Reaction of Rifamycins with Sodium Sulfinates[1]

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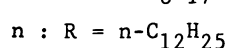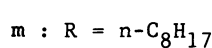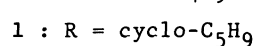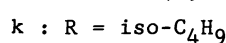(Received January 5, 1988)

The reaction of rifamycin S and the quinonic 3-(hydrazonomethyl)rifamycin derivatives with sodium sulfinates under neutral conditions were found to afford the hydroquinone-type 4-O-sulfonyl derivatives of rifamycin. 3-Amino-4-deoxo-4-iminorifamycin S also gave rise to the hydroquinone-type 4-deoxy-4-sulfonylamino derivatives of rifamycin when treated with sodium sulfinates. Under acidic conditions, rifamycin S and 3-bromorifamycin S produced the hydroquinone- and quinone-type 3-sulfonyl derivatives of rifamycin, respectively, by reactions with sodium sulfinates. Some of sodium salts of 4-O-sulfonylrifamycin SV derivatives afforded rifamycin S and sodium sulfinates and/or sodium sulfonates when heated in AcOEt.

We have recently reported on the reaction of rifamycin S (1A) with sodium sulfite.[2] In connection with this work, we investigated the reaction of 1A with sodium p-toluenesulfinate (2a), which is anticipated to formally resemble sodium sulfite, and found the unusual formation of sulfonic ester sodium salt 4Aa under neutral conditions. This paper describes the reaction of 1A with 2a under various conditions (alkaline, neutral, or acidic), the formation of sulfonic ester sodium salts 4, sulfonic esters 5 and sulfonamides 9, and the decomposition of some of 4A in AcOEt.

Results and Discussion

Reaction of 1A with 2a. We have reported that the reaction of 1A with sodium sulfite under mild alkaline conditions gives the 3-substituted product, sodium rifamycin SV-3-sulfonate.[2] In connection with this

A : X = H
B : X = Br
C : X = -CH=NN(CH₃)₂
D : X = -CH=NN◯
E : X = -CH=NN◯
F : X = -SO₂◯-CH₃
G : X = -SO₂◯
H : X = -SO₂CH₃

a : R = ◯-CH₃
b : R = ◯
c : R = ◯-Ac
d : R = ◯-Cl
e : R = ◯-OH
f : R = ◯-OCH₃
g : R = ◯-NO₂
h : R = ◯-N(CH₃)₂

i : R = CH₃
j : R = n-C₄H₉
k : R = iso-C₄H₉
l : R = cyclo-C₅H₉
m : R = n-C₈H₁₇
n : R = n-C₁₂H₂₅
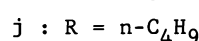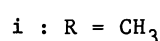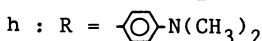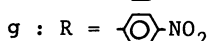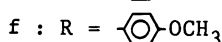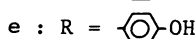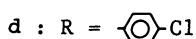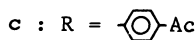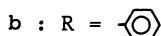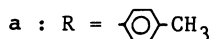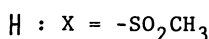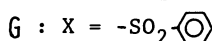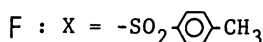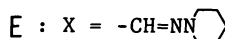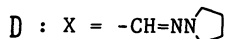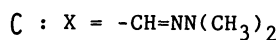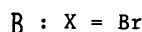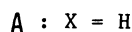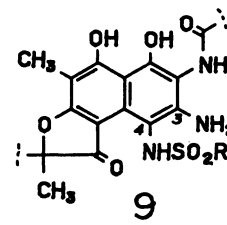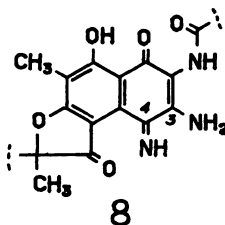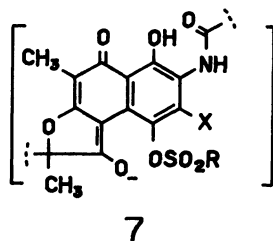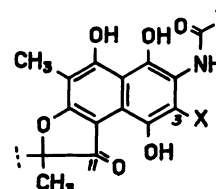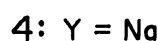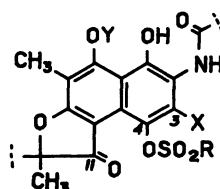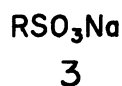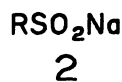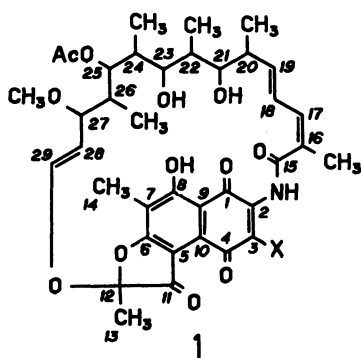
observation, 1A was allowed to react with 2a in an aq NaHCO₃-DMSO mixture (mild alkaline conditions). As a result, no products formed. However, in the absence of NaHCO₃ (neutral conditions) the reaction proceeded smoothly and almost quantitatively to produce a compound which fluoresced an orange color on a silica-gel TLC plate under an UV lamp (365 nm).³⁾ The reaction solution was poured into aq NaCl, and the extraction with AcOEt gave the sulfonic ester sodium salt 4Aa in 85% yield. Sodium salt 4Aa was converted to the corresponding acid form 5Aa by acidification. The 4-O-sulfonyl structure of 5Aa was deduced as follows. The UV spectrum (Table 2, footnote d) of 5Aa resembling that⁴⁾ of rifamycin SV (6A), confirmed the 1,4-naphthalenediol derivative structure for 5Aa; the NMR spectrum (CDCl₃) showed the signal at δ 7.42, which unfortunately overlapped with the signals of the p-tolyl group, but was attributed to the proton at the 3-position; the IR spectrum (KBr) showed the characteristic band of sulfonic ester at 1176 cm⁻¹ (νₛSO₂). These spectral data suggested the 4-O-sulfonyl structure for 5Aa, but the 1-O-sulfonyl structure is also possible. In order to distinguish these two possible structures, the 25-O-deacetyl derivative of 5Aa was prepared from 25-O-deacetylrifamycin S⁵⁾ and 2a. The IR spectrum (CDCl₃) of the 25-O-deacetyl derivative of 5Aa clearly showed the furanone νC(11)=O band at 1709 cm⁻¹ without disturbance of the 25-O-acetyl νC=O band.⁶⁾ This observation confirms the 4-O-sulfonyl structure for 5Aa, because if

5Aa takes the 1-O-sulfonyl structure the furanone νC(11)=O band should appear at ca. 1650 cm⁻¹ due to the intramolecular hydrogen-bonding between the furanone C(11)=O group and the 4-OH group.⁷⁾ The furanone νC(11)=O band of the 25-O-deacetyl derivative of sodium salt 4Aa in CDCl₃ appeared at 1675 cm⁻¹. A decrease of νC(11)=O in the salt form should be accounted for by the contribution of structure 7Aa.

The formation mechanism of sulfonic ester is not clear, but the oxidation potential of 1A seems to play an important role, because rifamycinol⁵⁾ (the 11-deoxo-11-hydroxy derivative of 1A) did not react with 2a under the same conditions as that described above.⁸⁾

The reaction of 1A with 2a in aq AcOH (acidic conditions) produced 3-(p-tolylsulfonyl)rifamycin SV (6F) as a main product (9% yield) along with many complex products in which a trace amount of 5Aa could be detected (analytical TLC). The IR spectrum (CDCl₃) of 6F showed the characteristic bands of sulfone at 1292 (νₐₛSO₂) and 1137 cm⁻¹ (νₛSO₂), and the singlet at δ 7.82 due to the proton at the 3-position of 1A was absent in the NMR spectrum (CDCl₃).

Formation of Sulfonic Ester Sodium Salts 4A and Their Acid Form 5A, and Decomposition of Some of 4A in AcOEt. Similarly to 2a, various sodium sulfinates were also found to react with 1A under neutral conditions to afford sulfonic ester sodium salts 4A, which upon acidification produced 5A. The results are summarized in Tables 1 and 2. All sulfonic esters, except for 5Ac and 5Ag, fluoresced similarly to

Table 1. Sulfonic Ester Sodium Salts 4A

Compound*⁾	Yield/%	νₛSO₂/cm⁻¹ (KBr)	Formula	Analysis^b⁾
4Aa	85	1176	C₄₄H₅₂NNaO₁₄S·2H₂O	C, H, N
4Ab	76	1188	C₄₃H₅₀NNaO₁₄S·H₂O	C, H, N
4Ac	87	1190	C₄₅H₅₂NNaO₁₅S·2H₂O	C, H, N
4Ad	77	1186	C₄₃H₄₉ClNNaO₁₄S	C, H, N
4Ae	62	1166	C₄₃H₅₀NNaO₁₅S·3H₂O	C, H, N
4Af	80	1169	C₄₄H₅₂NNaO₁₅S·H₂O	C, H, N
4Ag	76	1185	C₄₃H₄₉N₂NaO₁₆S·3/2H₂O	C, H, N
4Aj	85	1168	C₄₁H₅₄NNaO₁₄S·3/2H₂O	C, H, N

a) The melting points could not be specified due to gradual decomposition during heating. b) The values were within ±0.3% of the calculated theoretical values.

Table 2. Sulfonic Esters 5A

Compound*⁾	Procedure^b⁾	Yield/%	νₛSO₂/cm⁻¹ (KBr)	Formula	Analysis^c⁾
5Aa^d⁾	A	84	1176	C₄₄H₅₃NO₁₄S·1/2H₂O	C, H, N
5Ab	B	32	1192	C₄₃H₅₁NO₁₄S·3/2H₂O	C, H, N, S
5Ac	A	91	1193	C₄₅H₅₃NO₁₅S·3/2H₂O	C, H, N
5Ad	C	31	1192	C₄₃H₅₀ClNO₁₄S·H₂O	C, H, N, S
5Ae	C	16	1166	C₄₃H₅₁NO₁₅S·H₂O	C, H, N, S
5Af	A	75	1169	C₄₄H₅₃NO₁₅S·3/2H₂O	C, H, N
5Ag	A	84	1192	C₄₃H₅₀N₂O₁₆S·3/2H₂O	C, H, N
5Aj	A	92	1166	C₄₁H₅₅NO₁₄S·3/2H₂O	C, H, N

a) The melting points could not be specified due to gradual decomposition during heating. b) See Experimental. c) The values were within ±0.3% of the calculated theoretical values. d) UV λmax (pH 7.0 phosphate buffer) 226 (log ε 4.65), 296 (4.28), and 414 nm (4.24).

5Aa. The formations of 4A proceeded very cleanly, but 4A and 5A were proved to decompose during work up. Accordingly, the decomposition of some of 4A in AcOEt, which was used as an extraction solvent, was next investigated. The sodium salts 4Aa, 4Ac, 4Ad, and 4Af were heated at 70 °C in a solution of AcOEt for several hours. As a result, each salt decomposed to afford 1A as a main product and many complex compounds along with the formation of precipitates. The precipitate from 4Ac was found to be sodium p-acetylbenzenesulfinate (2c) by a comparison of the NMR spectra (D_2O) with that of the authentic sample. The identification was also confirmed by the reaction of 1A with the precipitate to afford the compound identical with 4Ac (analytical TLC). The IR spectra (KBr) of the precipitates from 4Aa and 4Af showed the sulfonate ν_sSO_2 bands at 1200 and 1190 cm⁻¹, respectively; these precipitates were confirmed to be sodium p-toluenesulfonate (3a) and sodium p-methoxybenzenesulfonate (3f), respectively, by comparing the NMR spectra (D_2O) with those of the authentic samples. The IR spectrum (KBr) of the precipitate from 4Ad showed the sulfonate ν_sSO_2 band at 1200 cm⁻¹, while its NMR spectrum (D_2O) showed that it consisted of two sorts of the compounds, sodium p-chlorobenzenesulfinate (2d) and sodium p-chlorobenzenesulfonate (3d) (molar ratio, 1:ca. 2). The results are summarized in Table 3. It is of interest that the decomposition reactions of sodium salts 4Aa, 4Ac, 4Ad, and 4Af in AcOEt commonly afforded 1A,

while the oxidation states of the precipitates were different depending upon the nature of the substituent involved in the phenylsulfonyl group. The mechanism of decomposition is not clear. Heating of 5Aa in AcOEt at 70 °C for 4 h resulted in the decomposition of 5Aa into many complex compounds in which 1A could not be detected (analytical TLC).

Formation of Sulfones 6G and 6H. Sodium benzenesulfinate (2b) was allowed to react with 1A in aq AcOH to afford 3-(phenylsulfonyl)rifamycin SV (6G) in 5% yield. On the other hand, it was observed by TLC analysis that the 1,4-naphthoquinone derivative 1G could be produced in good yield by the reaction of 3-bromorifamycin S[9] (1B) with 2b in aq AcOH. Indeed, 3-(methylsulfonyl)rifamycin SV (6H) was obtained in 63% yield by the reaction of 1B with sodium methanesulfinate (2i) in aq AcOH followed by reduction with L-ascorbic acid.

Formation of Sulfonic Esters 5C—E. The reactions of the 3-(hydrazonomethyl)rifamycin derivatives 1C—E with some of 2 under neutral conditions followed by acidification, afforded the corresponding sulfonic esters 5C—E. The sulfonic ester structures of 5C—E were supported by the characteristic ν_sSO_2 bands of the sulfonic esters. The results are summarized in Table 4.

Formation of Sulfonamides 9. When 3-amino-4-deoxo-4-iminorifamycin S[10] (8) were treated with some of 2 under neutral conditions, the reaction proceeded almost quantitatively to afford sulfona-

Table 3. Decomposition of Sulfonic Ester Sodium Salts 4Aa, 4Ac, 4Ad, and 4Af in AcOEt at 70°C

Compound	Time/h	Isolation yield/% of 1A	Identification of the precipitate (Yield/%)
4Aa	5.75	46	3a (ca. 71)
4Ac	4.75	70	2c (ca. 80)
4Ad	4	49	2d and 3d (ca. 98)[a]
4Af	6.25	37	3f (ca. 67)

a) The molar ratio of 2d to 3d was 1:ca. 2 (determined by the NMR spectrum in D_2O on the basis of integration of the signals of aromatic protons).

Table 4. Sulfonic Esters 5C—E

Compound[a]	Yield/%	ν_sSO_2/cm⁻¹ (KBr)	Formula	Analysis[b]
5Ce	52	1166	$C_{46}H_{57}N_3O_{15}S \cdot H_2O$	C, H, N, S
5Cf	51	1169	$C_{47}H_{59}N_3O_{15}S$	C, H, N, S
5Ch	41	1167	$C_{48}H_{62}N_4O_{14}S$	C, H, N, S
5Cj	33	1167	$C_{44}H_{61}N_3O_{14}S \cdot 1/2H_2O$	C, H, N, S
5Cl	45	1164	$C_{45}H_{61}N_3O_{14}S$	C, H, N, S
5Cn	24	1163	$C_{52}H_{77}N_3O_{14}S$	C, H, N, S
5Dj	41	1164	$C_{46}H_{63}N_3O_{14}S$	C, H, N, S
5Dk	41	1161	$C_{46}H_{63}N_3O_{14}S$	C, H, N, S
5Dm	31	1165	$C_{50}H_{71}N_3O_{14}S$	C, H, N, S
5Dn	29	1163	$C_{54}H_{79}N_3O_{14}S$	C, H, N, S
5Ej	51	1164	$C_{47}H_{65}N_3O_{14}S \cdot 1/2H_2O$	C, H, N

a) The melting points could not be specified due to gradual decomposition during heating. b) The values were within ±0.3% of the calculated theoretical values.

Table 5. Sulfonamides 9

Compound[a]	Yield/%	$\nu_s SO_2/cm^{-1}$ (CHCl$_3$)	Formula	Analysis[b]
9d	67	1162	$C_{43}H_{52}ClN_3O_{13}S \cdot H_2O$	C, H, N, S
9g	66	1168	$C_{43}H_{52}N_4O_{15}S$	C, H, N, S
9h	70	1152	$C_{45}H_{58}N_4O_{13}S \cdot H_2O$	C, H, N, S
9j	69	1148	$C_{41}H_{57}N_3O_{13}S \cdot 1/2H_2O$	C, H, N, S
9k	62	1148	$C_{41}H_{57}N_3O_{13}S \cdot H_2O$	C, H, N, S
9l	74	1145	$C_{42}H_{57}N_3O_{13}S \cdot H_2O$	C, H, N, S

a) The melting points could not be specified due to gradual decomposition during heating. b) The values were within ±0.3% of the calculated theoretical values.

mides **9** after acidification. The sulfonamide structures of **9** were supported by the characteristic $\nu_s SO_2$ bands of the sulfonamides. The results are summarized in Table 5. All sulfonamides in Table 5, except for **9g**, fluoresced similarly to **5Aa**.

Conclusion

Quinone- and quinone imine-type derivatives of rifamycin were found to react with sodium sulfinates under neutral conditions, giving the sulfonic esters and the sulfonamides, respectively. To our knowledge, only limited numbers of reports are concerned with the formation of sulfonic esters and sulfonamides in the reactions of quinonic or quinoniminic compounds with sulfinic acids or their salts.[11] Novel examples of such reactions are provided as described above.

Experimental

Analytical TLC was performed on Silica gel 60 F$_{254}$ pre-coated plates (0.25 mm, Merck), using CHCl$_3$–CH$_3$OH (10:1 or 4:1) as a developing solvent. Preparative TLC was performed on Silica gel 60 F$_{254}$ pre-coated plates (2 mm, Merck). IR spectra were measured on a JASCO IRA-1, a Shimadzu IR-440 spectrometer, or a Hitachi 270-50 infrared spectrometer. UV spectra were taken with a Shimadzu UV-210 spectrometer. Measurements of NMR spectra were carried out using a JEOL PS-100, a Hitachi R-24A spectrometer, or a Hitachi R-24B spectrometer. Tetramethylsilane was used as an internal reference for a solution of CDCl$_3$. NMR spectra of sodium sulfinates or sodium sulfonates were recorded in a solution of D$_2$O without an internal reference. Elemental analyses were performed with a Yanagimoto CHN-CORDER MT-3 or at the Elemental Analysis Center of Kyoto University.

Rifamycin Derivatives 1C—E. These compounds were prepared by oxidation of compounds[12] **6C—E** in CHCl$_3$ with MnO$_2$ (70%, Wako Pure Chemical Ind., Ltd.) followed by washing with dil H$_2$SO$_4$.

Sodium Sulfinates 2a—n and Sodium Sulfonates 3a, 3d, and 3f. Compounds **2a**, **2b**, **3a**, and **3d** were purchased. Compounds **2d**,[13a] **2g**,[13b] **2i**,[14b] **2j**,[14b] and **2k—n**[15] were prepared by the methods reported. Compounds **2c** and **2f** were prepared as **2d** from the corresponding sulfonyl chloride.[14a,16] Compound **2e** was prepared as **2g** from p-hydroxybenzenesulfonyl chloride.[17] Compound **2h** was prepared[18] from the corresponding sulfonyl chloride.[13c,d]

Compound **3f** was prepared by hydrolysis of p-methoxybenzenesulfonyl chloride with NaHCO$_3$

Preparation of Sulfonic Ester Sodium Salts in Table 1 and the 25-O-Deacetyl Derivative of 4Aa. General Procedure: A solution of an excess amount of **2** in H$_2$O was added to a solution of **1A** in DMSO. After being stirred for several hours, the reaction mixture was poured into aq NaCl, and extracted with AcOEt. The combined extracts were washed with aq NaCl, dried over Na$_2$SO$_4$, then evaporated in vacuo. The resulting residue was precipitated from AcOEt–hexane, AcOEt–benzene, or AcOEt–benzene–hexane to afford **4A**, tabulated in Table 1. As a typical run, the preparation of **4Aa** is described below.

A solution of **2a** (2.16 g, 12 mmol) in H$_2$O (10 ml) was added to a solution of **1A** (2.00 g, 2.9 mmol) in DMSO (50 ml). After being stirred at r.t. for 3 h, the reaction mixture was treated according to the general procedure to afford 2.24 g (85% yield) of **4Aa** as a dark yellow powder after precipitation from AcOEt–benzene–hexane.

The 25-O-deacetyl derivative of **4Aa** was obtained from 25-O-deacetylrifamycin S[5] and **2a** in 82% yield. The 25-O-deacetyl derivative of **4Aa**: IR (KBr) 1175 cm^{-1} ($\nu_s SO_2$). IR (CDCl$_3$) 1675 cm^{-1} (νC(11)=O). Anal. (C$_{42}$H$_{50}$NNaO$_{13}$S · 1/2H$_2$O) C, H, N.

Preparation of Sulfonic Esters 5Aa, 5Ac, 5Af, 5Ag, 5Aj and the 25-O-Deacetyl Derivative of 5Aa (Procedure A). General Procedure: A sodium salt **4A** was dissolved in AcOEt, then aq NaCl acidified with H$_2$SO$_4$ (acidic aq NaCl) was added to the solution. The mixture was shaken, and the organic layer was separated, washed with aq NaCl, dried over Na$_2$SO$_4$ or MgSO$_4$, and evaporated in vacuo. The resulting residue was precipitated from AcOEt–hexane or AcOEt–benzene–hexane to afford the title compounds. As a typical run, the preparation of **5Aa** is described below.

A solution of 1.13 g of **4Aa** in 80 ml of AcOEt was treated according to the general procedure, and the resulting residue was precipitated from AcOEt–hexane to afford 0.91 g (85% yield) of **5Aa** as a yellow powder. **5Aa**: ^{1}H NMR (CDCl$_3$) δ=2.33 (3H, s, the methyl protons of the p-tolylsulfonyl group), 7.04 (2H, d, the aromatic protons of the p-tolylsulfonyl group), 7.34—7.52 (3H, signals due to the aromatic protons of the p-tolylsulfonyl group and the proton at the 3-position).

The 25-O-deacetyl derivative of **5Aa** was obtained from the 25-O-deacetyl derivative of **4Aa** in 83% yield. The 25-O-deacetyl derivative of **5Aa**: IR (KBr) 1176 cm^{-1} ($\nu_s SO_2$). IR (CDCl$_3$) 1709 cm^{-1} (νC(11)=O). Anal. (C$_{42}$H$_{51}$NO$_{13}$S · H$_2$O) C, H, N.

Preparation of Sulfonic Ester 5Ab (Procedure B). A solution of **2b** (0.19 g, 1.2 mmol) in H$_2$O (1 ml) was added to

a solution of 1A (0.20 g, 0.29 mmol) in DMSO (8 ml). After being stirred overnight at r.t., the reaction mixture was poured into acidic aq NaCl. The resulting precipitate was collected, washed with acidic aq NaCl, and dissolved in AcOEt. The ethyl acetate solution was washed with aq NaCl, dried over $MgSO_4$, then evaporated in vacuo. The resulting residue was precipitated from AcOEt-benzene-hexane to afford 0.08 g (32% yield) of 5Ab as a dark yellow powder.

Preparation of Sulfonic Esters 5Ad and 5Ae (Procedure C). As a typical run, the preparation of 5Ad is described below.

A solution of 2d (0.27 g, 1.4 mmol) in H_2O (1.5 ml) was added to a solution of 1A (0.20 g, 0.29 mmol) in DMSO (7 ml). After being stirred overnight at r.t., the reaction mixture was treated by the same procedure as that described for 5Ab. The resulting residue was separated on preparative TLC plates (4:1 $CHCl_3$-CH_3OH). The yellow band was collected and extracted with CH_3OH. AcOEt was added to the methanolic extract. The ethyl acetate solution was washed successively with acidic aq NaCl and aq NaCl, dried over $MgSO_4$, and evaporated in vacuo. The resulting residue was precipitated from AcOEt-hexane to afford 0.08 g (31% yield) of 5Ad as a pale-yellow powder.

Compound 5Ae was obtained from 1A and 2e in 16% yield.

Preparation of 3-Sulfonylrifamycin Derivatives 6F and 6G. As a typical run, the preparation of 6F is described below.

A solution of 2a (2.5 g, 14 mmol) in H_2O (20 ml) was added to a solution of 1A (0.70 g, 1.0 mmol) in AcOH (30 ml). After being stirred at r.t. for 12 h, the reaction mixture was poured into H_2O. The resulting precipitate was collected, washed with H_2O, and dissolved in AcOEt. The ethyl acetate solution was washed with aq NaCl, dried over Na_2SO_4, and evaporated in vacuo. The resulting residue was separated on preparative TLC plates (two developments with 200:20:1 $CHCl_3$-EtOH-AcOH). The orange band was collected and extracted with CH_3OH. The methanolic solution was diluted with AcOEt, and the organic mixture was washed successively with acidic aq NaCl and aq NaCl, dried over Na_2SO_4, and evaporated in vacuo. The resulting residue was recrystallized from acetone to afford 0.08 g (9% yield) of 6F as orange crystals. Mp ca. 180 °C (decomp). IR (CDCl$_3$) 1292 ($\nu_{as}SO_2$) and 1137 cm^{-1} ($\nu_s SO_2$). ^{1}H NMR (CDCl$_3$) δ=2.41 (3H, s, the methyl protons of the p-tolylsulfonyl group), 7.28 (2H, d, the aromatic protons of the p-tolylsulfonyl group), 7.88 (2H, d, the aromatic protons of the p-tolylsulfonyl group). Anal. ($C_{44}H_{53}NO_{14}S \cdot 1/2H_2O$) C, H, N.

Physical data of 6G are as follows. Mp ca. 174 °C (decomp). IR (CDCl$_3$) 1295 ($\nu_{as}SO_2$) and 1140 cm^{-1} ($\nu_s SO_2$). ^{1}H NMR (CDCl$_3$) δ=7.3—7.7 (3H, m, the aromatic protons of the phenylsulfonyl group), 7.9—8.1 (2H, d, the aromatic protons of the phenylsulfonyl group). Anal. ($C_{43}H_{51}NO_{14}S \cdot H_2O$) C, H, N.

Preparation of 3-(Methylsulfonyl)rifamycin SV (6H). A solution of 2i (0.47 g, 4.6 mmol) in H_2O (1 ml) was added to a solution of 3-bromorifamycin S[9] (1B) (0.50 g, 0.65 mmol) in AcOH (6 ml). After being stirred at r.t. for 40 min, the reaction mixture was poured into H_2O. The resulting precipitate was collected, washed with H_2O, and dissolved in AcOEt. The ethyl acetate solution was added to a

solution of 2.5 g of L-ascorbic acid in aq CH_3OH. The mixture was shaken for several min, washed with aq NaCl, dried over $MgSO_4$, and evaporated in vacuo. The resulting residue was purified by preparative TLC in a similar manner to that described for 6F, affording 0.32 g (63% yield) of 6H as an orange powder after precipitation from AcOEt-ligroine. Mp ca. 204 °C (decomp). IR (CDCl$_3$) 1290 ($\nu_{as}SO_2$) and 1125 cm^{-1} ($\nu_s SO_2$). ^{1}H NMR (CDCl$_3$) δ=3.50 (3H, s, the methyl protons of the methylsulfonyl group). Anal. ($C_{38}H_{49}NO_{14}S$) C, H, N.

Decomposition of Sulfonic Ester Sodium Salts 4Aa, 4Ac, 4Ad, and 4Af in AcOEt. As a typical run, the decomposition of 4Aa is described below.

A 300 mg of 4Aa was dissolved in 20 ml of AcOEt. After being stirred at 70 °C for 5.75 h, the resulting precipitate was collected by filtration and washed with AcOEt, affording 46 mg of a brownish powder. IR (KBr) 1200 cm^{-1}. The NMR spectrum in D_2O was identical with that of the authentic sample of 3a. The filtrate and the washings were combined and evaporated in vacuo. The resulting residue was separated by a preparative TLC plate (10:1 $CHCl_3$-CH_3OH). The yellow band was collected and extracted with CH_3OH. The methanolic solution was diluted with AcOEt, and the organic mixture was washed successively with a mixture of a pH 4 buffer and aq NaCl and aq NaCl, dried over $MgSO_4$, and evaporated in vacuo. The resulting residue was crystallized from i-C_3H_7OH to afford 116 mg of yellow crystals. The IR spectrum in CHCl$_3$ was identical with that of 1A.

Preparation of Sulfonic Esters in Table 4. These compounds were prepared from 3-(hydrazonomethyl)rifamycin derivatives 1C—E and 2 by a similar procedure to that described for 5Ad. As developing solvents for preparative TLC, AcOEt-CH_3OH (60:1—20:1) or $CHCl_3$-CH_3OH (10:1) was used. AcOEt-hexane or AcOEt-ligroine was used as a crystallizing solvent.

Preparation of Sulfonamides in Table 5. General Procedure: A solution of an excess amount of 2 in H_2O was added to a solution of 3-amino-4-deoxo-4-iminorifamycin S[10] (8) in DMSO. After being stirred at r.t. for several min, the reaction mixture was poured into aq NaCl and extracted with $CHCl_3$. The chloroform extracts were combined and reextracted with H_2O. The aqueous layers were extracted again with $CHCl_3$ under acidic conditions which were made by addition of dil H_2SO_4. The combined extracts were washed with aq NaCl, dried over Na_2SO_4, and evaporated in vacuo. The resulting residue was precipitated from $CHCl_3$-hexane to afford a sulfonamide 9 in Table 5. As a typical run, the preparation of 9h is described below.

A solution of 2h (0.13 g, 0.59 mmol) in H_2O (0.4 ml) was added to a solution of 8 (0.14 g, 0.20 mmol) in DMSO (2.4 ml). After being stirred at r.t. for 5 min, the reaction mixture was treated according to the general procedure, affording 0.13 g (70% yield) of sulfonamide 9h as a yellow powder.

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