symmetry barrier to rearrangement to tetrahedral MnO_4^-. The photochemistry may be induced by both of the electronic transitions of permanganate occurring in the visible, but the quantum yield for the shorter wavelength band is significantly greater. Both the structure of the intermediate and its symmetry barrier to thermal decomposition have literature precedents.

Acknowledgment. We thank the National Science Foundation for support of this research as well as for fellowship support to C.R.M.

Registry No. MnO_4^-, 14333-13-2; MnO_4^{2-}, 14333-14-3; MnO_2^-, 85759-28-0; O_2, 7782-44-7; *p*-toluenesulfonic acid, 104-15-4; *p*-ethylbenzenesulfonic acid, 98-69-1; *p*-isopropylbenzenesulfonic acid, 16066-35-6; acetone, 67-63-0; *p*-(α,α-dimethylmethanol)benzenesulfonic acid, 107408-08-2; *p*-carboxybenzenesulfonic acid, 636-78-2; *p*-acetylbenzenesulfonic acid, 34074-93-6; *p*-toluenesulfonate, 16722-51-3; *p*-ethylbenzenesulfonate, 18777-64-5; *p*-isopropylbenzenesulfonate, 71407-44-8.

New Entry to the C-Glycosilation by means of Carbenoid Displacement Reaction. Its Application to the Synthesis of Showdomycin

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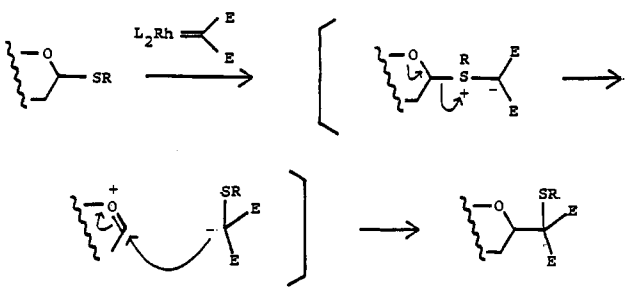
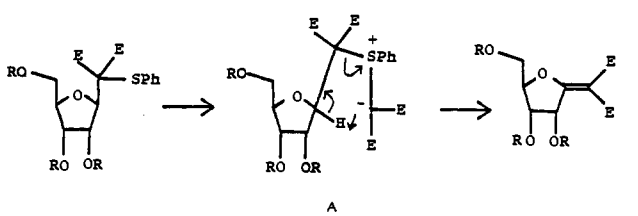
Abstract: The novel and stereoselective carbon–carbon bond-forming reaction at the anomeric center of carbohydrates has been developed by means of a carbenoid displacement reaction with phenyl thioglycosides. This reaction was suggested to proceed via the oxonium ion intermediates and has the following advantages: (i) the preferential participation of a carbenoid with a sulfur atom can restrict the reaction site; (ii) the reaction can be carried out under neutral reaction condition; and (iii) the introduction of various functionalities can be accomplished by manipulation of the organosulfur groups of the products. This synthetic strategy was successfully applied to the synthesis of antitumor agent, (+)-showdomycin, and would provide a general route to the other *C*-glycosides.

In recent years much attention has been focussed on the formation of carbon–carbon (C–C) bonds[1] at the anomeric center of carbohydrates directed at synthesizing physiologically interesting or naturally occurring *C*-nucleosides[2] and *C*-glycosides[3] and also at evaluating their synthetic potential as chiral templates.[4] During the course of our studies on the new C–C bond-forming reactions by employing a carbenoid displacement reaction,[5] we became interested in developing a method for the efficient C-glycosilation reaction.

Scheme I



Scheme II



A

Our design using a carbenoid displacement reaction for the C-glycosilation is based on the following considerations: (i) the use of phenyl thioglycosides as starting materials can restrict the reaction site by the preferential participation[6] of the sulfur atom with the carbenoid, (ii) the introduction of various functionalities can be accomplished by manipulation of the organosulfur groups

(1) For examples, see: (a) Kunz, H.; Weissmüller, J.; Müller, B. *Tetrahedron Lett.* **1984**, *25*, 3571. (b) Yougai, S.; Miwa, T. *J. Chem. Soc., Chem. Commun.* **1983**, 68. (c) Martin, O. R.; Mahnken, R. E. *Ibid.* **1986**, 497. (d) Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1982**, *23*, 2281. (e) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. (f) Schmidt, R. R.; Hoffmann, M. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 406. (g) Dawe, R. D.; Reid, B. F. *J. Chem. Soc., Chem. Commun.* **1981**, 1180. (h) Stewart, A. O.; Williams, R. M. *J. Am. Chem. Soc.* **1985**, *107*, 4289. (i) DeShong, P.; Slough, G. A.; Elango, V. *Ibid.* **1985**, *107*, 7788. (j) Cohen, T.; Lin, M.-T. *Ibid.* **1984**, *106*, 1130. (k) Rosenthal, A. *Adv. Carbohydr. Chem.* **1968**, *23*, 59. (l) Trainor, G. L.; Smart, B. E. *J. Org. Chem.* **1983**, *48*, 2447. (m) Dunkerton, L. V.; Serino, A. J. *Ibid.* **1982**, *47*, 2812. (n) Arai, I.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 287. (o) Arai, I.; Lee, T. D.; Hanna, R.; Daves, G. D., Jr. *Organometallics* **1982**, *1*, 742. (p) Dupuis, J.; Giese, B.; Hartung, J.; Leising, M. *J. Am. Chem. Soc.* **1985**, *107*, 4332. (q) Giese, B.; Dupuis, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 622.

(2) For reviews, see: (a) Suhadolnik, R. J. *Nucleoside Antibiotics*; Wiley-Interscience: New York, 1970. (b) Daves, G. D.; Cheng, C. C. *Prog. Med. Chem.* **1976**, *13*, 303. (c) Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111.

(3) For examples, see: (a) Markham, K. R.; Woolhouse, A. D. *Phytochemistry* **1983**, *22*, 2827. (b) Hochlowski, J. E.; Faulkner, J. D.; Matsumoto, G. K.; Clardy, J. *J. Am. Chem. Soc.* **1983**, *105*, 7413.

(4) (a) Cupps, T. L.; Wise, D. S.; Townsend, L. B. *J. Org. Chem.* **1982**, *47*, 5115. (b) Schmidt, R. R.; Hoffman, M. *Tetrahedron Lett.* **1982**, *23*, 409. (c) Danishefsky, S.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 3803.

(5) (a) Kametani, T.; Nakayama, A.; Itoh, A.; Honda, T. *Heterocycles* **1983**, *20*, 2355. (b) Kametani, T.; Kanaya, N.; Mochizuki, T.; Honda, T. *Ibid.* **1982**, *19*, 1023. (c) Kametani, T.; Kawamura, K.; Tsubuki, M.; Honda, T. *J. Chem. Soc., Chem. Commun.* **1985**, 1324. (d) Kametani, T.; Yukawa, H.; Honda, T. *Ibid.* **1986**, 651. (e) Mak, C.-P.; Baumann, K.; Mayerl, F.; Mayerl, C.; Fliri, H. *Heterocycles* **1982**, *19*, 1647.

(6) For examples, see: (a) Gillespie, R. J.; Rust, J. M.; Rust, P. M.; Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* **1978**, 83. (b) Gillespie, R. J.; Porter, A. E. A.; Willmontt, W. E. *Ibid.* **1978**, 85. (c) Nickon, A.; Rodriguez, A.; Shirhatti, V.; Ganguly, R. *Tetrahedron Lett.* **1984**, *25*, 3555. (d) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; Levsen, D. *J. Org. Chem.* **1984**, *49*, 1917. (e) Crow, W. D.; Gosney, I.; Ormiston, R. A. *J. Chem. Soc., Chem. Commun.* **1983**, 643.

0002-7863/87/1509-3010$01.50/0

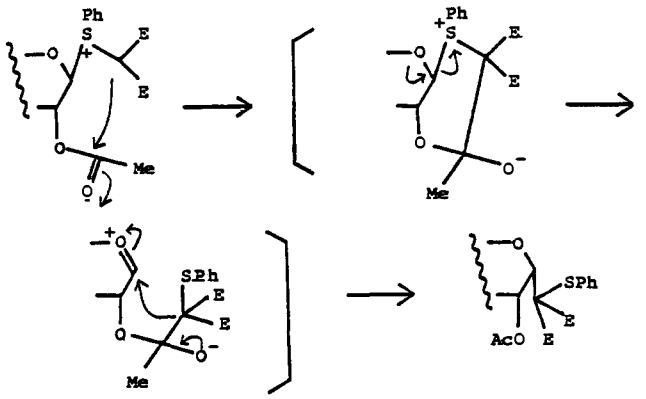


Figure 1. ORTEP drawing of the ylide **35** (top). ORTEP drawing of the rearranged product **36** (bottom).

of the product,[7] (iii) the reaction can be carried out under neutral condition, and (iv) the stereoselectivity in the C–C bond formation would be expected, if this reaction would proceed via the oxonium intermediate[1e] generated by a proposed reaction mechanism in the β-lactam series,[5b,e] as shown in Scheme I.

Thus, a number of phenylthioglycosides have been prepared according to the literatures[8] with a slight modification. We initially examined the intermolecular carbenoid displacement reaction of 2-(phenylthio)tetrahydropyran (**1**) and -furan (**2**) with dimethyl α-diazomalonate in appropriate solvent in the presence of a catalytic amount of rhodium(II) acetate and succeeded in obtaining the C–C bond-forming products **13** and **14** in reasonable yields, respectively. Since the above reaction was found to be effective to form a new carbon–carbon bond at the α-position to oxygen atom, a glycosilation for the thiophenylfuranosides was further investigated. The typical procedure is described below. A solution of 1-β-(phenylthio)triacetylglycoside (**8**) (368 mg, 1 mmol) and 3 equimolar amounts of dimethyl α-diazomalonate (474 mg, 3 mmol) in methylene chloride (20 mL) in the presence of rhodium(II) acetate (30 mg) was refluxed for 2 h. After evaporation of the solvent, the residue was chromatographed on silica gel by using benzene–ethyl acetate as the eluant to give *C*-glycoside **19** (352 mg) in 70.7% yield. Some examples of C-glycosilation and reductive dethiophenylation are given in Table I, and these reactions are completely stereospecific thereby yielding only one isomer as product.

Stereochemistry of the products was determined based on their NMR spectra.[9] Stereoselectivity exhibited in the formation of β-anomer in the above reaction of furanosides can be explained

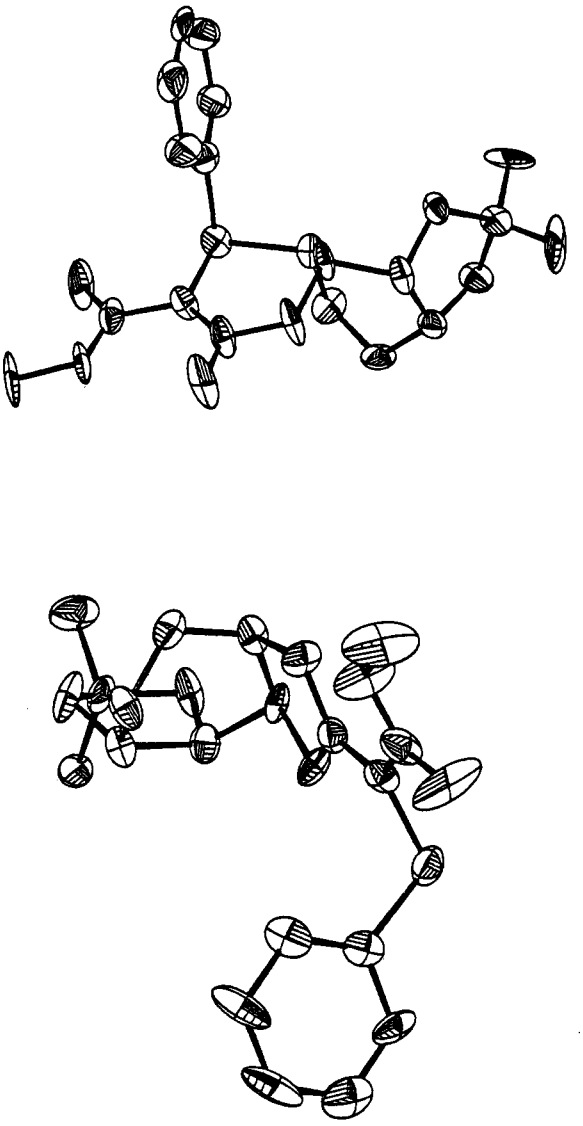
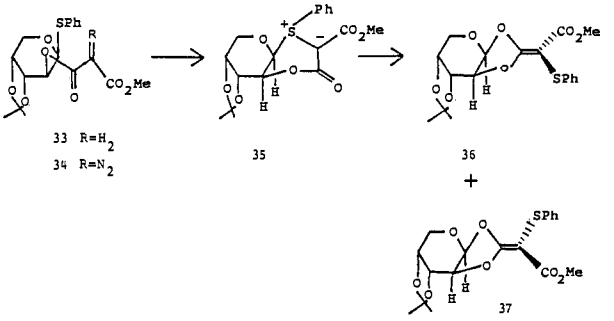


Figure 2.

Scheme III



by steric effect of the carbon α to the anomeric center, owing to great conformationl rigidity[10] (entry 8, 9, 11). Interestingly, the reaction of the tribenzyl ether **9** under similar reaction condition furnished the elimination product **21** as a major product, in 43.3% yield, presumably arising from the further reaction of **20** with the excess of the reagent via the ylide intermediate A together with the small amount of the displacement product **26** (entry 9, 10). This assumption was proven by further treatment of the isolated **20** with dimethyl α-diazomalonate to yield **21**. 1,4-Conjugated reduction[11] of **21** with sodium borohydride in methanol in the

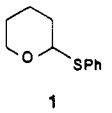
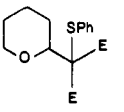
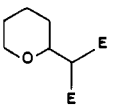
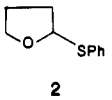
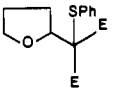
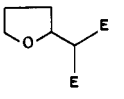
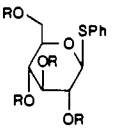
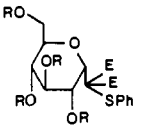
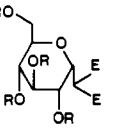
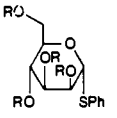
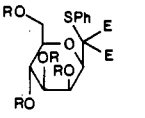
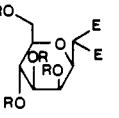
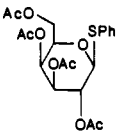
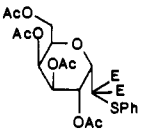
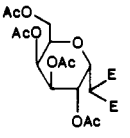
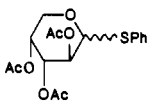
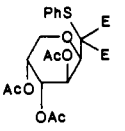
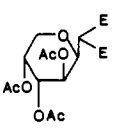
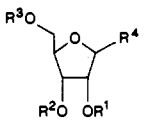
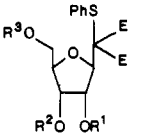
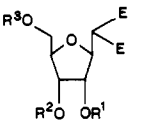
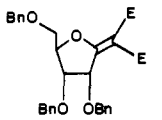
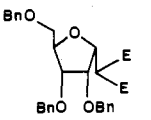
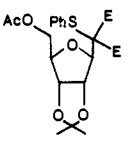
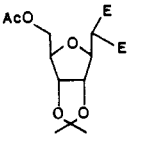
(7) (a) Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453. (b) Vedejs, E.; Kraft, G. A. *Tetrahedron* **1982**, *38*, 2857. (c) Vedejs, E. *Acc. Chem. Res.* **1984**, *17*, 358.

(8) For preparation of the thioglycoside **3**, see: (a) Wolfrom, M. L.; Wood, H. B. *J. Am. Chem. Soc.* **1949**, *71*, 3175. (b) Ferrier, R. J.; Furneaux, R. H. *Carbohydr. Res.* **1976**, *52*, 63. For preparation of **4**, see: (c) Purves, C. B. *J. Am. Chem. Soc.* **1929**, *51*, 3619. (d) VanCleve, J. W. *Carbohydr. Res.* **1979**, *70*, 161. For preparation of **6**, see: (e) Landge, A. B.; Ingle, T. R.; Bose, J. L. *Indian J. Chem.* **1969**, *7*, 1200. (f) Sinha, B.; Pansare, V. S. *Indian J. Chem., Sect. B.* **1980**, *19B*, 825. For preparation of 7, see: (g) Capon, B.; Collins, P. M.; Leuy, A. A.; Overend, W. G. *J. Chem. Soc.* **1964**, 3242. For preparation of **8**, see: (h) Guthrie, R. D.; Smith, S. C. *Chem. Ind. (London)* **1968**, 547. (i) Kam, B. L.; Barascut, J.-L.; Imbach, J.-L. *Carbohydr. Res.* **1979**, *69*, 135. (j) Hewehi, Z. E. *Chem. Ber.* **1958**, *91*, 2039. (k) Antkowiak, W. Z.; Krzyżosiak, W. J. *Bull. Acad. Pol. Sci., Ser. Sci. Chim.* **1977**, *25*, 173. (l) Antkowiak, W. Z.; Krzyżosiak, W. J. *J. Chromatogr.* **1974**, *90*, 399. For preparation of **9** and **10**, see: (m) Zinner, H. *Chem. Ber.* **1950**, *83*, 275. (n) Potgieter, D. J. J.; MacDonald, D. L. *J. Org. Chem.* **1961**, *26*, 3934. (o) Haga, M.; Mess, R. K.; Fletcher, H. G., Jr. *J. Org. Chem.* **1968**, *33*, 1810. For preparation of thioglycosides from carbohydrates see: (p) Zissis, E.; Glingman, A. L.; Richtmyer, N. K. *Carbohydr. Res.* **1966**, *2*, 461. (q) Ferrier, R. J.; Hay, R. W.; Vethaviyasar, N. *Ibid.* **1973**, *27*, 55. (r) Hanessian, S.; Bacquet, C.; Lehong, N. *Ibid.* **1980**, *80*, C17. (s) Hanessian, S.; Guindon, Y. J. *Ibid.* **1980**, *86*, C3. (t) Nicolaou, K. C.; Seitz, S. P.; Papahatjis, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 2430. (u) Korytnyk, W.; Mills, J. A. *J. Chem. Soc.* **1959**, 636.

(9) (a) Jackman, L.; Sternhell, S. *Applications of Nuclear Magnetic Resonance in Organic Chemistry*, 2nd ed.; Oxford: Pergamon Press, 1969; pp 281–304. (b) DeShong, P.; Dicken, C. M.; Staib, R. R.; Freyer, A. J.; Weinreb, S. M. *J. Org. Chem.* **1982**, *47*, 4397.

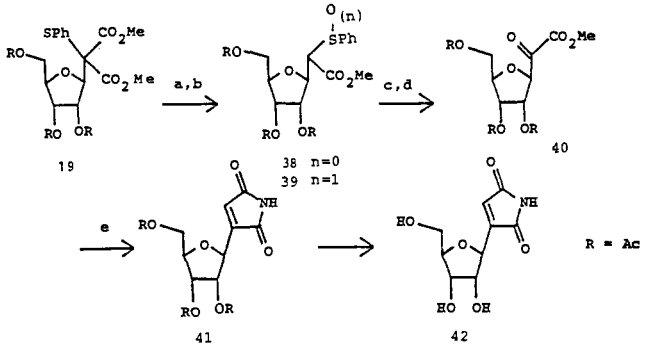
(10) (a) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 2870. (b) Cheng, J. C. Y.; Hacksell, U.; Davis, G. D., Jr. *Ibid.* **1986**, *51*, 3093.

Table I. C-Glycosidation of Thioglycosides and Reductive Dethiophenylation

entry	substrate	product	condtn (h)[a]	isoltd yield (%)	product	condtn (h)	isoltd yield (%)
1	 **1**	 **13** E = CO_2Me	A(0.5) B(24) C(2)	31.6 42 54	 **23**	D(11) E(1)	82.5 85.4
2	 **2**	 **14**	C(3)	88.5	 **24**	D(5)	85
3	 **3** R = Ac	 **15**	C(2)	84	 **25**	D(4)	84.5
4	**4** R = Bn		C(3)	0			
5	 **5** R = Ac	 **16**	C(2)	47	 **26**	E(2)	54
6	 **6**	 **17**	C(2)	73.7	 **27**	E(2)	80.7
7	 α,β-anomeric mixture **7**	 **18**	C(3)	57	 **28**	E(2)	80
8	 **8** $R^1 = R^2 = R^3 = Ac$, $R^4 = \beta$-SPh	 **19** **20** $R^1 = R^2 = R^3 = Bn$	C(2) C(2.5)	70.7 4.7	 **29** **30** $R^1 = R^2 = R^3 = Bn$	D(2) F(1.5)	80 62.1
9	**9** $R^1 = R^2 = R^3 = Bn$, $R^4 = \beta$-SPh	 **21**		43.3	 **31**		12
10	**10** $R^1 = R^2 = R^3 = Bn$, $R^4 = \alpha$-SPh	21	C(8)	56.7			
11	**11** $R^1 + R^2 = C(Me)_2$, $R^3 = Ac$, $R^4 = \beta$-SPh	 **22**	C(3)	34.3	 **32**	D(5)	70
12	**12** $R^1 + R^2 = C(Me)_2$, $R^3 = Ac$, $R^4 = \alpha$-SPh	**22**	C(7)	28			

[a] Reaction conditions were as follows: A, benzene, reflux; B, methylene chloride, room temperature; C, methylene chloride, reflux; D, Raney nickel, acetone, reflux; E, n-Bu_3SnH, AIBN, benzene, reflux; F, $NaBH_4$, $NiCl_2 \cdot 6H_2O$, methanol, room temperature.

Scheme IV[a]



[a](a) DABCO, celite, Me_2S, benzene, reflux, 24 h; (b) MCPBA, CH_2Cl_2, room temperature, 2 h; (c) $(CF_3CO)_2O$, 2,6-lutidine, CH_3CN, room temperature, 3 h; (d) $HgCl_2$, H_2O, room temperature, 1 h; (e) $Ph_3P{=}CHCONH_2$, $CHCl_3$, room temperature, 1 h.

presence of nickel(II) chloride afforded the β- and α-anomers **30** and **31** in 74% combined yield, in the ratio of ca. 5:1 (Scheme II).

This methodology could also be applied to the thiopyranosides[12] successfully to yield the desired *C*-glycosides. On the basis of the results obtained, it is noted that both α- and β-anomeric phenylthioglycosides can undergo the sulfonium ylide rearrangement and that the acyl protecting groups are required to proceed this reaction smoothly in good yield. This might suggest the existence of neighboring group participation which would bring about the coupling reaction from the opposite side of the C_2 substituent (Figure 1).[13] However, the stereochemistry at the anomeric position of the products was opposite (entry 3, 5, 6, 7), and this stereochemical control seemed to be affected by nucleophilic addition to the pyran oxonium ion due to the well-established anomeric effect.[14] Although the reaction mechanism is not immediately apparent, the observed stereoselectivity giving only one anomer as product can be rationalized by assuming the proposed reaction pathway as shown in Figure 1.

On the contrary, the intramolecular reaction of **34**[15] derived from **33** by diazo exchange reaction in methylene chloride in the presence of a catalytic amount of rhodium acetate gave the isolable ylide intermediate **35**, whose structure was unambiguously determined by its X-ray analysis.[16] Rearrangement of the ylide **35** was carried out in refluxing benzene to yield the *O*-glycosides **36** and **37**. On the basis of the spectroscopic data of the products, both compounds were deduced to be geometric isomers. Structure determination of **36** by X-ray analysis[17] led to the confirmation of the structures of both isomers, and this result suggested the reaction mechanism proposed here (Scheme III) (Figure 2).

The above C-glycosilation reaction was then applied to the synthesis of (+)-showdomycin.[18] Decarbomethoxylation[19] of **19** (DABCO, Celite, Me_2S, benzene, reflux, 24 h), followed by oxidation (MCPBA, CH_2Cl_2, room temperature, 2 h) afforded the sulfoxide **39** in 38% overall yield. The Pummerer rearrangement of **39** and subsequent dethiophenylation[20] provided the keto ester **40**. Finally, the Wittig reaction[21] of **40** furnished triacetylshowdomycin (**41**), which was identical with the authentic specimen.[22] Since **41** was already converted[23] into (+)-showdomycin (**42**), this constitutes its formal synthesis (Scheme IV).

In summary, we have shown unprecedental site- and stereoselective C-glycosilation reaction by means of carbenoid displacement reaction, and its successful application to the synthesis of (+)-showdomycin. This new process disclosed above demonstrates the versatility and practical utility.

Experimental Section

^1H NMR spectra were recorded on JEOL PMX-60 (60-MHz), JEOL JNM FX-100 (100-MHz), or JEOL JNM GX-400 (400-MHz) spectrometers and are reported in δ values. Infrared spectra were obtained with a Hitachi 260-10 spectrophotometer and mass spectra with a JEOL JMS D-300 spectrometer. Melting points were recorded on a Yanagimoto micro apparatus and are uncorrected. Thin-layer chromatography (TLC) was carried out on 0.25-mm E. Merck precoated silica gel glass plates (60F-254). Flash column chromatography was performed by using kieselgel 60.

α-1-Deoxy-1-*C*-(phenylthio)-2,3,4,5-tetra-*O*-acetyl-D-mannopyranose (5). A mixture of D-mannose (4 g, 22.2 mmol, 1.0 equiv) and sodium acetate (2.4 g, 29.26 mmol, 1.3 equiv) in acetic anhydride (40 mL) was heated at 100–120 °C for 2 h with stirring. The reaction mixture was poured into ice-cold saturated $NaHCO_3$ solution and extracted with $CHCl_3$. The organic phase was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue (8.3 g), which was directly used for the following transformation without further purification. To a stirred solution of the pentaacetate[8u] obtained above (8.3 g, 21.3 mmol, 1.0 equiv) and thiophenol (4 g, 36.36 mmol, 1.7 equiv) in anhydrous CH_2Cl_2 (30 mL) at room temperature was added boron trifluoride etherate (4.6 mL, 36.94 mmol, 1.74 equiv) dropwise under nitrogen. After stirring for 5 h at the same temperature, the reaction mixture was treated with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. Purification of a small portion (1 g) of the crude residue by silica gel chromatography (100 g) (eluted with 17% EtOAc in benzene) afforded 600 mg of the α anomer and 116 mg of the inseparable anomeric mixture (α:β = 1:1).

α anomer: (oil) $[\alpha]^{20}_D$ +88.6° (*c* 2, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 2.02 (3 H, s), 2.05 (3 H, s), 2.08 (3 H, s), 2.15 (3 H, s), 4.08 (1 H, dd, *J* = 12.2, 2.4 Hz), 4.23–4.40 (1 H, m), 4.42–4.60 (1 H, m), 5.29, 5.36 (2 H, each br s), 5.49 (2 H, br s), 7.27–7.51 (5 H, m); IR ($CHCl_3$) 1735 cm^{-1}; MS, *m/z* 440 (M^+); calcd for $C_{20}H_{24}O_9S$ 440.1128, found 440.1140.

β anomer: ^1H NMR (100 MHz) ($CDCl_3$) δ 1.99 (3 H, s), 2.04 (3 H, s), 2.09 (3 H, s), 2.21 (3 H, s), 4.19–4.22 (1 H, m), 4.91–5.19 (3 H, m),

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(12) In the preparation of the starting tetra- or pentaacetyl thioglycosides, 1,2-trans isomers were always major products; therefore, the pure 1,2-trans isomers were only examined in this reaction from the synthetic point of view.

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(15) For preparation of the thioglycoside **34**, see: (a) Ballou, C. E. *J. Am. Chem. Soc.* **1957**, *79*, 165. (b) McCormick, J. E. *Carbohydr. Res.* **1967**, *4*, 262.

(16) All the measurements were performed on a Rigaku AFC-5 diffractometer by using Cu Kα radiation. The unit cell dimensions were determined by least-squares calculation from 20 high-angle reflections. Intensity data were collected by using the $2\theta/\omega$ scan technique for $5° < 2\theta < 130°$ with an average scan rate of 5°/min. In total, 2136 independent reflections were collected, and 2068 satisfying the condition $F_o < 3\sigma(F)$ were used for calculations. Crystal data for **35**: $C_{18}H_{20}O_7S$, M_r = 380.42; orthorhombic *a* = 10.497 (10) Å, *b* = 17.516 (12)°, *c* = 9.685 (13) Å, D_c = 1.42 g cm^{-3}, *Z* = 4; space group $P2_12_12_1$. The structure was solved by the direct method with use of MULTAN (Main, P.; Woolfson, M. M.; Germin, G. *Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr.* **1971**, *27*, 368) and the Rigaku crystallographic package RASA-II. The structure was refined by the block-diagonal least-squares method with anisotropic thermal parameters for all non-hydrogen atoms. The *R* factor was finally reduced to 0.072.

(17) The structure of **36** was determined by using the 1705 reflections satisfying the condition $F_o < 3\sigma(F)$ for calculation. Crystal data for **36**: $C_{18}H_{20}O_7S$, M_r = 380.42; orthorhombic *a* = 11.297 (18) Å, *b* = 16.652 (11) Å, *c* = 9.892 (9) Å, D_c = 1.36 g cm^{-3}, *Z* = 4; space group $P2_12_12_1$. The structure was solved by the direct method with use of RANTAN and the Rigaku crystallographic package RASA-II, as described before. The *R* factor was finally reduced to 0.079.

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(23) Kalvoda, L.; Farkaš, J.; Šorm, F. *Tetrahedron Lett.* **1970**, 2297.

5.66 (1 H, d, J = 3.2 Hz), 7.27–7.54 (5 H, m).

1-Deoxy-1-*C*-(phenylthio)-2,3,4-tri-*O*-acetyl-D-arabinopyranose (7). To a stirred solution of 2,3,4-tri-*O*-acetyl-D-arabinopyranose (848 mg, 3.07 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (40 mL) at room temperature was added diphenyl disulfide (1.341 g, 6.15 mmol, 2.0 equiv) and tri-*n*-butylphosphine (1.245 g, 6.15 mmol, 2.0 equiv) under nitrogen. After having been stirred for 18 h at the same temperature, the reaction mixture was concentrated and separated by silica gel chromatography (30 g) (eluted with 9% EtOAc in benzene) to afford 932 mg (82.5%) of the thioglycoside 7 as an inseparable anomeric mixture: (oil) $[\alpha]^{24}_D$ −65.8° (c 1.2, CH_2Cl_2); ^{1}H NMR (60 MHz) ($CDCl_3$) δ 2.07 (3 H, s), 2.11 (6 H, s), 3.50–4.32 (2 H, m), 4.73–5.46 (4 H, m), 7.17–7.73 (5 H, m); IR ($CHCl_3$) 1740 cm^{-1}; MS, m/z 368 (M^+), 259 (M^+ − 109).

1-Deoxy-1-*C*-(phenylthio)-2,3,5-tri-*O*-benzyl-D-ribofuranose (9 and 10). To a stirred solution of 1-β-(thiophenyl)-3,5-di-*O*-benzyl-D-ribofuranose (483 mg, 1.143 mmol, 1.0 equiv) in anhydrous DMF at room temperature was added 60% sodium hydride in mineral oil (112 mg, 2.8 mmol, 2.5 equiv). After having been stirred for 0.5 h at room temperature, to this solution was added benzyl bromide (0.17 mL, 1.4 mmol, 1.2 equiv) dropwise, and stirring was continued for 15 h at room temperature. The reaction mixture was treated with saturated aqueous NH_4Cl and extracted with Et_2O. The combined organic layer was washed with saturated aqueous NH_4Cl, water, and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue which was subjected to silica gel flash column chromatography (10 g) (eluted with benzene) to afford 550 mg (94%) of the β anomer **9** [(oil) $[\alpha]^{21}_D$ −42.4° (c 0.8, CH_2Cl_2); ^{1}H NMR (60 MHz) ($CDCl_3$) δ 3.50 (2 H, d, J = 5.0 Hz), 3.82–4.03 (2 H, m), 4.33 (1 H, d, J = 5.0 Hz), 4.45 (4 H, s), 4.52 (2 H, s), 5.41 (1 H, d, J = 3.0 Hz), 7.04–7.60 (20 H, m); MS, m/z 403 (M^+ − 109), 311 (M^+ − 200). Anal. Calcd for $C_{32}H_{32}O_4S$ (512.67): C, 74.97; H, 6.29. Found: C, 74.68; H, 6.27]. Under identical reaction conditions, from 137 mg (0.33 mmol, 1.0 equiv) of 1-α-(thiophenyl)-3,5-di-*O*-benzyl-D-ribofuranose, 32 mg (0.8 mmol, 2.5 equiv) of sodium hydride, and 0.05 mL (0.39 mmol, 1.2 equiv) of benzyl bromide in anhydrous DMF (5 mL), was obtained 150 mg (89%) of the α anomer **10** (chromatographed on a silica gel column with benzene): (oil) $[\alpha]^{21}_D$ +160.3° (c 2.6, CH_2Cl_2); ^{1}H NMR (60 MHz) ($CDCl_3$) δ 3.53 (2 H, d, J = 3.5 Hz), 4.05 (1 H, dd, J = 7.0, 5.0 Hz), 4.46 (4 H, s), 4.57 (2 H, s), 4.62–4.97 (2 H, m), 5.69 (1 H, d, J = 5.5 Hz), 7.04–7.67 (20 H, m); MS, m/z 512 (M^+), 403 (M^+ − 109), 311 (M^+ − 200). Anal. Calcd for $C_{32}H_{32}O_4S$ (512.67): C, 74.97; H, 6.29. Found: C, 74.69; H, 6.31.

1-Deoxy-1-*C*-(phenylthio)-2,3-*O*-isopropylidene-5-*O*-acetyl-D-ribofuranose (11 and 12). Method A. To a stirred solution of 2,3-*O*-isopropylidene-5-*O*-acetyl-D-ribofuranose (127 mg, 0.55 mmol, 1.0 equiv) and diphenyl disulfide (240 mg, 1.1 mmol, 2.0 equiv) in anhydrous CH_2Cl_2 (3 mL) at room temperature was added tri-*n*-butylphosphine (223 mg, 1.1 mmol, 2.0 equiv) dropwise. After stirring for 4 h at room temperature, the reaction mixture was concentrated and separated by silica gel chromatography (10 g) (eluted with 2% EtOAc in benzene) to afford the two diastereomeric thioglycosides (82% combined): α anomer **12** (110 mg, 61.5%); β anomer **11** (36 mg, 20.5%).

Method B. To a stirred solution of β-1,5-di-*O*-acetyl-2,3-*O*-isopropylidene-D-ribofuranose (2.05 g, 7.48 mmol, 1.0 equiv) and thiophenol (902 mg, 8.2 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (15 mL) at room temperature was added boron trifluoride etherate (1 mL, 8.2 mmol, 1.1 equiv) dropwise under nitrogen. After stirring for 1 h at room temperature, the reaction mixture was treated with saturated aqueous $NaHCO_3$ at 0 °C and extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, and evaporated. Separation by silica gel column chromatography (50 g) (eluted with 2% EtOAc in benzene) afforded 1.2 g (49.5%) of the α anomer **12** and 850 mg (35.1%) of the β anomer **11**.

Method C. To a stirred solution of α-1-(thiophenyl)-2,3-*O*-isopropylidene-5-*O*-(*tert*-butyldiphenylsilyl)-D-ribofuranose (1.854 g, 3.6 mmol, 1.0 equiv) in THF (25 mL) at room temperature was added tetra-*n*-butylammonium fluoride in THF solution (1 M) (4 mL, 4 mmol, 1.1 equiv) dropwise. After having been stirred for 1 h at room temperature, the reaction mixture was diluted with Et_2O, washed with water and brine, dried over anhydrous sodium sulfate, and evaporated. Separation by silica gel (5 g) flash column chromatography (eluted with 30% EtOAc in benzene) gave 440 mg (43.3%) of the alcohol which was directly used for the following transformation [(oil) ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.41 (3 H, s), 1.64 (3 H, s), 3.71–3.94 (2 H, m), 4.28–4.51 (1 H, m), 4.68–5.18 (2 H, m), 5.71 (1 H, d, J = 5.0 Hz), 7.21–7.73 (5 H, m); IR ($CHCl_3$) 3400 cm^{-1}]. To a stirred solution of the alcohol obtained above (440 mg, 1.56 mmol, 1.0 equiv) was added triethylamine (0.28 mL, 2.0 mmol, 1.3 equiv), a catalytic amount of DMAP in anhydrous CH_2Cl_2 (10 mL) at −10 °C, and a solution of acetyl chloride (0.12 mL, 1.7 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (5 mL) dropwise under nitrogen. After having been stirred for 0.5 h at −10 °C, the reaction mixture was washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous sodium sulfate, and evaporated. Separation by silica gel chromatography (10 g) (eluted with 5% EtOAc in benzene) afforded 425 mg (84%) of the α anomer **12.**

α anomer **12**: (oil) $[\alpha]^{20}_D$ +105.7° (c 1.4, CH_2Cl_2); ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.38 (3 H, s), 1.61 (3 H, s), 2.07 (3 H, s), 4.10–4.80 (2 H, m), 4.26 (2 H, s), 4.99 (1 H, dd, J = 5.5, 5.0 Hz), 5.56 (1 H, d, J = 5.0 Hz), 7.13–7.70 (5 H, m); IR ($CHCl_3$) 1730 cm^{-1}; MS, m/z 324 (M^+), 309 (M^+ − 15), 215 (M^+ − 109); calcd for $C_{16}H_{20}O_5S$ 324.1030, found 324.1025.

β anomer **11**: (oil) $[\alpha]^{20}_D$ −202.1° (c 1, CH_2Cl_2); ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.95 (3 H, s), 1.52 (3 H, s), 2.10 (3 H, s), 3.93–4.96 (3 H, m), 4.75 (2 H, br s), 5.58 (1 H, d, J = 1.5 Hz), 7.19–7.81 (5 H, m); IR ($CHCl_3$) 1730 cm^{-1}; MS, m/z 324 (M^+), 309 (M^+ − 15), 215 (M^+ − 109); calcd for $C_{16}H_{20}O_5S$ 324.1031, found 324.1036.

General Procedure for C-Glycosilation Reaction. Method A. To a stirred solution of the thioglycoside (1.0 equiv) and rhodium(II) acetate (15% mol) in dry benzene (0.1 M) was added dropwise a solution of dimethyl diazomalonate (3.0 equiv) in dry benzene (1 M) at reflux under nitrogen, and stirring was continued until TLC analysis indicates disappearance of the starting material (see Table I). The reaction mixture was concentrated under reduced pressure to give a crude residue which was subjected to silica gel column chromatography. Solvent systems for separation are given with the reaction scale and spectral data for each compound.

Method B. The reaction was carried out in dry CH_2Cl_2 at ambient temperature employing the identical reaction scale.

Method C. The reaction was carried out in refluxing dry CH_2Cl_2.

General Procedure for Dethiophenylation Reaction of *C*-Glycosides. (a) To a stirred solution of the *C*-glycoside in acetone (0.03 M) was added Raney nickel (6 g/1 mmol), and stirring was continued until TLC analysis indicates disappearance of starting material at reflux temperature (see Table I). The reaction mixture was filtered through a small plug of Celite, and the filtrate was concentrated to give a residue, which was subjected to silica gel column chromatography. The solvent systems for separation are given with the reaction scale and spectral data for each compound. (b) To a stirred solution of the *C*-glycoside (1.0 equiv) in dry benzene (0.02 M) was added dropwise a solution of tri-*n*-butyltin hydride (2.0 equiv) and AIBN (2.0 equiv) in dry benzene (0.1 M) under nitrogen at reflux temperature, and stirring was continued until TLC analysis indicates disappearance of starting material at the same temperature (see Table I). After having been cooled to room temperature, the reaction mixture was diluted with EtOAc, washed twice with saturated aqueous NH_4Cl and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude residue which was subjected to silica gel column chromatography. The solvent systems for separation are given with the reaction scale and spectral data for each compound.

2-[(Phenylthio)bis(methoxycarbonyl)methyl]tetrahydropyran (13). From 388 mg (2 mmol) of **1**, 948 mg (6 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method A, B, and C was obtained 205 mg (31.6%) of **13** by method A, 270 mg (42%) of **13** by method B, and 350 mg (54%) of **13** by method C, respectively (chromatographed on a silica gel column, eluted with 5% EtOAc in benzene) (oil): ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.25–2.29 (6 H, m), 3.22–4.39 (3 H, m), 3.70 (6 H, s), 7.32–7.82 (5 H, m); IR ($CHCl_3$) 1725 cm^{-1}; MS, m/z 324 (M^+); calcd for $C_{16}H_{20}O_5S$ 324.1029, found 324.1013.

2-[Bis(methoxycarbonyl)methyl]tetrahydropyran (23). (a) From 100 mg (0.31 mmol) of **13** and 1.86 g of Raney nickel in acetone (10 mL) was obtained 55 mg (82.5%) of **23**. (b) From 100 mg (0.31 mmol) of **13**, 180 mg (0.62 mmol) of tri-*n*-butyltin hydride, and 102 mg (0.62 mmol) of AIBN in benzene (20 mL) was obtained 57 mg (85.4%) of **23** (chromatographed on a silica gel column, eluted with 1% EtOAc in benzene) (oil): ^{1}H NMR (100 MHz) ($CDCl_3$) δ 1.49–1.88 (6 H, m), 3.48 (1 H, d, J = 9.0 Hz), 3.73 (3 H, s), 3.76 (3 H, s), 3.86–4.09 (3 H, m); IR ($CHCl_3$) 1750, 1730 cm^{-1}; MS, m/z 216 (M^+), 85 (M^+ − 131). Anal. Calcd for $C_{10}H_{16}O_5$ (216.23): C, 55.54; H, 7.46. Found: C, 55.29; H, 7.49.

2-[(Phenylthio)bis(methoxycarbonyl)methyl]tetrahydrofuran (14). From 180 mg (1.0 mmol) of **2**, 474 mg (3.0 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 275 mg (88.5%) of **14** (chromatographed on a silica gel, eluted with 1% EtOAc in benzene) (oil): ^{1}H NMR (60 MHz) ($CDCl_3$) δ 1.18–2.50 (4 H, m), 3.82 (6 H, s), 4.44 (1 H, d, J = 7.0 Hz), 7.13–7.66 (5 H, m); IR ($CHCl_3$) 1725 cm^{-1}; MS, m/z 310 (M^+), 71 (M^+ − 239); calcd for $C_{15}H_{18}O_5S$ 310.0873, found 310.0863.

2-[Bis(methoxycarbonyl)methyl]tetrahydrofuran (24). From 300 mg (0.926 mmol) of **14** and 3 g of Raney nickel in acetone (30 mL) was obtained 165 mg (82.5%) of **24** (chromatographed on a silica gel, eluted with 2% EtOAc in benzene) (oil): ^{1}H NMR (60 MHz) ($CDCl_3$) δ

1.50–2.34 (4 H, m), 3.45 (1 H, d, J = 8.8 Hz), 3.74 (3 H, s), 3.76 (3 H, s), 4.21–4.65 (1 H, m); IR ($CHCl_3$) 1730, 1750 cm^{-1}; MS, m/z 202 (M^+), 71 ($M^+ - 131$). Anal. Calcd for $C_9H_{14}O_5$ (202.21): C, 53.46; H, 6.98. Found: C, 53.08; H, 7.33.

α-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (15). From 440 mg (1.0 mmol) of the β anomer **3**, 474 mg (3.0 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate employing the method C was obtained 480 mg (84%) of **15** (chromatographed on a silica gel, eluted with 10% EtOAc in benzene) (oil): $[\alpha]^{22}_D$ +11.6° (c 2, CH_2Cl_2); ^1H NMR (60 MHz) ($CDCl_3$) δ 1.91 (3 H, s), 2.07 (9 H, s), 3.54 (3 H, s), 3.62 (3 H, s), 3.70–4.04 (1 H, m), 4.10–4.35 (2 H, m), 4.43–4.67 (1 H, m), 4.93 (1 H, dd, J = 8.0, 5.0 Hz), 5.10–5.27 (1 H, m), 5.98 (1 H, d, J = 5.0 Hz), 7.20–7.71 (5 H, m); IR ($CHCl_3$) 1730 cm^{-1}; MS, m/z 570 (M^+), 511 ($M^+ - 59$), 331 ($M^+ - 239$).

α-1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (25). From 200 mg (0.35 mmol) of **15** and 2 g of Raney nickel in acetone (20 mL) was obtained 137 mg (84.5%) of **25** (chromatographed on a silica gel, eluted with 10% EtOAc in benzene) (oil): $[\alpha]^{23}_D$ +10.5° (c 1.5, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.87 (3 H, s), 2.09 (6 H, s), 2.11 (3 H, s), 3.73 (1 H, s), 3.76 (6 H, s), 4.00–4.36 (3 H, m), 4.82–4.94 (1 H, m), 5.17–5.24 (1 H, m), 5.74 (1 H, d, J = 5.1 Hz); IR ($CHCl_3$) 1740 cm^{-1}; MS, m/z 447 ($M^+ - 15$), 403 ($M^+ - 59$), 331 ($M^+ - 131$).

β-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3,4,6-tetra-*O*-acetyl-D-mannopyranose (16). From 543 mg (1.234 mmol) of **5**, 585 mg (3.7 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 329 mg (47%) of **16** (chromatographed on a silica gel, eluted with 9% EtOAc in benzene) (oil): $[\alpha]^{20}_D$ +6.3° (c 3, CH_2Cl_2); ^1H NMR (400 MHz) ($CDCl_3$) δ 1.98 (3 H, s), 2.05 (3 H, s), 2.08 (3 H, s), 2.15 (3 H, s), 3.50 (3 H, s), 3.61 (3 H, s), 3.68–3.73 (1 H, m), 4.14 (1 H, dd, J = 12.1, 2.5 Hz), 4.27 (1 H, dd, J = 12.1, 4.5 Hz), 5.11 (1 H, dd, J = 4.2, 2.7 Hz), 5.23 (1 H, dd, J = 9.7, 4.2 Hz), 5.36 (1 H, t, J = 9.7 Hz), 5.59 (1 H, d, J = 2.7 Hz), 7.25–7.36 (5 H, m); IR ($CHCl_3$) 1740 cm^{-1}; MS, m/z 570 (M^+), 497 ($M^+ - 73$), 461 ($M^+ - 109$); calcd for $C_{25}H_{30}O_{13}S$ 570.1421, found 570.1408.

β-1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3,4,6-tetra-*O*-acetyl-D-mannopyranose (26). From 194 mg (0.34 mmol) of **16**, 220 mg (0.68 mmol) of tri-n-butyltin hydride, and 112 mg (0.68 mmol) of AIBN in benzene (20 mL) was obtained 85 mg (54%) of **26** (chromatographed on a silica gel, eluted with 17% EtOAc in benzene) (oil): $[\alpha]^{20}_D$ −8.5° (c 1.5, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.86 (3 H, s), 2.05 (3 H, s), 2.06 (3 H, s), 2.09 (3 H, s), 3.63–3.78 (1 H, m), 3.74 (6 H, s), 4.13–4.21 (2 H, m), 4.58 (1 H, dd, J = 3.7, 2.2 Hz), 5.09–5.34 (2 H, m), 5.43 (1 H, d, J = 2.2 Hz); IR ($CHCl_3$) 1735 cm^{-1}; MS, m/z 447 ($M^+ - 15$).

α-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3,4,6-tetra-*O*-acetyl-D-galactopyranose (17). (a) From 440 mg (1 mmol) of the β anomer **6**, 474 mg (3 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 420 mg (73.7%) of **17** (chromatographed on a silica gel, eluted with 9% EtOAc in benzene) (oil): $[\alpha]^{20}_D$ +33.9° (c 2.5, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.89 (3 H, s), 2.06 (3 H, s), 2.08 (3 H, s), 2.10 (3 H, s), 3.58 (3 H, s), 3.61 (3 H, s), 3.76–3.89 (1 H, m), 4.10–4.18 (1 H, m), 4.29–4.38 (1 H, m), 4.55 (1 H, dd, J = 6.4, 4.6 Hz), 5.09 (1 H, dd, J = 6.4, 2.9 Hz), 5.51 (1 H, t, J = 2.9 Hz), 6.01 (1 H, d, J = 4.6 Hz), 7.27–7.39 (3 H, m), 7.58–7.68 (2 H, m); IR ($CHCl_3$) 1735 cm^{-1}; MS, m/z 570 (M^+); calcd for $C_{25}H_{30}O_{13}S$ 570.1391, found 570.1406.

α-1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3,4,6-tetra-*O*-acetyl-D-galactopyranose (27). From 335 mg (0.59 mmol) of **17**, 350 mg (1.17 mmol) of tri-n-butyltin hydride, and 192 mg (1.17 mmol) of AIBN in benzene (35 mL) was obtained 220 mg (80.7%) of **27** (chromatographed on a silica gel, eluted with 17% EtOAc in benzene (oil): $[\alpha]^{21}_D$ +54.1° (c, 2.5, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.80 (3 H, s), 2.06 (6 H, s), 2.10 (3 H, s), 3.76 (6 H, s), 4.09–4.50 (4 H, m), 4.16 (1 H, s), 5.07 (1 H, dd, J = 6.9, 3.2 Hz), 5.43 (1 H, t, J = 3.2 Hz), 5.80 (1 H, d, J = 4.6 Hz); IR ($CHCl_3$) 1740 cm^{-1}; MS, m/z 447 ($M^+ - 15$).

β-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3,4-tri-*O*-acetyl-D-arabinopyranose (18). From 368 mg (1.0 mmol) of 7, 474 mg (3.0 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 284 mg (57%) of **18** (chromatographed on a silica gel, eluted with 7% EtOAc in benzene) (oil): $[\alpha]^{23}_D$ +3.6° (c 1, CH_2Cl_2); ^1H NMR (400 MHz) ($CDCl_3$) δ 1.89 (3 H, s), 2.06 (3 H, s), 2.11 (3 H, s), 3.59 (3 H, s), 3.62 (3 H, s), 3.73 (1 H, dd, J = 12.5, 5.1 Hz), 4.09 (1 H, dd, J = 12.5, 4.9 Hz), 4.59–4.61 (1 H, m), 5.28–5.34 (1 H, m), 5.63 (1 H, d, J = 3.7 Hz), 7.26–7.38 (3 H, m), 7.62–7.64 (2 H, m); IR ($CHCl_3$) 1750, 1730 cm^{-1}; MS, m/z 498 (M^+), 259 ($M^+ - 239$).

β-1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3,4-tri-*O*-acetyl-D-arabinopyranose (28). From 342 mg (0.69 mmol) of **18**, 412 mg (1.38 mmol) of tri-n-butyltin hydride, and 226 mg (1.38 mmol) of AIBN in benzene (45 mL) was obtained 215 mg (80%) of **28** (chromatographed on a silica gel, eluted with 9% EtOAc in benzene) (oil): $[\alpha]^{23}_D$ −8.9° (c 0.8, CH_2Cl_2); ^1H NMR (60 MHz) ($CDCl_3$) δ 1.79 (3 H, s), 2.06 (3 H, s), 2.12 (3 H, s), 3.65–4.35 (4 H, m), 3.78 (6 H, s), 5.15–5.42 (2 H, m), 5.54 (1 H, d, J = 3.0 H); IR ($CHCl_3$) 1750, 1730 cm^{-1}; MS, m/z 259 ($M^+ - 131$).

β-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3,5-tri-*O*-acetyl-D-ribofuranose (19). From 1.376 g (3.74 mmol) of **8**, 1.77 g (11.2 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 1.317 g (70.7%) of **19** (chromatographed on a silica gel, eluted with 5% EtOAc in benzene): $[\alpha]^{22}_D$ +70.3° (c 0.4, CH_2Cl_2); mp 87–89 °C (EtOAc/hexane); ^1H NMR (60 MHz) ($CDCl_3$) δ 1.86 (3 H, s), 2.08 (3 H, s), 2.15 (3 H, s), 3.55 (6 H, s), 4.11–4.76 (4 H, m), 4.99 (1 H, t, J = 4.0 Hz), 5.99 (1 H, d, J = 4.0 Hz), 7.19–7.72 (5 H, m); IR ($CHCl_3$) 1735 cm^{-1}; MS, m/z 498 (M^+). Anal. Calcd for $C_{22}H_{26}O_{11}S$ (498.52): C, 53.01; H, 5.26. Found: C, 52.78; H, 5.25.

β-1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3,5-tri-*O*-acetyl-D-ribofuranose (29). (a) From 270 mg (0.54 mmol) of **19** and 3 g of Raney nickel in acetone (20 mL) was obtained 168 mg (80%) of **29**. (b) From 1.3 g (2.61 mmol) of **19**, 1.565 g (5.22 mmol) of tri-n-butyltin hydride, and 858 mg (5.22 mmol) of AIBN in benzene (170 mL) was obtained 650 mg (64%) of **29** (chromatographed on silica gel, eluted with 5% EtOAc in benzene) (oil): $[\alpha]^{22}_D$ +82.4° (c 1.5, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.77 (3 H, s), 2.09 (3 H, s), 2.12 (3 H, s), 3.70 (1 H, s), 3.74 (6 H, s), 4.04–4.71 (4 H, m), 4.92 (1 H, dd, J = 5.1, 3.9 Hz), 5.64 (1 H, d, J = 3.9 Hz); IR ($CHCl_3$) 1735 cm^{-1}; MS, m/z 391 ($M^+ + 1$), 375 ($M^+ - 15$), 259 ($M^+ - 131$).

β-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3,5-tri-*O*-benzyl-D-ribofuranose (20) and 1-Deoxy-1-*C*-[bis(methoxycarbonyl)-methylene]-2,3,5-tri-*O*-benzyl-D-ribofuranose (21). (a) From 512 mg (1 mmol) of **9**, 474 mg (3 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C were obtained 30 mg (4.7%) of **20** as a less polar product and 225 mg (43.3%) of **21** (chromatographed on a silica gel, eluted with 1% EtOAc in benzene).

20: (oil) ^1H NMR (100 MHz) ($CDCl_3$) δ 3.40–3.54 (2 H, m), 3.76 (6 H, s), 4.49–4.90 (4 H, m), 4.55 (4 H, s), 4.65 (2 H, s), 7.04–7.36 (5 H, m), 7.26 (5 H, s), 7.31 (5 H, s), 7.34 (5 H, s); IR ($CHCl_3$) 1735 cm^{-1}; MS, m/z 551 ($M^+ - 91$), 442 ($M^+ - 200$).

21: (oil) $[\alpha]^{23}_D$ +6.2° (c 1, CH_2Cl_2); ^1H NMR (60 MHz) ($CDCl_3$) δ 3.51–3.92 (2 H, m), 3.69 (3 H, s), 3.77 (3 H, s), 4.09 (1 H, dd, J = 7.5, 5.0 Hz), 4.40–4.90 (1 H, m), 4.50 (4 H, s), 4.69 (2 H, s), 5.30 (1 H, d, J = 5.0 Hz), 7.17–7.90 (5 H, m), 7.33 (10 H, s), 7.35 (5 H, s); IR ($CHCl_3$) 1710, 1640 cm^{-1}; MS, m/z 532 (M^+); calcd for $C_{31}H_{32}O_8$ 532.2097, found 532.2097.

(b) From 124 mg (0.242 mmol) of the α anomer **10**, 345 mg (2.18 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 73 mg (56.7%) of **21** (chromatographed on a silica gel, eluted with 1% EtOAc in benzene), whose NMR and IR spectra and R_f value were identical with those of the authentic specimen.

(c) A stirred mixture of the C-glycoside **20** (30 mg, 0.047 mmol, 1.0 equiv), dimethyl diazomalonate (22 mg, 0.14 mmol, 3.0 equiv), and a catalytic amount of rhodium(II) acetate in anhydrous CH_2Cl_2 (5 mL) was refluxed for 2.5 h under nitrogen. The reaction mixture was concentrated under reduced pressure to give a crude residue which was subjected to silica gel column chromatography (3 g) (eluted with 1% EtOAc in benzene) to afford 15 mg of **21** (60%). Its NMR and IR spectra and R_f value were identical with those of the authentic specimen.

β-1-Deoxy-1-*C*-[(phenylthio)bis(methoxycarbonyl)methyl]-2,3-*O*-isopropylidene-5-*O*-acetyl-D-ribofuranose (22). (a) From 730 mg (2.25 mmol) of **11**, 1.066 g (6.75 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 350 mg (34.3%) of **22** (chromatographed on a silica gel, eluted with 5% EtOAc in benzene) (oil): ^1H NMR (60 MHz) ($CDCl_3$) δ 1.37 (3 H, s), 1.55 (3 H, s), 2.08 (3 H, s), 3.82 (6 H, s), 5.93 (1 H, d, J = 2.0 Hz), 7.20–7.80 (5 H, m); IR ($CHCl_3$) 1735 cm^{-1}; MS, m/z 454 (M^+), 439 ($M^+ - 15$), 215 ($M^+ - 239$); calcd for $C_{21}H_{26}O_9S$ 454.1296, found 454.11289. (b) From 220 mg (0.68 mmol) of the α anomer **12**, 316 mg (2 mmol) of dimethyl diazomalonate, and a catalytic amount of rhodium(II) acetate by using the method C was obtained 86 mg (28%) of **22** (chromatographed on silica gel, eluted with 5% EtOAc in benzene), whose NMR and IR spectra and R_f value were identical with those of the authentic specimen.

β-1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3-*O*-isopropylidene-5-*O*-acetyl-D-ribofuranose (32). From 200 mg (0.44 mmol) of **22** and 2.4 g of Raney nickel in acetone (20 mL) was obtained 107 mg (70%)

of **32** (chromatographed on a silica gel, eluted with 5% EtOAc in benzene) (oil): $[\alpha]^{22}_D$ +2.27° (*c* 0.3, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.37 (3 H, s), 1.56 (3 H, s), 2.12 (3 H, s), 3.64 (1 H, d, *J* = 8.0 Hz), 3.78 (6 H, s), 4.10–4.27 (3 H, m); 4.48–4.66 (2 H, m), 4.84 (1 H, dd, *J* = 8.0, 3.5 Hz); ^{13}C NMR (100 MHz) ($CDCl_3$) δ ($CDCl_3$) 20.768, 25.507, 25.975, 27.379, 52.652, 54.583, 64.177, 81.728, 82.605, 83.015, 96.061, 114.314, 166.850, 166.967, 170.360; IR ($CHCl_3$) 1730 cm^{-1}; MS, *m/z* 347 (M^+ + 1), 331 (M^+ − 15), 215 (M^+ − 131).

1-Deoxy-1-*C*-[bis(methoxycarbonyl)methyl]-2,3,5-tri-*O*-benzyl-D-ribofuranose (30 and 31). (a) To a stirred solution of the malonylidene compound **21** (215 mg, 0.404 mmol, 1.0 equiv) and nickel (II) chloride (24 mg, 0.101 mmol, 0.25 equiv) in methanol (20 mL) was added sodium borohydride (31 mg, 0.81 mmol, 2.0 equiv) at room temperature. After having been stirred for 1.5 h at the same temperature, the reaction mixture was treated with 10 drops of acetic acid and filtered through a small plug of Celite.

The filtrate was concentrated under reduced pressure to give a crude residue which was subjected to silica gel column chromatography (7 g) (eluted with 2% EtOAc in benzene) to afford the two diastereomeric *C*-glycosides (74.1% combined): α anomer **31**, 26 mg (12%); β anomer **30**, 134 mg (62.1%).

α anomer: (oil) $[\alpha]^{24}_D$ +23.3° (*c* 0.16, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 3.44–3.53 (2 H, m), 3.59 (1 H, d, *J* = 7.5 Hz), 3.61 (3 H, s), 3.70 (3 H, s), 3.93 (1 H, t, *J* = 5.3 Hz), 4.04 (1 H, t, *J* = 5.3 Hz), 4.18–4.24 (1 H, m), 4.45–4.58 (6 H, m), 4.64 (1 H, dd, *J* = 7.5, 5.3 Hz), 7.26–7.36 (15 H, m); IR ($CHCl_3$), 1730 cm^{-1}; MS, *m/z* 535 (M^+ + 1), 443 (M^+ − 91).

β anomer: (oil) $[\alpha]^{21}_D$ +56.6° (*c* 2, CH_2Cl_2) [lit. $[\alpha]^{25}_D$ +16.5° (*c* 2, CH_2Cl_2)]; ^1H NMR (60 MHz) ($CDCl_3$) δ 3.50 (3 H, s), 3.72 (3 H, s), 4.14 (2 H, br s), 4.22–4.77 (3 H, m), 4.48 (4 H, s), 4.59 (2 H, s), 4.83 (1 H, d, *J* = 3.5 Hz), 7.25 (15 H, s); IR ($CHCl_3$) 1745, 1730 cm^{-1}; MS, *m/z* 534 (M^+), 443 (M^+ − 91).

(b) To a stirred solution of the *C*-glycoside **20** (30 mg, 0.047 mmol) in acetone (5 mL) was added Raney nickel (300 mg), and stirring was continued for 1 h at refluxing temperature. The reaction mixture was filtered through a small plug of Celite, and the filtrate was concentrated to give a residue, which was subjected to silica gel column chromatography (5 g) (eluted with 2% EtOAc in benzene) to afford the β anomer **30** (19 mg, 75%), whose NMR and IR spectra and R_f value were identical with those of the authentic specimen.

1-Deoxy-1-*C*-(phenylthio)-2-*O*-(1′-oxo-2′-(methoxycarbonyl)ethyl)-3,4-*O*-isopropylidene-D-arabinopyranose (33). To a stirred solution of β-2-*O*-(1′-oxo-2′-(methoxycarbonyl)ethyl)-3,4-*O*-isopropylidene-D-arabinopyranose (935 mg, 3.2 mmol, 1.0 equiv) and diphenyl disulfide (1.42 g, 6.5 mmol, 2.0 equiv) in anhydrous CH_2Cl_2 (20 mL) at room temperature was added tri-*n*-butylphosphine (1.32 g, 6.5 mmol, 2.0 equiv) dropwise. After having been stirred for 3 h at room temperature, the reaction mixture was concentrated to give a residue which was subjected to silica gel column chromatography (20 g) (eluted with 5% EtOAc in benzene) to afford 315 mg (30.4%) of the β anomer **33** and 550 mg (53.1%) of the α anomer.

α anomer: (prism) $[\alpha]^{24}_D$ −4.9° (*c* 1, CH_2Cl_2); mp 117–117.5 °C (recrystallized EtOAc/hexane); ^1H NMR (60 MHz) ($CDCl_3$) δ 1.35 (3 H, s), 1.54 (3 H, s), 3.45 (2 H, s), 3.75 (3 H, s), 4.89 (1 H, d, *J* = 7.0 Hz), 5.20 (1 H, dd, *J* = 7.0, 5.0 Hz), 7.18–7.71 (5 H, m); IR ($CHCl_3$) 1760, 1740, 1130 cm^{-1}; MS, *m/z* 382 (M^+), 367 (M^+ − 15), 273 (M^+ − 109). Anal. Calcd for $C_{18}H_{22}O_7S$ (382.44): C, 56.53; H, 5.80. Found: C, 56.51; H, 5.76.

β anomer 33: (oil) $[\alpha]^{24}_D$ −170.4° (*c* 0.85, CH_2Cl_2); ^1H NMR (60 MHz) ($CDCl_3$) δ 1.38 (3 H, s), 1.54 (3 H, s), 3.49 (2 H, s), 3.76 (3 H, s), 5.10–1.49 (1 H, m), 5.68 (1 H, d, *J* = 5.0 Hz), 7.20–7.67 (5 H, m); IR ($CHCl_3$) 1760, 1740, 1670 cm^{-1}; MS, *m/z* 382 (M^+), 367 (M^+ − 15), 273 (M^+ − 109); calcd for $C_{18}H_{22}O_7S$ 382.1087, found 382.1095.

β-1-Deoxy-1-*C*-(phenylthio)-2-*O*-(1′-oxo-2′-diazo-2′-(methoxycarbonyl)ethyl)-3,4-*O*-isopropylidene-D-arabinopyranose (34). To a stirred solution of **33** (315 mg, 0.825 mmol, 1.0 equiv) and triethylamine (0.23 mL, 1.65 mmol, 2.0 equiv) in anhydrous MeCN (10 mL) at room temperature was added a solution of *p*-toluenesulfonyl azide (195 mg, 0.989 mmol, 1.2 equiv) in anhydrous MeCN (10 mL) dropwise. After having been stirred for 4 h at room temperature, the reaction mixture was concentrated to give a residue which was subjected to silica gel column chromatography (10 g) (eluted with 5% EtOAc in benzene) to afford 286 mg (85%) of the diazo compound **34**: (oil) ^1H NMR (60 MHz) ($CDCl_3$) δ 1.35 (3 H, s), 1.53 (3 H, s), 3.80 (3 H, s), 3.97–4.57 (4 H, m), 5.10–5.49 (1 H, m), 5.66 (1 H, d, *J* = 5.0 Hz), 7.07–7.14 (5 H, m); IR ($CHCl_3$) 2150, 1760, 1740, 1700 cm^{-1}.

Methyl 2-(Phenylthio)-2-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)-acetate (38). A mixture of the *C*-glycoside **19** (498 mg, 1 mmol, 1.0 equiv), DABCO (1.122 g, 10 mmol, 10 equiv), dimethyl sulfide (620 mg, 10 mmol, 10 equiv), and Celite (500 mg) in anhydrous benzene was heated under reflux for 24 h with stirring. The reaction mixture was diluted with EtOAc, washed with brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue which was subjected to silica gel column chromatography (250 g) (eluted with 9% EtOAc in benzene) to afford 176 mg (40%) of the *C*-glycoside **38** as a diastereomeric mixture (2R:2S = 1:1): (oil) $[\alpha]^{24}_D$ +81.1° (*c* 0.11, CH_2Cl_2); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.76 (1.5 H, s), 1.78 (1.5 H, s), 2.09 (3 H, s), 2.13 (3 H, s), 3.71 (3 H, s), 3.73 (0.5 H, s), 3.78 (0.5 H, s), 4.09–4.76 (4 H, m), 4.80 (0.5 H, t, *J* = 4.0 Hz), 5.06 (0.5 H, t, *J* = 4.0 Hz), 5.89 (0.5 H, d, *J* = 4.0 Hz), 6.01 (0.5 H, d, *J* = 4.0 Hz), 7.26–7.45 (5 H, m); IR ($CHCl_3$) 1740 cm^{-1}; MS, *m/z* 331 (M^+ − 109), 259 (M^+ − 181).

Methyl 2-(Phenylsulfinyl)-2-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)-acetate (39). To a stirred two-phase solution of the *C*-glycoside **38** (160 mg, 0.364 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) and saturated $NaHCO_3$ (5 mL) at 0 °C was added a solution of *m*-chloroperbenzoic acid (86 mg, 0.4 mmol, 1.1 equiv) in CH_2Cl_2 (3 mL) dropwise. After stirring for 2 h at room temperature, the reaction mixture was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave residue, which was subjected to silica gel column chromatography (10 g) (eluted with 28% EtOAc in benzene) to afford 152 mg (91.6%) of the sulfoxide **39** as a diastereomeric mixture: (oil) $[\alpha]^{23}_D$ +67.6° (*c* 2, CH_2Cl_2); ^1H NMR (60 MHz) ($CDCl_3$) δ 1.75, 1.82, 1.89 (3 H, each s), 2.10 (3 H, s), 2.12, 2.14 (3 H, each s), 3.30, 3.62 (3 H, each s), 3.72 (1 H, br s), 4.10–5.21 (5 H, m), 5.76–6.17 (1 H, m), 7.41–7.85 (5 H, m); IR ($CHCl_3$) 1750, 1070 cm^{-1}; MS, *m/z* 456 (M^+), 259 (M^+ − 197).

2,3,5-tri-*O*-Acetylshowdomycin (41). To a stirred solution of the sulfoxide **39** (146 mg, 0.32 mmol, 1.0 equiv) and 2,6-lutidine (0.075 mL, 0.64 mmol, 2.0 equiv) in anhydrous MeCN (7 mL) at 0 °C was added a solution of trifluoroacetic anhydride (0.091 mL, 0.64 mmol, 2.0 equiv) in anhydrous MeCN (7 mL) dropwise under nitrogen. After stirring for 3 h at room temperature, to the above reaction mixture at room temperature was added a solution of mercuric chloride (130 mg, 0.48 mmol, 1.5 equiv) in water (20 mL), and stirring was continued for 1 h at the same temperature. The reaction mixture was diluted with EtOAc (50 mL), washed with 10% HCl, saturated $NaHCO_3$, and brine, and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded the crude α-keto ester (**40**), which was directly used for the following transformation. The above α-keto methyl ester is dissolved in $CHCl_3$ (7 mL) and treated with carbamoylmethylenetriphenylphosphorane (134 mg, 0.4 mmol, 1.25 equiv). The mixture was stirred for 1 h at ambient temperature. After removal of the solvent, the residue was subjected to silica gel column chromatography (20 g) (eluted with 30% EtOAc in benzene) to afford 70 mg (62%) of the fully protected showdomycin derivative **41**: $[\alpha]^{25}_D$ +10.9° (*c* 0.8, CH_2Cl_2); mp 114.5–116 °C [lit. mp 115–116 °C] (benzene/acetone); ^1H NMR (60 MHz) ($CDCl_3$) δ 2.31 (9 H, s), 4.07–4.50 (3 H, m), 4.72–5.05 (1 H, m), 5.17–5.64 (2 H, m), 6.60 (1 H, t, *J* = 1.5 Hz), 8.00 (1 H, br s); IR ($CHCl_3$) 1775, 1750, 1730, 1650 cm^{-1}; MS, *m/z* 313 (M^+ − 43).

Intramolecular Carbenoid Displacement Reaction of 34. To a stirred solution of the diazo compound **34** (280 mg, 0.686 mmol) in anhydrous CH_2Cl_2 (10 mL) at room temperature was added rhodium(II) acetate (15 mol%) under nitrogen, and the resultant mixture was heated for 2 h at reflux. The reaction mixture was concentrated under reduced pressure to give a crude residue which was subjected to silica gel column chromatography (10 g) (eluted with EtOAc) to afford 180 mg (69%) of the ylide compound **35**: $[\alpha]^{24}_D$ +58.6° (*c* 0.7, CH_2Cl_2); mp 151–151.5 °C (EtOAc/hexane); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.30 (3 H, s), 1.41 (3 H, s), 3.80 (3 H, s), 4.15–4.79 (4 H, m), 4.33 (1 H, t, *J* = 2.3 Hz), 5.16 (1 H, d, *J* = 2.3 Hz), 7.64 (5 H, s); IR ($CHCl_3$) 1665, 1635, 1345, 1310, 1105 cm^{-1}; MS, *m/z* 380 (M^+), 365 (M^+ − 15). Anal. Calcd for $C_{18}H_{20}O_7S$ (380.42): C, 56.83; H, 5.30. Found: C, 56.84; H, 5.32. The structure of **35** was determined by means of X-ray analysis.[16]

A solution of the ylide compound **35** obtained above (176 mg, 0.46 mmol) in anhydrous benzene (7 mL) was heated at reflux for 4 h under nitrogen. The reaction mixture was concentrated under reduced pressure to give a crude residue which was subjected to silica gel column chromatography (10 g) (eluted with 5% EtOAc in benzene) to afford 85 mg (48.3%) of the anti form *O*-glycoside **36** as a first elution and 55 mg (31.3%) of the syn form *O*-glycoside **37** as a second elution.

anti isomer: $[\alpha]^{25}_D$ −86.6° (*c* 1.7, CH_2Cl_2); mp 146–148 °C (EtOAc/hexane); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.31 (3 H, s), 1.46 (3 H, s), 3.45 (1 H, dd, *J* = 13.7, 1.7 Hz), 3.73 (3 H, s), 3.87 (1 H, d, *J* = 13.7 Hz), 4.08–4.15 (1 H, m), 4.62–4.79 (2 H, m), 6.24 (1 H, d, *J* = 5.6 Hz), 7.02–7.35 (5 H, m); IR ($CHCl_3$) 1700, 1585 cm^{-1}; MS, *m/z* 380 (M^+). Anal. Calcd for $C_{18}H_{20}O_7S$ (380.42): C, 56.83; H, 5.30.

Found: C, 56.75; H, 5.30. The structure of **36** was determined by means of X-ray analysis.[17]

syn isomer: $[\alpha]^{25}_D$ -120.3° (*c* 1.1, CH_2Cl_2); mp 58.5-61 °C (EtOAc/hexane); ^1H NMR (100 MHz) ($CDCl_3$) δ 1.36 (3 H, s), 1.47 (3 H, s) 3.49 (1 H, dd, J = 13.7, 1.7 Hz), 3.70 (3 H, s), 3.84 (1 H, d, J = 13.7 Hz), 4.31-4.39 (1 H, m), 4.81-5.00 (2 H, m), 6.05 (1 H, d, J = 5.6 Hz), 7.08-7.35 (5 H, m); IR ($CHCl_3$) 1690, 1585 cm^{-1}; MS, m/z 380 (M^+). Anal. Calcd for $C_{18}H_{20}O_7S$ (380.42): C, 56.83; H, 5.30. Found: C, 56.56; H, 5.27.

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Enantiospecific Total Synthesis of the Sesquiterpene Antibiotics (-)-Punctatin A and (+)-Punctatin D

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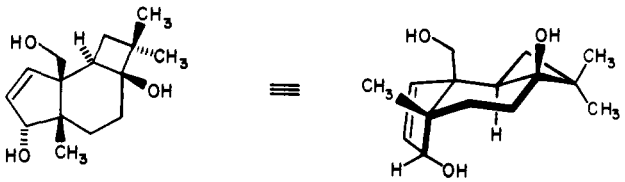
Abstract: Total syntheses of the levorotatory enantiomer of punctatin A (antibiotic M95464) and the dextrorotatory enantiomer of punctatin D (antibiotic M167906) have been achieved. The identities of the synthetic materials with the corresponding natural products, which were confirmed spectroscopically and by $[\alpha]_D$, permitted the assignment of absolute configuration. These structurally novel trans fused tertiary cyclobutyl alcohol antibiotics were constructed in 16-19 steps from optically pure (99.6% ee) dextrorotatory diketone **5**. Central to the synthetic strategy was (i) utilization of the Still rearrangement as a viable means for elaborating an angular hydroxymethylated *cis*-perhydroindan system and (ii) construction of the completely functionalized four-membered ring in proper stereochemical disposition by application of Norrish type II photochemistry. The conformational bias shown by selected intermediates and certain of their stereoisomers is also briefly touched upon.

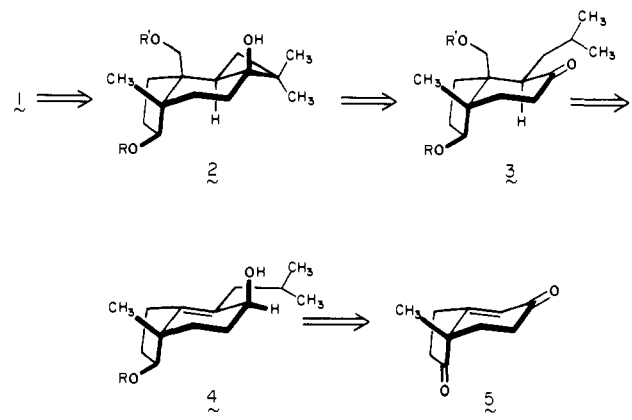
Growing of the dung fungus *Poronia punctata* (Linnaeus *ex* Fries) on malt solution in still culture has recently been shown to provide a rich source of new sesquiterpenes.[1,2] The major C_{15} constituent has been characterized as the trishydroxylated tricyclic substance **1** possessing a previously unknown caryophyllene-related



framework. The structural assignment to **1**, originally known as antibiotic M95464 but now recognized trivially as punctatin A,[3] rests upon chemical transformations and spectra as well as an X-ray crystallographic analysis.[1] A second more polar metabolite (punctatin D, antibiotic M167906) is epimeric with **1** at the allylic hydroxyl group.[2b]

The remarkable biological activity of these colorless, crystalline solids and the presence within their structure of a trans fused tertiary cyclobutyl alcohol hold particular fascination. Our interest in punctatins A and D stemmed also from the realization that their absolute configurations were unknown.

Scheme I



Accordingly, we embarked on stereospecific total syntheses of **1** and **33b** and set as our overall goal the assembling of their five contiguous chiral centers in proper relative configuration starting with a simple enantiomerically pure substrate.[4] From the retrosynthetic perspective, we envisioned introduction of the ring A double bond and setting of the associated allylic alcohol stereochemistry to be capable of implementation in the very late stages of the synthesis (Scheme I). This simplification would permit proper laboratory assessment of the elaboration of **2** from **3** by photochemical means. Thus, the plan was to construct the completely functionalized four-membered ring of punctatin A in its proper stereochemical disposition by utilization of Norrish type II photochemistry.[5] The success of this scenario rested on gaining access to **4** which we hoped to do from **5**, with appropriate at-

(1) Anderson, J. R.; Briant, C. E.; Edwards, R. L.; Mabelis, R. P.; Poyser, J. P.; Spencer, H.; Whalley, A. J. S. *J. Chem. Soc., Chem. Commun.* **1984**, 405.

(2) Five additional metabolites that co-occur with **1** have been assigned the names punctatin B-F and structurally characterized: (a) Anderson, J. R.; Edwards, R. L.; Fraer, A. A.; Mabelix, R. P.; Poyser, J. P.; Spencer, H.; Whalley, A. J. S. *J. Chem. Soc., Chem. Commun.* **1984**, 917. (b) Poyser, J. P.; Edwards, R. L.; Anderson, J. R.; Hursthouse, M. B.; Walker, N. P. C.; Sheldrick, G. M.; Whalley, A. J. S. *J. Antibiot.* **1986**, *39*, 167.

(3) Care should be exercised not to confuse punctatin A with punctatin, a germacranolide obtained from *Liatris punctata* Hook (Herz, W.; Wahlberg, I *Phytochemistry* **1973**, *12*, 1421). This substance was later renamed punctaliatrin (Herz, W.; Wahlberg, I. *Phytochemistry* **1974**, *13*, 315). An even earlier use of the name for a group of homoisoflavones has turned up (Heller, W.; Tamm, C. *Prog. Chem. Org. Nat. Prods.* **1981**, *40*, 105). We have been more recently informed by Dr. Edwards and Dr. Poyser that they are implementing a proposal to alter the names of punctatins A-F to punctaporonins A-F in order to eliminate further overlap of common nomenclature.

(4) Preliminary communication: Paquette, L. A.; Sugimura, T. *J. Am. Chem. Soc.* **1986**, *108*, 3841.

(5) (a) Fleming, I.; Kemp-Jones, A. V.; Long, W. E.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 2* **1976**, 7. (b) Fleming, I.; Long, W. E. *Ibid.* **1976**, 14. (c) Singh, S.; Usha, G.; Tung, C.-H.; Turro, N. J.; Ramamurthy, V. *J. Org. Chem.* **1986**, *51*, 941 and relevant references cited in these papers.

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