to that found for the two poorest leaving groups (k^H/k^D is the least for electron-withdrawing substituents). The conclusion is reached that for the two best leaving groups, the proton is *less* than one-half transferred to base at the transition state.

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The structure of ravidomycin

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The structure **1***a* is proposed for ravidomycin on the basis of chemical and spectroscopic data.

JOHN A. FINDLAY, JIA-SEN LIU, LAJOS RADICS et S. RAKHIT. Can. J. Chem. **59**, 3018 (1981).
En se basant sur les données chimiques et spectroscopiques on propose la structure **1***a* pour la ravidomycine.
[Traduit par le journal]

Ravidomycin, isolated from the fermentation broth of *Streptomyces ravidus*, possesses strong inhibitory effect on gram positive organisms and potent antitumor activity (1). We propose structure **1***a* for ravidomycin[1] based on chemical and spectral information.

Ravidomycin, $C_{31}H_{33}NO_9$ (M^+ 563.2148), mp 248–250°C, $[\alpha]_D^{26}$ −105.5°, has an infrared (ir) spectrum which shows the presence of two carbonyls (1740, 1720 cm^{-1}), an aromatic system (1620, 1600, 1580 cm^{-1}), and hydroxyl groups (3380 cm^{-1}). Its ultraviolet (uv) spectrum λ_{max}(MeOH) nm (log ε): 244 (4.68), 263 (4.54, sh), 277 (4.60), 285 (4.65), 308 (4.33), 320 (4.30), 335 (4.20), 350 (4.08), 392 (4.24) reveals the presence of a substituted naphthalene system (2). The ^1H nmr spectra of ravidomycin **1***a* and its diacetate **1***b* (see Table 1) attest to the presence of *ortho* (one pair), *meta* (one pair), and isolated (one) aromatic protons, which features can only be accommodated by inclusion of two tetrasubstituted and one pentasubstituted aromatic rings. Fusion of ravidomycin with alkali affords the aglycone **2***a* which features in its ^1H nmr ($CDCl_3$) spectrum six aromatic hydrogens, three of which (H-6, δ 7.00, dd, J = 8.0/0.8; H-7, δ 7.50, dd, J = 8.0/8.0; H-8, δ 8.04, dd, J = 8.0/0.8) are in a 1,2,3 relationship clearly demonstrating the position of the *C*-glycosidic moiety relative to the *ortho* hydrogens. This aglycone can be hydrogenated (Pt/glacial acetic acid) to a desoxohexahydro derivative **3** in which the original aglycone-containing ring has suffered reduction and has also been the site of hydrogenolysis of the phenolic hydroxyl. Alkali fusion of ravidomycin also furnishes diastereomeric hemiacetal carboxylic acids (~ 1:1) **4***a*, which provides compelling evidence for the relationship of the *C*-glycosidic bond and the

[1]Ravidomycin **1***a* possesses the same aglycone moiety as the newly reported antibiotics toromycin (4) and gilvogarcin V (5).

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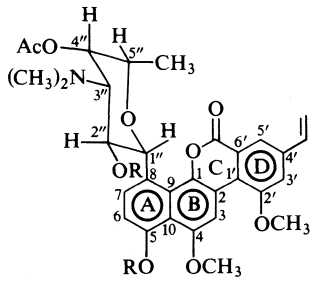
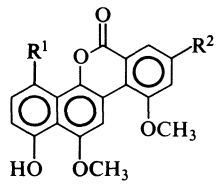
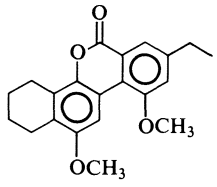


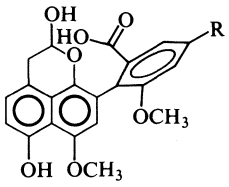
1a R = H
1b R = Ac



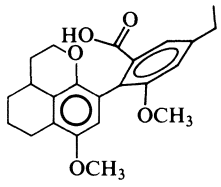
2a R^1 = H, R^2 = —CH=CH_2
2b R^1 = —CH_2CHO, R^2 = —CH_2CH_3



3



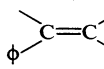
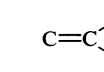
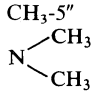
4a R = —CH=CH_2
4b R = —CH_2—CH_3



5

ethereal oxygen of the original lactone system in **1**. Thus the mixture **4a** displays in its ^{1}H nmr ($CDCl_3$) spectrum signals at δ 5.38 (dd, 0.5H, J = 3.0/7.2) and δ 5.67 (dd, 0.5H, J = 3.0/3.0) corresponding to the hemiacetal proton coupled to the CH_2-8 multiplet at δ 3.00–3.30. The existence of **4a** in diastereomeric form is no doubt due to restricted rotation around the C2—C1′ bond. Transformation of **4a** by catalytic hydrogenation (Pt/glacial acetic acid) into the dihydropyran **5** parallels the reduc-

TABLE 1. ^{1}H nmr parameters* of ravidomycin **1a** and its diacetate **1b**

Proton	**1a**	**1b**
H-3	8.47 (s)	8.59 (s)
H-7	7.99 (AB, $J_{6,7}$ = 8.4)	7.98† (AB, $J_{6,7}$ = 8.4)
H-6	7.07 (AB, $J_{6,7}$ = 8.4)	7.22† (AB, $J_{6,7}$ = 8.4)
H-5′	8.11 (d, $J_{3',5'}$ = 1.5)	8.16 (d, $J_{3',5'}$ = 1.5)
H-3′	7.36 (d, $J_{3',5'}$ = 1.5)	7.42 (d, $J_{3',5'}$ = 1.5)
OCH_3-4	4.11 (s)	4.00 (s)
OCH_3-2′	4.11 (s)	4.13 (s)
	5.47 (d, J_{cis} = 10.9) 5.96 (d, J_{trans} = 17.5)	5.49 (d, J_{cis} = 10.9) 5.98 (d, J_{trans} = 17.5)
	6.82 (dd, J_{cis} = 10.9, J_{trans} = 17.5)	6.84 (dd, J_{cis} = 10.9, J_{trans} = 17.5)
H-1″	5.87 (d, $J_{1'',2''}$ = 9.0)	6.31 (d, $J_{1'',2''}$ = 10.0)
H-2″	4.46 (dd, $J_{1'',2''}$ = 9.0, $J_{2'',3''}$ = 10.3)	5.75 (dd, $J_{1'',2''}$ = 10.0, $J_{2'',3''}$ = 10.3)
H-3″	3.10 (dd, $J_{3'',4''}$ = 2.4, $J_{2'',3''}$ = 10.3)	3.25 (dd, $J_{3'',4''}$ = 2.4, $J_{2'',3''}$ = 10.3)
H-4″	5.57 (dd, $J_{3'',4''}$ = 2.4, $J_{4'',5''}$ = 1.0)	5.60 (dd, $J_{3'',4''}$ = 2.4, $J_{4'',5''}$ = 1.0)
H-5″	4.51 (qd, J_{5'',CH_3} = 6.4, $J_{4'',5''}$ = 1.0)	4.44 (qd, J_{5'',CH_3} = 6.4, $J_{4'',5''}$ = 1.0)
CH_3-5″	1.07 (d, J_{5'',CH_3} = 6.4)	1.15 (d, J_{5'',CH_3} = 6.4)
	2.51 (s)	2.42 (s)
Ac-4″	2.13 (s)	2.17 (s)
Ac-2″		1.60 (s)
Ac-5		2.40 (s)
OH-5	9.83 (s)	
OH-2″	3.57 (br)	

*In $CDCl_3$. Chemical shifts, δ, in ppm relative to internal TMS. Coupling constants, J, in Hz.
†May be interchanged.

tion and hydrogenolysis of **2***a* to **3** and confirms the fact that the hemiacetal ring in **4***a* utilizes the phenolic oxygen derived from opening of the lactone. The lactone aldehyde **2***b* is obtainable by heating **4***b* in quinoline at 180°C in the presence of copper affording corroboration of the relationship of lactone and sugar in **1***a*.

The lactone ring in ravidomycin must unite the tetrasubstituted phenyl ring bearing the *meta* hydrogens to the pentasubstituted naphthalene ring and placement of the substituents on this ring D follows from the juxtaposition of groups on the known anisole-2,3,5-tricarboxylic acid obtainable by hot alkaline permanganate treatment of **1***a*, together with analysis of ^{1}H nmr chemical shift data on various compounds. For example, in compound **3** the solvent-induced chemical shift for the *meta* protons, $\Delta_{C_6H_6}(CDCl_3) = -0.23$ ppm for H-5′ and +0.46 ppm for H-3′ is as predicted by the "carbonyl plane rule" (3). Mutual proton decoupling experiments on ravidomycin diacetate **1***b* give rise to a significant narrowing of the resonance lines due to H-3′ (δ 7.42) and the OCH_3-2′ (δ 4.13) which indicates an *ortho* relationship between the respective carbons. In a similar manner it was shown that the isolated aromatic proton H-3 is *ortho* to the remaining methoxyl group. Furthermore, when the lactone ring is opened, as in **4***a*, the isolated aromatic proton and one methoxyl are shifted 1.58 ppm and 0.32 ppm upfield, respectively, relative to the corresponding signals in **2***a* and this can only be explained if the isolated aromatic proton and one methoxyl are located at C-3 and C-2′, respectively, where both are deshielded when the lactone ring is closed and shielded when it is open and the angle between the planes of the two aromatic systems is changed substantially.

The structure of the amino sugar moiety follows from consideration of ^{1}H nmr data on ravidomycin and its diacetate, together with a full set of appropriate decoupling experiments which confirmed the presence of the 3,6-dideoxy-3-*N*,*N*-dimethylamino pseudo altropyranose in the conformation (with H-7 and H-1″ *S-trans*) indicated in **1***a*. The absolute configuration of the molecule has yet to be determined.

The structures of all compounds are fully supported by infrared, ultraviolet, and mass spectral data and are consistent with ^{13}C nmr chemical shift, multiplicity data and selective ^{13}C–{^{1}H} decoupling experiments.

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