Reaction of Rifamycin S with Hexahydro-1,3,5-triazines Prepared from Formaldehyde and Primary Aliphatic Amines

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Rifamycin S (**1**) and 25-*O*-deacetylrifamycin S reacted with 1,3,5-tri-*t*-butylhexahydro-1,3,5-triazine to give deep-blue compounds. The structures of the deep-blue compounds are discussed based on ^{13}C NMR data, and it is concluded that the earlier structures[1] should be partly re-revised. The mechanism of formation of the deep-blue compounds and the reaction of **1** with several hexahydro-1,3,5-triazines, which were prepared from formaldehyde and primary aliphatic amines, are also described.

We previously reported[1] that rifamycin S (**1**) was allowed to react with 1,3,5-tri-*t*-butylhexahydro-1,3,5-triazine (**2c**) to afford a characteristic deep-blue colored compound, which was identical with the compound prepared according to the method of Marsili and Pasqualucci,[2] who proposed that the structure of the deep-blue compound was **3c**. We suggested[1] that the deep-blue compound did not consist of an oxazinium ring but, rather, a dihydropyrimidinium ring. We partly revised the earlier structure, **4c**, suggested by Maggi et al.,[3-5] in which the 4-hydroxyl group was dissociated, to the enolized structure, **5c**, based on the IR spectral data and the interpretation[3] of Maggi et al. on a polarographic oxidation wave.[1] Here, we report that the structure of the deep-blue compound should be re-revised based on the ^{13}C NMR data to **6c** in which the 8-hydroxyl group is dissociated. Moreover, the mechanism of formation of the deep-blue compound and the reaction of **1** with several hexahydro-1,3,5-triazines **2** prepared from formaldehyde and aliphatic primary amines are reported.

Results and Discussion

The Structure of the Deep-Blue Compound Obtained in the Reaction of 1 with 2c. We previously suggested that the deep-blue compound, **A**, which was obtained in the reaction of **1** with **2c**, had the enolized structure **5c**.[1] The suggestion was based on the IR spectral data of **A** and its 25-*O*-deacetyl derivative **B** (no furanone νC(11)=O band was observed at ca. 1740 cm^{-1}; the amide νC(15)=O band was observed at ca. 1660 cm^{-1}) and the interpretation of Maggi et al.[3] on a polarographic oxidation wave. Later, we prepared *N*-methylrifamycin S (**8**),[6] 25-*O*-deacetyl-4-*O*-(*p*-tolylsulfonyl)rifamycin SV (**9**) and its sodium salt (**10**),[7] and from their IR spectral data ($CDCl_3$) we knew that the amide νC(15)=O band might appear at rather low frequency, owing to a structural factor of the amide group (**8**, tertiary amide, 1659 cm^{-1}) and that the furanone νC(11)=O band also might appear at rather low frequency, owing to a dissociation of the 8-hydroxyl group (**9**, 1709cm^{-1}; **10**, 1675 cm^{-1}). Moreover, it has been known that the occurrence of a polarographic two-step oxidation wave can be interpreted as being due to the presence of a stable intermediate radical,[8] but not due to the nonequivalence of the hydroquinone hydroxyls, the interpretation of Maggi et al.[3] This information brought us another possible structure, **6c**, in which the 8-hydroxyl group was dissociated, to the chromophores of **A** and **B**. The structure **6c** can be used to interpret the IR

Table 1. ^1H NMR Data of Compound **A** (**6c**) in $CDCl_3$ (Concn ca. 10^{-2} mol dm^{-3}) at 300 MHz

Proton	Multipl.	*J*/Hz	δ	Proton	Multipl.	*J*/Hz	δ
OH-1	s		16.57	H-25	dd	25,26=5[b]	4.95
OH-4	s		14.87	H-26	c)	26,27=3	2.10
CH=N^+	s		8.98	H-27	ddd	27,28=5	3.66
H-13	s		1.77	H-28	dd	28,29=12	5.27
H-14	s		2.08	H-29	dd	27,29=1.5	6.11
H-17	b.d	17,18=11	5.88	H-30	b.s	30,17=n.d.	2.14
H-18	a)	18,19=15.5	5.31	H-31	d	31,20=7	0.74
H-19	dd	19,20=4	6.01	H-32	d	32,22=7	0.95
H-20	ddq	20,21=9.5	2.25	H-33	d	33,24=7	0.71
H-21	b.d	21,22=n.d.	3.28	H-34	a)	34,26=n.d.	0.70
OH-21	b.	21,OH=n.d.	4.27	H-36	s		2.12
H-22	a)	22,23=n.d.	1.63	H-37	s		3.17
H-23	b.d	23,24=8.5	3.23	H-2′(α)[d]	d	2′(α),2′(β)=12	4.55
OH-23	b.	23,OH=n.d.	3.57	H-2′(β)[d]	d	2′(α),2′(β)=12	6.56
H-24	a)	24,25=6[b]	2.03	*t*-butyl	s		1.66

s: singlet, d: doublet, q: quartet, b.: broad, n.d.: not determined. a) This signal partly overlapped on another signal. b) These coupling constants may be interchanged. c) This signal entirely overlapped on another signal. d) The determination of the configuration was made by reference to the literature.[13]

spectral data of **A** and **B**, as well as their characteristic ^{1}H NMR spectral data, which showed two singlets due to the phenolic hydroxyl protons in the very low field (**A**, δ 16.57 and 14.87; **B**, δ 16.44 and 14.74). Namely, the amide νC(15)=O band appears at a rather low frequency (ca. 1660 cm^{-1}), owing to the structural factor of the amide group (tertiary amide), not owing to an intramolecular hydrogen bonding between the amide C(15)=O and the 1-hydroxyl group. The furanone νC(11)=O band appears at low frequency, perhaps at ca. 1590 cm^{-1} owing to dissociation of the 8-hydroxyl group and an intramolecular hydrogen bonding between the furanone C(11)=O and 4-hydroxyl group. The large chemical shift values of the two phenolic hydroxyl protons are due to strong intramolecular hydrogen bonding between the ionized 8-hydroxyl group and the 1-hydroxyl group and between the furanone C(11)=O and the 4-hydroxyl group (the oxygen atom of the furanone C(11)=O is considered to be charged much negatively due to contribution of a limiting structure **7c**). The possible structure of **6c** was substantiated by ^{13}C NMR data. Chemical shifts and assignments in ^{1}H and ^{13}C NMR spectra of **A** (**6c**) and **B** (25-OH-**6c**) in $CDCl_3$ are summarized in Tables 1—3. Assignments for protons and carbon atoms, except for two phenolic hydroxyl protons and all quaternary carbon atoms, were made based on H–H and C–H correlation spectroscopy. For assignments of quaternary carbon atoms, proton nondecoupling spectra were recorded, and assignments were performed with reference to the chemical shifts and the multiplicities of the quaternary carbon atoms of rifampicin (**11**) and 3-[(dimethylhydrazono)methyl]rifamycin SV.[9] The assignments for the

Table 2. ^{1}H NMR Data of Compound **B** (25-OH-**6c**) in $CDCl_3$ (Concn ca. 10^{-2} mol dm^{-3}) at 300 MHz

Proton	Multipl.	J/Hz	δ	Proton	Multipl.	J/Hz	δ
OH-1	s		16.44	H-25	dd	25,26=8.5	3.78
OH-4	s		14.74	OH-25	b.		4.13
CH=N$^+$	s		9.15	H-26	ddq	26,27=4.5	1.95
H-13	s		1.79	H-27	ddd	27,28=6	3.89
H-14	s		2.08	H-28	dd	28,29=12.5	5.13
H-17	dq	17,18=11	5.77	H-29	dd	27,29=1	6.19
H-18	dd	18,19=15.5	5.26	H-30	d	30,17=1	2.13
H-19	dd	19,20=6.5	5.87	H-31	d	31,20=7	0.94
H-20	ddq	20,21=3	2.66	H-32	d	32,22=7	0.93
H-21	dd[a]	21,22=6	3.23	H-33	d	33,24=7	0.86
OH-21	b.	21,OH=n.d.	3.09	H-34	d	34,26=7	0.69
H-22	ddq	22,23=7.5	1.30	H-37	s		3.29
H-23	dd[a]	23,24=5	3.16	H-2′(α)[b]	d	2′(α),2′(β)=12.5	4.51
OH-23	b.	23,OH=n.d.	4.11	H-2′(β)[b]	d	2′(α),2′(β)=12.5	6.69
H-24	ddq	24,25=2	1.59	t-butyl	s		1.72

s: singlet, d: doublet, q: quartet, b.: broad, n.d.: not determined. a) After treatment with D_2O. b) The determination of the configuration was made by reference to the literature.[13]

Table 3. ^{13}C NMR Chemical Shifts of Compound **A** (**6c**) and Compound **B** (25-OH-**6c**) in $CDCl_3$ at 75.47 MHz

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
A[a]	146.75	122.26	107.42	154.83	99.58	172.09	107.87	183.29	112.50
B[b]	147.11	121.67	107.58	153.24	98.79	172.04	107.36	183.39	113.50
Compound	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18
A[a]	119.16	188.94	107.97	22.09	7.53	170.46	129.42	130.97	122.04
B[b]	118.92	188.56	106.69	21.99	7.35	172.09	128.96	130.84	124.75
Compound	C-19	C-20	C-21	C-22	C-23	C-24	C-25	C-26	C-27
A[a]	140.20	37.31	74.02	35.89	79.41	37.76	76.43	39.97	79.41
B[b]	139.49	37.00	78.87	41.86	79.28	36.21	72.46	39.06	83.43
Compound	C-28	C-29	C-30	C-31	C-32	C-33	C-34	C-35	C-36
A[a]	112.86	140.13	21.02	14.57	11.27	11.93	12.69	171.78	20.85
B[b]	106.90	140.78	20.45	17.85	14.40	11.50	12.99	—	—
Compound	C-37	CH=N$^+$	C-2′	$\underline{C}(CH_3)_3$	$C(\underline{C}H_3)_3$				
A[a]	57.30	154.27	56.32	64.79	27.50				
B[b]	57.13	155.86	55.36	65.02	27.27				

a) Concn ca. 10^{-2} mol dm^{-3}. b) Concn ca. 10^{-1} mol dm^{-3}.

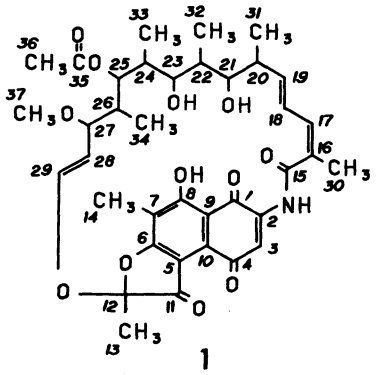
Table 4. ^{13}C NMR Chemical Shifts and Multiplicities of Quaternary Carbon Atoms in a Proton Non-Decoupling Spectrum of Compound **B** (25-OH-**6c**) in $CDCl_3$ (Concn ca. 10^{-1} mol dm^{-3}) and Change of Multiplicities by Long-Range Selective Proton Decoupling (LSPD)

Chemical shift	Multiplicity (J/Hz)	Assignment	Change of Multiplicity (J/Hz) by LSPD		
			CH=N$^+$ (δ=9.09)	OH-4 (δ=14.59)[a]	OH-1 (δ=16.44)
188.56	q(2)	C-11	—	—	—
183.39	q(3.5)	C-8	—	—	—
172.09	n.d.	C-15	—	—	—
172.04	q(4)	C-6	—	—	—
153.24	n.d.	C-4	—	—	—
147.11	d(4)	C-1	—	—	s
128.96	dq(2, 7)	C-16	—	—	—
121.67	d(6)	C-2	—	—	s
118.92	d(1)	C-10	—	s	—
113.50	n.d.	C-9	—	—	—
107.58	dd(2.5, 6.5)	C-3	d(6.5)	d(2.5)	—
107.36	q(6)	C-7	—	—	—
106.69	quintet(4.5)	C-12	—	—	—
98.79	s	C-5	—	—	—

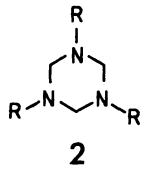
s: singlet, d: doublet, q: quartet, n.d.: not determined. a) This chemical shift was slightly different from the value on Table 2, maybe, due to different concentration.

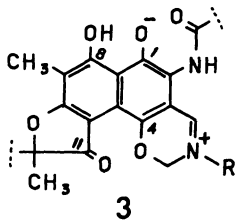
two phenolic hydroxyl protons were carried out by long-range selective proton decoupling (LSPD) experiments. The results of LSPD experiments for **B** (25-OH-**6c**) are summarized in Table 4.[10] The LSPD of the δ 14.59 proton affected the signals at 118.92 and 107.58, which were attributed to C-10 and C-3, respectively; hence, the δ 14.59 proton are assigned to the 4-hydroxyl proton. This implies that the 4-hydroxyl proton is not dissociated. The LSPD of the δ 16.44 proton affected the signals at 147.11 and 121.67, which were attributed to C-1 and C-2, respectively; hence, the 1-hydroxyl proton is also not dissociated. Therefore, the remaining 8-hydroxyl proton must be dissociated. The signals due to C-8 of **A** (**6c**) and **B** (25-OH-**6c**) are shifted downfield compared with that of **11** for 14 ppm (**A**, 183.29; **B**, 183.39; **11**, 169.19). This phenomenon is interpreted in terms of the contribution of a limiting structure **7c**,[11] and supports the structure of **6c**, in which the 8-hydroxyl group is completely dissociated. Thus, the structures of the deep-blue compounds, which have been reported by Marsili and Pasqualucci,[2] Maggi et al.,[3-5] and the authors,[1,12,13] should be revised to structures comprising a dihydropyrimidinium ring in which the 8-hydroxyl group is dissociated.

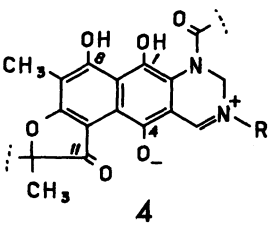
Mechanism of the Formation of Compound 6c. The process of the reaction of **1** with **2c** in pyridine at 63 °C was investigated by analytical silica-gel TLC. In the early stages of the reaction (after ca. 30 min from beginning) an intermediate product **C**, **6c** and the remaining starting material **1** were detected. At the end of the reaction (after ca. 1.5 h from beginning) **C** and **1** disappeared, while 3-[(t-butylamino)methylene]rifamycin (**12c**)[14] and rifamycin SV (**14**) as well as **6c** were detected. From this reaction mixture, **6c** was isolated in 38% yield. The intermediate product **C** was detected more clearly when the reaction was carried out at r.t., and it was considered that **C** was an intermediate for **6c**, because two-dimensional TLC showed that **C** gradually transformed on TLC plates into several compounds in which **6c** was included. Attempts to isolate **C** were not successful, due to its instability. However, it was observed by TLC that L-ascorbic acid reduced **C**, while the resulting reduction product **D** reverted to **C** upon treatment with MnO_2. The reduction product **D** was also observed by TLC to be the same compound which was formed by reduction of **6c** with $NaBH_4$ in EtOH. Additionally, it was observed by TLC that 3-[(t-butylamino)methyl]rifamycin S (**13c**), which was prepared by oxidation of 3-[(t-butylamino)methyl]rifamycin SV (**15c**) with MnO_2, transformed immediately and completely into **C** by treatment with **2c** in pyridine at r.t., and after warming at 62 °C for 1 h **6c** was obtained in 41% yield.[15] These facts imply that the structure of the intermediate product **C** can be assigned to **17c**, and it is concluded that in the reaction of **1** with **2c** the Mannich derivative **13c** is formed at first, then **17c**, and finally **6c** is formed by isomerization of **17c**. The formation of **17c** from **13c** is very fast, and this is the reason for the failure of the detection of **13c** by TLC. It is described above that **12c** and **14** were also detected at the end of the reaction of **1** with **2c**. This is interpreted as meaning that **6c** partly underwent aminolysis into **16c** by the action of t-butylamine, which was released during the course of the reaction; then, the redox reaction between the resulting **16c** and the remaining **1** proceeded to afford **12c** and **14**. In fact, it was observed by TLC that **12c** and **14** were formed by treating **6c** with t-butylamine

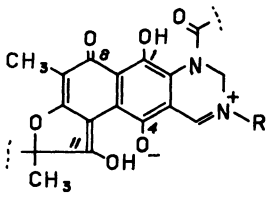


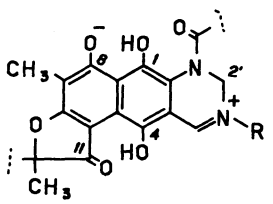
a: R = CH_3
b: R = C_2H_5
c: R = t-C_4H_9
d: R = t-C_5H_{11}
e: R = cyclo-C_6H_{11}

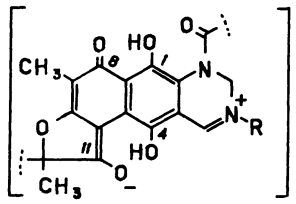


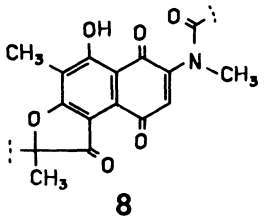


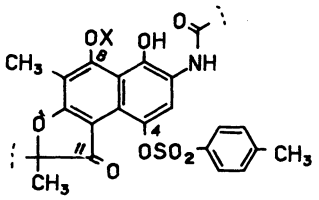




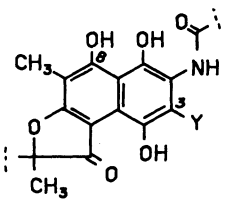




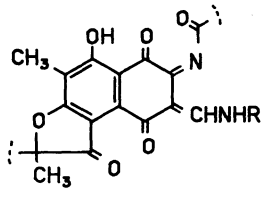


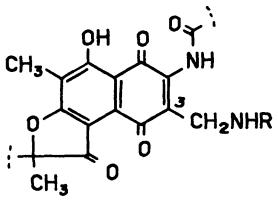


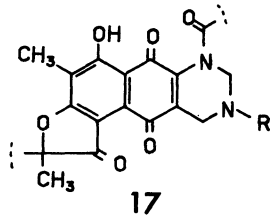
9: X = H (25-O-deacetyl)
10: X = Na (25-O-deacetyl)

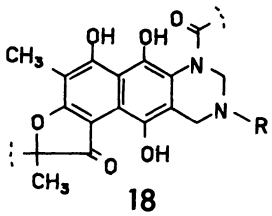


11: Y = -CH=NN⟨⟩NCH$_3$
14: Y = H
15: Y = -CH_2NHR
16: Y = -CH=NR









in the presence of **1** in pyridine at 65 °C.

Reaction of 1 with Other Hexahydro-1,3,5-triazines 2. Hexahydro-1,3,5-triazine **2d** reacted with **1** exactly like **2c**, and at the end of the reaction **6d**, **12d** and **14** were detected by TLC. The isolation yield of **6d** was 48%. Hexahydro-1,3,5-triazines **2a**, **2b**, or **2e** also reacted with **1**, but the results of the reaction were very different from the results described for **2c** and **2d**. The yields of compounds **6a**, **6b**, or **6e** were very low and the major products were observed by TLC to be the hydroquinone-type derivatives **18a**, **18b**, or **18e** and **14**. The formations of **12a**, **12b**, or **12e** were not observed. These different results from that of a reaction of **1** with **2c** or **2d** are attributed to the reducing power of hexahydro-1,3,5-triazines **2a**, **2b**, and **2e**.[12] As a representative example the result of the reaction of **1** with **2a** is interpreted as follows. At first, compound **17a** is formed via **13a**, then isomerizes into **6a**; however, the iminium bond of **6a** is reduced with the remaining **2a**, and **18a** is formed. The redox reaction between **18a** and the remaining **1** results in the formation of **17a** and **14**. Thus, the transformation of **1** into **18a** and **14** continues until **1** disappears; at the end of the reaction, **18a** and **14** are formed as major

Table 5. Reaction of Rifamycin S (**1**) with Hexahydro-1,3,5-triazines **2**

2 (Molar ratio to **1**)	Reaction condition[a]		Product	Yield/%
	Temp/°C	Time/h		
2a (1.9)	r.t.	48	**6a**	2
2b (2.0)	r.t.	48	**6b**	2
2c (0.69)	63	1.5	**6c**	38
2c (2.0)[b]	60	1.5	25-OH-**6c**	31
2d (2.4)	40	3.5	**6d**	48
2e (4.0)	r.t.	3.5	**6e**	4

a) Pyridine was used as a solvent. b) The 25-O-deacetyl derivative of **1** was used.

products, while **6a** is obtained in very low yield. The results are summarized in Table 5.

Experimental

Analytical TLC was performed on silica gel 60 F_{254} pre-coated plates (layer thickness 0.25 mm, Merck), using $CHCl_3$–CH_3OH (10:1) as a developing solvent. Preparative TLC was performed on silica gel 60 F_{254} pre-coated plates (layer thickness 0.5 mm, Merck). ^1H NMR spectra were recorded on a JEOL PS-100 spectrometer or a Bruker AM-300 spectrometer and TMS was used as an internal reference. ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer and TMS was used as an internal reference. IR spectra were obtained with a Hitachi Perkin-Elmer model 225 spectrometer. UV spectra were obtained with a Shimadzu UV-210A spectrometer. Melting points were measured with a Yanagimoto micro melting-point apparatus and are uncorrected. Elemental analyses were performed with a Yanagimoto CHN-CORDER MT-3 or at the Elemental Analysis Center of Kyoto University.

Preparation of Hexahydro-1,3,5-triazines 2a—e. A similar method to that described by Smolin and Rapoport[16] was employed. Under cooling with ice-cold water, formalin was gradually added to an equimolar amount of amine. Isolation procedures were as follows.

2a, 2b, and 2d: A powder of K_2CO_3 was added to the reaction solution, and the products were extracted with $CHCl_3$. The extract was dried over K_2CO_3, evaporated in vacuo, and the residue was distilled. **2a**: Bp 40—42 °C/15 mmHg.** **2b**: Bp 63 °C/7 mmHg. In the case of **2d**, *N*-methylene-*t*-pentylamine (bp 92—93 °C) was obtained by distillation; however, this *N*-methyleneamine trimerized spontaneously into **2d** on standing.

2c: Pellets of NaOH were added to the reaction solution, and the resulting organic layer was separated, dried over KOH, and distilled in the presence of *d*-10-camphorsulfonic acid to afford *N*-methylene-*t*-butylamine (bp 67—68 °C); however, this *N*-methyleneamine trimerized spontaneously into **2c** on standing.

2e: The reaction products were extracted with ether, then the extract was dried over NaOH, evaporated in vacuo, and the residue was recrystallized from hexane. Mp 72—73 °C.

Reaction of 1 with Hexahydro-1,3,5-triazines 2a—e. As a typical run, the reaction of **1** with **2c** is described below.

To a solution of 300 mg of **1** in 3 ml of pyridine was added 76 mg of **2c**. After being stirred at 63 °C for 1.5 h, the reaction solution was poured into 10% AcOH, and the products were extracted with AcOEt. The extract was washed with 10% AcOH, brine, dried over Na_2SO_4, and evaporated in vacuo, then preparative TLC was carried out using $CHCl_3$–CH_3OH (20:1) as a developing solvent. The deep blue band was collected, and extracted with $CHCl_3$–CH_3OH (10:1). The extract was evaporated in vacuo, and the residue was further purified by column chromatography (Wakogel C-200, 10 g, Wako Pure Chemical Ind., Ltd.) using $CHCl_3$–CH_3OH (100:1, then 50:1) as an eluent. The deep-blue eluate was collected, and evaporated in vacuo to afford 133 mg (yield, 38%) of **6c** as a deep-blue powder. The reaction conditions and yields of **6a—e** are summarized in Table 5. The 25-*O*-deacetyl derivative of **6c** was prepared from 25-*O*-deacetylrifamycin S[17] and **2c**. Compounds **6a,b**, and **6e** were identical with authentic samples.[12] ^1H and ^{13}C NMR data of **6c** and its 25-*O*-deacetyl derivative are summarized in Tables 1—4. Other physical data of **6c** and its 25-*O*-deacetyl derivative have already been reported.[1] **6d**: UV λ_{max} (CH_3OH) 225 (log ε 4.58), 276 (4.35), 314 (sh, 4.17), 360 (4.28), and 600 nm (4.03); IR ($CHCl_3$) 3440, 1720, 1655 and 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ=9.00 (1H, s, iminium proton), 15.02 (1H, s, 4-OH), and 16.52 (1H, s, 1-OH). Found: C, 61.66; H, 6.95; N, 3.12%. Calcd for $C_{44}H_{58}N_2O_{12}\cdot 3H_2O$: C, 61.38; H, 7.14; N, 3.25%.

Preparation of 15c. To a solution of 8.0 g of 3-formylrifamycin SV[18–20] in 50 ml of pyridine was added 4.0 g of *t*-butylamine. The mixture was stirred at r.t. for 10 min; then 0.5 g of $NaBH_4$ was added to the mixture at 0 °C. After being stirred at 0 °C for 10 min, the reaction mixture was added to 1 l of cold 10% H_2SO_4. The products were extracted with AcOEt, and the extract was washed with H_2O, dried over Na_2SO_4, and evaporated in vacuo. The residue was dissolved in $CHCl_3$–AcOEt (1:1), and the solution was concentrated in vacuo to afford 2.0 g (yield, 22%) of **15c** as orange crystals. ^1H NMR ($CDCl_3$, after treatment with D_2O) δ=1.51 (9H, s, *t*-butyl), 3.76 (1H, d, *J*=11 Hz, $C\underline{H}_2NH$), and 4.15 (1H, d, *J*=11 Hz, $C\underline{H}_2NH$). Found: C, 62.08; H, 7.35; N, 3.62%. Calcd for $C_{42}H_{58}N_2O_{12}\cdot 3/2H_2O$: C, 62.28; H, 7.59; N, 3.45%.

Reaction of 13c with 2c. To a solution of 200 mg of **15c** in 20 ml of $CHCl_3$ was added 2.0 g of MnO_2 (70%, Wako Pure Chemical Ind., Ltd.). After being stirred at r.t. for 15 min, the mixture was filtered, and the filtrate was evaporated in vacuo. The residue, in which **13c** and **12c** were included,[15] was dissolved in 4 ml of pyridine, and to the solution 23 mg of **2c** was added. After being stirred at 62 °C for 1 h, the reaction mixture was extracted with AcOEt under acidic conditions (10% AcOH). The extract was washed with brine, dried over Na_2SO_4, and evaporated in

** (1 mmHg≈133.33 Pa.)

vacuo; then, preparative TLC was carried out using $CHCl_3$–CH_3OH (10:1) as a developing solvent. From the orange band 40 mg (yield, 20%) of **12c** was obtained (AcOEt was used as an eluent). From the deep-blue band 85 mg (yield, 41%) of **6c** was obtained (10:1 $CHCl_3$–CH_3OH was used as an eluent).

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15) Compound **13c** employed in this reaction was contaminated with **12c**. Contamination of **12c** into **13c** is not avoid, because **13c** is rather unstable and easily undergoes disproportionation into **12c** and **15c**. The latter compound **15c** reverts into **13c** during the preparation of **13c**. The disproportionation of **13c** into **12c** and **15c** is considered as that **13c** isomerizes into **16c** in a similar way described for **17c** into **6c**, then the redox reaction between the resulting **16c** and the remaining **13c** affords **12c** and **15c**.

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