Experimentelles

Chemikalien. Benzol (p.a., *Merck*); Acetonitril (puriss. *Fluka*) wurde mit Phosphorpentoxid versetzt und destilliert; Trimethylphosphit, CIBA-GEIGY AG, wurde destilliert, wobei die bei 110°/748 Torr siedende Fraktion (gemäss GC.-Analyse) 1% Trimethylphosphat enthaltend) verwendet wurde. Technisches Chloracetessigsäuremethylamid wurde 3mal aus Wasser, einmal aus Tetrachlorkohlenstoff/Benzol 9:1 (*g/g*) umkristallisiert, mit Äther gewaschen und bei 45° im Vakuum getrocknet (Reinheit: 97%).

Kinetik. Die Reaktion wurde durch Zusatz von TMP zur thermostatisierten Lösung von RCl in Gang gesetzt. Proben des Reaktionsgemisches (im allg. etwa 5 g) wurden in geeigneten Zeitintervallen entnommen, mit Äthanol auf 250 ml verdünnt und kolorimetriert.

Die kolorimetrische Bestimmung von RCl wurde in Anlehnung an die Erfahrungen bei der Bestimmung von Dimethyl-(2-methylcarbamoyl-1-methyl-vinyl)-phosphat [5] wie folgt ausgeführt: Von der äthanolischen Lösung der Proben wurden 5 ml in einen 100 ml Messkolben pipettiert, in dem 30 ml Äthanol und 10,0 ml der Reagenzlösung (0,1 M $FeCl_3 \cdot 6H_2O$ in Äthanol) vorgelegt waren, und mit Äthanol zur Marke aufgefüllt. Diese Lösung wurde nach 10 Min. gegen die entsprechende Blindprobe als Referenz bei 560 nm in einer 1-cm-Küvette kolorimetriert. Die lineare Eichkurve wurde mit Hilfe einer Stammlösung von RCl nach dem gleichen Vorgang erstellt.

Die Bestimmung der Ausbeuten bei vollständigem Umsatz an RCl wurde nach der Entfernung des Lösungsmittels titrimetrisch [6] ausgeführt.

LITERATURVERZEICHNIS

[1] *W. Perkow, K. Ulrich & F. Meyer,* Naturwissenschaften *39,* 353 (1952).
[2] *F. W. Lichtenthaler,* Chem. Reviews *61,* 607 (1961); *P. A. Chopard, V. M. Clark, R. F. Hudson & A. J. Kirby,* Tetrahedron *21,* 1961 (1965).
[3] *A. Arcoria & S. Fisichella,* Tetrahedron Letters *36,* 3347 (1971).
[4] *I. J. Borowitz, S. Firstenberg, G. B. Borowitz & D. Schuessler,* J. Amer. chem. Soc. *94,* 1623 (1972).
[5] *J. Rosales, R. Dousse & A. Becker,* Analyt. chim. Acta *56,* 127 (1971).
[6] *J. Rosales,* Z. analyt. Chem. (im Druck).

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308. Antibiotic X-5108. II[1]). Structure of Goldinono-1,4-lactone-3,7-hemiketal, a Degradation Product of the Antibiotic

Preliminary Communication

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Zusammenfassung. Antibioticum X-5108 ist ein Naturprodukt mit neuartiger Struktur. Behandlung des Antibioticums mit Essigsäure führte zu einem kristallinen Abbauprodukt, das als 3(*S*)-Äthyl-3,3a,5(*S*),6,7,7a(*R*)-hexahydro-3a(*R*),7(*R*)-dihydroxy-6,6-dimethyl-5-[1(*cis*),3(*trans*)-pentadienyl]-2*H*-furo[3,2-*b*]pyran-2-on (**5**) identifiziert wurde.

[1]) Part I, see [1].

We have recently described the production of antibiotic X-5108 by *Streptomyces goldiniensis*[2]), its isolation and properties [1].

Periodate oxidation of the antibiotic sodium salt afforded one major, unstable, solvent extractable fragment **3**, $C_{10}H_{16}O_2$, calcd. mol. wt. 168; found: *m/e* (%) 168 (38), 97 (100) with $\lambda_{max}^{dioxane}$ 235 nm (ε 18,770) indicating a diene identified as *2,2-dimethyl-3*(S)*-hydroxy-4*(trans),*6*(cis)*-octadienal.* Reduction of **3** with lithium aluminium hydride afforded *2,2-dimethyl-4*(trans),*6*(cis)*-octadiene-1,3*(S)*-diol,* **3a**, $C_{10}H_{18}O_2$, calcd. mol. wt. 170, found: *m/e* (%) 170 (6), 97 (100), $\lambda_{max}^{2\text{-propanol}}$ 233 nm (ε 24,700). The NMR. spectrum of **3a** revealed signals at $\delta_{TMS}^{CDCl_3}$ 0.88 (*s*, 2 gem. CH_3), 1.76 (*dd*, CH_3, $J_{6,8} = 1.5$ and $J_{7,8} = 7$ Hz), 3.31 (*s*, 2 OH), 3.43, 3.53 (AB, H-1a and H-1b, $J_{1a,1b} = 11$ Hz), 4.04 (*d*, H-3, $J_{3,4} = 8$ Hz), 5.53 (*dq*, H-7, $J_{6,7} = 11$ and $J_{7,8} = 7$ Hz), 5.73 (*dd*, H-4, $J_{3,4} = 8$ and $J_{4,5} = 15$ Hz), 6.04 (*tq*, H-6, $J_{5,6} = J_{6,7} = 11$ and $J_{6,8} = 1.5$ Hz) and 6.54 (*dd*, H-5, $J_{4,5} = 15$ and $J_{5,6} = 11$ Hz).

Diol **3a** was converted to *mono-(4-nitrobenzoyl)ester* **3b**, $C_{17}H_{21}NO_5$, calcd. mol. wt. 319, found: *m/e* (%) 319 (1.5), 97 (100); NMR. spectra were similar to those of **3a**, the AB-pattern for H-1a and H-1b, however, was shifted paramagnetically to δ 4.18 and 4.35 ($J_{1a,1b} = 11$ Hz). Both **3a** and **3b** were converted to *di-(4-nitrobenzoyl)ester* **3c**, $C_{24}H_{24}N_2O_8$, calcd. mol. wt. 468, found: *m/e* (%) 468 (1.5), 150 (100), obtained as colorless needles[3]), mp. 115°, $[\alpha]_D$ −107.8° (*c* 0.5, dioxane) with an NMR. spectrum similar to that of **3b**, but the two geminal methyl groups appeared as two separate signals at δ 1.17 and 1.22 and the doublet for H-3 was shifted paramagnetically to δ 5.65 ($J_{3,4} = 8$ Hz).

Periodate oxidation of the hydrogenated antibiotic sodium salt (Pd/C, ethanol), followed by reduction with lithium aluminium hydride, afforded *2,2-dimethyl-octane-1,3*(S)*-diol* **4** as colorless needles, mp. 39°, $C_{10}H_{22}O_2$, calcd. mol. wt. 174; found: *m/e* (%) 156 (0.5), 56 (100), $[\alpha]_D$ −39° (*c* 1.0, dioxane). The NMR. spectrum exhibited signals at $\delta_{TMS}^{CDCl_3}$ 0.82, 0.83 (*s*, 2 gem. CH_3), 0.86 (*t*, CH_3, $J_{7,8} = 6$ Hz), 1.28 (broad, 4 CH_2), 3.37, 3.48 (AB, H-1a and H-1b, $J_{1a,1b} = 11$ Hz), 3.41 (*m*, H-3) and 3.63 (*s*, 2 OH).

Hydrogenation of antibiotic X-5108 in acetic acid (Pt/C) yielded crystalline **6a**, $C_{16}H_{28}O_5$, in 97% yield, mp. 93–94°, $[\alpha]_D$ −21.6° (*c* 1.0, $CHCl_3$), $\nu_{max}^{CHCl_3}$ 1785 cm^{-1} indicating a γ-lactone [2]. Compound **6a** was converted to 4-bromobenzoate **6b**, mp. 180°, $[\alpha]_D$ +27.2° (*c* 1.0, $CHCl_3$), $\nu_{max}^{CHCl_3}$ 1720, 1270 (aromatic ester), 1785 cm^{-1} (γ-lactone). Crystals of **6b** are triclinic, space group P1, with two independent molecules in a unit cell of dimensions a = 6.855, b = 13.144, c = 14.371 Å, $\alpha = 91.63$, $\beta = 97.67$, $\gamma = 103.68°$. The structure was elucidated by the heavy atom method and refined by least squares. The final unweighted R value for an anisotropic model without hydrogen atoms is 5.5%. The absolute configuration was established by calculating structure factors for both enantiomers ($R_2 = 7.5\%$ and 7.9%). The structure of **6a** was found to be *3*(S)*-ethyl-3,3a,5*(S),*6,7,7a*(R)*-hexahydro-3a*(R),*7*(R)*-dihydroxy-6,6-dimethyl-5*-n*-pentyl-2*H*-furo[3,2-*b*]pyran-2-one.*

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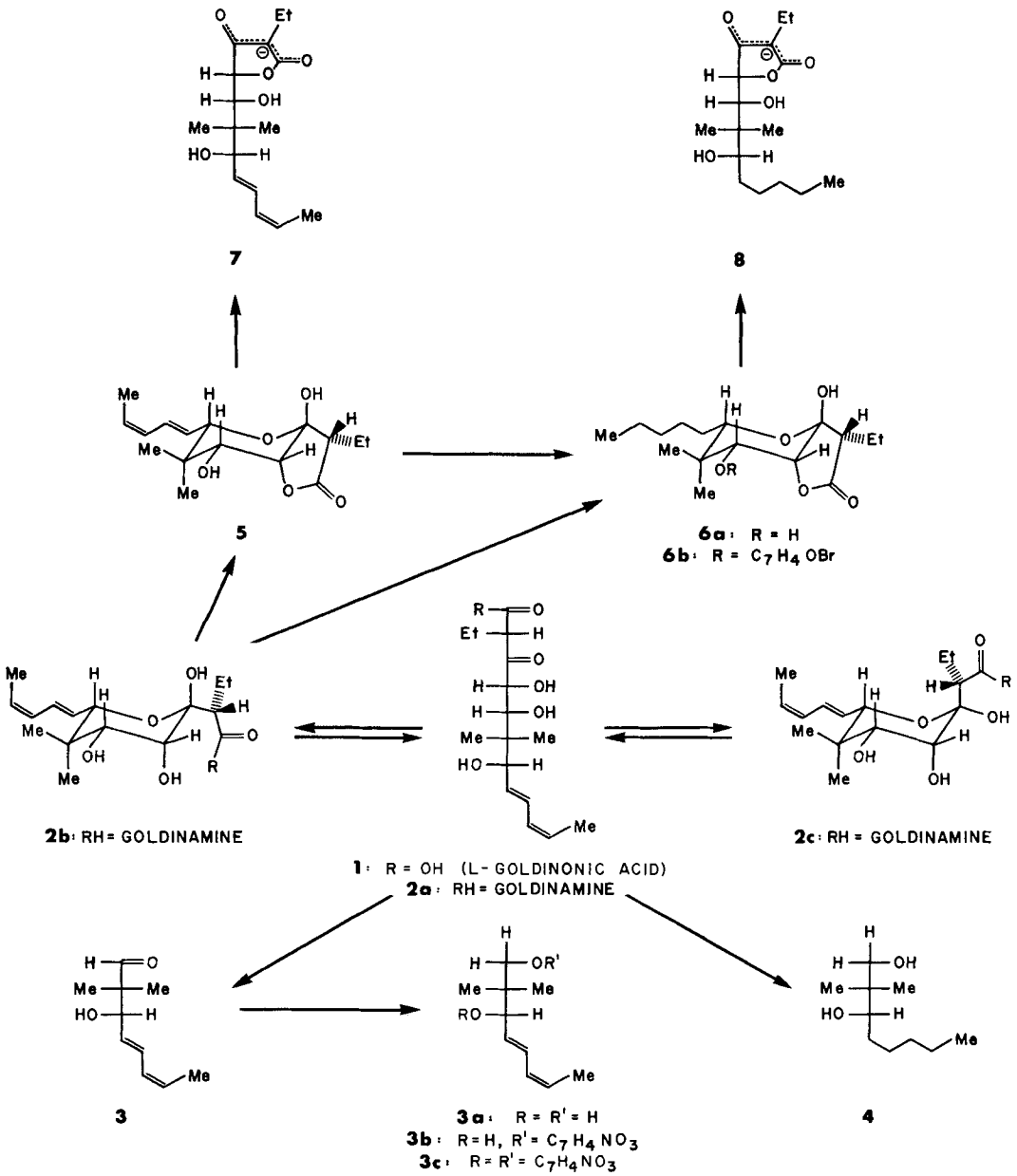
[2]) Trivial names of degradation products of antibiotic X-5108 are derived from the name of the producing organism.

[3]) Satisfactory elemental analyses were obtained for all crystalline compounds.

Compound **6a** exhibited only end absorption in the UV. spectrum but 0.1 N ethanolic NaOH produced a chromophore as shown in **8** with λ_{max} 262 nm (ε 15,000).

Treating antibiotic X-5108 with acetic acid yielded diene **5**, $C_{16}H_{24}O_5$, as colorless needles, mp. 180°, $[\alpha]_D$ −14.3° (*c* 1.0, $CHCl_3$) identified as *3*(S)-*ethyl-3, 3a, 5*(S),*6, 7, 7a*(R)-*hexahydro-3 a*(R), *7*(R)-*dihydroxy-6, 6-dimethyl-5-*[*1* (cis), *3*(trans)-*pentadienyl*]-



2H-furo-[3,2-b]pyran-2-one. The NMR. spectrum of **5** revealed signals at $\delta_{TMS}^{DMSO\text{-}d_6}$ 0.70, 0.83 (*s*, 2 gem. CH_3), 1.06 (*t*, CH_3–CH_2, $J = 7.5$ Hz), 1.60 (*m*, CH_3–CH_2), 1.70 (*d*, CH_3–CH=, $J = 7$ Hz), 2.60 (*t*, H-3, $J = 7$ Hz), 3.55 (broad, H-7), 4.10 (*d*, H-5, $J = 7$ Hz), 4.16 (*d*, H-7a, $J_{7,7a} = 4$ Hz), 5.49 (*dq*, CH_3–CH=, $J = 11$ and $J = 7$ Hz), 5.60 (*dd*, CH_3–CH^{c}=CH–CH^{t}=CH–, $J = 6$ and $J = 15$ Hz), 6.00 (*tq*, CH_3–CH^{c}=CH–, $J = 11$ and $J = 1.5$ Hz), 6.50 (*dd*, CH_3–CH^{c}=CH–CH^{t}=CH–, $J = 11$ and $J = 15$ Hz). Catalytic reduction of **5** gave **6a** in quantitative yield establishing the absolute stereochemistry of **6a** as that of **5**. Compound **5** exhibited λ_{max}^{EtOH} 233 nm (ε 26,800) with shifts to 233 nm (ε 27,200) and 260 nm (ε 15,700) in 0.1 N ethanolic NaOH due to conversion of **5** to **7**. Formally, compound **5** can be considered as a derivative of the hypothetical acid **1**, 2-deoxy-2-C-ethyl-6,6-di-C-methyl-7-[1(*trans*),3(*cis*)-pentadienyl]-L-*galacto*-3-heptulosonic acid, named L-goldinonic acid. The established absolute stereochemistry of tetrahydro-L-goldinonolactone **6a** permits assignment of the 3(*S*) configuration in compounds **3** and **4**.

The facile liberation of **5** from the antibiotic and **6a** from its reduced form under mild acidic conditions suggests an acid-labile linkage in the parent substance; the ease of cleavage is due to anchimeric participation of the axial hydroxyl group of the substrate, resulting in the concomitant formation of a γ-lactone.

In addition to **5**, mild acetic acid treatment of antibiotic X-5108 liberated an amine, termed goldinamine. The immediate precursor of **5** can thus be regarded as **2b**. The presence of a hemiketal in the antibiotic, suggested by the absence of a ketone absorption in the IR. spectrum, indicates possible isomerism of **2b** and **2c** *via* **2a**. The partial structure of antibiotic X-5108 is thus represented by **2b** and **2c**. Although a mechanism leading to inversion at the carbon atom bearing the ethyl group has been demonstrated by conversion of **5** to **7** and **6a** to **8**, the 97% yield of **6a** from the antibiotic confirms the preponderance of the 3(*S*) configuration of **5** in the antibiotic.

BIBLIOGRAPHY

[1] *J. Berger, H. H. Lehr, S. Teitel, H. Maehr & E. Grunberg*, J. Antibiotics, in press (1972).
[2] *A. L. Pape*, Ph.D. Thesis, Georgia Inst. Technol., 1971.

309. Antibiotic X-5108. III[1]). Structure of the Chromophore

Preliminary Communication

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Zusammenfassung. Antibioticum X-5108 wurde in den 4-Brombenzyläther übergeführt, der, durch oxydative Spaltung mit Perjodat, eine Carbonsäure (**5a**) lieferte, deren UV.-Spektra im langwelligen Bereich denen des Antibioticums ähnlich sind. Der Chromophor des Antibioticums

[1]) Part II, s. [1].