ortho-Thioquinones, New Acceptors for the Stereoselective Synthesis of Aryl 2-Deoxy-*O*-Glycosides

Giuseppe Capozzi,* Chiara Falciani, Stefano Menichetti, Cristina Nativi,* and Barbara Raffaelli[a]

Abstract: α-Hydroxynaphthylthiophthalimide (**1**) is a suitable precursor of the reactive *ortho*-thioquinone **2**, which can be generated in situ and trapped by glycals. The reaction is an inverse electron-demand [4+2] cycloaddition that occurs in a totally regioselective and highly stereoselective way. A series of differently substituted glycals (**3**, **5**–**12**, **21**, **22**, **38**) as well as various *ortho*-thioquinones (**25**–**27**) are successfully used as electron-rich dienophiles and electron-poor dienes, respectively, with chloroform, dimethylformamide, and dimethyl sulfoxide as solvents. The stereochemistry of substituents on the dienophile strongly influences the selectivity of the cycloaddition, which becomes totally stereoselective when galactals **8**–**10** or arabinals **21** and **22** are employed as dienophiles. Among the heterodienes tested, the α-naphthol derivative **25** and the tyrosine derivative **26** were successfully used to prepare the naphthyl-α-*O*-rhamnoside **32**$\boldsymbol{\alpha}$ and the tyrosine-α-*O*-glucoside **34**, respectively. Cycloadducts **4**$\boldsymbol{\alpha}$, **17**, **24**, and **33**$\boldsymbol{\alpha}$ were successfully desulfurized, affording the corresponding aryl 2-deoxy-α-*O*-glycosides **39** and **40**–**42**.

Keywords: cycloadditions · desulfurizations · glycosides · *ortho*-thioquinones

Introduction

Aryl *O*-glycoside antibiotics represent an important class of bioactive molecules which are an attractive target for many organic chemists.[1] Several types of α- and β-2-deoxyglycosides frequently appear as glycon moieties in naturally occurring molecules such as the aureolic acid antibiotic family.[2] The activity of these chemotherapeutic agents, resulting from the selective inhibition of the DNA-dependent RNA polymerization,[3] is strongly influenced by their carbohydrate components. For these reasons, the stereoselective formation of aryl–glycoside bonds has been the topic of wide-ranging studies and is still a challenge for the synthetic carbohydrate chemist. However, the efficient and stereocontrolled *O*-glycosidation of 2-deoxy sugars is a difficult problem to solve, because of the lack of anchimeric assistance from the substituent at C-2 and the instability of 2-deoxyglycosyl donors in acidic media.[4]

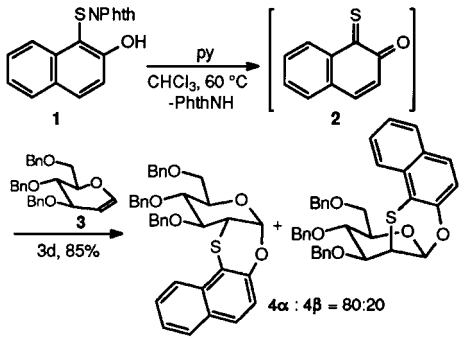
We reported recently an efficient method for the generation of *ortho*-thiobenzoquinones and *ortho*-thionaphthoquinones, a new class of electron-poor heterodienes which can be trapped in situ with suitable electron-rich dienophiles to synthesize various benzo- and naphtho-condensed thio-substituted heterocycles[5] and in particular an isovanillin-containing derivative known to be a powerful nonclassical sweetener.[5] In this paper we report a new protocol for the stereoselective synthesis of differently substituted 2-thio-*O*-benzo- and *O*-naphthoglycosides and their successful transformation into the corresponding aryl 2-deoxyglycosides.

[a] G. Capozzi, C. Nativi, C. Falciani, S. Menichetti, B. Raffaelli
Centro C.N.R. Chimica dei Composti Eterociclici
Università di Firenze
via G. Capponi 9, I-50121 Firenze (Italy)
Fax: (+39) 055-2476964
E-mail: capozzi@chimorg.unifi.it
nativi@chimorg.unifi.it

Results and Discussion

The easily prepared thiophthalimide derivative **1**[5] is the precursor of the *ortho*-thionaphthoquinone **2**, an electron-poor heterodiene which can be trapped by the tri-*O*-benzyl-glucal **3** to give, with high stereoselectivity and complete regioselectivity, the aryl *O*-glucosides **4**$\boldsymbol{\alpha}$ and **4**$\boldsymbol{\beta}$ in an 80:20 ratio and in 85% overall yield[6] (Scheme 1). The [4+2] cycloaddition is performed in chloroform and in the presence of 0.8 equivalents of pyridine[7] at 60 °C for three days. As shown in Scheme 1, the single regioisomer formed affords the oxygen of the *ortho*-thioquinone linked to the anomeric carbon, while the sulfur is linked to the C-2 of the carbohydrate moiety. The analysis of ^{1}H NMR chemical shifts and coupling constants allowed the determination of the regiochemistry and stereochemistry of the major isomer **4**$\boldsymbol{\alpha}$ (δ

0947-6539/99/0506-1748 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 6



Scheme 1. Route from thiophthalimide derivative **1** to aryl *O*-glucosides **4*α*** and **4*β***.

H-1 = 5.82, H-2 = 3.46; $J_{1,2}$ = 3.0 Hz, $J_{2,3}$ = 10.2 Hz) and of the minor isomer **4*β*** (δ H-1 = 5.43, H-2 = 3.75; $J_{1,2}$ = 1.1 Hz, $J_{2,3}$ not detectable) (see Experimental Section). Quantum mechanics calculations indicated that the reaction was controlled by the LUMO of the diene and the HOMO-1 of the dienophile,[6, 8] and the orbital coefficients showed a favored interaction between the sulfur of the *ortho*-thioquinone **2** and the C-2 of the glucal **3**. The stereochemistry of the result obtained (see Scheme 1) clearly demonstrates a preferred attack of the heterodiene from the α site of glucal **3**, as it is known for a glucal with three equatorial substituents.[9, 10]

To evaluate the suitability of this method for the general synthesis of aryl 2-deoxy-2-thio-*O*-glycosides and to understand the factors which could influence the stereoselectivity of the reaction, we prepared a series of unsubstituted and differently substituted glycals[11] to undergo cycloaddition with the electron-poor diene **2**. Moreover, the cycloadditions were performed in chloroform, dimethylformamide, and dimethyl sulfoxide to appraise possible solvent effects. The dienophiles used (**3**, **5**–**12**) and the corresponding cycloadducts (**4**, **13**–**20**), obtained as single regioisomers, are reported in Table 1 and Scheme 2.

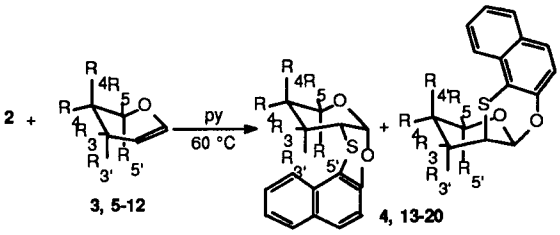
Unlike the regiochemistry, the stereochemical outcome of the cycloadditions cannot be explained by a single variable. In chloroform the all-equatorial glycal series satisfies the general

Abstract in Italian: *L'orto-tiochinone **2**, generato in situ a partire dall' α-idrossinaftiltiottalimmide **1**, può essere intrappolato da glicali attraverso reazioni regiospecifiche e stereoselettive, di cicloaddizione [4+2] a domanda elettronica inversa. Vari glicali diversamente sostituiti (**3**, **5**–**12**, **21**, **22**, **38**) e ortotiochinoni (**25**–**27**) sono stati provati rispettivamente come dienofili elettron-ricchi e dieni elettron-poveri, utilizzando come solventi cloroformio, dimetilformammide e dimetilsolfossido. La stereochimica dei sostituenti presenti sul dienofilo influenza sensibilmente la selettività della cicloaddizione che risulta totale nel caso di dienofili quali i galattali **8**–**10** o gli arabinali **21** e **22**. Tra gli eterodieni studiati il derivato dell' α-naftolo, **25** e il derivato della tirosina **26** sono stati utilizzati per la sintesi del naftil-α-O-ramnoside **32*α*** e del tirosin-α-O-glucoside **34**. La desolforazione dei cicloaddotti **4*α***, **17**, **24** e **33*α*** ha portato alla formazione dei corrispondenti 2-deossi-α-O-glicosidi **39**, **40**–**42**.*

Table 1. Reaction of *ortho*-thioquinone **2** with glycals **3**, **5**–**12**.

Entry	Glycal	Product	Solvent	α/β ratio	Reaction time[a]	Yield [%]
1	**3**	**4**	$CHCl_3$	80/20	3 d	85
2	**3**	**4**	DMF[b]	60/40	4 d	79
3	**3**	**4**	DMSO[b]	55/45	5 d	73
4	**5**	**13**	DMF[b]	43/57	2 d	92
5	**5**	**13**	DMSO[b]	74/26	6 d	39
6	**6**	**14**	$CHCl_3$	95/5	12 d	69
7	**6**	**14**	DMF[b]	52/48	6 d	57
8	**6**	**14**	DMSO[b]	73/27	27 h	56
9	**7**	**15**	$CHCl_3$	90/10	5 d	80
10	**8**	**16**	DMF[b]	α	3 d	51
11	**8**	**16**	DMSO[b]	α	4 h	64
12	**9**	**17**	$CHCl_3$	α	5 d	68
13	**9**	**17**	DMF[b]	α	9 d	49
14	**9**	**17**	DMSO[b]	α	4 d	56
15	**10**	**18**	$CHCl_3$	α	6 d	33
16	**10**	**18**	DMF[b]	α	4 d	41
17	**10**	**18**	DMSO[b]	α	30 min	55
18	**11**	**19**	DMF[b]	32/68	4 d	53
19	**12**	**20**	$CHCl_3$	63/37	12 d	70
20	**12**	**20**	DMF[b]	58/42	9 d	52

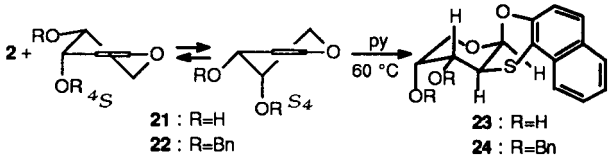
[a] The reaction was monitored by tlc until the glycal was completely consumed. [b] Diene/dienophile ratio = 2/1.



Scheme 2. [4+2] Cycloadditions between the electron-poor diene **2** and electron-rich glycals **3**, **5**–**12**.

	R^3	R^4	R^5	$R^{3'}$	$R^{4'}$	$R^{5'}$
3, 4	OBn	OBn	CH_2OBn	H	H	H
5, 13	OH	OH	CH_2OBn	H	H	H
6, 14	OH	OH	$CH_2OtBDMS$	H	H	H
7, 15	OBn	OBn	$CH_2OtBDMS$	H	H	H
8, 16	OH	OH	CH_2OH	H	H	H
9, 17	OBn	OBn	CH_2OBn	H	H	H
10, 18	OH	OH	$CH_2OtBDMS$	H	H	H
11, 19	H	H	H	OH	OH	H
12, 20	H	H	H	OBn	OBn	Me

rule[10, 11] of a preferred α-site attack; the α-site selectivity becomes strongly favored when a bulky group is present at C-6 (bottom face; Table 1, entry 1 < entries 6 and 9). The presence of an axial substituent determines an anti attack (with respect to the axial group) on glycals, affording completely stereoselective cycloadditions. In the galactal series (axial group at C-4) (entries 10–17), the α-cycloadducts were obtained as single stereoisomers. Moreover, in the arabinal series (S_4, axial group at C-4) the β-cycloadducts were stereospecifically formed (Scheme 3). The assignment of the exact structure of **23** and **24** was accomplished by ^{1}H NMR analysis. Compound **23** showed a diagnostic doublet ($J_{1,2}$ = 2.2 Hz) at δ = 5.8 for H-1 and a doublet of doublets ($J_{2,3}$ = 12.0 Hz) at δ = 4.2 for H-2, while cycloadduct **24** presented a doublet ($J_{1,2}$ = 2.8 Hz) at δ = 5.8 for H-1 and a doublet of



Scheme 3. Stereochemistry of the cycloaddition in the arabinal series.

doublets ($J_{2,3} = 11.0$ Hz) at $\delta = 3.6$ for H-2. The stereochemistry depicted in Scheme 3 for both the cycloadducts is in perfect agreement with the NMR data.

The use of the polar solvents dimethyl sulfoxide and dimethylformamide generally reduces the face selectivity of the cycloaddition. It is interesting that selectivity is still observed in entries 5 and 8 of Table 1, where hydrogen bonding between the solvent and the hydroxyl groups on the dienophiles is possible. However, selectivity is diminished when this H-bonding interaction is not possible (Table 1, entry 3). The effect of solvent on cycloaddition rate is a complex phenomenon since the heterodiene **2** in dimethylformamide or dimethyl sulfoxide undergoes side reactions which effectively reduce the concentration of the diene in the reaction mixture.[12] In fact, when the cycloadditions are performed in the above solvents, an excess of **2** is necessary to complete the reaction. An interesting acceleration of the cycloaddition is evident when glycals **6**, **8**, and **10** are reacted in dimethyl sulfoxide (Table 1, entries 8, 11 and 17). Surprisingly it does not occur with other glycals (entries 3, 5, 14). Although the coordinative character of the solvent plays a role (in dimethyl sulfoxide, cycloadditions take place even in the absence of added pyridine), it does not in itself completely explain the experimental data, which are too limited to suggest any rationalization.

The extension of the cycloaddition to heterodienes **25**–**27**, formed in situ from the parent phthalimidesulfenyl derivatives **28**–**30**, gave the aryl 2-thio-*O*-glycosides **31**–**37** as single regioisomers (see Table 2). The heterodiene **25** came from the phthalimide derivative **28**, a precursor of the aglycon of the antitumor antibiotic BE-12604B[13] (Figure 1), while **26** was obtained from the phthalimide derivative **29**, which in turn was prepared by treatment of the N(Cbz) (phenylmethoxycarbonyl)-protected[14] tyrosine methyl ester with phthalimidesolfenyl chloride[5] (Scheme 4). The cycloaddition results for dienes **25**–**27** are summarized in Table 2.

The general trend highlighted for data reported in Table 1 is reproduced in Table 2. Worthy of mention are the cycloadducts **32**α and **34** (entries 2 and 4) obtained by reaction of glycals **11** and **3** with **25** and **26**, respectively. The α-naphthyl-2,6-dideoxy-2-thio-L-glucoside **32**α, completely separable from **32**β by flash chromatography on silica gel, is a precursor of the 2-thio analogue of the antibiotic BE-12406B[13, 15] (Figure 1), while the α-glycoside **34**, formed in chloroform with complete regio and stereoselectivity, is an example of a glycoamino acid, the synthesis of which demonstrates the potential of this new approach. Cycloadduct **33** was procured by treating, in dimethylformamide, diene **25** with glycal **38**, prepared from commercially available quinovose following a literature procedure[11] (Figure 1).

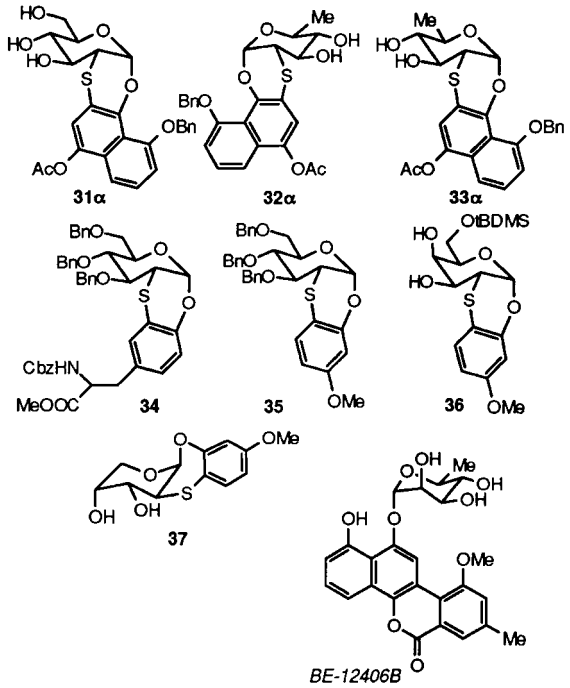
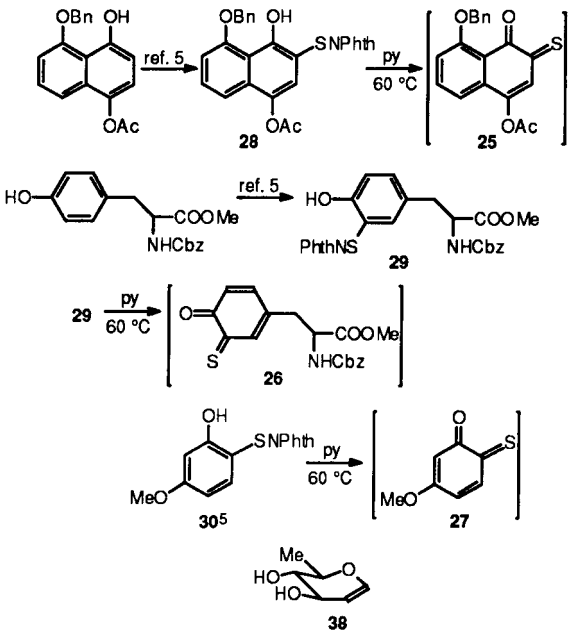


Figure 1. Molecular structure of cycloadducts reported in Table 2.



Scheme 4. Preparation of heterodienes **25**–**27**.

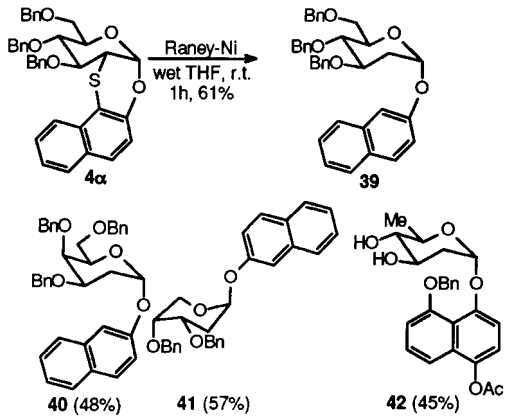
Table 2. Reaction of heterodienes **25**–**27** with glycals **3, 5, 10, 11, 21**, and **38**.

Entry	Diene	Glycal	Product	Solvent	α/β ratio	Reaction time	Yield [%]
1	**25**	**5**	**31**	DMF[a]	4/1[b]	1.5 d[b]	52[b]
2	**25**	**11**	**32**	DMF[a]	2/1	4 d	43
3	**25**	**38**	**33**	DMF[a]	2/1	3 d	58
4	**26**	**3**	**34**	$CHCl_3$	α	9 d	40
5	**27**	**3**	**35**	$CHCl_3$	10/1	8 d	61
6	**27**	**3**	**35**	DMF[a]	3/1	7 d	47
7	**27**	**10**	**36**	$CHCl_3$	α	14 d	18
8	**27**	**21**	**37**	DMSO[a]	β	5 d	13

[a] Diene/dienophile ratio = 2/1. [b] After acetylation of the crude product.

0947-6539/99/0506-1750 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 6

Synthesis of aryl 2-deoxy-*O*-glycosides: The cycloaddition protocol reported above allows the stereoselective formation of an anomeric bond and the introduction of a thio group at C-2 in a single step. The 2-thioglycosides obtained (Tables 1 and 2) were excellent intermediates, after removal of the sulfur atom, for the synthesis of the corresponding aryl 2-deoxy-*O*-glycosides.[16] In fact, treatment of cycloadducts **4α**, **17**, and **24** with Raney nickel[17] in wet THF at room temperature afforded the corresponding 2-deoxy-α- or 2-deoxy-β-*O*-glycosides **39, 40, 41** in good yield and without any undesired rearrangement, which usually occurs when acidic conditions are used[18, 19] (Scheme 5).



Scheme 5. Desulfurization of 2-thioglycoside **4α** with Raney nickel to give **39**, and the structures of 2-deoxy-*O*-glycosides **40**–**42**.

Desulfurization of **33α** with Raney nickel proved unsatisfactory (10% yield) because of its instability in the reaction medium. Better results were obtained by treating the cycloadduct with $NiCl_2$–$NaBH_4$ in a methanol/tetrahydrofuran solvent mixture[20] at −10 °C for 10 min. The 2-deoxy glycoside **42** was prepared in 45% yield under these milder conditions.

Conclusion

We have shown that *ortho*-thioquinones, easily formed in situ from their phthalimido derivatives, represent an interesting class of electron-poor heterodienes. The heterodienes can cycloadd to a variety of glycals, with their hydroxyls blocked or completely unprotected, to form regio- and stereoselectively the corresponding aryl 2-deoxy-2-thio-α- or β-*O*-glycosides. Reductive desulfurization of four different 2-thioglycosides gave the expected 2-deoxy-*O*-glycosides in good yield. Thus, in a few simple steps, aryl 2-deoxyglycosides were prepared without recourse to conventional glycoside chemistry. Further aspects of the reactivity of this 1,4-oxathiin system are currently under investigation in our laboratories.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini in $CDCl_3$ (unless otherwise specified) at 200 and 50 MHz, respectively; residual $CHCl_3$ at $\delta = 7.26$ (for ^{1}H) and a central peak of $CDCl_3$ at $\delta = 77.0$ (for ^{13}C) served as reference lines. Mass spectra and GC-MS analyses were obtained with a Carlo Erba gas chromatograph equipped with an OV 101 30 m capillary column, interfaced on a mass spectrometer. Melting points (uncorrected) were determined on a Büchi 510 apparatus. Rotations are measured on a Jasco DIP-370 polarimeter at 25 °C. IR spectra were recorded on a Perkin–Elmer 881 spectrophotometer. Elemental analyses were carried out with a Perkin–Elmer 245 Elementary Analyser. $CHCl_3$, CH_2Cl_2 and THF were dried following standard procedures, and all commercial reagents were used without further purification as obtained from freshly opened containers. Phthalimidesulfenyl chloride was prepared as reported elsewhere.[21]

3,4-Di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-D-glucal (7): Compound **7** was prepared by the monosilylation[22] and benzylation[23] of glucal **5** (216 mg, 1.5 mmol) following literature procedures, followed by flash column chromatography (dichloromethane); 75% yield; glassy solid; ^{1}H NMR: $\delta = 0.10$ (s, 6H), 0.94 (s, 9H), 3.91–4.04 (m, 4H), 4.22–4.25 (m, 1H), 4.64 (AB system, $J_{AB} = 11.7$ Hz, 2H), 4.75–4.93 (m, 3H), 6.42 (dd, $J = 6.3$, 1.1 Hz, 1H, H-1), 7.31–7.38 (m, 10H); ^{13}C NMR: $\delta = -5.4$, −5.2, 18.3, 25.9, 61.7, 70.6, 73.9, 74.2, 75.8, 78.0; 99.8 (C-2), 127.6, 127.7, 127.8, 127.9, 128.4, 138.4, 144.7 (C-1); elemental analysis: calcd for $C_{26}H_{36}O_4Si$ (440.6): C 70.87, H 8.23; found: C 70.72, H 8.13.

3,4,6-Tri-*O*-benzyl-D-galactal (9):[17, 23] Flash column chromatography (ethyl acetate:petroleum ether = 1:6); 80% yield; oil; ^{1}H NMR: $\delta = 3.66$ (A part of an ABX system, $J_{AB} = 10.1$ Hz, 1H), 3.80 (B part of an ABX system, $J_{AB} = 10.1$ Hz, 1H), 3.94–3.98 (m, 1H), 4.18–4.24 (m, 2H), 4.40–4.71 (m, 5H), 4.82–4.92 (m, 2H), 6.38 (dd, $J = 6.3$ Hz, 1.5 Hz, 1H), 7.29–7.37 (m, 15H); ^{13}C NMR: $\delta = 68.4$, 70.7, 70.8, 71.3, 73.3, 73.4, 75.6, 99.9 (C-2), 127.4, 127.5, 127.6, 127.8, 128.1, 128.3, 128.3, 138.0, 138.3, 138.5, 144.1 (C-1).

6-*O*-*tert*-Butyldimethylsilyl-D-galactal (10):[22] Flash column chromatography (ethyl acetate:petroleum ether = 1:2); 50% yield; oil; ^{1}H NMR: $\delta =$ 0.11 (s, 6H), 0.91 (s, 9H), 2.28 (br s, 2H), 3.88–4.00 (m, 3H), 4.09–4.12 (m, 1H), 4.30–4.33 (m, 1H), 4.72 (dt, $J = 6.2$, 2.0 Hz, 1H), 6.38 (dd, $J = 6.2$, 1.4 Hz, 1H, H-1); ^{13}C NMR: $\delta = 18.2$, 25.7, 62.9, 64.1, 65.6 (C-3, C-4, C-5), 76.0 (C-6), 102.9 (C-2), 144.3 (C-1); elemental analysis: calcd for $C_{12}H_{24}O_4Si$ (260.4): C 55.35, H 9.29; found: C 55.02, H 9.20.

6-Deoxy-L-glucal (11):[11] Flash column chromatography (dichloromethane:methanol = 5:1); 92% yield; oil; ^{1}H NMR ($[D_4]CH_3OH$): $\delta =$ 1.36 (d, $J = 7.0$ Hz, 3H, CH_3), 3.25–3.53 (m, 1H), 3.71–3.85 (m, 1H), 4.09–4.13 (m, 1H), 4.70 (dd, $J = 5.8$, 2.1 Hz, 1H), 4.98 (s, 2H), 6.33 (d, $J = 5.8$ Hz, 1H, H-1); ^{13}C NMR ($[D_4]CH_3OH$): $\delta = 18.1$ (C-6), 71.0 (C-5), 76.4 (C-3), 76.5 (C-4), 105.1 (C-2), 145.5 (C-1); elemental analysis: calcd for $C_6H_{10}O_3$ (130.1): C 55.37, H 7.74; found: C 55.50, H 7.76.

D-arabinal (21):[11] Flash column chromatography (dichloromethane:methanol = 10:1); 98% yield; oil; ^{1}H NMR ($[D_4]CH_3OH$): $\delta =$ 3.88–4.00 (m, 3H, CH_2-5, H-4), 4.18–4.23 (m, 1H, H-3), 4.92–4.99 (m, 3H), 6.52 (dd, $J = 6.0$, 0.8 Hz, 1H); ^{13}C NMR ($[D_4]CH_3OH$): $\delta = 65.7$, 68.4, 70.1 (C-3, C-4, C-5), 104.9 (C-2), 149.6 (C-1); elemental analysis: calcd for $C_5H_8O_3$ (130.1): C 51.72, H 6.94; found: C 51.50, H 6.91.

3,4-Di-*O*-benzyl-D-arabinal (22):[23] Flash column chromatography (ethyl acetate:petroleum ether = 1:5) gave a glassy solid; 73% yield; ^{1}H NMR: $\delta = 3.75$ (dt, $J = 9.8$, 3.8 Hz, 1H), 3.97–4.12 (m, 3H), 4.50–4.72 (m, 4H), 4.87 (t, $J = 5.8$ Hz, 1H), 6.40 (d, $J = 5.8$ Hz, 1H, H-1), 7.28–7.41 (m, 10H). ^{13}C NMR: $\delta = 63.2$ (C-5), 66.7, 73.2 (C-3, C-4), 70.87, 71.0, 98.8 (C-2), 127.5, 127.7, 127.8, 127.8, 128.4, 138.05, 138.8, 146.5 (C-1); elemental analysis: calcd for $C_{19}H_{20}O_3$ (296.4): C 77.00, H 6.80; found: C 76.70, H 6.84.

General procedure for cycloaddition reactions: All the cycloadditions were performed at 60 °C by adding 0.8 equiv of freshly distilled pyridine to a mixture of the sulfenamide and glycal in a 0.8:1 ratio; 0.4 equiv of sulfenamide was subsequently added in two portions (1.2 equiv in four portions for reactions performed in DMF or DMSO). The reactions were monitored by NMR (0.1 mmol scale/$CDCl_3$ or $[D_6]$DMSO) or by TLC (DMF). The crude reaction mixtures were diluted with CH_2Cl_2 (30 mL), washed with saturated NH_4Cl (2 × 15 mL) and water (2 × 20 mL) and dried over anhydrous Na_2SO_4. Flash chromatography on silica gel (ethyl acetate/petroleum ether) was used to purify the crude products (solids were recrystallized when necessary). Physical and spectroscopic data of compounds **4, 13–20, 23, 24, 31–37** obtained by this general procedure are as follows.

3,4,6-Tri-*O*-benzyl-2-deoxy-D-glucopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (4α): A white solid was obtained; m.p. 134–135 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = +4.0$ ($c = 2.4$ in $CHCl_3$); ^{1}H NMR: $\delta = 3.46$ (dd, $J = 3.0$, 10.2 Hz, 1H, H-2), 3.72–3.92 (m, 4H), 4.22 (dt, $J = 9.4$ Hz, 1H), 4.53–4.87 (m, 6H), 5.82 (d, $J = 3.0$ Hz, 1H, H-1), 7.07–7.61 (m, 19H), 7.79 (d, $J = 7.4$ Hz, 1H), 7.95 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR: $\delta = 42.5$ (C-2), 68.2 (C-6), 72.9, 73.6, 75.2, 76.4, 78.4, 78.8 (C-3, C-4, C-5, $3CH_2$), 95.1 (C-1), 107.2, 123.0, 124.4, 126.8, 126.8, 127.9, 128.0, 128.1, 128.4, 128.4, 129.7, 131.2, 137.9, 138.0, 149.7; elemental analysis: calcd for $C_{37}H_{34}O_5S$ (590.7): C 75.23, H 5.80; found: C 75.07, H 5.60.

Compound 4β: A glassy solid was obtained; ^{1}H NMR: $\delta = 3.69–3.78$ (m, 3H), 4.08–4.25 (m, 3H), 4.48 (AB system, J_{AB} 12.1 Hz, 2H), 4.62 (t, J 11.0 Hz, 2H), 4.90 (AB system, J_{AB} 11.1 Hz, 2H), 5.43 (d, $J = 1.1$ Hz, 1H, H-1), 7.12–7.58 (m, 19H), 7.77 (d, J 7.8 Hz, 1H), 8.03 (d, J 7.8 Hz, 1H,); ^{13}C NMR: $\delta = 41.2$ (C-2), 68.6, 71.0, 73.4, 75.3 (C-6, $3CH_2$), 73.7, 77.0, 80.5, (C-3, C-4, C-5), 91.8 (C-1), 110.2, 119.4, 122.5, 124.4, 126.0, 126.4, 127.4, 127.8, 127.8, 128.0, 128.2, 128.3, 128.4, 128.6, 129.7, 130.9, 137.3, 138.1, 138.2, 145.7; MS (70 eV, EI): m/z (%) = 591 (1) [M+1], 91 (100).

2-Deoxy-D-glucopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (13α): Compound **13α** was obtained as a waxy solid after acetylation under standard conditions; $[\alpha]_D^{20} = +104.6$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.98$, 2.05, 2.13 (3s, 9H), 3.54 (dd, $J = 10.6$, 2.8 Hz, 1H, H-2), 4.16–4.48 (m, 3H), 5.17–5.33 (m, $J = 9.8$ Hz, 2H), 5.79 (d, $J = 2.8$ Hz, 1H, H-1), 7.08 (d, $J = 8.8$ Hz, 1H), 7.28–7.94 (m, 5H); ^{13}C NMR: $\delta = 20.5$, 20.7, 20.9 ($3CH_3$), 40.5 (C-2), 60.2 (C-6), 68.8, 69.6, 69.7 (C-3, C-4, C-5), 93.8 (C-1), 106.8; 118.9, 122.8, 124.6, 126.6, 126.9, 128.3, 130.6, 135.3, 148.6; 169.6, 169.6, 170.6 (3CO); elemental analysis: calcd for $C_{22}H_{22}O_8S$ (446.5): C 59.18, H 4.97; found: C 59.29, H 5.03.

Compound 13β: Compound **13β** was obtained as an oil after acetylation under standard conditions; $[\alpha]_D^{20} = -73.8$ ($c = 0.1$ in $CHCl_3$); ^{1}H NMR: $\delta =$ 1.99, 2.08, 2.12 (3s, 9H), 3.83–3.93 (m, $J = 9.4$, 4.0 Hz, 1H), 4.06 (br dd, $J =$ 4.4, 1.6 Hz, 1H, H-2), 4.21 (br d, 2H), 5.41 (dd, $J = 9.2$, 4.4 Hz, 1H), 5.56 (d, $J = 1.6$ Hz, 1H, H-1), 5.63 (br t, $J = 9.4$ Hz, 1H), 7.10 (d, $J = 8.8$ Hz, 1H, 1H), 7.28–7.94 (m, 5H); ^{13}C NMR: $\delta = 20.5$ (3 CH_3), 40.8 (C-2), 62.2 (C-6), 65.2, 71.9, 73.4 (C-3, C-4, C-5), 91.1 (C-1), 108.8, 119.0, 122.1, 124.4, 126.2, 126.4, 128.2, 130.4, 135.2, 145.1, 169.4, 169.7, 170.5 (3CO); MS (70 eV, EI): m/z (%) = 446 (21.0) [$M^{\bullet+}$], 146 (100).

6-*O*-*tert*-Butyldimethylsilyl-2-deoxy-D-glucopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (14α): Compound **14α** was obtained as a white solid; m.p. 134–136 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = -1.3$ ($c = 10.55$ in $CHCl_3$); ^{1}H NMR: $\delta = 0.14$ (s, 6H), 0.93 (s, 9H), 2.87 (br s, 1H), 3.27–3.34 (m, $J = 2.9$ Hz, 2H), 3.76–4.078 (m, 5H), 5.75 (d, $J = 2.9$ Hz, 1H, H-1), 7.07 (d, $J = 8.8$ Hz, 1H), 7.28–7.94 (m, 5H); ^{13}C NMR: $\delta = -5.4$ ($2CH_3$), 18.3, 25.9 ($3CH_3$), 42.8 (C-2), 63.9 (C-6), 70.4, 72.4, 72.9 (C-3, C-4, C-5), 94.4 (C-1), 119.2, 122.9, 123.6, 124.5, 126.8, 126.9, 128.4, 129.6, 134.3, 149.41; elemental analysis: calcd for $C_{22}H_{30}O_5SSi$ (434.6): C 60.80, H 6.96; found: C 60.53, H 6.85.

Compound (14β): Compound **14β** was obtained as a yellowish solid; m.p. 55–60 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = -4.4$ ($c = 6.70$ in $CHCl_3$); ^{1}H NMR: $\delta = -0.01$ (s, 3H), 0.03 (s, 3H), 0.84 (s, 9H), 3.16 (s, 1H), 3.56–3.63 (m, 1H), 3.76–3.85 (m, 2H), 3.97–4.26 (m, 4H), 5.47 (d, $J = 1.6$ Hz, 1H, H-1), 7.09 (d, $J = 8.8$ Hz, 1H), 7.38–7.55 (m, 3H), 7.74 (d, $J = 7.6$ Hz, 1H); 7.99 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR: $\delta = -5.8$, -5.7; 18.0 (C_q); 25.7 ($3CH_3$), 42.6 (C-2), 65.3 (C-6), 71.2, 73.4, 74.8 (C-3, C-4, C-5), 91.7 (C-1), 110.2, 119.2, 122.5, 124.5, 125.9, 126.4, 128.2 129.74, 130.78, 145.35; MS (70 eV, EI): m/z (%) = 434 (6) [$M^{\bullet+}$], 117 (100).

6-*O*-*tert*-Butyldimethylsilyl-3,4-di-*O*-benzyl-2-deoxy-D-glucopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (15α): Compound **15α** was obtained as a pale yellow oil; $[\alpha]_D^{20} = +48.5$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR: $\delta = 0.12$ (s, 3H), 0.13 (s, 3H), 0.94 (s, 9H), 3.40 (dd, $J = 2.8$, 10.2 Hz, 1H, H-2), 3.71–4.08 (m, 5H), 4.57–4.90 (m, 4H), 5.79 (d, $J = 2.6$ Hz, 1H, H-1), 7.09–7.60 (m, 14H), 7.78 (d, $J = 8.4$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR: $\delta = -5.3$, -5.0, 18.3, 25.9, 42.7 (C-2), 61.6 (C-6), 72.1, 75.2, 74.1, 78.2, 78.6 (C-3, C-4, C-5), 95.2 (C-1), 107.3, 119.1, 123.0, 124.4, 126.2, 126.4, 126.7, 127.6, 127.8, 127.9, 128.3, 128.4, 128.5, 128.9, 129.1, 129.7, 131.2, 138.0, 138.2,149.8; elemental analysis: calcd for $C_{37}H_{42}O_5SSi$ (614.9): C 70.32, H 6.88; found: C 70.36, H 6.91.

(1*S*,2*S*)-2-Deoxy-α-D-galactopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (16): Compound **16** was obtained as a white solid after acetylation under standard conditions; m.p. 169–172 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = +8.0$ ($c = 4.5$ in $CHCl_3$); ^{1}H NMR: $\delta = 2.02$, 2.10, 2.20 (3s, 9H), 3.80 (dd, $J = 2.6$, 11.8 Hz, 1H, H-2), 4.21–4.24 (m, 2H), 4.62–4.68 (m, 1H), 5.16 (dd, $J = 11.8$, 3.1 Hz, 1H), 5.47–5.48 (m, 1H), 5.86 (d, $J = 2.6$ Hz, 1H, H-1), 7.10 (d, $J = 8.8$ Hz, 1H), 7.36–7.60 (m, 3H), 7.74–7.83 (m, 2H); ^{13}C NMR: $\delta = 20.5$, 20.6, 20.7 ($3CH_3$), 36.7 (C-2), 61.6 (C-6), 67.3, 67.4, 68.6 (C-3, C-4, C-5), 94.49 (C-1), 106.9, 119.1, 122.8, 124.6, 126.6, 126.8, 128.4, 129.8, 130.6, 148.5, 169.7, 169.9, 170.4; elemental analysis: calcd for $C_{22}H_{22}O_8S$ (446.5): C 59.18, H 4.97; found: C 59.00, H 4.99.

(1*S*,2*S*)-3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-galactopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (17): Compound **17** was obtained as a glassy solid; ^{1}H NMR: $\delta = 3.65–3.71$ (m, 3H), 3.97–4.04 (m, 2H), 4.32 (t, $J = 6.7$ Hz, 1H), 4.45–4.65 (2 AB system and B part of an AB system, 5H), 4.98 (A part of an AB system, $J_{AB} = 11.2$ Hz, 1H), 5.86 (d, $J = 2.8$ Hz, 1H, H-1), 7.02–7.60 (m, 19H), 7.78 (d, $J = 8.2$ Hz, 1H), 7.99 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR: $\delta = 38.8$ (C-2), 68.5 (C-6), 71.7, 73.5, 74.9 (C-3, C-4, C-5), 72.7, 73.6, 74.8, 95.56 (C-1), 107.6, 123.0, 128.3, 136.5, 126.6, 127.6, 127.6, 127.7, 127.8, 127.9, 128.2, 128.2, 128.3, 128.4, 129.6, 131.1, 137.4, 137.7, 138.2, 149.4; elemental analysis: calcd for $C_{37}H_{34}O_5S$ (590.8): C 75.23, H 5.80; found: C 75.34, H 5.87.

(1*S*,2*S*)-6-*O*-*tert*-Butyldimethylsilyl-2-deoxy-α-D-galactopyranose[1,2-*b*]-naphtho[1,2-*e*]-1,4-oxathiin (18): Compound **18** was obtained as a white solid after acetylation under standard conditions; m.p. 62–63 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = +4.1$ ($c = 16.7$ in $CHCl_3$); ^{1}H NMR: $\delta =$ 0.05, 0.07 (2s, 6H), 0.87 (s, 9H), 2.02, 2.18 (2s, 6H), 3.63–3.85 (m, 3H), 4.44–4.52 (m, 1H), 5.18 (dd, $J = 11.5$, 3.1 Hz, 1H), 5.65–5.58 (m, 1H), 5.84 (d, $J = 2.6$ Hz, 1H, H-1), 7.09 (d, $J = 8.8$ Hz, 1H), 7.36–7.83 (m, 5H); ^{13}C NMR: $\delta = -5.7$, 18.2, 20.6, 20.7, 25.7, 37.1 (C-2), 60.6 (C-6), 67.3, 67.8, 71.0 (C-3, C-4, C-5), 94.7 (C-1), 107.0, 119.2, 122.8, 124.5, 126.6, 126.7, 128.4, 129.8, 130.7, 148.69, 169.74; elemental analysis: calcd for $C_{26}H_{34}O_7SSi$ (518.7): C 60.21, H 6.61; found: C 60.20, H 6.64.

2,6-Dideoxy-L-glucopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (19α): Compound **19α** was obtained as a white solid after acetylation under standard conditions; m.p. 148–150 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = -16.7$ ($c = 3.1$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.30$ (d, $J = 6.2$ Hz, 3H), 2.00 (s, 3H), 2.06 (s, 3H), 3.51 (dd, $J = 2.8$, 11.0 Hz, 1H, H-2), 4.26–4.40 (m, 1H), 4.90 (t, $J = 9.7$ Hz, 1H), 5.24 (dd, $J = 9.4$, 10.8 Hz, 1H), 5.74 (d, $J =$ 2.6 Hz, 1H, H-1), 7.09 (d, $J = 8.8$ Hz, 1H), 7.35–7.60 (m, 3H), 7.73–7.80 (m, 2H); ^{13}C NMR: $\delta = 17.4$, 20.6, 41.0 (C-2), 67.7, 69.8, 74.5 (C-3, C-4, C-5), 93.9 (C-1), 107.0, 119.1, 123.0, 124.6, 126.7, 127.0, 128.4, 129.8, 130.8, 149.0, 167.8, 169.8; elemental analysis: calcd for $C_{20}H_{20}O_6S$ (388.4): C 61.84, H 5.19; found: C 61.55, H 5.20.

Compound 19β: Compound **19β** was obtained as a pale yellow solid after acetylation under standard conditions; m.p. 188–190 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = +13.5$ ($c = 2.4$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.29$ (d, $J = 5.8$ Hz, 3H), 2.09 (s, 3H), 2.16 (s, 3H), 3.70–3.84 (m, 1H), 4.11 (dd, $J =$ 1.2, 4.0 Hz, 1H, H-2), 5.32–5.46 (m, 2H), 5.53 (d, $J = 1.2$ Hz, 1H, H-1), 7.12 (d, $J = 8.8$ Hz, 1H), 7.30–7.58 (m, 3H), 7.75 (d, $J = 7.8$ Hz, 1H), 7.96 (d, $J =$ 8.4 Hz, 1H); ^{13}C NMR: $\delta = 17.6$, 20.7, 41.4 (C-2), 70.2, 72.0, 72.3 (C-3, C-4, C-5), 91.2 (C-1), 109.1, 119.2, 122.3, 124.6, 126.3, 126.5, 128.3, 129.8, 130.72, 145.3, 169.7, 170.1.

3,4-Di-*O*-benzyl-2,6-dideoxy-L-glucopyranose[2,1-*b*]naphtho[1,2-*e*]-1,4-oxathiin (20α): Compound **20α** was obtained as a white solid; m.p. 94–97 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = -7.0$ ($c = 3.1$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.41$ (d, $J = 6.4$ Hz, 3H, CH_3), 3.33 (t, $J = 9.1$ Hz, 1H), 3.43 (dd, $J = 3.0$, 10.6 Hz, 1H, H-2), 3.73 (dd, J =8.8, 10.6 Hz, 1H), 4.12–4.27 (m, 1H), 4.58–4.93 (m, 4H), 5.74 (d, $J = 3.0$ Hz, 1H, H-1), 7.12 (d, $J = 8.8$ Hz, 1H), 7.27–7.62 (m, 13H), 7.79 (d, $J = 8.4$ Hz, 1H), 7.96 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR: $\delta = 17.9$ (C-6), 42.9 (C-2), 69.6 (C-5), 75.5, 76.4, 78.6, 84.6 (C-3, C-4), 94.9 (C-1), 107.2, 119.2, 123.0, 124.4, 126.8, 126.9, 127.7, 127.8, 127.9, 128.2, 128.4, 128.5, 129.7, 131.2, 137.9, 138.0, 149.8; elemental analysis: calcd for $C_{30}H_{28}O_4S$ (484.6): C 74.35, H 5.82; found: C 74.15, H 5.90.

Compound 20β: Compound **20β** was obtained as a white solid; m.p. 80–82 °C (ethyl acetate/petroleum ether); ^{1}H NMR: $\delta = 1.38$ (d, $J = 6.2$ Hz, 3H, CH_3), 3.55–3.70 (m, 1H), 3.77–3.88 (m, 1H), 4.03–4.10 (m, 2H), 4.66 (AB system, $J_{AB} = 11.0$ Hz, 2H), 4.94 (AB system, $J_{AB} = 11.3$ Hz, 2H), 5.40 (d, $J = 1.2$ Hz, 1H, H-1), 7.13 (d, $J = 8.8$ Hz, 1H), 7.29–7.58 (m, 13H), 7.76 (d, $J = 7.0$ Hz, 1H), 8.03 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR: 18.0 (C-6), 41.3 (C-2), 70.9, 73.2, 75.6, 79.2, 80.4 (C-3, C-4, C-5), 91.8 (C-1), 109.9, 119.3, 122.5, 124.4, 126.1, 126.4, 127.8, 128.1, 128.3, 128.4, 128.6, 129.7, 131.0, 137.3, 138.2, 145.6.

0947-6539/99/0506-1752 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 6

(1*R*,2*R*)-2-Deoxy-β-D-arabinopyranose[1,2-*b*]naphtho[1,2-*e*]-1,4-oxathiin (23): Compound **23** was obtained as a waxy solid; m.p. 192–195 °C (decomp) (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = -9.0$ ($c = 3.05$ in MeOH); ^{1}H NMR ([D$_4$]CH$_3$OH): $\delta = 3.71$ (A part of an ABX system, $J_{AB} = 10.6$ Hz, 1H), 3.78 (B part of an ABX system, $J_{AB} = 10.6$ Hz, 1H), 3.86–3.95 (m, 2H), 4.22–4.28 (d, $J = 12.0$ Hz, 1H), 5.53 (s, 2H), 5.80 (d, $J = 2.2$ Hz, 1H, H-1), 7.10 (d, $J = 8.8$ Hz, 1H), 7.38–7.65 (m, 3H), 7.81 (d, $J = 8.0$ Hz, 1H), 7.95 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR ([D$_4$]CH$_3$OH): $\delta = 41.2$ (C-2), 66.4, 67.7, 70.2 (C-3, C-4, C-5), 96.8 (C-1), 108.8, 120.11, 124.0, 125.4, 127.5, 129.4, 131.1, 132.5, 135.4, 150.7; elemental analysis: calcd for $C_{15}H_{14}O_4S$ (290.3): C 62.05, H 4.86; found: C 61.87, H 4.81.

(1*R*,2*R*)-3,4-Di-*O*-benzyl-2-deoxy-β-D-arabinopyranose[1,2-*b*]naphtho-[1,2-*e*]-1,4-oxathiin (24): Compound **24** was obtained as a glassy solid; $[\alpha]_D^{20} = -15.0$ ($c = 1.1$ in CHCl$_3$); ^{1}H NMR: $\delta = 3.65$ (dd, $J = 2.8$ Hz, 11.0 Hz, 1H), 3.78–3.80 (m, 1H), 3.99–4.06 (m, 3H), 4.52 (s, 2H), 4.79 (AB system, $J_{AB} = 12.4$ Hz, 2H), 5.87 (d, $J = 2.6$ Hz, 1H, H-1), 7.03–7.58 (m, 14H), 7.78 (d, $J = 8.8$ Hz, 1H), 8.01 (d, $J = 8.6$ Hz, 1H); ^{13}C NMR (75 MHz): $\delta = 38.2$ (C-2), 62.6 (C-5), 71.8, 72.2, 72.5, 73.2 (C-3, C-4), 95.6 (C-1), 107.8, 118.9, 122.8, 123.1, 124.3, 126.4, 126.6, 126.8, 127.5, 127.6, 127.8, 127.9, 128.1, 128.3, 129.6, 131.1, 137.4, 138.0, 149.2; elemental analysis: calcd for $C_{29}H_{26}O_4S$ (470.6): C 74.02, H 5.57; found: C 73.60, H 5.80.

2-Deoxy-D-glucopyranose[1,2-*b*](4-acetoxy-8-benzyloxy)naphtho[2,1-*e*]-1,4-oxathiin (31α): Compound **31α** was obtained as a glassy solid after acetylation under standard conditions; ^{1}H NMR: $\delta = 1.96$, 2.02, 2.05 (3s, 9H), 2.41 (s, 3H), 3.23 (A part of an ABX system, $J_{AB} = 12.8$ Hz, 1H), 3.41 (dd, $J = 10.6$, 2.8 Hz, 1H), 3.94 (B part of an ABX system, $J_{AB} = 12.8$ Hz, 1H), 4.05–4.11 (m, 1H), 5.06–5.36 (m, 4H), 5.86 (d, $J = 2.6$ Hz, 1H, H-1), 6.91 (s, 1H), 7.01 (t, $J = 4.4$ Hz, 1H), 7.36–7.57 (m, 7H); ^{13}C NMR: $\delta = 20.5$, 20.6, 20.9, 41.0 (C-2), 60.9 (C-6), 68.5, 69.5, 69.9 (C-3, C-4, C-5), 71.7, 94.8 (C-1), 107.8, 109.7, 114.1, 119.7, 123.5, 126.6, 127.1, 128.0, 128.1, 128.6, 134.2, 136.6, 140.6, 145.4, 155.4, 169.3, 169.5, 169.8, 170.5; elemental analysis: calcd for $C_{31}H_{30}O_{11}S$ (610.6): C 60.98, H 4.95; found: C 60.65; H 5.00.

2,6-Dideoxy-α-L-glucopyranose[1,2-*b*](4-acetoxy-8-benzyloxy)naphtho-[2,1-*e*]-1,4-oxathiin (32α): Compound **32α** was obtained as a pale yellow solid; m.p. 175–179 °C (ethyl acetate/petroleum ether); $[\alpha]_D^{20} = -326.3$ ($c = 0.1$ in CHCl$_3$); ^{1}H NMR: $\delta = 0.95$ (d, $J = 6.4$ Hz, 3H, CH$_3$-6), 2.41 (s, 3H), 2.49 (brs, 1H), 2.92 (brs, 1H), 3.16 (dd, $J = 2.8$, 10.8 Hz, 1H, H-2), 3.26 (t, $J = 9.4$ Hz, 1H), 3.71 (t, $J = 9.7$ Hz, 1H), 3.86–3.94 (m, 1H), 5.14 (AB system, $J_{AB} = 11.7$ Hz, 2H), 5.74 (d, $J = 2.6$ Hz, 1H, H-1), 6.93–6.70 (m, 2H), 7.32–7.57 (m, 7H); ^{13}C NMR: $\delta = 17.3$ (C-6), 20.9, 43.5 (C-2), 69.8, 70.7, 71.9 (C-3, C-4, C-5), 76.5, 95.3 (C-1), 107.0, 110.1, 114.0, 117.8, 126.7, 127.7, 127.81, 128.5, 136.9, 140.1, 146.4, 155.6, 169.6; elemental analysis: calcd for $C_{25}H_{24}O_7S$ (468.5): C 64.09, H 5.16, found: C 64.20, H 5.35.

Compound 32β: Compound **32β** was obtained as a glassy solid; $[\alpha]_D^{20} = +43.3$ ($c = 0.14$ in CHCl$_3$); ^{1}H NMR: $\delta = 1.33$ (d, $J = 6.2$ Hz, 3H, CH$_3$-6), 2.39 (s, 3H), 3.04 (brs, 1H), 3.38–3.52 (m, 2H), 3.70 (t, $J = 8.2$ Hz, 1H), 3.80–3.85 (m, 2H), 5.14 (AB system, $J_{AB} = 11.9$ Hz, 2H), 5.32 (s, 1H), 6.83–6.97 (m, 2H), 7.23–7.59 (m, 7H); ^{13}C NMR: $\delta = 17.6$ (C-6), 20.9, 43.4 (C-2), 72.4, 73.2, 73.7 (C-3, C-4, C-5), 91.4 (C-1), 107.2, 111.7, 114.6, 118.0, 126.1, 127.2, 128.1, 128.3, 137.6, 140.3, 142.0, 155.1, 169.8.

2,6-Dideoxy-α-L-glucopyranose[1,2-*b*](4-acetoxy-8-benzyloxy)naphtho-[2,1-*e*]-1,4-oxathiin (33α): Compound **33α** was obtained as a waxy solid; ^{1}H NMR: $\delta = 0.95$ (d, $J = 5.8$ Hz, 3H, CH$_3$-6), 2.41 (s, 3H), 2.64 (brs, 1H), 3.10 (brs, 1H), 3.16 (dd, $J = 2.8$, 10.4 Hz, 1H, H-2), 3.27 (brt, $J = 9.2$ Hz, 1H), 3.72 (dd, $J = 8.9$, 10.4 Hz, 1H), 3.86–3.95 (m, 1H), 5.14 (AB system, $J_{AB} = 10.0$ Hz, 2H), 5.74 (d, $J = 2.8$ Hz, 1H, H-1), 6.93 (s, 1H), 6.98 (t, $J = 4.2$ Hz, 1H), 7.33 (m, 4H), 7.56 (m, 2H); ^{13}C NMR: $\delta = 17.4$, 31.0, 43.4 (C-2), 63.51 (C-5), 69.8, 70.6 (C-3, C-4), 71.8, 95.3 (C-1), 107.1, 110.1, 112.3, 114.0, 117.8, 118.7, 126.6, 127.8, 128.4, 128.50, 136.8, 140.7, 146.3, 156.0, 169.6; elemental analysis: calcd for $C_{25}H_{24}O_7S$ (468.5): C 64.09, H 5.16; found: C 63.89, H 5.31.

Compound (33β): Compound **33β** was obtained as a waxy solid; ^{1}H NMR: $\delta = 1.33$ (d, $J = 6.3$ Hz, 3H, CH$_3$-6), 2.39 (s, 3H), 2.81 (brs, 1H), 3.19 (brs, 1H), 3.38–3.52 (m, 1H), 3.66–3.84 (m, 3H), 5.14 (AB system, $J_{AB} = 11.8$ Hz, 2H), 5.31 (d, $J = 1.1$ Hz, 1H, H-1), 6.90 (s, 1H), 6.94–6.98 (m, 1H), 7.28–7.59 (m, 7H).

(1*S*,2*S*)-3,4,6-Tri-*O*-benzyl-2-deoxy-α-D-glucopyranose[1,2-*b*](4-*N*-carbobenzyloxyalaninebenzylester)benzo[2,1]-1,4-oxathiin (34): Compound **34** was obtained as a glassy solid; ^{1}H NMR: $\delta = 3.00–3.02$ (m, 2H), 3.24–3.31 (X part of a AMX system, $J = 3.0$, 10.6 Hz, 1H), 3.67–3.86 (m, 7H), 4.10–4.14 (m, 1H), 4.50–4.86 (m, 7H), 5.10 (s, 2H), 5.23 (br d, 1H), 5.68 (d, $J = 2.6$ Hz, 1H, H-1), 6.76–6.81 (m, 3H), 7.11–7.33 (m, 20H); ^{13}C NMR: $\delta = 37.5$, 43.1, 52.3, 54.7 (C-2), 67.0, 68.1 (C-6), 72.9 (C-4), 73.6 (C-3), 75.2, 78.5, 79.0, 95.2 (C-5), 101.7 (C-1), 118.0, 118.2, 123.6, 127.4, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.5, 128.6, 129.6, 132.6, 137.8, 137.9, 138.0, 151.1, 155.8, 171.8; elemental analysis: calcd for $C_{45}H_{45}O_9NS$ (775.9): C 69.66, H 5.85; found: C 69.50, H 5.91.

3,4,6-Tri-*O*-benzyl-2-deoxy-D-glucopyranose[2,1-*b*](5-methoxy)benzo-[2,1-*e*]-1,4-oxathiin (35α): Compound **35α** was obtained as a white solid; m.p. 85–87 °C (ethyl acetate/petroleum ether); ^{1}H NMR: $\delta = 3.22–3.29$ (dd, $J = 2.8$, 10.2 Hz, 1H, H-2), 3.65–3.86 (m, 7H); 4.09–4.14 (m, 1H); 4.50–4.90 (m, 6H), 4.74, (d, $J = 2.8$ Hz, 1H, H-1), 6.47–6.54 (m, 2H), 6.99 (d, $J = 8.2$ Hz, 1H), 7.14–7.36 (m, 15H); ^{13}C NMR: $\delta = 42.9$ (OCH$_3$), 55.4 (C-2), 68.1 (C-6), 72.8 (C-4), 73.6, 75.2; 76.3 (C-3), 95.6 (C-5), 103.2 (C-1), 104.8, 109.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.6, 129.4, 137.8, 138.0, 153.0, 158.9; MS (70 eV, EI): m/z (%) = 570 (10.7) [$M^{\cdot+}$], 462 (33), 208 (26), 91 (100); elemental analysis: calcd for $C_{34}H_{34}O_6S$ (570.7): C 71.56, H 6.00; found: C 71.38, H 6.25.

Compound 35β: Compound **35β** was obtained as an oil; ^{1}H NMR: $\delta = 3.68–4.11$ (m, 9H), 4.51–4.89 (m, 6H), 5.31 (d, $J = 1.8$ Hz, 1H, H-1), 6.52–6.57 (m, 2H), 6.99 (d, $J = 9.7$ Hz, 1H), 7.18–7.37 (m, 15H); ^{13}C NMR: $\delta = 41.3$ (OCH$_3$), 55.4 (C-2), 68.6 (C-6), 70.8 (C-3), 73.4, 73.5, 75.2 (C-4), 80.4 (C-5), 92.2 (C-1), 103.8, 107.4, 109.6, 127.5, 127.8, 127.9, 128.0, 128.2, 128.4, 128.5, 137.3, 138.1, 158.3.

(1*S*,2*S*)-6-*tert*-Butyldimethylsilyl-2-deoxy-α-D-galactopyranose[1,2-*b*]-(5-methoxy)benzo[2,1-*e*]-1,4-oxathiin (36): Compound **36** was obtained as an oil; ^{1}H NMR: $\delta = 0.01$, 0.12 (2s, 6H), 0.90 (s, 9H), 2.69 (d, 1H); 3.50 (dd, $J = 3.2$, 10.8 Hz, 1H, H-2), 3.65–4.22 (m, 9H), 5.75 (d, $J = 3.0$ Hz, 1H, H-1), 6.40–6.53 (m, 2H), 6.99 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR: $\delta = -5.6$, 18.2, 25.8, 39.9 (C-2), 55.4 (OCH$_3$), 63.7, 67.0, 69.2, 71.1 (C-3, C-4, C-5, C-6), 95.5 (C-1), 107.8, 103.2, 109.3, 123.6, 152.8, 158.9; elemental analysis: calcd for $C_{19}H_{30}O_6SiS$ (414.6): C 55.04, H 7.29; found: C 55.18, H 7.13.

(1*R*,2*R*)-2-Deoxy-β-D-arabinopyranose[1,2-*b*](5-methoxy)benzo[2,1-*e*]-1,4-oxathiin (37): Flash column chromatography (dichloromethane/methanol) gave compound **37** as an oil; ^{1}H NMR ([D$_4$]CH$_3$OH): $\delta = 3.60$ (dd, $J = 2.8$, 10.8 Hz, 1H, H-2), 3.77–4.06 (m, 6H), 4.25–4.32 (m, 1H), 5.05 (brs, 2H), 5.83 (d, $J = 3.0$ Hz, 1H, H-1), 6.61–6.71 (m, 2H), 7.15 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR ([D$_4$]CH$_3$OH): $\delta = 41.3$ (OCH$_3$), 55.8 (C-2), 66.3, 67.3, 70.0 (C-3, C-4, C-5), 97.4 (C-1), 106.3, 104.1, 110.1, 129.0, 154.2, 160.3; elemental analysis: calcd for $C_{12}H_{14}O_5S$ (270.3): C 53.32, H 5.22; found: C 53.12, H 5.23.

***N*-(4-Acetoxy-8-benzyloxy-1-hydroxynaphthyl-2-thio)phthalimide (28)**: 143 mg (0.67 mmol) of phthalimidesulfenyl chloride was added to a solution of 204 mg (0.42 mmol) of 4-acetoxy-8-benzyloxy-1-hydroxynaphthalene[24] in 3 mL dry CHCl$_3$. The reaction mixture was refluxed for 2 h, diluted with CH$_2$Cl$_2$ (40 mL), washed with saturated NH$_4$Cl and water and dried over anhydrous Na$_2$SO$_4$. Flash column chromatography (dichloromethane) gave 169 mg (83% yield) of **28** as a yellow solid; m.p. 98–100 °C (decomp); ^{1}H NMR: $\delta = 2.38$ (s, 3H), 5.27 (s, 2H), 6.93 (dd, $J = 7$, 1.8 Hz, 1H), 7.28–7.46 (m, 8H), 7.45–7.80 (m, 4H), 10.08 (s, 1H); ^{13}C NMR: $\delta = 20.8$, 71.9, 107.0, 113.6, 115.1, 115.2, 122.4, 123.8, 127.8, 127.9, 128.9, 134.4, 138.4, 152.2, 155.5, 167.8, 169.3; elemental analysis: calcd for $C_{27}H_{19}O_6NS$ (485.5): C 66.79, H 3.94; found: C 66.68, H 3.57.

***N*[(*S*)-2-*N*-carbobenzyloxyamino-3-(4-hydroxyphenylthio)methylpropionate]phthalimide (29)**: Compound **29** was obtained as a waxy solid by flash column chromatography (dichloromethane), as for **28**; 55% yield; ^{1}H NMR: $\delta = 3.01–3.08$ (m, 2H), 3.78 (s, 3H), 4.59–4.63 (m, 1H), 5.02 (s, 2H), 5.19 (brs, 1H), 6.92 (d, $J = 8.4$ Hz, 1H), 7.09–7.14 (dd, $J = 8.4$, 2.2 Hz, 1H), 7.33 (m, 5H), 7.60 (d, $J = 2.2$ Hz, 1H), 7.74–7.89 (m, 4H), 8.29 (brs, 1H); ^{13}C NMR: $\delta = 36.8$, 52.5, 54.7, 66.9, 117.1, 118.2, 124.2, 127.9, 128.1, 128.5, 131.8, 134.8, 135.8, 138.8, 155.5, 158.0, 168.3, 171.6; elemental analysis: calcd for $C_{26}H_{22}N_2O_7S$ (506.5): C 61.65, H 4.38; found: C 61.79, H 4.30.

2-*O*-(2-Deoxy-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl)naphthalene (39): To a solution of 23 mg (0.04 mmol) of **4α** in 1.5 mL of THF was added 150 mg Raney nickel, activated according to a literature procedure.[25] The mixture was vigorously stirred for 2 h at room temperature, diluted with 3 mL of THF, and filtered over Celite®. After evaporation of the solvent, the crude product was chromatographed (petroleum ether/ethyl acetate = 2.5–1) to give 14.8 mg of **39** (68% yield) as colorless oil. $[\alpha]_D^{20} = +165.3$ ($c = 0.16$ in

$CHCl_3$); ^{1}H NMR: $\delta = 1.92-2.05$ (A part of an AMPX system, $J = 3.4$, 9.8, 13.2 Hz, 1H, H-2ax), 2.54–2.63 (M part of an AMPX system, $J = 1.0$, 5.2, 13.1 Hz, 1H, H-2eq), 3.58–4.97 (m, 11H), 5.88 (m, 1H), 7.15–7.79 (m, 22H); ^{13}C NMR: $\delta = 35.4$ (C-2), 68.6 (C-6), 71.4, 72.0, 73.3, 75.0, 77.4, 77.9, 95.8 (C-1), 110.4, 118.9, 124.1, 126.3, 127.2, 127.6, 127.7, 127.9, 128.3, 128.4, 129.3, 129.4, 134.4, 138.0, 138.4, 138.6, 154.2; elemental analysis: calcd for $C_{37}H_{36}O_5$ (560.7): C 79.26, H 6.47; found: C 79.41, H 6.52.

2-*O*-(2-Deoxy-3,4,6-tri-*O*-benzyl-*α*-D-galactopyranosyl)naphthalene (40): Flash column chromatography (dichloromethane) gave compound **40** as an oil; 48% yield; ^{1}H NMR: $\delta = 2.24-2.30$ (m, 1H, H-2ax), 2.39–2.53 (m, 1H, H-2eq), 3.54 (A part of an ABX system, $J_{AB} = 9.3$ Hz, 1H), 3.67 (B part of an ABX system, $J_{AB} = 9.3$ Hz, 1H), 4.04–4.23 (m, 3H), 4.36 (AB system, $J_{AB} = 11.6$ Hz, 2H), 4.66 (A part of an AB system, $J_{AB} = 11.6$ Hz, 1H), 4.70 (s, 2H), 4.99 (B part of an AB system, $J_{AB} = 11.6$ Hz, 1H), 5.88 (d, 1H), 7.16–7.47 (m, 19H), 7.67–7.88 (m, 3H); ^{13}C NMR: $\delta = 31.2$ (C-2), 69.2, 70.6, 70.7, 72.9, 73.3, 74.4, 74.5, 96.6 (C-1), 110.8, 124.0, 126.3, 127.2, 127.4, 127.6, 127.6, 127.7, 128.2, 128.3, 128.5, 129.3, 129.5, 134.4, 137.9, 138.5, 138.8, 154.6; elemental analysis: calcd for $C_{37}H_{36}O_5$ (560.7): C 79.26, H 6.47; found: C 79.18, H 6.52.

2-*O*-(2-Deoxy-3,4-di-*O*-benzyl-*β*-D-arabinopyranosyl)naphthalene (41): Flash column chromatography (ethyl acetate:petroleum ether = 1:4) gave compound **41** as a white solid; 57% yield (21% of 3,4-di-*O*-benzyldihydropyran was also obtained); m.p. 58–60 °C; ^{1}H NMR: $\delta = 2.15-2.25$ (m, 1H, H-2ax), 2.42–2.56 (m, 1H, H-2eq), 3.76–4.08 (m, 3H), 4.12–4.20 (m, 1H), 4.65 (s, 2H), 4.79 (s, 2H), 5.86 (t, $J = 2.9$ Hz, 1H), 7.17–7.48 (m, 14H), 7.72–7.80 (m, 3H); ^{13}C NMR: $\delta = 31.9$ (C 2), 61.8, 70.4, 71.6, 72.3, 72.5, 96.6 (C-1), 110.4, 118.8, 124.0, 126.3, 127.1, 127.6, 127.6, 127.8, 128.4, 128.4, 129.3, 129.4, 134.4, 138.5, 138.5, 154.5; elemental analysis: calcd for $C_{29}H_{28}O_4$ (440.5): C 79.07, H 6.41; found: C 79.26, H 6.50.

4-Acetoxy-8-benzyloxy-1-*O*-(2,6-dideoxy-*α*-D-glucopyranosyl)naphthalene (42): 141 mg (0.6 mmol) of $NiCl_2 \cdot 6H_2O$ and 67 mg (1.8 mmol) of $NaBH_4O$ were added to a solution of 40 mg (0.08 mmol) of **33*α*** in 2.4 mL THF/MeOH (3/1) kept at −10 °C. After 30 min at −10 °C, the reaction mixture was diluted with MeOH (10 mL) and filtered over Celite®. Flash chromatography (ethyl acetate:petroleum ether:dichloromethane = 2:1:1) gave 17 mg (45% yield) of **42** as a glassy solid; ^{1}H NMR: $\delta = 1.21$ (d, $J =$ 6.2 Hz, 3H), 1.48–1.62 (m, 1H, H-2ax), 1.85–1.95 (m, 1H, H-2eq), 2.44 (s, 3H), 2.98–3.08 (m, 1H), 3.33–3.40 (m, 1H), 3.65–3.74 (m, 1H), 5.10 (s, 2H), 5.52 (dd, $J = 0.4$, 3.6 Hz, 1H), 6.96–7.20 (m, 1H), 7.13 (s, 2H), 7.41–7.62 (m, 7H); ^{13}C NMR: $\delta = 17.7$, 21.0, 37.8 (C-2), 68.5, 69.1, 71.4, 96.9 (C-1), 107.6, 109.7, 113.8, 118.7, 119.9, 128.1, 128.7, 129.4, 130.0, 137.3, 151.2, 152.0, 154.1, 156.5, 169.7; HRSM calcd for $C_{25}H_{26}O_7$ [$M^{\cdot+}$] 438.1678; found: $m/e =$ 438.1678.

Acknowledgments

This work was funded by MURST Progetto Nazionale Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni and by CNR, Italy.

[1] K. Toshima, K. Tatsuta, *Chem. Rev.* **1993**, *93*, 1503.
[2] a) W. R. Roush, X.-F. Lin, *Tetrahedron Lett.* **1993**, *43*, 6829; b) K. Toshima, Y. Nozaki, S. Mukaiyama, T. Tamai, M. Nakata, K. Tatsuta, M. Kinoshita, *J. Am. Chem. Soc.* **1995**, *117*, 3717; c) D. P. Sebesta, W. R. Roush, *J. Org. Chem.* **1992**, *57*, 4799.
[3] a) W. A. Remers, *The Chemistry of Antitumor Antibiotics*, Wiley-Interscience, New York, **1979**, Ch. 3; b) G. R. Pettit, *Biosynthetic Products for Cancer Chemotherapy*, *Vol. 1*, Plenum, New York, **1977**, p. 143.
[4] For reviews on the synthesis of 2-deoxyglycosides, see a) R. W. Franck, S. M. Weinreb, *Studies in Natural Products Chemistry* (Ed.: Atta-Ur-Rahman), Elsevier, Amsterdam, **1989**, p. 173; b) J. Thiem, W. Klaffke, *Top. Curr. Chem.* **1990**, *154*, 285.
[5] G. Capozzi, C. Falciani, S. Menichetti, C. Nativi, *J. Org. Chem.* **1997**, *62*, 2611.
[6] For preliminary communication, see G. Capozzi, C. Falciani, S. Menichetti, C. Nativi, R. W. Franck, *Tetrahedron Lett.* **1995**, *36*, 6755.
[7] Pyridine and lutidine are suitable bases for generation of the heterodiene. The optimal base/substrate ratio is 0.5–0. 8. The reaction becomes very sluggish when less than 0.5 equiv base is used. No improvement is observed with amounts of base above 0.8 equiv.
[8] AM1 calculations carried out on **2** and **3** were obtained with geometrical optimization implemented by a Spartan program. Calculated energies (eV): **2** HOMO = −8.824, LUMO = −2.046; **3** HOMO − 1 = −9.370, LUMO = 0.327.
[9] Examples of below-plane selectivity in glycal cycloaddition: a) Y. Leblanc, B. J. Fitzsimmons, J. P. Springer, J. Rokach, *J. Am. Chem. Soc.* **1989**, *111*, 2995; b) R. B. Gupta, R. W. Franck, *J. Am. Chem. Soc.* **1989**, *111*, 7668.
[10] R. W. Franck, N. Kaila, M. Blumenstein, R. Geer, X. L. Huang, J. J. Dannenberg, *J. Org. Chem.* **1993**, *58*, 5335.
[11] For the preparation of glycals, see L. Somsak, I. Nemeth, *J. Carbohydr. Chem.* **1993**, *12*, 679.
[12] When glycal **3** was reacted with **2** in MeOH as solvent, 10% of methyl-2-deoxy-2-thio(2-naphthyl)-D-glucopyranoside was also formed.
[13] T. Hosoya, E. Takashiro, T. Matsumoto, K. Suzuki, *Tetrahedron Lett.* **1994**, *35*, 4591.
[14] T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, Wiley, New York, **1991**.
[15] S. Nakajima, K. Kojiri, H. Suda, M. Okanishi, *J. Antibiotics* **1991**, *44*, 1061.
[16] K. Toshima, S. Mukaiyama, T. Ishiyama, K. Tatsuta, *Tetrahedron Lett.* **1990**, *31*, 3339.
[17] G. Capozzi, A. Dios, R. W. Franck, A. Geer, C. Marzabadi, S. Menichetti, C. Nativi, M. Tamarez, *Angew. Chem.* **1996**, *108*, 805; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 777.
[18] We proved that aryl *O*-glycoside **39** undergoes *O*- to *C*-glycoside rearrangement when treated with catalytic amounts of BF_3OEt_2 in CH_2Cl_2 at room temperature; see ref. [19].
[19] a) T. Hosoya, E. Takashiro, T. Matsumoto, K. Suzuki, *J. Am. Chem. Soc.* **1994**, *116*, 1004; b) G. Matsuo, S. Matsumura, K. Toshima, *Chem. Commun.* **1996**, 2173.
[20] T. G. Back, D. L. Baron, K. Yang, *J. Org. Chem.* **1993**, *58*, 2407.
[21] M. U. Bombala, S. V. Ley, *J. Chem. Soc. Perkin Trans. 1* **1979**, 3013.
[22] B. Lou, G. V. Reddy, H. Wang, S. Hanessian, in *Preparative Carbohydrate Chemistry* (Ed.: S. Hanessian), Dekker, New York, **1996**, p. 401.
[23] M. T. Bilodeau, T. K. Park, S. Hu, J. T. Randolph, S. J. Danishefsky, P. O. Livingstone, S. Zhang, *J. Am. Chem. Soc.* **1995**, *117*, 7840.
[24] H. Laatsch, *Liebigs Ann. Chem.* **1985**, 1847.
[25] A. I. Vogel, in *Practical Organic Synthesis*, Longman, Birmingham, AL, **1962**, p. 870.

Received: May 25, 1998 [F1170]

  0947-6539/99/0506-1754 $ 17.50+.50/0