# Serial Radical Reactions of Glycals: Ready Routes to Highly Functionalized *C*-Glycosyl Derivatives[1]

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The C3-OH of partially protected glycals can be readily converted into mixed acetals of 2-bromoacetaldehyde or into silylmethylene bromides. Reaction of these derivatives with tri-*n*-butyltin hydride gives a radical that cyclizes efficiently to generate a stabilized radical at C1. The latter can be trapped very efficiently with acrylonitrile, *tert*-butyl isocyanide, allyltri-*n*-butyltin, tributyltin acrylates, or a complex pyranoside enone to afford C-glycosides in which a 1,2 disubstitution has taken place. The stereochemistry of the resulting 1,2 disubstituted product is dependent, at C-2, on the stereochemistry of the C3-OH and at the anomeric center (C-1) upon the interplay of (a) steric effects and (b) the electronic bias of the radical anomeric effect.

Recognition of differences in behavior between carbohydrate derivatives and their carbocyclic counterparts[3] and the leverage of these differences into synthetically useful transformations of carbohydrates into natural products[4] are interwoven areas of interest in our group. In this connection we,[5] as well as others,[6–13] have devoted special attention to stereoselective radical reactions of carbohydrate substrates because such procedures are particularly well suited for manipulations of highly functionalized systems owing to their mildness, their ability to tolerate unprotected hydroxyl groups, and the attendant low incidence of $\beta$-elimination of oxygen functionalities.[14]

Cyclohexyl radicals, e.g. **1** (Scheme 1) add preferentially to alkenes from the sterically favored equatorial position,[15] whereas glycosyl radicals, e.g. **2**, because of the stereoelectronic effect of the ring oxygen, lead predominantly to axial attack.[16,17] On the other hand, the bicyclic cyclohexyl radical **3**, developed by Stork and coworkers,[18] has shown remarkable "shape selectivity" and reacts stereoselectively *anti* to the fused five-membered ring.[17,18]

It was in this context that we became interested in (potential) differences in behavior of anomeric radicals **4** and **5**, *vis a vis* the cyclohexyl analogue **3**. Thus, the anomeric radicals are (a) stabilized,[19] (b) more nucleophilic,[20] and (c) susceptible to facial selectivity in their reactions, not only because of normal steric factors, but also because of the above mentioned radical anomeric effect.[21] As a result of the latter, axial attack on the anomeric radical (i.e. addition from the α-face in the D-series) that would maintain the overlap between the nonbonding electron pair of the ring oxygen and the

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(3) (a) Fraser-Reid, B.; Underwood, R.; Osterhout, M.; Grossman, J. A.; Liotta, D. *J. Org. Chem.* **1986**, *51*, 2152. (b) Fraser-Reid, B.; Tsang, R.; Lowe, D. *Chem. Scri.* **1985**, *25*, 117. (c) Benkö, Z.; Fraser-Reid, B.; Mariano, P. S.; Beckwith, A. L. J. *J. Org. Chem.* **1988**, *53*, 2066.

(4) (a) Fraser-Reid, B.; Anderson, R. C. *Prog. Chem. Org. Nat. Prod.* **1980**, *39*, 1. (b) Fraser-Reid, B.; Tsang, R. *Strategies and Tactics in Organic Synthesis;* Lindberg, T., Ed.; Academic Press: New York, 1989; Vol. 2, pp 123–162.

(5) (a) Fraser-Reid, B.; Holder, N. L.; Yunker, M. B. *J. Chem. Soc., Chem. Commun.* **1972**, 1286. (b) Fraser-Reid, B.; Holder, N. L.; Hicks, D. R.; Walker, D. L. *Can. J. Chem.* **1977**, *55*, 3978. (c) Fraser-Reid, B.; Anderson, R. C.; Hicks, D. R.; Walker, D. L. *Can. J. Chem.* **1977**, *55*, 3986. (d) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 2116. (e) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 8102.

(6) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, England, 1986.

(7) (a) Barton, D. H. R.; Zard, S. Z. *Pure Appl. Chem.* **1986**, *58*, 675. (b) Barton, D. H. R.; Motherwell, W. B. *Heterocycles* **1984**, *21*, 1. (c) Barton, D. H. R.; Motherwell, W. B. *Pure Appl. Chem.*, **1981**, *53*, 15. (d) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. I* **1975**, 1574.

(8) (a) Keck, G. E.; Yates, B. E. *J. Am. Chem. Soc.* **1982**, *104*, 5829. (b) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079. (c) Keck, G. E.; Enholm, E. J.; Kachensky, D. F. *Tetrahedron Lett.* **1984**, *25*, 1867.

(9) RajanBabu, T. V. *J. Am. Chem. Soc.* **1987**, *109*, 609.

(10) (a) Wilcox, C. S.; Thomasco, L. M. *J. Org. Chem.* **1985**, *50*, 546. (b) Wilcox, C. S.; Gaudino, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 3102.

(11) Bartlett, P. A.; McLaren, K. L.; Ting, P. C. *J. Am. Chem. Soc.* **1988**, *110*, 1633.

(12) Crich, D.; Ritchie, T. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1461. Crich, D.; Ritchie, T. *J. Carbohydr. Res.* **1989**, *190*, c3. Crich, D.; Ritchie, T. J. *J. Chem. Soc., Perkin Trans. I* **1990**, 945. Crich, D.; Lim, L. B. L. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2209. Crich, D.; Hermann, F. *Tetrahedron Lett.* **1993**, *34*, 3385.

(13) Kahne, D.; Yang, D.; Lim, J. J.; Miller, R.; Paguaya, E. *J. Am. Chem. Soc.* **1988**, *110*, 8716.

(14) (a) Curran, D. P. *Synthesis* **1988**, 417, 489. (b) Ramaiah, H. *Tetrahedron* **1987**, *43*, 3541. (b) Walling, C. *Tetrahedron* **1985**, *41*, 3887. (c) Hart, D. J. *Science* **1984**, *223*, 883. (d) Surzur, J. M. *Reactive Intermediates*, Vol. 2; Abramovitch, R. A., Ed.; Plenum Press: New York, 1982; Chapter 3.

(15) Damm, W.; Giese, B.; Hartung, J.; Hasskerl, T.; Houk, K. N.; Hüter, O.; Zipse, H. *J. Am. Chem. Soc.* **1992**, *114*, 4067.

(16) Praly, J. P. *Tetrahedron Lett.* **1983**, *24*, 3075. Baumberger, F.; Vasella, A. *Helv. Chim. Acta* **1983**, *66*, 2210. Adlington, R. M.; Baldwin, J. E.; Basak, A.; Kozyrod, R. P. *J. Chem. Soc., Chem. Commun.* **1983**, 944. Giese, B.; Dupuis, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 622.

(17) (a) Giese, B. *Pure Appl. Chem.* **1988**, *60*, 1655. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969.

(18) (a) Stork, G. *Bull. Soc. Chim. Fr.* **1990**, *127*, 675. (b) Stork, G. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 149. (c) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303. (d) Stork, G.; Sher, P. M.; Chen, H.-C. *J. Am. Chem. Soc.* **1986**, *108*, 6384. (e) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765. (f) Stork, G.; Mook, R. Jr.; Biller, S. A.; Rychnovsky S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741.

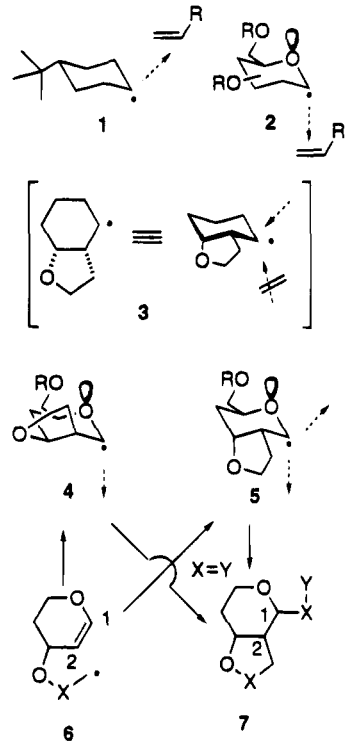
(19) Dupuis, J.; Giese, B.; Riegge, D.; Fischer, H.; Korth, H.-G.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 896. Korth, H.-G.; Lommes, P.; Sicking, W.; Sustmann, R. *Chem. Ber.* **1985**, *118*, 4627. Korth, H.-G.; Sustmann, R. Groninger, K. S.; Leisung, M.; Giese, B. *J. Org. Chem.* **1988**, *53*, 4364.

(20) Giese, B.; Mehl, W. *Tetrahedron Lett.* **1991**, *34*, 4275. Giese, B.; Dupuis, J.; Hasskerl, T.; Meixner, J. *Tetrahedron Lett.* **1983**, *24*, 703.

(21) (a) Giese, B.; Dupuis, J. *Tetrahedron Lett.* **1984**, *25*, 1349. (b) Rychnovsky, S. D.; Powers, J. P.; LePage, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 8375. (c) Juaristi, E.; Cuevas, G. *Tetrahedron* **1992**, *48*, 5019.

0022-3263/95/1960-3871$09.00/0 

**Scheme 1**



unpaired electron of the radical center (or the forming bond) will be preferred.[17b]

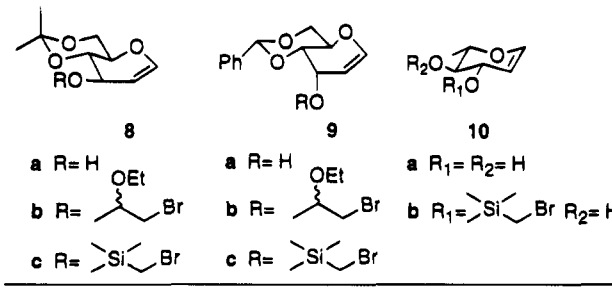
Accordingly, in the case of **4**, steric as well as stereoelectronic factors jointly favor axial attack, whereas stereoselectivity in the reaction of **5** will be the result of a counterplay of steric and electronic effects. Interest from a synthetic standpoint arises from the possibility of completely stereoselective access to α-C-glycosides from **4** and to the β-C-counterparts from **5**.[22]

We report herein our studies[23] on serial radical reactions on C-3-tethered, $\Delta^{1,2}$ unsaturated sugar derivatives (glycals), **6**, leading to intermediates **4** and **5**, trapping of which by a suitable reagent, **X=Y**, should afford **7**, in which stereocontrolled, vicinal 1,2-substitution of the glycal double bond has occurred. The overall result of the operation (**6** → **7**, Scheme 1) would be the ready preparation of polyfunctionalized *C*-glycosyl derivatives from commercially available, or easily accessible, glycals.

## Results and Discussion

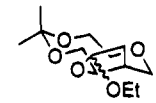
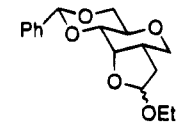
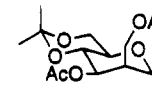
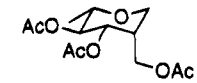
**Preparation of Radical Precursors.** The readily available glycals **8a**[24] and **9a**[25] (Table 1) were converted into the mixed bromo acetals[18,26] **8b** and **9b** by reaction with 1,2-dibromoethyl ethyl ether ($Et_3N$, $CH_2Cl_2$, 0 °C → RT). Silicon-tethered bromides **8c**, **9c**, and **10b** were prepared from the corresponding alcohols following the general guidelines from the groups of Nishiyama[27] and Stork[28] [$ClSi(CH_3)_2CH_2Br$, $Et_3N$, $CH_2Cl_2$, rt].

**Table 1. Radical Cyclization of C-2-Tethered Radicals onto the $\Delta^{1,2}$ Double Bond of a Glycal**



**8** **9** **10**

a R= H; b R= OEt, Br; c R= Si, Br — a R= H; b R= OEt, Br; c R= Si, Br — a $R_1 = R_2 = H$; b $R_1$= Si, Br, $R_2$= H

| Entry | Substrate | Reaction Conditions[a] | Products | Yield (%) |
|---|---|---|---|---|
| i | **8b** | A |  **11** | 80 |
| ii | **8b** | B | **11** | 76 |
| iii | **9b** | A |  **12** | 80 |
| iv | **9b** | B | **12** | 74 |
| v | **8c** | C |  **13** | 70 |
| vi | **10b** | C |  **14** | 52 |
| vii | **9c** | C | no cyclization product | |

[a] For Reaction Conditions A-C see Experimental

**Intramolecular Radical Cyclization onto the Glycal Double Bond.** Although intermolecular addition of a nucleophilic, carbon-centered radical to an electron-rich vinyl ether is not favored,[29] studies by Newcomb[30] and Beckwith[31] have shown that intramolecular versions proceed at rates which are comparable to those of the corresponding reaction of olefins.[32]

Our first task was to demonstrate that the first step (**6** → **4**, Scheme 1) could be carried out efficiently (Table

(22) For recent leading examples of stereocontrolled entry to β-C-glycosides based on radical procedures, see: Stork, G.; Suh, H. S.; Kim, G. *J. Am. Chem. Soc.* **1991**, *113*, 7054. Crich, D.; Lim, L. B. L. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2205. Crich, D.; Lim, L. B. L. *Tetrahedron Lett.* **1991**, *32*, 2565. Crich, D.; Lim, L. B. L. *Tetrahedron Lett.* **1990**, *31*, 1897. De Mesmaeker, A.; Hoffmann, P.; Ernst, B.; Hug, P.; Winkler, T. *Tetrahedron Lett.* **1989**, *30*, 6307.

(23) A preliminary communication of this work has already appeared: López, J. C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1989**, *111*, 3450.

(24) Fraser-Reid, B.; Walker, D. L.; Tam, S. Y.-K.; Holder, N. L. *Can. J. Chem.* **1973**, *51*, 3950.

(25) Feast, A. R.; Overend, W. G.; Williams, N. A. *J. Chem. Soc.* **1965**, 7378.

(26) Ueno, Y.; Moriya, O.; Chino, K.; Watanabe, M.; Okawara, M. *J. Chem. Soc., Perkin Trans. I* **1986**, 1351.

(27) Nishiyama, H.; Kitajima, T.; Matsumoto, M.; Itoh, K. *J. Org. Chem.* **1984**, *49*, 2298.

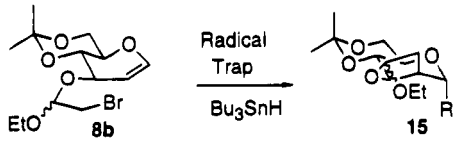
(28) Stork, G.; Kahn, M. *J. Am. Chem. Soc.* **1985**, *107*, 500. Stork G.; Sofia, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 6826.

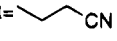
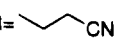
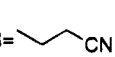
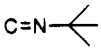
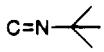
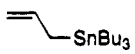
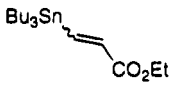
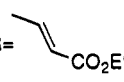
(29) For a study of the influence of substituents on the rate of intermolecular addition of free radicals to alkenes, see: Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 753.

(30) Park, S.-U.; Chung, S.-K.; Newcomb, M. *J. Am. Chem. Soc.* **1986**, *108*, 240.

(31) Beckwith, A. L. H.; Roberts, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 5893. Beckwith, A. L. J.; O'Shea, D. M.; Roberts, D. H. *J. Chem. Soc., Chem. Commun.* **1983**, 1445.

**Table 2. Sequential Radical Cyclization–Intermolecular Trapping of C-2-Tethered Radicals Derived from 8b**




| Entry | Reaction Conditions[a] | Radical Trap | Product | Yield (%) |
|---|---|---|---|---|
| i | A |  | **15a** R=  | 75 |
| ii | B |  | **15a** R=  | 78 |
| iii | A[b] |  | **15a** R=  | 87 |
| iv | A |  | **15b** R= CN | 28[c] |
| v | B |  | **15b** R= CN | 76 |
| vi | C |  | **15c** R=  | 68 |
| vii | D |  | **15d** R=  | 63[d] |

[a] For Reaction Conditions A-D see Experimental

[b] Converted to its corresponding iodide before cyclization (See Experimental)

[c] Reduced compound **11** was also isolated in 31% yield

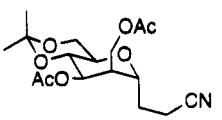
[d] The corresponding *cis* isomer was also isolated in 8% yield

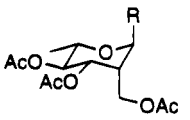
1). This was established by treatment of mixed bromo acetals **8b** and **9b** with tri-*n*-butyltin hydride and AIBN in benzene solutions, which afforded the tricyclic compounds **11** and **12** in 80% yields (entries i and iii). Similar results were obtained by treating **8b** and **9b** under the conditions recommended by Stork and Sher ($Bu_3SnCl$, $NaCNBH_3$, tBuOH)[18c] (entries ii and iv).

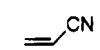
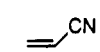
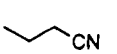
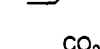
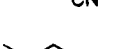
Treatment of silylmethylene derivatives **8c** and **10b** (Table 1, entries v and vi) under Stork and Sher conditions[18c] followed by Tamao oxidation[33] (KF, $KHCO_3$, $H_2O_2$) and acetylation led to compounds **13** and **14** in good yields. In our hands, treatment of 4,6-*O*-benzylidene derivative **9c**, under identical reaction conditions as used with **8c** and **10b**, failed to yield any product resulting from cyclization, the known acetate **9** (R = Ac)[34] being the only material isolated.

**Radical Cyclization–Intermolecular Trapping Sequence.** We then repeated the above-described reaction of compound **8b** in the presence of a 10-fold excess of acrylonitrile (Table 2). The *C*-glycosyl compound **15a** was obtained in 75% yield when the reaction was carried out in benzene under syringe pump conditions (entry i) or 78% when the catalytic method of Stork was used (entry ii), there being no evidence of the reduced product **11** in either case. Replacing the bromide of **8b** with iodide (entry iii) prior to cyclization improved the yield of **15a** to 87%, presumably because of better propagation at the alkyl iodide–stannyl radical step.[35]

**Table 3. Sequential Radical Cyclization–Intermolecular Trapping of C-3 Silicon-Tethered Radicals 8c and 10b under Stork's Catalytic Conditions**




| Entry | Substrate | Radical Trap X=Y | Product | Yield (%) |
|---|---|---|---|---|
| i | **8c** |  | **16** | 61 (12)[a] |
| ii | **10b** |  | **17a** R=  | 32 (25)[b] |
| iii | **10b** |  | **17b** R=  | 37 (23)[b,c] |

[a] Recovered acetylated unreacted starting material **8e** in %

[b] Recovered acetylated unreacted starting material **10c** in %

[c] Some telomers (6%) also obtained

Attempts to trap the radical intermediate with *tert* butyl isocyanide under similar conditions ($Bu_3SnCl$, $NaCNBH_3$, tBuOH, 0.01 M) afforded a mixture of the glycosyl cyanide **15b** and the reduced product **11** in ≈1:1 ratio. Increase of the concentration to 0.04 M (entry v), however, permitted us to obtain **15b** as the sole reaction product in 76% yield.

Another example of the ready introduction of a functionalized alkyl substituent at C1 was demonstrated by using allyltributyltin as a radical trap in an SH2′ process,[8] which afforded **15c** in 68% yield (entry vi). Evidence for the rapid rate of the intramolecular cyclization step (**6** → **4**, Scheme 1) in this experiment comes from the failure to detect products from the reaction of the pendant radical **6** with allyltributyltin.[36,37] A similar trend was observed from the reaction of **8b** with a 3:1 *Z*/*E* mixture of tin acrylates[38] in the presence of AIBN (Table 2, entry vii), whereby **15d** was obtained in 63% along with ≈8% of the isomeric *cis* product.

We next turned our attention to tethered silyl bromides **8c** and **10b** (Table 3). Serial radical ring closure followed

(32) For radical cyclizations onto enol ethers, see: (a) Ladlow, M.; Pattenden, G. *Tetrahedron Lett.* **1984**, *25*, 4317. (b) Begley, M. J.; Ladlow, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. I* **1988**, 1095. (c) Begley, M. J.; Ladlow, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. I* **1988**, 1107.

(33) Tamao, K.; Ishida N.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2120.

(34) Hicks, D. R.; Fraser-Reid, B. *Can. J. Chem.* **1975**, *53*, 2017.

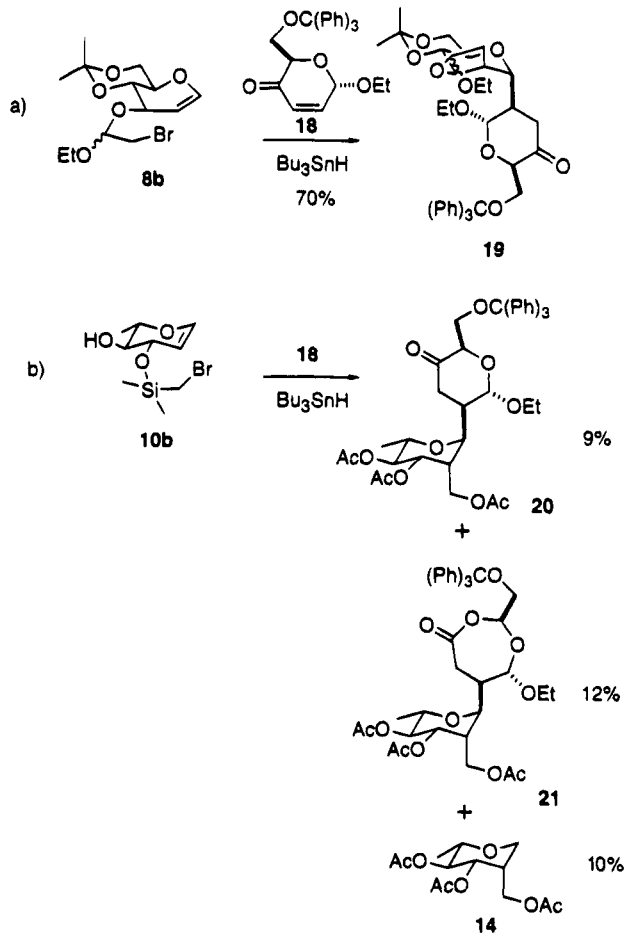
(35) Porter, N. A.; Magnin, D. R.; Wright, B. T. *J. Am. Chem. Soc.* **1986**, *108*, 2787. Ingold, K. U.; Lusztyk, J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 343.

(36) For example, Giese has shown that acyloxy migration to the anomeric carbon is faster than radical allylation described by Keck:[8] (a) Giese, B., in ref 6, p 101.

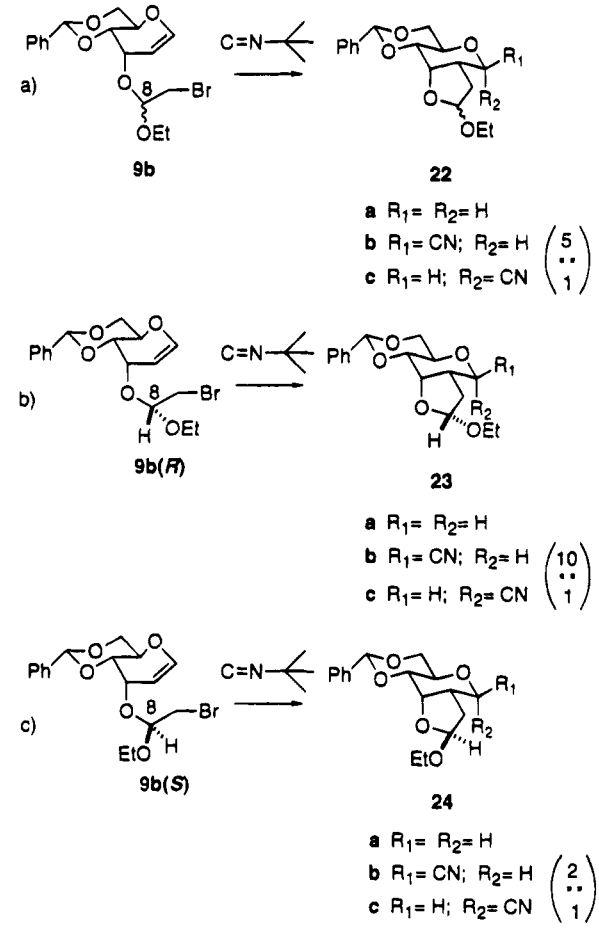
(37) For a related example, see: Ferrier, R. J.; Petersen, P. M. *Tetrahedron* **1990**, *46*, 1. Ferrier, R. J.; Petersen, P. M.; Taylor, M. A. *J. Chem. Soc., Chem. Commun.* **1989**, 1247.

(38) (a) Gómez, A. M.; López, J. C.; Fraser-Reid, B. *J. Chem. Soc., Perkin Trans. I* **1994**, 1689. (b) Russell, G. A. *Acc. Chem. Res.* **1989**, *22*, 1. (c) Russell G. A.; Ngoviwatchai, P. *Tetrahedron Lett.* **1985**, *26*, 4975. (d) Baldwin J. E.; Kelly, D. R. *J. Chem. Soc., Chem. Commun.* **1985**, 682. (e) Russell, G. A.; Tashtoush, H.; Ngoviwatchai, P. *J. Am. Chem. Soc.* **1984**, *106*, 4622. (f) Baldwin, J. E.; Kelly, D. R.; Ziegler, C. B. *J. Chem. Soc., Chem. Commun.* **1984**, 133.

**Scheme 2. –Intermolecular Trapping of C-2-Tethered Radicals with Enone 18**




**Scheme 3. Sequential Radical Cyclization/ Intermolecular Trapping of C-3-Tethered Radicals 9b in the Presence of *tert*-Butyl Isocyanide**




by intermolecular trapping with acrylonitrile took place smoothly with both substrates and led, after Tamao oxidation[33] and acetylation, to **16** and **17a**, respectively (entries i and ii). In both cases some acetylated unreacted starting materials **8** (R = Ac) or **10** ($R_1 = R_2$ = Ac) were isolated. For glycal **10b**, trapping with methyl acrylate (10 equiv) could also be effected (entry iii).

A substrate of special interest to our group was the hex-2-enopyranosid-4-ulose **18**[39] as the radical trap (Scheme 2). This α-enone has often been used in this laboratory for a variety of synthetic and mechanistic studies involving radical reactions.[3c,5a-c] In the present study, isolation of the highly functionalized product **19** in 70% yield (Scheme 2a) was most encouraging. However, the yield of the desired product **20** in Scheme 2b suffered from the fact that the C-4 keto group did not survive the Tamao oxidation. Thus a facile Baeyer–Villiger reaction of the highly reactive 4-ketopyranose system, as previously reported by us,[40] led to acylal **21** as a byproduct. A substantial amount of the reduced intermediate **14** was also obtained.

Reactions of glycal **9b** (Scheme 3) were expected to be less stereocontrolled because steric effects favor the 1,2-*trans* product with β anomeric orientation, whereas the radical anomeric effect favors the 1,2 *cis* product with α orientation. Indeed, a trapping experiment with *tert*-butyl isocyanide indicated that β:α anomeric mixtures of **22b/22c** were obtained in 5:1 ratio, along with equal amounts of the reduced intermediate **22a**.

A more careful study of the crude reaction mixtures ($^1$H NMR), however, suggested that the ratio of **22b/22c** depended on the C-8 configuration of the starting epimeric bromides. In order to gain some insight into this matter, the C-8 epimeric mixed bromo acetals **9b** were separated and independently subjected to reaction in the presence of *tert*-butyl isocyanide. The results in Schemes 3b, c confirmed the fact that one of the isomers, **9b(*R*)**, does indeed display a much larger stereochemical bias than the other, **9b(*S*)**, for β-C-glycoside formation.

## Discussion

The 5-*exo-trig* radical intramolecular radical addition of C-3 bromomethyl acetals to the double bond of glycals takes place efficiently to generate anomeric α-oxy radicals, which are trapped readily by deactivated olefins, thereby leading to the formation of 1,2 di-C-alkylated glycosides.

On the other hand, the 5-*exo-trig* radical cyclizations of tethered silyl bromomethyl ethers seem to be substrate dependent. In our hands the axially oriented silyl ether **9c** did not yield any cyclized product (Table 1), whereas equatorially-disposed silyl ethers **8c** and **10b** did cyclize, albeit to different extents. The reaction of **10b**, for instance, always left unreacted starting material (23–27%), recovered as the diacetate **10** ($R_1 = R_2$ = Ac).[41]

Regardless of the nature of the tether involved, once

(39) Fraser-Reid, B.; McLean, A.; Usherwood, E. W.; Yunker, M. *Can. J. Chem.* **1970**, *48*, 2877.

(40) Tsang, R.; Battista, R.; Fraser-Reid, B. Unpublished result. See also: Tsang, R.; Fraser-Reid, B. *J. Org. Chem.* **1992**, *57*, 1065.

the first cyclization has taken place, trapping of the resulting anomeric radical is a very efficient process. However it is best to use the trap in excess, since when only 1 equiv of enone **18** was used (Scheme 2b) a substantial amount of reduced material (from hydrogen transfer to the anomeric radical) was observed.

In the case of anomeric radicals of type **4**, complete stereoselectivity was observed for the formation of the corresponding α-C-glycosides (Tables 2 and 3). The α configurations assigned to these products were supported by $J_{1,2}$ coupling constants which were in the range of 1.5–3.9 Hz in all cases.

The reactions of the *allal* derivative **9b** summarized in Scheme 3 (cf. **5**, in Scheme 1) illustrates that the radical anomeric effect overrides, to a certain extent, the otherwise dominant steric factors related with the "shape selectivity" in cyclohexane analogues.[17,18]

The different behavior observed for the *R* and *S* forms of bromo acetals **9b** is noteworthy since the configuration at the anomeric acetal center has always been regarded as irrelevant. We have previously noted different stereoselectivities in some of our other substrates. Thus we have found that a pair of diastereomeric tethered bromo acetals of pyranosidic dienes exhibit epimer-dependent selectivities in serial radical cyclizations.[42]

The structures assigned to isomers **23** and **24** in Scheme 3 are the result of X-ray analysis, and we have used these data as the basis for making the C-8 assignments for the pendant acetal precursors as shown in Scheme 3b,c, on the assumption that additional steric hindrance by the *endo* ethoxy group in the intermediate anomeric radicals will lead to more β-C-glycoside product. Thus the higher β/α ratio in **23** was deemed to imply *R* configuration at C-8 of **9b** and, by corollary, *S* configuration for the precursor of **24**.

## Conclusions

Novel, stereocontrolled avenues to 2-deoxy-2-C-alkylated *C*-glycopyranosides have been described involving intramolecular 5-*exo*-*trig* radical cyclizations of C-3 tethered glycals, followed by intermolecular trapping of the anomeric radical intermediates. When the tether is a mixed haloacetal, the cyclization step is a very efficient process, whereas when silyl bromomethyl ethers are used reduction of the intermediate may depreciate the amount of cyclized product, the extent of which depends on the nature of the substrate. When the orientation of the tether is such that the independent constraints of "shape selectivity" and radical anomeric effect operate in the same direction, just one isomer at C-1, resulting from axial attack, is observed. However when these constraints are not in unison, C-1 mixtures of anomeric C-glycosides are obtained. Furthermore, the otherwise irrelevant configuration at the anomeric center of the halo acetal moiety exerts additional stereodirecting effect in the formation of the C-glycosidic bond. Thus different ratios of α- and β-C-glycosides are obtained depending on the configuration at the pendant anomeric center of the starting bromo acetals.

(41) The axial or equatorial nature of the tethered silyl ether, however, does not seem to be the reason for the different reactivity observed, see: Pedretti, V.; Mallet, J.-M.; Sinaÿ, P. *Carbohydr. Res.* **1993**, *244*, 247.

(42) López, J. C.; Gómez, A. M.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1994**, 1533. López, J. C.; Gómez, A. H.; Fraser-Reid, B. *Aust. J. Chem.* **1995**, *48*, 333.

## Experimental Section

**General Procedures.** Melting points were determined in capillary tubes and are uncorrected. Optical rotations were determined at the sodium D line and are measured in chloroform. $[\alpha]_D$ values are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. High-field NMR spectra were recorded at 300 MHz in $CDCl_3$; chemical shifts (δ) are relative to $CHCl_3$ as internal reference. Mass spectra were recorded by chemical ionization (with methane ammonia as the reagent gas). TLC was conducted in precoated kieselgel 60 $F_{254}$. Detection was first by UV (254 nm) and then charring with a solution of ammonium molybdate(VI) tetrahydrate (12.5 g) and cerium(IV) sulfate tetrahydrate (5.0 g) in 10% aqueous sulfuric acid (500 mL). Column chromatography was carried out on kieselgel (230–400 mesh) and mixtures of petroleum ether–ethyl acetate (PE–EtOAc) as eluant. All reactions were conducted under an atmosphere of argon. Anhydrous $MgSO_4$ or $Na_2SO_4$ was used to dry the organic solutions during workups, and the removal of the solvents was done under vacuum with a rotoevaporator. Unless otherwise noted, materials were obtained from commercially available sources and used without further purification. Solvents were dried and purified using standard methods.

**General Procedure for the Preparation of Bromo Acetals.**[18,26] A solution of methyl 1,2-dibromoethyl ether was prepared by dropwise addition of bromine to a stirred solution of ethyl vinyl ether (6 equiv) in dry dichloromethane ($CH_2Cl_2$) (1/mL/mmol) maintained at −78 °C under argon. The solution was kept at −78 °C for 90 min and then was allowed to warm to room temperature (rt) for about 60 min. A solution of the alcohol in triethylamine ($Et_3N$) (2 mL/mmol) was then added, and the resulting mixture was stirred at rt overnight. Concentration under reduced pressure and flash chromatography afforded the pure mixed bromo acetals. In the cases in which the isomeric acetals could be separated, characterization has been provided for each of the isomers.

**General Procedure for the Preparation of (Bromomethyl)silyl Ethers.**[27,28] Typically, to an ice-cooled solution of the alcohol in $CH_2Cl_2$ was added $Et_3N$ (2 mL/mmol) and (bromomethyl)dimethylchlorosilane (1.2 equiv). The solution was allowed to warm to rt and kept at that temperature overnight. The reaction mixture was poured into aqueous $NaHCO_3$ and extracted twice with $CH_2Cl_2$. The combined organic extracts were washed with water and brine and dried. Evaporation of the solvent furnished crude (bromomethyl)silyl ethers that were azeotroped with toluene and without further purification were subjected to the radical cyclization reaction.

**General Procedure for the Radical Cyclization Reactions. Method A.** Typically, a thoroughly degassed (argon) solution of alkyl halide (halo acetal or (bromomethyl)silyl ether) in benzene (0.02 M) was heated to reflux under argon. A solution of $Bu_3SnH$ (1.5 equiv) and AIBN (0.1 equiv) was then added via a syringe-driven pump over 12 h. After cooling, the reaction mixture was treated sequentially with carbon tetrachloride and then with a diluted solution of iodine in $Et_2O$, which was added dropwise till no decoloration was observed. The organic solvents were removed and the residue taken up in EtOAc and washed several times with a saturated solution of potassium fluoride. The separated organic phase was dried, the solvent was removed, and the residue was purified by flash chromatography.

**Method B.** To a thoroughly degassed (argon) solution of the alkyl halide, tributyltin chloride (0.1 equiv), and AIBN (0.1 equiv) in *tert*-butyl alcohol (0.04 M) was added sodium cyanoborohydride (2 equiv) and the reaction mixture was immediately refluxed in a preheated bath for 4 h. The reaction mixture was diluted with $CH_2Cl_2$ and shaken with a 3% aqueous ammonia solution, followed by addition of brine and separation of the organic phase. The aqueous layer was extracted twice with $CH_2Cl_2$ and dried. Solvents were removed by azeotroping with toluene, and the residue was subjected to flash chromatography.

**General Procedure for the Tamao Oxidations.**[33] The crude silyl ether resulting from the radical cyclization was dissolved in THF/MeOH (1:1, 1 mL/mmol), and the solution

was treated with potassium hydrogen carbonate (2 equiv), potassium fluoride (4 equiv), and 30% hydrogen peroxide (20 equiv). The resulting mixture was refluxed for 10 h. After cooling, the remaining hydrogen peroxide was decomposed by careful addition of well-ground $Na_2S_2O_3 \cdot 5H_2O$ (25 equiv) at rt. After 1 h, an iodine starch test was negative. The mixture was then diluted with $Et_2O$ (1 mL/mmol) and filtered through Celite. The precipitate was washed with THF/MeOH/$Et_2O$ (1:1:2), and the filtrate was concentrated under reduced pressure. The resulting crude diols were subjected to acetylation, with acetic anhydride and catalytic DMAP in pyridine (rt, 24 h).

**4,6-Di-*O*-isopropylidene-3-*O*-(2-bromo-1-ethoxyethyl)-D-glucal (8b).** This compound was prepared by the general method from alcohol **8a** (300 mg, 0.48 mmol) followed by chromatography (PE–EtOAc, 8:2) to give **8b** (503 mg, 92%) as a colorless oil: $^1$H NMR (for two isomers) $\delta$ 1.22 (t, $J$ = 7.0 Hz, 3H one isomer), 1.24 (t, $J$ = 7.0 Hz, 3H other isomer), 1.41 (s, 3H one isomer), 1.42 (s, 3H one isomer), 1.52 (s, 3H other isomer), 1.53 (s, 3H other isomer), 3.32 (m, 1H), 4.0–3.5 (m, 3H), 4.33 (m, 1H), 4.72 (m, 1H), 4.85 (t, $J$ = 5.4 Hz, 1H one isomer), 4.95 (t, $J$ = 5.4 Hz, 1H other isomer), 6.34 (dt, $J$ = 1.9, 6.2 Hz, 1H); $^{13}$C NMR 15.0, 15.1, 18.9, 19.0, 28.9, 29.0, 32.4, 32.5, 61.5, 61.6, 62.0, 62.6, 69.5, 69.7, 71.2, 71.6, 72.3, 72.5, 99.5, 99.6, 101.0, 102.3, 102.4, 144.5, 144.7; MS $m/z$ 354 $(M + NH_4)^+$.

**4,6-Di-*O*-benzylidene-3-*O*-(2-bromo-1-ethoxyethyl)-D-glucal (9b).** This compound was prepared according to the general method from alcohol **9a** (256 mg, 0.48 mmol) followed by chromatography (PE–EtOAc, 95:5) to give **9b** (273 mg, 66%) as a colorless oil. More careful chromatography of the mixture (PE–EtOAc, 98:2) afforded pure materials of each isomer.

**For the faster moving isomer**: $[\alpha]^{21}_D$ +16.9° ($c$ 2.4); $^1$H NMR $\delta$ 1.09 (t, $J$ = 7.0 Hz, 3H), 3.38 (d, $J$ = 5.0 Hz, 2H), 3.55 (m, 1H), 3.79 (m, 1H), 3.83 (d, $J$ = 10.2 Hz, 1H), 3.92 (dd, $J$ = 3.5 Hz, 10.5 Hz, 1H), 4.24 (m, 2H), 4.47 (dd, $J$ = 5.3, 10.5 Hz, 1H), 4.88 (t, $J$ = 5.3 Hz, 1H), 4.95 (t, $J$ = 6.2 Hz, 1H), 5.59 (s, 1H), 6.42 (d, $J$ = 6.2 Hz, 1H), 7.36 (m, 3H), 7.48 (m, 2H); $^{13}$C NMR $\delta$ 15.0, 32.4, 62.5, 63.8, 64.3, 68.8, 77.8, 99.7, 100.5, 101.8, 104.9, 126.2, 128.2, 129.1, 137.2, 145.9; MS $m/z$ 404 $(M + NH_4)^+$.

**For the slower moving isomer**: $[\alpha]^{21}_D$ +103.6° ($c$ 0.8); $^1$H NMR $\delta$ 1.23 (t, $J$ = 7.0 Hz, 3H), 3.39 (dd, $J$ = 7.0, 10.5 Hz, 2H), 3.51 (dd, $J$ = 3.7, 10.5 Hz, 1H), 3.94 (dd, $J$ = 3.4, 10.4 Hz, 1H), 4.23 (m, 1H), 4.30 (dd, $J$ = 3.5, 6.1 Hz, 1H), 3.79 (m, 1H), 3.83 (d, $J$ = 10.2 Hz, 1H), 3.92 (dd, $J$ = 3.5 Hz, 10.5 Hz, 1H), 4.24 (m, 2H), 4.46 (dd, $J$ = 5.3, 10.5 Hz, 1H), 4.98 (m, 2H), 5.58 (s, 1H), 6.44 (d, $J$ = 6.1 Hz, 1H), 7.39 (m, 3H), 7.49 (m, 2H); $^{13}$C NMR $\delta$ 15.2, 32.1, 61.5, 64.4, 66.5, 68.7, 78.7, 99.6, 99.7, 101.9, 102.3, 126.1, 128.4, 129.2, 137.1, 146.2; MS $m/z$ 404 $(M + NH_4)^+$.

**Preparation of Tricyclic Acetals 11.** Bromo acetals **8b** (60 mg, 0.18 mmol) were subjected to radical cyclization (method A) to give after flash chromatography (PE–EtOAc, 9:1) the tricyclic acetals **11** (36 mg, 80%). In a different experiment, **8b** (454 mg, 1.35 mmol) was allowed to react according to method B and provided the acetals **11** (263 mg, 76%) as a 1:1 mixture of isomers. A more careful chromatography (PE–EtOAc, 95:5) led to the isolation of pure samples.

**For the faster moving isomer**: mp 56–57 °C, $[\alpha]^{21}_D$ −111.5° ($c$ 1.0); $^1$H NMR $\delta$ 1.16 (t, $J$ = 7.0 Hz, 3H), 1.44 (s, 3H), 1.51 (s, 3H), 1.93 (dd, $J$ = 7.1, 12.6 Hz, 3H), 2.09 (dt, $J$ = 5.1, 12.6 Hz, 1H), 2.73 (m, 1H), 3.06 (dt, $J$ = 5.5, 10.0 Hz, 1H), 3.45 (m, 1H), 3.53 (t, $J$ = 8.0 Hz, 1H), 3.60–4.00 (m, 5H), 4.11 (t, $J$ = 8.0 Hz, 1H), 5.18 (d, $J$ = 4.9 Hz, 1H); $^{13}$C NMR $\delta$ 15.2, 19.1, 29.2, 35.9, 37.4, 62.1, 62.7, 66.8, 70.5, 74.1, 78.0, 99.7, 103.0; MS $m/z$ 259 $(MH)^+$, 276 $(M + NH_4)^+$.

Anal. Calcd for $C_{13}H_{22}O5$: C, 60.45; H, 8.58. Found: C, 60.71; H, 8.39.

**For the slower moving isomer**: $[\alpha]^{21}_D$ −15.9° ($c$ 1.1); $^1$H NMR $\delta$ 1.19 (t, $J$ = 7.0 Hz, 3H), 1.43 (s, 3H), 1.51 (s, 3H), 2.01 (m, 1H), 2.35 (m, 1H), 2.49 (m, 1H), 3.05 (dt, $J$ = 5.5, 10.0 Hz, 1H), 3.49 (m, 1H), 3.18–4.10 (m, 7H), 5.25 (d, $J$ = 4.7 Hz, 1H); $^{13}$C NMR $\delta$ 15.2, 19.1, 29.2, 35.6, 40.1, 62.4, 63.6, 66.7, 71.3, 72.61, 78.3, 99.6, 105.0; MS $m/z$ 259 $(MH)^+$, 276 $(M+NH_4)^+$.

Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.37; H, 8.34.

**Preparation of Tricyclic Acetals 12.** Bromo acetals **9b** were subjected to the standard radical cyclization conditions according to method A (58 mg, 0.151 mmol) or method B (230 mg, 0.60 mmol). Flash chromatography (PE–EtOAc, 9:1) of the reaction crudes afforded an inseparable mixture of acetals **12** (37 mg, 80% and 136 mg, 74% respectively): $^1$H NMR (selected signals) $\delta$ 1.18 (t, $J$ = 7.0 Hz, 3H one isomer), 1.23 (t, $J$ = 7.0 Hz, 3H other isomer), 5.24 (d, $J$ = 6.3 Hz, 1H one isomer), 5.35 (dd, $J$ = 4.0, 5.6 Hz, 1H other isomer), 5.58 (s, 1H both isomers); $^{13}$C NMR $\delta$ 15.1, 15.4, 35.3, 35.4, 37.7, 39.0, 63.8, 65.8, 66.2, 67.5, 68.0, 69.4, 69.5, 73.7, 76.6, 78.3, 78.8, 102.6, 102.7, 104.2, 126.4, 128.1, 128.2, 129.0, 137.4; MS $m/z$ 307 $(MH)^+$, 324 $(M + NH_4)^+$.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.45; H, 7.24. Found: C, 66.23; H 7.07.

**1,2-Dideoxy-2-*C*-(acetoxymethyl)-3-*O*-acetyl-4,6-*O*-isopropylidene-D-mannopyranose (13).** (Bromomethyl)silyl ether **8c**, prepared by the standard procedure from alcohol **8a** (200 mg, 1.07 mmol), was subjected to radical cyclization (method B) to furnish a reaction crude that was submitted to sequential Tamao oxidation and acetylation. Flash chromatography (PE–EtOAc, 9:1) afforded recovered **acetyl-8a** (30 mg, 12%) and **13** (224 mg, 70%): $[\alpha]^{21}_D$ −94.3° ($c$ 0.9); $^1$H NMR $\delta$ 1.32 (s, 3H), 1.42 (s, 3H), 2.00 (s, 3H), 2.04 (s, 3H), 2.45 (m, 1H), 3.20 (dt, $J$ = 5.2, 9.9 Hz, 1H), 3.56 (d, $J$ = 12 Hz, 1H), 3.67 (m, 2H), 3.81 (dd, $J$ = 5.2, 10.7 Hz, 1H), 3.95 (d, $J$ = 11.9 Hz, 1H), 4.16 (t, $J$ = 9.8 Hz, 1H), 4.26 (dd, $J$ = 4.1, 11.1 Hz, 1H), 2.72 (dd, $J$ = 6.0, 10.1 Hz, 1H); $^{13}$C NMR $\delta$ 19.1, 19.2, 20.8, 21.0, 39.1, 60.9, 62.1, 67.2, 69.4, 72.1, 73.8, 99.9, 170.3, 170.9; MS $m/z$ 303 $(MH)^+$, 320 $(M + NH_4)^+$.

Anal. Calcd for $C_{14}H_{22}O_7$: C, 55.62; H, 7.33. Found: C, 55.74; H, 7.14.

**1,3,6-Trideoxy-2-*C*-(acetoxymethyl)-3,4-di-*O*-acetyl-L-mannopyranose (14).** (Bromomethyl)silyl ether **10b**, prepared by the general procedure (carried out at −20 °C) from diol **10a** (2 g, 15.4 mmol), was subjected to radical cyclization (method B) to furnish a reaction crude that was submitted to sequential Tamao oxidation and acetylation. Flash chromatography (PE–EtOAc, 8:2) afforded recovered di-*O*-acetylrhamnal (890 mg, 27%) and **14** (2.16 g, 51%): $[\alpha]^{21}_D$ +27.1° ($c$ 1.0); $^1$H NMR $\delta$ 1.14 (d, $J$ = 6.1 Hz, 3H), 1.99 (s, 3H), 2.00 (s, 3H), 2.01 (s, 3H), 2.39 (m, 1H), 3.34 (m, 1H), 3.48 (bd, $J$ = 12.1 Hz, 1H), 3.95 (dd, $J$ = 1.5, 12.1 Hz, 1H), 4.17 (t, $J$ = 10.1 Hz, 1H), 4.30 (dd, $J$ = 4.0, 10.1 Hz, 1H), 4.77 (t, $J$ = 9.8 Hz, 1H), 5.02 (dd, $J$ = 5.8, 10.1 Hz, 1H); $^{13}$C NMR, 17.8, 20.6, 20.7, 38.9, 60.5, 66.0, 71.3, 72.6, 75.1, 169.7, 170.1, 170.6; MS $m/z$ 306 $(M + NH_4)^+$.

Anal. Calcd for $C_{13}H_{20}O_7$: C, 54.16; H, 6.99. Found: C, 53.89; H, 6.73.

**Cyclization Reaction of Bromo Acetals 8b in the Presence of Acrylonitrile. Preparation of Bicyclic Acetals 15a.** Bromo acetals **8b** (60 mg, 0.18 mmol) were subjected to the general radical cyclization conditions according to method A in the presence of acrylonitrile (117.2 mL, 1.8 mmol, 10 equiv). Careful flash chromatography (PE–EtOAc, 9:1) of the reaction mixture allowed for isolation of both isomers of **15a**.

**For the faster moving isomer** (19 mg, 34% yield): mp 87–89 °C; $[\alpha]^{21}_D$ −48.0° ($c$ 0.8); $^1$H NMR $\delta$ 1.17 (t, $J$ = 7.0 Hz, 3H), 1.43 (s, 3H), 1.53 (s, 3H), 1.70 (m, 1H), 1.81 (q, $J$ = 7.1 Hz, 2H), 2.06 (dd, $J$ = 8.1, 13.0 Hz, 1H), 2.46 (t, $J$ = 7.1 Hz, 1H), 2.60 (m, 1H), 3.42 (m, 2H), 3.65–4.00 (m, 5H), 4.16 (t, $J$ = 8.1 Hz, 1H), 5.17 (d, $J$ = 5 Hz, 1H); $^{13}$C NMR $\delta$ 13.5, 13.6, 15.1, 19.0, 29.1, 29.9, 36.3, 40.9, 62.7, 62.9, 64.7, 72.1, 72.7, 77.1, 99.5, 102.7, 119.2; MS $m/z$ 312 $(MH)^+$, 329 $(M + NH_4)^+$.

Anal. Calcd for $C_{16}H_{25}O_5N$: C, 61.72; H, 8.09; N, 4.50. Found: C, 61.51; H, 7.86; N, 4.12.

**For the slower moving isomer** (23 mg, 41% yield): $[\alpha]^{21}_D$ +65.0° ($c$ 1.25); $^1$H NMR $\delta$ 1.11 (t, $J$ = 7.1 Hz, 3H), 1.34 (s, 3H), 1.42 (s, 3H), 1.81–1.72 (m, 3H), 2.17 (m, 1H), 2.39–2.30 (m, 3H), 3.25 (m, 1H), 3.38 (m, 1H), 3.60 (t, $J$ = 10 Hz, 1H), 3.80–3.69 (m, 2H),4.06–3.93 (m, 3H), 5.09 (dd, $J$ = 1.4, 2.3 Hz, 1H); $^{13}$C NMR $\delta$ 13.6, 15.2, 19.0, 29.1, 29.9, 36.0, 42.4, 63.1, 63.2, 64.8, 71.9, 72.5, 78.8, 99.5, 104.0, 119.3; MS $m/z$ 312 $(MH)^+$, 329 $(M + NH_4)^+$. Anal. Calcd for $C_{16}H_{25}O_5N$: C, 61.72; H, 8.09; N, 4.50. Found: C, 61.66; H 7.94; N, 4.26.

In a different experiment, the mixture of bromo acetals **8b** (61 mg, 0.181 mmol) was treated according to the conditions reported in method B in the presence of acrylonitrile (117 mL, 1.8 mmol) to yield after chromatography the acetals **15a** as a 1:1 mixture (44 mg, 78% yield).

**Cyclization Reaction of Iodo Acetals 8d in the Presence of Acrylonitrile.** A solution of bromo acetals **8b** (66 mg, 0.196 mmol) in ethyl methyl ketone (10 mL) was treated with NaI (293 mg, 1.96 mmol) and heated to reflux. After 4 h, the reaction was diluted with $CH_2Cl_2$, washed with sodium bisulfite, and dried. Analysis by $^1H$ NMR of the resulting residue showed a 1:1 mixture of **8b** and **8d**, which was then resubjected to the same reaction conditions. Heating was continued for 3 h, and after workup the $^1H$ NMR analysis showed a 95:5 ratio of **8d**:**8b** which was used without further purification in the next reaction. A thoroughly degassed solution of the resulting iodo acetals **8d** in benzene was subjected to the radical reaction conditions in the presence of acrylonitrile (127 mL, 1.96 mmol) to yield after chromatography the acetals **15a** (53 mg, 87%) as a 1:1 mixture of isomers.

**Cyclization Reaction of Bromo Acetals 8b in the Presence of *tert*-Butyl Isocyanide. Preparation of Glycosyl Cyanides 15b.** Bromo acetals **8b** (90 mg, 0.27 mmol) were subjected to the general radical cyclization conditions according to method A in the presence of *tert*-butyl isocyanide (603.7 mL, 5.34 mmol, 20 equiv). Flash chromatography (PE–EtOAc, 9:1) of the reaction mixture afforded the reduced products **11** (22 mg, 31%) along with the glycosyl cyanides **15b** (21 mg, 28% yield): $^1H$ NMR (for two isomers) $\delta$ 1.15 (t, $J$ = 7.1 Hz, 3H one isomer), 1.20 (s, $J$ = 7.1 Hz, 3H other isomer), 1.44 (s, 3H), 1.50 (s, 3H), 1.99 (m, 1H one isomer), 2.06 (m, 2H other isomer), 2.47 (m, 1H one isomer), 2.80 (m, 1H one isomer), 3.06 (m, 1H other isomer), 3.40–4.30 (m, 7H), 4.83 (bd, 1H one isomer), 4.86 (d, $J$ = 2.5 Hz, 1H other isomer), 5.18 (t, $J$ = 3.4 Hz, 1H one isomer), 5.24 (dd, $J$ = 4.0, 6.0 Hz, 1H); $^{13}C$ NMR $\delta$ 15.1, 15.2, 18.9, 19.0, 28.9, 29.0, 35.4, 35.6, 40.5, 42.5, 61.4, 61.7, 62.8, 63.8, 64.5, 64.6, 64.7, 64.8, 67.4, 68.1, 71.4, 72.8, 75.9, 76.5, 99.8, 99.9, 102.3, 102.4, 104.2, 104.3, 117.3; MS $m/z$ 284 $(MH)^+$, 301 $(MNH_4)^+$.

Anal. Calcd for $C_{14}H_{21}O_5N$: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.17; H, 7.21; N, 5.03.

In a different experiment the mixture of bromo acetals **8b** (1.04 g, 3.075 mmol) was treated according to the conditions reported in method B in the presence of *tert*-butyl isocyanide (6.95 mL, 61.5 mmol) to yield after chromatography the glycosyl cyanides **15b** as a 1:1 mixture at the acetalic carbon (661 mg, 76% yield).

**Cyclization Reaction of Bromo Acetals 8b in the Presence of Allyltributyltin. Preparation of *C*-Allyl Glycosides 15c.** Bromo acetals **8b** (50 mg, 0.148 mmol), allyltributyltin (91.2 mL, 0.297 mmol), and AIBN (4.9 mg, 0.0297 mmol) were heated in degassed benzene (297 mL, 2 mL/mmol) at 80 °C for 36 h. Concentration in vacuo and flash chromatography of the reaction crude afforded **15c** (30 mg, 68%) as a 1:1 mixture of epimers: $^1H$ NMR $\delta$ 1.16 (t, $J$ = 7.1 Hz, 3H one isomer), 1.19 (t, $J$ = 7.1 Hz, 3H other isomer), 1.42 (s, 3H), 1.50 (s, 3H), 1.75 (m, 1H one isomer), 1.90 (m, 1H one isomer), 2.01 (dd, $J$ = 4.5, 13.0 Hz, 1H one isomer), 2.20–2.52 (m, 3H), 2.64 (m, 1H one isomer), 3.28–3.51 (m, 2H), 3.62–3.90 (m, 4H), 4.11 (m, 1H), 5.10 (m, 2H), 5.78 (m, 1H); $^{13}C$ NMR $\delta$ 15.1, 15.2, 19.0, 19.1, 29.1, 29.2, 36.4, 36.6, 38.3, 38.4, 40.4, 42.0, 62.7, 63.0, 63.1, 63.3, 64.3, 64.5, 72.7, 73.5, 74.4, 77.2, 78.1, 99.4, 99.5, 102.7, 104.2, 117.4, 117.5, 134.0, 134.2; MS $m/z$ 299 $(MH)^+$.

Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78. Found: C, 64.27; H, 8.54.

**Cyclization reaction of Bromo Acetals 8b in the Presence of Ethyl (*Z*)-(Tributylstannyl)propenoate. Preparation of Crotonates 15d.** Bromo acetals **8b** (476 mg, 1.41 mmol), a 3:1 mixture of (*Z*)- and (*E*)-ethyl (tributylstannyl)propenoate (1.1 g, 2.86 mmol), and AIBN (37.1 mg, 0.22 mmol) were heated in degassed toluene (2.12 mL, 1.5 mL/mmol) at 80 °C for 24 h. Concentration in vacuo and flash chromatography of the reaction crude afforded **15d-*cis*** (40 mg, 8%) and **15d-*trans*** (316 mg, 63%), both as a 1:1 mixture of isomers at the acetalic center.

**For 15d-*cis*:** $^1H$ NMR $\delta$ 1.16 (t, $J$ = 7.1 Hz, 3H one isomer), 1.19 (t, $J$ = 7.1 Hz, 3H other isomer), 1.28 (t, $J$ = 7.0 Hz, 3H), 1.43 (s, 3H), 1.52 (s, 3H), 1.98 (m, 2H), 2.52 (m, 1H), 3.46 (m, 2H), 3.66–4.04 (m, 4H), 4.17 (m, 3H), 5.18 (m, 1H), 5.41 (t, $J$ = 8.0 Hz, 1H one isomer), 5.48 (bd, $J$ = 6.2 Hz, 1H other isomer), 5.87 (bd, $J$ = 11.8 Hz, 1H), 6.16 (dd, $J$ = 8.7, 11.8 Hz, 1H one isomer), 6.41 (dd, $J$ = 7.9, 11.8 Hz, 1H other isomer); $^{13}C$ NMR $\delta$ 14.1, 14.2, 14.3, 15.1, 15.2, 15.3, 19.0, 19.1, 29.1, 29.2, 35.4, 36.6, 41.4, 43.9, 60.4, 60.5, 62.7, 62.8, 62.9, 63.4, 64.8, 65.0, 72.2, 72.5, 77.3, 99.5, 99.6, 102.9, 103.0, 104.0, 104.1, 121.2, 121.7, 146, 148, 165.8, 165.9; MS $m/z$ 357 $(MH^+)$, 374 $(M + NH_4)^+$.

Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.92. Found: C, 60.38; H 7.67.

**For 15d-*trans*:** $^1H$ NMR $\delta$ 1.16 (t, $J$ = 7.1 Hz, 3H one isomer), 1.19 (t, $J$ = 7.1 Hz, 3H other isomer), 1.28 (t, $J$ = 7.0 Hz, 3H), 1.42 (s, 3H), 1.51 (s, 3H), 1.83–1.92 (m, 1H), 3.11 (dd, $J$ = 8.1, 13.1 Hz, 1H one isomer), 2.25 (ddd, $J$ = 5.5, 9.6, 13.1 Hz, 1H one isomer), 2.56 (m, 1H, one isomer), 2.75 (quint, $J$ = 8.4 Hz, 1H one isomer), 3.42 (m, 2H), 3.64–3.96 (m, 4H), 4.08–4.24 (m, 3H), 4.33 (m, 1H one isomer), 4.64 (m, 1H other isomer), 5.18 (d, $J$ = 4.3 Hz, 1H), 6.04 (d, $J$ = 15.8 Hz, 1H), 6.84 (ddd, $J$ = 5.0, 8.1, 15.8 Hz, 1H); $^{13}C$ NMR $\delta$ 14.1, 14.2, 15.0, 15.1, 15.2, 15.3, 18.8, 18.9, 29.0, 29.1, 35.8, 36.1, 40.3, 41.8, 60.6, 62.7, 62.8, 63.2, 64.9, 65.3, 72.5, 72.7, 72.9, 73.7, 77.0, 78.7, 99.4, 99.5, 102.6, 102.7, 104.0, 104.1, 122.7, 123.0, 145.2, 146.3, 165.8, 165.9; MS $m/z$ 357 $(MH^+)$, 374 $(M + NH_4)^+$.

Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.92. Found: C, 60.43; H, 7.84.

**Cyclization Reaction of Bromo Acetals 8c in the Presence of Acrylonitrile. Preparation of C-Glycoside 16.** (Bromomethyl)silyl ether **8c**, prepared by the standard procedure from alcohol **8a** (400 mg, 2.14 mmol), was subjected to radical cyclization (method B) in the presence of acrylonitrile (1.1 mL, 21.4 mmol) to furnish a reaction crude that was submitted to sequential Tamao oxidation and acetylation. Flash chromatography (PE–EtOAc, 9:1 and then 6:4) afforded recovered **8** (R = Ac) (89 mg, 12%) and the C-glycoside **16** (463 mg, 61%): m p 182–184 °C; $[\alpha]^{21}_D$ −47.0° ($c$ 0.6); $^1H$ NMR $\delta$ 1.35 (s, 3H), 1.45 (s, 3H), 1.78 (m, 2H), 2.05 (s, 3H), 2.08 (s, 3H), 2.42 (m, 4H), 3.42 (dt, $J$ = 5.1, 9.8 Hz, 1H), 3.71 (q, $J$ = 10.1 Hz, 2H), 3.82 (dd, $J$ = 5.2, 10.8 Hz, 1H), 4.05 (m, 1H), 4.17 (t, $J$ = 10.2 Hz, 1H), 4.33 (dd, $J$ = 3.3, 10.9 Hz, 1H), 5.10 (dd, $J$ = 5.7, 10.4 Hz, 1H); $^{13}C$ NMR $\delta$ 14.0, 19.2, 20.9, 21.1, 25.9, 29.1, 41.9, 61.6, 62.4, 66.3, 69.2, 69.6, 73.2, 100.2, 118.7, 170.3, 170.9; MS $m/z$ 356 $(MH)^+$, 373 $(M + NH_4)^+$. Anal. Calcd for $C_{17}H_{25}O_7N$: C, 57.45; H, 7.09; N, 3.94. Found: C, 57.21; H, 6.87; N, 3.73.

**Cyclization Reaction of (Bromomethyl)silyl Ethers 10b in the Presence of Acrylonitrile. Preparation of C-Glycoside 17a.** (Bromomethyl)silyl ether **10b**, prepared by the standard procedure from diol **10a** (202 mg, 1.55 mmol), was subjected to radical cyclization (method B) in the presence of acrylonitrile (921 mL, 15.5 mmol) to afford a reaction crude that was subjected to sequential Tamao oxidation and acetylation. Flash chromatography (PE–EtOAc, 9:1) afforded recovered **10** ($R_1 = R_2$ = Ac) (85 mg, 25%) and the C-glycoside **17a** (58 mg, 32%): $[\alpha]^{21}_D$ −8.3° ($c$ 1.2); $^1H$ NMR $\delta$ 1.30 (d, $J$ = 6.6 Hz, 3H), 1.88 (m, 1H), 2.06 (s, 3H), 2.08 (s, 3H), 2.09 (s, 3H), 2.08 (m, 1H), 2.29 (m, 1H), 2.50 (m, 2H), 3.85 (quint, $J$ = 6.6 Hz, 1H), 3.99 (m, 1H), 4.10 (dd, $J$ = 7.8, 11.2 Hz, 1H), 4.22 (dd, $J$ = 5.9, 11.2 Hz, 1H), 4.76 (t, $J$ = 6.6 Hz, 1H), 5.16 (dd, $J$ = 4.8 Hz, 6.6 Hz, 1H); $^{13}C$ NMR $\delta$ 13.6, 16.7, 20.8, 20.9, 27.2, 40.1, 60.9, 68.3, 68.6, 69.3, 70.4, 119.0, 169.6, 169.7, 170.6; MS $m/z$ 359 $(M + NH_4)^+$.

Anal. Calcd for $C_{16}H_{23}O_7N$: C, 56.3; H, 6.79; N, 4.10. Found: C, 56.12; H, 7.13; N, 3.93.

**Cyclization Reaction of (Bromomethyl)silyl Ethers 10b in the Presence of Methyl Acrylate. Preparation of C-Glycoside 17b.** (Bromomethyl)silyl ether **10b**, prepared by the standard procedure from diol **10a** (170 mg, 1.30 mmol), was subjected to radical cyclization (method B) in the presence of methyl acrylate (1.17 mL, 13.0 mmol) to afford a reaction mixture that was subjected to sequential Tamao oxidation and acetylation. Flash chromatography (PE–EtOAc, 9:1) afforded recovered **10** ($R_1 = R_2$ = Ac) (66 mg, 23%) and the C-glycoside

**17b** (181 mg, 37%): $[\alpha]^{21}_D$ +4.6° (*c* 1.8); $^1$H NMR δ 1.15 (d, *J* = 6.4 Hz, 3H), 1.77 (m, 1H), 2.00 (s, 3H), 2.01 (s, 3H), 2.02 (s, 3H), 2.13 (m, 1H), 2.25 (m, 1H), 2.38 (m, 2H), 3.65 (s, 3H), 3.70 (quint, *J* = 6.6 Hz, 1H), 3.87 (dd, *J* = 3.8, 10.7 Hz, 1H), 4.09 (dd, *J* = 8.5, 11.2 Hz, 1H), 4.23 (dd, *J* = 5.2, 11.2 Hz, 1H), 4.71 (t, *J* = 6.6 Hz, 1H0, 5.15 (dd, *J* = 6.6 Hz, 8.1 Hz, 1H); $^{13}$C NMR δ 17.4, 20.8, 26.0, 30.3, 41.0, 51.6, 61.3, 68.0, 69.3, 70.8, 71.2, 69.7, 169.8, 170.6, 173.4; MS *m/z* 392 $(M + NH_4)^+$, 375 $(MH)^+$.

Anal. Calcd for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00. Found: C, 54.73; H, 6.86.

**Cyclization Reaction of Bromo Acetals 8b in the Presence of Enone 18. Preparation of 19.** Bromo acetals **8b** (78 mg, 0.23 mmol) were subjected to the general radical cyclization conditions according to method A in the presence of enone **18** (287.3 mg, 0.69 mmol). Flash chromatography (PE−EtOAc,9:1) of the reaction mixture afforded **19** (109 mg, 70%). More careful flash chromatography (PE−EtOAc, 95:5) allowed the isolation of the two single isomers at the acetalic center.

**For the faster moving isomer**: $[\alpha]^{21}_D$ +34.9° (*c* 1.2); $^1$H NMR δ 1.23 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 6.9 Hz, 3H), 1.43 (s, 3H), 1.53 (s, 3H), 2.00 (m, 2H), 2.34 (m, 2H), 2.66 (m, 2H), 3.22−4.22 (m, 8H), 4.99 (d, *J* = 4.9 Hz, 1H), 5.17 (d, *J* = 4.8 Hz, 1H), 7.18−7.55 (m, 15H); $^{13}$C NMR δ 15.2, 19.1, 29.1, 34.9, 36.2, 37.8, 41.7, 62.7, 63.0, 63.1, 63.4, 65.1, 72.0, 74.3, 74.9, 77.2, 86.9, 98.9, 99.4, 102.8, 127.0, 127.2, 127.8, 128.6, 128.7, 143.8, 210.0; MS *m/z* 673 $(MH)^+$, 690 $(M + NH_4)^+$.

Anal. Calcd for $C_{40}H_{48}O_9$: C, 71.41; H, 7.19. Found: C, 71.17; H 7.01.

**For the slower moving isomer**: $[\alpha]^{21}_D$ +28.3° (*c* 1.2); $^1$H NMR δ 1.26 (t, *J* = 6.9 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.43 (s, 3H), 1.52 (s, 3H), 1.84 (m, 1H), 2.23 (m, 2H), 2.37 (m, 1H), 2.55 (m, 2H), 3.18−4.22 (m, 8H), 4.94 (d, *J* = 4.6 Hz, 1H), 5.18 (dd, *J* = 1.7, 2.8 Hz, 1H), 7.20−7.50 (m, 15H); $^{13}$C NMR δ 15.1, 15.3, 19.1, 29.1, 35.5, 36.1, 39.4, 41.8, 63.0, 63.2, 63.3, 63.4, 65.0, 72.5, 73.9, 75.0 78.7, 86.7, 99.1, 99.5, 104.2, 127.0, 127.8, 128.7, 143.8,209.98; MS *m/z* 673 $(MH)^+$, 690 $(M + NH_4)^+$.

Anal. Calcd for $C_{40}H_{48}O_9$: C, 71.41; H, 7.19. Found: C, 71.19; H, 7.09.

**Cyclization Reaction of (Bromomethyl)silyl Ethers 10b in the presence of Enone 18. Preparation of C-Glycosides 20 and 21.** (Bromomethyl)silyl ether **10b**, prepared by the standard procedure from diol **10a** (378 mg, 2.6 mmol), was subjected to radical cyclization (method B) in the presence of enone **18** (1.07 g, 2.6 mmol) to afford a reaction crude that was subjected to sequential Tamao oxidation and acetylation. Flash chromatography (PE−EtOAc, 9:1) afforded recovered **10** ($R_1$ = $R_2$ = Ac) (131 mg, 27%), reduced **14** (77 mg, 10%), and the C-glycosides **20** (152 mg, 9%) and **21** (214 mg, 12%).

**For 20**: $[\alpha]^{21}_D$ −57.7° (*c* 0.5); $^1$H NMR δ 1.25 (d, *J* = 6.5 Hz, 3H), 1.26 (t, *J* = 6.9 Hz, 3H), 1.99 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 2.26 (dd, *J* = 4.1, 14.0 Hz, 1H), 2.42 (m, 2H), 2.62 (t, *J* = 14.0 Hz, 1H), 3.39 (dd, *J* = 6.0, 10.1 Hz, 1H), 3.47 (dd, *J* = 2.0, 10.1 Hz, 1H), 3.47 (dd, *J* = 2.0, 10.1 Hz, 1H), 3.64 (m, 1H), 3.87 (m, 1H), 3.96 (m, 2H), 4.25 (m, 3H), 4.78 (t, *J* = 7.1 Hz, 1H), 5.14 (dd, *J* = 4.6, 7.2 Hz, 1H), 5.22 (d, *J* = 4.5 Hz, 1H), 7.32 (m, 15H); $^{13}$C NMR δ 14.9, 16.9, 20.7, 20.8, 20.9, 37.4, 38.5, 39.0, 60.6, 62.8, 63.2, 68.4, 69.4, 70.5, 71.7, 74.4, 86.6, 97.9, 126.9, 127.7, 128.6, 143.6, 169.6, 170.6, 209.7; MS *m/z* 720 $(M + NH_4)^+$.

Anal. Calcd for $C_{40}H_{46}O_{11}$: C, 68.36; H, 6.60. Found: C, 68.16; H, 6.39.

**For 21**: $[\alpha]^{21}_D$ +21.9° (*c* 1.1); $^1$H NMR δ 1.22 (d, *J* = 5.9 Hz, 3H), 1.29 (t, *J* = 6.9 Hz, 3H), 2.02 (s, 6H), 2.05 (s, 3H), 2.60 (m, 3H), 3.36 (m, 3H), 3.63 (m, 2H), 3.96 (d, *J* = 11.3 Hz, 1H), 4.13 (m, 2H), 4.49 (dd, *J* = 10.7 Hz, 1H), 4.81 (t, *J* = 9.7 Hz, 1H), 5.10 (m, 2H), 5.79 (dd, *J* = 3.2, 6.3 Hz, 1H), 7.32 (m, 15H); $^{13}$C NMR δ 14.7, 18.0, 20.6, 20.7, 30.6, 36.1, 38.2, 60.1, 64.0, 64.8, 68.1, 68.9, 71.1, 71.9, 87.2, 90.7, 97.3, 127.1, 127.6, 128.6, 143.6, 169.6, 170.1, 170.9, 171.0. MS *m/z* 736 $(M + NH_4)^+$. Anal. Calcd for $C_{40}H_{45}O_{12}$: C, 66.93; H, 6.32. Found: C, 66.57; H, 6.07.

**Cyclization Reaction of Bromo Acetals 9b in the Presence of *tert*-Butyl Isocyanide. Preparation of Glycosyl Cyanides 22.** Bromo acetals **9b** (71 mg, 0.184 mmol) were subjected to the general radical cyclization conditions according to method A in the presence of *tert*-butyl isocyanide (0.416 mL, 3.68 mmol, 20 equiv). Evaporation of the solvent and $^1$H NMR and $^{13}$C NMR of the reaction crude showed the presence of six compounds which were tentatively assigned to reduced **22a** (≡**12**) and glycosyl cyanides **22b,c**. The ratio could be established by $^1$H NMR from the integration of the anomeric protons on **22b** and **22c** compared with the benzylic proton on the crude and was shown to be 6:5:1, **22a:22b:22c** (40 mg, 68%). $^{13}$C NMR showed signals corresponding to the CN groups of **22b,c** at 116.2, 116.9, 117.4, and 117.7.

**Cyclization Reaction of Bromo Acetal 9b(R) in the Presence of *tert*-Butyl Isocyanide. Preparation of Glycosyl Cyanides 23.** Bromo acetal **9b(R)** (200 mg, 0.52 mmol) was subjected to the general radical cyclization conditions according to method B in the presence of *tert*-butyl isocyanide (1.17 mL, 10.4 mmol). $^1$H NMR of the reaction crude showed the presence **23a**, **23b**, and **23c** in a ratio of 5:10:1. Flash chromatography (PE−EtOAc, 8:2) and separation by HPLC allowed for isolation of **23a** (27 mg, 17%) and **23a** (59 mg, 34%)). α-Isomer **23c** could not be obtained in pure form.

**For 23a**: $[\alpha]^{21}_D$ +19.2° (*c* 0.5); $^1$H NMR δ 1.23 (t, *J* = 7.0 Hz, 3H), 1.61 (d, *J* = 13.6 Hz, 1H), 2.12 (dt, *J* = 7.0, 13.6 Hz, 1H), 2.51 (m, 1H), 3.48 (m, 1H), 3.66 (t, *J* = 10.6 Hz, 1H), 3.78 (m, 2H), 3.90 (d, *J* = 12.1 Hz, 1H), 3.93 (m, 1H), 4.34 (m, 1H), 5.24 (d, *J* = 6.6 Hz, 1H), 5.58 (s, 1H), 7.34 (m 3H), 7.52 (m, 2H); $^{13}$C NMR δ 14.9, 32.4, 62.5, 63.8, 64.3, 68.8, 77.8, 99.7, 100.5, 101.8, 104.9, 126.1, 128.2, 129.1, 129.2, 137.2, 145.9, 146.0; MS *m/z* 307 $(MH)^+$, 324 $(M + NH_4)^+$.

**For 23b**: mp 158−160 °C; $[\alpha]^{21}_D$ +4.5° (*c* 0.4); $^1$H NMR δ 1.23 (t, *J* = 7.0 Hz, 3H), 1.93 (d, *J* = 14.2 Hz, 1H), 2.26 (dt, *J* = 6.3, 14.1 Hz, 1H), 2.74 (m, 1H), 3.50 (m, 1H), 3.81 (m, 3H), 4.39 (m, 1H), 4.96 (d, *J* = 10.9 Hz, 1H), 5.28 (d, *J* = 6.2 Hz, 1H), 5.58 (s, 1H), 7.35 (m 3H), 7.52 (m, 2H); $^{13}$C-NMR δ 15.4, 35.4, 42.5, 64.3, 66.1, 66.3, 68.6, 76., 77.2, 102.7, 104.5, 104.9, 117.5, 126.3, 128.3, 129.2, 136.9; MS *m/z* 332 $(MH)^+$, 349 $(M + NH_4)^+$.

Anal. Calcd for $C_{18}H_{21}O_5N$: C, 65.26; H, 6.34; N, 4.22. Found: C, 65.47; H, 6.18; N, 3.98.

**Cyclization Reaction of Bromo Acetal 21 in the Presence of *tert*-Butyl Isocyanide. Preparation of Glycosyl Cyanides 24.** Bromo acetal **21** (150 mg, 0.39 mmol) was subjected to the general radical cyclization conditions according to method B in the presence of *tert*-butyl isocyanide (0.88 mL, 7.8 mmol). $^1$H NMR of the reaction crude showed the presence of **24a**, **24b**, and **24c** in a ratio of 3:2:1. Flash chromatography (PE−EtOAc, 8:2) and separation by HPLC allowed for isolation **24a** (29 mg, 24%) and **24b** (16 mg, 12%). α-Isomer **24c** could not be obtain in pure form.

**For 24a**: $[\alpha]^{21}_D$ +29.6° (*c* 0.8); $^1$H NMR δ 1.19 (t, *J* = 7.1 Hz, 3H), 1.78 (dd, *J* = 5.7, 13.6 Hz, 1H), 1.89 (ddd, *J* = 4.0, 6.8, 13.6 Hz, 1H), 2.60 (m, 1H), 3.21 (t, *J* = 11.5 Hz, 1H), 3.51 (m, 1H), 3.79 (m, 4H), 4.34 (dd, *J* = 2.7, 10.4 Hz, 1H), 4.41 (m, 1H), 5.35 (dd, *J* = 3.9, 5.6 Hz, 1H), 5.58 (s, 1H), 7.34 (m 3H), 7.52 (m, 2H); MS *m/z* 307 $(MH)^+$, 324 $(M + NH_4)^+$.

**For 24b**: mp 120−122 °C, $[\alpha]^{21}_D$ +103.5° (*c* 0.4); $^1$H NMR δ 1.19 (t, *J* = 7.0 Hz, 3H), 2.07 (t, *J* = 3.5 Hz, 2H), 2.80 (m, 1H), 3.48 (m, 1H), 3.74 (m, 1H), 3.86 (m, 2H), 4.07 (d, *J* = 10.8 Hz, 1H), 4.37 (m, 1H), 4.45 (m, 1H), 5.36 (t, *J* = 4.5 Hz, 1H), 5.58 (s, 1H), 7.35 (m 3H), 7.52 (m, 2H); MS *m/z* 332 $(MH)^+$, 349 $(M + NH_4)^+$.

Anal. Calcd for $C_{18}H_{21}O_5N$: C, 65.26; H, 6.34; N, 4.22. Found: C, 65.08; H, 6.15; N, 3.81.

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