for the Cope rearrangement are very similar to the ones found in isotropic solution[10] and liquid-crystalline solution.[13] These results are supported by a T_1 study of a nonirradiated sample, where an activation energy of 60 kJ/mol, very close to the 55 kJ/mol observed in liquid phase,[10] was found.[21] Although the agreement may be fortuitous we tentatively interpret this to mean that the dynamics of the Cope rearrangement in the solid is governed by the same intramolecular forces as in the liquid phase.

In conclusion, the Cope rearrangement can be clearly identified and described by chemical shift resolved NMR spectroscopy, an aim that cannot be achieved by X-ray or wide-line NMR spectroscopy.

Acknowledgment. We are grateful to Prof. G. Schroeder (University of Karlsruhe) and Dr. C. S. Yannoni (IBM Research) for graciously providing us with samples of bullvalene. This work was performed under the auspices of the U.S. Department of Energy.

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A Synthesis of Methoxatin

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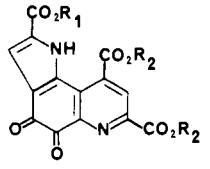
Received June 3, 1985

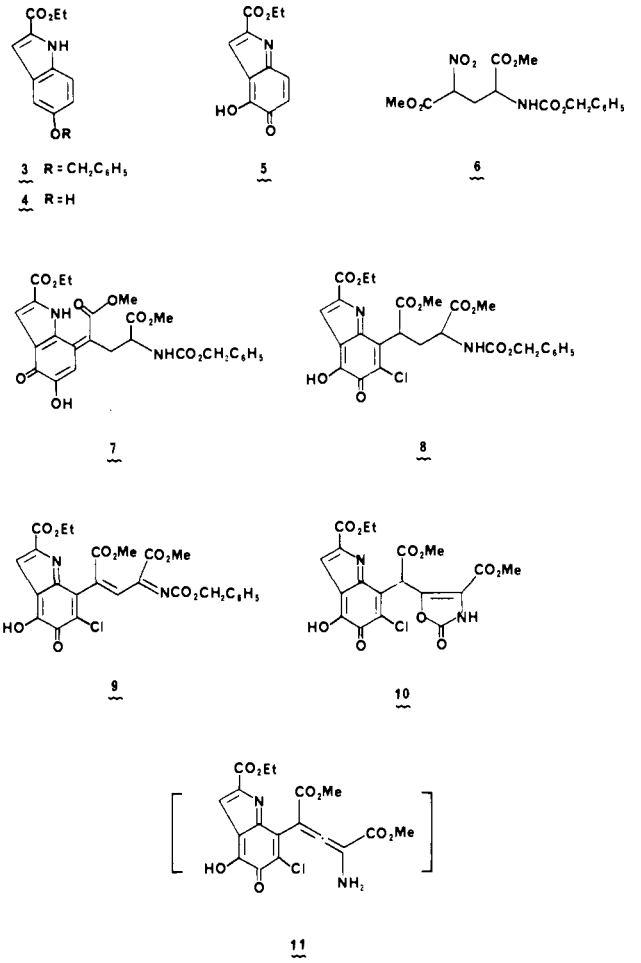
Methylotrophic bacteria use one-carbon compounds as their sole source of energy. The function of the critical enzyme methanol dehydrogenase was found to be dependent on a cofactor called methoxatin. An X-ray diffraction study of a derivative revealed structure **1**[1] for methoxatin, and syntheses were accomplished subsequently.[2-5]



1 $R_1 = R_2 = H$

2 $R_1 = Et$, $R_2 = Me$

To our knowledge the biosynthetic pathway to methoxatin remains unknown but phenylalanine or *o*-tyrosine and glutamic acid appear to be attractive precursors. We describe a total synthesis of methoxatin (**1**) from derivatives of these hypothetical forerunners. Oxidation of the hydrochloride of *o*-tyrosine ethyl ester with Fremy's salt gave the quinone imine **5**[6] (mp >270 °C, orange needles) but in poor yield. Intermediate **5** was produced more efficiently when phenol **4**,[7] prepared by debenzylation of



commercial **3**, was oxidized with Fremy's salt (2.2 equiv, CH_3CN, H_2O, KH_2PO_4, 20 °C, 30 min, 94% yield).[8] To render one hydrogen atom adjacent to the γ-carboxy group of glutamic acid more acidic and to simultaneously introduce a leaving group we prepared a mixture of diastereomeric nitro esters **6** by adding methyl nitroacetate to *N*-(benzyloxycarbonyl)dehydroalanine methyl ester[9] ($^1/_2$ equiv of Et_3N, 3 equiv of nitro ester, 20 °C, 3 days, 75% yield). Michael addition of **6** to **5** (Et_3N, THF, 20 °C, 1 h, 47% yield) afforded **7**[10] (yellow needles, mp 180–182 °C, dec). When a solution of **7** in methylene chloride containing triethylamine (1 equiv) was treated with *N*-chlorosuccinimide (1 equiv, 20 °C, 30 min), followed by addition of DDQ (5 equiv) or MnO_2 (30 equiv) and Et_3N (1 equiv) (20 °C, 90 min), two diastereomeric chlorides **8** (mp 126–129 °C dec and 171–174 °C dec) and the bright red imine **9**[11] (mp 88–91 °C dec) were formed in 35–50% and 27–31% yield, respectively. Dehydrogenation of **8** to **9** could be accomplished with MnO_2 or NiO (CH_2Cl_2, Et_3N, 1 equiv). Absence of intramolecular hydrogen bonding and lack of indole NH–C_3 proton coupling demand the presence of tautomer **9** and suggest nonplanarity of quinone imine and azadiene chromophores.

Trifluoroacetic acid (20 °C, 1 h, 85% yield) caused cleavage of the benzyl group in **9** with formation of the yellow 4-oxazolin-2-one **10**,[12] mp 182–184 °C dec. Heating **10** in chlorobenzene

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(6) ^{1}H NMR ($CDCl_3$) δ 1.40 (t, 3 H, J = 7.2 Hz), 4.38 (q, 2 H, J = 7.2 Hz), 6.25 (d, 1 H, J = 10 Hz), 7.27 (s, 1 H), 7.28 (d, 1 H, J = 10 Hz), 10.23 (br, 1 H, exchanged with D_2O); UV λ_{max} (C_2H_5OH) 272, 331, 465 nm.
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(10) ^{1}H NMR ($CDCl_3$) revealed a hydroxy proton δ 7.11 (s, 1 H, exchanged with D_2O). An indole proton at δ 7.35 (d, 1 H, J = 1.9 Hz) and a hydrogen bonded indole NH at δ 12.76 (br, 1 H, exchanged with D_2O); UV λ_{max} (C_2H_5OH) 273 (log ϵ 4.4), 311 (4.0), 330 (4.0), 367 (4.2), 540 nm (3.2).
(11) ^{1}H NMR (acetone-d_6) δ 6.76 (s, 1 H) vinyl proton; 7.40 (br, 1 H, exchanged with D_2O), 7.43 (s, 1 H) indole proton; UV λ_{max} (C_2H_5OH) 286 (log ϵ 4.5), 332 (3.7), 490 nm (3.3).
(12) ^{1}H NMR ($CDCl_3$) δ 5.74 (s, 1 H), 7.50 (s, 1 H), 7.30 (s, 1 H) and 7.6 (br, 1 H), both exchanged with D_2O; UV λ_{max} (C_2H_5OH) 274 (log ϵ 4.4), 359 (3.7), 568 nm (3.5); IR ($CHCl_3$) 3400, 1790, 1760, 1727 cm^{-1}.

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(131 °C, 4 h, 82% yield) produced methoxatin triester **2**[4,13] probably via the aminoallene **11** and the corresponding imine, followed by electrocyclic ring closure and elimination of HCl. Hydrolysis to methoxatin (**1**) was effected with lithium hydroxide.[3]

Acknowledgment. This work was supported by a National Research Service Award (No. 2T32CA09112) from the National Cancer Institute, DHEW, the National Institutes of Health (Grant GM 09868), and Hoffmann-La Roche Inc. High-resolution mass spectra were provided by the facility, supported by the National Institutes of Health (Grant RR 00317) (Principle Investigator, Professor K. Biemann), from the Biotechnology Resources Branch, Division of Research Resources. We thank Ajinomoto Inc. for a gift of *o*-tyrosine.

(13) We are indebted to Professor J. B. Hendrickson and Dr. DeVries for an authentic sample of **2**.

Stereospecific Synthesis of Rhynchosporosides: A Family of Fungal Metabolites Causing Scald Disease in Barley and Other Grasses

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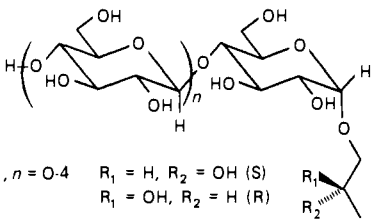
Received April 25, 1985

In addition to insect and weed pests, another major cause of destruction in plants used for food, fiber, and recreation originates from phytotoxin-producing fungi and bacteria. The rhynchosporosides are a family of such destructive compounds produced by *Rhynchosporium secalis* and recognized over the last few years as the causal agents of scald disease in barley, rye, wheat, and other grasses.[1] Although the detection of these toxins was made as early as 1971 in Australia by Ayesu-Offei and Clare,[2] culture and isolation difficulties hampered elucidation of their structures until recently when investigations by Strobel in the USA and Auriol in France suggested the mixture of oligosaccharides (I) (n = 0–4, R and/or S series) were responsible for the phytotoxic



activity.[3] Syntheses of mono- and disaccharides were recently reported by the groups of Ogawa,[4a] Strobel,[4b] and Auriol,[4c] but the more potent, higher homologues still remain elusive to both full structural elucidation and synthesis. In view of the importance of these compounds and in an effort to assist in their isolation from their natural source, structural elucidation, and biological investigation we initiated a synthetic program directed toward these structures. In this paper we wish to report the first synthesis of six rhynchosporosides (I, n = 2–4, R and S series) by an efficient and stereospecific route based on our recently reported two-stage activation procedure for oligosaccharide synthesis.[5]

† Recipient of a Camille and Henry Dreyfus Teacher-Scholar Award, 1980–1985; J. S. Guggenheim Fellow, 1984–1985.

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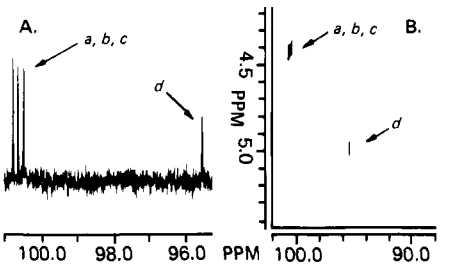

Figure 1. NMR Experiments with peracetylated [4*S*]-rhynchosporoside (Bruker AM-500, $CDCl_3$). (A) Expansion of the anomeric region of a 125.7-MHz ^1H-decoupled ^{13}C NMR spectrum showing the three β-linkages (signals a, b, and c) and the one α-linkage (signal d). (B) Contour plot of the anomeric region of a 125.7-MHz 2D ^1H–^{13}C heteronuclear chemical shift-correlated NMR spectrum showing the shifts for the anomeric carbons and protons (β-bonds, a, b, c; α-bond, d).

As in most oligo- and polysaccharide syntheses, the challenging issues in the present undertaking were (i) efficient and convenient couplings of the components of the chains and (ii) stereocontrol in the formation of the glycoside bonds. The mild, two-stage activation method involving phenylthio and fluoro sugars and the choice of suitable protecting groups and reaction medium allowed efficient, convenient, and stereospecific synthesis of both the *S* and the *R* series of tri-, tetra-, and pentasaccharides I. *Thus, β-glycoside bond specificity was secured by strategic placement of an acetoxy group at the 2-position (α)[6] and performing the coupling reaction in CH_2Cl_2, whereas α-glycoside bond specificity was observed when a benzyloxy group was present at the 2-position (α) and the glycosidation was performed in ether as solvent.*

Scheme I outlines the construction of the targeted rhynchosporosides **15a** ([3*R*]-rhynchosporoside)[8], **15b** ([3*S*]-rhynchosporoside), **19a** ([4*R*]-rhynchosporoside), **19b** ([4*S*]-rhynchosporoside), **25a** ([5*R*]-rhynchosporoside), and **25b** ([5*S*]-rhynchosporoside) from the simple building blocks **1**,[9] **3**,[10] **4**,[10] **5**[10], **6a**[12] and **6b**.[12] Thus, conversion of the phenylthioglycoside **1** to fluoride **2** with NBS–DAST (CH_2Cl_2, 0–25 °C, 85%) followed by coupling with **3** ($AgClO_4$, $SnCl_2$, 4-Å MS, CH_2Cl_2, −15–0 °C) led to the

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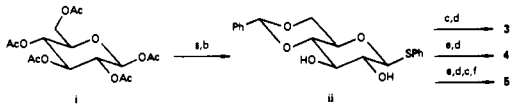
(8) The designation [*nR* or *nS*]-rhynchosporoside, where n = number of glucose units and R or S configuration of the aglycon, is suggested to describe members of this family (I) of phytotoxins.

(9) Cellobiose derivative **1** was prepared from D-(+)-cellobiose peracetate by treatment with PhSH (1.2 equiv) in the presence of $SnCl_4$ (0.3 equiv) (PhH, 60 °C) in 82% yield.

(10) Compounds **3**–**5** were prepared from D-(+)-glucose pentaacetate (i)



via intermediate ii as follows: (a) 1.2 equiv of PhSH, 0.7 equiv of $SnCl_4$, PhH, 60 °C, then 1.0 equiv of NaOMe, MeOH, 25 °C, 85%; (b) 3.0 equiv of $PhCH(OMe)_2$, 0.05 equiv of CSA, PhH, 25 °C, 90%; (c) 2.5 equiv of Ac_2O, 2.0 equiv of DMAP, CH_2Cl_2, 0–25 °C, 95%; (d) (i) excess $NaCNBH_3$,[11] 4-Å MS, THF, 25 °C, 92%; (ii) HCl(g), Et_2O; (e) 6.0 equiv of NaH, 4.0 equiv of $PhCH_2Br$, THF, Δ, 90%; (f) 1.5 equiv of NBS, 1.3 equiv of DAST, CH_2Cl_2, −15 °C, 85%.

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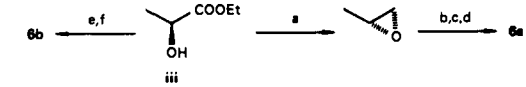
(12) Compounds **6a** and **6b** were synthesized from L-(+)-ethyl lactate (iii)



as follows: (a)[13] TsCl–pyr, then BH_3–THF, then 50% NaOH, 40% overall; (b) NaH–$PhCH_2OH$ (5.0 equiv of each) THF, 50 °C, 65%; (c) 1.1 equiv of Ph_2-*t*-BuSiCl, 1.1 equiv of imidazole, DMF, 25 °C, 95%; (d) H_2, Pd/C, EtOH, 25 °C, 90%; (e) 1.4 equiv of Ph_2-*t*-BuSiCl, 2.6 equiv of Et_3N, 0.1 equiv of DMAP, CH_2Cl_2, 25 °C; (f) 2.0 equiv of BH_3, THF, 25 °C, 92%.

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