Ferrier Rearrangement under Nonacidic Conditions Based on Iodonium-Induced Rearrangements of Allylic *n*-Pentenyl Esters, *n*-Pentenyl Glycosides, and Phenyl Thioglycosides[1]

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Iodonium-promoted rearrangements of easily accessible allylic *n*-pentenyl esters, *n*-pentenyl glycosides, or phenyl thioglycosides result in the generation of the allylic oxocarbenium ion intermediate **II** of the Ferrier rearrangement, **I** → **II** → **IIIa**, of glycals leading to 2,3-unsaturated glycosides. Thus the Ferrier rearrangement can now be carried out under nonacidic conditions, with NIS or iodonium dicollidinium perchlorate as promoter, to afford good yields of disaccharides in which acid-labile functionalities, either in the glycosyl donor or glycosyl acceptor, have been preserved.

Introduction

The Lewis acid-catalyzed rearrangement of glycals in the presence of alcohols, known as the Ferrier reaction,[4] **I** → **IIIa** is the method of choice for the synthesis of 2,3-unsaturated glycosides.[5] The reaction as originally stated by Ferrier[4a] involves intermediacy of a cyclic allylic oxocarbenium ion **II** (Scheme 1) to which the nucleophile adds preferentially in quasi-axial orientation. The most commonly employed Lewis acid to effect this transformation has been boron trifluoride etherate ($BF_3{\cdot}Et_2O$) although stannic chloride has been found to be more successful with particular substrates.[6,7]

However, the synthetic value of the Ferrier reaction is not limited to the preparation of unsaturated glycosides, since ion **II** can be intercepted by a variety of nucleophiles to form sugar fluorides **IIIb**,[8] hydride reduction to give **IIIc**,[9] and thiols to give thioglycosides **IIId**.[10] Ion **II** can also be trapped with carbon nucleophiles to generate allylic C-glycosides **IIIe**.[11,12]

However the requirement of an acid catalyst restricts both the glycal and the nucleophilic partner that can be used. Thus although tri-*O*-acetyl-D-glucal (**1**) reacts with diacetone galactose (**2**) to give a good yield of disaccharide **3** (Scheme 2a),[4d] it failed, in our hands, with some other acid-sensitive "alcohols" such as diacetone glucose (**4**) and 1,3,4,6-tetra-*O*-acetyl-D-fructose (**5**).[13] Furthermore, when the allal derivative **6**[14] was treated with ethanol under Ferrier conditions (Scheme 2d), a complex reaction mixture was obtained.

A nonacidic alternative for triggering formation of the allylic oxocarbenium ion **II** would clearly extend the scope of the Ferrier reaction, and some of our contributions to this objective have appeared as preliminary communications.[15,16] Since then several reports have focused on nonacidic alternatives for the Ferrier rearrangement[17,18] or synthetic applications thereof.[19,20] In this manuscript we give a full report of our studies on nonacidic, iodonium-induced Ferrier-type rearrangements which, *inter alia*, helps to clarify mechanistic aspects of the Ferrier reaction.

Preparation of the Substrates (Scheme 3). Allylic *n*-pentenyl esters (nPEs) **7b**, **8b**, and **9b** were prepared in good yields by Steglich esterification[21] of the corre-

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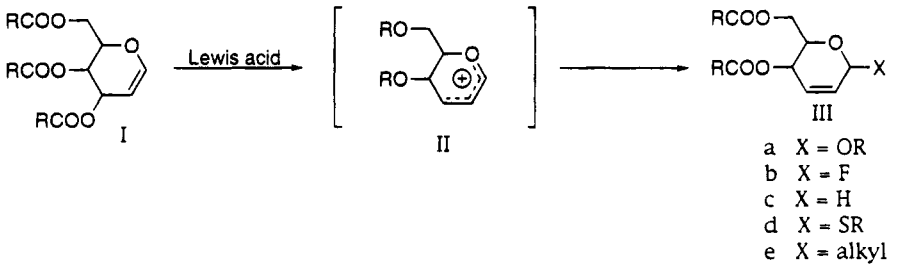
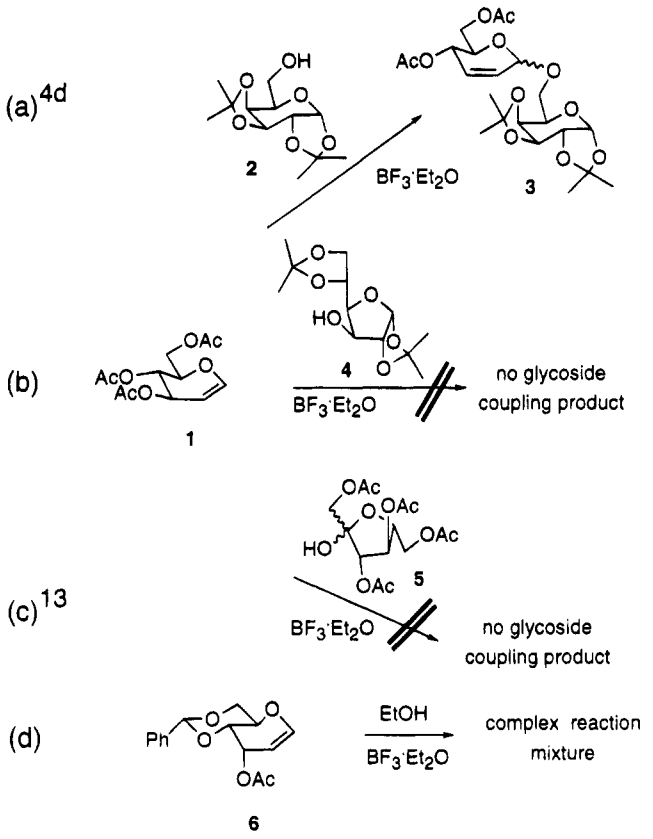
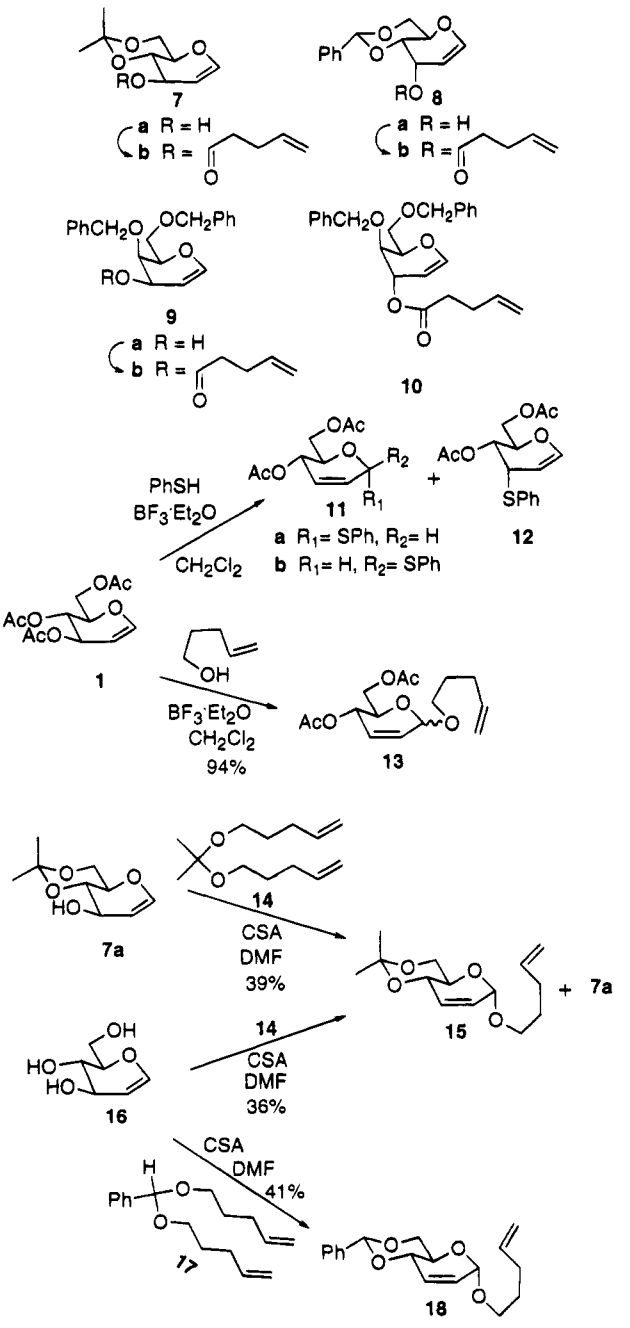
Scheme 1. Ferrier Rearrangement of Glycals



Scheme 2



Scheme 3. Preparation of Substrates for Ferrier Oxidative Rearrangement



sponding 3-hydroxy glycals **7a**,[22] **8a**,[23] and **9b**.[24] The ester **10** was obtained from **9a**, by a Mitsunobu reaction[25] utilizing *n*-pentenoic acid.

Reaction of triacetylglucal **1** with benzenethiol in CH_2Cl_2 in the presence of $BF_3{\cdot}Et_2O$ according to Valverde et al.[10b,c,26,27] afforded a mixture of α and β phenyl thioglycosides **11a,b** in a 8:1 ratio in 78% yield, together with the 3-thiophenyl glycal **12** in 5–10% yield.[28] Analogously, reaction of **1** with 4-penten-1-ol in CH_2Cl_2 yielded allylic *n*-pentenyl glycoside (NPG) **13** in 92% yield as a 11:1 mixture of α and β anomers.

The preparation of the *n*-pentenyl glycoside **15** was effected in one step from either **7a** or unprotected glycal **16** by treatment with dipent-4-enyl acetal **14**[29] (1.2 or 2.5 equiv, respectively) in DMF in the presence of a catalytic amount of camphorsulfonic acid (CSA) (see Discussion

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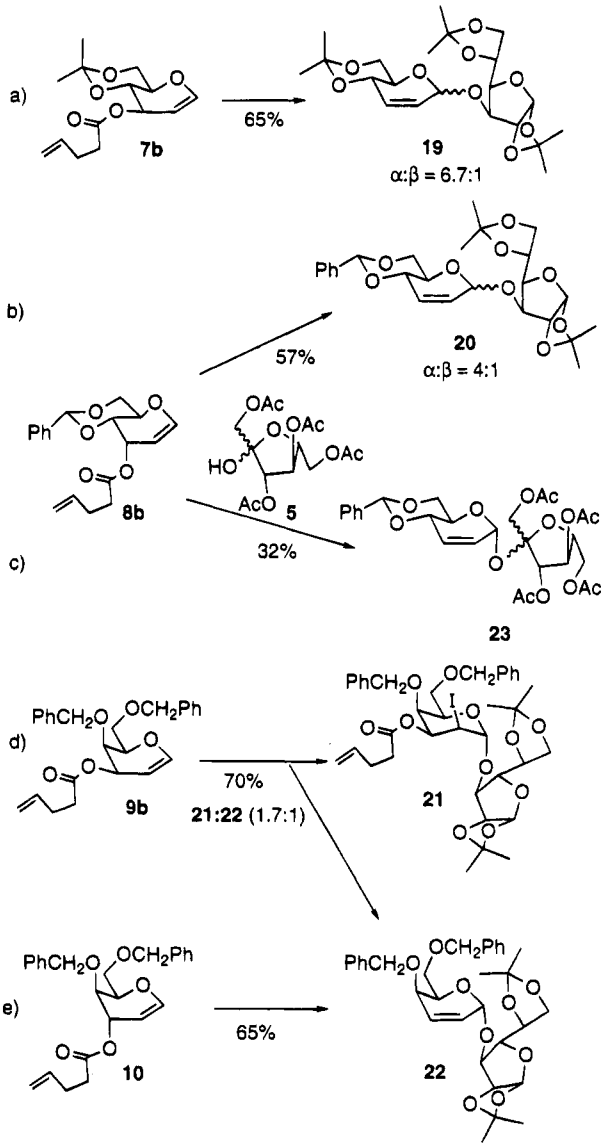
Scheme 4. Ferrier Rearrangement of 3-*O*-Pentenoyl Glycals with Diacetone Glucose 4 Using Iodonium Dicollidine Perchlorate (IDCP) as Promotor (α:β Ratio)



section below). Analogously benzylidene derivative **18** was prepared by use of dipent-4-enyl acetal **17**.

3-*O*-Pentenoyl Glycals in Nonacidic Ferrier Rearrangements. The results of rearrangements of the glycal *n*-pentenyl esters in dichloromethane with iodonium dicollidine perchlorate (IDCP)[30] as promoter are shown in Scheme 4. Esters **7b** and **8b** proceeded smoothly to give good yields of **19** and **20**, respectively, the α anomers predominating as is usually the case.[4]

The *galacto* derivative **9b** (Scheme 4d) was of particular interest. Thus Zamojski and co-workers[6] have shown that specially prescribed conditions are neccesary for 3,4,6-tri-*O*-acetyl-D-galactal to undergo the Ferrier rearrangement,[6] since anomalous behavior is exhibited under the standard conditions.[4] Fortunately reaction of glycal **9b** with diacetone glucose (**4**) under our oxidative conditions gave a 1.7:1 mixture of **21** and **22** (70% yield). Interestingly with the C-3-epimer **10**, the α-D derivative **22** was obtained as the only product in 65% yield.

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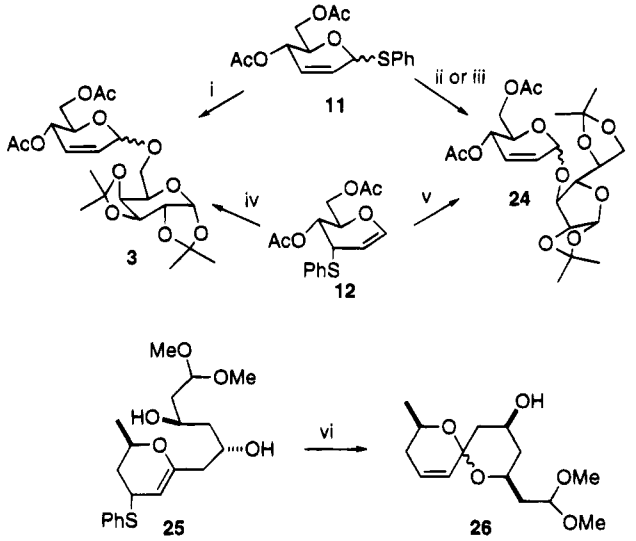
Scheme 5. Oxidative Coupling of Allylic Thioglycosides to Glycosyl Acceptors (α:β)[a]



[a] (i) NIS, **2**, 85%, [α:β] 1.8:1; (ii) NIS, **4**, 84%, [α:β] 1.8:1; (iii) NIS, **4**, 71%, [α:β] 3.5:1; (iv) IDCP, **4**, 63%, [α:β] 3.3:1; (v) NIS, **4**, 70%, [α:β] 3.5:1; (vi) NIS, 56%, [α:β] 3:1.

In light of the failure noted for the fructose addition in Scheme 2c, reaction of pentenoylated glycal **8b** with the highly hindered tertiary hydroxyl group of 1,3,4,6-tetra-*O*-acetyl-D-fructofuranose **5**[31] was regarded as a demanding test. In the event, disaccharide **23** (Scheme 4c) was obtained in 32% yield.

Phenyl Thioglycosides. Allylic phenyl thioglycoside **11** as an 8:1 anomeric mixture (Scheme 5) was treated with NIS in the presence of a primary hydroxyl derivative (**2**) to give disaccharide **3** in 85% yield. Analogously the pure **11**α reacted with diacetone glucose (**4**) to furnish **24** in good yield. The 3-phenylthio glycal **12** also underwent coupling with sugar derivatives **2** and **4** to yield rearranged allylic glycosides **3** and **24**. Ready formation of spiroketals is also possible as demonstrated by the reaction of **25** with NIS which yielded **26** as a 3:1 mixture of α,β anomers in 56% yield (Scheme 5).

***n*-Pentenyl Glycosides.** *n*-Pentenyl hex-2-enopyranosides undergo coupling reactions with IDCP as a promoter in dichloromethane as shown in Scheme 6. Thus substrate **13** (as an 11:1 anomeric mixture) reacted with glycosyl acceptors **2** and **4** to give disaccharides **3** and **24** in 69 and 52% yields, respectively, with similar α:β ratios (1.6:1 and 1.8:1).

Reactions of the acetalated glycosyl donors **15** and **18** with diacetone glucose (**4**) provided disaccharides **19** and **20** in good yields. The latter donor, **18**, also reacted with fructose derivative **5** to afford the above described disaccharide **23** in 34% yield.

Discussion

The present study grew out of our investigation of *n*-pentenyl esters as glycosyl donors,[32] **IVa** → **V** (Scheme 7a). Although these substrates, **IVa**, underwent coupling reactions readily, they did not display armed/disarmed

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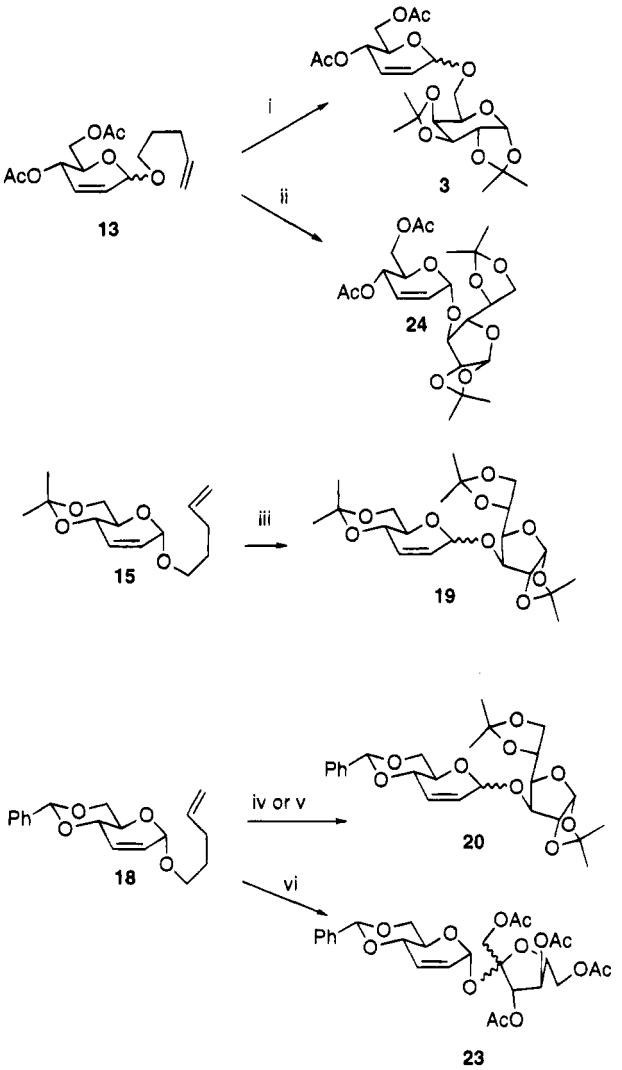
Scheme 6. Oxidative Hydrolysis of Allylic Pent-4-enyl Glycosides with Iodonium-Based Promoters[a]



[a] (i) IDCP, **2**, 69%, [α:β] 1.6:1; (ii) IDCP, **4**, 52%, [α:β] 9:1; (iii) IDCP, **4**, 55%, [α:β] 8.9:1; (iv) IDCP, **4**, 68%, [α:β] 4:1; (v) NIS, **4**, 35%, [α:β] 4:1; (vi) NIS, **5**, 32%.

effects[33] to the extent that had been observed with their *n*-pentenyl glycoside counterparts **IVb**.[34-36] Since our original communication,[33] these observations have been extended to other glycosyl donors.[37-39] In attempting to develop chemistry that would be unique for these glycosyl esters, we noted that by placing the pentenoate substituent at C-3 of a glycal the resulting molecule, **VII**, would be a vinylogous glycosyl ester, whose iodonium ion induced cleavage would generate the same allyl oxocarbenium **II** of the Ferrier reaction (**I** → **II**, Scheme 7b). Notably, further reaction of the hex-2-enopyranoside products (i.e. **IIIa**, Scheme 7) is not expected to occur in view of the well-documented resistance of hex-2-enopyranosides to reaction with electrophiles.[40a]

However an additional feature of substrate **VII** was the presence of two possible sites for electrophilic attack, and thus the question of chemoselectivity arose. Although in **VII** the vinyl ether (A, Scheme 7b) should be more reactive toward an iodonium ion than the isolated pentenyl double bond (B, Scheme 7b), we were mindful of the work of Friesen and Danishefsky which shows that C-3 esters disarm a glycal double bond.[38a] Whether this delicate counterplay of electronic forces could be resolved was one of the original impetuses of this study.

Conceivably the formation of disaccharides from 3-pentenoates would involve (a) chemoselective attack by the electrophile at the terminal double bond (B) in **VII** rather than at the electron-rich enol ether[40] (A); (b) formation of an allylic oxocarbenium ion **II**; and (c) quenching at the anomeric position by the nucleophile R'OH to give **IIIa**.

The fact that thioglycosides can also be used in iodonium-promoted reactions to generate oxocarbenium ions **VI**→ **V** (Scheme 7a) was recognized early in Fraser-Reid's laboratory[41] and elsewhere.[37b,c] In this context the (phenylthio)glycal **VIII** is seen as analogous to the 3-pentenoyl derivative **VII** (Scheme 7). The behavior of the relevant substrate **12** was therefore of interest (vide supra). Accordingly, when compound **12** was treated with NIS in the presence of glycosyl acceptors **2** and **4** (Scheme 5), coupled products **3** and **24**, respectively, were obtained, thereby demonstrating a preferred attack at the phenyl sulfide moiety (C, Scheme 7b).

Reaction of **25** to give **26** (Scheme 5), in which the delicate dimethoxy acetal group has survived, is a remarkable example of the synthetic possibilities of this method.[16]

The reactions assembled in Table 1 were all very fast and required less than 15 min for disappearance of the starting materials. Phenyl thioglycosides can be readily activated by either NIS or IDCP (entries a,b,d–j). On the other hand, NPG's require the action of IDCP. Thus with the less potent promoter NIS, 24 h was required for the coupling of **18** with diacetone glucose to give **20** (entries h and i).

Allylic *n*-pentenyl esters, NPG's, and phenyl thioglycosides undergo coupling reactions with monosaccharides to afford disaccharides, the yields seemingly dependent on the nature of the hydroxyl group, decreasing in the order primary, secondary, and tertiary **2**, **4**, and **5**, respectively (Table 1). The table also shows that under these neutral conditions α-coupling is always preferred, as in the case of the normal acid-catalyzed Ferrier rearrangement. Therefore acid-catalyzed equilibration

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Scheme 7. *n*-Pentenyl Esters in Glycosidation Reactions

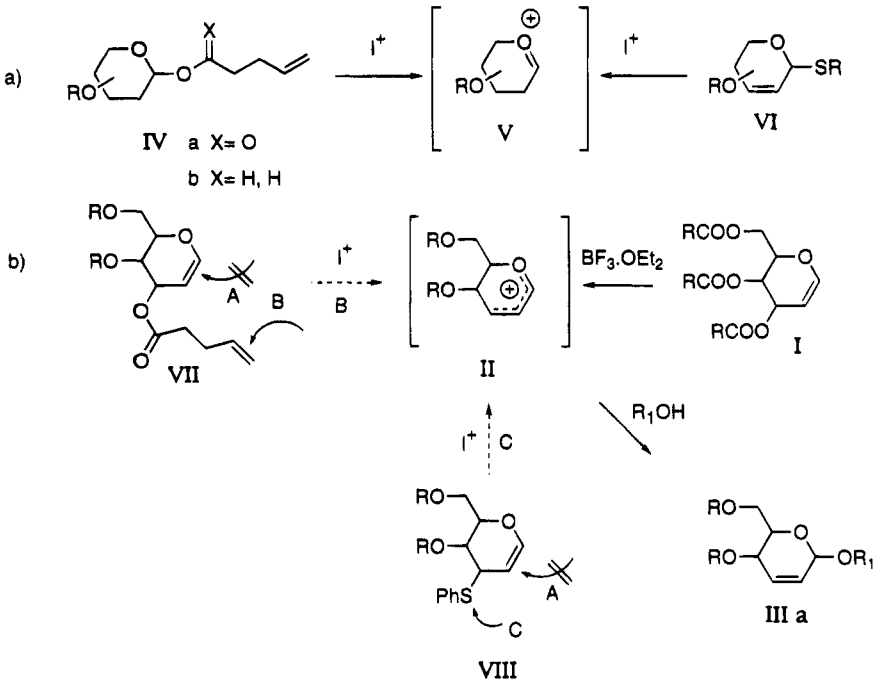


Table 1. Coupling of Unsaturated Glycosyl Donors with Diacetone Glucose (2) and Galactose (4) Using IDCP or NIS as Promoters

Entry	Alcohol	Substrate	Promoter	Product	Yield	(α:β) Ratio
a)	2	11	NIS	3	85%	1.8:1
b)	2	12	NIS	3	84%	1.8:1
c)	2	13	IDCP	3	69%	1.6:1
d)	4	11α	NIS	24	71%	3.5:1
e)	4	12	IDCP	24	63%	3.3:1
f)	4	12	NIS	24	70%	3.5:1
g)	4	13	IDCP	24	52%	9:1
h)	4	18	IDCP	20	68%	4:1
i)	4	18	NIS	20	35%	4:1
j)	4	8b	IDCP	20	57%	4:1
k)	4	7b	IDCP	19	65%	6.7:1
l)	4	15	IDCP	19	55%	8.9:1
m)	5	8b	IDCP	23	32%	
n)	5	18	IDCP	23	34%	

does not appear to be a factor. Interestingly, Table 1 also shows that α:β selectivity, does not depend on the promoter (entry e versus f; h versus i) or on the location of the triggering group (entry a versus b; d versus f; h versus j).

The possibility of anchimeric assistance by the 4-acetoxy group of **1** (Scheme 2), first hypothesized by Ferrier,[4d] can be excluded in several of the cases here described, in view of our use of nonparticipating protecting groups at C-4. Thus our results with the allylic *n*-pentenyl esters and the allylic thioglycoside **12** (Scheme 5) are in agreement with the rationalization of Zamojski et al. for the Ferrier rearrangement, which is based on the leaving properties of the group at C-3.[6c,42]

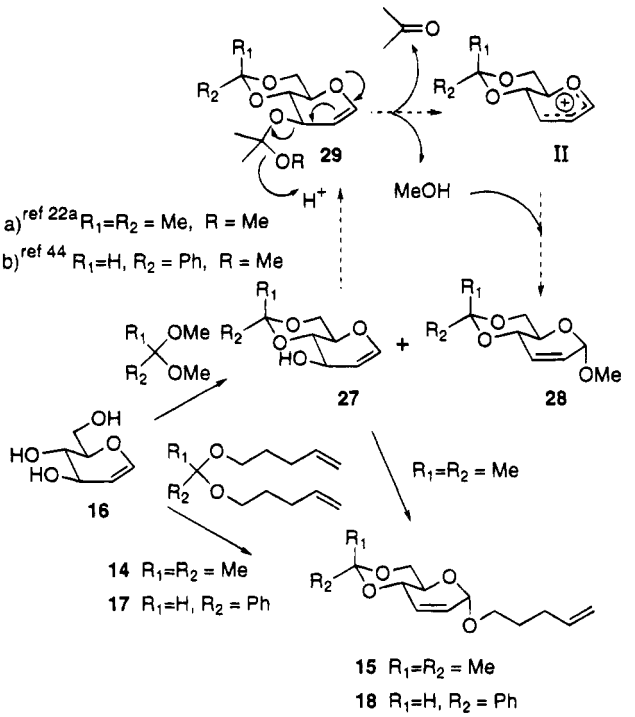
Our results with esters **9b** and **10** (Scheme 4d,e) also seem to indicate that the leaving group properties are reinforced when the anomeric oxygen lone pair is anti to the leaving group at C-3. The vinylogous anomeric effect, first postulated by Curran,[43] provides a rationalization for these observations.

The question of the leaving group properties of the substituent at C-3 had been of concern to us earlier when it was observed that, upon treatment with dimethoxypropane, D-glucal **16** gave the acetonated hex-2-enopyranoside **28a** with only minor amounts of the desired glucal **27a**(≡ **7a**)[22a] (Scheme 8). We suggested that the latter was formed but reacted further to give the mixed acetal **29a** which underwent elimination of the allylic oxygen with concomitant liberation of methanol. The latter then intercepted the allylic oxocarbenium ion **II** to form **28a**. A similar result was later reported by Florent and Monneret[44] by reaction of glucal **16** with α,α-dimethoxytoluene which gave the glycoside **28b** in 92% yield.

The present work has given us the opportunity to revisit this hypothesis in the context of the synthesis of the unsaturated NPGs **15** and **18**. We reasoned that with the recently described dipent-4-enyl acetals **14** and **17**[29] the overall result (Scheme 8) would be formation of

(42) Descotes, G.; Martin, J.-C. *Carbohydr. Res.* **1977**, *56*, 168.
(43) Curran, D. P.; Suh, Y.-S. *J. Am. Chem. Soc.* **1984**, *106*, 5002.
(44) Florent, J. C.; Monneret, C. *Synthesis*, **1982**, 29.

Scheme 8. One-Step Preparation of 4,6-*O*-Acetal Derivatives of Allylic nPGs from d-Glucal by Means of Dipent-4-enyl Acetals



n-pentenyl hex-2-enopyranoside with an acetal protecting group bridging **O4** and **O6**. This proved to be the case. Thus treatment of **16** with the dipent-4-enyl acetals **14** and **17** in the presence of CSA led to compounds **15** and **18** in appreciable quantities (also see Scheme 3).

In the first stereoselective synthesis of sucrose, Fraser-Reid and Iley[45ab] prepared compound **23** as an advanced intermediate by a much longer route. The result in Scheme 4c therefore provides a ready alternative that paves the way for a more expeditious synthesis of sucrose and its derivatives.

Conclusions

NPEs, NPGs, and phenylthio groups in unsaturated monosaccharide glycosyl donors can be used to generate allylic oxocarbenium ion **II**, the key intermediate of the Ferrier rearrangement, by the use of iodonium ion as promoter. As in the normal Ferrier rearrangement, α-glycosides, resulting from quasi-axial interception of **II** by the glycosyl acceptors, were obtained as the major products. This oxidative modification of the Ferrier rearrangement allows the reaction to take place under nonacidic conditions, from easily accessible starting materials, and with fairly unreactive secondary and tertiary hydroxyl groups of monosaccharide acceptors to afford coupling products in fairly good yields.

Experimental Section

General Procedure. Melting points were determined in capillary tubes and are uncorrected. Optical rotations were determined at the sodium D line and measured in chloroform. 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 rotoeavaporator. Unless otherwise noted, materials were obtained from commercially available sources and used without further purification. Solvents were dried and purified using standard methods. For preparation and characterization of compounds **11**α, **11**β, and **12** see refs 26–28.

General Procedure for *n*-Pentenoylation of Glycals.[15] A stirred solution of alcohol (1 equiv) and pent-4-enoic acid (1.4 equiv) in dry CH_2Cl_2 (1 mL/mmol) was treated sequentially with DCC (1.6 equiv) and a catalytic amount of DMAP at room temperature. The reaction was left overnight, the *N*,*N*-dicyclohexylurea was filtered off, and the filtrate was poured into water. The resulting mixture was extracted with CH_2Cl_2, the combined organic fractions were dried, and the solvent was removed. The residue was purified by flash column chromatography.

4,6-Di-*O*-isopropylidene-3-*O*-(4-pentenoyl)-D-glucal (7b): 80% from **7a**; $[\alpha]^{21}_D$ −92.2° (*c* 2.7); ^{1}H NMR δ 1.34 (s, 3H), 1.46 (s, 3H), 2.35 (m, 4H), 3.76 (m, 2H), 3.90 (dd, J = 4.7, 9.9 Hz, 1H), 3.97 (dd, J = 7.8, 9.9 Hz, 1H), 4.66 (dd, J = 1.8, 6.3 Hz, 1H), 4.96 (m, 2H), 5.36 (dt, J = 1.8, 7.8 Hz, 1H), 5.76 (m, 1H), 6.28 (d, J = 6.3 Hz, 1H); ^{13}C NMR δ 18.9, 28.8, 28.9, 33.5, 61.5, 69.3, 69.8, 99.7, 100.9, 115.5, 136.5, 145.2, 172.6; MS m/z 286 $(M + NH_4)^+$.

Anal. Calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.94; H, 7.43.

4,6-Di-*O*-benzylidene-3-*O*-(4-pentenoyl)-D-allal (8b): 94% from **8a**; $[\alpha]^{21}_D$ +218.5° (*c* 1.6); ^{1}H NMR δ 2.70 (m, 4H), 3.80 (t, J = 10.5 Hz, 1H), 3.94 (dd, J = 4.0, 10.3 Hz, 1H), 4.14 (ddd, J = 5.1, 10.3, 10.5 Hz, 1H), 4.42 (dd, J = 5.1, 10.5 Hz, 1H), 4.94 (m, 3H), 5.42 (dd, J = 4.0, 6.0 Hz, 1H), 5.56 (s, 1H), 5.76 (m, 1H), 6.45 (d, J = 5.9 Hz, 1H), 7.35 (m, 5H); ^{13}C NMR δ 28.4, 33.2, 61.4, 64.5, 68.1, 75.5, 98.0, 101.0, 115.0, 125.6, 127.8, 128.6, 136.1, 136.6, 146.9, 172.1; MS m/z 334 $(M + NH_4)^+$.

Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.13; H, 6.13.

4,6-Di-*O*-benzyl-3-*O*-(4-pentenoyl)-D-galactal (9b): 86% from **9a**; $[\alpha]^{21}_D$ −49.7° (*c* 0.8); ^{1}H NMR δ 2.32 (m, 4H), 3.59 (dd, J = 4.4, 10.5, 1H), 3.74 (dd, J = 4.4, 10.5, 1H) 3.98 (t, J = 3.5 Hz, 1H), 4.24 (m, 1H), 4.46 (m, 4H), 4.69 (m, 1H), 4.98 (m, 2H), 5.45 (m, 1H), 5.76 (m, 1H), 6.39 (dd, J = 1.3, 6.1 Hz, 1H), 7.35 (m, 10H); ^{13}C NMR δ 28.4, 33.2, 61.4, 64.5, 68.1, 75.5, 98.0, 101.0, 115.0, 125.6, 127.8, 128.6, 136.1, 136.6, 146.9, 172.1; MS m/z 426 $(M + NH_4)^+$.

Anal. Calcd for $C_{25}H_{28}O_5$: C, 73.49; H, 6.91. Found: C, 73.17; H, 7.04.

4,6-Di-*O*-benzyl-3-*O*-(4-pentenoyl)-D-gulal (10). To a cooled (0 °C) and stirred solution of **9a** (2.0 g, 6.1 mmol), PPh_3 (3.2 g, 12.2 mmol), and pent-4-enoic acid (1.1 mL, 9.1 mmol) in dry toluene (40 mL) was added a solution of DEAD (1.4 mL, 9.1 mmol) in toluene (3 mL). The reaction mixture was stirred overnight at rt, the solution was concentrated *in vacuo*, and the residue was chromatographed (PE–EtOAc 9:1) to afford **10** (870 mg, 35%, 86% corrected yield): $[\alpha]^{21}_D$ −160.4° (*c* 1.2); ^{1}H NMR δ 2.39 (m, 4H), 3.49 (dd, J = 6.0, 9.8, 1H), 3.57 (m, 1H), 3.73 (dd, J = 6.0, 9.8, 1H), 4.01 (t, J = 6.0 Hz, 1H), 4.42 (d, J = 11.9 Hz, 1H), 4.52 (d, J = 11.9 Hz, 1H), 4.53 (d, J = 12.0 Hz, 1H), 4.76 (d, J = 12.0 Hz, 1H), 4.91 (ddd, J = 1.7, 5.8, 6.1 Hz, 1H), 4.97 (m, 1H), 5.04 (m, 1H), 5.18 (dd, J = 1.9, 5.8 Hz, 1H), 5.80 (m, 1H), 6.66 (d, J = 6.1 Hz, 1H), 7.31 (m, 10H); ^{13}C NMR δ 28.8, 33.7, 66.6, 69.0, 71.1, 72.0, 73.6, 88.5, 115.7, 127.7, 127.8, 128.2, 128.3, 128.4, 136.5, 138.2, 138.3, 171.9; MS m/z 426 $(M + NH_4)^+$.

Anal. Calcd for $C_{25}H_{28}O_5$: C, 73.49; H, 6.91. Found: C, 73.22; H, 6.62.

(45) (a) Iley, D. E.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1975**, *97*, 2563. (b) Fraser-Reid, B.; Iley, D. E. *Can. J. Chem.* **1979**, *57*, 645. (c) Barret, A. G. M.; Bezuidenhoudt, B. C. B.; Melcher, L. M. *J. Org. Chem.* **1990**, *55*, 5196.

Ferrier Rearrangement with Thiophenol. To a stirred and cooled (−20 °C) solution of tri-*O*-acetyl-D-glucal (12.4 g, 45.6 mmol) in dry CH_2Cl_2 (1 mL/mmol) were added thiophenol (4.68 mL, 45.6 mmol) and a catalytic amount of $BF_3{\cdot}Et_2O$ (0.1 mL). The reaction was allowed to warm to rt, stirred for 2 h, and then neutralized by addition of Na_2CO_3. After the solution was stirred for 30 min, the solids were filtered off and the filtrate was evaporated *in vacuo*. The residue was chromatographed (PE−EtOAc 8:2) to give two fractions, the first one containing an 8:1 mixture of **11a** and **11b** (11.5 g, 78%), from which **11a** could be purified by crystallization (hexane/diethyl ether) and a second fraction composed by **12** (1.26 g, 9%).

Pent-4-enyl 4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (13). To a stirred and cooled (0 °C) solution of glucal (2.0 g, 7.35 mmol) in dry CH_2Cl_2 (20 mL) were added 4-pentenol (1.0 mL, 9.7 mmol) and a catalytic amount of $BF_3{\cdot}Et_2O$ (0.5 mL, 4.0 mmol). The mixture was allowed to react for 1 h and then neutralized by addition of Na_2CO_3. After the solution was stirred for 30 min, the solids were filtered off and the filtrate was evaporated *in vacuo*. The residue was chromatographed (PE−EtOAc 8:2) to yield **13** as a 11:1 mixture of α and β pentenylglycosides: ^{1}H NMR δ 1.71 (m, 2H), 2.06 (s, 3H), 2.08 (s, 3H), 2.12 (m, 2H), 3.50 (m, 1H), 3.77 (m, 1H), 4.09 (m, 1H), 4.21 (m, 2H), 4.99 (m, 3H), 5.29 (dd, J = 1.4, 9.6 Hz, 1H), 5.84 (m, 3H); ^{13}C NMR δ 20.8, 21.0, 28.9, 30.4, 63.0, 65.3, 66.9, 68.2, 94.4, 114.9, 127.9, 129.0, 138.0, 170.3, 170.8; MS m/z 316 $(M + NH_4)^+$.

Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.37; H, 7.44. Found: C, 60.21; H, 7.38.

General Procedure for the Reaction of Glycals with Dipent-4-enyl Acetals. To a solution of glycal in dry DMF was added the dipent-4-enyl acetal (2.3 equiv for **16** and 1.1 equiv for **7a**). The mixture was acidified with a catalytic amount of CSA and allowed to stand at room temperature for 2 days. The reaction was quenched with $NaHCO_3$ solution, and the solution was extracted three times with CH_2Cl_2. The combined organic fractions were dried, the solvent removed, and the residue was purified by flash chromatography.

Penten-4-yl 2,3-dideoxy-4,6-*O*-isopropylidene-α-D-*erythro*-hex-2-enopyranoside (15): 39% from **7a** and 36% from **16**; $[\alpha]^{21}_D$ +45.1° (*c* 0.7); ^{1}H NMR δ 1.42 (s, 3H), 1.50 (s, 3H), 1.68 (m, 2H), 2.12 (m, 2H), 3.47 (m, 1H), 3.73 (m, 4H), 3.87 (dd, J = 5.0, 10.1 Hz, 1H), 4.17 (dd, J = 1.2, 8.8 Hz, 1H), 4.94 (s, 1H), 5.01 (m, 2H), 5.67 (dt, J = 2.4, 10.3 Hz, 1H), 5.86 (m, 1H), 5.96 (d, J = 10.3 Hz, 1H); ^{13}C NMR δ 18.9, 28.9, 29.2, 30.2, 63.1, 65.0, 67.7, 67.9, 95.0, 99.8, 114.9, 126.6, 131.4, 138.0.

Anal. Calcd for $C_{14}H_{22}O_4$: C, 65.6; H, 9.44. Found: C, 65.25; H, 9.13.

Penten-4-yl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (18): 41% from **16**; mp 65−66 °C; $[\alpha]^{21}_D$ +97.2° (*c* 0.7); ^{1}H NMR δ 1.72 (m, 2H), 2.16 (m, 2H), 3.51 (m, 1H), 3.86 (m, 3H), 4.15 (m, 1H), 4.29 (dd, J = 4.1, 9.7 Hz, 1H), 5.00 (s, 1H), 5.02 (m, 2H), 5.58 (s, 1H), 5.73 (dt, J = 2.5, 10.4 Hz, 1H), 5.83 (m, 1H), 6.13 (d, J = 10.4 Hz, 1H), 7.30 (m, 2H), 7.58 (m, 3H); ^{13}C NMR δ 29.0, 30.3, 63.9, 68.1, 69.5, 75.3, 95.1, 102.2, 114.9, 126.3, 126.9, 128.2, 128.4, 129.2, 129.6, 130.6; MS m/z 320 $(M + NH_4)^+$.

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.5; H, 7.33. Found: C, 71.73; H, 7.48.

General Procedure for the Iodonium-Induced Glycosidation Reaction. The glycosyl donor (1 equiv) and the acceptor alcohol (1.1 equiv) were azeotropically dried with toluene and kept under vacuum for 1 h. The resulting mixture was dissolved in dry CH_2Cl_2 (0.1 mL/mmol) under argon, and pulverized activated molecular sieves were added. The promotor (NIS or IDCP, 1.6 equiv) was added, and after TLC showed consumption of the starting material, the reaction was diluted with CH_2Cl_2 and filtered off. The filtrate was washed with 10% sodium thiosulfate solution, saturated $NaHCO_3$ solution, and brine. Flash chromatography of the residue afforded the corresponding products.

3-*O*-(4,6-*O*-Isopropylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (19α): mp 102−104 °C; $[\alpha]^{21}_D$ +13.6° (*c* 0.8); ^{1}H NMR δ 1.26 (s, 3H), 1.27 (s, 3H), 1.35 (s, 3H), 1.38 (s, 3H), 1.44 (s, 3H), 1.47 (s, 3H), 3.76 (t, J = 10.5 Hz, 1H), 3.85 (dd, J = 5.1, 10.5 Hz, 1H), 3.91 (dd, J = 5.2, 8.3 Hz, 1H), 4.02 (dd, J = 2.7, 9.3 Hz, 1H), 4.07 (m, 1H), 4.14 (m, 2H), 4.48 (d, J = 3.3 Hz, 1H), 5.14 (s, 1H), 5.62 (dt, J = 1.5, 10.3 Hz, 1H); ^{13}C NMR δ 18.4, 24.9, 25.8, 26.3, 26.4, 28.7, 62.5, 64.6, 67.1, 67.3, 72.1, 80.6, 80.8, 84.1, 95.5, 99.5, 104.9, 108.6, 111.5, 125.4, 131.2; MS m/z 429 $(MH)^+$.

Anal. Calcd for $C_{21}H_{32}O_9$: C, 58.87; H, 7.53. Found: C, 58.68; H, 7.39.

3-*O*-(4,6-*O*-Isopropylidene-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (19β): mp 102−104 °C, $[\alpha]^{21}_D$ +23.4° (*c* 0.5); ^{1}H NMR δ 1.31 (s, 3H), 1.35 (s, 3H), 1.41 (s, 3H), 1.42 (s, 3H), 1.49 (s, 3H), 1.54 (s, 3H), 3.55 (m, 1H), 3.85 (m, 2H), 4.01 (m, 2H), 4.19 (dd, J = 3.0, 6.6 Hz, 1H), 4.28 (m, 2H), 4.34 (m, 1H), 4.60 (d, J = 3.6 Hz, 1H), 5.50 (t, J = 1.4 Hz, 1H), 5.65 (ddd, J = 1.4, 2.4, 10.5 Hz, 1H), 5.88 (d, J = 3.6 Hz, 1H), 6.06 (d, J = 10.5 Hz, 1H); ^{13}C NMR δ 19.2, 25.5, 26.3, 26.7, 26.8, 29.2, 62.7, 66.8, 67.4, 71.9, 72.8, 77.4, 80.5, 84.0, 97.5, 100.0, 105.1, 108.8, 111.8, 127.4, 133.4; MS m/z 429 $(MH)^+$.

3-*O*-(4,6-*O*-Benzylidene-2,3-dideoxy-α-*d*-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (20α): mp 133−135 °C, $[\alpha]^{21}_D$ +48.1° (*c* 0.7); ^{1}H NMR δ 1.28 (s, 3H), 1.30 (s, 3H), 1.37 (s, 3H), 1.46 (s, 3H), 3.82 (m, 2H), 3.94 (dd, J = 5.3, 8.5 Hz, 1H), 4.05 (m, 2H), 4.14 (m, 2H), 4.52 (d, J = 3.6 Hz, 1H), 5.20 (bs, 1H), 5.68 (dt, J 2.4, 10.2 Hz, 1H), 5.85 (d, J = 3.6 Hz, 1H), 6.10 (d, J = 10.2 Hz, 1H), 7.25 (m, 3H), 7.43 (m, 2H); ^{13}C NMR δ 24.9, 25.8, 26.4, 26.5, 63.6, 67.3, 68.9, 72.2, 74.6, 80.7, 80.8, 84.1, 95.5, 101.7, 104.9, 108.6, 111.5, 125.7, 125.8, 127.9, 128.7, 130.4, 136.7; MS m/z 494 $(M + NH_4)^+$.

Anal. Calcd for $C_{25}H_{32}O_9$: C, 63.01; H, 6.77. Found: C, 62.85; H, 6.43.

3-*O*-(4,6-*O*-Benzylidene-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (20β): $[\alpha]^{21}_D$ +45.3° (*c* 0.1); ^{1}H NMR δ 1.3 (s, 3H), 1.37 (s, 3H), 1.43 (s, 3H), 1.50 (s, 3H), 3.77 (m, 1H), 3.89 (t, J = 10.2 Hz, 1H), 4.03 (m, 2H), 4.20 (dd, J = 3.0, 6.9 Hz, 1H), 4.32 (m, 4H), 4.63 (d, J = 3.7 Hz, 1H), 5.56 (bs, 1H), 5.63 (s, 1H), 5.71 (dt< J = 2.1, 10.3 Hz, 1H), 5.90 (d, J = 3.7 Hz, 1H), 6.23 (d, J = 10.3, 1H), 7.40 (m, 5H); ^{13}C NMR δ 25.1, 26.3, 27.7, 28.3, 66.4, 68.5, 70.4, 72.2, 74.3, 77.9, 80.0, 83.5, 97.0, 101.6, 104.7, 108.3, 111.8, 125.7, 127.1, 127.9, 128.7, 132.3; MS m/z 477 $(MH)^+$.

Anal. Calcd for $C_{25}H_{32}O_9$: C, 63.01; H, 6.77. Found: C, 62.72; H, 6.49.

3-*O*-(4,6-Di-*O*-benzyl-2-deoxy-2-iodo-3-(4-pentenoyl)-α-D-talopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (21): $[\alpha]^{21}_D$ +6.71° (*c* 0.5); ^{1}H NMR δ 1.21 (s, 3H), 1.37 (s, 3H), 1.41 (s, 3H), 1.48 (s, 3H), 2.47 (m, 4H), 3.50 (dd, J = 5.4, 10.2 Hz, 1H), 3.77 (dd, J = 7.2, 10.2 Hz, 1H), 3.94 (m, 2H), 4.07 (dd, J = 2.7, 8.1 Hz, 1H), 4.15 (dd, J = 6.3, 8.4 Hz, 1H), 4.24 (m, 2H), 4.31 (m, 1H), 4.50 (m, 2H), 4.70 (d, J = 3.3 Hz, 1H), 4.88 (d, J = 11.7 Hz, 1H), 4.96 (t, J = 3.9 Hz, 1H), 5.03 (bd, J = 10.2 Hz, 1H), 5.84 (m, 1H), 5.86 (d, J = 3.3 Hz, 1H), 7.28 (m, 10H); ^{13}C NMR δ 21.8, 25.4, 26.1, 26.2, 26.7, 26.8, 28.6, 33.6, 67.8, 68.5, 68.7, 71.2, 72.4, 73.1, 73.5, 73.8, 81.5, 81.6, 83.5, 102.7, 105.3, 109.3, 111.9, 115.8, 127.7, 127.9, 128.3, 128.4, 136.3, 137.9, 171.6.

Anal. Calcd for $C_{37}H_{47}O_{11}I$: C, 55.92; H, 5.96. Found: C, 55.67; H, 5.58.

6-*O*-(4,6-Di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (22): $[\alpha]^{21}_D$ −103.9° (*c* 0.6); ^{1}H NMR δ 1.12 (s, 3H), 1.29 (s, 3H), 1.37 (s, 3H), 1.43 (s, 3H), 3.67 (dd, J = 2.7, 5.2 Hz, 1H), 3.75 (d, J = 5.9 Hz, 2H), 3.93 (dd, J = 5.4, 8.4 Hz, 1H), 4.05 (dd, J = 5.7, 8.4 Hz, 1H), 4.08 (d, J = 2.7 Hz, 1H), 4.19 (m, 2H), 4.27 (d, J = 2.7 Hz, 1H), 4.55 (m, 4H), 4.77 (d, J = 3.6 Hz, 1H), 5.27 (d, J = 3.0 Hz, 1H), 5.80 (d, J = 3.6 Hz, 1H), 5.94 (dd, J = 3.0, 10.2 Hz, 1H), 6.09 (dd, J = 5.2 Hz, 10.2 Hz, 1H); ^{13}C NMR δ 25.4, 26.1, 26.9, 27.0, 67.3, 67.7, 70.0, 70.4, 70.9, 72.7, 73.7, 81.2, 81.4, 83.9, 95.7, 105.4, 109.0, 111.8, 127.1, 127.6, 127.8, 128.4, 129.2, 138.2, 138.3; MS m/z 586 $(M+NH_4)^+$.

Anal. Calcd for $C_{32}H_{40}O_9$: C, 67.59; H, 7.09. Found: C, 67.73; H, 7.24.

2-*O*-(4,6-Di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,3:4,6-tetra-*O*-acetyl-α(and β)-D-gluco-

furanose (23): ^{1}H NMR (mixture 2.4:1 two isomers) δ 2.06 (s, 3H major isomer), 2.08 (s, 3H, major isomer), 2.10 (s, 6H major isomer and 3H minor isomer), 2.11 (s, 3H minor isomer), 2.13 (s, 3H minor isomer), 2.16 (3H minor isomer), 3.79 (m, 2H), 3.99 (m, 1H), 4.06–4.60 (m, 6H), 4.93 (m, 1H), 5.48–5.78 (m, 4H), 6.17 (m, 1H), 7.26 (m, 3H), 7.47 (m, 2H); ^{13}C NMR δ 20.6, 20.7, 20.8, 20.9, 61.0, 61.7, 63.1, 63.3, 64.6, 64.8, 65.5, 69.0, 69.1, 69.4, 70.8, 73.7, 74.7, 74.8, 75.6, 77.4, 77.7, 77.8, 78.1, 79.2, 80.1, 80.9, 81.7, 87.8, 87.9, 92.3, 102.1, 102.2, 102.3, 102.4, 107.4, 107.5, 126.2, 126.3, 126.4, 126.5, 126.7, 128.1, 128.2, 128.4, 129.0, 129.3, 131.1, 131.2, 131.3, 131.4, 137.1, 137.2, 137.4, 168.2, 168.3, 169.4, 169.6, 170.0; MS m/z 565 $(MH)^+$.

Anal. Calcd for $C_{27}H_{32}O_{13}$: C, 57.44; H, 5.71. Found: C, 57.11; H, 6.02.

6-*O*-(4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (3): ^{1}H NMR (mixture α and β isomers) δ 1.31 (s, 3H α isomer and 6H α isomer), 1.33 (s, 3H α isomer), 1.41 (s, 3H α isomer), 1.42 (s, 3H β isomer), 1.51 (s, 3H), 2.06 (s, 3H β isomer), 2.07 (s, 3H β isomer), 2.09 (s, 6H α isomer), 3.66–4.31 (m, 8H), 4.59 (m, 1H), 5.08 (s, 1H), 5.16 (t, J = 4.4 Hz, 1H β isomer), 5.19 (d, J = 1.1 Hz, 1H α isomer), 5.32 (s, 1H β isomer), 5.51 (t, J = 4.4 Hz, 1H α isomer), 5.80–6.01 (m, 2H); ^{13}C NMR δ 20.8, 20.9, 24.3, 24.5, 24.9, 25.9, 62.8, 63.3, 64.2, 65.2, 66.1, 66.9, 67.0, 97.2, 67.4, 70.4, 70.5, 70.6, 70.9, 71.1, 72.6, 94.5, 95.3, 96.2, 96.3, 108.5, 109.2, 125.6, 127.7, 129.1, 130.5, 170.2, 170.5, 170.8; MS m/z 490 $(M + NH_4)^+$.

Anal. Calcd for $C_{22}H_{32}O_{11}$: C, 55.93; H, 6.83. Found: C, 55.79; H, 6.59.

3-*O*-(4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (24α): $[\alpha]^{21}_D$ +47.0° (c 0.8); ^{1}H NMR δ 1.29 (s, 3H), 1.31 (s, 3H), 1.39 (s, 3H), 1.48 (s, 3H), 2.07 (s, 3H), 2.10 (s, 3H), 3.95 (dd, J = 5.1, 8.4 Hz, 1H), 4.02–4.26 (m, 6H), 4.31 (d, J = 2.7 Hz, 1H), 4.61 (d, J = 3.6 Hz, 1H), 5.36 (m, 2H), 5.82 (m, 3H); ^{13}C NMR δ 25.3, 26.5, 26.8, 27.0, 63.3, 65.5, 67.2, 67.7, 72.6, 81.2, 81.3, 84.3, 95.4, 105.4, 109.5, 112.0, 127.2, 129.4, 170.2, 170.8; MS m/z 490 $(M + NH_4)^+$.

Anal. Calcd for $C_{22}H_{32}O_{11}$: C, 55.93; H, 6.83. Found: C, 55.86; H, 6.78.

3-*O*-(4,6-Di-*O*-acetyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (24β): $[\alpha]^{21}_D$ +63.2° (c 0.6); ^{1}H NMR δ 1.30 (s, 3H), 1.31 (s, 3H), 1.40 (s, 3H), 1.48 (s, 3H), 2.30 (s, 6H), 4.00 (m, 4H), 4.14 (dd, J = 2.9, 7.3 Hz, 1H), 4.25 (m, 3H), 4.31 (d, J = 2.9 Hz, 1H), 4.59 (d, J = 3.7 Hz, 1H), 5.27 (m, 1H), 5.38 (d, J = 1.6 Hz, 1H), 5.88 (m, 2H), 6.02 (dt, J = 1.6, 10.4 Hz, 1H); ^{13}C NMR δ 20.8, 21.0, 25.3, 26.30, 26.8, 62.7, 64.3, 67.0, 72.4, 73.2, 76.6, 80.6, 83.6, 94.6, 105.1, 108.9, 111.8, 128.8, 129.5, 170.2, 170.7; MS m/z 490 $(M + NH_4)^+$.

Anal. Calcd for $C_{22}H_{32}O_{11}$: C, 55.93; H, 6.83. Found: C, 55.79; H, 6.75.

Spiroketal 26: ^{1}H NMR (mixture of two isomers) δ 1.16 (d, J = 7.3 Hz, 3H β isomer), 1.22 (d, J = 6.38 Hz, 3H α isomer), 1.70–2.10 (m, 8H), 3.40 (s, 3H), 3.44 (s, 3H), 3.90–4.30 (m, 3H), 4.60 (dd, J = 4.0, 7.7 Hz, 1H), 5.61 (ddd, J = 1.8, 2.2, 9.9 Hz, 1H), 5.93 (ddd, J = 3.0, 4.6, 9.9 Hz, 1H). MS m/z 315 $(MH)^-$.

Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.63; H, 8.59.

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