dative enzyme. The disubstituted guanidine alkaloid, pterogynine (N_1,N_1-diisopentenylguanidine),[10] may prove to be a biosynthetic intermediate.

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Supplementary Material Available: ^1H and ^{13}C NMR, IR, and MS data for **1**, **2**, and **5–14**, all racemic, where applicable (4 pages). Ordering information is given on any current masthead page.

(10) Hart, N. K.; Johns, S. R.; Lamberton, J. A.; Willing, R. I. *Aust. J. Chem.* **1970**, *23*, 1679.

Synthetic 8-Vinylbenzo[*d*]naphtho[1,2-*b*]pyran-6-one *C*-Glycoside

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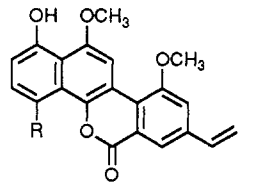
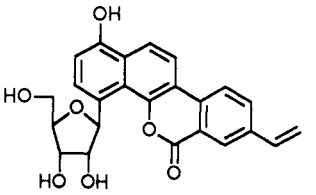
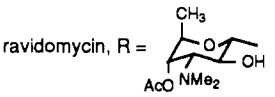
Summary: Synthesis of 8-ethenyl-1-hydroxy-4-(β-D-ribofuranosyl)benzo[*d*]naphtho[1,2-*b*]pyran-6-one, a *C*-glycoside analogue of ravidomycin and gilvocarcin V, has been achieved by a sequence of reactions involving Lewis acid catalyzed coupling of the aglycon and carbohydrate followed by introduction of the vinyl group and unmasking of the carbohydrate and phenolic hydroxyls.

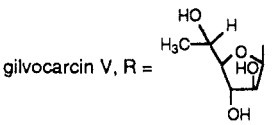
Sir: We have reported palladium-mediated[1,2] and Lewis acid catalyzed[3] aglycon–carbohydrate coupling reactions for syntheses of benzo[*d*]naphtho[1,2-*b*]pyran-6-one *C*-glycosides related to the *C*-glycoside antitumor antibiotics,[4] ravidomycin,[5] the gilvocarcins[6] (toromycin[7]), and the chrysomycins[8] (virenomycin,[9] the albacarcins[10]). We now report the synthesis of a *C*-glycoside (**1**) that possesses an underivatized C-1 phenolic hydroxyl and a vinylic substituent at C-8,[11] the functional groups considered critical for the photolytic nicking of DNA.[11a,12]





1





defucogilvocarcin, R = H

In in vitro studies,[11a,12-15] gilvocarcin V, its naturally occurring[16] aglycon defucogilvocarcin, and the synthetic aglycon analogue 8-ethenyl-1-hydroxybenzo[*d*]naphtho-[1,2-*b*]pyran-6-one[11a] (**2e**) have been shown to intercalate into DNA and to cause single-strand breaks (nicks) when irradiated. The ability of synthetic aglycon analogue **2** to nick DNA[11a] establishes the 1-hydroxy and 8-vinyl (ethenyl) substituents as sufficient for bioactivity; however, neither **2** nor defucogilvocarcin is nearly as effective as the *C*-glycoside gilvocarcin V[12] or ravidomycin.[17] The evidence that the carbohydrate moieties of these *C*-glycoside antibiotics play significant (but perhaps not structurally specific) roles in their antibiotic actions[4,11a,12-15] provides a rationale for synthesis of *C*-glycoside analogues[18] such as **1**.

(1) Outten, R. A.; Daves, G. D.; Jr. *J. Org. Chem.* **1987**, *52*, 5064–5066.
(2) Outten, R. A.; Daves, G. D. Jr. *J. Org. Chem.* **1989**, *54*, 29–35.
(3) Kwok, D.-I.; Outten, R. A.; Huhn, R.; Daves, G. D., Jr. *J. Org. Chem.* **1988**, *53*, 5359–5361.
(4) For a recent review of *C*-glycoside antibiotics see: Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1–65.
(5) Findlay, J. A.; Liu, J. S.; Radics, L.; Rakhit, S. *Can. J. Chem.* **1981**, *59*, 3018–3020.
(6) Hirayama, N.; Takahashi, K.; Shirahata, K.; Ohashi, Y. Sasada, Y. *Bull. Soc. Chem. Jpn.* **1981**, *54*, 1338–1342.
(7) Horii, S.; Fukase, H.; Mizuta, E.; Hatano, K.; Mizuno, K. *Chem. Pharm. Bull.* **1980**, *28*, 3601–3611. Jain, T. C.; Simolike, G. C.; Jackman, L. M. *Tetrahedron* **1983**, *39*, 599–605.
(8) Weiss, U.; Yoshihira, K.; Highet, R. J.; White, R. J.; Wei, T. T. *J. Antibiot.* **1982**, *35*, 1194–1201.
(9) Brazhnikova, M. G.; Kudinova, M. K.; Kulyaeva, V. V.; Potapova, N. P.; Rubasheva, L. M.; Rozynov, B. V.; Horvath, G. *Antibiotiki* **1984**, *29*, 884–892.
(10) Matson, J. A.; Myllymaki, R. W.; Doyle, T. W.; Bush, J. A. U.S. Patent 4,461,831, July 24, 1984; *Chem. Abstr.* **1985**, *102*, 4456a.
(11) Synthetic studies of the aglycon system and of the carbohydrate present in ravidomycin, (–)-methyl ravidosaminide, have been reported. See: (a) McGee, L. R.; Confalone, P. N. *J. Org. Chem.* **1988**, *53*, 3695–3701. (b) Findlay, J. A.; Daljeet, A.; Murray, P. J.; Rej, R. N. *Can. J. Chem.* **1987**, *65*, 427–431. (c) Macdonald, S. J. F.; McKenzie, T. C.; Hassen, W. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1528–1530. (d) Patten, A. D.; Nguyen, N. H.; Danishefsky, S. *J. Org. Chem.* **1988**, *53*, 1003–1007. (e) McKenzie, T. C.; Hassen, W.; Macdonald, S. J. F. *Tetrahedron Lett.* **1987**, *28*, 5435–5436. (f) McKenzie, T. C.; Hassen, W. *Tetrahedron Lett.* **1987**, *28*, 2563–2566. (g) Knapp, S.; Lal, G. S.; Sahai, D. *J. Org. Chem.* **1986**, *51*, 380–383.
(12) Tse-Dinh, Y.-C.; McGee, L. R. *Biochem. Biophys. Res. Commun.* **1987**, *143*, 808–812.
(13) Greenstein, M.; Monji, T.; Yeung, R.; Maiese, W. M.; White, R. J. *Antimicrob. Agents Chemother*, **1986**, *29*, 861–866.
(14) Elespuru, R. K.; Gonda, S. K. *Science* **1984**, *223*, 69–71.
(15) Wei, T. T.; Byrne, K. M.; Warnick-Pickle, D.; Greenstein, M. *J. Antibiot.* **1982**, *35*, 545–548.
(16) Misra, R.; Tritch, H. R., III; Pandey, R. C. *J. Antibiot.* **1985**, *38*, 1280–1283.
(17) Rakhit, S.; Eng, C.; Baker, H.; Singh, K. *J. Antibiot.* **1983**, *36*, 1490–1494.
(18) Acid- or base-catalyzed rearrangements of gilvocarcin V and ravidomycin have yielded analogues not found in nature; see ref 7 and 17.

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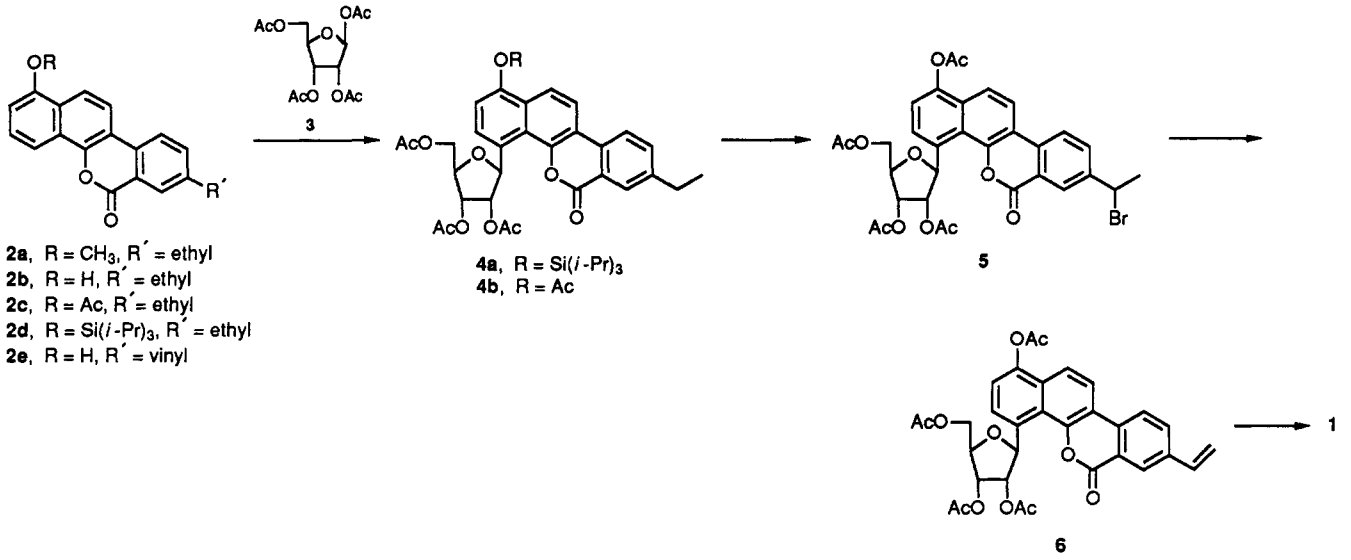
Scheme I



1-Hydroxy-4-(β-D-ribofuranosyl)-8-vinylbenzo[*d*]-naphtho[1,2-*b*]pyran-6-one (**1**) was prepared as shown in Scheme I. Achievement of this synthesis required that a number of tactical problems be solved. Lewis acid catalyzed coupling of the tetracyclic aglycon system with 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose[19] (**3**) was first achieved[3] by using the *O*-methyl aglycon **2a**. However, no conditions were found that would permit removal of the *O*-methyl group of the resulting *C*-glycoside without effecting partial anomerization of the glycosidic linkage. Efforts to effect coupling of the carbohydrate with the free phenolic compound **2b** or its acetyl derivative **2c** were unsuccessful. Similarly, attempts to use aglycon derivatives with an 8-vinyl substituent in Lewis acid catalyzed glycosidic coupling reactions failed.

Stannic chloride catalyzed coupling of 8-ethyl-1-[(triisopropylsilyl)oxy]benzo[*d*]naphtho[1,2-*b*]pyran-6-one[20] (**2d**) with carbohydrate **3** yielded a 1:1 mixture of *C*-glycoside **4a**[21] and its α-anomer[3] in 80% combined yield. Following anomer separation by silica gel chromatography, removal of the triisopropylsilyl protective group (CsF) and acetylation (acetic anhydride/pyridine) yielded tetraacetate **4b**[21] (95%). This change in phenolic protective group was necessary because attempted benzylic bromination of **4a** with *N*-bromosuccinimide yielded a complex mixture that included products with apparent substitution within the triisopropylsilyl group.

Benzylic bromination[11a] of tetraacetate **4b** (NBS, benzoyl peroxide) was effected, producing **5**[21] (62%). It is noteworthy that no bromination occurred at C-1 of the carbohydrate moiety, which is also benzylic. Dehydrobromination of **5** for introduction of the 8-vinyl substituent of **6**[21] was achieved (73%) by using tetrakis(triphenylphosphine)palladium(0).[22] The synthesis of **1**[21] was completed by removal of the four protecting acetyl groups using sodium carbonate in methanol in 83% yield.

This synthesis foreshadows the preparation of a number of *C*-glycoside analogues of the antibiotics of this class for detailed biological evaluation of the structural parameters associated with antitumor and antiviral activities.

Acknowledgment. We thank the American Cancer Society for generous financial support of this research.

(19) Brown, G. B.; Davoll, J. A.; Lowy, B. A. *Biochem. Prepr.* **1955** *4*, 70.

(20) Prepared by demethylation of **2a**[3,11a] (BBr_3, 97%) followed by silylation (chlorotriisopropylsilane, imidazole, 92%).

(21) All new compounds have been characterized by ^1H and ^{13}C nuclear magnetic resonance and elemental analysis and/or high-resolution mass spectrometry.

(22) We found Pd(0)-catalyzed dehydrobromination to be preferable to procedures using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), LiBr/Li_2CO_3,[11a] or phenyl selenoxide (Findlay, J. A.; Daljeet, A.; Murray, P. J.; Rej, R. N. *Can. J. Chem.* **1986**, *65*, 427-431).

Highly Stereoselective Radical Cyclization: Copper- or Ruthenium-Catalyzed Preparation of *cis*- and *trans*-β,γ-Dialkyl γ-Lactams from Acyclic *N*-Allyltrichloroacetamide Derivatives

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Summary: Efficient 1,2-asymmetric induction was achieved in the copper-catalyzed cyclization of *N*-allyltrichloroacetamides derived from 3-amino-1-butene or 3-amino-1-heptene, in which the stereochemical course was dependent on nitrogen protecting groups.

Sir: Although free-radical cyclization has become an attractive synthetic method for five-membered ring skele-

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