra of **3** also showed a profile similar to those of oxopropaline A (**1**). Oxopropaline D gave more simple ^{13}C and ^1H NMR spectra than **1** or **2** (Table 2 and Fig. 4). Examination of the molecular formula and the ^{13}C and ^1H NMR spectra suggested that the structure of **3** was de-rhamnosyl oxopropaline A. The ^1H NMR spectra and Rf values of the aglycone produced by the acidic hydrolysis of **1** and **2** were identical to those of **3**. Hence the structure of **3** was determined to be 4-methyl-1-(1-oxo-2,3-dihydroxy-propyl)-9*H*-pyrido[3,4-*b*]indole. The stereochemistry at the C-11 of oxopropaline D is currently being investigated.

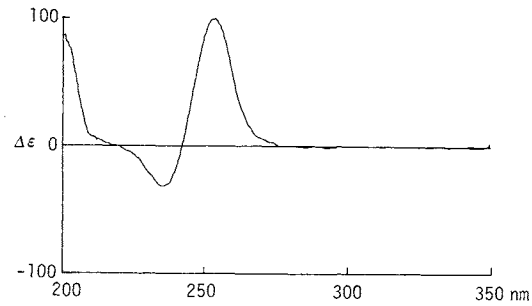
Oxopropaline E (**4**) has the molecular formula $C_{21}H_{24}N_2O_6$ based on HRFAB-MS [*m/z* 401.1713

Scheme 1. Acidic methanolysis and perbromobenzoylation of oxopropaline A and L-(+)-rhamnose.



$(M+H)^+$; calcd. 401.1713], and thus contains one oxygen less than oxopropalines A (**1**) and B (**2**). The UV and IR spectra of **4** resemble those of **1** and **2**. In the ^1H NMR spectrum of **4**, *geminal* methylene protons at C-11 (δ 3.61 and δ 3.94) were observed instead of the methine proton (δ 5.72) of **2**. The ^{13}C NMR spectrum of oxopropaline E (**4**) also contain a methylene carbon at δ 38.7, in place of the oxygenated methine carbon at C-11 (δ 74.3). These spectroscopic investigations supported the

Fig. 7. CD spectrum of 2,3,4-tri-*p*-bromobenzoyloxy-1-methoxy-rhamnose derived from oxopropaline A in CH_3CN at 22°C.



fact that the structure of **4** is 11-dehydroxy-oxopropaline B. Acidic hydrolysis with 1 N HCl at 100°C for 1.5 hours and acidic methanolysis followed by per-*p*-bromobenzoylation were carried out. These experiments yielded an unknown aglycone but the same sugar derivative as that derived from **1**, **2** and authentic L-(+)-rhamnose. The polarity of the aglycone was lower than that of **3**, which is the aglycone of **1** and **2**. Furthermore, the Rf value and the HPLC retention time of the aglycone from **4** were identical to those of oxopropaline G (**5**)[2].

The molecular formula of oxopropaline G (**5**) was determined to be $C_{15}H_{14}N_2O_2$ by analysis of the HRFAB-MS [*m/z* 255.1141 $(M+H)^+$; calcd. 255.1133]. The UV and IR spectra of **5** resembled those of **1**~**4**. The ^{13}C and ^1H NMR spectra of **5** were simple like those of oxopropaline D (**3**). In the ^1H NMR spectrum of **5**, a characteristic A_2B_2 ^1H-^1H spin system was observed as two triplets at δ 3.54 and δ 4.08 in the C-1 substituent, while the ^{13}C NMR experiment showed two methylene carbons at δ 41.8 and δ 58.8, corresponding to the A and B protons; respectively. These spectroscopic characteristics revealed that the structure of **5** is 11-dehydroxy-oxopropaline D (4-methyl-1-(1-oxo-3-hydroxy-propyl)-9*H*-pyrido[3,4-*b*]indole). These results established the structures of **4** and **5** as shown in Fig. 1.

Experimental

General

FAB-MS spectra were measured using a JEOL JMS-SX102 spectrometer. UV spectra were measured using a Hitachi 200-20 spectrometer and a Hewlett-Packard diode array instrument of the HP1090 liquid chromatography system. IR spectra were recorded using a Hitachi 270-30 spectrometer. Optical rotations were taken with a Horiba SEPA-200 spectrometer. CD spectra were recorded using a JASCO J-20A automatic recording spectropolarimeter driven by a JASCO DP-500N data processor. ^1H and ^{13}C NMR measurements were performed using a Varian VXR400 spectrometer. The HMBC experiment were carried out using a Bruker AM 500 instrument.

Acidic Hydrolysis

Samples (4.6 mg, 2.2 mg and 4.0 mg of oxopropalines A, B, and E, respectively) in 1 N HCl were heated at 100°C for 1.5 hours and the component sugar and aglycone were determined by TLC and HPLC, respectively. The sugar moieties were developed with the solvent system of *n*-PrOH - H_2O - NH_4OH (6 : 2 : 1) and detected with an anthrone reagent. The sugars from oxopropalines A, B and E gave the same Rf value, 0.45, as that of authentic L-(+)-rhamnose (obtained from Tokyo Chemical Industry Co. Ltd.) when directly compared on TLC. The aglycones from oxopropalines A and B (3.9 mg and 1.1 mg, respectively) showed the same retention time as oxopropaline D, while the retention time of the aglycone from oxopropaline E (1.6 mg) was identical to the retention time of oxopropaline G from HPLC analyses as previously described[2].

Acidic Methanolysis and per-*p*-Bromobenzoylation

Samples (4.0 mg and 5.0 mg of oxopropaline A and authentic L-(+)-rhamnose, respectively) in 0.5 ml of 5% HCl - methanol (obtained from Tokyo Chemical Industry Co. Ltd.) were heated at 100°C for 2 hours. The sample from oxopropaline A was concentrated *in vacuo* and then dissolved in 10 ml of H_2O. The aqueous solution was extracted with 10 ml of EtOAc. The H_2O layer was concentrated *in vacuo*. Each methyl glycoside was purified by PTLC (Merck Art. No. 16485, *n*-PrOH - H_2O - NH_4OH (6 : 2 : 1)) to remove impurities. The ^{13}C NMR data of the purified methyl glycosides indicated that the structure was 1-α-*O*-Me-rhamnose, comparable with those of α-L-(+)-rhamnose and β-L-(+)-rhamnose[7]. The sample from oxopropaline and the evaporated sample from L-(+)-rhamnose were dissolved in separate 0.5 ml portions of pyridine, adding 1.0 mg of *p*-bromobenzylchloride. Each solution was left at room temperature for 24 hours. The resulting solutions were evaporated *in vacuo* and purified by PTLC (Merck Art. No. 16485, *n*-hexane - EtOAc = 4 : 1), to give 0.25 mg and 0.65 mg of product from oxopropaline A and

L-(+)-rhamnose, respectively. The Rf values of both products gave concordant results (Rf=0.42) on TLC Merck Art. No. 5554, *n*-hexane - EtOAc=4:1). The CD spectra of both products were measured in CH_3CN and gave the same curve described in the text. The sugar moieties from the acidic methanolysis of oxopropalines B and E as described above gave the same behavior as the derivative from authentic L-(+)-rhamnose on TLC (Merck Art. No. 16485). Methyl glycosides from oxopropalines B and E and authentic L-(+)-rhamnose were developed with the solvent system of *n*-PrOH - H_2O - NH_4OH (6:2:1) and the same Rf value gave 0.58.

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References

1) BALITZ, D. M.; J. A. BUSH, W. T. BRADNER, T. W. DOYLE, F. A. O'HERRON & D. E. NETTLETON: Isolation of lavendamycin. A new antibiotic from *Streptomyces lavendulae*. J. Antibiotics 35: 259~265, 1982
2) ABE, N.; Y. NAKAKITA, T. NAKAMURA, N. ENOKI, H. UCHIDA, S. TAKEO & M. MUNEKATA: Novel cytocidal compounds, oxopropalines from *Streptomyces* sp. G324 producing lavendamycin. I. Taxonomy of the producing organism, fermentation, isolation and biological activities. J. Antibiotics 46: 1672~1677, 1993
3) AOYAGI, T.; M. KUMAGAI, T. HAZATO, M. HAMADA, T. TAKEUCHI & UMEZAWA: Pyridindolol, a new β-galactosidase inhibitor produced by actinomycetes. J. Antibiotics 28: 555~557, 1975
4) SCOTT, A. I.: Interpretation of the ultra-violet spectra of natural products. *In* International Series of Monographs of Organic Chemistry. Vol. 7. pp. 176~177, 297~303, Pergamon Press, 1964
5) STUART, K. & R. WOO-MING: b-Carboline alkaloids. Heterocycles 3: 223~264, 1975
6) WIESLER, W. T.; N. BEROVA, M. OJIKA, H. V. MAYERS, M. CHANG, P. ZHOU, L-C. LO, M. NIWA, R. TAKEDA & K. NAKANISHI: A CD-spectroscopic alternative to methylation analysis of oligosacchrides: reference spectra for identification of chromophoric glycopyranoside derivatives. Helv. Chim. Acta 73: 509~551, 1990
7) BREITMAIER, E. & W. VOELTER: ^{13}C NMR Spectroscopy. *In* Monographs in Modern Chemistry. Vol. 5. p 251, Verlag Chemie Weinheim, New York, 1978