of 41 mg of **13c** in 1 mL of MeOH was treated with 0.11 mL of 1 N NaOH and 2 mL of water to provide 44 mg of **13d**.

6,9α-Epoxy-5-fluoro-11α,15(*S*)-dihydroxyprosta-5(*E*),13(*E*)-dien-1-oic Acid, Sodium Salt (14d). A solution of 275 mg of **14c** in 1 mL of MeOH was treated with 0.75 mL of 1 N NaOH and 5 mL of water to provide 271 mg of **14d**.

6,9α-Epoxy-5(*R*)-fluoro-11α,15(*S*)-dihydroxyprosta-6,13(*E*)-dien-1-oic Acid, Sodium Salt (15d). A solution of 347 mg of **15c** in 2 mL of MeOH was treated with 0.93 mL of 1 N NaOH and 5 mL of water to provide 325 mg of **15d**.

6,9α-Epoxy-5(*S*)-fluoro-11α,15(*S*)-dihydroxyprosta-6,13(*E*)-dien-1-oic Acid, Sodium Salt (16d). A solution of 264 mg of **16c** in 1 mL of MeOH was treated with 0.72 mL of 1 N NaOH and 5 mL of water to provide 263 mg of **16d**.

6,9α-Epoxy-5-fluoro-11α,15(*S*)-dihydroxyprosta-5(*Z*),13(*E*)-dien-1-oic Acid, Sodium Salt (17d). A solution of 5 mg of **17c** in 1 mL of MeOH was treated with 0.18 mL of 0.1 N NaOH and 2 mL of water for 24 h to provide 5 mg of **17d**.

Methyl 6,9α:7(*R*),11α-Diepoxy-15(*S*)-hydroxyprosta-5(*Z*),13(*E*)-dien-1-oate (47) and Methyl 6,9α:7(*R*),11α-Diepoxy-15(*S*)-hydroxyprosta-5(*E*),13(*E*)-dien-1-oate (48). A solution of 108 mg of the mixture of **25c** and **26c** above in 20 mL of MeOH was added to a solution prepared from 30 mg of sodium metal in 10 mL of MeOH. After 4 h at ca. 25 °C, TLC analysis showed no sign of reaction. The mixture was refluxed for 20 h until little starting material remained. After evaporation to a small volume, the mixture was diluted with ether and washed twice with water and brine. After drying over sodium sulfate and evaporation, DCLC (60% EtOAc) provided 21 mg of a mixture of isomers, ca. 82% **47** and 18% **48**, R_f 0.47.

Methyl 6,9α-Epoxy-5(*S*)-fluoro-6(*S*),11α,15(*S*)-trihydroxyprost-13(*E*)-en-1-oate (45) and Methyl 6,9α-Epoxy-5(*S*)-fluoro-6(*R*),11α,15(*S*)-trihydroxyprost-13(*E*)-en-1-oate (46). A sample of 148 mg of **16a**, which had become gummy with moisture after standing for about 8 months, was redried and found by ^{13}C NMR to contain about 20% of other materials. This sample was dissolved in 1 mL of water and chilled in an ice bath. After the addition of 20 mL of EtOAc, 5 mL of 2.5 % citric acid was added with vigorous stirring. The organic layer was separated and washed with brine. After removal of solvent the residue was dissolved in methanol and esterified with diazomethane. DCLC (20%, 50%, 100% EtOAc) provided 17 mg of crude **47**, 10 mg of a complex mixture, R_f 0.17, and 97 mg of a mixture, R_f 0.08, of ca. 55% **45** and 45% **46**.

6,9α:7(*R*),11α-Diepoxy-15(*S*)-hydroxyprosta-5(*Z*),13(*E*)-dien-1-oic Acid, Sodium Salt (49) and 6,9α:7(*R*),11α-Diepoxy-15(*S*)-hydroxyprosta-5(*E*),13(*E*)-dien-1-oic Acid, Sodium Salt (50). A solution of 21 mg of the mixture of **47** and **48** in 1 mL of MeOH was treated with 0.08 mL of 1 N NaOH and 1 mL of water to provide 23 mg of a mixture of ca. 84% **49** and 16% **50**.

Acid Decomposition of 14d. A solution of 113 mg of **14d** in 50 mL water was acidified to pH 5.3 by the addition of small pieces of dry ice and stored for 72 h at ca. 24 °C. After adding 1 N NaOH to return the pH to 8, lyophilization left a residue of 119 mg. ^{13}C NMR analysis (based on the relative intensities of the C-9 signals) indicated that the mixture contained ca. 20% **14d**, 34% 6,9α-epoxy-5(*S*)-fluoro-6(*S*),11α,15(*S*)-trihydroxyprost-13(*E*)-en-1-oic acid, sodium salt (**41**), 18% 6,9α-epoxy-5(*S*)-fluoro-6(*R*),11α,15(*S*)-trihydroxyprost-13(*E*)-en-1-oic acid, sodium salt (**42**), 15% 6,9α-epoxy-5(*R*)-fluoro-6(*S*),11α,15(*S*)-trihydroxyprost-13(*E*)-en-1-oic acid, sodium salt (**43**), and 13% 6,9α-epoxy-5(*R*)-fluoro-6(*R*),11α,15(*S*)-trihydroxyprost-13(*E*)-en-1-oic acid, sodium salt (**44**).

Decomposition of 15d. 1. To a solution of 259 mg of **15d** in 50 mL of water was added sufficient 1 N NaOH to raise the pH to 11. After 24 h the pH had fallen to 9.5, so additional base was added to return it to 11. After an additional 48 h (pH 9.5) lyophilization provided 282 mg of a mixture containing ca. 10% of **15d**, 30% of **49**, 45% of material that is assigned 6,9α-epoxy-5,11α,15(*S*)-trihydroxyprosta-6,13(*E*)-dien-1-oic acid, sodium salt (**51**), and 10% and 5% of two other materials. The composition was assigned on the basis of relative intensities of the C-6 signals.

2. To a solution of 267 mg of **15d** in 50 mL water were added a few small pieces of dry ice, which lowered the pH to 6.0. After 48 h at 24 °C lyophilization left a residue of 281 mg that was composed of **15d**, **43**, **44**, and **49** in ca. 3:3:2:2 as well as one or more unidentified minor impurities.

3. A solution of 270 mg of **15d** in 50 mL of water was acidified by the addition of small portions of Dowex 50W-X2 resin until a faint cloudiness developed. The resin was removed by filtration and rinsed with 50 mL of water. After 16 h at 24 °C the filtrate (pH 4.2) was returned to pH 8 and lyophilized, leaving a residue of 243 mg that was composed of ca. 20% **15d**, 45% **43**, and 35% **44**.

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Supplementary Material Available: The carbon and proton NMR assignments of compounds discussed and some related compounds in tabular form together with the spectrum of **14d** (14 pages). Ordering information is given on any current masthead page.

Translactonization in Erythromycins

Isaac O. Kibwage, Roger Busson, Gerard Janssen, Jos Hoogmartens, and Hubert Vanderhaeghe*

Laboratorium voor Farmaceutische Chemie, Katholieke Universiteit Leuven, B-3000 Leuven, Belgium

Johan Bracke

Janssen Pharmaceutica, B-2340 Beerse, Belgium

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When erythromycin A is heated in diethylamine–acetic acid, an erythromycin hemiketal is obtained, which can be further transformed into a new enol ether and spiroketal. The new enol ether is also obtained in equilibrium with the normal one on heating erythromycin A or B in pyridine–acetic acid. The novel compounds, which will be called pseudoerythromycin derivatives, are characterized by a translactonization between the C_{11}-hydroxyl and the lactone group. Their structure was proved by mass and ^1H and ^{13}C NMR spectrometry, by acetylation experiments, and by degradation with lead tetraacetate.

In endeavoring to obtain a larger amount of the novel erythromycin A hemiketal, which we recently isolated from mother liquors of industrial production of erythromycin A,[1] the latter compound was treated with different com-

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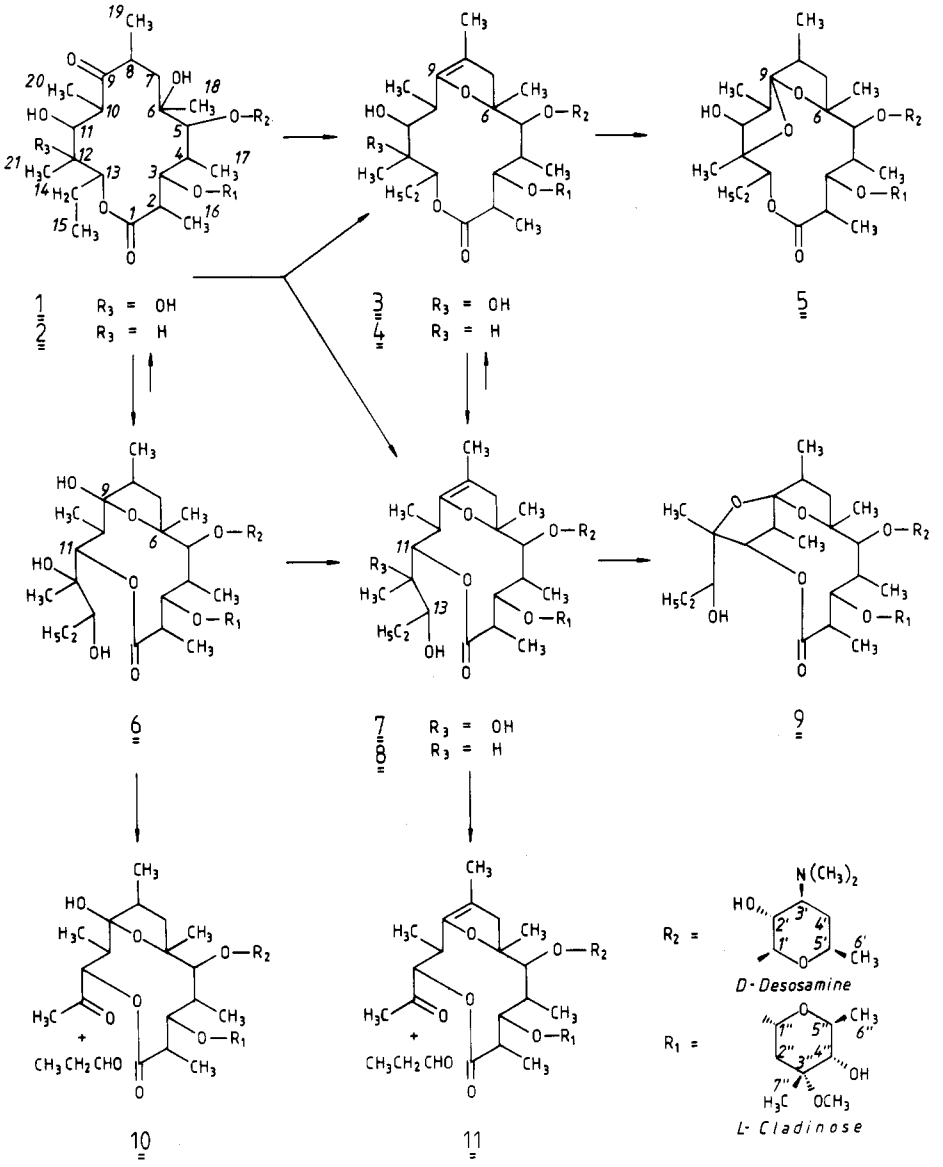
Scheme I



binations of acid–base mixtures. These reagents were chosen since treatment of erythromycin A (1) with glacial acetic acid or with dilute mineral acid does not give a hemiketal but leads to 8,9-anhydroerythromycin A 6,9-hemiketal (3) (usually called erythromycin A enol ether) or to erythromycin A 6,9:9,12-spiroketal (5) (usually called anhydroerythromycin A), respectively (Scheme I).[2,3]

The desired hemiketal 6 could be readily prepared by heating 1 for 3 days in a 3:1 mixture of diethylamine–acetic acid at 45–50 °C. The compound was obtained in a crystalline form in a yield of about 25%. Attempts to increase the yield by changing the reaction time or temperature or by using other secondary amines, such as pyrrolidine or piperidine, were all unsuccessful. In triethylamine–acetic acid no reaction took place, whereas on heating in a 3:1 mixture of pyridine–acetic acid, 1 was converted into two other products, namely,the already known enol ether 3 and a new enol ether 7, which we also isolated previously from mother liquor concentrates.[1] Examination of the reaction mixture by high-performance liquid chromatography (HPLC) indicated complete transformation of erythromycin A, after being heated for 24 h at 70 °C, into a 20:80 equilibrium mixture of 3 and 7. This equilibrium, which could also be attained under the same conditions from either 3 or 7, did not shift significantly by substitution of acetic acid for other acids, although the reaction rate was influenced, e.g., 4 h for complete equilibration with pyridine–formic acid and 5 days with pyridine–trimethylacetic acid.

When hemiketal 6 was kept in acetic acid for 4 h at room temperature, the method of choice for preparing enol ether from erythromycin A, it was completely transformed into the new enol ether 7. This observation indicates a close structural relationship between 7 and 6, and, for reasons outlined hereafter, these compounds will be called pseudoerythromycin A enol ether (7) and pseudoerythromycin A hemiketal (6).

The structural assignment of 7 was based on the following chemical and spectral evidence. Mass spectrometry as well as normal ^{13}C NMR spectrometry indicated that 7 has two intact sugars and an aglycon framework similar to that of the normal enol ether 3. From a comparison of the ^{13}C chemical shifts of 7 (Table I) with those of eryth-

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Table I. Aglycon ^{13}C NMR Chemical Shifts[a] of Erythromycin Derivatives

	chem shift, ppm					
C	6[b]	7[b]	8	9[b]	10	11
1	176.7	175.7	176.1	173.4	175.5	172.9
2	46.9	46.8	46.8	46.6	46.5	46.1
3	80.3	80.6	80.5	82.4	80.7	80.3
4	39.9	38.8	39.0	39.6	39.8	38.5
5	85.9	81.6	81.8	85.6	85.8	81.5
6	84.1	86.0	85.9	85.6	84.5	85.9
7	40.9	43.4	43.4	43.3	41.0	43.3
8	37.5	101.2	101.4	38.0	38.0	102.3
9	106.6	149.5	149.7	118.1	105.9	147.6
10	38.1	31.7	31.3	45.3	39.7	32.2
11	72.9	77.5	78.1	89.0	77.9	80.2
12	76.5	76.6	38.2	83.6	207.0	205.8
13	77.7	76.8	71.1	77.0		
14	22.9	22.5	26.7	24.0		
14-Me(15)	11.6	11.7	10.9	11.6		
2-Me(16)	14.0	15.0	15.2	14.8	13.3	14.6
4-Me(17)	10.3	9.3	8.9	9.5	10.3	9.2
6-Me(18)	29.7	26.7	26.9	28.9	29.7	26.7
8-Me(19)	11.9	10.8	11.0	15.0	11.8	10.4
10-Me(20)	10.0	11.1	7.9	16.3	9.8	10.7
12-Me(21)	17.1	16.7	9.3	21.8	27.6	27.2

[a] Complete listing of the chemical shifts as well as the NMR data for the acetyl derivatives will be published elsewhere together with a detailed discussion of the assignments. [b] Assignments are based on a ^{13}C ^{1}H shift correlated 2D NMR spectrum; analogous measurements on erythromycin A were recently reported by: Everett, J. R.; Tyler, J. W. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2599.

romycin A,[4,5] the presence of an enol ether structure at C_9 was inferred. This conclusion was based on the absence of the low-field C_9 ketone signal and of one of the signals from the group of nonoxygenated methine carbons (C_2, C_4, C_8, or C_{10}), together with the appearance of two new sp^2 carbon resonances at 149.5 and 101.2 ppm (both being a singlet in the off-resonance decoupled spectrum) and also on the characteristic 10 ppm downfield shift for one of the signals due to C_6 or C_{12}, participating in the ether bridge. Further deductions of structure could not be made on the basis of this spectrum, because of uncertain assignment of similarly substituted carbons such as C_6 and C_{12} or the methine carbons C_2, C_4, C_8, and C_{10} or the group of oxygenated carbons C_3, C_5, C_{11}, and C_{13} and also because of ambiguity in interpretation of observed substitution effects, mainly as a result of induced conformational reorganization of the flexible macrolide ring.

As the structure of the normal enol ether **3** has been established unambiguously as the 8,9-anhydro 6,9-hemiketal,[3,6] the following possibilities were retained for the new enol ether **7**: (a) the double bond is located between C_9 and C_{10} rather than C_8 and C_9 as described recently for an erythronolide analogue,[7] (b) the C_{12}-OH is involved in the ether bridge rather than the C_6-OH, and (c) a C_8–C_9 or C_9–C_{10} double bond could be accompanied by an epimerization at C_{10} or C_8, respectively. The third possibility was eliminated on the following evidence: heating of erythromycin A (after exchange of all labile hydrogens for deuterium) with pyridine–deuteriated acetic acid afforded, after usual workup, **3** and **7** with no incorporation of deuterium in either compound, thus excluding epimerization at C_8 or C_{10}.

The localization of the internal ether bond in **7** is based on a comparison of its CMR spectrum with that of an analogous compound (**8**) obtained from erythromycin B. Indeed, heating of erythromycin B (**2**) in pyridine–acetic acid in the same way as described for **1** similarly gave a mixture of the known[3] enol ether **4** and a new enol ether **8** (Scheme I). As erythromycin B has no C_{12} hydroxyl group, a C_9–O–C_{12} ether bridge in **8** is excluded, and since the CMR shifts of **8** (Table I) relative to erythromycin B[4,5] compare very well with those of **7** relative to erythromycin A, one can safely assume that the internal ether bond in **7** is also between C_6 and C_9.

Table II. ^{1}H NMR Chemical Shifts[a] and Coupling Constants for 3 and 7

	chem shift, ppm		coupling constants, Hz		
	3	7		3	7
H-2	2.72	2.83	$J_{2,3}$	3.7	10.0
H-3	4.10	4.29	$J_{3,4}$	2.4	0
H-4	1.89	1.76	$J_{4,5}$	7.8	9.5
H-5	3.89	3.70	$J_{7e,7a}$	15.5	16.0
H-7e	2.65	2.79	$J_{7e,19}$	1.8	1.5
H-7a	1.96	2.03	$J_{7a,19}$	1.1	1.5
H-10	2.80	2.94	$J_{10,11}$	8.0	2.7
H-11	3.46	5.05	$J_{13,14e}$	2.6	2.5
H-13	4.86	2.83	$J_{13,14a}$	10.7	10.0
H-14e	1.89	1.68	$J_{14a,14e}$	14.5	nd
H-14a	1.47	1.36	$J_{14,15}$	7.5	7.5
14-Me(15)	0.89	1.00	$J_{2,16}$	7.5	7.0
2-Me(16)	1.15	1.28	$J_{4,17}$	7.5	7.0
4-Me(17)	1.09	1.11	$J_{10,20}$	7.0	7.0
6-Me(18)	1.35	1.42			
8-Me(19)	1.57	1.55			
10-Me(20)	1.05	1.23			
12-Me(21)	1.06	1.20			

[a] δ values in ppm from Me_4Si; as determined from a 2D homonuclear shift correlated (COSY-45) experiment; only the aglycon protons are given. nd = not determined because of overlapping by sugar protons.

The position of the double bond in **7** was deduced from two-dimensional ^{1}H NMR which allowed complete and unambiguous assignment of all proton resonances. The chemical shift values for the aglycon protons of **3** and **7** as determined from a 360-MHz 2D proton–proton shift correlation spectrum (COSY-45 experiment) are collected in Table II. Both compounds lack a H-8 signal and this immediately fixes the double bond in both isomers between C_8 and C_9. Another argument is the existence of allylic long-range coupling between the C_8-methyl protons and the protons on C_7 in **3** as well as in **7**. Further examination of the ^{1}H NMR data shows that apart from a change of some coupling constants which points to a different conformation, the shift values for both compounds are very similar, except for H-11 (+1.59 ppm for **3** → **7**) and H-13 (−2.03 ppm for **3** → **7**). The downfield shift of H-11, which is characteristic for esterification of a secondary α-hydroxyl group,[8] together with the concomitant upfield shift of H-13 led to the hypothesis of an intramolecular transesterification between the C_{11}-OH and the C_{13} lactone group. This explanation is confirmed by inspection of the 2D-COSY spectrum of **7**, which clearly shows coupling between H-13 and a hydroxyl proton located at 3.28 ppm, a coupling which is absent in the spectrum of **3**.

Conclusive evidence for the proposed structure of **7** was obtained by oxidation of **7** with lead tetraacetate. This reaction gave propionaldehyde and a new carbonyl compound **11**. The molecular ion of **11** at m/e 655 and a weak ketone absorption at 280 nm ($A_{1\,cm}^{1\%}$ 2.8) are in agreement with the expected cleavage reaction between the two adjacent hydroxylated carbons C_{12} and C_{13}. ^{13}C NMR shifts

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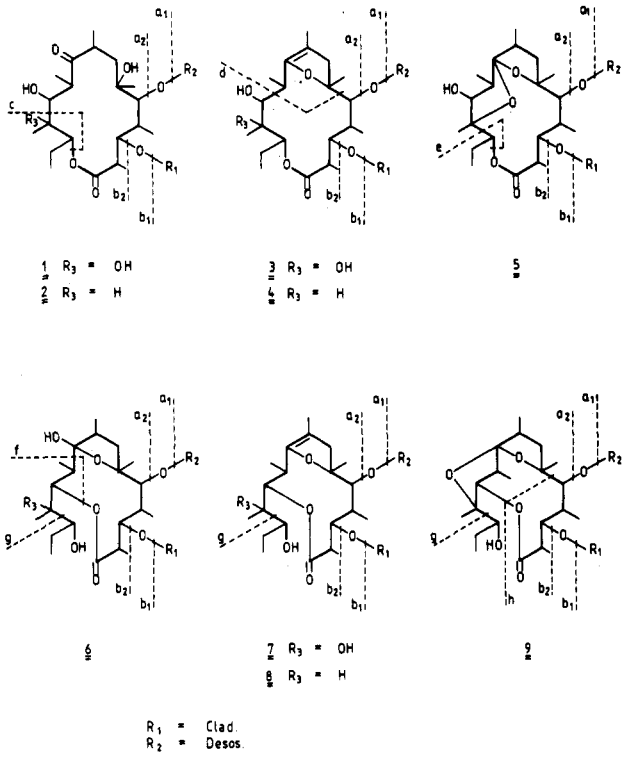
Scheme II



of 11 (Table I) are almost identical with those of **7**, except for C_{13}, C_{14}, and C_{15}, which are absent, and for the new carbonyl carbon C_{12}, which has shifted downfield to 205.8 ppm, as well as the adjacent carbons C_{21} (+10.5 ppm) and C_{11} (+2.7 ppm).

Similarly, treatment of hemiketal **6** with lead tetraacetate liberated propionaldehyde and afforded a new compound **10** with molecular ion at *m/e* 673 and a weak UV absorption at 280 nm ($A_{1\,cm}^{1\%}$ 2.3). The ^{13}C NMR spectrum of **10** (Table I) was again fully in agreement with a cleavage product derived from the 6,9-hemiketal of ring-contracted erythromycin A or pseudoerythromycin A in which a transesterification from C_{13} to C_{11} had taken place.

One further step in the acid degradation of erythromycin derivatives is the transformation of erythromycin A enol ether into the 6,9:9,12-spiroketal **5** by treatment of **3** or of **1** with dilute hydrochloric acid.[2,3] Likewise, treatment of **7** with hydrochloric acid gave the analogous compound **9** (Scheme I). The second ether bridge in **9** was positioned between C_9 and C_{12} and not between C_9 and C_{13} on the basis of its mass spectrum and of the 9 ppm downfield shift of the C_{12} signal in its ^{13}C NMR spectrum and also on the basis of the easy formation of a triacetyl derivative which is indicative of the presence of three secondary hydroxyl groups.

Although the mass spectrometric fragmentation of the pseudo compounds largely parallels that of the normal compounds, a few differences are characteristic of their structure (Scheme II). First, all pseudo compounds exhibit the weak but distinct loss of the C_{13}–C_{15} moiety, ion g, with or without back-transfer of a hydrogen. Second, some cleavages occuring in the normal compounds are absent in the corresponding pseudo compounds and vice versa. Thus, ion c in erythromycin A, d + H in the enol ethers **3** and **4**, and e in the spiroketal **5**, followed by loss of one or both sugar moieties, are absent in the pseudo compounds. On the other hand, the mass spectra of the pseudo compounds **6** and **9** show ions which may be represented by f and h, respectively.

Further confirmation for the structure of the compounds is obtained by acetylation of pseudoerythromycin derivatives **6**, **7**, or **9** with acetic anhydride in pyridine at room temperature for 3 days, affording the corresponding 2′,4″,13-triacetyl esters. Under the same conditions, esterification of the normal derivatives **1**, **3**, or **5** yields the respective 2′,4″,11-triacetates.[6,9,10] It has been stated[9] that reaction of **1** at 70 °C for 24 h yields the same triacetyl compound as that obtained at room temperature. We have now observed that the normal derivative is indeed the main product at 70 °C, but, according to HPLC analysis, some triacetyl derivative of **5** and **9** was formed.

It should be noted that the observed translactonization is a reversible reaction. At room temperature the pseudo compounds undergo a parallel sequence of reactions as the normal erythromycin analogues, but at increased temperature and with appropriate catalysts pseudo and normal compounds are in equilibrium with each other, at least as far as the C_{11}-hydroxyl group is unsubstituted and the conformational reorganization of the macrolide ring is not too pronounced. This is clearly shown by the partial reconversion of pseudo enol ether **7**, when heated in pyridine–acetic acid, into **3** or **6** into **1** and by the failure to equilibrate the more constrained spiroketals **5** and **9** or the triacetates of **7** and **3** or of **6** and **1**.

The conformational change accompanying the ring contraction as a result of the translactonization was not studied in detail, but the fact that pseudoerythromycin A exists as the 6,9-hemiketal isomer (**6**) and not in the hydroxy ketone tautomer points to a conformational reorganization of the 12-membered macrolide ring which is similar to that observed for 11-acylated erythromycins and which is favorable for the formation of a 6,9-hemiketal structure.[11] Indeed, the triacetyl derivative of erythromycin A[9,10] as well as the 11,12-cyclic carbonate[12] is isolated in the hemiketal form as is evidenced from the characteristic chemical shift (ca. 106 ppm) of C_9 in their ^{13}C NMR spectra. On the other hand, the 6,9-hemiketal of erythromycin A has never been isolated. We have monitored the reaction course during the preparation of the enol ether **3** and the spiroketal **5** by TLC, HPLC, and ^{13}C NMR, but we did not find evidence for the presence of the 6,9-hemiketal. These results, however, do not necessarily exclude this intermediate step. A 9,12-hemiketal derivative of erythromycin A has been mentioned in biological studies.[13] This information, however, was not correct, since the compound was in fact the enol ether **3**.[14]

The pseudoerythromycins, which actually may be considered as a new class of 12-membered macrolide compounds, show an activity that is therapeutically unimportant.[15]

Experimental Section

Thin-layer chromatography (TLC) was performed on precoated silica gel 60 F_{254} plates (E. Merck) with the mobile phases mentioned in Table III. The HPLC apparatus consisted of a Waters Model M-45 solvent delivery system, a Waters Model 440 detector provided with an extended wavelength module at 214 nm and a Hewlett-Packard Model 3390A recording integrator. The

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Table III. Chromatographic Data

	TLC R_f values in mobile phase[a]		HPLC t_r,[b] min
	A	B	
erythromycin A (1)	0.51	0.09	5.70
erythromycin B (2)	0.53	0.11	7.77
erythromycin A enol ether 3	0.60	0.22	11.86
pseudoerythromycin A enol ether 7	0.45	0.07	7.94
pseudoerythromycin A hemiketal 6	0.32	0.01	7.42
erythromycin A spiroketal 5	0.43	0.08	6.53
pseudoerythromycin A spiroketal 9	0.54	0.03	7.75
erythromycin B enol ether 4	0.61	0.21	
pseudoerythromycin B enol ether 8	0.51	0.09	
erythromycin A triacetate	0.69	0.27	13.48 (9.35*)
erythromycin A enol ether triacetate	0.74	0.41	33.11
pseudoerythromycin A enol ether triacetate	0.76	0.35	31.18 (21.59*)
pseudoerythromycin A hemiketal triacetate	0.75	0.38	
erythromycin A spiroketal triacetate	0.78	0.55	(8.66*)
pseudoerythromycin A spiroketal triacetate	0.76	0.42	(13.34*)

[a] TLC: silica gel; mobile phases: A, CH_2Cl_2–MeOH–33% NH_3 (90:9:1.5); B, CH_2Cl_2–CH_3CN–33% NH_3 (70:30:1.5). [b] HPLC: Zorbax C8 7 μm; mobile phase, CH_3CN–CH_3OH–$NH_4H_2PO_4$/$(NH_4)_2HPO_4$ (0.2 M, pH 6.5)–$(CH_3)_4N^+OH^-$ (0.2 M, neutralized to pH 6.5)–H_2O (300:270:50:200:240); *, 300:270:50:200:180).

column, 25 cm × 4.6 mm (i.d.) was packed in the laboratory with Zorbax 7 μm C8. See Table III for the mobile phases. Melting points were determined with a Büchi–Tottoli apparatus. Specific optical rotations were obtained with a Thorn-NPL Model Type 243 automatic polarimeter. UV spectra were recorded on a Beckman Model 25 spectrophotometer. IR spectra were run on a Perkin Elmer Model 197 spectrophotometer. Low-resolution mass spectra (MS) were recorded on a AEI MS-12 mass spectrometer by direct insertion, at 8 kV, 70 eV, and source temperature 150–170 °C. High-resolution mass spectra (HRMS) were recorded on a AEI MS-902 S mass spectrometer equipped with a VG-2020 data system. For the identification of propionaldehyde by gas chromatography–mass spectrometry, the reaction mixture was analyzed on a Pye Series 104 gas chromatograph. A coiled glass column 5 ft, 1/4 in. i.d., packed with Porapak Q was used with a helium flow of 60 mL per min and a column temperature of 120 °C. A Varian Type V5620 membrane separator was used.

^1H and ^{13}C FT nuclear magnetic resonance spectra were taken with a Jeol FX90Q NMR spectrometer operating at 89.60 or at 22.53 MHz in 5-mm tubes and at ordinary probe temperature (30 °C). Samples were prepared in deuteriochloroform solution at concentrations of about 0.2–0.4 M. ^{13}C peak positions were measured relative to $CDCl_3$ taken as 76.9 ppm relative to tetramethylsilane (Me_4Si). The two-dimensional NMR spectra were recorded on a Bruker AM 360 spectrometer.

Pseudoerythromycin A 6,9-Hemiketal (6). Erythromycin A (1.0 g) was dissolved in 20 mL of acetonitrile. After addition of 9 mL of diethylamine and 3 mL of glacial acetic acid, the solution was warmed at 45–50 °C. Examination of the reaction mixture by TLC indicated the transformation of erythromycin into a new compound (6). After 3 days the formation of 6 did not improve further: a substantial amount of the erythromycin remained unchanged but a certain amount of two more compounds was formed. The 3 day old reaction mixture was diluted with 120 mL of water, brought to pH 9 with ammonia, and extracted four times with 50 mL of dichloromethane. The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was chromatographed on a column containing 60 g of silica gel with CH_2Cl_2–CH_3OH–33% NH_3 (100:3.5:0.35). After control with TLC the appropriate fractions were combined. The first eluted product was erythromycin A (500 mg) followed by a mixture of erythromycin A, the minor components, and some hemiketal and finally by the hemiketal (200 mg). Crystallization from acetonitrile gave a crystalline product with mp 218–221 °C dec: $[\alpha]^{20}_D$ – 16.5° (c 1, CH_3OH); UV (CH_3OH) no absorption in the 280-nm region; IR (KBr) 3575–3375, 3000–2750, 1690, 1455, 1375, 1330, 1260, 1160 cm^{-1}; MS,[16] m/e (relative intensity) 733 (1.3, M), 715 (4.0, M – H_2O), 657 (1.8, g + H – H_2O), 656 (1.9, g – H_2O), 590 (2.5, f + H), 574 (0.6, b_1), 558 (2.3, b_2), 557 (1.1, 715 b_1 + H), 432 (2.8, 590 b_1 + H), 383 (1.9, a_1b_2 + H – H_2O), 365 (1.2, 383 – H_2O), 159 (35.9, R_1), 158 (100, R_2), 127 (16.5), 115 (25.8); HRMS, calcd for $C_{37}H_{67}NO_{13}$ 733.4612, found 733.4553.

Erythromycin A Enol Ether 3. Erythromycin A (1.0 g) in 10 mL of glacial acetic acid was kept at room temperature. After 4 h, 50 mL of saturated sodium bicarbonate solution and 100 mL of dichloromethane were added. The two layers were separated, and the aqueous layer was further extracted twice with dichloromethane. The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The residue was crystallized from ethanol, yielding 0.7 g of 3 with mp 138–141.5 °C, $[\alpha]^{20}_D$ –43° (c 1.0, CH_3OH) (lit.[3] mp 133–135 °C, $[\alpha]^{25}_D$ – 43° (c 1.19, CH_3OH)): UV (CH_3OH) λ_{max} 212 nm ($A_{1\,cm}^{1\%}$ 98); IR (KBr) 3500–3400, 3000–2700, 1725 (lactone), 1630, 1450, 1375, 1275, 1160 cm^{-1}; MS, m/e (relative intensity) 715 (13.3, M), 592 (0.7, d + H), 557 (4.7, b_1 + H), 556 (2.8, b_1), 540 (1.8, b_2), 434 (2.4, 592 b_1 + H), 383 (1.5, a_1b_2 + H), 382 (2.8, a_1b_2), 365 (2.2, 383 – H_2O), 364 (1.2, 382 – H_2O), 159 (41.1, R_1), 158 (100, R_2), 127 (12.2), 115 (20.9).

Pseudoerythromycin A Enol Ether 7 and Erythromycin A Enol Ether 3. A solution of 1.0 g of erythromycin A in 15 mL of a 3:1 mixture of pyridine and acetic acid was heated for 24 h at 70 °C. After cooling, the mixture was diluted with 50 mL of saturated sodium bicarbonate solution and 100 mL of dichloromethane. After separation of the two layers, the aqueous solution was further extracted twice with dichloromethane. The combined organic layers were dried over Na_2SO_4 and evaporated. The residue was taken up in toluene, which was removed by distillation to eliminate most of the pyridine, and finally purified by chromatography on a column containing 60 g of silica gel. Elution with CH_2Cl_2–MeOH (96:4) and collecting 5-mL fractions yielded in fractions 39–49 a product (20 mg) which on the basis of TLC, HPLC, and MS corresponded to the monoacetyl derivative of 7. Further elution gave 170 mg (18.5%) of 3. The following fractions yielded 0.69 g (71%) of 7. Recrystallization of 7 from acetonitrile gave a product with mp 131–136 °C: $[\alpha]^{20}_D$ –45° (c 1.0, CH_3OH); UV (CH_3OH) λ_{max} 211 nm ($A_{1\,cm}^{1\%}$ 102); IR (KBr) 3450, 3000–2700, 1705 (lactone), 1450, 1375, 1315, 1260, 1160 cm^{-1}; MS, m/e (relative intensity) 715 (21.5, M), 657 (0.9, g + H), 656 (0.8, g), 557 (1.0, b_1 + H), 556 (1.0, b_1), 540 (0.7, b_2), 382 (2.5, a_1b_2), 365 (0.8, a_1b_2 + H – H_2O), 364 (0.3, 382 – H_2O), 159 (26.5, R_1), 158 (100, R_2), 127 (12.4), 115 (25.9); HRMS, calcd for $C_{37}H_{65}NO_{12}$ 715.4506, found 715.4498. In another experiment, when the reaction mixture was heated for 4 days at 70 °C, some 11% of the monoacetyl derivative of 7 was obtained. On the basis of the mass spectrum, the acetyl group is located in the desosamine fragment: m/e (relative intensity) 757 (39.2, M), 715 (1.4, M – CH_2CO), 699 (1.3, g + H), 698 (1.1, g), 599 (0.8, b_1 + H), 598 (0.5, b_1), 582 (1.3, b_2), 382 (9.6, a_1b_2), 365 (1.7, a_1b_2 + H – H_2O), 364 (1.0, 382 – H_2O), 200 (100, R_2Ac), 159 (9.0, R_1), 127 (22.6), 115 (36.7).

Isomerization of 3 into 7 and Vice Versa. Compound 3 (or 7) was dissolved in a 3:1 mixture of pyridine and acetic acid and heated at 70 °C as described above. The composition of the reaction mixture was examined by HPLC. A 80:20 mixture of 7 and 3 was obtained after 24 h.

Pseudo Enol Ether 7 and Enol Ether 3 Formation in Deuterioacetic Acid. Erythromycin A (1.0 g) was dissolved in 10 mL of acetone and 5 mL of D_2O. The solution was evaporated under reduced pressure, the residue was taken up in the same mixture and evaporated again. The residue was dissolved in 15 mL of a 3:1 mixture of pyridine–deuterioacetic acid and kept at 70 °C for 4 days. The reaction mixture was purified as described above, yielding 120 mg of 3, 300 mg of a mixture of 3 and 7, and 500 mg of 7. Examination by ^1H NMR and ^{13}C NMR revealed that there was no deuterium incorporation in either 3 or 7.

(16) Ion structures are indicated in Scheme II. Obviously, fragmentation a_1b_2 cannot be distinguished from a_2b_1. Owing to the composite nature of m/e 159, or m/e 201 in the triacetyl derivatives, the presence of cladinose was checked by the presence of the daughter ions m/e 127 and 115, shifted to m/e 169 and 157, respectively, in the triacetyl derivatives.

Erythromycin B Enol Ether 4. Erythromycin B (250 mg) was dissolved in 3 mL of acetic acid and kept at room temperature for 4 h. The enol ether **4** was isolated as described for **3**, yielding 150 mg of product. Crystallization from ethanol gave enol ether **4** with mp 139–142 °C (lit.[3] mp 80–82 °C, $[\alpha]^{25}_D$ –33° (*c* 1.14, CH_3OH)): UV (CH_3OH) λ_{max} 211 nm ($A_{1\,cm}^{1\%}$ 95); IR (KBr) 3430, 3000–2700, 1725 (lactone), 1450, 1375, 1325, 1275, 1160 cm^{-1}; MS, *m/e* (relative intensity) 699 (16.3, M), 576 (1.1, d + H), 541 (7.4, b_1 + H), 540 (2.7, b_1), 524 (1.2, b_2), 418 (3.4, 576 b_1 + H), 367 (1.7, a_1b_2 + H), 366 (3.7, a_1b_2), 349 (1.2, 367 – H_2O), 348 (0.7, 366 – H_2O), 159 (38.4, R_1), 158 (100, R_2), 127 (14.0), 115 (25.6).

Pseudoerythromycin B Enol Ether 8 and Erythromycin B Enol Ether 4. Erythromycin B (150 mg) was heated in pyridine–acetic acid for 24 h at 70 °C as described for the preparation of **7** and **3**. Extraction and chromatography yielded some of the minor component **4** and 110 mg of **8**. Crystallization of **8** from acetonitrile gave crystals with mp 110–116 °C: $[\alpha]^{22}_D$ –57° (*c* 0.5, CH_3OH); UV (CH_3OH) λ_{max} 211 nm ($A_{1\,cm}^{1\%}$ 88.4); IR (KBr) 3470, 3000–2700, 1705 (lactone), 1455, 1375, 1320, 1260, 1160 cm^{-1}; MS, *m/e* (relative intensity) 699 (38.5, M), 641 (0.8, g + H), 640 (0.1, g), 541 (2.5, b_1 + H), 540 (1.8, b_1), 524 (0.9, b_2), 366 (3.2, a_1b_2), 349 (1.0, a_1b_2 + H – H_2O), 348 (0.4, 366 – H_2O), 159 (33.2, R_1), 158 (100, R_2), 127 (11.7), 115 (23.1); HRMS, calcd for $C_{37}H_{65}NO_{11}$ 699.4557, found 699.4562.

Erythromycin A 6,9:9,12-Spiroketal (5). To a stirred suspension of 0.40 g of erythromycin A enol ether **3** in 10 mL of water was added 10% hydrochloric acid to obtain pH 2.5, at which point **3** was dissolved. After 30 min at room temperature, 20 mL of dichloromethane was added, and the mixture was brought to pH 8.0 with 1 M NaOH. The organic layer was separated and the aqueous layer was extracted two more times with dichloromethane. The combined organic layers were dried (Na_2SO_4) and evaporated, yielding 340 mg of **5**. TLC and HPLC indicated the formation of one compound. By recrystallization in dichloromethane–hexane, a crystalline product was obtained: mp 146.5–149.5 and then 161–165 °C (lit.[2] mp 142–150 °C); $[\alpha]^{22}_D$ –54.5° (*c* 1.0, CH_3OH); UV (CH_3OH) no absorption in the 280-nm region; IR (KBr) 3430, 3000–2700, 1725 (lactone), 1450, 1375, 1165, 905 cm^{-1}; MS, *m/e* (relative intensity) 715 (14.0, M), 557 (3.0, b_1 + H), 556 (1.3, b_1), 540 (4.4, b_2), 383 (1.4, a_1b_2 + H), 365 (3.0, 383–H_2O), 341 (6.0, a_1b_2e), 159 (16.0, R_1), 158 (100, R_2), 127 (11.4), 115 (21.1).

Pseudoerythromycin A 6,9:9,12-Spiroketal (9). Pseudoerythromycin A enol ether **7** (1.0 g) was dissolved in 75 mL of water by adjusting the pH to 2.5 with concentrated hydrochloric acid. After 5 h at room temperature, the reaction mixture was alkalinized with ammonia and extracted four times with 50 mL of dichloromethane. After drying (Na_2SO_4) and evaporation of the organic layers, the residue (1 g) was crystallized from warm acetonitrile, yielding 810 mg of crystals of **9**: mp 221–223 °C dec; $[\alpha]^{22}_D$ –56.3° (*c* 1.0, CH_3OH); UV (CH_3OH) no absorption in the 280-nm region; IR (KBr) 3440, 3000–2700, 1715 (lactone), 1450, 1375, 1320, 1260, 1165, 905 cm^{-1}; MS, *m/e* (relative intensity) 715 (2.7, M), 657 (1.4, g + H), 656 (1.5, g), 557 (0.4, b_1 + H), 556 (0.2, b_1), 540 (0.4, b_2), 476 (4.4, h + H), 383 (0.4, a_1b_2 + H), 181 (38.6), 159 (23.2, R_1), 158 (100, R_2), 127 (7.8), 123 (38.2), 115 (16.4); HRMS, calcd for $C_{37}H_{65}NO_{12}$ 715.4506, found 715.4470.

Transformation of 6 into 1. Hemiketal **6** (50 mg) was dissolved in 0.75 mL of diethylamine and 0.25 mL of acetic acid and warmed at 50 °C. The reaction was followed by TLC, system A. After 3 days, the relative amounts of **1** and **6** were the same as when starting from **1**.

Transformation of 6 into 7. Hemiketal **6** (50 mg) was dissolved in 1 mL of acetic acid and the reaction was checked by TLC, system A. After 4 h at room temperature compound **6** was completely transformed into **7**.

Lead Tetraacetate Oxidation of 6. (a) Compound **6** (0.5 g) and lead tetraacetate (0.56 g) in 20 mL of dichloromethane were stirred for 30 min at room temperature. The precipitate, which formed during the reaction, was filtered off and washed with 80 mL of dichloromethane. The combined filtrates were washed with sodium bicarbonate solution and water and dried on Na_2SO_4. After evaporation of the filtrate, the residue was chromatographed on silica gel with CH_2Cl_2–CH_3OH–33% NH_3 (100:8:0.35) as eluent. The appropriate fractions were evaporated, yielding 450 mg of **10**, which crystallized from acetonitrile: mp 138–142 °C; R_f 0.46 (mobile phase A); $[\alpha]^{22}_D$ –3.5° (*c* 1.0, CH_3OH); UV (CH_3OH) λ_{max} 206 nm ($A_{1\,cm}^{1\%}$ 15.5), 280 ($A_{1\,cm}^{1\%}$ 2.3); IR (KBr) 3540–3470, 3000–2700, 1725, 1705 (sh) (lactone, ketone), 1450, 1375, 1240, 1160 cm^{-1}; MS, *m/e* (relative intensity) 673 (7.1, M), 655 (1.5, M – H_2O), 514 (1.1, b_1), 499 (3.7, b_2 + H), 498 (4.6, b_2), 481 (1.5, 499 – H_2O), 323 (9.5, a_1b_2 + H – H_2O), 159 (61.5, R_1), 158 (100, R_2), 127 (13.8), 115 (27.7).

(b) Compound **6** (20 mg) was mixed with 20 mg of lead tetraacetate and 1 mL of ethyl acetate was added. The solution, obtained by sonication, was kept for 30 min at room temperature. The precipitate was removed by centrifugation, and the supernatant was analyzed by GC–MS, ad described in the General section. Priopionaldehyde was identified.

Lead Tetraacetate Oxidation of 7. (a) Compound **7** (1.0 g) was oxidized with lead tetraacetate (1.0 g) as described for **6**, yielding 0.68 g of **11**: mp 110–114 °C; R_f 0.56 (mobile phase A); $[\alpha]^{23}_D$ –42.5° (*c* 1, CH_3OH); UV (CH_3OH) λ_{max} 215 nm ($A_{1\,cm}^{1\%}$ 97), 280 ($A_{1\,cm}^{1\%}$ 2.8); IR (KBr) 3430, 3000–2700, 1750 and 1730 (sh) (lactone, ketone) 1450, 1360, 1235, 1160 cm^{-1}; MS, *m/e* (relative intensity) 655 (38.7, M), 497 (3.9, b_1 + H), 496 (1.6, b_1), 480 (1.1, b_2), 322 (2.1, a_1b_2), 159 (31.7, R_1), 158 (100, R_2), 127 (10.9), 115 (27.5).

(b) Propionaldehyde was identified by GC–MS after oxidation with $Pb(OAc)_4$ as described for **6**.

General Procedure for Acetylation. The compound was dissolved in 25 mL of pyridine and 5 mL of acetic anhydride per gram of product. After 3 days at room temperature, the solution was poured into 100 mL of saturated sodium bicarbonate solution, and the mixture was extracted three times with dichloromethane. The organic layers were combined, washed with water and dried over Na_2SO_4. After evaporation of the filtrate, the residue was crystallized from the solvent given.

Erythromycin A 2′,4″,11-Triacetate. (1) The reaction was carried out at room temperature, yielding crystals from diisopropyl ether, 94% yield, mp 102–105 °C. After recrystallization first from acetone–hexane and then from acetonitrile, the mp was 142–145 °C, $[\alpha]^{20}_D$ –46° (*c* 1.0, CH_3OH) (lit.[9,10] mp 143–145 °C, $[\alpha]^{20}_D$ –49° (*c* 2.0, $CHCl_3$)): MS, *m/e* (relative intensity) 859 (1.8, M), 841 (1.8, M – H_2O), 800 (1.6, M – AcO), 658 (0.6, b_1), 642 (2.0, b_2), 641 (1.4, 841 b_1 + H), 425 (1.0, a_1b_2 + H – H_2O), 365 (1.6, 425 – HOAc), 201 (32.4, R_1Ac), 200 (100, R_2Ac), 169 (11.0), 157 (7.2).

(2) The reaction was carried out at 70 °C for 24 h. Erythromycin A was dissolved in pyridine–acetic anhydride and warmed at 70 °C for 24 h. Examination of the reaction mixture by HPLC and TLC indicated that the main product was erythromycin A 2′,4″,11-triacetate but that a certain amount of the triacetyl derivative of **5** and of **9** was present.

Pseudoerythromycin A 6,9-hemiketal 2′,4″,13-triacetate: crystals from acetone–hexane, 57% yield; mp 190–193 °C; $[\alpha]^{20}_D$ –20.5° (*c* 1.0, CH_3OH), IR (KBr) 3450, 3000–2700, 1730, 1700, 1450, 1370, 1230, 1160 cm^{-1}; MS, *m/e* (relative intensity) 859 (0.8, M), 841 (11.4, M – H_2O), 800 (1.2, M – AcO), 740 (6.1, g – H_2O), 658 (0.7, b_1), 642 (2.7, b_2), 641 (1.4, 841 b_1 + H), 425 (3.9, a_1b_2 + H – H_2O), 424 (5.0, a_1b_2 – H_2O), 201 (29.3, R_1Ac), 200 (100, R_2Ac), 169 (14.6), 157 (22.5).

Erythromycin A enol ether 2′,4″,11-triacetate: crystals from dichloromethane–pentane, 83% yield; mp 129–132 °C (lit.[6] mp 122–125 °C); $[\alpha]^{22}_D$ –29° (*c* 1.0, CH_3OH); UV (CH_3OH) λ_{max} 210 nm ($A_{1\,cm}^{1\%}$ 115); IR (KBr) 3475, 3000–2700, 1730 (ester, lactone), 1455, 1375, 1230, 1160 cm^{-1}; MS, *m/e* (relative intensity) 841 (29.1, M), 641 (2.0, b_1 + H), 640 (0.9, b_1), 624 (1.9, b_2), 424 (14.9, a_1b_2), 201 (37.3, R_1Ac), 200 (100, R_2Ac), 169 (10.1), 157 (26.1).

Pseudoerythromycin A enol ether 2′,4″,13-triacetate: crystals from acetone–water, 67% yield; mp 115–118 °C; $[\alpha]^{23}_D$ –39.5° (*c* 0.5, CH_3OH); UV (CH_3OH) λ_{max} 210 nm ($A_{1\,cm}^{1\%}$ 110); IR (KBr) 3475, 3000–2700, 1730 (ester, lactone), 1455, 1375, 1230, 1160 cm^{-1}; MS, *m/e* (relative intensity) 841 (29.0, M), 799 (3.7, M – CH_2CO), 740 (1.5, g), 641 (0.5, b_1 + H), 640 (0.3, b_1), 624 (1.1, b_2), 424 (6.7, a_1b_2), 407 (1.5, a_1b_2 + H – H_2O), 406 (1.0, 424 – H_2O), 201 (43.3, R_1Ac), 200 (100, R_2Ac), 169 (11.7), 157 (26.7).

Erythromycin A 6,9:9,12-spiroketal 2′,4″,11-triacetate: crystals from acetone–water after column chromatographic purification, 57 % yield; mp 126–138 °C (lit.[9] mp 128–139 °C; $[\alpha]_D$ –33° (*c* 2, $CHCl_3$)); IR (KBr) 3360, 3000–2700, 1715 (ester, lactone), 1440, 1360, 1225, 1160, 890 cm^{-1}; MS, *m/e* (relative intensity) 841 (14.5, M), 798 (4.3, M – Ac), 782 (5.3, M – AcO), 781 (5.7, M – HOAc), 641 (5.6, b_1 + H), 624 (2.2, b_2), 581 (3.6, 641– HOAc), 564

(9.3, 624 - HOAc), 425 (1.0, a_1b_2 + H), 365 (1.9, 425 - HOAc), 201 (32.5, R_1Ac), 200 (100, R_2Ac), 169 (13.3), 157 (6.5).

Pseudoerythromycin A 6,9:9,12-spiroketal 2,4″,13-triacetate: crystals from acetone–water after column chromatographic purification, 49% yield; mp 110–116 °C; IR (KBr) 3400, 3000–2700, 1720 (ester, lactone), 1440, 1365, 1230, 1160, 895 cm^{-1}; MS, *m/e* (relative intensity), 841 (0.8, M), 799 (3.3, M - CH_2CO), 741 (5.7, g + H), 740 (5.2, g), 641 (0.2, b_1 + H), 624 (0.3, b_2), 560 (5.7, h + H), 201 (44.6, R_1Ac), 200 (100, R_2Ac), 181 (78.6), 169 (10.7), 157 (5.0), 123 (47.2).

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Registry No. 1, 114-07-8; 1 (triacetate), 31357-45-6; 2, 527-75-3; 3, 33396-29-1; 3 (triacetate), 105882-74-4; 4, 33275-72-8; 5, 23893-13-2; 5 (triacetate), 23893-10-9; 6, 105900-46-7; 6 (triacetate), 105882-69-7; 7, 105882-69-7; 7 (triacetate), 105882-75-5; 8, 105900-47-8; 9, 105882-70-0; 9 (triacetate), 105882-76-6; 10, 105882-71-1; 11, 105882-72-2.

Elsamicins A and B, New Antitumor Antibiotics Related to Chartreusin. 2. Structures of Elsamicins A and B

Koko Sugawara, Mitsuaki Tsunakawa, Masataka Konishi,* and Hiroshi Kawaguchi

Bristol-Myers Research Institute, Ltd., Tokyo Research Center, 2-9-3, Shimomeguro, Meguroku, Tokyo 153, Japan

Bala Krishnan

Bristol-Myers Company, Pharmaceutical Research and Development Division, Wallingford, Connecticut 06492

He Cun-heng and Jon Clardy*

Department of Chemistry—Baker Laboratory, Cornell University, Ithaca, New York 14853-1301

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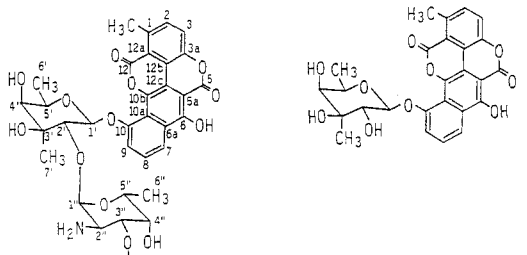
The structures of new antitumor antibiotics elsamicins A (**1a**) and B (**1b**), produced by an unidentified actinomycete strain J907-21, have been established by a combination of chemical degradation, spectral analysis, and X-ray diffraction. They are structurally similar to chartreusin containing chartarin as an aglycon, but differ to each other in sugar moieties. Elsamicin A possesses two novel sugars, 2-amino-2,6-dideoxy-3-*O*-methyl-D-galactose and 6-deoxy-3-*C*-methyl-D-galactose. The presence of the amino sugar makes elsamicin A remarkably water-soluble and more bioactive than chartreusin. Elsamicin B differs from elsamicin A in that it lacks the amino sugar moiety.

Results and Discussion

The search for anticancer drugs, especially drugs with novel chemotypes, has been accelerated by the demands of modern cancer chemotherapy. In our continuing screening for antitumor antibiotics in the fermentation broths using mouse leukemia P388, we have isolated two new antibiotics, elsamicins A (**1a**) and B (**1b**) from an



1a

1b

unidentified actinomycete strain No. J907-21 (ATCC-39417) collected in El Salvador.[1] Both antibiotic components showed antibacterial activity against gram-positive bacteria and anaerobic organisms. **1a**, the predominant component, produced a strong effect in prolonging the life span of mice with leukemia P388, leukemia L1210, and melanoma B16, while **1b** was devoid of antitumor activity.

In this report we present structural studies which show that **1a** and **1b** are similar to chartreusin[2] (**2**). They have the same aglycon, chartarin, but differ in the sugar moieties. **2** was extensively studied because of its promising activity in experimental tumor models.[3] However, it did not proceed to clinical study primarily because of its poor water solubility and rapid bile excretion. Since **1a** contains a new amino sugar (elsaminose) and a neutral sugar (elsarose), it is soluble in water, especially under acidic conditions, and exhibits different pharmacokinetics from **2**.

1a and **1b** were isolated from the fermentation broth of strain J907-21 by 1-BuOH extraction followed by column chromatography on nonionic porous polymer resin and silica gel.[1] **1a** and **1b** were obtained as yellow rods from $CHCl_3$–MeOH. **1a** crystals contain 1 equiv of MeOH as solvate: $C_{33}H_{35}NO_{13}$–CH_3OH, mp 225–226 °C, $[\alpha]^{26}_D$ +124° (*c* 0.5, pyridine); **1b**, $C_{26}H_{22}O_{10}$, mp 271–272 °C dec., $[\alpha]^{26}_D$ −8° (*c* 0.5, pyridine). The UV spectra of **1a** and **1b** exhibited absorption maxima at 236, 266, 398, and 422 nm in neutral and acidic solution and at 240, 268, and 436 nm in alkaline solution, suggesting a chartarin-like chromophore.[4] Comparison of the ^{13}C NMR spectra with that

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