Acetal Transfer *via* Halonium-Ion Induced Reactions of Dipent-4-enyl Acetals: Scope and Mechanism[1,2]

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Introduction

Although there have been steady gains in the use of unprotected sugars for selective synthetic operations,[4] the nonenzymatic manipulation of complex sugars, whether as chiral synthons[5] or for oligosaccharide construction, will continue to require the judicious use of protecting groups. In this context cyclic acetals have a long history of service, their obvious advantages being the simultaneous protection of two hydroxyl groups and their easy removal under mild conditions.[6] With respect to their installation, the classical procedure involving acid-catalyzed reactions with aldehydes or ketones[6] has been supplanted by less harsh alternatives which, for example, can give access to products of kinetic control.[7] The hazards of acid-catalyzed procedures can be circumvented by using α,α-dihalomethyl derivatives with sodium hydride or pyridine as promoters,[8,9] but the yields from such reactions are usually only modest. The same holds true for a variety of neutral acetalization agents that have been described.[10–12] Of special interest is the use of arylhalocarbenes generated from aromatic halodiazirines which has been introduced by Vasella and co-workers.[13] These reagents have the unique advantage of being able to acetalize either *cis* or *trans* vicinal diols.

Our studies on *n*-pentenyl glycosides (NPGs)[14] have sensitized us to the advantages of synthesis and/or cleavage of glycosides under neutral conditions, the mechanism of which is outlined in Scheme 1a. Extension to the dipent-4-enyl acetals such as **3** may be envisaged as outlined in Scheme 1b, where the first stage of reaction leads to the oxocarbenium ion **5**. Capture of the latter by a diol would then afford the mixed acetal **7** which could react in a second episode to give the cyclic acetal **10**.

Glycosyl pent-4-enoates (*n*-pentenyl esters, NPEs), **1b**, have also been shown by Kunz[15] and us[16] to be excellent donors of the glycosyl oxocarbenium ion **2**. The corresponding dialkenoate acetals, **4** (Scheme 1b), were therefore of interest since a comparable cascade of ions leading to the same key intermediate **9**, *via* **6** and **8**, should also be possible.

In this paper we give a full account of our synthetic and mechanistic studies on the prototypical acetalating reagents **3** and **4**.[2]

Preparation of Reagents

The reagents **3** (**a** → **d**) were readily prepared under the standard conditions[17] shown in Scheme 2a using the aldehyde or ketone of interest, with a slight excess of 4-penten-1-ol in hexane at 0 °C. However, our efforts to prepare the corresponding dialkenoate derivatives met with modest success.[18] Thus, acceptable results were obtained only for the preparation of reagent **4a** from benzaldehyde and pent-4-enoic anhydride (Scheme 2b). With anisaldehyde under the same conditions, the acetalization turned out to be reversible which resulted in poor yields of **4b**. Only **4a** was chosen for subsequent investigation.

Exploratory Acetalizations (Conditions)

Reagents **3a**, **3c**, and **4a** were selected for exploratory acetalizations with the readily prepared diol **11**[19] as the test substrate. Preliminary experiments showed that acetal transfer failed in polar solvents such as dimethylformamide and dimethyl sulfoxide, and so acetonitrile was adopted for general use. The results in Table 1 show that for both benzylidination and isopropylidination (entries i, ii, vii, and viii) *N*-halosuccinimides gave moderate yields, a problem that was compounded by the sluggishness of reactions. With iodonium dicollidine perchlorate (IDCP)[20] acetalization was much faster (entry iii) but ketalization was still slow (entry ix), and interestingly, faster reactions and excellent yields seemed to go hand in hand. Notable, in entry ix, was the recovery of a substantial amount of the starting material **11**. These results are in keeping with our experiences with NPGs, where IDCP-promoted reactions sometimes "stop", leaving large amounts of unreacted partners.[14]

Protic acids have long been known to enhance the heterolytic cleavage of *N*-haloamides,[21] and the effect is apparent from entries iv and x (Table 1). It is evident

(1) This work was supported by grants from NIH (GM 41071) and NSF (CHE 9311 356).

(2) A preliminary account of this work has been published: Madsen, R.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1994**, 749.

(3) Danish Technical Research Council Postdoctoral Fellow.

(4) See, for example: Klotz, W.; Schmidt, R. R. *Liebigs Ann. Chem.* **1993**, 683. Bellosta, V.; Benhaddou, R.; Czernecki, S. *Synlett* **1993**, 861. Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 5500. Prenner, R. H.; Binder, W. H.; Schmid, W. *Liebigs Ann. Chem.* **1994**, 73. Haeckel, R.; Troll, C.; Fischer, H.; Schmidt, R. R. *Synlett* **1994**, 84. Lundt, I.; Madsen, R.; Al Daher, S.; Winchester, B. *Tetrahedron* **1994**, *50*, 7513 and references cited therein.

(5) Fraser-Reid, B.; Anderson, R. C. *Prog. Chem. Org. Nat. Prod.* **1980**, *39*, 1. Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*; Pergamon: New York, 1983.

(6) de Belder, A. N. *Adv. Carbohydr. Chem.* **1965**, *20*, 219. Bradly, R. F., Jr. *Adv. Carbohydr. Chem. Biochem.* **1971**, *26*, 197. de Belder, A. N. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 179. Clode, D. M. *Chem. Rev.* **1979**, *79*, 491.

(7) Gelas, J.; Horton, D. *Heterocycles* **1981**, *16*, 1587.

(8) Brimacombe, J. S.; Foster, A. B.; Jones, B. D.; Willard, J. J. *J. Chem. Soc.* C **1967**, 2404.

(9) Garegg, P. J.; Swahn, C.-G. *Methods in Carbohydrate Chemistry*; Whistler, R. L., BeMiller, J. N., Eds.; Academic Press: New York, 1980; Vol. VIII, p 317.

(10) Munavu, R. M.; Szmant, H. H. *Tetrahedron Lett.* **1975**, 4543

(11) Hanessian, S.; Lavallee, P.; Pernet, A. G. *Carbohydr. Res.* **1973**, *26*, 258.

(12) Oikawa, Y.; Nishi, T.; Yonemitsu, O. *Tetrahedron Lett.* **1983**, *24*, 4037.

(13) Li, C.; Vasella, A. *Helv. Chim. Acta* **1993**, *76*, 211.

(14) Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *Synlett* **1992**, 927.

(15) Kunz, H.; Wernig, P.; Schultz, M. *Synlett* **1990**, 631.

(16) Lopez, J. C.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1991**, 159.

(17) Roelofsen, D. P.; Wils, E. R. J.; van Bekkum, H. *Rec. Trav. Chim. Pays-Bas* **1971**, *90*, 1141.

(18) For preparation of other dialkanoate acetals see: McKusick, B. C. *J. Am. Chem. Soc.* **1948**, *70*, 1982. Michie, J. K.; Miller, J. A. *Synthesis* **1981**, 824. Kochhar, K. S.; Bal, B. S.; Deshpande, R. P.; Rajadhyaksha, S. N.; Pinnick, H. W. *J. Org. Chem.* **1983**, *48*, 1765.

(19) Akerfeldt, K.; Bartlett, P. A. *Carbohydr. Res.* **1986**, *158*, 137.

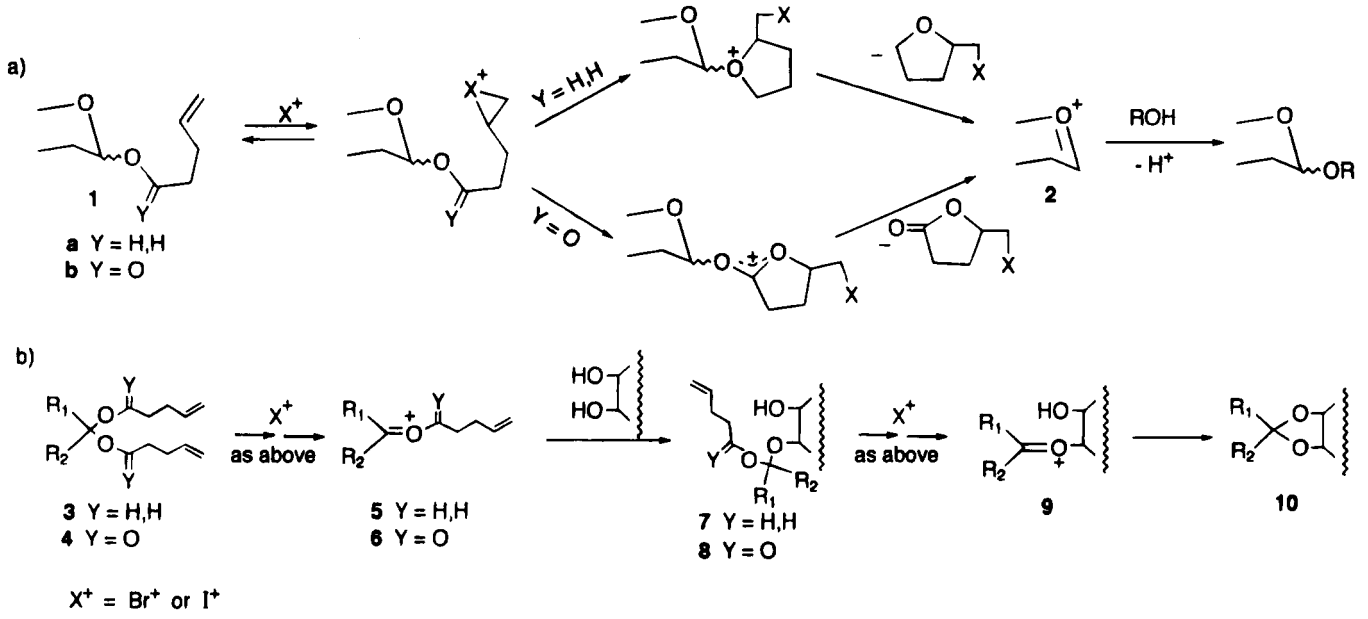
(20) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190.

(21) Lambert, F. L.; Ellis, W. D.; Parry, R. J. *J. Org. Chem.* **1965**, *30*, 304.

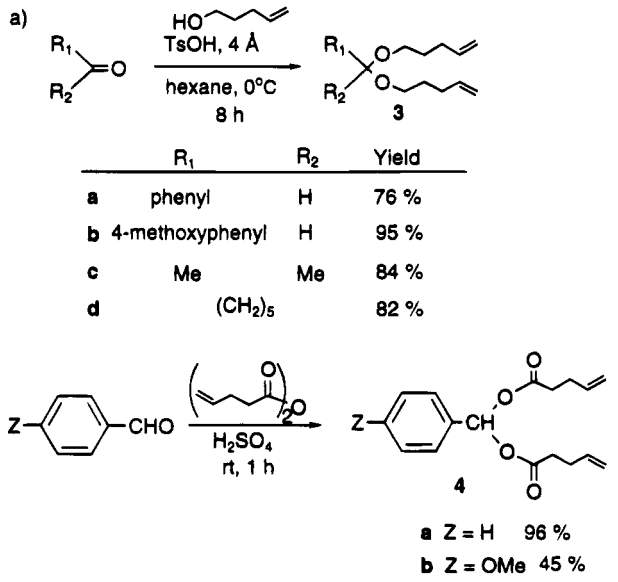
(22) Konradsson, P.; Mootoo, D. R.; McDevitt, R. E.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1990**, 270.

0022-3263/95/1960-0772$09.00/0

Scheme 1



Scheme 2



	R_1	R_2	Yield
a	phenyl	H	76 %
b	4-methoxyphenyl	H	95 %
c	Me	Me	84 %
d	$(CH_2)_5$		82 %

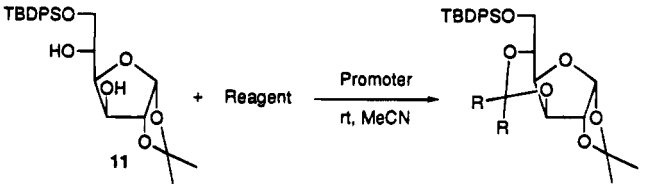
from entries v, vi and xi, xii that the combination of *N*-halosuccinimides and catalytic amounts of Lewis acids[22] also provide excellent results.

Entries xiii and xiv show that the dialkenoate acetal **4a** can be used for benzylidination, but that in terms of yields and reaction times, it does not compare favorably with the dialkyl counterpart **3a**. The sluggishness of the reaction may be rationalized by noting that the carbonyl group of the key intermediate **6** would induce destabilization relative to the ether counterpart **5** (Scheme 1).

Exploratory Acetalizations (Test Substrates)

The above exploratory studies showed that the use of NBS (and also NIS, which is more expensive) and an acid (Lewis or Brönsted) gave the best combination of yields and efficiency. The benzylidene reagent **3a** generally reacts faster than the ketal **3c** (entries iii *versus* ix and iv *versus* x), and this accounts for the fact that the weaker acid CSA is so much better with **3a** than **3c** (entries iv and x). On the other hand with the potent Lewis acids,

Table 1. Acetalization of 6-*O*-(*tert*-Butyldiphenylsilyl)-1,2-*O*-isopropylidene-α-d-glucofuranose



entry	reagent[a]	promoter[b]	reaction time	product	yield (%) (C-7 epimers)
i	**3a**	NBS	24 h	**12**	61 (1/1)
ii		NIS	18 h		77 (3/2)
iii		IDCP	5 min		79 (2/1)
iv		NBS/CSA	15 min		91 (6/1)
v		NBS/Et_3SiOTf	5 min		91 (2/1)
vi		NBS/BF_3·OEt_2	5 min		90 (2/1)
vii	**3c**	NBS	30 h	**13**	46
viii		NIS	20 h		49
ix		IDCP	30 h		2 (+ 79 of rec. **11**)
x		NBS/CSA	7 h		44 (+ 51 of rec. **11**)
xi		NBS/Et_3SiOTf	5 min		93
xii		NBS/BF_3·OEt_2	5 min		94
xiii	**4a**	NBS/Et_3SiOTf	1 h	**12**	45 (3/2)
xiv		NBS/CSA	8 h		60 (3/2)

[a] 1.2 Equiv of reagent was used. [b] 2.7 equiv of IDCP or the *N*-halosuccinimide (with or without 1.0 equiv of the acid) was used.

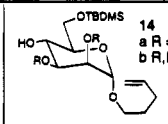
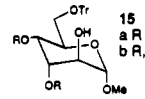
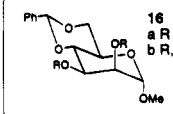
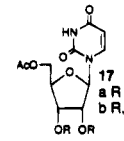
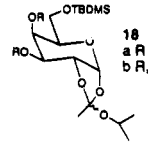
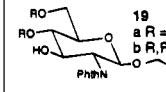
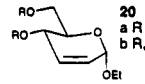
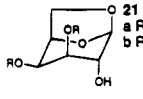
both reagents react rapidly. This is reminiscent of our observation that with IDCP there is substantial rate difference in the reactions of armed and disarmed NPGs, but with NIS/Et_3SiOTf, both react within the time it takes to run a TLC sample.[22]

With these data in hand we were now in a position to examine a wider array of test substrates in order to develop guidelines for use of the reagents.

The acetonating reagent **3c** was first tested on a variety of substrates to see how well acid labile protecting groups would survive under the reaction conditions (Table 2). Substrates **14a**[14] and **15a**[23] (entries i → iv) showed that silyl and trityl ethers are accommodated well

(23) Garegg, P. J.; Hoffman, J.; Lindberg, B.; Samuelsson, B. *Carbohydr. Res.* **1978**, *67*, 263.
(24) Buchanan, J. G.; Saunders, R. M. *J. Chem. Soc.* **1964**, 1796.

Table 2. Acetalization of Various Test Substrates

Entry	Substrates and Products	Reagent	Conditions (yields%)[a]
i	 14 a R = H b R,R = CMe_2	3c	A(87%)
ii		–	B(87%)
iii	 15 a R = H b R,R = CMe_2	–	A(86%)
iv		–	B(86%)
v	 16 a R = H b R,R = CMe_2	–	A(85%)
vi		–	B(88%)
vii	 17 a R = H b R,R = $C(CH_2)_5$	3d	A(72%)
viii		–	B(70%)
ix	 18 a R = H b R,R = CMe_2	3c	E(46%)
x	 19 a R = H b R,R = PhCH	3a	A(82%)
xi		–	B(80%)
xii		–	C(78%)
xiii	 20 a R = H b R,R = PhCH	–	D(45%)
xiv		–	A(66%)
xv		–	B(72%)
xvi		–	C(80%)
xvii	 21 a R = H b R,R = CHC_6H_4OMe (endo)	3b	C(82%)

[a] Key: NBS, Et_3SiOTf, MeCN, 5 min; (B) NBS, $BF_3{\cdot}OEt_2$, MeCN, 5 min; (C) NBS, CSA, MeCN, 15 min; (D) IDCP, MeCN, 5 min; (E) NIS (4 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (2 eq), MeCN, 24 h.

judging from the excellent yields in which products **14b** and **15b**,[24] respectively, were obtained. Similarly, the benzylidene ring of substrate **16a**[25] was unaffected during the formation of **16b**.[25]

The nucleoside **17a**[26] also underwent smooth acetalization with the cyclohexylidene derivative **3d** although the yields of the product, **17b**, were somewhat lower. In this context it should be noted that Marnett and coworkers[27] have used *n*-pentenyl ribosides for NBS-promoted preparation of nucleoside analogs.

The Lewis acid conditions were therefore suitable for the cases in entries i → viii.

On the other hand, the orthoester **18a**[28] was too acid labile even for these relatively mild conditions (entry ix). Indeed, even omission of the Lewis acid catalyst was only modestly rewarded. Inclusion of the highly hindered proton acceptor 2,6-di-*tert*-butyl-4-methylpyridine[29] was necessary, but even then the acetonide **18b** was obtained in only moderate amounts after 24 h of reaction.

For the benzylidenating agent **3a**, the allyl glycoside **19a**[30] was tested to show that allyl groups could survive the reaction conditions. This is in keeping with reports from our laboratory which demonstrate that allyl groups react much less readily under conditions for activating NPGs[31] and that allyl glycosides tend to give bromohydrins rather than suffer hydrolysis.[32]

In this connection, the conversion of **14a** into **14b** (Table 2) is intriguing, in that the glycosidic *n*-pentenyl group is unaffected during the acetalization. However, whether this chemoselectivity can be generalized to all NPGs is at present not known.

The hex-2-enopyranoside **20a**[33] was considered to be a more severe test substrate because of the extreme sensitivity to acids.[34] On the other hand, the double bond of **20a** has been shown to be highly resistant to electrophilic attack by Horton and co-workers[35] a circumstance which is readily rationalized by the presence of three deactivating allylic oxygens.[32]

The best yield of the benzylidenated product **20b**[36] is seen to be with camphorsulfonic acid (CSA), while IDCP gave the poorest (entries xvi and xiii), respectively. The last result (entry xiii) was attributed to the above-mentioned idiosyncrasies of IDCP. The lesser yields with the Lewis acids (entries xiv, xv) were expected because TLC monitors gave evidence of substantial decomposition. The high yields obtained with the weaker acid CSA is a tribute to the mildness of the reaction conditions.

In entry xvii it is noted that upon acetalization of the 1,6-anhydrogalactose **21a**,[37] the product **21b**[38] carries the aryl group in the more sterically hindered endo orientation. It should be noted that the reported synthesis employing 4-methoxy-α,α-dimethoxytoluene and *p*-toluenesulfonic acid also gave **21b** as the only product, in spite of the possibility for equilibration under the reaction conditions.[38]

Mechanistic Issues

Table 1 shows that acid catalysis is needed for the acetalization reactions to proceed at acceptable rates. A question may therefore be raised as to whether the process being observed is not simply an acid-catalyzed acetal transfer between the reagent and the diol concerned.

We have assumed that the role of the added acid is to enhance production of the halonium ion,[21,22] as shown in Scheme 3a and, by corollary, formation of the key oxocarbenium ion intermediate **5**. However, the bromonium ion could be functioning only to scavenge the pent-

(25) Patroni, J. J.; Stick, R. V.; Skelton, B. W.; White, A. H. *Aust. J. Chem.* **1988**, *41*, 91. Thiem, J.; Gerken, M.; Bock, K. *Liebigs Ann. Chem.* **1983**, 462.
(26) Ishido, Y.; Sakairi, N.; Okazaki, K.; Nakazaki, N. *J. Chem. Soc., Perkin Trans. 1* **1980**, 563.
(27) Chapeau, M.-C.; Marnett, L. J. *J. Org. Chem.* **1993**, *58*, 7258.
(28) Tsui, D. S. K.; Gorin, P. A. J. *Carbohydr. Res.* **1985**, *144*, 137.
(29) Barresi, F.; Hindsgaul, O. *Synlett* **1992**, 759.
(30) Pinto, B. M.; Reimer, K. B.; Morissette, D. G.; Bundle, D. R. *J. Org. Chem.* **1989**, *54*, 2650. El-Sokkary, R. I.; Silwanis, B. A.; Nashed, M. A.; Paulsen, H. *Carbohydr. Res.* **1990**, *203*, 319.
(31) Udodong, U. E.; Madsen, R.; Roberts, C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1993**, *115*, 7886.
(32) Rodebaugh, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1994**, *116*, 3155.
(33) Ferrier, R. J.; Prasad, N. *J. Chem. Soc. C* **1969**, 570.
(34) Albano, E.; Horton, D.; Tsuchiya, T. *Carbohydr. Res.* **1966**, *2*, 349.
(35) Albano, E. L.; Horton, D.; Lauterbach, J. H. *Carbohydr. Res.* **1969**, *9*, 149.
(36) Radatus, B.; Fraser-Reid, B. *Can. J. Chem.* **1972**, *50*, 2909. Mukhopadhyay, A.; Suryawanshi, S. N.; Bhakuni, D. S. *Indian J. Chem.* **1988**, *27B*, 1009.
(37) Lafont, D.; Boullanger, P.; Cadas, O.; Descotes, G. *Synthesis* **1989**, 191.
(38) Kloosterman, M.; Slaghek, T.; Hermans, J. P. G.; van Boom, J. H. *Recl. Trav. Chim. Pays-Bas* **1984**, *103*, 335.

Scheme 3

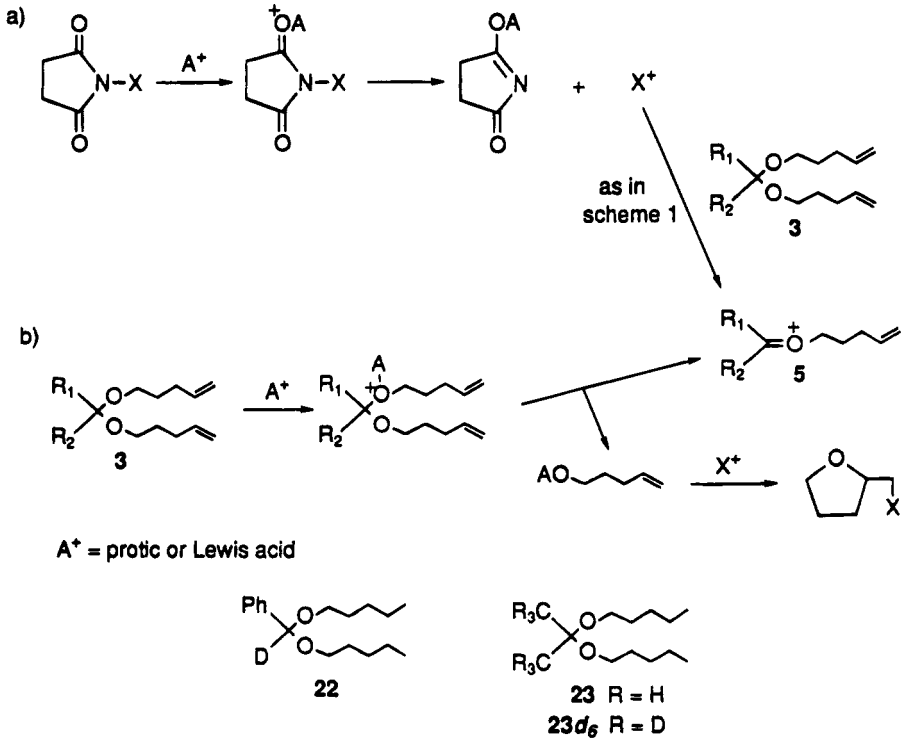
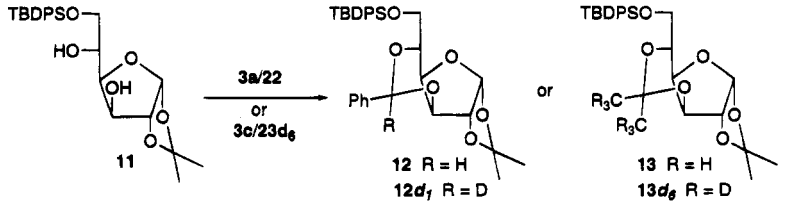


Table 3. Competitive Acetalizations with Pentenyl and Pentanyl Reagents



entry	reagents[a]	promoter	reaction time (min)	product(s)	yield (%)
i	**3a** and **22** (1:1)	IDCP	5	Only **12**	79
ii		NBS/Et_3SiOTf	5	**12** and **12**-d_1 (1:1)	98
iii		NBS/BF_3·OEt_2	5	**12** and **12**-d_1 (1:1)	94
iv		NBS/CSA	15	**12** and **12**-d_1 (1:1)	95
v	**3c** and **23**-d_6 (1:1)	NBS/Et_3SiOTf	5	**13** and **13**-d_6 (1:1)	96
vi		NBS/BF_3·OEt_2	5	**13** and **13**-d_6 (1:1)	97

[a] 1.2 equiv of the reagents was used.

4-enol which is liberated from **3** by the normal acid-catalyzed process depicted in Scheme 3b. The implication, in the latter case, would be that the acid, and not Br^+, is the electrophile in the rate-determining step. In such a case a saturated counterpart of **3**, i.e., a dipentanyl acetal, should function equally well.

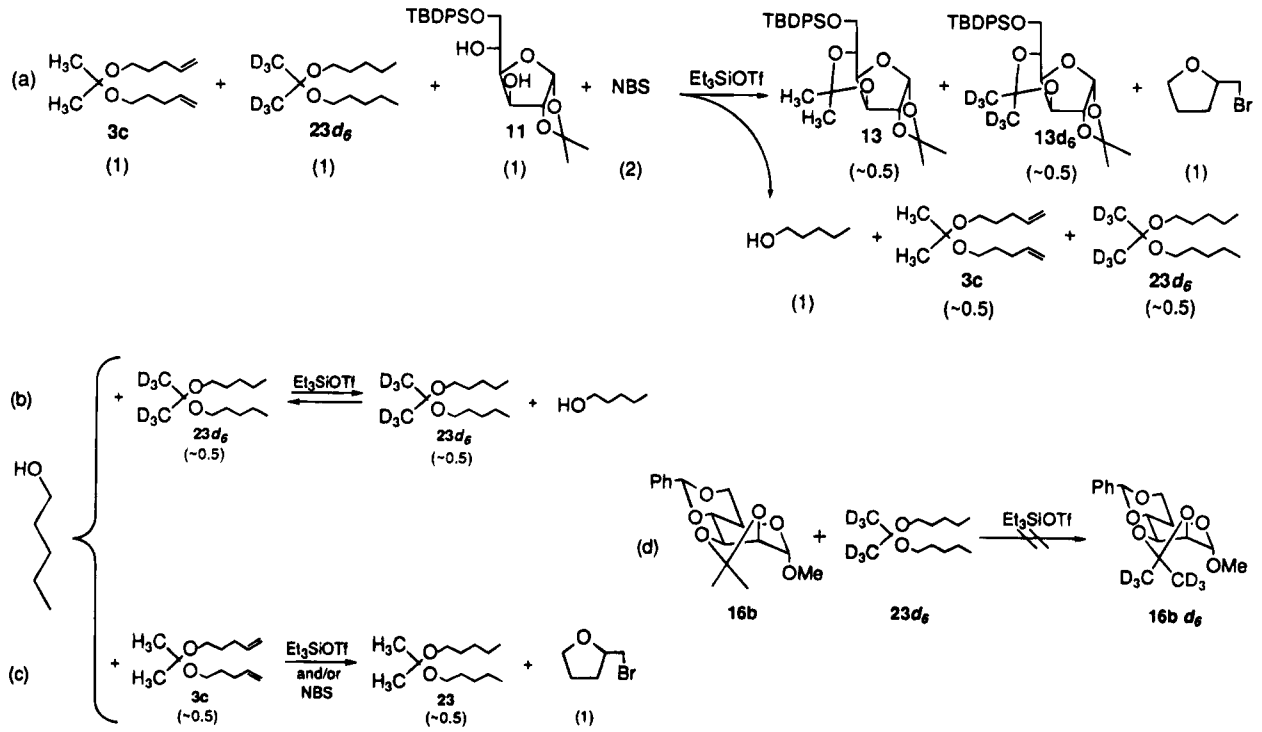
Table 3 records six experiments that address the issue of whether the "real" promoter is Br^+ or the acid. In order to probe these questions, the deuterated dipentanyl derivatives **22** and **23**-d_6 were prepared from benzaldehyde-d_1[39] and acetone-d_6 for use in competing studies. The substrate was again diol **11**. In entry i, the promoter was IDCP, and not surprisingly, compound **12** was the only product. This result establishes clearly that halonium ion driven acetal transfer, as outlined in Scheme 3a, is indeed operational. However, entries ii–vi show that under acidic conditions the acid-catalyzed acetal transfer as outlined in Scheme 3b is also occurring.

Interpretation of these results must take account of the fact that the undeuterated and deuterated counterparts **12**/**12**-d_1 and **13**/**13**-d_6 were obtained in a ~1:1 ratio in all cases except entry i, Table 3, where I^+ is the only available electrophile. The pent-4-enyl residue is immediately converted into iodomethyl tetrahydrofuran and therefore prevented from engaging further reactions. On the other hand, in Table 3, entries ii → vi, where Br^+ and Lewis acid are available as electrophiles, 1-pentanol is also produced and is free to engage in equilibration reactions whereby acetal scrambling can occur.

In this connection, acetal scrambling is a problem that plagues normal acid-catalyzed acetalizations,[6] and some experiments were designed to probe this issue. The situation in Scheme 4a encaptulates that in Table 3, entries ii → vi (*vide supra*), the correspondence in the numbers of equivalents between reactants and products being powerful evidence that equilibration is dynamic. The acid-catalyzed process in Scheme 4b is "invisible" since the equilibrium is dynamic. The comparable process in Scheme 4c is promoted by either acid or Br^+, and with the removal of the pent-4-enol, the 1-pentanol is free to produce **23** completely.

(39) Nasipuri, D.; Ghosh, C. K.; Martin, R. J. L. *J. Org. Chem.* **1970**, *35*, 657.

Scheme 4[a]



[a] The numbers in parentheses refer to equivalents.

In order to see whether such scrambling was occurring under the Br^+-induced conditions, the bis-acetal **16b** was incubated with the hexadeuteriodipentanyl reagent **23**-d_6 for 5 min, the same period of time that was required to convert **16a** into **16b** (Table 2). As is noted in Scheme 4d the starting material was recovered completely, there being no evidence for **16b**-d_6.

Furthermore, attempts to acetonate **16a** with reagent **3c** and Et_3SiOTf produced a poor yield of **16b** with TLC evidence for gross decomposition. Decomposition was even more evident when acid-catalyzed benzylidenation of the hex-2-enopyranoside **20** was attempted.

In conclusion, acetalization with the dipent-4-enyl reagents can be carried out under neutral conditions with halonium salts or NBS. However, addition of an acid to the latter potentiates Br^+ formation in addition to independently inducing acetal transfer.

Relevance to NPG Activation

The results in Table 3 raised the possibility that NIS/Et_3SiOTf-promoted reactions of NPGs[14] might also be simple acid-catalyzed processes instead of the iodonium-induced alternative depicted in Scheme 1. In order to address this issue we prepared the disarmed and armed NPGs **25a** and **25b**[14] and their saturated, deuterated counterparts **27b** and **27c**, respectively, by the routine procedures outlined in Scheme 5. The *n*-pentenyl glycosides **25a** and **b** could experience either oxidative or acid-catalyzed cleavage, while their saturated counterparts **27b** and **c**, respectively, could experience only the acid-catalyzed alternative.

The experimental process we chose involved competitive acetal exchange with methanol.[40] Thus, equimolar amounts of the pentenyl and pentanyl substrates were allowed to compete for 1 equivalent of methanol under standard NIS/Et_3SiOTf-promoted conditions. The results in Table 4 show that the iodonium-induced option occurs overwhelmingly judging from the ^1H NMR spectra of the reaction products. These spectra revealed (a) that C1-deuterio analogs of methyl glucosides **28a** and **28b** were completely absent and (b) that none of the recovered pentanyl glucosides were protonated at C1. Had the reaction been even partly acid-catalysed, the results in a and b would not have been observed.

In summary, dipent-4-enyl acetals have been shown to be effective acetal transfer agents. The reactions can be promoted under neutral conditions by IDCP or an *N*-halosuccinimide, but in the case of the latter addition of a Lewis or protic acid enhances the rates substantially, most reactions being complete within 5 min. The reaction conditions are so mild that highly acid labile substrates can be acetalized in near quantitative yields. Acetal protecting groups already present in the substrate are neither scrambled nor exchanged, and the reactions are nearly always completed within 5 min.

Experimental Section

General Procedures. Melting points were obtained on a Büchi 510 melting point apparatus, and distillation temperatures are uncorrected. Optical rotations were determined at the Sodium D line with a Perkin-Elmer 241 polarimeter. NMR spectra were recorded on a Varian XL-300 spectrometer. Chemical shifts were measured in ppm. All NMR spectra were recorded in $CDCl_3$ using $CHCl_3$ ($\delta = 7.26$) as internal reference for ^1H NMR spectra and $CDCl_3$ ($\delta = 77.1$) for ^{13}C NMR spectra. All reactions were conducted under an atmosphere of argon. Thin layer chromatography was performed on aluminum plates precoated with silica gel (Merck 5554). Compounds were visualized by charring after dipping in a solution of ammonium molybdate (6.25 g) and cerium(IV) sulfate (2.5 g) in 10% aqueous sulfuric acid (250 mL). Anhydrous Na_2SO_4 was used to dry organic solutions during workup. Flash column chromatography

(40) Fraser-Reid, B.; Wu, Z.; Udodong, U. E.; Ottosson, H. *J. Org. Chem.* **1990**, *55*, 6068.

Scheme 5

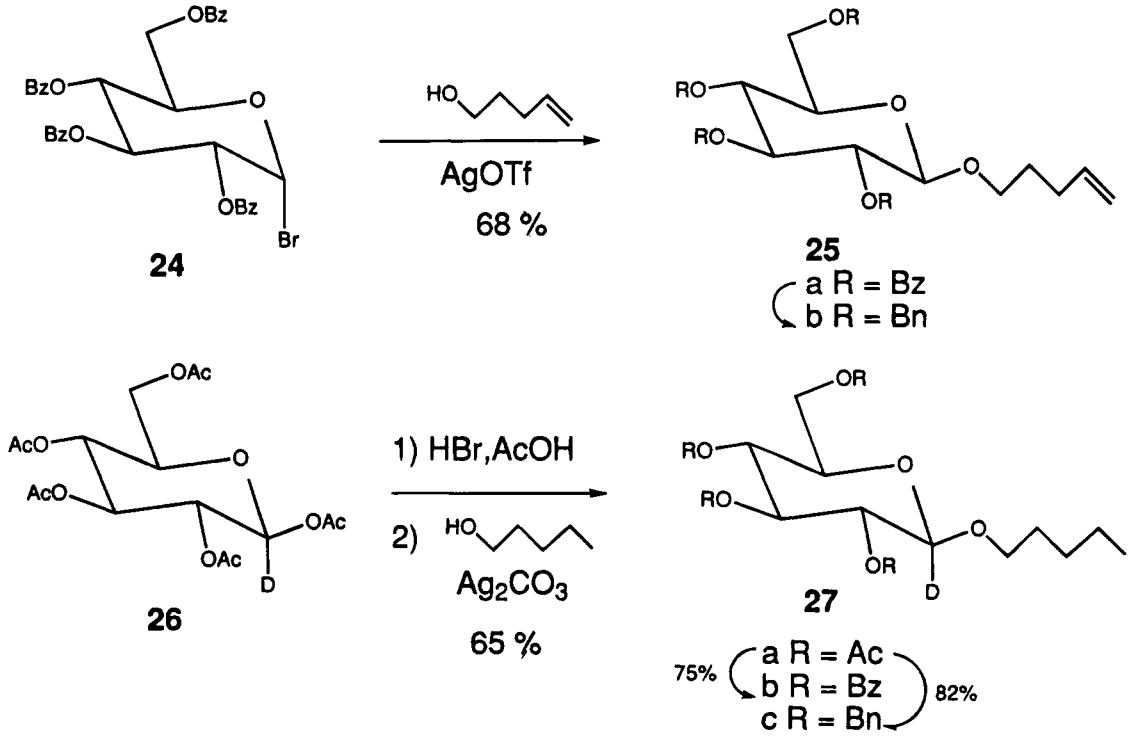
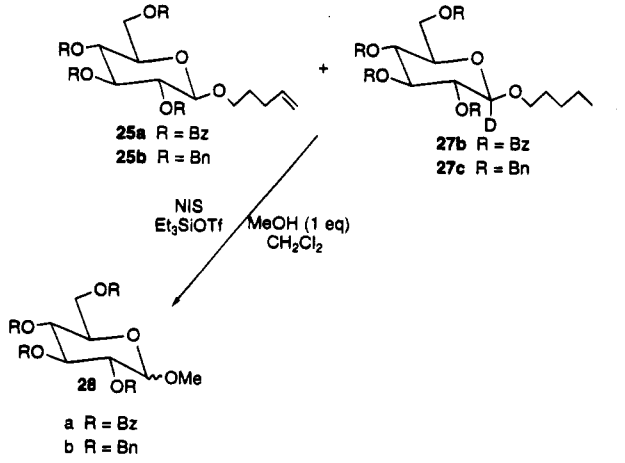


Table 4. Acid *versus* Halonium Ion Catalyzed Reactions of NPGs



entry	substrates	product	yield(%)
i	**25a** and **27b** (1:1)	**28a**(β)	71 (91% of rec. **27b**)
ii	**25b** and **27c** (1:1)	**28b**(α/β)	86 (84% of rec. **27c**)

was performed using Kieselgel 60 (230–400 mesh, Merck). Microanalyses were conducted by Atlantic Microlab, Inc., P.O. Box 2288, Norcross, GA, 30091. Acetonitrile was distilled from CaH_2 and kept over 3 Å molecular sieves. Dichloromethane was distilled from P_2O_5. Iodonium di-*sym*-collidine perchlorate (IDCP) was prepared by the procedure of Lemieux and Morgan.[20] *N*-Bromosuccinimide (NBS) was used as purchased, and *N*-iodosuccinimide (NIS) was recrystallized from *p*-dioxane/CCl_4.

General Procedure for Preparing Dipent-4-enyl Acetals 3a–d. To an ice-cooled mixture of the corresponding aldehyde/ketone (30 mmol) and 4-penten-1-ol (7.75 mL, 75.0 mmol) in hexane (30 mL) were added *p*-toluenesulfonic acid (1g) and powdered, activated 4 Å molecular sieves (6 g). The reaction was stirred for 8 h at 0 °C before being quenched with solid $NaHCO_3$. The mixture was filtered through Celite, and the molecular sieves were washed with hexane (20 mL). The filtrate was washed with 1 M aqueous NaOH (25 mL), dried, and concentrated. The residue was distilled to purify the dipent-4-enyl acetal.

Benzaldehyde Dipent-4-enyl acetal (3a): yield 76%; bp 129–131 °C/0.9 mm (lit.[41] bp 102–103 °C/0.2 mm); *d* 0.938; ^{1}H NMR δ 7.51–7.31 (m, 5H, Ph), 5.82 (m, 2H, 2 –CH=), 5.51 (s, 1H, PhCH), 5.07–4.94 (m, 4H, 2 =CH_2), 3.52 (m, 4H, 2 OCH_2), 2.16 (m, 4H, 2 CH_2) 1.72 (m, 4H, 2 CH_2); ^{13}C NMR 139.0, 138.3, 128.3, 128.1, 126.7, 114.8, 101.6, 64.5, 30.5, 29.0.

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.23; H, 9.34.

4-Methoxybenzaldehyde dipent-4-enyl acetal (3b): yield 95%; bp 159–162 °C/0.9 mm; *d* 0.976; ^{1}H NMR δ 7.39 (m, 2H, Ph), 6.89 (m, 2H, Ph), 5.83 (m, 2H, 2 –CH=), 5.47 (s, 1H, PhCH), 5.07–4.94 (m, 4H, 2 =CH_2), 3.82 (s, 3H, OMe), 3.51 (m, 4H, 2 OCH_2), 2.16 (m, 4H, 2 CH_2), 1.71 (m, 4H, 2 CH_2); ^{13}C NMR 159.5, 138.2, 131.3, 127.9, 114.7, 113.4, 101.4, 64.6, 55.2, 30.5, 29.0.

Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.22; H, 9.06.

Acetone dipent-4-enyl acetal (3c): yield 84%; bp 221–223 °C; *d* 0.845; ^{1}H NMR δ 5.83 (m, 2H, 2 –CH=), 5.07–4.93 (m, 4H, 2 =CH_2), 3.91 (t, J = 6.8 Hz, 4H, 2 OCH_2), 2.12 (m, 4H, 2 CH_2), 1.64 (m, 4H, 2 CH_2), 1.35 (s, 6H, 2 Me); ^{13}C NMR 138.4, 114.6, 99.6, 60.0, 30.6, 29.3, 25.0.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.51; H, 11.40.

Cyclohexanone dipent-4-enyl acetal (3d): yield 82%; bp 110–112 °C/0.8 mm; *d* 0.905; ^{1}H NMR δ 5.84 (m, 2H, 2 –CH=), 5.07–4.94 (m, 4H, 2 =CH_2), 3.38 (t, J = 6.7 Hz, 4H, 2 OCH_2), 2.13 (m, 4H, 2 CH_2), 1.69–1.35 (m, 14H, 7 CH_2); ^{13}C NMR 138.5, 114.6, 99.8, 58.8, 33.8, 30.7, 29.3, 25.7, 23.0.

Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.03; H, 11.10.

Benzaldehyde dipent-4-enoate acetal (4a). To a solution of benzaldehyde (2.0 mL, 19.7 mmol) and pent-4-enoic anhydride[42] (3.6 mL, 19.2 mmol) was added concd H_2SO_4 (3 drops). The mixture was stirred at room temperature for 1 h and then diluted with Et_2O (25mL) and washed with saturated aqueous $NaHCO_3$ (15 mL). The organic phase was dried and concentrated and the residue distilled to afford **4a** (5.32g, 96%); bp 161–164 °C/0.7 mm; *d* 1.04; ^{1}H NMR δ 7.73 (s, 1H, PhCH), 7.56–7.37 (m, 5H, Ph), 5.82 (m, 2H, 2 –CH=), 5.10–4.96 (m, 4H, 2 =CH_2), 2.53–2.35 (m, 8H, 4 CH_2); ^{13}C NMR 170.8, 136.2, 135.5, 129.7, 128.6, 126.6, 115.7, 89.7, 33.3, 28.5.

(41) Crawford, R. J.; Raap, R. *Can. J. Chem.* **1965**, *43*, 356.
(42) Ellervik, U.; Magnusson, G. *Acta Chem. Scand.* **1993**, *47*, 826.

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.65; H, 6.97.

General Procedure for Acetalization. The substrate (1 mmol) was azeotroped with toluene and dried for 30 min under high vacuum. It was then dissolved in acetonitrile (3–8 mL), and the dipent-4-enyl acetal (1.2 mmol), NBS (470 mg, 2.64 mmol), and the acid (Et_3SiOTf, $BF_3{\cdot}OEt_2$ or camphorsulfonic acid, 0.1 mmol) were added. The mixture was stirred at room temperature, with protection from light, for 5 min (with Et_3SiOTf and $BF_3{\cdot}OEt_2$) or for 15 min (with camphorsulfonic acid) before quenching with Et_3N (25 μL) at 0 °C. The solution was diluted with CH_2Cl_2 (15 mL) and washed successively with 10% aqueous $Na_2S_2O_3$ (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The organic solution was dried, concentrated, and azeotroped with xylene (five times) to remove 2-(bromomethyl)-oxolane. The residue was purified by flash chromatography to give the corresponding acetal.

3,5-*O*-(*R*)-Benzylidene-6-*O*-(*tert*-butyldiphenylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (12*R*): R_f = 0.55 (91:9 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +35.7° (*c* 1, $CHCl_3$) (lit.[19] $[\alpha]^{25}_D$ +36.8° (*c* 1.05, $CHCl_3$)); ^1H NMR δ 7.74–7.32 (m, 15H, Ph), 6.06 (d, *J* = 3.7 Hz, 1H), 5.90 (s, 1H, PhCH), 4.67 (m, 2H), 4.39 (d, *J* = 3.4 Hz, 1H), 4.15 (m, 1H), 3.92 (m, 2H), 1.51 (s, 3H, Me), 1.34 (s, 3H, Me), 1.01 (s, 9H, tBu); ^{13}C NMR 105.4, 96.2, 84.6. NMR data were in accordance with literature values.[19]

3,5-*O*-(*S*)-Benzylidene-6-*O*-(*tert*-butyldiphenylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (12*S*): R_f = 0.42 (91:9 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +8.8° (*c* 1, $CHCl_3$); ^1H NMR δ 7.72–7.35 (m, 15H, Ph), 6.08 (s, 1H, PhCH), 6.06 (d, *J* = 3.7 Hz, 1H), 4.68 (d, *J* = 3.7 Hz, 1H), 4.59 (d, *J* = 2.0 Hz, 1H), 4.36–4.30 (m, 2H), 4.13 (dd, *J* = 4.4, 11.2 Hz, 1H), 3.95 (dd, *J* = 4.4, 11.2 Hz, 1H), 1.56 (s, 3H, Me), 1.36 (s, 3H, Me), 1.10 (s, 9H, tBu); ^{13}C NMR 104.8, 95.4, 84.0.

Anal. Calcd for $C_{32}H_{38}O_6Si$: C, 70.30; H, 7.01. Found: C, 70.33; H, 7.03.

6-*O*-(*tert*-Butyldiphenylsilyl)-1,2;3,5-di-*O*-isopropylidene-α-D-glucofuranose (13): R_f = 0.67 (91:9 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +11.7° (*c* 1, $CHCl_3$); ^1H NMR δ 7.74–7.68 (m, 4H, Ph), 7.45–7.34 (m, 6H, Ph), 5.99 (d, *J* = 3.7 Hz, 1H), 4.57 (d, *J* = 3.9 Hz, 1H), 4.36 (dd, *J* = 3.7, 6.8 Hz, 1H), 4.18 (d, *J* = 3.9 Hz, 1H), 3.88 (dd, *J* = 3.1, 10.9 Hz, 1H), 3.80 (dd, *J* = 6.8, 10.9 Hz, 1H), 3.70 (dt, *J* = 3.1, 6.8 Hz, 1H), 1.47 (s, 3H, Me), 1.36 (s, 6H, 2 Me), 1.32 (s, 3H, Me), 1.05 (s, 9H, tBu); ^{13}C NMR 112.1, 106.4, 100.8.

Anal. Calcd for $C_{28}H_{38}O_6Si$: C, 67.44; H, 7.68. Found: C, 67.28; H, 7.71.

Pent-4-enyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-α-D-mannopyranoside (14b): R_f = 0.55 (85:15 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +8.8° (*c* 1, $CHCl_3$); ^1H NMR δ 5.81 (m, 1H, –CH=), 5.07–4.95 (m, 2H, $=CH_2$), 4.96 (s, 1H), 4.18–4.11 (m, 2H), 3.91–3.69 (m, 4H), 3.61 (m, 1H), 3.44 (m, 1H), 2.13 (m, 2H), 1.69 (m, 2H), 1.52 (s, 3H, Me), 1.35 (s, 3H, Me), 0.90 (s, 9H, tBu), 0.09 (s, 6H, 2 Me); ^{13}C NMR 109.5, 97.1.

Anal. Calcd for $C_{20}H_{38}O_6Si$: C, 59.67; H, 9.51. Found: C, 59.44; H, 9.46.

Methyl 3,4-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-altropyranoside (15b): R_f = 0.50 (65:35 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +35.6° (*c* 1, $CHCl_3$) (lit.[24] $[\alpha]^{22}_D$ +32.8° (*c* 2.1, $CHCl_3$)); ^1H NMR δ 7.52–7.20 (m, 15H, Ph), 4.60 (d, *J* = 5.6 Hz, 1H), 4.15–4.09 (m, 2H), 3.96 (m, 1H), 3.80 (m, 1H), 3.56 (s, 3H, OMe), 3.33 (dd, *J* = 3.0, 10.3 Hz, 1H), 3.27 (dd, *J* = 6.7, 10.3 Hz, 1H), 1.46 (s, 3H, Me), 1.30 (s, 3H, Me); ^{13}C NMR 110.7, 101.9.

Methyl 4,6-*O*-benzylidene-2,3-*O*-isopropylidene-α-D-mannopyranoside (16b): R_f = 0.44 (9:1 petroleum ether/EtOAc); mp 106–108 °C; $[\alpha]^{20}_D$ –18.5° (*c* 1, $CHCl_3$) (lit.[25] $[\alpha]_D$ –10° (*c* 1, $CHCl_3$)); ^1H NMR δ 7.53–7.33 (m, 5H, Ph), 5.57 (s, 1H, PhCH), 4.96 (s, 1H), 4.36–4.21 (m, 3H), 3.82–3.67 (m, 3H), 3.41 (s, 3H, OMe), 1.59 (s, 3H, Me), 1.37 (s, 3H, Me); ^{13}C NMR 109.7, 102.0, 99.0. NMR data were in accordance with literature values.[25]

5′-*O*-Acetyl-2′,3′-*O*-cyclohexylideneuridine (17b): R_f = 0.48 (7:3 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +4.4° (*c* 1, $CHCl_3$); ^1H NMR δ 8.88 (bs, 1H, NH), 7.27 (d, *J* = 8.0 Hz, 1H), 5.73 (dd, *J* = 2.2, 8.0 Hz, 1H), 5.65 (d, *J* = 2.0 Hz, 1H), 4.99 (dd, *J* = 2.0, 6.4 Hz, 1H), 4.81 (dd, *J* = 3.9, 6.4 Hz, 1H), 4.40–4.24 (m, 3H), 2.09 (s, 3H, Ac), 1.80–1.37 (m, 10H, 5 CH_2); ^{13}C NMR 115.4, 102.6, 95.3.

Anal. Calcd for $C_{17}H_{22}N_2O_7$: C, 55.73; H, 6.05; N, 7.65. Found: C, 55.56; H, 6.10; N, 7.59.

6-*O*-(*tert*-Butyldimethylsilyl)-3,4-*O*-isopropylidene-α-D-galactopyranose 1,2-(2-propyl)orthoacetate (18b): R_f = 0.44 (94:6 petroleum ether/EtOAc); ^1H NMR (exo isomer) δ 5.60 (d, *J* = 5.3 Hz, 1H), 4.59 (dd, *J* = 2.0, 8.0 Hz, 1H), 4.43 (dd, *J* = 2.0, 5.3 Hz, 1H), 4.28 (dd, *J* = 1.0, 7.8 Hz, 1H), 3.91 (dt, *J* = 6.0, 6.3 Hz, 1H), 3.82–3.66 (m, 3H), 1.66 (s, 3H, Me), 1.93 (s, 3H, Me), 1.32 (s, 3H, Me), 1.15 (d, *J* = 6.3 Hz, 3H, Me), 1.14 (d, *J* = 6.0 Hz, 3H, Me), 0.88 (s, 9H, tBu), 0.06 (s, 6H, 2 Me); ^{13}C NMR 120.5, 109.1, 97.0.

Anal. Calcd for $C_{20}H_{38}O_7Si$: C, 57.39; H, 9.15. Found: C, 56.38; H, 9.00.

Allyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (19b): R_f = 0.56 (65:35 petroleum ether/EtOAc); mp 180–182 °C; $[\alpha]^{20}_D$ –33.8° (*c* 1, $CHCl_3$) (lit.[30] mp 173–175 °C; $[\alpha]^{20}_D$ –37.0° (*c* 1.4, $CHCl_3$)); ^1H NMR δ 7.91–7.71 (m, 4H, Phth), 7.55–7.32 (m, 5H, Ph), 5.70 (m, 1H, -CH=), 5.58 (s, 1H, PhCH), 5.32 (d, *J* = 8.5 Hz, 1H), 5.19–5.03 (m, 2H, $=CH_2$), 4.65 (m, 1H), 4.40 (dd, *J* = 4.4, 10.4 Hz, 1H), 4.32–4.26 (m, 2H), 4.04 (dd, *J* = 5.0, 12.2 Hz, 1H), 3.85 (t, *J* = 10.4 Hz, 1H), 3.69–3.57 (m, 2H); ^{13}C NMR 101.5, 97.8. NMR data were in accordance with literature values.[30]

Ethyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (20b): R_f = 0.48 (95:5 petroleum ether/EtOAc); mp 94–96 °C; $[\alpha]^{20}_D$ +101.7° (*c* 1, $CHCl_3$) (lit.[36] $[\alpha]^{20}_D$ +91.3° (*c* 1.9, $CHCl_3$)); ^1H NMR δ 7.55–7.35 (m, 5H, Ph), 6.13 (bd, *J* = 10.4 Hz, 1H), 5.74 (dt, *J* = 2.5, 10.3 Hz, 1H), 5.59 (s, 1H, PhCH), 5.12 (bs, 1H), 4.30 (dd, *J* = 4.3, 10.1 Hz, 1H), 4.15 (m, 1H), 3.97–3.77 (m, 3H), 3.57 (dq, *J* = 7.0, 9.7 Hz, 1H), 1.26 (t, *J* = 7.0 Hz, 3H, Me); ^{13}C NMR 102.1, 99.8.

1,6-Anhydro-*endo*-3,4-*O*-(4-methoxybenzylidene)-β-D-galactopyranose (21b): R_f = 0.42 (1:1 petroleum ether/EtOAc); mp 160–162 °C; $[\alpha]^{20}_D$ +21.3° (*c* 1, $CHCl_3$) (lit.[38] mp 154–155 °C; $[\alpha]^{25}_D$ +35° (*c* 1, $CHCl_3$)); ^1H NMR δ 7.45 (m, 2H, Ph), 6.94 (m, 2H, Ph), 5.80 (s, 1H, PhCH), 5.43 (s, 1H), 4.55 (m, 2H), 4.22 (m, 1H), 4.15 (d, *J* = 7.6 Hz, 1H), 4.05 (d, *J* = 9.0 Hz, 1H), 3.83 (s, 3H, OMe), 3.55 (m, 1H); ^{13}C NMR 103.1, 101.2. NMR data were in accordance with literature values.[38]

Benzaldehyde-*d* di-*n*-pentanyl acetal (22): yield 85%; bp 126–127 °C/0.3 mm; *d* 0.923; ^1H NMR δ 7.50–7.31 (m, 5H, Ph), 3.50 (m, 4H, OCH_2), 1.62 (m, 4H, 2 CH_2), 1.35 (m, 8H, 4 CH_2), 0.91 (t, 6H, 2 Me); ^{13}C NMR 139.1, 128.2, 128.1, 126.7, 65.3, 29.5, 28.5, 22.6, 14.1.

Anal. Calcd for $C_{17}H_{27}DO_2$: C, 76.94; H+D, 10.63. Found: C, 76.96; H+D, 10.67.

Acetone-d_6 di-*n*-pentanyl acetal (23-d_6): yield 79%; bp 224–227 °C; *d* 0.846; ^1H NMR δ 3.38 (t, 4H, 2 OCH_2), 1.54 (m, 4H, 2 CH_2), 1.33 (m, 8H, 4 CH_2), 0.91 (t, 6H, 2 Me); ^{13}C NMR 99.3, 60.7, 29.8, 28.6, 22.6, 14.1.

Anal. Calcd for $C_{13}H_{22}D_6O_2$: C, 70.23; H + D, 12.69. Found: C, 70.03; H + D, 12.77.

Competing Experiments between 3a and 22 and 3c and 23-d_6 for 11. The general procedure for acetalizations described above was followed. Diol **11** (459 mg, 1 mmol) was dissolved in acetonitrile (5 mL), and the dipent-4-enyl acetal **3a** or **3c** (1.2 mmol), the di-*n*-pentanyl acetal **22** or **23**-d_6 (1.2 mmol), IDCP or NBS (2.7 mmol), and the acid (0.1 mmol) were mixed as indicated in Table 3. The reaction mixture was stirred at room temperature and then worked up as described above to give the corresponding acetals, which were analyzed by ^1H NMR.

Pent-4-enyl 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranoside (25a). To a mixture of 4-penten-1-ol (0.5 mL, 4.84 mmol), AgOTf (1.2 g, 4.67 mmol), and powdered, activated 4 Å molecular sieves (1 g) in CH_2Cl_2 (10 mL) was added at –30 °C, *via* a syringe, a solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide **24**[43] (2.5 g, 3.79 mmol) in CH_2Cl_2 (4 mL) during 10 min. The reaction mixture was stirred at –30 °C for 2 h, quenched with saturated aqueous $NaHCO_3$, and then filtered through Celite. The molecular sieves were washed with CH_2Cl_2 (20 mL). The organic phase was washed with saturated aqueous $NaHCO_3$ (20 mL), dried, and concentrated. The residue was purified by flash chromatography (4:1 petroleum ether/EtOAc) to afford **25a** (1.71 g, 68%); R_f = 0.55; mp 113–114 °C; $[\alpha]^{20}_D$ +18.7° (*c* 1, $CHCl_3$);

(43) Fletcher, H. G., Jr. *Methods in Carbohydrate Chemistry*; Whistler, R. L., Wolfrom, M. L., Eds.; Academic Press: New York, 1963; Vol. II, p 226.

^{1}H NMR δ 8.06–7.83 (m, 8H, Ph), 7.57–7.28 (m, 12H, Ph), 5.91 (t, J = 9.7 Hz, 1H), 5.68 (t, J = 9.7 Hz, 1H), 5.65 (m, 1H, –CH=), 5.53 (dd, J = 8.0, 9.7 Hz, 1H), 4.83 (d, J = 8.0 Hz, 1H), 4.82 (m, 2H, =CH_2), 4.64 (dd, J = 3.1, 12.1 Hz, 1H), 4.51 (dd, J = 5.2, 12.1 Hz, 1H), 4.16 (m, 1H), 3.93 (m, 1H), 3.56 (m, 1H), 1.98 (m, 2H), 1.65 (m, 2H); ^{13}C NMR 101.3.

Anal. Calcd for $C_{39}H_{36}O_{10}$: C, 70.47; H, 5.46. Found: C, 70.27; H, 5.50.

Pentanyl 2,3,4,6-Tetra-*O*-acetyl-β-D-[1-^{2}H]glucopyranoside (27a). To an ice-cooled solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-[1-^{2}H]glucopyranose[44] (3.5 g, 8.94 mmol) in CH_2Cl_2 (8 mL) was added *via* a syringe 30% HBr in AcOH (12 mL). The reaction was stirred at room temperature for 3 h. It was then diluted with CH_2Cl_2 (25 mL) and washed successively with ice-cooled water (2 × 25 mL) and saturated aqueous $NaHCO_3$ (4 × 25 mL). The organic solution was dried and concentrated to give a syrupy residue. This was taken up in CH_2Cl_2 (20 mL) and cooled to 0 °C while 1-pentanol (2 mL, 18.4 mmol), Ag_2CO_3 (3.0 g, 10.9 mmol), and powdered, activated 4 Å molecular sieves (2 g) were added. The mixture was stirred for 16 h at room temperature and then filtered through Celite. The molecular sieves were washed with CH_2Cl_2 (10 mL), and the filtrate was washed with saturated aqueous $NaHCO_3$ (20 mL), dried, and concentrated. The residue was flash chromatographed (1:1 petroleum ether/ether) to give **27a** (2.42 g, 65%): R_f = 0.61; $[\alpha]^{20}_D$ –17.5° (*c* 1.5, $CHCl_3$); ^{1}H NMR δ 5.18 (t, J = 9.6 Hz, 1H), 5.06 (t, J = 9.6 Hz, 1H), 4.96 (d, J = 9.6 Hz, 1H), 4.24 (dd, J = 4.7, 12.4 Hz, 1H), 4.11 (dd, J = 2.4, 12.4 Hz, 1H), 3.84 (m, 1H), 3.67 (m, 1H), 3.44 (m, 1H), 2.07 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.00 (s, 3H, Ac), 1.97 (s, 3H, Ac), 1.57 (m, 2H), 1.26 (m, 4H), 0.87 (t, 3H, Me), no signal from H-1.

Anal. Calcd for $C_{19}H_{29}DO_{10}$: C, 54.41; H + D, 7.21. Found: C, 53.99; H + D, 7.13.

Pentanyl 2,3,4,6-Tetra-*O*-benzoyl-β-D-[1-^{2}H]glucopyranoside (27b). Compound **27a** was deacetylated with methanolic sodium methoxide, and the product was benzoylated with BzCl in pyridine in the usual way to give **27b**: R_f = 0.5 (99:1 CH_2Cl_2/EtOAc); mp 110–111 °C; $[\alpha]^{20}_D$ +16.6° (*c* 1, $CHCl_3$); ^{1}H NMR δ 8.05–7.82 (m, 8H, Ph), 7.57–7.27 (m, 12H, Ph), 5.91 (t, J = 9.7 Hz, 1H), 5.67 (t, J = 9.7 Hz, 1H), 5.53 (d, J = 9.7 Hz, 1H), 4.64 (dd, J = 3.3, 12.1 Hz, 1H), 4.51 (dd, J = 5.2, 12.1 Hz, 1H), 4.16 (m, 1H), 3.82 (m, 1H), 3.54 (m, 1H), 1.53 (m, 2H), 1.16 (m, 4H), 0.69 (t, 3H, Me), no signal from H-1.

Anal. Calcd for $C_{39}H_{37}DO_{10}$: C, 70.15; H + D, 5.74. Found: C, 69.99; H + D, 5.89.

(44) Breven, L. A.; Withers, S. G. *Carbohydr. Res.* **1986**, *156*, 282.

Pentanyl 2,3,4,6-Tetra-*O*-benzyl-β-D-[1-^{2}H]glucopyranoside (27c). Compound **27a** was deacetylated with NaOMe in MeOH, and the product was benzylated with BnBr/NaH/Bu_4NI in DMF in the usual way to afford **27c**: R_f = 0.52 (9:1 petroleum ether/EtOAc); mp 59–60 °C; $[\alpha]^{20}_D$ +5.6° (*c* 2, $CHCl_3$); ^{1}H NMR δ 7.42–7.16 (m, 20H, Ph), 4.99 (d, J = 10.7 Hz, 1H), 4.96 (d, J = 10.7 Hz, 1H), 4.85 (d, J = 10.6 Hz, 1H), 4.83 (d, J = 10.6 Hz, 1H), 4.75 (d, J = 10.7 Hz, 1H), 4.65 (d, J = 12.2 Hz, 1H), 4.59 (d, J = 12.2 Hz, 1H), 4.55 (d, J = 10.7 Hz, 1H), 4.00 (m, 1H), 3.80–3.46 (m, 7H), 1.70 (m, 2H), 1.40 (m, 4H), 0.92 (t, 3H, Me), no signal from H-1.

Anal. Calcd for $C_{39}H_{45}DO_6$: C, 76.57; H + D, 7.58. Found: C, 76.73; H + D, 7.61.

Competition Experiments between 25a/25b and 27b/27c. To a solution of **25a** or **25b** (0.247 mmol), **27b** or **27c** (0.247 mmol), and MeOH (10 μL, 0.247 mmol) in CH_2Cl_2 (1.5 mL) were added NIS (65 mg, 0.289 mmol) and Et_3SiOTf (65 μL, 0.287 mmol). The reaction was stirred at room temperature for 15 min. It was cooled to 0 °C and quenched with Et_3N (50 μL). The mixture was diluted with CH_2Cl_2 (10 mL) and washed successively with 10% saturated aqueous $Na_2S_2O_3$ (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The dried solution was concentrated and the residue purified by flash chromatography to give unreacted **27b** or **27c** (~0.220 mmol) and methyl glucosides **28a** or **28b** α/β (~0.200 mmol).

Methyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (28a): R_f = 0.57 (3:1 petroleum ether/EtOAc); mp 159–160 °C; $[\alpha]^{20}_D$ +28.0° (*c* 1, $CHCl_3$) (lit.[45] mp 161–162 °C; $[\alpha]_D$ +26.9° (*c* 2.5, $CHCl_3$)); ^{1}H NMR δ 8.05–7.81 (m, 8H, Ph), 7.58–7.25 (m, 12H, Ph), 5.92 (t, J = 9.7 Hz, 1H), 5.69 (t, J = 9.7 Hz, 1H), 5.53 (dd, J = 7.8 Hz, 1H), 4.77 (d, J = 7.8 Hz, 1H), 4.66 (dd, J = 3.2, 12.1 Hz, 1H), 4.52 (d, J = 5.2, 12.1 Hz, 1H), 4.16 (m, 1H), 3.55 (s, 3H, OMe); ^{13}C NMR 102.1, 57.2.

Methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (28bβ): R_f = 0.59 (85:15 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +11.4° (*c* 1, $CHCl_3$) (lit.[46] $[\alpha]^{27}_D$ +12.6 (*c* 2.7, $CHCl_3$)); ^{1}H and ^{13}C NMR in accordance with literature values.[47]

Methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (28bα): R_f = 0.41 (85:15 petroleum ether/EtOAc); $[\alpha]^{20}_D$ +17.8° (*c* 1, $CHCl_3$) (lit.[48] $[\alpha]^{20}_D$ +18.7° (*c* 1.5, $CHCl_3$)); ^{1}H and ^{13}C NMR in accordance with literature values.[47]

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(45) Maradufu, A.; Perlin, A. S. *Carbohydr. Res.* **1974**, *32*, 261.
(46) Weygand, F.; Ziemann, H. *Liebigs Ann. Chem.* **1962**, *657*, 179.
(47) Briner, K.; Vasella, A. *Helv. Chim. Acta* **1992**, *75*, 621. Dhawan, S. N.; Chick, T. L.; Goux, W. J. *Carbohydr. Res.* **1988**, *172*, 297.
(48) Tate, M. E.; Bishop, C. T. *Can. J. Chem.* **1963**, *41*, 1801.