Pergamon

Tetrahedron 57 (2001) 4405–4410

TETRAHEDRON

Ionic liquids as recyclable reaction media for the tetrahydropyranylation of alcohols

Luís C. Branco and Carlos A. M. Afonso*

Departamento de Química, Centro de Química Fina e Biotecnologia, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, 2825-114 Caparica, Portugal

Received 20 November 2000; revised 26 March 2001; accepted 29 March 2001

Abstract—A comparative study of the catalysed tetrahydropyranylation of 1-phenylethanol by *p*-toluenesulphonic acid (TsOH), pyridinium *p*-toluenesulphonate (PPTS) and triphenylphosphine hydrobromide (TPP.HBr) using 3,4-dihydro-2*H*-pyran in dichloromethane or in the ionic liquids 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) or 1-*n*-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]) showed that the reaction occurs readily in [bmim][PF_6] for PPTS or TPP.HBr by a non-reversible process. These reaction media were recycled on 22 occasions without loss of activity and their scope of application to other alcohols was also studied.

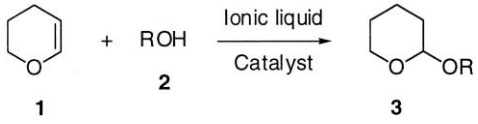
1. Introduction

Room temperature ionic liquids, mainly consisting of 1,3-dialkylimidazolium cations are attracting increasing interest as alternative environmentally benign reaction media.[1] These solvents are non-volatile, thermally stable and, depending on the anion, can present low miscibility with water, alkanes and dialkyl ethers while also being compatible with transition metal catalysts. These media have been applied in non-catalytic[1,2] and catalytic reactions[1,3] and also in selective extraction procedures.[4] Catalysts that have polar or ionic character can be immobilised in these ionic media permitting a practical method of recycling by the simple extraction of products from the ionic reaction media.[3a–c,e,g–l]

3,4-Dihydro-2*H*-pyran **1** is a versatile and low-cost reagent for the protection of hydroxyl groups giving tetrahydropyranyl ethers **3**, which are robust protective groups, easy to remove[5] and also useful intermediates for further functional transformations.[5,6] The tetrahydropyranylation generally requires protic or Lewis acid catalysis. Among a considerable number of reported methods,[5,7] including heterogeneous catalysis,[5,8] *p*-toluenesulphonic acid (TsOH), pyridinium *p*-toluenesulphonate (PPTS)[5,9] and triphenylphosphine hydrobromide (TPP.HBr)[5,10] are the most reliable and readily accessible catalysts for the tetrahydropyranylation of alcohols using **1**. According to the observation that the catalysts TsOH, PPTS and TPP.HBr are soluble in the ionic liquids based on the 1-*n*-butyl-3-methylimidazolium [bmim] unit and also the possibility of the product being further extracted with diethyl ether, prompted us to study the tetrahydropyranylation of alcohols under this potentially reusable reaction medium (Scheme 1).

2. Results and discussion

Using 1-phenylethanol **2a** as an example and following by GLC the conversion of **2a** into the corresponding tetrahydropyran **3a**, a comparative study was performed between the catalysts TsOH, PPTS and TPP.HBr in the common organic solvent dichloromethane (DCM) and in the ionic solvents 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) and 1-*n*-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]), (Table 1). In the absence of catalyst no reaction was observed in all solvents during the first 3 h. For longer time periods some formation of product **3a** was detected, where after 24 h the conversion was higher in DCM (30%) than in [bmim][PF_6] (14.4%) or [bmim][BF_4] (4.9%) (Table 1, entries 1, 2 and 3). In contrast, when the reaction was performed in DCM and in the presence of catalyst (10 mol%) at room temperature, the conversion was almost complete after 5 min for the three catalysts tested (Table 1, entries 4–6). In the case of the ionic liquids [bmim][PF_6] and [bmim][BF_4] the milder catalysts



Scheme 1.

Keywords: ionic liquid; recyclable reaction media; tetrahydropyranylation; alcohols.

* Corresponding author. Tel.: +351-21-294-8358; fax: +351-21-294-8550; e-mail: cma@dq.fct.unl.pt

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00373-8

Table 1. Comparative conversion study (by GLC) of the tetrahydropyranylation of 1-phenylethanol **2a**[a]

Entry	Solvent	Catalyst	Time	Conversion **3a**[b] (%)
1	DCM	No	3 h	0.0
			6 h	15.0
			24 h	30.0
2	[bmim][PF_6]	No	3 h	0.0
			6 h	2.8
			24 h	14.4
3	[bmim][BF_4]	No	6 h	0.0
			10 h	2.2
			24 h	4.9
4	DCM	TPP.HBr	5 min	96.6[c]
5	DCM	TsOH	5 min	95.9
			15 min	98.7[c]
6	DCM	PPTS	5 min	97.0[c]
7	[bmim][PF_6]	TPP.HBr	5 min	96.8
			15 min	97.4
			2 h	98.9
8	[bmim][PF_6]	TsOH	5 min	40.5
			15 min	67.2
			2 h	74.1
9	[bmim][PF_6]	PPTS	5 min	75.8
			15 min	96.9
			2 h	97.4
10	[bmim][BF_4]	TPP.HBr	5 min	94.4[c]
11	[bmim][BF_4]	TsOH	5 min	12.2
			15 min	36.9
			2 h	66.5
12	[bmim][BF_4]	PPTS	5 min	28.1
			15 min	80.1
			1 h	90.3[c]

[a] **2a** (0.82 mmol), 3,4-dihydro-2*H*-pyran **1** (2 equiv.), and catalyst (10 mol%) in solvent (1 ml) at room temperature (18°C).
[b] Conversion of **3a** obtained by GLC analysis.
[c] Minimum time necessary to achieve the maximum conversion observed for the time-scale studied (2 h).

PPTS and TPP.HBr gave higher final conversions and cleaner reaction mixtures than the catalyst TsOH (Table 1, entries 7–12). In the case of TPP.HBr the reaction is still complete after 5 min in both ionic liquids, while for PPTS the reaction is considerably slower in the ionic solvent [bmim][BF_4] (Table 1, entries 7 and 10 vs. entries 9 and 12). By performing a comparative study at lower temperature (3°C) using the catalyst PPTS, we observed that the reaction in [bmim][PF_6] is slightly faster than in the conventional solvent DCM and much faster than in [bmim][BF_4] (Fig. 1). The relative rates observed in [bmim][PF_6], DCM and [bmim][BF_4] are, respectivelly, 5.2, 3.6 and 1.0.

We observed that for the milder catalysts PPTS and TPP.HBr at room temperature or at 3°C and in all the solvents tested (DCM, [bmim][PF_6] or [bmim][BF_4]) the diastereomeric ratio (d_r) of the tetrahydropyran **3a** was constantly between 0.95 and 1.0. In contrast, for the TsOH the d_r was higher at room temperature and also increased with reaction time as presented in Fig. 2. Only at lower temperature (3°C) was the observed d_r similar to that obtained for PPTS and TPP.HBr catalysts. A similar dependence was also observed for camphorsulphonic acid (CSA). When a 1:1 diastereomer reaction mixture of **3a** (previously obtained at −13°C using TsOH) was left at room temperature for 1 h, the d_r value changed to 3.32. A similar result was observed by adding the catalyst TsOH (10 mol%) to a solution of the previously isolated 1:1 diastereomer mixture of **3a** in DCM at room temperature. The

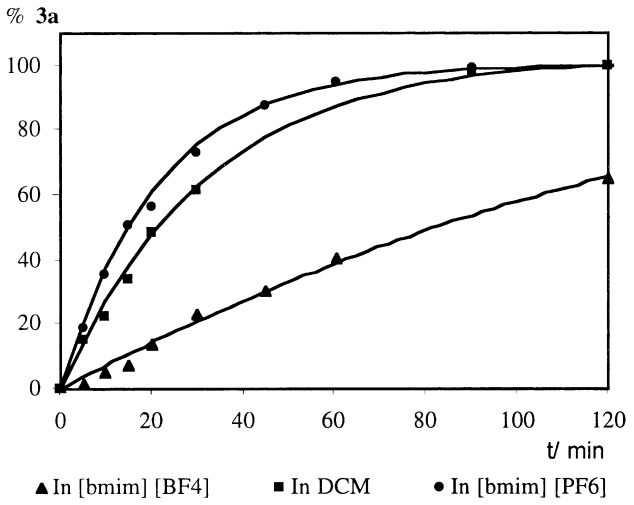


Figure 1. Conversion (by GLC) of 1-phenylethanol **2a** into tetrahydropyranyl ether **3a** at 3°C in the presence of PPTS (10 mol%). Relative rates for [bmim][PF_6]:DCM:[bmim][BF_4] are 5.2:3.6:1.0; obtained by comparison of initial rate constants ($t \leq t_{1/2}$).

above results imply that at room temperature the tetrahydropyranylation is reversible for TsOH (or CSA) and irreversible for the catalysts PPTS and TPP.HBr. This fact is consistent with the stronger acidity of the TsOH. On the other hand, the lower reactivity observed for the catalyst TsOH in the ionic solvents [bmim][PF_6] and [bmim][BF_4] could eventually result from the effect of the solvent on the reaction equilibrium.

Using the ionic solvent [bmim][PF_6] and the catalysts PPTS

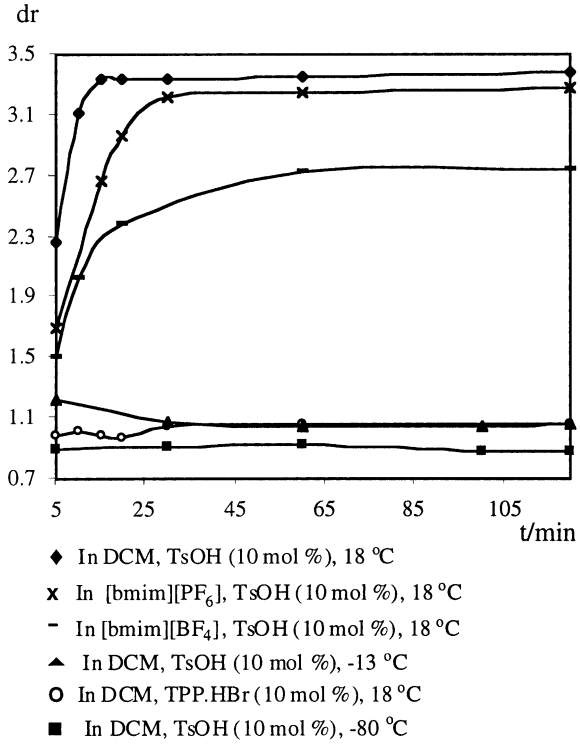


Figure 2. Dependence of the diastereomeric ratio (d_r) of **3a** on the reaction conditions. The d_r values were determined by GLC and refer, respectively, to diastereomer retention times (t_R) of 4.0 min and 4.7 min.

Table 2. Representative examples for the preparation of tetrahydropyranes **3a–3f** in ionic solvent[a]

Entry	Alcohol **2**	Solvent	Catalyst	Yield **3**[b] (%)
1[c]	$PhCH_2OH$ **2b**	DCM	TsOH	99
2[c]	$PhCH_2OH$ **2b**	DCM	TPP.HBr	87
3[c]	$PhCH_2OH$ **2b**	[bmim][BF_4]	TPP.HBr	96
4[c]	$PhCH_2OH$ **2b**	[bmim][PF_6]	TsOH	28
5[c]	$PhCH_2OH$ **2b**	[bmim][PF_6]	TPP.HBr	92
6[c]	$PhCH_2OH$ **2b**	[bmim][PF_6]	PPTS	91
7[d]	PhCHMeOH **2a**	[bmim][PF_6]	TPP.HBr	78
8[d]	PhCHMeOH **2a**	[bmim][PF_6]	PPTS	81
9[c]	(−)-Menthol **2c**	[bmim][PF_6]	TPP.HBr	81
10[c]	(−)-Menthol **2c**	[bmim][PF_6]	PPTS	83
11[e]	Cholesterol **2d**	[bmim][PF_6]	TPP.HBr	62
12[e]	Cholesterol **2d**	[bmim][PF_6]	PPTS	80
13[c]	Geraniol **2e**	[bmim][PF_6]	TPP.HBr	74
14[c]	Geraniol **2e**	[bmim][PF_6]	PPTS	69
15[f]	1-Adamantanol **2f**	[bmim][PF_6]	TPP.HBr	75
16[f]	1-Adamantanol **2f**	[bmim][PF_6]	PPTS	86

[a] **2** (0.82–1.64 mmol), 3,4-dihydro-2*H*-pyran **1** (2 equiv.), and catalyst (10 mol%) in solvent (0.2–1.0 M) at room temperature.
[b] Isolated product after flash chromatography.
[c] Reaction time of 4 h.
[d] Reaction time of 1 h.
[e] Reaction time of 5 h.
[f] Reaction time of 7 h.

and TPP.HBr as the best conditions previously identified by GLC, we then prepared in moderate to high yields the tetrahydropyranes **3a–3f** from several representative alcohols **2a–2f** (Table 2). In all examples the product was removed from the ionic reaction mixture by successive extractions with diethyl ether. The use of catalyst TsOH in the ionic solvent is inappropriate (Table 2, entries 1 and 4; 99% in DCM vs. 28% in [bmim][PF_6]), and the catalysts PPTS and TPP.HBr appeared very similar. These preparative results are in accordance with the comparative conversion GLC studies described above.

Our attention was then directed towards the possibility of recycling the reaction media. Using 1-phenylethanol **2a** as a representative example, all reactions were performed for 1 h using 3,4-dihydro-2*H*-pyran **1** (2 equiv.) at room temperature. After each cycle the reaction mixture was extracted with diethyl ether, the conversion determined by GLC and in some representative examples, the tetrahydropyran **3a** was isolated by flash chromatography. Then, more alcohol **2a** and pyran **1** were added into the next cycle. New catalyst was added only when the last cycle gave low conversion. Table 3 presents the results obtained for the catalysts PPTS and TPP.HBr.

By changing the catalyst (6 mol% for run A, D and 10 mol% for run B, C, E, F) under identical extraction procedures, we verified that the number of cycles that allow a conversion of greater than 40% is dependent on the initial amount and type of catalyst: TPP.HBr (4 cycles for 6 mol% in run D vs. 5 cycles for 10 mol% in run E); PPTS (2 cycles for 6 mol% in run A vs. 6 cycles for 10 mol% in run B). We also observed that long-time extraction procedures (2 h) considerably reduce the conversion of the next cycle, with this effect being more relevant for the catalyst TPP.HBr (cycle 15 of run E and cycle 4 of run F). To circumvent this problem we used instead fast-time extractions (5 min, cycles 11–22 in run C and cycles 6–22 in run F). The strong dependence of the conversion on the type of extraction is due to simultaneous extraction of the catalyst by diethyl ether from the ionic phase. We also observed that the volume of the ionic reaction medium was reduced to approximately 80% of the initial volume after the maximum of 22 cycles tested (run C and run F), which result from some solubillity of the ionic liquid [bmim][PF_6] in diethyl ether. The isolated yields obtained for some representative cycles are also in the same range as those observed for the one-cycle reaction presented in Table 2 (entries 7 and 8). It is particularly noteworthy that the same ionic liquid was used for 22 cycles and also could be used without further addition of catalyst for 12 and 17 cycles, respectively, for PPTS (run C) and TPP.HBr (run F) with a reduction in the conversion of less than 7%.

In summary, this study presented here shows that at room temperature the catalyst TsOH promotes the tetrahydropyranylation of alcohols under reversible conditions, while for the milder catalysts PPTS and TPP.HBr the transformation occurs under a non-reversible process. The ionic liquid [bmim][PF_6] is a convenient medium for this transformation using the catalysts PPTS or TPP.HBr giving moderate to high yields for representative substrates. This reaction medium can also be successfully recycled on at least 22 occasions without an appreciable loss of activity. The decrease in the activity of the process is due to loss of catalyst and volume reduction of the ionic reaction mixture, which occurs during the extraction of the product with diethyl ether.

3. Experimental

3.1. General remarks

All glassware was oven-dried and cooled in a desiccator (P_2O_5 desiccant) prior to use. Commercially supplied reagents were used as supplied, except for benzyl alcohol which was distilled and stored under argon atmosphere and protected from light. Dichloromethane was distilled over calcium hydride powder under an argon atmosphere. 1-*n*-Butyl-3-methylimidazolium hexafluorophosphate [bmim][PF_6] and 1-*n*-butyl-3-methylimidazolium tetrafluoroborate [bmim][BF_4] were prepared following reported procedures.[4b,11]

^{1}H NMR spectra were recorded on a Bruker AMX 400 Spectrometer. Chemical shifts are reported downfield in parts per million (ppm) from a tetramethylsilane reference. Infrared (IR) spectra were recorded on a Perkin–Elmer FTIR 683 as thinly dispersed films. Gas liquid chromatography (GLC) was carried out on a Varian Star 3400 C_x gas chromatograph, using He as carrier gas and capillary column Supelco C315602 SW-10. Optical rotations were carried out using an Optical Activity Mod. AA-1000 digital polarimeter with a cell path length of 5 cm. Melting points were carried out on a Gallenkamp melting point apparatus and are uncorrected.

Flash chromatography was carried out using an MN Kieselgel 60M gel (40–63 μm, Art. 815381) column. All eluents were distilled prior to use. Preparative and analytical thin

Table 3. Reuse of ionic liquid [bmim][PF_6] reaction medium for the tetrahydropyranylation of **3a**[a]

	Run A **3a** (1.6 mmol) PPTS (6 mol%)	Run B **3a** (1.6 mmol) PPTS (10 mol%)	Run C **3a** (2.5 mmol) PPTS (10 mol%)	Run D **3a** (1.6 mmol) TPP.HBr (6 mol%)	Run E **3a** (1.6 mmol) TPP.HBr (10 mol%)	Run F **3a** (2.5 mmol) TPP.HBr (10 mol%)
Cycle	Conversion **3a** (% by GLC)[b]	Conversion **3a** (% by GLC)[b]	% **3a** GLC[b] (Yield)[c]	Conversion **3a** (% by GLC)[b]	Conversion **3a** (% by GLC)[b]	% **3a** GLC[b] (Yield)[c]
1	37.0	98.8	97.2 (77.9)	97.3	97.8	95.9 (77.8)
2	48.9	97.6	95.3	88.9	99.1	94.8
3	31.3	99.0	95.7	98.6	99.5	94.8
4	21.8	97.9	97.2	42.9	99.6	95.2[e] (80.1)
5	5.4	93.7	96.3[e] (81.0)	5.1	85.6	44.0[e] (56.2)
6	5.4	97.5	74.8[e] (66.0)	0.8	31.7	96.4[d,f] (71.7)
7	86.2[d]	31.4	72.5[e]	95.1[d]	93.7[d]	94.5[f]
8	64.2	27.2	68.2[e] (60.2)	67.9	99.3	96.4[f]
9	40.4	87.8[d]	64.0[e]	19.1	97.9	97.4[f]
10	71.4[d]	92.6	58.7[e] (62.0)	93.9[d]	95.3	97.2[f]
11	95.7	94.9	93.7[d,f] (68.8)	84.2	21.7	91.4[f] (72.1)
12	29.4	97.3	96.0[f]	96.9	28.5	92.4[f]
13		86.9	96.2[f]		95.6[d]	99.1[f]
14		98.4	93.9[f] (71.6)		98.6	98.0[f] (68.1)
15		97.7[e]	97.8[f]		99.7[e]	93.0[f]
16		71.2[e]	93.1[f]		2.8[e]	97.3[f]
17		72.0[e]	92.8[f]		0.3[e]	97.4[f]
18		96.6[d]	93.1[f]		0.1[e]	97.0[f]
19		92.9	98.9[f] (69.6)		98.3[d]	97.1[f] (72.0)
20			96.5[f]			97.9[f]
21			89.8[f]			95.0[f]
22			86.0[f]			92.3[f]

[a] **2a** (1.6 or 2.5 mmol), 3,4-dihydro-2*H*-pyran **1** (2 equiv.), and catalyst (6 or 10 mol%) in [bmim][PF_6] (2 or 4 ml) at room temperature (18°C) was reacted for 1 h, extracted with diethyl ether (4×3 ml or 5×5 ml, 15 min for each extraction) and then **2a** and **1** were added again for the next cycle.

[b] Conversion of **3a** obtained by GLC analysis.

[c] Isolated product **3a** after flash chromatography.

[d] New addition of the catalyst was performed.

[e] Slow extraction of the reaction mixture was performed (2 h for each extraction).

[f] Fast extraction of the reaction mixture was performed (5 min for each extraction).

layer chromatography (TLC) was carried out using, respectively, MN Kieselgel G/UV_{254} (Art. 816320) glass-backed plates and MN Alugram® SIL G/ UV_{254} (Art. 818133). The plates were visualised using ultraviolet light (254 nm).

3.2. General procedure for the conversion analysis of 1-phenylethanol 2a to 1-phenylethanol tetrahydropyranyl ether 3a followed by GLC

3,4-Dihydro-2*H*-pyran (150 μl, 1.64 mmol) was added to a stirred solution of 1-phenylethanol (100 mg, 0.82 mmol) and catalyst [10 mol%, triphenylphosphine hydrobromide (TPP.HBr, 36 mg); *p*-toluenesulphonic acid monohydrate (TsOH, 19 mg) or pyridinium *p*-toluenesulphonate (PPTS, 25 mg)] in a classic solvent (dry dichloromethane, 1ml) or ionic liquid ([bmim][PF_6] or [bmim][BF_4], 1 ml), under argon atmosphere at room temperature (18°C, water bath) or at 0°C. The course of the reaction was followed by GLC by taking 20 μl samples of the reaction medium at determined time intervals (5, 10, 15, 20, 30, 45, 60 and 120 min) and diluting in diethyl ether (0.3 ml) in the presence of Na_2CO_3, followed by injection into the gas chromatographer [carrier gas flow: 21 ml min^{-1}, *T* (oven)=130°C, *T* (injector)=150°C and *T* (detector)=230°C]. The conversion of the reaction for each sample was determined by comparing the peak areas of the product **3a** (t_R=4.0 min, t_R=4.7 min) with 1-phenylethanol (t_R=2.4 min).

3.3. Recycling of tetrahydropyranylation of 1-phenylethanol 2a

A solution of 3,4-dihydro-2*H*-pyran (310 μl, 3.28 mmol or 465 μl, 4.92 mmol) was added to a stirred mixture of 1-phenylethanol (200 μl, 1.64 mmol or 300 μl, 2.46 mmol) and the catalyst [6 or 10 mol%: triphenylphosphine hydrobromide (TPP.HBr), 30 or 65 mg; or pyridinium *p*-toluenesulphonate (PPTS), 25 or 50 mg] in ionic liquid ([bmim][PF_6], 2 or 4 ml), under an argon atmosphere. The resulting mixture was further stirred for 1 h at room temperature. The reaction medium was extracted with diethyl ether (4×3 ml or 5×5 ml) through normal extraction (corresponding to 15 min for every extraction). In some cycles different extractions were perfomed: slow extraction (corresponding to 2 h for every extraction) and fast extraction (corresponding to 5 min for every extraction). The combined ethereal extracts were injected on a GLC for analysis of the reaction conversion as described above. In certain cycles, the resulting etheral solution was evaporated under *in vacuo* and purified on a flash chromatography column (silica gel, eluent:*n*-hexane/diethyl ether 9:1). A new portion of reactants was added to the recycled [bmim][PF_6] and the cycle repeated. When lower yields of product were observed a new portion of catalyst (TPP.HBr or PPTS) was added into the ionic reaction mixture.

3.4. General procedure for preparative tetrahydropyranylation of alcohols 2a–2f

A solution of 3,4-dihydro-2*H*-pyran (1.92 mmol for benzyl alcohol **2b**, 1.64 mmol for cholesterol **2d** and 3.28 mmol for other alcohols) was added to a stirred solution of alcohol (0.96 mmol for benzyl alcohol **2b**, 0.82 mmol for cholesterol **2d** and 1.64 mmol for other alcohols) and the catalyst [(10 mol%), TPP.HBr or PPTS] in ionic liquid ([bmim][PF_6], 1 ml for benzyl alcohol **2b**, 4 ml for cholesterol **2e** and 2 ml for other alcohols). The resulting mixture was further stirred (1 h for benzyl alcohol **2b**, 5 h for cholesterol **2d**, 7 h for 1-adamantanol **2f** and 4 h for other alcohols) at room temperature under an argon atmosphere. The reaction mixture was extracted with diethyl ether (5×5 ml) and the resulting solution was evaporated in vacuo and purified by TLC or flash chromatography.

3.4.1. 1-Phenylethanol tetrahydropyranyl ether 3a. 3,4-Dihydro-2*H*-pyran (310 μl), 1-phenylethanol **2a** (200 μl, 1.64 mmol) and TPP.HBr (65 mg) in 2 ml of [bmim][PF_6], were stirred for 1 h. Purification by flash chromatography using hexane/diethyl ether 9:1 gave **3a** as a yellow oil (263 mg, 78%; 273 mg, 81% in the case of PPTS). Spectral data are identical to those previously reported.[12]

3.4.2. Benzyl alcohol tetrahydropyranyl ether 3b. 3,4-Dihydro-2**H**-pyran (175 μl), benzyl alcohol **2b** (100 μl, 0.96 mmol) and TPP.HBr (33 mg) in 1 ml of ionic liquid ([bmim][PF_6]) were stirred for 4 h. Purification by TLC using hexane/ethyl acetate 9.5:0.5 gave **3b** as a colourless oil (170 mg, 92%; 168 mg, 91% in the case of PPTS). Spectral data are identical to those previously reported.[12–14]

3.4.3. (−)-Menthol tetrahydropyranyl ether 3c. 3,4-Dihydro-2*H*-pyran (310 μl), (−)-menthol **2c** (391 mg, 1.64 mmol) and TPP.HBr (65 mg) in 2 ml of [bmim][PF_6] were stirred for 4 h. Purification by flash chromatography using hexane/diethyl ether 9:1 gave **3c** as a colourless oil (431 mg, 81%; 439 mg, 83% in the case of PPTS). Spectral data are identical to those previously reported;[13] $[\alpha]_D^{25}$=−86.8 (c=1.0, $CHCl_3$).

3.4.4. Cholesterol tetrahydropyranyl ether 3d. 3,4-Dihydro-2*H*-pyran (160 μl), cholesterol **2d** (317 mg, 0.82 mmol) and TPP.HBr (65 mg) in 4 ml of [bmim][PF_6] were stirred for 5 h. Purification by flash chromatography using hexane/diethyl ether 9:1 gave **3d** as a white solid (240 mg, 62%; 308 mg, 80% in the case of PPTS); mp 149.0–149.5°C, lit.[13] mp 150°C; $[\alpha]_D^{25}$=+16.2 (c=1.0, $CHCl_3$). Spectral data are identical to those previously reported.[12,13]

3.4.5. Geraniol tetrahydropyranyl ether 3e. 3,4-Dihydro-2*H*-pyran (310 μl), geraniol **2e** (288 μl, 1.64 mmol) and TPP.HBr (65 mg) in 2 ml of [bmim][PF_6] were stirred for 4 h. Purification by flash chromatography using hexane/diethyl ether 9:1 gave **3e** as a colourless oil (289 mg, 74%; 270 mg, 69% in the case of PPTS). Spectral data are identical to those previously reported.[12,13]

3.4.6. 1-Adamantanol tetrahydropyranyl ether 3f. 3,4-Dihydro-2*H*-pyran (310 μl), 1-adamantanol **2f** (250 mg, 1.64 mmol) and TPP.HBr (65 mg) in 2 ml of [bmim][PF_6] were stirred for 7 h. Purification by flash chromatography using hexane/diethyl ether 9:1 gave **3f** as a colourless oil (292 mg, 75%; 333 mg, 86% in the case of PPTS). Spectral data are identical to those previously reported.[13]

Acknowledgements

This work was supported by the Fundação para a Ciência e Tecnologia, project PRAXIS/C/QUI/10069/98 and the Instituto de Biologia Experimental e Tecnológica. We also acknowledge Ana S. C. Rodrigues for technical support.

References

1. (a) Welton, T. *Chem Rev.* **1999**, *99*, 2071–2083. (b) Seddon, K. R. *Kinetics and Catalysis* **1996**, *37*, 693–697 http://www.ch.qub.ac.uk/resources/ionic/review/review.html. (c) Hussey, C. L. *Pure Appl. Chem.* **1988**, *60*, 1763–1772.
2. (a) Gordon, C. M.; McCluskey, A. *Chem. Commun.* **1999**, 1431–1432. (b) Green, L.; Hemeon, I.; Singer, R. D. *Tetrahedron Lett.* **2000**, *41*, 1343–1346. (c) Stark, A.; MacLean, B. L.; Singer, R. D. *J. Chem. Soc., Dalton Trans.* **1999**, 63–66. (d) Adams, C. J.; Earle, M. J.; Seddon, K. R. *Chem. Commun.* **1999**, 1043–1044. (e) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Chem. Commun.* **1998**, 2245–2246.
3. (a) Chen, W.; Xu, L.; Chatterton, C.; Xiao, J. *Chem. Commun.* **1999**, 1247–1248. (b) Song, C. E.; Roh, E. J. *Chem. Commun.* **2000**, 837–838. (c) Carmichael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Organic Lett.* **1999**, *1*, 997–1000. (d) Bellefon, C.; Pollet, E.; Grenouillet, P. *J. Mol. Catal. A: Chemical* **1999**, *145*, 121–126. (e) Dyson, P. J.; Ellis, D. J.; Parker, D. G.; Welton, T. *Chem. Commun.* **1999**, 25–26. (f) Owens, G. S.; Abu-Omar, M. M. *Chem. Commun.* **2000**, 1165–1166. (g) Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Green Chem.* **1999**, 23–25. (h) Carmichael, A. J.; Haddleton, D. M.; Bon, S. A. F.; Seddon, K. R. *Chem. Commun.* **2000**, 1237–1238. (i) Mathews, C. J.; Smith, P. J.; Welton, T. *Chem. Commun.* **2000**, 1249–1250. (j) Howarth, J.; Dallas, A. *Molecules* **2000**, *5*, 851–855. (k) Howarth, J. *Chem. Comm.* **2000**, 1743–1744. (l) Song, C. E.; Oh, C. R.; Roh, E. J.; Choo, D. J. *Chem. Comm.* **2000**, 1743–1744.
4. (a) Blanchard, L. A.; Hancu, D.; Beckman, E. J.; Brennecke, J. F. *Nature* **1999**, *399*, 28. (b) Huddleston, J. G.; Willauer, H. D.; Swatloski, R. P.; Visser, A. E.; Rogers, R. D. *Chem. Commun.* **1998**, 1765–1766. (c) Cull, S. G.; Holbrey, J. D.; Vargas-Mora, V.; Seddon, K. R.; Lye, G. J. *Biotechnology and Bioengineering* **2000**, *69*, 227–233.
5. (a) Greene, T. H.; Wuts, P. G. M. In *Protective Groups in Organic Synthesis*, John Wiley & Sons: New York, 1999; pp 49–54. (b) Kierkus, P. C. In *Handbook of Reagents for Organic Synthesis: Activating Agents and Protecting Groups*, Pearson, A. J., Roush, W. R., Eds.; John Wiley & Sons: New York, 1999; pp 147–150.
6. (a) Schlama, T.; Gouverneur, V.; Mioskowski, C. *Tetrahedron Lett.* **1997**, *38*, 3517–3520. (b) Bhar, S.; Ranu, B. C. *J. Org. Chem.* **1995**, *60*, 745–747.
7. (a) Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. *Chem. Lett.* **1999**, 857–858. (b) Chandrasekhar, S.; Takhi, M.; Reddy, Y. R.; Mohapatra, S.; Rao, C. R.; Reddy, K. V. *Tetrahedron* **1997**, *53*, 14997–15004.
8. (a) Ballini, R.; Bigi, F.; Carloni, S.; Maggi, R.; Sartori, G. *Tetrahedron Lett.* **1997**, *38*, 4169–4172. (b) Thompson, L. A.; Ellman, J. A. *Tetrahedron Lett.* **1994**, *35*, 9333–9336.
9. Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772–3774.
10. Bolitt, V.; Mioskowski, C. *Tetrahedron Lett.* **1988**, *29*, 4583–4586.
11. (a) Suarez, P. A. Z.; Dullius, J. E. L.; Einloft, S.; de Souza, R. F.; Dupont, J. *Polyhedron* **1996**, *15*, 1217–1219. (b) Holbrey, J. D.; Seddon, K. R. *J. Chem. Soc., Dalton Trans.* **1999**, 2133–2139.
12. Hoyer, S.; Laszlo, P. *Synthesis* **1986**, 655–657.
13. Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S. *Synthesis* **1979**, 618–620.
14. Brown, D. S.; Ley, S. V.; Vile, S.; Thompson, M. *Tetrahedron* **1991**, *47*, 1329–1342.