trations of both 2 and 3 decreased such that the rate dropped slowly. In support of this rationale, the steady second-stage rate was observed from the start in a 1-g hydrolysis of 2 with the solution phase saturated with 3 initially.

Experimental Section

Materials. Acetonitrile (Fisher HPLC-grade) and trifluoroacetic acid (Fisher certified) were used to prepare the HPLC mobile phase. Triton X-100 (Roehm and Haas), lipase (Amano LPL-80 with activity of 889 000 u/g), and aqueous phosphate buffer, prepared from potassium phosphate dibasic (Fisher certified ACS) and concentrated HCl (Mallinckrodt Analytical Reagent), were used for hydrolysis reaction mixtures. Compounds 2, 3, the corresponding racemic ester–acid and diacid, and 4, all described previously,[1,2] were available in these laboratories.

Kinetics Runs. In heterogeneous enzymatic hydrolyses, solid diester 2 (1.00, 0.50, or 0.25 g) was added to 0.1 M pH 7.5 phosphate buffer (30 mL) containing Triton X-100 (0.5 mL). The slurries were stirred mechanically and thermostated in a water bath at 40 °C or were agitated using an ultrasonic probe (Heat Systems-Ultrasonics, Inc., Model W-370). The probe was used in a reaction vessel equipped with a circulating water jacket kept at 36 °C to compensate for heat generated by the probe, and the reaction temperature of about 40 °C was monitored using a thermocouple. The hydrolysis was found to proceed the same with mechanical stirring or ultrasonic agitation; mechanical stirring was preferred for better control of the reaction temperature.

In preliminary runs, assays of stirred mixtures of the buffer, Triton X-100, and 2 or 3, without enzyme, showed initial supersaturation followed by equilibration within a half hour to filtrate concentrations (solubilities) of 0.8 mg/mL of 2 or 6 mg/mL of 3. In hydrolysis kinetic runs the lipase (40 mg) was added last to initiate hydrolysis after stirring for a half hour. Aliquots of the slurry, taken periodically while stirring, were analyzed for the diester, ester–acid, and diacid using HPLC; see below. Aliquots of the solution phase, obtained by filtration through an immersed fine-porosity glass frit, were analyzed similarly.

In homogeneous enzymatic hydrolyses, solutions of Triton X-100 (0.5 mL) and diester 2 (15 mg) in the pH 7.5 buffer (30 mL) were thermostated in the water bath at 40 °C, and again the lipase (20 or 40 mg) was added last to initiate hydrolysis. Some hydrolyses of 2 were performed with 3, the racemic ester–acid, the diacid, or 4 present initially.

High-Performance Liquid Chromatography. A 250- × 4.6-mm Partisil 10 ODS column (Whatman) was used for liquid chromatography with an isocratic mobile phase of acetonitrile/0.2 wt % aqueous trifluoroacetic acid 44:56 v/v, delivered at a rate of 2 mL/min with the column at ambient temperature (23 °C). Compounds 2, 3 (or the racemate), the diacid, and 4 eluted at retention times of 9, 5, 3, and 4 min, respectively, and all exhibited the same UV spectrum. Chromatograms were monitored at 292 nm, chosen as a peak wavelength at which Triton X-100 and the lipase did not absorb.

Appendix

The reversible inhibition of enzyme E by (*S*)-ester–acid product P was modeled assuming rapid equilibria involving unreactive complexes EP_1 and EP_2 in solution.

$$E + P \rightleftharpoons EP_1 \qquad K_1 = [EP_1]/[E][P] \qquad (1)$$

$$EP_1 + P \rightleftharpoons EP_2 \qquad K_2 = [EP_2]/[EP_1][P] \qquad (2)$$

Hydrolysis of diester substrate S was assumed to occur via complex ES, in rapid equilibrium also.

$$E + S \rightleftharpoons ES \qquad K_S = [ES]/[E][S] \qquad (3)$$

The apparent diester reactivity relative to that in the absence of P (the ordinate function in Figure 3) was calculated as $[E]/[E_{total}]$. Assuming [ES] low for the sake of simplicity, EP_1 and EP_2 were eliminated by substitution from eqs 1 and 2 and the enzyme material balance, eq 4, to obtain eq 5.

$$[E_{total}] = [E] + [EP_1] + [EP_2] \qquad (4)$$

$$[E]/[E_{total}] = 1/[1 + K_1[P]^1 + K_1K_2[P]^2] \qquad (5)$$

This function of [P], evaluated for various values of the *K*'s, was compared to the relative reactivity data curve, Figure 3. No good fit was obtained assuming a single equilibrium , eq 1, but calculated curves fitting the data curve were obtained using two equilibria, eqs 1 and 2. For example, the curve for $K_1 = K_2 = 0.5$ (mg/mL)$^{-1}$ fit, but considerable variation was found tolerable. The agreement was just as good with K_1 two or three times larger and K_2 moderately smaller, or with K_1 two or three times smaller and K_2 larger. Since [P] exceeded the solubility value of 6 mg/mL during most of the heterogeneous hydrolysis, *K* values of 0.5 connote $[EP_1]/[E]$ and $[EP_2]/[EP_1]$ ratios greater than 3, eqs 1 and 2.

Acknowledgment. The authors thank Dr. D. L. Hughes for helpful discussions and Mrs. H. R. Graham for typing the manuscript.

Cross Coupling Reactions of 2-(Allyloxy(thio))benzothiazoles with Organocopper Reagents in Dihydropyranoid Systems. Mechanistic Implications of the Substrate and the Reagent: Regio- and Stereocontrolled Access to Branched-Chain Sugars

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Received March 2, 1992

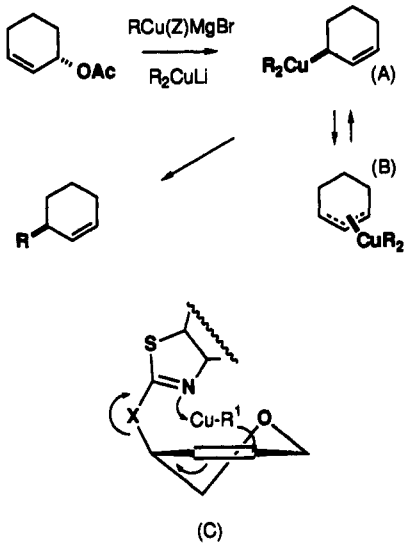
Allylic derivatives are very useful compounds from a synthetic, mechanistic and biochemical point of view.[1] One of the chemical aspects which has attracted more attention is the regio- and stereochemistry of nucleophilic displacement reactions, and in particular those related to the applications of organometallic reagents in the selective formation of C,C bonds. In general, little regioselectivity has been achieved when working under stoichiometric conditions, and the regioselectivity of the reaction has been shown to depend on such factors as solvent, substrate, reagents, etc. Goering et al.[2a-d] have achieved a high degree of regiocontrol by using allylic carboxylates in the presence of Grignard reagents and catalytic amounts of cuprous cyanide. The stereochemistry of this reaction with regard to the relative disposition of the metal and the leaving groups is predominantly anti, as in most reactions of allylic electrophiles with electron-rich complexes.[2e] For these particular substrates these authors have postulated the formation of a σ-copper(III) complex (A) which can either undergo stereospecific reductive elimination to give anti-γ alkylation or isomerize to the π-allyl complex (B) (Scheme I). The active species are considered to be RCu(Z)MgBr

(1) (a) Magid, R. D. *Tetrahedron* **1980**, *36*, 1901. (b) Erdik, E. *Tetrahedron* **1984**, *40*, 641.

(2) (a) Underiner, T. L.; Goering, H. L. *J. Org. Chem.* **1991**, *56*, 2563. (b) Underiner, T. L.; Paisley, S. D.; Schmitter, J.; Lesheski, L.; Goering, H. L. *J. Org. Chem.* **1989**, *54*, 2369. (c) Underiner, T. L.; Goering, H. L. *J. Org. Chem.* **1989**, *54*, 3239. (d) Underiner, T. L.; Goering, H. L. *J. Org. Chem.* **1988**, *53*, 1140. (e) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 19.

0022-3263/92/1957-4546$03.00/0

Scheme I



R^1 = alkyl or phenyl

and is postulated that when Z = CN the γ-cross-coupling prevails, but when Z = R, the allylic rearrangement (σ–π rearrangement mechanism) is observed. Mitsunobu et al.[3] have also studied the reaction of allylic mesyl derivatives with methyl cuprates, obtaining the methyl derivative corresponding to an α-anti substitution. Though they explain this result as invoking the principle of hard and soft acids and bases (position C-3 is considered softer than position C-1) it is obvious that it could be also explained through Goering's mechanism as well.

There are not many examples of the use of allyl ethers in cross-coupling reactions with organocopper reagents. Using an extensive variety of allylic ethers, Normant et al.[4] found that the α–γ ratio was very much dependent on steric effects regardless of the particular CuX used. In this context, the behavior of a particular type of allylic ethers (2-thio- or 2-oxybenzothiazoles) attracted our attention.[5] Its use with acyclic substrates has permitted workers to secure a certain regiocontrol of the reaction by the choice of appropriate solvents and modification of the addition order of the reagents.

We recently showed how this methodology could be adapted to the preparation of pyranoses bearing a methyl branch at C-2 and C-4 with excellent control of regio and stereochemistry.[6]

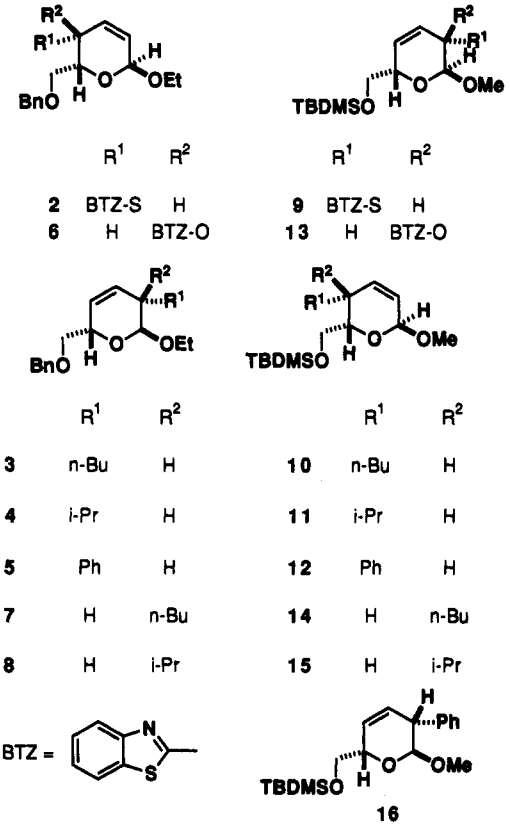
In this context we wondered whether the same methodology could be utilized for introduction of other alkyl groups and for alkyl branching at other sites of the pyranoses. In this report we describe some recent studies in our laboratory dealing with the scope of this protocol.

Results and Discussion

Substrate **2** reacted in the expected manner to afford the *n*-butyl, isopropyl, and phenyl derivatives corresponding to a γ-substitution with syn stereochemistry (**3**, **4**, and **5** respectively) (see Table I). On the other hand, when the cross-coupling reaction was carried out using compound **6**, the *n*-butyl and isopropyl derivatives still reacted in the predicted manner to afford compounds **7** and **8**, respectively. However, the organocopper reagent derived from phenyl bromide yielded selectively compound **5** (entry vi). This product still corresponds to a γ-substitution, but the stereochemistry, though selective, indicates an antistereofacial approach of the incoming group.

Table I. Products and Yields Obtained during the Cross-Coupling Reactions of Substrates 2, 6, 9, and 13

entry	substrate	product	yield (%)
i	2	3	80
ii	2	4	78
iii	2	5	64
iv	6	7	74
v	6	8	50
vi	6	5	52
vii	9	10	60
viii	9	11	60
ix	9	12	88
x	13	14	80
xi	13	15	76
xii	13	16	36



Alkylation of the thiobenzothiazole **9** and oxybenzothiazole **13** took place yielding the respective *n*-butyl and isopropyl derivatives, according to the expected regio- and stereochemistry (**10**, **11**, **14**, **15**). When phenylmagnesium bromide in presence of copper iodide was used in the cross-coupling reaction of **9**, compound **12** was exclusively produced in 88% yield, showing that the reaction follows the same pattern as the alkylation process. However, when the oxybenzothiazole derivative **13** was allowed to react under similar conditions compound **16** was obtained in 36% yield (entry xii). Arylation has thus occurred with stereo- and regicontrol, but no allylic transposition was observed. As an additional example of this cross-coupling reaction, compound **23** was next investigated. Treatment of **23** (Scheme II) with methyl cuprate or phenyl cuprate afforded the expected products **24** and **25**, respectively.

(3) Mitsunobu, O.; Yoshida, M.; Takiya, M.; Kubo, K.; Maruyama, S.; Satoh, I.; Iwami, H. *Chem. Lett.* **1989**, 809.
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Table II. ^{1}H NMR Significant Spectral Parameters for Compounds 2–5, 7, 8, 10–12, 14–16, and 23–25

	2	3	4[a]	5	7[a]	8	10	11	12[a]	14	15	16	23[a]	24[a]	25[a]
H-1	5.123	4.749	4.810	4.861	4.850	4.987	4.825	4.814	4.848	4.847	4.757	4.613	6.449	6.132	6.088
H-2	5.897	2.024	1.995	3.343	2.334	2.059	5.718	5.866	5.784	5.732	5.719	3.219	5.236	4.510	4.304
H-3	6.229	5.810	5.630	5.864	5.571	5.818	6.131	6.039	5.854	5.920	5.818	5.725	5.553	2.219	3.175
H-4	5.909	5.675	5.828	5.920	5.738	5.699	2.020	2.010	3.162	2.180	2.096	5.842	3.851	3.909	3.791
H-5	4.227	4.358	4.478	4.450	4.485	ca. 4.33	4.036	4.059	4.610	3.602	ca. 3.62	4.467	3.692	3.741	3.520
H-6	3.717	3.513	3.444	3.679	3.500	ca. 3.53	3.646	3.717	3.551	3.743	nd[b]	3.671	3.345	3.676	3.378
H-6′	3.732	3.566	3.582	3.716	3.622	ca. 3.56	3.726	3.781	3.639	3.813	nd[b]	3.744	3.520	3.940	3.585
J_{12}	2.8	0.9	0.9	1.1	4.4	4.1	2.7	2.9	2.9	3.0	3.0	1.2	2.7	5.9	6.0
J_{13}	−1.5	−1.2	−1.2	−1.2	−1.1	−1.3	−1.1	−1.1	−1.0	−1.4	−1.3	−1.2	−2.0	−1.6	−1.3
J_{14}	1.6	−0.3	−0.3	−0.3	−0.3	ca. 0	0.3	ca. 0	ca. 0	1.5	1.6	ca. 0	2.5	ca. 0	ca. 0
J_{15}	−0.7	−0.5	−0.5	−0.4	−0.7	ca. 0	−0.6	−0.9	−0.6	−0.3	ca. 0	−0.4	−0.5	ca. 0	ca. 0
J_{23}	10.3	5.0	4.8	4.9	2.2	1.8	10.1	10.2	9.9	10.1	10.2	4.8	10.1	5.8	5.9
J_{24}	−1.8	−1.6	−1.8	−1.9	2.4	−2.7	−1.2	−1.3	−1.4	−2.8	−3.0	−1.7	−2.6	ca. 0	ca. 0
J_{25}	ca. 0	2.7	3.6	3.1	3.9	4.3	ca. 0	ca. 0	ca. 0	ca. 0	ca. 0	3.1	ca. 0	ca. 0	ca. 0
J_{34}	1.8	10.4	10.6	10.4	10.3	10.5	5.9	5.5	5.7	1.9	2.0	10.4	1.7	6.4	6.1
J_{35}	ca. 0	−2.3	−2.3	−2.3	−2.2	−2.1	ca. 0	−0.2	ca. 0	ca. 0	ca. 0	−2.3	−0.3	ca. 0	ca. 0
J_{45}	9.5	1.6	1.8	1.8	2.1	2.0	3.1	3.9	3.6	10.0	10.0	1.7	9.0	9.9	9.7
J_{56}	4.2	4.6	5.7	4.3	5.5	nd[b]	6.5	6.2	6.7	5.7	nd[b]	5.5	10.6	10.3	10.2
$J_{56'}$	2.5	6.6	6.1	5.8	6.0	nd[b]	7.0	7.4	6.5	2.5	nd[b]	5.3	5.0	5.4	5.3
$J_{66'}$	−11.1	−10.0	−9.6	−9.9	−9.7	nd[b]	−10.3	−10.4	−10.3	−11.3	nd[b]	−10.4	−10.5	−10.7	−10.6

[a] Solvent: C_6D_6. [b] nd = not determined.

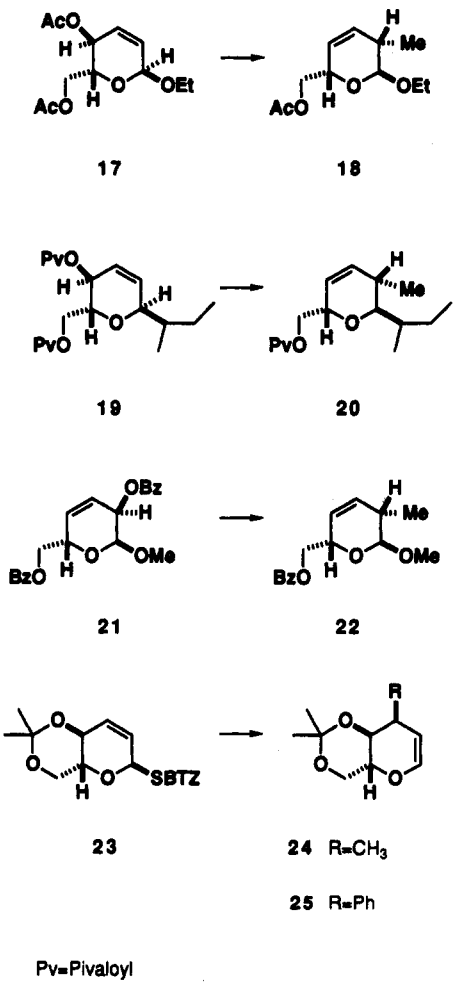
Clearly alkylation always followed the same pattern, regardless of the substrate, affording the alkyl derivatives that correspond to a γ-syn substitution. In all these cases alkylation could take place through the mechanism depicted in C (Scheme I).

On the contrary, arylation has followed different patterns for substrates **2**, **9**, and **23** (on one hand) and **6** and **13** (on the other). In the first case, when the benzothiazole group is on the β-face (e.g., opposite to the substituent at the anomeric center) the reaction proceeds in a γ-syn manner, affording compounds **5** and **12** (entries iii and ix) as in the case of alkylation. However, substrates **6** and **13** with the benzothiazole group at the α-face afforded compounds **5** and **16**, respectively (entries vi and xii), which correspond to anti substitutions.

In order to explain the specific formation of α- or γ-anti products we postulate that in the last two cases the reaction proceeds through the formation of a π-allyl complex B as reaction intermediate, following the suggestion of Goering et al.[2a-d]

To support this interpretation we carried out the reaction of **21** with methylmagnesium iodide and CuI (Scheme II). As previously reported in the literature,[7] for methylations of unsaturated dihydropyrans (compounds **18** and **20**) and according to the mechanism previously proposed[2c] for cross-coupling allylic carboxylates with alkyl(sp^3)copper reagents, this reaction should take place through complex A affording the methyl derivative corresponding to a γ-anti substitution. In fact, compound **21** afforded **22**. To explain this result, in terms of the mechanism proposed by Goering et al.,[2a-d] it is necessary that the σ-allyl–copper(III) complex A isomerizes to the π-allyl complex B prior to methylation. Since the only isolated product corresponds to an α-anti substitution, the dihydropyran substrate must be strongly biased in favor of substitution taking place at C-2 (pyranose numbering). An analogous explanation would be valid for the reaction of phenyl(sp^2)copper reagents with substrates **6** and **13** which also led to C-2 anti-substituted products, independently of whether the starting material was a 2,3 or a 3,4-unsaturated pyranose. Finally, in the case of **23**, where the benzothiazole group is in the anomeric position, a γ-syn substitution was observed both for the alkylation and arylation reactions.

Scheme II



Possibly, in the case of the phenyl(sp^2)copper reagents, the formation of complex C has such electronic or steric requirements that cannot be provided by substrates **6** and **13** (due to the proximity of the substituent at the anomeric center). Consequently, the reaction occurs through the alternative pathway represented by complex B. Compound **23** where no interference from the anomeric substituent was possible reacted with phenylcopper reagents yielding the γ-syn product. None of the substrates men-

(7) (a) Danishefsky, S. J.; Armistead, S. M.; Wincott, F. E.; Selnick, H. G.; Hungate, R. *J. Am. Chem. Soc.* **1989**, *111*, 2967. (b) Chapleur, Y.; Grapsas, Y. *Carbohydr. Res.* **1985**, *141*, 153. (c) Boquel, P.; Chapleur, Y. *Tetrahedron Lett.* **1990**, *31*, 1869.

tioned above (2, 6, 9, 13, and 23) afforded alkyl derivatives when the cross-coupling reaction was attempted using *tert*-butylmagnesium bromide.

Structural Features. The structures of all the compounds obtained were assigned through the analyses of their ^{1}H NMR data (see Table II). The 300-MHz ^{1}H NMR spectra of all derivatives were analyzed iteratively, and the best computed data of chemical shifts and coupling constants are given in Table II. The sign of the coupling constants were assessed from the literature[8] or obtained from the calculations.

The value of $J_{1,2}$ (ca. 4 Hz in compounds 7 and 8 and ca. 1 Hz in derivatives 3, 4, 5, and 16) indicates equatorial–quasi-axial and equatorial–quasi-equatorial geometries for H-1 and H-2, respectively. On the other hand, the magnitude of the coupling constants $J_{4,5}$ (3–4 Hz in compounds 10–12 and ca. 10 Hz in derivatives 14 and 15) suggest quasi-equatorial–axial and quasi-axial–axial arrangements of H-4 and H-5, respectively, and are in accordance with the values calculated from Altona's equation.[9] The negligible values of homoallylic couplings ($J_{1,4}$) and those of $J_{3,4}$ (ca. 5.5) are in support of H-4 being quasi-equatorial in compounds 10–12, while the magnitudes of $J_{3,4}$ (ca. 2 Hz) and $J_{1,4}$ (ca. 1.5 Hz) suggest a quasi-axial geometry for H-4 in compounds 14 and 15.

Concerning the stereochemistry of the bicyclic derivatives 24 and 25, the values of $J_{3,4}$ (6.1–6.4 Hz) are in agreement with those calculated according to Altona's equation for angles in the neighborhood of 40°, which indicates quasi-axial arrangements of the substituents at C-3.

NOE experiments were also performed on selected compounds, leading to unambiguous location of the double bond and providing additional support to the structures deduced from coupling constants. Thus, irradiation of H-5 produced around a 6% increase in the intensity of H-4 in 10 and 11, and no noticeable variation in analogous proton of 14, while irradiation of H-2 led to increments of 4% in the intensity of H-1 in compounds 5 and 16 and 6% in that of 7. Finally, irradiation of H-3 in compound 25 induced a 5% increase in the intensity of H-4.

As expected, all the data are in accordance with predominant $^0H_5$ conformations for compounds 2 and 10–15 and $^0H_1$ conformations for 3–8 and 16.

From the results obtained it could be concluded that a complete control of the regio- and stereoselectivity can be achieved in the formation of C–C bonds in dihydropyrans by the use of the oxy(thio)benzothiazolyl group. *C*-Alkyl or *C*-aryl derivatives of predefined stereochemistry can be obtained at positions C-2, C-3, and C-4 of the pyranosidic ring. In the alkylation process the regio- and stereochemical outcome is dictated by coordination effects, in such a manner that a complex is formed between the copper species and the substrate. However, in the arylation reaction the substrate has a decisive role on the control of the process.

Experimental Section

For general experimental details see ref 6.

Starting Materials. The known diols, ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (1a) and methyl 3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (1b) were prepared from D-glucose, as previously described.[6] 4,6-*O*-Isopropylidene-D-glucal was prepared from commercial glucal.[10] Ethyl 2,3-dideoxy-6-*O*-benzyl-α-D-*erythro*-hex-2-enopyranoside (1c),[11] methyl 3,4-dideoxy-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hex-3-enopyranoside (1d),[6] and substrates 2,[12] 9,[6] and 13[6] were identified either by identity with authentic samples or comparison with previously published spectroscopic information. All known compounds gave satisfactory physical and spectral data consistent with their structures.

Product 3[12] was also identified through its spectroscopic data.

General Procedure for the Synthesis of (Allylthio)benzothiazoles 2, 9, and 23. The allylic alcohol (5 mmol) was dissolved in toluene (20 mL) together with PPh_3 (6 mmol) and 2-mercaptobenzothiazol (5.5 mmol). While the temperature was maintained below 5 °C, diethyl azodicarboxylate (5.5 mmol) dissolved in toluene was added dropwise and with stirring. Once the allylic alcohol was consumed the suspension was filtered and washed with toluene, and the solution was concentrated in vacuo. The residue was then directly applied on a silica gel column.

General Procedure for the Synthesis of the (Allyloxy)benzothiazoles 6 and 13. To the allylic alcohol (7 mmol) dissolved in dry ether (50 mL) was added metallic potassium (10.5 mmol) in small pieces at 0 °C and with stirring. Once the reaction was complete, 2-chlorobenzothiazole (10.5 mmol) dissolved in ether (5 mL) was added, and the reaction mixture was left at room temperature for 24 h. Methanol was then added until complete disappearance of excess metal. The reaction mixture was washed with water, dried, and evaporated. The oily residue was chromatographed (hexane–ethyl acetate (8:2)) to give the product.

Ethyl 2,3-Dideoxy-6-*O*-benzyl-4-*O*-(2-benzothiazolyl)-α-D-*erythro*-hex-2-enopyranoside (6). This compound, a thick oil, was synthesized from 1c (70%): $[\alpha]_D$ 115.0° (*c* 0.71, $CHCl_3$); ^{1}H NMR (300 MHz) δ 1.26 (3 H, t, J = 6.3 Hz, OCH_2CH_3), 3.60 and 3.90 (2 H, 2 dq, J_{gem} = 9.8 Hz, OCH_2CH_3), 3.72 (2 H, q, $J_{6,6'}$ = 12.0 Hz, H-6, H-6'), 4.15 (1 H, m, H-5), 4.56 (2 H, q, J_{gem} = 12.0 Hz, OCH_2Ph), 5.12 (1 H, d, $J_{1,2}$ = 2.6 Hz, H-1), 5.91 (1 H, dd, $J_{2,1}$ = 2.6 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.90 (1 H, m (overlapping with H-2), H-4), 6.22 (1 H, d, $J_{3,2}$ = 10.0 Hz, H-3), plus signals due to the benzothiazolyl group and aromatic benzyl group. Anal. Calcd for $C_{22}H_{23}NO_4S$: C, 66.48; H, 5.83; N, 3.52; S, 8.0. Found: C, 66.75; H, 5.75; N, 3.70; S, 8.30.

General Procedure for the Reaction of (Allyloxy(thio))benzothiazole Derivatives with Organocopper Reagents. The Grignard reagent was prepared in anhydrous ether (10 mL) from Mg (4.0 mmol) and RBr (R = *n*-Bu, *i*-Pr, *t*-Bu, Ph) (4.0 mmol). This solution was cooled to −30 °C and CuI (1.5 mmol) was added in one portion under argon. Stirring was continued during 30 min at −30 °C, and then a solution (15 mL) of the substrate (1.0 mmol) in ether was added. In order to obtain acceptable yields and to ensure high regio- and stereoselectivity, a good stirring of the reaction mixture was critical. The mixture was allowed to warm slowly to room temperature and stirred for 6 h. The reaction was diluted with ether and treated with concentrated aquous NH_4Cl and a few drops of NH_4OH, while vigorously stirring. The ethereal phase was separated and dried over anhydrous sodium sulfate and concentrated in vacuo. Flash chromatography of the crude residue (hexane–ethyl acetate (9:1)) yielded the product.

Ethyl 2,3,4-Trideoxy-2-*C*-isopropyl-6-*O*-benzyl-α-D-*threo*-hex-3-enopyranoside (4). This compound was prepared from 2 and isopropylmagnesium bromide as a syrup (78%): $[\alpha]_D$ 50.9° (*c* 0.21, $CHCl_3$). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.40; H, 9.05.

Ethyl 2,3,4-Trideoxy-2-*C*-phenyl-6-*O*-benzyl-α-D-*threo*-hex-3-enopyranoside (5). Prepared from 2 or 6 and phenylmagnesium bromide as a syrup (64% and 52%, respectively): $[\alpha]_D$ 148.6° (*c* 0.95, $CHCl_3$). Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.74; H, 7.46. Found: C, 77.92; H, 7.20.

Ethyl 2,3,4-Trideoxy-2-*C*-*n*-butyl-6-*O*-benzyl-α-D-*erythro*-hex-3-enopyranoside (7). This compound was synthesized from 6 and *n*-butylmagnesium bromide as a colorless oil (74%): $[\alpha]_D$ −23.0° (*c* 0.51, $CHCl_3$). Anal. Calcd for $C_{19}H_{28}O_3$:

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74.96; H, 9.27. Found: C, 75.13; H, 9.33.

Ethyl 2,3,4-Trideoxy-2-*C*-isopropyl-6-*O*-benzyl-α-D-*erythro*-hex-3-enopyranoside (8). This product was prepared from **6** and isopropylmagnesium bromide as a syrup (50%): $[\alpha]_D$ −19.6° (*c* 0.7, $CHCl_3$). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.41; H, 8.87.

Methyl 2,3,4-Trideoxy-4-*C*-*n*-butyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*threo*-hex-2-enopyranoside (10). Prepared from **9** and *n*-butylmagnesium bromide as a colorless oil (60%): $[\alpha]_D$ −71.6° (*c* 0.72, $CHCl_3$). Anal. Calcd for $C_{17}H_{34}O_3Si$: C, 64.92; H, 10.9. Found: C, 64.65; H, 10.65.

Methyl 2,3,4-Trideoxy-4-*C*-isopropyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*threo*-hex-2-enopyranoside (11). Prepared from **9** and isopropylmagnesium bromide as a syrup (60%): $[\alpha]_D$ −85.0° (*c* 1.4; $CHCl_3$). Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.74. Found: C, 64.13; H, 10.60.

Methyl 2,3,4-Trideoxy-4-*C*-phenyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*threo*-hex-2-enopyranoside (12). Prepared from **9** and phenylmagnesium bromide as a syrup (88%): $[\alpha]_D$ −104.2° (*c* 0.8; $CHCl_3$). Anal. Calcd for $C_{19}H_{30}O_3Si$: C, 68.22; H, 9.04. Found: C, 68.41; H, 8.82.

Methyl 2,3,4-Trideoxy-4-*C*-*n*-butyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hex-2-enopyranoside (14). Prepared from **13** and *n*-butylmagnesium bromide as a colorless oil (80%): $[\alpha]_D$ 33.2° (*c* 0.42, $CHCl_3$). Anal. Calcd for $C_{17}H_{34}O_3Si$: C, 64.92; H, 10.9. Found: C, 65.12; H, 10.72.

Methyl 2,3,4-Trideoxy-4-*C*-isopropyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hex-2-enopyranoside (15). Prepared from **13** and isopropylmagnesium bromide as a syrup (76%): $[\alpha]_D$ 77.4° (*c* 0.44; CH_2Cl_2). Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.74. Found: C, 64.15; H, 10.50.

Methyl 2,3,4-Trideoxy-2-*C*-phenyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*threo*-hex-3-enopyranoside (16). Prepared from **13** and phenylmagnesium bromide as a syrup (36%). Starting material (50%) was recovered unchanged: $[\alpha]_D$ 77.3° (*c* 0.7; $CHCl_3$). Anal. Calcd for $C_{19}H_{30}O_3Si$: C, 68.22; H, 9.04. Found: C, 68.33; H, 8.77.

Methyl 2,3,4-Trideoxy-2-*C*-methyl-6-*O*-benzyl-α-D-*threo*-hex-3-enopyranoside (22). Methyl iodide (568 mg, 4.0 mmol) was reacted with metallic Mg (97 mg, 4.0 mmol) in anhydrous ether. This solution was cooled at −30 °C, and CuI (285 mg, 1.5 mmol) was added in one portion under argon. Stirring was continued during 30 min at −30 °C, and a solution of **21**[13] (368 mg, 1.0 mmol) in ether (15 mL) was added. This mixture was allowed to warm slowly to room temperature and stirred for 6 h. The reaction was diluted with ether and treated with concentrated aqueous NH_4Cl and a few drops of NH_4OH while vigorously stirring. The ethereal layer was separated and dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was rebenzoylated (Bz_2O/Py) and chromatographed on silica gel to yield the product, a thick oil (80 mg, 30%).

2-Benzothiazolyl 2,3-Dideoxy-4,6-*O*-isopropylidene-1-thio-α-D-*erythro*-hex-2-enopyranoside (23). A syrupy product prepared from 4,6-di-*O*-isopropylidene-D-glucal[10] and 2-mercaptobenzothiazole using the general conditions described above for (allylthio)benzothiazoles:[14] $[\alpha]_D$ 310.9° (*c* 0.7, $CHCl_3$). Anal. Calcd for $C_{16}H_{17}NO_3S_2$: C, 57.29; H, 5.11; N, 4.18; S, 19.12. Found: C, 57.40; H, 5.11; N, 4.15; S, 19.44.

1,5-Anhydro-4,6-*O*-isopropylidene-2,3-dideoxy-3-*C*-methyl-D-*ribo*-hex-1-enitol (24). Prepared from **23** and MeMgBr as a syrup: $[\alpha]_D$ 160.9° (*c* 1.4, $CHCl_3$). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.10; H, 8.90.

1,5-Anhydro-4,6-*O*-isopropylidene-2,3-dideoxy-3-*C*-phenyl-D-*ribo*-hex-1-enitol (25). Prepared from **23** and PhMgBr as a syrup: $[\alpha]_D$ 244.3° (*c* 0.85, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.31; H, 7.60.

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Registry No. 1a, 23339-15-3; **1b**, 51385-38-7; **1c**, 80516-25-2; **1d**, 124944-63-4; **2**, 130619-57-7; **3**, 130641-42-8; **4**, 142041-72-3; **5**, 142041-73-4; **6**, 142041-74-5; **7**, 142041-75-6; **8**, 142041-76-7; **9**, 124944-67-8; **10**, 142041-77-8; **11**, 142041-78-9; **12**, 142041-79-0; **13**, 124944-66-7; **14**, 142041-80-3; **15**, 142041-81-4; **16**, 142041-82-5; **21**, 34254-52-9; **22**, 142041-83-6; **23**, 142041-84-7; **24**, 142041-85-8; **25**, 142041-86-9; BTZ-Cl, 615-20-3; BTZ-SH, 149-30-4; 4,6-D-isopropylidene-D-glucal, 51450-36-3.

Nickel-Catalyzed Geminal Dimethylation of Allylic Cyclic Dithioketals. A Convenient Procedure To Form a *tert*-Butyl Substituent at the Olefinic Carbon Atom

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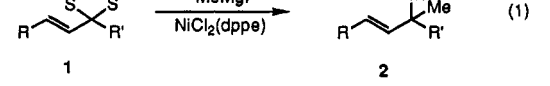
Received January 2, 1992

Much effort has been devoted to the introduction of a *tert*-butyl group or a quaternary carbon to olefinic carbon atom(s) with the aim of synthesizing crowded olefins.[1] Most of the procedures that have been developed use reagents containing a *tert*-butyl group. Although Tebbe-like reagents are effective for converting a carbonyl group into a *gem*-dimethyl substituent, their application to allylic carbonyl substrates is limited by poor regioselectivity.[2] We recently reported a series of nickel-catalyzed cross-coupling reactions of benzylic and allylic dithioacetals with Grignard reagents.[3-5] In the presence of $NiCl_2$(dppe), cinnamaldehyde dithioacetals **1** (R = Ar, R′ = H) react with MeMgI to give the geminally dimethylated products (eq 1, R = Ar, R′ = H).[4] We have extended this reaction to geminal dimethylation of allylic dithioketals and now report a facile procedure for the regioselective preparation of *tert*-butyl-substituted olefins **2** (eq 1, R′ ≠ H).



(1)

1 **2**

Dithioketals **1** were prepared according to a modified literature procedure.[6] Treatment of **1** with 4 equiv of MeMgI in the presence of 5 mol % of $NiCl_2$(dppe) in refluxing ether–THF for 10 h afforded *gem*-dimethyl

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