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Design and synthesis of novel ionic liquid/liquid crystals (IL^2Cs) with axial chirality

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Abstract—As the first examples of axially chiral ionic liquids, new pyridinium salts having a 1,3-dioxan ring in their central core were synthesized. Enantioselective dehydrohalogenation using chiral alkoxides provided a simple and practical approach for their synthesis. Some structures exhibit both low melting point and liquid crystalline behaviour.

Owing to their unique chemical and physical properties, ionic liquids (ILs) have received recent attention for applications as potential replacements for volatile solvents.[1] For example, ILs can favourably be used in place of organic solvents for electrophilic fluorination,[2] Suzuki cross-coupling reactions,[3] and Diels–Alder reactions,[4] suggesting this modern class of solvents to be suitable for most of organic synthesis. Besides green chemistry applications, one fascinating aspect of ILs chemistry is the possibility to design an infinite number of structures and to imagine a new paradigm in organic synthesis, that is, the concept of 'tailor-made' solvents. Surprisingly, the number of published examples of asymmetric synthesis in this media has been limited so far.[5] Recently, chiral ionic liquids have attracted significant attention for their potential application to chiral discrimination, including asymmetric synthesis.[5] In this search for a renewal in the chemistry of chiral solvents, the previously described chiral ILs were directly obtained from the chiral pool,[6] the stereogenic unit being a chiral center. Recently was disclosed access to a planar dissymmetric derivative,[7] while ILs with axial chirality remain hitherto unknown compounds.

Ionic liquid presenting thermotropic mesophases are attractive new materials because they can be considered as structured solvents. They could increase the selectivity in reactions by ordering reactants,[8] or be used as templates for the synthesis of mesoporous materials,[9] and in the formation of ordered thin films.[10] Inspired by a series of publications from Haramoto et al.,[11] in which achiral compounds having both properties of ionic liquids and liquid crystals are examined, we describe herein the first synthesis of a novel family of chiral ionic liquids in which:

(i) *the stereogenic unit is a chiral axis*,
(ii) '*ionic liquid/liquid crystals*' (*IL^2Cs*) *properties are tuned by the constitution of the salts* (*geometry of the rod-like core and nature of the anion*).[12]

The construction of chiral precursors was realized by means of the methodology of chiral alkoxides that we described some years ago.[13] Indeed, we expected this route to be particularly efficient for our purpose since high enantioselectivities as well as versatility were previously demonstrated.[13] Thus, we selected 1,3-dioxans in the pyridine series as target compounds.

Ethylenic substrate **1** was simply obtained by acetalization of pyridine-4-carboxaldehyde (Scheme 1). The stereospecific bromination of **1** yielded exclusively *cis*-**2a**, which was isomerized into its isomer *trans*-**2b** by treatment with hydrobromic acid vapours. Both

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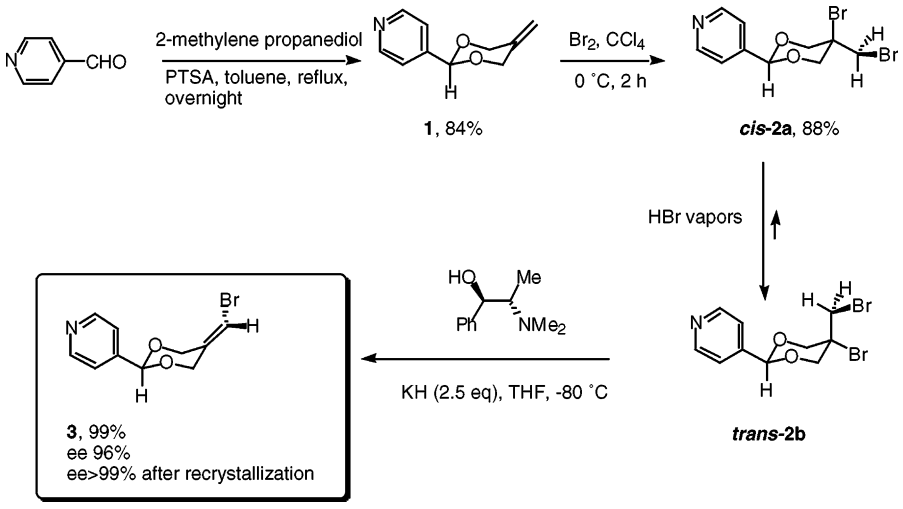


Scheme 1. Synthesis of chiron **3**.

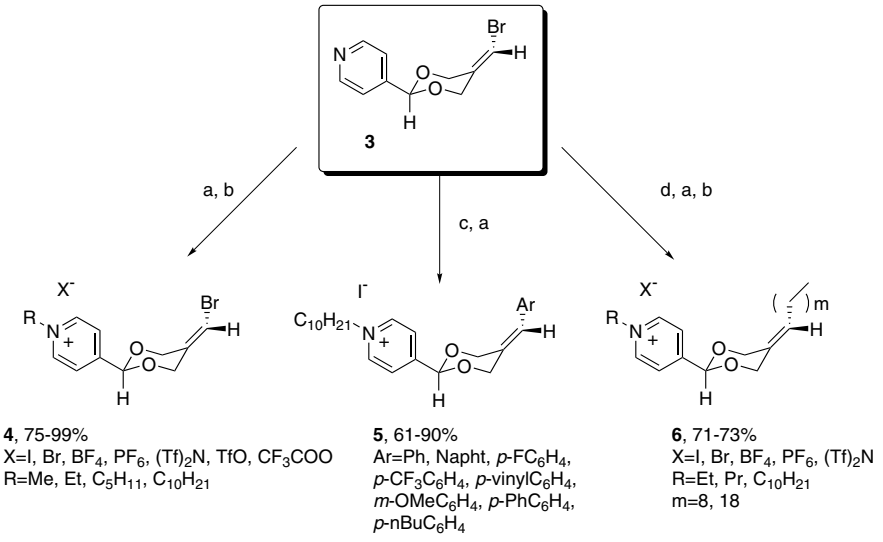
stereoisomers **2a** and **2b** were obtained as pure materials bearing two enantiotopic protons, which can be discriminated by a chiral base.

We then submitted compound *trans*-**2b** to an excess of potassium chiral alkoxide derived from *N*-methylephedrine; the dehydrobromination proceeded to give quantitatively **3** in high enantiomeric purity. Finally, a single recrystallization of **3** provided the optically pure compound, which was transformed into a variety of IL^{2}Cs taking advantage of the pyridinic ring and of the vinylic bromine substituent.

For example, ionic liquids **4** were directly synthesized by alkylation of the pyridine with an alkyl halide, followed or not by anion metathesis. The anionic counter-ion plays a crucial role for the physical properties of ionic liquids (solubility, viscosity, melting point). Reaction of **3** with an alkyl halide during 24–48 h in acetonitrile under reflux gave the corresponding chiral ILs **4** in excellent yields (Scheme 2). We were delighted to observe that the majority of compounds **4** are liquid at room temperature.

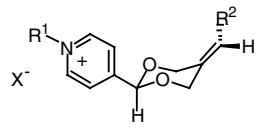
In a second set of experiments, we elaborated IL^{2}Cs **5** and **6**, taking advantage of the vinylic bromine of chiron **3**, which allows simple Suzuki cross-coupling between **3** and various aromatics or aliphatics. Thus, a new series of ionic liquids was prepared by coupling with boronic acid in anhydrous DMF under reflux and subsequent quaternization in CH_3CN to provide compounds **5**. ILs **6** were obtained in about 70% yield (Scheme 2).

Physico-chemical properties of selected examples (either in racemic or enantiomerically pure form) of new IL^{2}Cs were examined. The presence and the nature of anisotropic phases were checked by polarized microscopy and the transition temperatures were obtained with a



Scheme 2. Synthesis of IL^{2}Cs **4**, **5** and **6**. Reagents and conditions: (a) alkyl halide, reflux, CH_3CN, 48 h; (b) anion metathesis; (c) $ArB(OH)_2$, KOH, 5 mol% $Pd(PPh_3)_4$, DMF, reflux, 48 h; (d) alkene, 9-BBN, THF, 0 °C–rt, 2 h then 5 mol% $PdCl_2(dppf)_2$, K_2CO_3, DMF, reflux, 48 h.

Table 1.



	R^1	R^2	X	
4a (*RS*)	$C_{10}H_{21}$	Br	I	G −20 I
4b (*RS*)	$C_{10}H_{21}$	Br	Br	G −23 I
4b (*R*)	$C_{10}H_{21}$	Br	Br	G −23 I
4c (*RS*)	$C_{10}H_{21}$	Br	PF_6	G −17 I
4d (*RS*)	$C_{10}H_{21}$	Br	BF_4	G −30 I
4e (*RS*)	$C_{10}H_{21}$	Br	$(Tf)_2N$	G −40 I
4e (*R*)	$C_{10}H_{21}$	Br	$(Tf)_2N$	G −39 I
5a (*RS*)	$C_{10}H_{21}$	Ph	I	G −1 I
5a (*R*)	$C_{10}H_{21}$	Ph	I	G −6 I
5b (*RS*)	$C_{10}H_{21}$	*p*-MeO–C_6H_4	I	G 17 I
5c (*RS*)	$C_{10}H_{21}$	*p*-BuO–C_6H_4	I	N 47 I
5c (*R*)	$C_{10}H_{21}$	*p*-BuO–C_6H_4	I	N* 39/45 I
5d (*RS*)	$C_{10}H_{21}$	*p*-OctO–C_6H_4	I	G 22 Sm 92 I
6a (*RS*)	C_3H_7	$C_{18}H_{37}$	Br	K 52 Sm 149 I
6b (*RS*)	$C_{10}H_{21}$	$C_{18}H_{37}$	I	Sm 41 N 90 I_{decomp}
6b (*R*)	$C_{10}H_{21}$	$C_{18}H_{37}$	I	Sm_1 50 Sm_2 90 I
6c (*RS*)	$C_{10}H_{21}$	C_8H_{17}	I	Sm 44/55 I
6c (*R*)	$C_{10}H_{21}$	C_8H_{17}	I	N* 35/40 I
6d (*RS*)	$C_{10}H_{21}$	C_8H_{17}	Br	SmC 55 I
6e (*RS*)	$C_{10}H_{21}$	C_8H_{17}	BF_4	G −25 Sm 92 I
6f (*RS*)	$C_{10}H_{21}$	C_8H_{17}	PF_6	G −35 I
6g (*RS*)	$C_{10}H_{21}$	C_8H_{17}	$(Tf)_2N$	G −43 I

(*RS*): racemic; K: crystal, G: glass, N: nematic, N*: chiral nematic (cholesteric), Sm: smectic, SmC: smectic C.

differential scanning calorimeter (DSC, heating rate of 10 °C/min). Table 1 describes representative structures taken respectively from series **4**, **5** and **6**.

Most of these new compounds exhibit the expected properties: low melting or glass transition temperatures, thermal stability up to 150 °C and more, allowing chemistry in a large temperature range. Even more interestingly, compounds **5c**,**d** and **6a**–**e** present liquid crystalline state in a wide range of temperatures. Different phases can be observed depending on the structure of the rod-like cation and the nature of the anion. Some conclusions can be drawn as follows:

Influence of the cation moiety:

(i) Generally, mesophases can be observed only when the central core bears long chains on both sides. The central core of this molecule is rather small and these two chains are necessary to obtain rod-like calamitic molecules.[14]

(ii) The transition temperatures (glass transition, melting point, mesomorphic transitions) are not strongly affected between racemic and single-enantiomer compounds (see **5a**, **5c**, **6b** and **6c**). However, the nature of the mesophase is affected by the enantiomeric purity: cholesteric (N*) phases are observed for pure (*R*) compounds while nematic or smectic phase are observed for the racemic mixtures, which were obtained as in Scheme 1 when using potassium *tert*-butoxide instead of the chiral alkoxide.

Figure 1. Photography of compound (*RS*) **6d** (SmC; 30 °C).

Influence of the anion:

(i) Melting point is lowered when replacing the halogen counter-ion by either hexafluorophosphate or triflimide anion (see compounds **4b**–**e** and **6c**–**g**).

(ii) On the other hand, obtention of liquid crystalline properties is more easily observed with halogen or tetrafluoroborate anions (**6c**–**g**). Such effect of the size (but also probably charge delocalization) was already observed in some other series presenting mesomorphic properties.[14,15] The bigger anions should decrease the packing of the cationic mesomorphic units. For a typical photography in this series, see Figure 1.

In conclusion, we have designed and synthesized the first series of pyridinium IL^2Cs with axial chirality.[16] These novel compounds can readily be prepared via enantioselective dehydrohalogenation by means of chiral bases and are currently examined as chiral solvents for asymmetric synthesis.[17]

Acknowledgements

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16. Access to compound **3** is performed with procedures given in Ref. 13. (*R*) **6c**: to a solution of 9-BBN (0.5 M in THF, 4.68 mL, 2.3 mmol) was added 1-octene (0.34 mL, 2.2 mmol) under argon at 0 °C. After stirring for 20 min at 0 °C, the solution was warmed to rt. After stirring for 3 h, freshly distilled and degassed DMF (10 mL), **3** (2 mmol), 5 mol% $PdCl_2$(dppf) and potassium carbonate (4 mmol) were successively added. The reaction was then refluxed for 48 h. After cooling to rt, water (10 mL) and diethylether (10 mL) were successively added. Standard work-up and drying over magnesium sulfate afforded the crude product, which was purified by flash chromatography (cyclohexane–ethylacetate 7:3) to give the product in 73% yield. (*R*)-2-Pyridyl-5-(octylmethylidene)-1,3-dioxane (1 mmol) was dissolved in freshly distilled acetonitrile (10 mL) under argon and iododecane (5 mmol) was added. The mixture was refluxed for 48 h. After evaporation, the pyridinium salt was washed with diethylether (3×5 mL) and dried under vacuum.
^{1}H NMR (300 MHz, $CDCl_3$): 0.86–0.90 (m, 6H); 1.25–1.28 (m, 26H); 1.79–1.84 (m, 4H); 4.45 (t, 2H, $J = 13.2$ Hz); 4.62 (d, 1H, $J = 12.4$ Hz); 4.90 (d, 1H, $J = 12.4$ Hz); 5.50 (t, 2H, $J = 7.5$ Hz); 5.41 (t, 1H, $J = 7.5$ Hz); 5.88 (s, 1H); 8.17 (d, 2H, $J = 6.6$ Hz); 9.26 (d, 2H, $J = 6.6$ Hz).^{13}C NMR (75 MHz, $CDCl_3$): 14.5; 23.0; 26.3; 27.1; 29.4; 29.5; 29.6; 29.7; 29.8; 29.9; 32.2; 32.3; 62.3; 67.0; 73.0; 97.4; 126.1; 127.7; 128.9; 145.2; 156.3.
$[\alpha]^{25}$ 1 (546 nm, *c* 4, $CHCl_3$).
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