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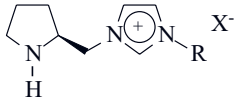
Ionic liquids as the catalysts for asymmetric reactions

Summary — A new 7 functionalized chiral ionic liquids (CILs) based on pyrrolidine have been synthesized from (*S*)-proline as a main substrat. The obtained compounds have 1-[(*S*)-(pyrrolidin-2-yl)methyl]-3-alkylimidazolium cation and bis(trifluoromethylsulfonyl)imide and hexafluorophosphate anions. The structures of the obtained catalysts were determined by spectroscopic analysis ^{1}H NMR, ^{13}C NMR and ^{19}F NMR. This chiral ionic liquids have been applied as efficient catalysts for Michael addition of cyclohexanone to nitroalkenes.
Keywords: chiral ionic liquids, asymmetric synthesis, Michael addition, imidazole, pyrrolidine, enantioselectivity.

CIECZE JONOWE JAKO KATALIZATORY REAKCJI ASYMETRYCZNYCH
Streszczenie — Na bazie (*S*)-proliny zsyntezowano 7 nowych funkcjonalizowanych chiralnych cieczy jonowych zawierających kation 1-[(*S*)-(pirolidyno-2-ylo)metylo]-3-alkiloimidazoliowy oraz aniony: bis(trifluorometylosulfonylo)imidkowy i heksafluorofosforanowy. Struktury uzyskanych związków określono metodami spektroskopowymi ^{1}H NMR, ^{13}C NMR i ^{19}F NMR. Zsyntezowane ciecze jonowe zastosowano jako skuteczne katalizatory addycji Michaela cykloheksanonu do nitroalkenów.
Słowa kluczowe: chiralne ciecze jonowe, synteza asymetryczna, addycja Michaela, imidazol, pirolidyna, enancjoselektywność.

INTRODUCTION

Ionic liquids for many years have been used as new type of media for material science [1, 2], electrochemistry [3, 4] and especially for organic synthesis [5—7]. The chiral ionic liquids (CILs) are compounds of increasing importance due to their application for asymmetric synthesis, stereoselective polymerization and chiral chromatography. Since 1999, when Seddon *et al.* reported the first example of CILs having lactate anion [8], more chiral ionic liquids have been synthesized [9—17]. Then, chiral ionic liquids and other catalysts for asymmetric organic synthesis have been intensively investigated. (*S*)-proline was a first compound used as a catalysts for Michael addition of carbon nucleophiles to nitroalkenes to afford the adducts with good diastereoselectivity, but poor enantioselectivity [18]. Therefore, new catalysts such as proline derivatives and other compounds based pyrrolidine for example chiral ionic liquids having pyrrolidine moiety, have been synthesized. Recently, some functionalized chiral ionic liquids have been obtained and used as catalysts for asymmetric C-C bond forming reactions such as Michael addition [19—25], aldol reaction [26—28] and reduction of aromatic ketones with borane-dimethyl sulfide complex [29]. Luo *et al.* [19, 20], Headley *et al.* [21, 22] and Wang *et all* [23] reported the chiral ionic liquids having imidazolium ring as efficient catalysts for asymmetric Michael addition of carbonyl compounds to nitroalkenes. The application of 1-ethyl-3-methylimidazolium (*S*)-prolinate as catalysts for asymmetric addition of cyclohexanone to chalcone in different solvents was presented by Qiang *et al.* [25]. Later, Headley *et al.* described the synthesis of pyrrolidine-based pyridinium ionic liquids for asymmetric Michael reaction [30]. Last year,



(I)—(IV)

where:
(Ia) R = Bu, $X^- = (CF_3SO_2)_2N^-$
(IIa) R = *i*-Pr, $X^- = (CF_3SO_2)_2N^-$
(IIb) R = *i*-Pr, $X^- = PF_6^-$
(IIIa) R = Pent, $X^- = (CF_3SO_2)_2N^-$
(IIIb) R = Pent, $X^- = PF_6^-$
(IVa) R = Hex, $X^- = (CF_3SO_2)_2N^-$
(IVb) R = Hex, $X^- = PF_6^-$

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novel pyrrolidine-based chiral ionic liquids and other pyrrolidine analogues were synthesized and applied for asymmetric organic reactions, especially for Michael addition [31—33]. We designed a new chiral ionic liquids of the structure similar to described in literature [19] but with different alkyl substituents incorporated to imidazolium ring and anions [Formula (I)—(IV)] as catalysts for asymmetric synthesis.

EXPERIMENTAL

Materials

All starting materials: L-proline, $LiAlH_4$, imidazole, di-*tert*-butyl dicarbonate, *p*-toluenesulfonyl chloride were commercial products (Aldrich and Merck) of analytical grade.

Methods of testing

^1H NMR and ^{13}C NMR spectra were recorded on a Varian 200 MHz spectrometer.

^{19}F NMR spectra were recorded on Varian 500 MHz spectrometer. Chemical shifts of ^1H and ^{13}C were given in δ ppm relative to tetramethylsilane (TMS) as an internal standard. Chemical shifts of ^{19}F were given in δ ppm relative to trifluoroacetic acid as an internal standard. The coupling constants J were given in hertz. The reaction products were purified by column chromatography methods on silica gel 230—400 mesh ASTM (Merck).

The HPLC analysis were made with liquid chromatograph Lachrom (firm Merck Hitachi) equipped with pump and variable wavelength UV-VIS spectrophotometric detector. Chromatographic measurements were performed with column Atlantis® T3, 25.0 cm × 0.46 cm. The mixture of methanol with 0.05 M phosphate buffer pH = 2.5 was used as the mobile phase (flow 1 cm^3/min). Chiral HPLC analysis was performed on Shimadzu SPD 6-AV, using a Chiralcel OD-H column and eluent: hexane/iPrOH (90:10).

Synthesis of (*S*)-prolinol

In a 3 dm^3 round-bottomed flask equipped with reflux condenser was placed 1 dm^3 of anhydrous THF and $LiALH_4$ (25 g, 0.66 mol).The suspension was heated under reflux for 15 min, then (*S*)-proline (24 g, 0.42 mol) was added in small portions for 40 min. The mixture was magnetically stirred under reflux for 1 h. The excess of $LiAlH_4$ was decomposed by cautiously adding of KOH (11.67 g, 0.21 mol) in water (47 cm^3). The mixture was refluxed for 15 min. The solution and precipitated solid were separated by filtration. The removing (*S*)-prolinol was extracted from the precipitate by extraction with hot THF. The combined filtrates were concentrated under reduced pressure to afford of (*S*)-prolinol (41 g, 0.41 mmol, 97 %) as a pale-yellow oil.

Synthesis of *N-tert*-butoxycarbonyl-(*S*)-prolinol *p*-toluenesulfonate

To 100 cm^3 the solution of (*S*)-prolinol (10 g, 0.1 mol) in CH_2Cl_2 27.5 cm^3 (20 g, 0.2 mol) of triethylamine was added and cooled down to 0 °C. Then di-*tert*-butyl dicarbonate (27.5 g, 0.11 mol) was added and the mixture was stirred at room temperature for 6 h. After this time, to the reaction mixture 35 cm^3 (25.2 g, 0.25 mol) of Et_3N was added and cooled to 0 °C. Then, *p*-toluenesulfonyl chloride (25.3 g, 0.123 mol) was added and the mixture was stirred at room temperature for 18 h. The reation mixture was diluted with CH_2Cl_2 (200 cm^3) and washed with water, 1 M HCl, saturated $NaHCO_3$ and water. The organic layer was dried with sodium sulfate, filtered and concentrated under reduced pressure to yield 27.8 g of *N*-Boc-prolinol *p*-toluenesulfonate, which was used in the next step without further purification.

Synthesis of *N-tert*-butoxycarbonyl-[(*S*)-(pyrrolidin-2-yl)methyl]imidazole

To the suspension of freshly synthesized sodium imidazolate (10.8 g, 0,12 mol from imidazole and NaH) in CH_3CN (100 cm^3) *N*-Boc-prolinol *p*-toluenesulfonate (27.8 g, 0,078 mmol) in CH_3CN (100 cm^3) was added and the mixture was stirred under reflux until the HPLC control indicated the disappearance of the starting material. The solvent was distilled off under reduced pressure and the residue was diluted with water (250 cm^3) and extracted with CH_2Cl_2. The organic layer was washed 2 times with water (2 × 200 cm^3), dried over Na_2SO_4 and concentrated in vacuo. To the residue 11 cm^3 of acetone was added, mixed and cooled down to 0 °C. The obtained white solid was filtrated, washed with cold acetone and dried. The filtrate was concentrated under reduced pressure and chromatographed on silica gel using a mixture of hexane:acetone (3:2) as eluent. The total yield of *N-tert*-butoxycarbonyl-[(*S*)-(pyrrolidin-2- yl)methyl]imidazole was 10.58 g (0.042 mol, 54 %). $[\alpha]_D^{20}$ = + 25.3 (CH_3OH c ~ 1,0 m/v). ^1H NMR ($CDCl_3$, 200 MHz): δ 1.51 (s, 9H, *t*-Bu), 1.60—1.80 (m, 2H), 1.82—2.02 (m, 2H), 3.05—3.50 (m, 2H, CH_2-**CH_2**-N[C=O]), 3.90—4.18 (m, 2H, CH-**CH_2**-imidazole), 4.20—4.36 (m, 1H, CH), 6.89 (s, 1H, CH imidazole), 7.05 (s, 1H, CH imidazole), 7.43 (s, 1H, CH imidazole) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ 23.48 (CH_2), 28.45 (CH_2), 28.63 (3 x CH_3, *t*-Bu), 47.18 (CH_2), 48.78 (CH_2), 57.37 (CH), 79.98 (C, *t*-Bu), 120.01 (CH), 129.47 (CH), 137.83 (CH), 154.86 (C=O) ppm.

General procedure for the alkylation of *N-tert*-butoxycarbonyl-[(*S*)-(pyrrolidin-2-yl)methyl]imidazole (Boc-Im-Prol)

To the solution of Boc-Im-Prol (0.021 mol) in toluene bromoalkane (0.084 mol) was added and the mixture was stirred at about 75 °C (reaction with 2-bromopropane was

carried out at 60 °C). After completion, the solvent was removed by decantation and the obtained oil was washed with diethyl ether (5 cm^3) and purified by column chromatography method on silica gel, using a mixture of dichlorometane:methanol as eluent. *N-tert*-butoxycarbonyl-[(*S*)-(pyrrolidin-2-yl)methyl]imidazolium bromides were obtained with yield about 70 %.

General procedure for the synthesis of 1-[(*S*)-(pyrrolidin-2-yl)methyl]-3-alkylimidazolium dibromides (Va)—(Vd)

A mixture of 1-Boc-[(*S*)-(pyrrolidin-2-yl)methyl]-3-alkylimidazolium bromide (0.01 mol) and 25 % HBr aqueous solution (25 cm^3) was stirred magnetically. When HPLC control indicated the disappearance of the starting material, aqueous solution was removed under reduced pressure and the residue was dried in vacuo over KOH. The crude product was purified by column chromatography using a mixture of dichloromethane:methanol (from 8:1 to 5:1). The desired products were obtained with yields 78—80 %.

1-[2(S)-(pyrrolidin-2-yl)methyl]-3-butylimidazolium dibromide (Va)

^{1}H NMR (DMSO-d_6, 200 MHz): δ 0.92 (t, 3H, CH_3, J = 7.3 Hz), 1.20—1.42 (m, 2H, CH_3-**CH_2**-CH_2), 1.60—2.24 (m, 6H), 3.18—3.42 (m, 2H, CH_2-**CH_2**-NH_2^+), 3.98—4.16 (m, 1H, CH), 4.17—4.30 (m, 2H, CH_2-**CH_2**-imidazole), 4.62—4.80 (m, 2H, CH-**CH_2**-imidazole), 7.95 (s, 1H, CH imidazole), 7,99 (s, 1H, CH, imidazole), 9.32 (s, 1H, CH imidazole), 9.46 (s, 2H, NH_2^+) ppm.

^{13}C NMR (DMSO-d_6, 50 MHz): δ 13.26 (CH_3), 18.71 (CH_2), 22.57 (CH_2), 27.30 (CH_2), 31.07 (CH_2), 44.60 (CH_2), 48.34 (CH_2), 48.64 (CH_2), 58.71 (CH), 122.46 (CH), 122.57 (CH), 136.45 (CH) ppm.

1-[2(S)-(pyrrolidin-2-yl)methyl]-3-isopropylimidazolium dibromide (Vb)

^{1}H NMR (DMSO-d_6, 200 MHz): δ 150 (d, 6H, *i*-Pr, J = 6.6 Hz), 1.67—2.18 (m, 4H, 2 x CH_2), 3.18—3.35 (m, 2H, CH_2-**CH_2**-NH_2^+), 3.95—4.15 (m, 1H, CH), 4.58—4.73 (m, 3H), 7.90 (s, 1H, CH, imidazole), 7.99 (s, 1H, CH, imidazole), 9.13 (s, 1H, CH, imidazole), 9.39 (t, 2H, NH_2^+, J = 1,4 Hz) ppm.

^{13}C NMR (DMSO-d_6, 50 MHz), δ 22.25 (CH_3), 22.34 (CH_3), 22.75 (CH_2), 27.47 (CH_2), 44.70 (CH_2), 48.61 (CH_2), 52.46 (CH), 58.92 (CH), 120.91 (CH), 122.81 (CH), 135.52 (CH) ppm.

1-[2(S)-(pyrrolidin-2-yl)methyl]-3-pentylimidazolium dibromide (Vc)

^{1}H NMR (DMSO-d_6, 200 MHz): δ 0.88 (t, 3H, CH_3, J = 6,6 Hz), 1.26—1.38 (m, 4H, 2 x CH_2), 1.69—2.20 (m, 6H, 3 x CH_2), 3.17—3.36 (m, 2H, CH_2-**CH_2**-NH_2^+), 4.05—4.16 (m, 1H, CH), 4.21 (t, 2H, CH_2-**CH_2**-imidazole, J = 7,2 Hz), 4.58—4.79 (m, 2H, CH-**CH_2**-imidazole), 7.90 (s, 1H, CH, imidazole), 7.99 (s, 1H, CH, imidazole), 9.29 (s, 1H, CH, imidazole), 9.42 (s, 2H, NH_2) ppm.

^{13}C NMR (DMSO-d_6, 50 MHz): δ 13.63 (CH_3), 21.42 (CH_2), 22.58 (CH_2), 27.34 (CH_2), 27.55 (CH_2), 28.80 (CH_2), 44.67 (CH_2), 48.45 (CH_2), 48.94 (CH_2), 58.66 (CH), 122.55 (2 x CH), 136.54 (CH) ppm.

1-[2(S)-(pyrrolidin-2-yl)methyl]-3-hexylimidazolium dibromide (Vd)

^{1}H NMR (DMSO-d_6, 200 MHz): δ 0.87 (t, 3H, CH_3 = 6,6 Hz), 1.18—1.40 (m, 6H, 3 x CH_2), 1.69—2.20 (m, 6H, 3 x CH_2), 3.20—3.40 (m, 2H, CH_2-**CH_2**-NH_2^+), 4.00—4.15 (m, 1H, CH), 4.21 (t, 2H, CH_2-**CH_2**-imidazole, J = 7,2 Hz), 4.58—4.79 (m, 2H, CH-**CH_2**-imidazole), 7,93 (s, 1H, CH, imidazole), 7.97 (s, 1H, CH, imidazole), 9.30 (s, 1H, CH, imidazole), 9.42 (s, 2H, NH_2^+) ppm.

^{13}C NMR (DMSO-d_6, 50 MHz): δ 13.63 (CH_3), 21.42 (CH_2), 22.58 (CH_2), 25.09 (CH_2), 27.30 (CH_2), 29.10 (CH_2), 30.10 (CH_2), 44.61 (CH_2), 48.38 (CH_2), 48.94 (CH_2), 58.66 (CH), 122.50 (CH), 122.56 (CH), 136.54 (CH) ppm.

Synthesis of the catalysts (I)—(IVb)

[(S)-(pyrrolidin-2-yl)methyl]-3-butylimidazolium bis(trifluoromethylsulfonyl)imide (Ia)

1-[(*S*)-(pyrrolidin-2-yl)methyl]-3-butylimidazolium dibromide (Va) (575.4 mg, 1.56 mmol) was dissolved in water (0,6 cm^3), alkalized with saturated solution of $NaHCO_3$ (2 cm^3) and stirred for 2 h. After this time, $Li(CF_3SO_2)_2N$ (447.7 mg, 1.56 mmol) was added and the mixture was stirred for 24 h. The aqueous solution was extracted 3 times with CH_2Cl_2 (3 × 10 cm^3). The combined extracts were washed with water (8 cm^3) and dried over $MgSO_4$. The solvent was removed under reduced pressure. The crude product was purified by column chromatography using the mixture of dichloromethane:methanol (16:1). Yield 426.2 mg (0.872 mmol, 56 %).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.96 (t, 3H, CH_3, J = 7.3 Hz), 1.31—1.56 (m, 4H), 1.75—1.90 (m, 3H), 2.01—2.17 (m, 1H), 2.84 (s, 1H, NH), 2.93—3.10 (m, 2H, **CH_2**NH), 3.58—3.71 (m, 1H), 3.98—4.10 (m, 1H), 4,17 (t, 2H, CH_2-**CH_2**-imidazole, J = 7.4 Hz), 4.29 (dd, 1H, J_1 = 4.0 Hz, J_2 = 13.6 Hz), 7.27 (m, 1H, CH, imidazole), 7.49 (m, 1H, CH, imidazole), 8.79 (s, 1H, CH, imidazole) ppm.

^{13}C NMR ($CDCl_3$, 50 MHz): δ 13.37 (CH_3), 19.52 (CH_2), 25.59 (CH_2), 28.91 (CH_2), 31.97 (CH_2), 46.88 (CH_2), 50,15 (CH_2), 53.66 (CH_2), 58.26 (CH), 119.87 (q, 2 x **CF_3**[SO_2], J ^{13}C-^{19}F = 319.2 Hz), 121.86 (CH), 123.41 (CH), 135.94 (CH) ppm.

1-[(S)-(pyrrolidin-2-yl)methyl]-3-isopropylimidazolium bis(trifluoromethylsulfonyl)imide(IIa)

The title compound was prepared according to the procedure for (Ia) from dibromide (Vb) (492.1 mg, 1.39 mmol), saturated solution of $NaHCO_3$ (1.7 cm^3) and $Li(CF_3SO_2)_2N$ (397.6 mg, 1.38 mmol). The crude product was purified by column chromatography using a mixture of dichloromethane:methanol (15:1) to afford 330 mg (0.674 mmol, 50 %) of the desired ionic liquid.

^{1}H NMR (CD_2Cl_2, 200 MHz): δ 1.58 (d, 6H, 2 x CH_3, J = 6.8 Hz), 1.62—1.69 (m, 1H), 1.79—1.98 (m, 2H), 2.11—2.28 (m, 1H), 3.06—3.27 (m, 2H, **CH_2**NH), 3.71—3.85 (m, 1H), 4.14—4.43 (m, 2H), 4.54—4.68 (m, 1H), 7.34—7.36 (m, 1H, CH, imidazole), 7.50—7.52 (m, 1H, CH, imidazole), 8,73 (s, 1H, CH, imidazole) ppm.

^{13}C NMR (CD_2Cl_2, 50 MHz): δ 22.79 (CH_3), 22.84 (CH_3), 25.22 (CH_2), 28.97 (CH_2), 47.43 (CH_2), 52.86 (CH_2), 54.24 (CH), 59.35 (CH), 120.10 (q, 2 x **CF_3**[SO_2], J ^{13}C-^{19}F = 319.2 Hz), 120.76 (CH), 123.65 (CH),134.62 (CH,) ppm.

^{19}F NMR (CD_2Cl_2, 470.4 MHz): δ -79.86 ppm.

1-[(S)-(pyrrolidin-2-yl)methyl]-3-isopropylimidazolium hexafluorophosphate (IIb)

To the solution of dibromide (Vb) (509 mg, 1.43 mmol) in water (0.5 cm^3) saturated solution of $NaHCO_3$ (1.7 cm^3) was added and the mixture was stirred for 2 h. Then, KPF_6 (263.2 mg, 1.43 mmol) was added and the mixture was stirred for 24 h. After this time, the aqueous solution was extracted 3 times with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were washed with water (6 cm^3), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of dichlorometane:methanol (15:1) to afford 228.5 mg (0.674 mmol, 47 %) of (IIb).

^{1}H NMR (DMSO-d_6, 200 MHz): δ 1.48 (d, 6H, 2 x CH_3, *i*-Pr, J = 6.6 Hz), 1.54—1.63 (m, 1H), 1.72—1.88 (m, 2H), 1.91—2.06 (m, 1H), 3.04 (t, 2H, CH_2-**CH_2**-NH, J = 7.0 Hz), 3.64—3.78 (m, 1H), 4.13—4.37 (m, 2H), 4.56—4.76 (m, 1H, *i*-Pr), 7.76—7.78 (m, 1H, CH, imidazole), 7.91—7.92 (m, 1H, CH, imidazole), 9.15 (s, 1H, CH, imidazole) ppm.

^{13}C NMR (DMSO-d_6, 50 MHz): δ 22.15 (CH_3), 23.79 (CH_2), 27.80 (CH_2), 45.39 (CH_2), 50.89 (CH_2), 52.18 (CH), 58.00 (CH), 120.37 (CH), 122.83 (CH,),135.12 (CH) ppm.

^{19}F NMR (DMSO-d_6, 470.4 MHz): δ -70.55 (d, 6F, PF_6^-, J = 710.3 Hz) ppm.

1-[(S)-(pyrrolidin-2-yl)methyl]-3-pentylimidazolium bis(trifluoromethylsulfonyl)imide (IIIa)

This compound was prepared according to the procedure for (Ia) from compound (Vc) (335.3 mg, 0.875 mmol), saturated solution of $NaHCO_3$ (1.2 cm^3) and $Li(CF_3SO_2)_2N$ (397.6 mg, 1.38 mmol). Chromatography of the crude product afforded 238 mg (0.474 mmol, 54 %) of (IIIa). A mixture of dichloromethane:methanol (16:1) was used as eluent.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.90 (t, 3H, CH_3, J = 6.4 Hz), 1.29—1.39 (m, 4H), 1.41—1.59 (m, 1H), 1.78—1.94 (m, 4H), 2.03—2.20 (m, 1H), 2.95—3.17 (m, 2H), 3.50 (s, 1H, NH), 3.62—3.75 (m, 1H), 4.04—4.11 (m, 1H), 4.16 (t, 2H, CH_2-**CH_2**-imidazole, J = 7,4 Hz), 4.33 (dd, 1H, J_1 = 3.9 Hz, J_2 = 13.8 Hz), 7.72 (s, 1H, CH, imidazole), 7.50 (m, 1H, CH, imidazole), 8.77 (s, 1H, CH, imidazole) ppm.

^{13}C NMR ($CDCl_3$, 50 MHz): δ 13.80 (CH_3), 22.06 (CH_2), 25.32 (CH_2), 28.29 (CH_2), 28.79 (CH_2), 29.87 (CH_2), 46.93 (CH_2), 50.41 (CH_2), 53.23 (CH_2), 58.54 (CH), 119.84 (q, 2 x **CF_3**[SO_2], J = 319 Hz), 122.02 (CH), 123.39 (CH), 135.86 (CH) ppm.

^{19}F NMR ($CDCl_3$, 470.4 MHz), δ: -79.45 ppm.

1-[(S)-(pyrrolidin-2-yl)methyl]-3-pentylimidazolium hexafluorophosphate (IIIb)

The title compound was prepared according to the procedure for (IIb) from compound (Vc) (355.2 mg, 0.927 mmol), saturated solution of $NaHCO_3$ (1.2 cm^3) and KPF_6 (170.1 mg, 0.924 mmol). The obtained product was purified by column chromatography on silica gel. Elution with a mixture of dichloromethane:methanol (16:1) afforded 170.3 mg (0.464 mmol, 50 %) of ionic liquid (IIIb).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.91 (t, 3H, CH_3, J = 6.6 Hz), 1.30—1.45 (m, 5H), 1.65—1.80 (m, 4H), 1.96—2.09 (m, 1H), 2.90—3.06 (m, 2H, **CH_2**NH), 3.53—3.66 (m, 1H), 3.87—3.98 (m, 1H), 4.16 (t, 2H, CH_2-**CH_2**-imidazole, J = 7.3 Hz), 4.18—4.26 (m, 1H), 7.20 (t, 1H, CH, imidazole), 7.44 (t, 1H, CH, imidazole), 8.68 (s, 1H, CH, imidazole) ppm.

^{13}C NMR ($CDCl_3$, 50 MHz): δ 13.93 (CH_3), 22.14 (CH_2), 26.14 (CH_2), 28.38 (CH_2), 29.15 (CH_2), 29.88 (CH_2), 46.80 (CH_2), 50.37 (CH_2), 54.48 (CH_2), 57.61 (CH), 121.40 (CH), 123.37 (CH), 136.00 (CH) ppm.

^{19}F NMR ($CDCl_3$, 470.4 MHz): δ -72.86 (d, 6F, PF_6^-, J = 711.3 Hz) ppm.

1-[(S)-(pyrrolidin-2-yl)methyl]-3-hexylimidazolium bis(trifluoromethylsulfonyl)imide (IVa)

The title compound was prepared according to the procedure for (Ia) from compound (Vd) (401.5 mg, 1.01 mmol), saturated $NaHCO_3$ (1.2 cm^3) and $Li(CF_3SO_2)_2N$ (290,9 (mg, 1.01 mmol). The crude product was purified by column chromatography using a mixture of dichloromethane:methanol (17:1) to afford 261.7 mg (0.507 mmol, 50 %) of (IVa) as a pale yellow liquid.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.88 (t, 3H, CH_3, J = 6.3 Hz), 1.28—1.36 (m, 6H), 1.40—1.58 (m, 1H), 1.74—1.90 (m, 4H), 2.02—2.18 (m, 1H), 2.93—3.15 (m, 2H, **CH_2**NH), 3.38 (s, 1H, NH), 3.60—3.73 (m, 1H, CH), 4.03—4.14 (m, 1H), 4.16 (t, 2H, CH_2-**CH_2**-imidazole, J = 7.6 Hz), 4.31 (dd, 1H, J_1 = 4.0 Hz, J_2 = 14.0 Hz), 7.28 (m, 1H, CH, imidazole), 7.50 (m, 1H, CH, imidazole), 8.76 (s, 1H, CH, imidazole) ppm.

^{13}C NMR ($CDCl_3$, 50 MHz): δ 13.94 (CH_3), 22.44 (CH_2), 25.37 (CH_2), 25.88 (CH_2), 28.81 (CH_2), 30.00 (CH_2), 31.07 (CH_2), 46.85 (CH_2), 50.38 (CH_2), 53.33 (CH_2), 58.40 (CH), 119.84 (q, 2 x **CF_3**[SO_2], J ^{13}C-^{19}F = 319.2 Hz), 122.00 (CH), 123.39 (CH), 135.83 (CH) ppm.

1-[(S)-(pyrrolidin-2-yl)methyl]-3-hexylimidazolium hexafluorophosphate (IVb)

The compound (IVb) was synthesized according to the procedure for (IIb) from compound (Vd) (404.9 mg, 1.02 mmol), saturated $NaHCO_3$ (1.2 cm^3) and KPF_6 (187.5 mg, 1.02 mmol). The desired product was isolated by column chromatography on silica gel. Elution with a mixture of dichloromethane:methanol (17:1) afforded 190.7 mg (0,5 mmol, 49 %) of (IVb).

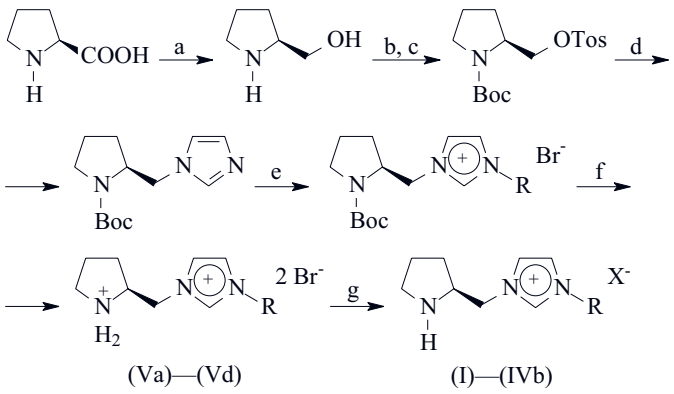
^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.87 (t, 3H, CH_3, J = 6.4 Hz), 1.29—1.36 (6H), 1.40—1.50 (1H), 1.66—1.90 (m, 4H), 1.94—2.11 (m, 1H), 2.84—3.06 (m, 2H), 3.54—3.67 (m, 1H), 3.98 (dd, 1H, J_1 = 8.2 Hz, J_2 = 13,8 Hz), 4.15 (t, 2H, CH_2-**CH_2**-imidazole, J = 7.5 Hz), 7.26 (m, 1H, CH, imidazole), 7.44 (m, 1H, CH, imidazole), 8.60 (s, 1H, CH, imidazole) ppm.

^{13}C NMR ($CDCl_3$, 50 Hz): δ 14.05 (CH_3), 22.51 (CH_2), 25.78 (CH_2), 25.95 (CH_2), 28.97 (CH_2), 29.95 (CH_2), 31.14 (CH_2), 46.73 (CH_2), 50.30 (CH_2), 53.91 (CH_2), 121.77 (CH), 123.31 (CH), 135.75 (CH) ppm.

^{19}F NMR (470.4 MHz): δ -72.60 (d, 6F, PF_6^-, J = 711.7 Hz) ppm.

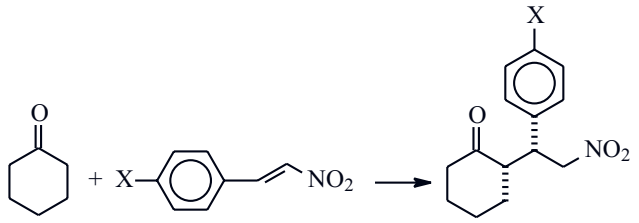
Asymmetric Michael addition of cyclohexanone to nitrostyrene — typical procedure

To a mixture of cyclohexanone (546.4 mg, 5.567 mmol), catalyst (I) (65.95 mg, 0,135 mmol) and benzoic acid (16.54 mg, 0.135 mmol) in CH_2Cl_2 (1 cm^3) a solution of *trans*-β-nitrostyrene (177.5 mg, 1.19 mmol) in CH_2Cl_2 (1 cm^3) was added. The mixture was magnetically stirred. The reaction was monitored by TLC and HPLC methods. After disappearance of nitrostyrene, dichloromethane and cyclohexanone were removed under reduced pressure. The residue was extracted with diethyl ether (3 × 10 cm^3). The organic layer was washed twice with aqueous $NaHCO_3$ (2 × 8 cm^3) to remove of benzoic acid and water (8 cm^3), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 7:1) to afford the Michael adduct (177.0 mg, 0.571 mmol, 60 %) (see Scheme A, Table 1).



Scheme A. Synthesis of chiral ionic liquids: (a) $LiAlH_4$, THF; (b) Boc_2O, Et_3N; (c) TosCl, Et_3N; (d) imidazole, NaH; (e) RBr, toluene; (f) HBr aq.; (g) $NaHCO_3$, then KPF_6 or $LiTf_2N$

T a b l e 1. Asymmetric addition of cyclohexanone to nitroalkenes *via* Scheme A



(VI) (VIIa, b) (VIIIa, b)

where: (VIIa) X = H, nitrostyrene; (VIIb) X = Cl, *p*-chloronitrostyrene

Entry	Substrate	Catalyst	Time h	Yield[a] %	Syn/anti[b]	Ee[c] %
1	(VIIa)	(Ia)	120	60	90/10	>99
2	(VIIa)	(IIa)	120	60	91/9	>99
3	(VIIa)	(IIb)	144	65	91/9	>99
4	(VIIb)	(IIa)	120	65	91/9	96
5	(VIIb)	(IIb)	120	61	91/9	95
6	(VIIa)	(IIIa)	72	60	89/11	>99
7	(VIIa)	(IIIb)	72	50	88/12	>99
8	(VIIb)	(IIIa)	72	65	91/9	99
9	(VIIb)	(IIIb)	72	58	91/9	87
10	(VIIa)	(IVa)	72	59	87/13	>99
11	(VIIa)	(IVb)	72	50	87/13	>99
12	(VIIb)	(IVa)	72	64	91/9	95
13	(VIIb)	(IVb)	72	65	92/8	93

[a] Yield of the product isolated by column chromatography.
[b] Determined by ^{1}H NMR analysis.
[c] Determined by chiral HPLC analysis.

(S)-2-[(R)-2-nitro-1-phenylethyl]cyclohexanone (VIIIa) — diastereomer syn [26]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.14—1.33 (m, 1H), 1.46—1.81 (m, 4H), 2.00—2.12 (m, 1H), 2.30—2.51 (m, 2H, CH_2-**CH_2**[C=O]), 2.62—2.76 (m, 1H, **CH**[C=O]), 3.76 (dt, 1H, J_1 = 4,6 Hz, J_2 = 10,0 Hz), 4.63 (dd, 1H, J_1 = 10.0 Hz, J_2 = 12.6 Hz), 4.95 (dd, 1H, J_1 = 4.6 Hz, J_2 = 12.6 Hz), 7.14—7.19 (m, 2H, Ar), 7.26—7.37 (m, 3H, Ar) ppm.

^{13}C NMR ($CDCl_3$, 200 MHz): δ 25.04 (CH_2), 28.55 (CH_2), 33.23 (CH_2), 42.76 (**CH_2**[C=O]), 43.95 (CH), 52.52 (CH), 78.92 (**CH_2**[NO_2]), 127.78 (CH, Ar), 128.18 (2 x CH, Ar), 128.94 (2 x CH, Ar), 137.77 (C, Ar), 212.00 (C=O) ppm.

The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, λ = 254 nm, hexane/*i*-PrOH = 90:10, 0,5 ml/min, t_R (minor) = 21.3 min, t_R (major) = 22.7 min, ee > 99 %), $[\alpha]_D^{20}$ = -28.6°.

(S)-2-[(S)-2-nitro-1-phenyloethyl]cyclohexanone diastereomer anti

^{1}H NMR ($CDCl_3$, 50 MHz): δ 1.34—1.48 (m, 1H), 1.58—1.74 (m, 2H), 1.84—1.96 (m, 1H), 1.99—2.16 (m, 2H), 2.21—2.34 (m, 1H), 2.36—2.39 (m, 1H), 2.68—2.79 (m, 1H), 3.96—4.06 (m, 1H), 4.84—4.89 (m, 2H, **CH_2**[NO_2]), 7.23—7.31 (m, 5H, Ar) ppm.

^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.24 (CH_2), 27.55 (CH_2), 30.16 (CH_2), 42.52 (CH_2), 53.96 (CH), 76.74 (CH_2), 127.74 (CH, Ar), 128.54 (2 x CH, Ar), 128.94 (2 x CH, Ar), 138.52 (C, Ar), 210.69 (C=O) ppm.

The reaction addition of cyclohexanone to *p*-chloro-*trans*-β-nitrostyrene was carried out according to the procedure described above.

(S)-2-[(R)-2-nitro-1-(4-chlorophenyl)ethyl]cyclohexanone (VIIIb) — diastereomer syn

^{1}H NMR ($CDCl_3$, 200 MHz) δ: 1.14—1.33 (m, 1H), 1.52—1.81 (m, 4H), 2.05—2.12 (m, 1H), 2.30—2.51 (m, 2H, CH_2-**CH_2**[C=O]), 2.62—2.76 (m, 1H, **CH**[C=O]), 3.76 (dt, 1H, J_1 = 4.6 Hz, J_2 = 10,0 Hz), 4.60 (dd, 1H, J_1 = 10.0 Hz, J_2 = 12.6 Hz). 4.94 (dd, 1H, J_1 = 4.6 Hz, J_2 = 12.6 Hz), 7.10—7.32 (2d, 4H, *p*-Ar, J = 8.2 Hz) ppm.

^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.26 (CH_2), 28.64 (CH_2), 33.26 (CH_2), 42.94 (**CH_2**[C=O]), 43.55 (CH), 52.58 (CH), 78.78 (**CH_2**[NO_2]), 129.33 (2 x CH, Ar), 129.75 (2 x CH, Ar), 133.81 (C, Ar), 136.47 (C, Ar), 212,00 (C=O) ppm, $[\alpha]_D^{20}$ = -27.8°.

(S)-2-[(S)-2-nitro-1-(4-chlorophenyl)ethyl]cyclohexanone — diastereomer anti

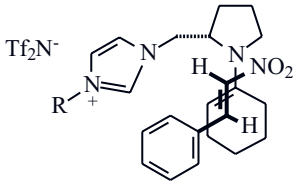
^{1}H NMR ($CDCl_3$, 50 MHz): δ 1.32—1.46 (m, 1H), 1.56—1.73 (m, 2H), 1.86—1.97 (m, 1H), 2.02—2.14 (m, 2H), 2.27—2.45 (m, 2H, **CH_2**[C=O]), 2.66—2.78 (m, 1H, **CH**[C=O]), 3.88—3.98 (m, 1H), 4.82—4.87 (m, 2H, **CH_2**[NO_2]), 7.18—7.31 (2d, 4H, *p*-Ar) ppm.

RESULTS AND DISCUSSION

Synthesis of chiral ionic liquids

The new chiral ionic liquids (CILs) were synthesized from (*S*)-proline as a starting material [19]. Reduction of this compound with $LiAlH_4$ gave (*S*)-prolinol. Luo *et al.* described reduction of aminoacids with $NaBH_4/I_2$ [34]. Boc-protection of (*S*)-prolinol carried out under basic condition followed by reaction of obtained product with *p*-toluenesulfonyl chloride afforded Boc-prolinol *p*-toluenesulfonate. Nucleophilic substitution of this compound with sodium imidazolate carried out under reflux in CH_3CN gave *N*-*tert*-butoxycarbonyl-[(pyrrolidin-2-yl)methyl]imidazole. *N*-alkylation of the product with bromoalkanes gave the corresponding Boc-protected pyrrolidinylimidazolium bromides. Removal of Boc group with aqueous HBr afforded the pyrrolidine-based imidazolium bromide salts (Va)—(Vd) which were identified by ^{1}H and ^{13}C NMR spectroscopy methods. The compounds in the reaction with KPF_6 or $LiTf_2N$ carried out under basic conditions ($NaHCO_3$) afforded the desired chiral ionic liquids (I)—(IVb) (Scheme A) which were purified by flash column chromatography. The ionic liquids are soluble in moderately polar solvents such as methanol, acetone, and dichloromethane [except (IIb)] but insoluble in less polar solvents (diethyl ether, toluene, and hexane). The structure of obtained chiral ionic liquids was determined by spectroscopic analysis of ^{1}H NMR and ^{13}C NMR. The presence of fluorine in anion was confirmed by ^{19}F NMR spectra.

Initially, we utilized the obtained chiral ionic liquids for the direct asymmetric Michael addition of cyclohexanone (VI) to *trans*-β-nitrostyrene (VII) to afford Michael adduct (VIII) using CH_2Cl_2 as reaction medium. Reaction was carried out at room temperature at the presence of benzoic acid as the cocatalyst. As shown in the Table 1, application of the obtained catalysts give the desired product in good yield, diastereoselectivity (from 87/13 to 91/9) and excellent enantioselectivity (>99 %). We next examined the influence of temperature on the stereoselectivity of the reaction. The Michael addition catalyzed with (IVa) and carried out at lower temperature (4 °C) afforded the adduct product (VIIIa) with better diastereoselectivity (94:6; *syn*/*anti*) and comparable enantioselectivity. The results in the table show the influence of the substituent on aryl group on yield and enantioselectivity. The relative and absolute configuration of the Michael adduct was determined by ^{1}H NMR spectroscopic analysis, comparison of chemical shift and coupling constants J values and optical rotation with described in literature [30]. The stereoselectivity of this reaction may be explained by an acyclic synclinal transition state proposed by Seebach and Goliński [Formula (IX)] [35] and presented by Zhu *et al.* [36]. The transition state of Michael reaction was also presented in other papers [19, 30].



(IX)

CONCLUSIONS

In conclusion, we designed and prepared seven chiral ionic liquids based on pyrrolidine with bis(trifluoromethylsulfonyl)imide and hexafluorophosphate anions as catalysts for asymmetric organic synthesis. The ionic liquids were obtained from (*S*)-proline and identified by spectroscopic methods. Next, we used the obtained chiral ionic liquids for asymmetric Michael addition of cyclohexanone to nitrostyrene and *p*-chloronitrostyrene. The Michael adducts were obtained with good yields, diastereselectivities and excellent enantioselectivities (93—99.9 %). Further investigation on the application of this catalysts in asymmetric synthesis is currently in progress and will be reported.

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