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Carbon-Ferrier rearrangements in ionic liquids using $Yb(OTf)_3$ as catalyst

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Abstract

The ionic liquids [bmim][BF_4] and [bmim][NTf_2] are used as efficient recyclable solvents in the ytterbium triflate catalysed carbon-Ferrier rearrangement of triacetyl glucal with allyl silanes, propargyl silane, and silyl enolethers.

Keywords: Ionic liquids; Carbon-Ferrier rearrangement; Ytterbium triflate; Glycal

1. Introduction

Room temperature ionic liquids (RTILs) appear of much current interest as novel reaction media and as one of the most promising alternatives to volatile organic solvents (VOS) [1]. This is mainly due to their unique physical properties which makes them as very attractive solvents for organic synthesis [2,3], organometallic catalysis [4,5], as well as for biotransformations [6,7]. One of their potential advantages is that, in many cases, such solvents could be recycled for performing several times the same reaction on the same substrates or could even be reused for performing similar reactions on different substrates. Several examples of efficient catalysis by lanthanide salts in RTILs have been already described. This includes Friedel Crafts type reactions [8], Diels–Alder catalysis [9], multicomponent condensations [10], thioacetalization [11], or the synthesis of *O*-glycosides using the Ferrier rearrangement [12]. *C*-glycosides are very important compounds in bioorganic chemistry [13,14]. One of the most versatile methods for their preparation is the reaction of sugar derived electrophiles with carbon nucleophiles. The carbon-Ferrier rearrangement generally involves the reaction of glycals under Lewis acid catalysis with nucleophiles such as silyl enolethers [15], allylsilanes [16,17], and organometallic derivatives [18]. Recently, it has been established that lanthanides salts are also efficient Lewis acid catalysts for this carbon-Ferrier rearrangement [19,20]. The stereoselectivity of the latter reaction is usually good in favor of the α-anomer, except in cases of conformational control [21]. Finally, it has to be noted that this reaction was one of the key steps of several elegant total synthesis of bioactive natural products [22–25]. As part of our ongoing studies on the potential uses of RTILs [26,27], we have studied this carbon-Ferrier rearrangement in ionic liquids, under lanthanide salt catalysis. The purpose of this paper is to demonstrate that the latter reaction is easily performed in 1-butyl-3-methyl imidazolium tetrafluoroborate [bmim][BF_4] or 1-butyl-3-methyl imidazolium bis *N*-trifluoro imidate [bmim][NTf_2] and using $Yb(OTf)_3$ at 5 mol% as a catalyst. Commercially available 2,4,6-tri-*O*-acetyl-D-glucal was selected as a model for the sugar component and using allyl silanes, propargylsilane as well as silyl enolethers as nucleophiles, moderate to good yields of adducts have been obtained with an excellent stereoselectivity. Furthermore, it proved to be possible to recycle and/or reuse the solvent for these reactions.

2. Experimental

The ionic liquids [bmim][BF_4] and [bmim][NTf_2] were prepared according to literature procedures [28,29]. Allyl and propargyl silanes, as well as $Yb(OTf)_3$ are commercially

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available and were used as received. The silyl enol ethers were prepared according to literature procedures and their purity was checked by ^{1}H NMR before use.

2.1. Typical procedure

To a stirred solution 2,4,6- tri-*O*-acetyl-D-glucal (272 mg, 1 mM) in [bmim][BF_4] (3 ml) were added Yb(OTf)$_3$ (31 mg, 5 mol%), allyl trimethylsilane (171 mg, 1.5 mM) at RT. The reaction was monitored by TLC and after 3 h the product was extracted with ether (3 × 10 ml), and purified by flash chromatography on SiO_2 to obtain glycoside **3a** in 80% yield. ^{1}H NMR (400 MHz $CDCl_3$): δ 2.07 (s, 3H), 2.09 (s, 3H), 2.35–2.45 (m, 2H), 3.91 (ddd, 1H, $J_{5,6a}$ = 3.4 Hz, $J_{5,6b}$ = 6.3 Hz, $J_{5,4}$ = 9.9 Hz, 5-H), 4.14 (dd, 1H, $J_{6a,5}$ = 3.4 Hz, $J_{6a,6b}$ = 11.9 Hz, 6a-H), 4.21 (dd, 1H, $J_{6b,5}$ = 6.3 Hz, $J_{6b,6a}$ = 11.9 Hz, 6b-H), 4.38 (ddd, 1H, $J_{1,2}$ = 2.4 Hz, $J_{1,1a}$ = 5.0 Hz, $J_{1,1b}$ = 8.8 Hz, 1-H), 5.06 (s, 1H, terminal methylene), 5.11 (dd, 1H, $J_{4,3}$ = 2.3 Hz, $J_{4,5}$ = 9.9 Hz, 4-H), 5.16 (s, 1H, terminal methylene), 5.88 (dd, 1H, $J_{3,4}$ = 2.3 Hz, $J_{3,2}$ = 10.4 Hz, 3-H), 5.91 (dd, 1H, $J_{2,1}$ = 2.4 Hz, $J_{2,3}$ = 10.4 Hz, 2-H). ^{13}C NMR (100 MHz, $CDCl_3$): 20.27, 20.54, 37.28, 62.29, 64.40, 69.15, 70.80, 117.07, 123.13, 132.25, 133.41, 169.91, 170.32.

The other glycosides were obtained following a similar procedure.

2.2. Compound 3b

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84 (s, 3H), 2.07 (s, 3H), 2.08 (s, 3H), 2.35–2.45 (m, 2H), 3.91 (ddd, 1H, $J_{5,6a}$ = 3.4 Hz, $J_{5,6b}$ = 6.3 Hz, $J_{5,4}$ = 9.9 Hz, 5-H), 4.14 (dd, 1H, $J_{6a,5}$ = 3.4 Hz, $J_{6a,6b}$ = 11.9 Hz, 6a-H), 4.21 (dd, 1H, $J_{6b,5}$ = 6.3 Hz, $J_{6b,6a}$ = 11.9 Hz, 6b-H), 4.38 (ddd, 1H, $J_{1,2}$ = 2.4 Hz, $J_{1,1a}$ = 5.0 Hz, $J_{1,1b}$ = 8.8 Hz, 1-H), 5.06 (s, 1H, terminal methylene), 5.11 (dd, 1H, $J_{4,3}$ = 2.3 Hz, $J_{4,5}$ = 9.9 Hz, 4-H), 5.16 (s, 1H, terminal methylene), 5.88 (dd, 1H, $J_{3,4}$ = 2.3 Hz, $J_{3,2}$ = 10.4 Hz, 3-H), 5.91 (dd, 1H, $J_{2,1}$ = 2.4 Hz, $J_{2,3}$ = 10.4 Hz, 2-H). ^{13}C NMR (100 MHz, $CDCl_3$): 21.22, 21.50, 22.80, 41.74, 63.31, 65.44, 69.89, 70.68, 113.63, 123.98, 133.56, 142.08, 170.86, 171.29.

2.3. Compound 5

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.05 (s, 3H), 2.06 (s, 3H), 3.88 (ddd, 1H, $J_{5,6a}$ = 2.9 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.4 Hz, 5-H), 4.14 (dd, 1H, $J_{6a,5}$ = 2.9 Hz, $J_{6a,6b}$ = 12.1 Hz, 6a-H), 4.17 (dd, 1H, $J_{6b,5}$ = 5.4 Hz, $J_{6b,6a}$ = 12.1 Hz, 6b-H), 4.81 (dd, 1H, $J_{1,2}$ = 2.6 Hz, $J_{1,1}$ = 5.2 Hz, 1-H), 4.83 (m, 2H, terminal methylene), 5.21 (dd, 1H, $J_{4,3}$ = 2.1 Hz, $J_{4,5}$ = 8.4 Hz, 4-H), 5.25 (m, 1H), 5.78 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{3,2}$ = 10.4 Hz, 3-H), 5.88 (dd, 1H, $J_{2,1}$ = 2.6 Hz, $J_{2,3}$ = 10.4 Hz, 2-H). ^{13}C NMR (100 MHz, $CDCl_3$): 21.23, 21.47, 63.54, 65.46, 69.16, 70.98, 89.86, 125.56, 131.10, 170.81, 171.37, 209.53.

2.4. Compound 7a

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (s, 3H) 2.09 (s, 3H), 3.15 (dd, 1H), 3.46 (dd, 1H), 3.97 (ddd, 1H, $J_{5,6a}$ = 2.9 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.4 Hz, 5-H), 4.13 (dd, 1H, $J_{6a,5}$ = 2.9 Hz, $J_{6a,6b}$ = 12.1 Hz, 6a-H), 4.25 (dd, 1H, $J_{6b,5}$ = 5.4 Hz, $J_{6b,6a}$ = 12.1 Hz, 6b-H), 4.94 (ddd, 1H, $J_{1,2}$ = 2.4 Hz, $J_{1,1a}$ = 5.0 Hz, $J_{1,1b}$ = 8.8 Hz, 1-H), 5.15 (dd, 1H, $J_{4,3}$ = 2.1 Hz, $J_{4,5}$ = 8.4 Hz, 4-H), 5.82 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{3,2}$ = 10.4 Hz, 3-H), 6.06 (dd, 1H, $J_{2,1}$ = 2.6 Hz, $J_{2,3}$ = 10.4 Hz, 2-H), 7.63 (m, 3H, aromatic), 7.92 (m, 2H, aromatic). ^{13}C NMR (100 MHz, $CDCl_3$): 21.20, 21.46, 51.35, 63.03, 65.09, 68.49, 70.57, 123.93, 127.07, 127.92, 129.07, 133.00, 133.91, 133.94, 144.43, 170.88, 171.22, 197.18.

2.5. Compound 7b

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 (m, 4H), 1.60 (m, 2H), 2.00 (s, 3H) 2.03 (s, 3H), 2.32 (m, 2H), 2.56 (m, 1H), 3.88 (ddd, 1H, $J_{5,6a}$ = 2.9 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.4 Hz, 5-H), 4.15 (dd, 1H, $J_{6a,5}$ = 2.9 Hz, $J_{6a,6b}$ = 12.1 Hz, 6a-H), 4.19 (dd, 1H, $J_{6b,5}$ = 5.4 Hz, $J_{6b,6a}$ = 12.1 Hz, 6b-H), 4.40 (dd, 1H, $J_{1,2}$ = 2.4 Hz, $J_{1,1}$ = 2.1 Hz, 1-H), 5.05 (dd, 1H, $J_{4,3}$ = 2.1 Hz, $J_{4,5}$ = 8.4 Hz, 4-H), 5.69 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{3,2}$ = 10.4 Hz, 3-H) 6.05 (dd, 1H, $J_{2,1}$ = 2.6 Hz, $J_{2,3}$ = 10.4 Hz, 2-H). ^{13}C NMR (100 MHz, $CDCl_3$): 21.24, 21.48, 25.07, 28.34, 30.71, 43.15, 53.82, 63.30, 65.42, 70.54, 70.66, 123.92, 133.44, 170.82, 171.26, 211.44.

2.6. Compound 7c

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.03 (s, 3H), 2.07 (s, 3H), 2.37 (s, 3H), 2.41 (dd, 1H, $J_{1,1}$ = 5.1 Hz, 10.4 Hz,), 2.66 (dd, 1H, $J_{1,1}$ = 8.1 Hz, 7.8 Hz), 3.76 (ddd, 1H, $J_{5,6a}$ = 2.9 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.4 Hz, 5-H), 3.94 (dd, 1H, $J_{6a,5}$ = 2.9 Hz, $J_{6a,6b}$ = 12.1 Hz, 6a-H), 4.03 (dd, 1H, $J_{6b,5}$ = 5.4 Hz, $J_{6b,6a}$ = 12.1 Hz, 6b-H), 4.53 (ddd, 1H, $J_{1,2}$ = 2.4 Hz, $J_{1,1a}$ = 5.0 Hz, $J_{1,1b}$ = 8.8 Hz, 1-H), 4.90 (dd, 1H, $J_{4,3}$ = 2.1 Hz, $J_{4,5}$ = 8.4 Hz, 4-H), 5.60 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{3,2}$ = 10.4 Hz, 3-H), 5.73 (dd, 1H, $J_{2,1}$ = 2.6 Hz, $J_{2,3}$ = 10.4 Hz, 2-H). ^{13}C NMR (100 MHz, $CDCl_3$): 21.20, 21.46, 30.97, 47.36, 63.03, 65.09, 68.49, 70.57, 124.45, 132.76, 170.77, 171.22, 206.18.

2.7. Compound 7d

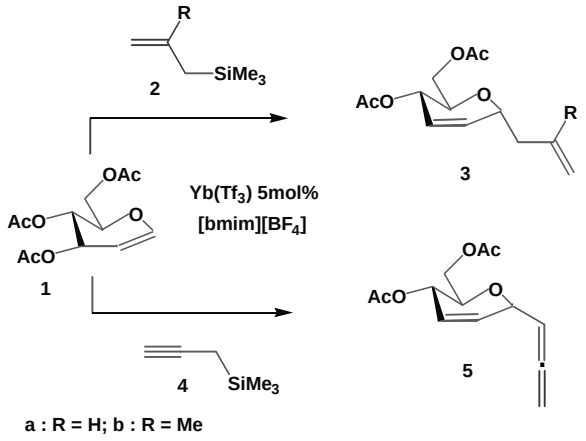
^{1}H NMR (400 mHz, $CDCl_3$) δ 2.02 (s, 3H), 2.07 (s, 3H), 2.15–2.25 (m, 2H), 2.07 (m, 1H), 2.28 (m, 2H), 3.90 (ddd, 1H, $J_{5,6a}$ = 2.9 Hz, $J_{5,6b}$ = 5.4 Hz, $J_{5,4}$ = 8.4 Hz, 5-H), 4.12 (dd, 1H, $J_{6a,5}$ = 2.9 Hz, $J_{6a,6b}$ = 12.1 Hz, 6a-H), 4.25 (dd, 1H, $J_{6b,5}$ = 5.4 Hz, $J_{6b,6a}$ = 12.1 Hz, 6b-H), 4.73 (dd, 1H, $J_{1,2}$ = 2.4 Hz, $J_{1,1}$ = 2.1 Hz, 1-H), 5.08 (dd, 1H, $J_{4,3}$ = 2.1 Hz, $J_{4,5}$ = 8.4 Hz, 4-H), 5.82 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{3,2}$ = 10.4 Hz, 3-H), 6.15 (dd, 1H, $J_{2,1}$ = 2.6 Hz, $J_{2,3}$ =

10.4 Hz, 2-H), 7.23 (m, 2H, aromatic), 7.45 (m, 1H) 7.93 (m, 1H). ^{13}C NMR (100 mHz, $CDCl_3$): 21.24, 21.48, 24.54, 28.63, 51.52, 62.94, 65.08, 69.68, 71.36, 123.93, 127.07, 127.92, 129.09, 133.00, 133.94, 144.43, 170.88, 171.22, 197.18.

3. Results and discussion

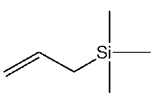
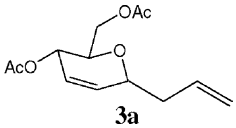
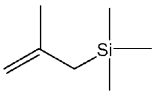
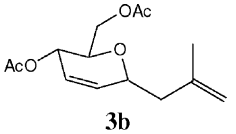
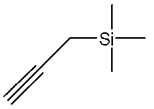
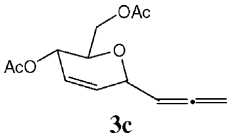
3.1. Allylsilanes and propargylsilane

The 2,4,6-tri-*O*-acetyl-D-glucal was found to react smoothly with allyl trimethylsilane **2a** in [bmim][BF_4] under Yb(OTf)$_3$ catalysis (5 mol%): after 3 h at room temperature the reaction is completed and the adduct **3a** was isolated in 80% yield after extraction with ether followed by a short SiO_2 chromatography (Scheme 1, Table 1). High field NMR analysis of the crude reaction mixture indicates that the reaction is highly stereoselective (>95%) in favor of the α-anomer. The spectral data of **3a** are in full agreement with literature. In the same way, the methallyl silane **2b** reacted with **1** to give the adduct **3b** in 80% yield (entry 2). Here again the α-anomer was the only isomer formed in this reaction.



Scheme 1.

Table 1
C-glycosidation of various allyl silanes using Yb(OTf)$_3$ at 5 mol% in [bmim][BF_4]

Entry	Acceptor	Glycoside	Time (h)	Yield (%)
1		 **3a**	3	80
2		 **3b**	3	80
3		 **3c**	8	65

The propargylsilane **4** also reacts with **1** under the same reaction conditions, although more slowly: after 8 h at room temperature the adduct **5** is obtained in 65% yield (entry 3). The structure of this compound is easily established from its spectral data: particularly relevant is the central allenic carbon atom at 209 ppm. The α-anomer was the only isomer formed in this reaction and these results are in agreement with those obtained using CH_2Cl_2 as solvent [19].

It has to be noted that Sc(OTf)$_3$ was found to be as effective as Yb(OTf)$_3$ to catalyse these carbon-Ferrier rearrangements in [bmim][BF_4]; however, the latter catalyst was selected since it is less expensive.

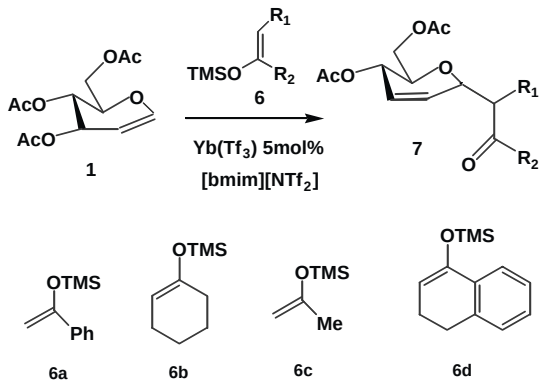
Using allylsilane as the nucleophile it was demonstrated that it is possible to recycle the ionic solvent in this reaction. After the first run the ionic liquid was dried under vacuum (8 h at 80 °C) then readdition of glycal, allylsilane and catalyst to this solvent afforded, under the same conditions as previously, the adduct **3a** in similar yield. This experiment was performed until three runs. However it must be noted that readdition of the catalyst is necessary at each run since, otherwise the reaction does not go to completion. Independent experiments have demonstrated that ether did not extract Yb(OTf)$_3$ from the ionic liquid solution. Therefore, some evolution and/or decomposition of the catalyst is probably occuring under these reaction conditions, but this could not be established unambiguously at this stage.

The possibility of reusing the solvent for successive reactions with different substrates was also examined using two different silanes. After performing a first run using **2a**, which afforded **3a** as previously indicated, for the second run the silane **2b** was used as the nucleophile: it afforded **3b** as expected and careful analysis using high field NMR excluded the presence of residual **3a** in the crude reaction mixture of this second run. Therefore, such carbon-Ferrier rearrangements, with allylsilanes as nucleophiles, can be performed in this ionic liquid without cross contamination of the final products.

3.2. Silyl enol ethers

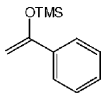
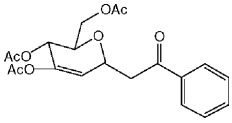
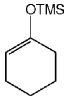
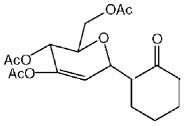
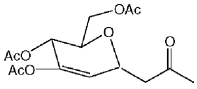
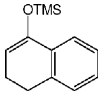
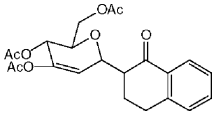
The 2,4,6-tri-*O*-acetyl-D-glucal was also found to react smoothly with the silyl enolethers **6** in [bmim][NTf_2] under Yb(OTf)$_3$ catalysis (5 mol%): after 0.5–1.5 h at room temperature the reactions are complete and the adducts **7** were isolated in 40–65% yields after extraction with ether followed by a short SiO_2 chromatography (Scheme 2, Table 2). High field NMR analysis of the crude reaction mixture indicates that the reactions are again highly stereoselective (>95%) in favor of the α-anomer. The spectral data of adducts **7** are in full agreement with literature.

The possibility of recycling the solvent was extended to these enol ethers. Using the previously described procedure,



Scheme 2.

Table 2
C-glycosidation of silyl enol ethers using $Yb(OTf)_3$ at 5 mol% in $[bmim][NTf_2]$

Entry	Acceptor	Glycoside	Time (h)	Yield (%)
1			0.5	65
2			0.5	60
3			0.5	40
4			1.5	60

three consecutive runs of reactions of **1** with **6a** were successfully performed with similar yields. Here again it proved to be necessary to add the $Yb(OTf)_3$ catalyst after each run. Finally, the reuse of the solvent was confirmed by using first **2b** as the nucleophile and, in a second run the silyl enol ether **6d**. In the latter reaction only **7d** was isolated without cross contamination by **3b**.

4. Conclusion

Yttterbium triflate is an efficient catalyst for the carbon-Ferrier rearrangement in the ionic liquids $[bmim][BF_4]$ and $[bmim][NTf_2]$. The reactions of allylsilanes, propargylsilane, or silyl enolethers afford the corresponding *C*-glycosides in fair to good yields with an excellent stereoselectivity. Furthermore, it is possible to recycle or reuse the ionic liquid used as the solvent of these reactions.

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