

## Glycosylation with Trichloroacetimidates in Ionic Liquids: Influence of the Reaction Medium on the Stereochemical Outcome

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The glycosylation with trichloroacetimidates derived from different glycopyranoses bearing a nonparticipating group at C-2 was explored in different ionic liquids as solvents. The stereoselectivity of the reaction was significantly affected by the reaction media and by the anomeric configuration of the donor.

Ionic liquids (ILs) have recently found increasing applicability as solvents in organic reactions.<sup>1</sup> Due to their high polarity, reactions in ILs have kinetic and thermodynamic behavior different from classical solvents, which often leads to improved process performance.<sup>2</sup>

Relatively few papers have appeared in the literature describing glycosylation reaction performed in ILs,<sup>3</sup> where they emerged as suitable solvents. In a preliminary communication, we reported on the use of [emim]- $[OTf]^4$  and [bmim][PF<sub>6</sub>]<sup>5</sup> (Figure 1) as solvents for glycosylation of 2-propanol or carbohydrate acceptors with



**FIGURE 1.** Structure of [emim][OTf],  $[bmim][PF_6]$ , and  $[emim][BF_4]^{6a}$  (a) water-soluble coordinating anion; (b) hydrophobic noncoordinating anion; (c) water-soluble noncoordinating anion.

various trichloroacetimidate donors, under trimethylsilyl trifluoromethanesulfonate (TMSOTf) catalysis.<sup>3d</sup> The coupling reactions proceeded under mild conditions, at room temperature, and, in some cases, avoiding the use of the Lewis acid catalyst. Moreover, the ionic liquid could be recycled without loss of the Lewis acid catalytic properties, rendering the glycosylation reaction performed in these media appealing especially from an industrial point of view.

During these preliminary experiments, we observed that, in [emim][OTf], trichloroacetimidates bearing nonparticipating groups at C-2 yielded preferentially the  $\beta$ -glycoside.<sup>3d</sup> Similar results were subsequently reported by Toshima et al.,<sup>3e</sup> who invoked a possible coordination from the  $\alpha$ -side of the oxonium ion by the triflate, inducing the nucleophilic attack of the acceptor from the  $\beta$ -side. A similar coordination effect is described for nitriles at low temperature and in the presence of a strong acid catalyst (such as TMSOTf)<sup>7</sup> and in Crich's works on glycosyl triflates for the synthesis of 1,2-*cis*glycosides.<sup>8</sup>

To gain further insight into the glycosylation mechanism in ILs, we report herein a systematic study describing the glycosylation with anomerically pure  $\alpha$ - and  $\beta$ -trichloroacetimidate donors both in coordinating and noncoordinating ILs.

First, the general efficiency of [emim][OTf] and "classical" solvents in the glycosylation of 2-propanol with  $\alpha$ and  $\beta$ -2,3,4,6-tetra-O-benzyl glucopyranose trichloroacetimidate 1<sup>9</sup> was compared. The results are reported in Table 1.

Among the classical solvents, dichloromethane and diethyl ether (entries 1, 2, 7, and 8) provided products  $2\alpha,\beta^{10}$  with a prevalent inversion of the anomeric configuration of the starting donor, while acetonitrile (entries 3 and 9) gave predominantly the  $\beta$ -glycoside. Interest-

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TABLE 1.	<b>Glycosylation</b> d	of Isopropanol	with α- and
β-2,3,4,6-Tet	ra-O-benzyl Glu	ucopyranose	
Trichloroac	etimidates 1 in	Different Solv	ents <sup>a</sup>

Entry	Donor Solvent		Product	Yield (%)	α/β ratio⁵	Reaction time
1		$CH_2Cl_2$		85	16/84	20 min.
2		$Et_2O$	BnO BnO BnO OiPr	96	40/60	20 min.
3		CH <sub>3</sub> CN		84	18/82	20 min.
4	<sup>BnO</sup> ÓTCA 1α	[emim][OTf]	2α,β	67	16/84	2 h
5		[emim][OTf] <sup>°</sup>		79	15/85	30 min.
6		CH <sub>2</sub> Cl <sub>2</sub> :[emim][OTf]	1:1	65	25/75	20 min.
7		$CH_2Cl_2$		86	70/30	20 min.
8		$Et_2O$		68	72/28	20 min.
9		A CH <sub>3</sub> CN		58	43/57	20 min.
10	BnO 1β	[emim][OTf]	2α,β	Quant.	45/55	20 min.
11		[emim][OTf] <sup>c</sup>		85	20/80	48 h
12		1:1	72	54/46	20 min.	

<sup>*a*</sup> All reactions were carried out with 20 equiv of 2-propanol and 0.01 equiv of TMSOTf in 0.5 mL of solvent at room temperature. <sup>*b*</sup> Determined by NMR. <sup>*c*</sup> Reaction performed without Lewis acid catalysis.

## SCHEME 1



ingly, in [emim][OTf], both  $1\alpha$  and  $1\beta$  afforded mainly the  $\beta$ -isopropyl glycoside  $2\beta$  (entries 4, 5, 10, and 11). This was particularly evident when donor  $1\beta$  was allowed to react in the absence of the acidic catalyst (entry 11; 20/ 80  $\alpha/\beta$ ). In addition, experiments performed in a 1:1 [emim][OTf]/CH<sub>2</sub>Cl<sub>2</sub> mixture evidenced that donor  $2\beta$ provided lower  $\alpha/\beta$  ratios with growing concentration of [emim][OTf] (compare entries 7 and 12 with entry 10 in Table 1).

The investigation of the reaction in [emim][OTf] was extended to various anomerically pure  $\alpha$ - and  $\beta$ -donors bearing nonparticipating groups at C-2, according to Scheme 1. Each reaction was run both in the presence (0.01 equiv) and in the absence of the acidic promoter (TMSOTf).

The results are reported in Table 2. Regardless of their anomeric configuration, all the glycosyl donors provided predominantly the  $\beta$ -glycoside, with  $\alpha$ -donors showing higher selectivities. The only exception emerged with mannosyl donors  $8\alpha$  and  $8\beta$  (entries 13–16), in line with the known difficulty in the direct synthesis of  $\beta$ -mannosides, where steric effects dominate the reactivity.<sup>18</sup>

TABLE 2.	<b>Glycosylation of Isopropanol wit</b>	th
Trichloroad	etimidate Donors in [emim][OTf]	

Entrv	Donor	Acceptor	Yield (%)	α/β	Reaction	Product
		F		ratio*	time	
1	PhTODO	3	68	5/95	1 h	
	BnO N <sub>3</sub>					9α,β
2	<b>5α</b> <sup>12</sup> <b>ΟΤ</b> CA	3	22 <sup>b,c</sup>	<2/98	48 h	
3	PhTOT 0	3	68	40/60	2 h	
	BNO					9a.B
4	<b>5</b> β <sup>12</sup>	3	n.r. <sup>b</sup>	-	24 h	,,P
5	OTCA	3	Quant	18/82	4 h	
	OAC					10a.B
6	οΑc 6α <sup>13</sup>	3	Quant. <sup>b</sup>	16/84	24 h	100,p
7		3	85	37/63	10 min.	
	OAc OAc	-				10α,β
8	6β	3	96 <sup>b</sup>	28/72	15 min.	
9	BnOCOBn	3	89	18/82	1,5 h	
	BnO					11α B <sup>14</sup>
10	<sup>ΒΠΟ</sup> ΌΤCΑ <b>7α</b> <sup>9</sup>	3	64 <sup>b</sup>	30/70	1,5 h	110,p
11	BnO_OBn	3	72	46/54	45 min.	
		-				11 a B
12	BnÒ <b>7</b> 8 <sup>9</sup>	3	$78^{b}$	47/53	45 min.	Πu,p
12	/p	2	22	50/50	2.1	
15	BnO OBII	3	82	50/50	2 n	- 16
	OTCA		- b			12α,β'
14	<b>8α</b> <sup>9</sup>	3	Quant."	50/50	2 h	
15	BnO- OBn	3	36	80/20	45 min.	
	BnO OTC	A				12α,β
16	<b>8β</b> <sup>16</sup>	3	28 <sup>b</sup>	87/13	45 min.	4
17	1α	4	83	16/84	4 h	<b>13α,β</b> <sup>17</sup>
18	1β	4	68 <sup>d</sup>	25/75	48 h	13α,β

 $^a$  Determined by NMR.  $^b$  Reaction performed without Lewis acid catalysis.  $^c$  Also isolated was 28% of the glycoside lacking the benzylidene group in a 14/86  $\alpha/\beta$  ratio.  $^d$  TMSOTf 0.02 equiv.

Nevertheless, donor  $8\alpha$  gave a 50/50  $\alpha/\beta$  ratio: This result is worthy of note when compared with the data obtained by Crich<sup>8a</sup> with an analogue thioglycoside donor at -78°C and considering that the reaction was run at room temperature. 2-Deoxy-2-azido glucopyranosyl donors **5** were poorly reactive in the absence of the acidic promoter. In fact, compound **5** $\alpha$  reacted only in 48 h (entry 2) providing only 22% of the expected product. The corresponding donor **5** $\beta$  did not yield any product after 24 h (entry 4).

The same trend in selectivity was observed by using carbohydrate acceptors (entries 17 and 18): Glucosyl donors  $1\alpha$  and  $1\beta$  reacted with armed acceptor  $4,^9$  affording disaccharides  $13\alpha,\beta$  mainly as the  $\beta$ -anomer.

An analogous series of experiments was performed in ILs containing a noncoordinating anion such as [bmim]- $[PF_6]$  and  $[emim][BF_4]$  (Figure 1). The results are summarized in Table 3. In this case, the stereochemistry of the products was strongly dependent on the anomeric

<sup>(11)</sup> Discrepancies in the reaction times were mainly due to the diverse solubility of the substrates in the reaction media. This was noted even between different batches of the same trichloroacetimidate (e.g., entries 4 and 5 in Table 1).

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TABLE 3. Glycosylation of Isopropanol with Trichloroacetimidates 5–8 in [bmim][PF<sub>6</sub>] and [emim][BF<sub>4</sub>]

entry	donor	solvent	yield (%)	$\alpha/eta$ ratio <sup>a</sup>	reaction time	product no.
1	1α	$[bmim][PF_6]$	98	18/82	20 min	2α,β
2	1α	$[emim][BF_4]$	80	12/88	4 h	$2\alpha,\beta$
3	$1\beta$	$[bmim][PF_6]$	98	76/24	24  h	$2\alpha,\beta$
4	$1\beta$	$[emim][BF_4]$	74	85/15	4 h	$2\alpha,\beta$
5	5α	$[bmim][PF_6]$	64	7/93	2 h	9α,β
6	$5\beta$	$[bmim][PF_6]$	$43^b$	95/5	48 h	9α,β
7	6α	$[bmim][PF_6]$	quant	25/75	1 h	10α,β
8	$6\beta$	$[bmim][PF_6]$	quant	73/27	$5 \min$	10α,β
9	$7\alpha$	$[bmim][PF_6]$	91	17/83	$20 \min$	$11\alpha,\beta$
10	$7\beta$	$[bmim][PF_6]$	93	67/33	$20 \min$	$11\alpha,\beta$
11	8α	$[bmim][PF_6]$	94	47/53	1.5 h	$12\alpha,\beta$
12	$8\beta$	$[bmim][PF_6]$	75	76/24	$30 \min$	$12\alpha,\beta$
$^a$ Determined by NMR. $^b$ Performed with 0.1 equiv of TMSOTf.						

configuration of the donor:  $\alpha$ -donors gave predominantly  $\beta$ -glycosides, while  $\beta$ -donors mainly afforded  $\alpha$ -products. Once more, tetra-O-benzyl-mannose donor  $8\alpha$  gave the poorest stereoselectivity (47/53  $\alpha/\beta$  in entry 11).

To date, the study of the influence of ILs in the mechanism of a reaction is still in its early stages. Since the interaction between the substrate and these media depends on many factors (H-bonding ability and reciprocal ion pairing, viscosity, polarity, presence of cavities in the ILs, etc.), general trends can hardly be established.<sup>19</sup>

Taken together, our results show a different ability of [emim][OTf] and noncoordinating ILs in addressing the stereochemistry of glycosylation products. In particular, the prevalence of  $\beta$ -products observed in [emim][OTf] suggests a possible coordination of the triflate anion from the  $\alpha$ -side of the oxonium ion. This hypothesis was investigated through two low-temperature <sup>1</sup>H NMR spectroscopy experiments.<sup>20</sup> Glucosyl imidates  $1\alpha$  and  $1\beta$ were dissolved in  $CD_2Cl_2$  at  $-78^\circ$  in the presence of 1.5 equiv of [emim][OTf]. The donors were subsequently activated by addition of 0.01 equiv of TMSOTf. <sup>1</sup>H NMR spectra were recorded at regular time intervals (see Supporting Information). Inspection of the spectra revealed that compound  $1\beta$  (H-1, doublet at 5.74 ppm, J =7.4 Hz; NH, singlet at 8.83 ppm) converted within 30 min to glucosyl imidate  $1\alpha$  (H-1, doublet at 6.40 ppm, J =3.4 Hz; NH, singlet at 8.71 ppm) and to a third carbohydrate species whose anomeric proton appeared as a doublet at  $\delta$  6.16 ppm with J = 2.9 Hz. This was identified as the  $\alpha$ -glucosyl triflate according to the chemical shift reported in the literature.<sup>8b</sup> The peaks corresponding to  $1\alpha$  and to the  $\alpha$ -glucosyl triflate disappeared after 40 and 100 min, respectively, affording degradation byproducts.<sup>21</sup> On the contrary, the kinetics of the reaction of the  $\alpha$ -glucosyl imidate was sluggish. The H-1 peak intensity decreased slowly, and only a small amount of anomeric triflate (H-1, doublet at  $\delta$  6.16

ppm, J = 2.9 Hz) was generated. Its concentration remained low and constant for the duration of the experiment (210 min).

Although the experimental conditions used in NMR experiments were far from those reported in Tables 1–3, the data obtained disclose some possible reaction intermediates. Starting both from  $1\alpha$  and  $1\beta$ , the covalent anomeric  $\alpha$ -triflate is formed as a transient species, demonstrating that the triflate of the IL is able to coordinate the oxonium ion generated by trichloroace-timidate displacement. In the case of  $\beta$ -imidate, preanomerization to the  $\alpha$ -imidate also occurs: To our knowledge, this phenomenon has never been described previously, and we cannot exclude that it occurs also at room temperature and in neat IL.

According to these NMR results, a possible interpretation of the data reported in Tables 1 and 2 is that, in [emim][OTf],  $\alpha$ -donors react directly with the acceptor and/or through an  $\alpha$ -triflate intermediate, affording mainly  $\beta$ -products.  $\beta$ -Donors seem to provide the  $\beta$ -glycosides both by donor preanomerization and by formation of the  $\alpha$ -triflate intermediate. Moreover, in both cases, the incomplete stereoselectivity of the glycosylation can be due to the concurrent contribution of the highly reactive oxonium ion intermediate, present as a tight/ loose ionic couple. Finally, the higher amount of the  $\alpha$ -glycosides obtained from  $\beta$ -trichloroacetimidates is most likely due to the direct attack by the acceptor on the donors.

In conclusion, we showed that ionic liquid triflate in [emim][OTf] is sufficiently nucleophilic to interact with the oxonium ion. This influences the stereochemical outcome of the glycosylation performed in this medium. On the other hand, when the reaction is performed in noncoordinating ILs, the prevailing mechanism leads to inversion of the donor anomeric configuration, as observed in "classical" noncoordinating solvents under the same reaction conditions.

## **Experimental Section**

General Procedure for the Preparation of Monosaccharide Glycosides 2, 9–12. The donor (100 mg, 1 equiv) and 2-propanol (20 equiv) were dissolved in the solvent (0.5 mL), and TMSOTF (0.01 equiv) was added unless specifically mentioned otherwise. The reaction was stirred at room temperature until TLC showed complete conversion of the donor. For reaction in classical organic solvents, workup consisted of neutralization with triethylamine and evaporation of the solvent. For reactions in ILs, the workup was performed by addition of water and extraction of the product with chloroform. The crude mixture was purified by flash chromatography.

General Procedure for the Preparation of Disaccharides 13 $\alpha$  and 13 $\beta$ . The acceptor (60 mg, 1 equiv) and TMSOTf (0.01 equiv) were dissolved [emim][OTf] (0.5 mL). The donor (1.5 equiv) was added as a solid, and the reaction was stirred at room temperature until completion. After addition of water and extraction with chloroform, the crude was purified by flash chromatography.

Compounds  $2\alpha,\beta,9$   $11\alpha,\beta,12$   $12\alpha,\beta,13$  and  $13\alpha,\beta^{15}$  displayed the same chemical-physical characteristics already reported in the literature.

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<sup>(20)</sup> Low-temperature NMR experiments in neat [emim][OTf] are unfeasible, as it freezes at -9 °C.

<sup>(21)</sup> Chromatography of the mixture revealed the formation of different degradation byproducts, including the glucosyl-trichloro-acetamide, the reducing sugar derived from hydrolysis of the trichlo-roacetimidate, and the penta-O-benzyl glycoside.

Donors 1 and 4-7 were synthesized according to the procedures already published in the literature,  $^{9,12,13,16}$  except donor  $6\beta$ , whose preparation is described herein.

**<sup>3,4-</sup>Di-O-acetyl-2-O-benzyl-\beta-L-fucopyranosyl Trichloro-acetimidate** (6 $\beta$ ). To a solution of 2-O-benzyl-3,4-di-O-acetyl

fucopyranose (1392 mg, 4.11 mmol) in dry  $CH_2Cl_2$  (20 mL), trichloroacetonitrile (2.06 mL), and K<sub>2</sub>CO<sub>3</sub> (2270 mg, 16.4 mmol) were added. The reaction was stirred at room temperature until completion, then it was filtered over a celite pad and the solvent was evaporated. The crude was purified by flash chromatography (eluent: 7/3 hexane/EtOAc) providing 1298 mg of the product (2.67 mmol, 65%).  $[\alpha]_D^{22}$  –52.4 (c 1.1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.74 (s, 1H), 7.34–7.28 (m, 5H), 5.84 (d, 1H, J = 8.1 Hz), 5.28 (d, 1H, J = 3.4 Hz), 5.10 (dd, 1H, J = 3.4, J = 3.410.1 Hz), 4.91 (d, 1H, J = 11.4 Hz), 4.68 (d, 1H, J = 11.4 Hz), 3.98 (q, 1H, J = 6.5 Hz), 3.91 (dd, 1H, J = 8.2, J = 10.1 Hz),2.19 (s, 3H), 1.97 (s, 3H), 1.25 (d, 3H, J = 6.5 Hz). <sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  171.1, 170.5, 161.8, 98.9, 76.0, 75.6, 73.3, 71.0, 70.7, 21.3, 21.2, 16.6. FT IR (CHCl<sub>3</sub>) v 1678, 1742, 3038 cm<sup>-1</sup>. Anal. Calcd for  $C_{19}H_{22}O_7NCl_3$  (482.74): C, 47.27; H, 4.59; N, 2.90. Found: C, 47.32; H, 4.52, N, 2.93.

**O-Isopropyl-2-azido-2-deoxy-3-O-benzil-4,6-O-benziliden**α-**D-glucopyranoside** (9α). Eluent: 9/1 hexane/EtOAc.  $[α]_D^{22}$ + 115.7 (*c* 0.51, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.52– 7.25 (m, 15H), 5.59 (s, 1H), 4.98 (d, 1H, *J* = 3.5 Hz), 4.96 (d, 1H, *J* = 11.0 Hz), 4.80 (d, 1H, *J* = 11.0 Hz), 4.27 (dd, 1H *J* = 4.7, 10.1 Hz), 4.11 (t, 1H, *J* = 9.3 Hz), 4.02–3.89 (m, 2H), 3.75 (t, 1H, *J* = 10.1 Hz), 3.70 (t, 1H, *J* = 9.3 Hz), 3.29 (dd, 1H, *J* = 3.5, 9.3 Hz), 1.27–1.22 (m, 6H). <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): δ 101.3, 97.1, 83.0, 76.0, 75.0, 71.3, 68.9, 62.8, 23.3, 21.5. FT IR (CHCl<sub>3</sub>)  $\nu$  1261, 2110, 2255, 2875, 2924, 2970 cm<sup>-1</sup>. Anal. Calcd for C<sub>23</sub>H<sub>27</sub>O<sub>5</sub>N<sub>3</sub> (425.48): C, 64.93; N, 9.88; H, 6.40. Found: C, 64.90; N, 9.92; H, 6.35.

**O-Isopropyl-2-azido-2-deoxy-3-O-benzil-4,6-O-benziliden**β-**D-glucopyranoside** (9β). Eluent: 9/1 Hexane/EtOAc.  $[\alpha]_D^{22}$ -61.3 (*c* 1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.49-7.25 (m, 15H), 5.57 (s, 1H), 4.91 (d, 1H, J = 11.4 Hz), 4.79 (d, 1H, J = 11.4 Hz), 4.44 (d, 1H, J = 7.8 Hz), 4.32 (dd, 1H, J = 4.9, 10.3 Hz), 3.99 (septuplet, 1H, J = 6.2 Hz), 3.80 (t, 1H, J = 1.25 (m, 6H). <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>): δ 101.2, 81.5, 78.9, 66.2, 73.1, 74.9, 68.7, 23.5, 21.9. FTIR (CHCl<sub>3</sub> solution)  $\nu$  2115, 2245, 2880, 2968, 3010 cm<sup>-1</sup>. Anal. Calcd for C<sub>23</sub>H<sub>27</sub>O<sub>5</sub>N<sub>3</sub> (425.48): C, 64.93; N, 9.88; H, 6.40. Found: C, 64.92; N, 9.86; H, 6.38

**O-Isopropyl-3,4-di-O-acetyl-2-O-benzyl-\alpha-L-fucopyranoside (10\alpha) and O-Isopropyl-3,4-di-O-acetyl-2-O-benzyl-\beta-Lfucopyranoside (10\beta). The two compounds were obtained in a \alpha/\beta anomeric mixture that could not be separated by flash chromatography. The ratio between the anomers was determined by NMR, and the peaks of the major component of a 72/ 28 and 18/82 \alpha/\beta mixture are reported, respectively, to describe the \alpha- and \beta-anomer.**  **10**α. Eluent: 95/5 toluene/EtOAc. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.36–7.28 (m, 5H), 5.38–5.29 (m, 2H), 4.95 (d, 1H, J = 3.7 Hz), 4.70 (d, 1H, J = 12.2 Hz), 4.61 (d, 1H, J = 12.2 Hz), 4.22 (q, 1H, J = 6.6 Hz), 3.88 (septuplet, 1H, J = 6.0 Hz), 3.83 (dd, 1H, J = 3.7, 10.0 Hz), 2.15 (s, 3H), 2.01 (s, 3H), 1.25 (d, 3H, J = 6.0 Hz), 1.19 (d, 3H, J = 6.0 Hz), 1.11 (d, 3H, J = 6.6 Hz). <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  171.2, 170.8, 96.2, 74.0, 73.3, 72.4, 71.4, 64.8, 23.8, 22.0, 21.3, 16.5. FTIR (CHCl<sub>3</sub>): 1740 cm<sup>-1</sup>. Anal. Calcd for C<sub>20</sub>H<sub>28</sub>O<sub>7</sub> (380.43): C, 63.14; H, 7.42. Found: C, 63.12; H, 7.40.

**10** $\dot{\beta}$ . Eluent: 95/5 toluene/EtOAc. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.29 (m, 5H), 5.18 (d, 1H, J = 3.4 Hz), 4.95 (dd, 2H, J = 3.4, 10.1 Hz), 4.88 (d, 1H, J = 11.6 Hz), 4.61 (d, 1H, J = 11.6 Hz), 4.49 (d, 1H, J = 7.8 Hz), 4.01 (septuplet, 1H, J = 6.2 Hz), 3.74 (bq, 1H, J = 6.5 Hz), 3.57 (dd, 1H, J = 7.8, 10.1 Hz), 2.11 (s, 3H), 1.94 (s, 3H), 1.29 (d, 3H, J = 6.2 Hz), 1.23 (d, 3H), J = 6.2 Hz), 1.18 (d, 1H, J = 6.4 Hz). <sup>13</sup>C NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  170.6, 170.2, 102.1, 76.4, 72.7, 70.8, 68.7, 74.7, 23.6, 22.1, 20.7, 16.2. FTIR (CHCl<sub>3</sub>) 1740 cm<sup>-1</sup>. Anal. Calcd for C<sub>20</sub>H<sub>28</sub>O<sub>7</sub> (380.43): C, 63.14; H, 7.42. Found: C, 63.10; H, 7.45.

**Low-Temperature** (-78 °C) <sup>1</sup>H NMR Experiments. Glucosyl imidate  $1\beta$  (or  $1\alpha$ ) was dissolved in CD<sub>2</sub>Cl<sub>2</sub> in a 5 mm NMR tube, at  $-78^{\circ}$ , in the presence of 1.5 equiv of [emim][OTf]. The mixture was stable at these conditions, and therefore the shimming of the sample (lock on the 2H nuclei of CD<sub>2</sub>Cl<sub>2</sub> solvent) and the acquisition of the first 1H spectrum (labeled with t = 0) was performed using a 500 MHz spectrometer, equipped with a 5 mm QNP probe (13C, 13P, 19F/1H coils) and with an N<sub>2</sub> evaporator cooling system unit. The donor was activated by addition at  $-78^{\circ}$  of 0.01 equiv of TMSOTf, and a second spectrum was acquired after the necessary manipulation and lock stabilization time (t = 5 min). <sup>1</sup>H experiments (35 s each one) were subsequently acquired at regular time intervals (see Supporting Information) until the spectrum appearance was stable.

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**Supporting Information Available:** General experimental methods, NMR spectral data for [emim][OTf], [bmim][PF<sub>6</sub>], and compounds  $9\alpha$ ,  $9\beta$ ,  $5\beta$ ,  $10\alpha$ , and  $10\beta$ , and <sup>1</sup>H NMR spectra of low-temperature experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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