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NMR spectroscopy in studies of new chiral ionic liquids

Summary — Chiral ionic liquids (CILs) were discussed as new potential media for enantioselective organic synthesis, including enantioselective polymer synthesis. NMR spectra of new CILs, whose structures are shown in formulas (I)–(IV), were investigated in detail. In the case of ^1H NMR analysis of those compounds two characteristic doublets were observed — diastereotopic protons (AB spin system). In order to precisely determine the spectral position of each proton and carbon, but also to attribute in a detailed way the type of their signals, two-dimensional spectra were obtained. Additionally, ^1H NMR and ^{13}C NMR spectra indicated notable differences in the chemical shifts depending on the anion used. Comparing the differences between values of the chemical shifts, the anions, but also the quaternary ammonium salts, depending on the amine used, were ordered according to their increasing shielding capacities.

Keywords: quaternary ammonium salt, ionic liquid, chirality, diastereotopic protons, chemical shift.

SPKTROSKOPIA NMR W BADANIACH NOWYCH CHIRALNYCH CIECZY JONOWYCH

Streszczenie — Przedstawione w pracy chiralne ciecze jonowe [CILs, wzory (I)–(IV)] badano by ocenić możliwość ich zastosowania w roli katalizatorów, reagentów oraz rozpuszczalników w syntezie asymetrycznej, jak również w polimeryzacji stereoselektywnej. Omówiono szczegółowo wykorzystanie spektroskopii NMR do badań nowych CILs. Analizując widma NMR czwartorzędowych soli amoniowych z podstawnikiem (1*R*,2*S*,5*R*)-(–)-mentoksymetylowym zwrócono uwagę na charakterystyczne dwa dublety pochodzące od diastereotopowych protonów grupy metylenowej (układ spinowy AB) znajdującej się między czwartorzędowym atomem azotu i tlenem (rys. 1). W celu precyzyjnego określenia położenia każdego protonu i węgla części mentolowej oraz szczegółowego przypisania rodzaju sygnałów wykonano i omówiono widma dwuwymiarowe 2D NMR (rys. 2). Analiza widm ^1H NMR i ^{13}C NMR badanych CILs wykazała przesunięcia sygnałów chemicznych, w stosunku do położenia analogicznych sygnałów grup atomów wodoru (widma ^1H NMR) oraz grup atomów węgla (widma ^{13}C NMR) w chlorkach. Uszeregowano zarówno aniony, jak i syntezowane związki (w zależności od rodzaju aminy będącej częścią strukturalną czwartorzędowej soli amoniowej), pod względem zdolności ekranujących.

Słowa kluczowe: czwartorzędowa sól amoniowa, ciecz jonowa, chiralność, protony diastereotopowe, przesunięcie chemiczne.

Ionic liquids (ILs) are organic salts (built from the organic cation and organic or inorganic anion) that are generally liquid at ambient temperatures or melt below 100 °C [1]. This general definition makes the cation-anion combinations enormous. ILs possess a number of interesting properties, such as their very low vapor pressure (they cannot contribute to air pollution) and their wide liquid region. They have high solvating properties, however they have a non-coordinating nature and a wide accessible temperature range within which the ILs are not flammable. They are also compatible with various organic compounds, organometallic catalysts and even some inorganic compounds and generally can be easily

separated from reaction products. It is very important that the ionic liquids can be recycled. They are receiving considerable global attention because they offer a unique environment for processes in chemistry, biocatalysis, separation science, material synthesis, and electrochemistry.

In recent years, ionic liquids have also been intensively investigated by polymer chemists [2, 3]. The applications of ILs as solvents for polymerization processes, as components of polymeric materials, as templates for porous polymers and as novel electrolytes for electrochemical polymerizations have been reviewed [4–7]. ILs can be used among other possibilities as solvents in poly-

merization processes. For example, 1-ethyl-3-methylimidazolium tetrachloroaluminate ($[\text{EMIM}]^+[\text{AlCl}_4]^-$), 1-*n*-butyl-3-methylimidazolium tetrachloroaluminate ($[\text{BMIM}]^+[\text{AlCl}_4]^-$), 1-*n*-octyl-3-methylpyridinium tetrachloroaluminate $[\text{C}_8\text{-}\beta\text{-mpy}]^+[\text{AlCl}_4]^-$ and tetrachloroaluminate 1-*n*-octyl-4-methylpyridinium $[\text{C}_8\text{-}\gamma\text{-mpy}]^+[\text{AlCl}_4]^-$ ionic liquids were applied in biphasic ethylene polymerization as a medium of titanocene catalyst (Cp_2TiCl_2) [8, 9]. Other IL, *i.e.* *N*-butyl-*N*-methylpyrrolidonium bis(trifluoromethanesulfonyl)amide was used as a solvent with bis(oxalato)boric acid as an initiator in living cationic polymerization of styrene [10].

ILs exceptional popularity has resulted in the emergence of new groups such as: room temperature ionic liquids (RTILs) [11–13], energetic ionic liquids [14–16], task-specificity ionic liquids (TSILs) [17, 18], chiral ionic liquids (CILs) [19–23] *etc.*

CILs have attracted significant attention due to their potential applications in asymmetric synthesis, stereoselective polymerization, gas chromatography and spectroscopy [24].

Because ILs are nonvolatile and, depending on their structure, may be soluble or insoluble in typical organic solvents, they may be easily and quantitatively recovered after the reaction. This has stimulated interest in using CILs as chiral solvents in enantioselective organic chemistry, but also to control the stereochemistry of polymerization processes. Small but clearly detectable effect on polymer tacticity was observed for atom transfer radical polymerization (ATRP) of acrylates in chiral imidazolium IL [25, 26]. Ma *et al.* [27] have used CILs for the free radical polymerization of vinyl monomers. Two chiral ILs were designed for this purpose: the 1-(–)-menthoxy-carbonylmethylene-3-methylimidazolium hexafluorophosphate and the 1-(–)-menthoxycarbonylmethylene-3-hexadecylimidazolium hexafluorophosphate.

These new chiral solvents should play a central role in enantioselective organic chemistry (including enantioselective polymer chemistry) and hopefully expand the scope of chiral solvents. From the structural point of view, chirality in these new solvents can arise either from the anion or the cation, or seldom from both of them.

Previously CILs directly obtained in my laboratory from the natural chiral pool of (1*R*,2*S*,5*R*)-(–)-menthol based ammonium [28], pyridinium [29], alkylimidazolium [30] and alkoxyethylimidazolium [31] ionic liquids were described. They have been characterized by physical properties such as specific rotation, density, viscosity, thermal degradation and glass transition temperature. All of ammonium, pyridinium and imidazolium CILs are colorless liquids, and are nonvolatile, nonflammable, insoluble in hexane and diethyl ether, but are soluble in other organic solvents. They are stable in the air, in contact with water, and in commonly used organic solvents.

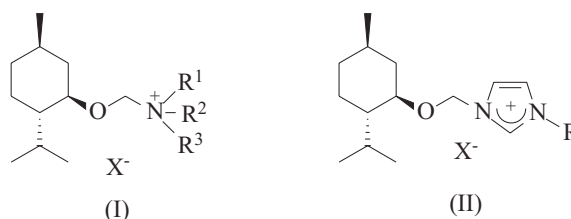
The aim of this study was the investigation of those, mentioned above new chiral ionic liquids using NMR

spectroscopy. ^1H NMR and ^{13}C NMR spectra including two-dimensional spectra were analyzed to discuss possibilities of use of this CILs as a new potential media for enantioselective organic synthesis, including polymer synthesis.

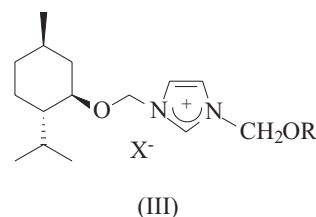
EXPERIMENTAL

Materials

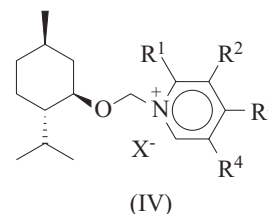
All investigated CILs with a (1*R*,2*S*,5*R*)-(–)-methoxy-methyl substituent, presented by formulas (I)–(IV), were synthesized according to the procedure described



$\text{R}, \text{R}^1 = \text{CH}_3\text{—C}_{12}\text{H}_{25}, \text{R}^2, \text{R}^3 = \text{CH}_3$



$\text{R} = \text{C}_2\text{H}_5\text{—C}_{12}\text{H}_{25}$



$\text{R}^1 = \text{H}, \text{CH}_3, \text{R}^2 = \text{H}, \text{CH}_3, \text{CONH}_2, \text{OH}, \text{N}(\text{CH}_3)_2$
 $\text{R}^3 = \text{H}, \text{CH}_3, \text{C}_2\text{H}_5, \text{tert-Bu}, \text{N}(\text{CH}_3)_2, \text{R}^4 = \text{H}, \text{OH}$

previously [28–31]. In all CILs as anions were used $\text{X}^- = \text{BF}_4^-, \text{ClO}_4^-, \text{I}^-, \text{PF}_6^-, \text{CF}_3\text{COO}^-, \text{Ace}^-, \text{Tf}_2\text{N}^-$.

Methods of testing

^1H NMR spectra were recorded on a Mercury Gemini 300 spectrometer at 300 MHz with tetramethylsilane as the standard. ^{13}C NMR spectra were recorded on the same instrument at 75 MHz. Two-dimensional spectra were performed using standard pulse sequences from the Bruker Drx puls library at 600 MHz. All spectra measurements were carried out in CDCl_3 . Each sample concentration of the quaternary ammonium salt in the solution was always constant and was 20 mg of each compound in $0.600 \text{ cm}^3 \text{ CDCl}_3$.

RESULTS AND DISCUSSION

Diastereotopic protons

In the case of ^1H NMR analysis attention should be paid to characteristic two doublets. Diastereotopic protons of the CH_2 group (AB spin system) which links menthol and amine derivatives appear in the spectrum in the form of two doublets. Diastereotopic protons are the protons that are topologically identical but non-

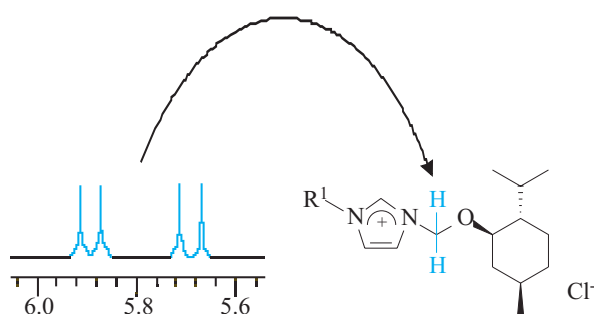


Fig. 1. Location and shape of the signals coming from the diastereotopic protons for 1-[(1R,2S,5R)-(-)-menthoxy-methyl]-3-methylimidazolium chloride

ternate towards symmetry operations of the molecule. Because the molecule has C_1 symmetry, thus protons of the methylene group are diastereotopic and as such have different chemical shifts. The AB system presented in Figure 1 is insulated, so its spectrum is a system of two doublets.

Protons like these are always non-equivalent both chemically and magnetically and in general they absorb at different frequency. The situation like this often takes place in the case of chiral compounds where symmetric center is located not far from diastereotopic protons. The manifestation of the diastereotopic protons was typical for all the studied salts, e.g., for 1-[(1R,2S,5R)-(-)-menthoxy-methyl]-3-methylimidazolium chloride (Fig. 1) δ [ppm] = 5.69 and 5.89 (d, $J = 10.4$ Hz, 2H, AB system).

Two-dimensional spectra

For synthesized compounds a precise determination of spectral position of each proton belonging to substituted cyclohexane is impossible when using ^1H NMR. The reason for it is the same as has been explained above (diastereotopic protons). In order to precisely determine the spectral position of each proton and carbon, but also attribute in a detailed way the type of their signals, two-dimensional spectra were obtained, such as:

- ^1H , ^1H COSY (corelation spectroscopy);
- NOESY (nuclear overhauser effect spectroscopy);
- ^{13}C , ^1H COSY, often called ^{13}C , ^1H HETCOR (heteronuclear correlations).

Figure 2 shows a fragment of ^1H , ^1H COSY spectroscopy of butyldimethyl[(1R,2S,5R)-(-)-menthoxy-methyl]ammonium chloride. As was already accentuated, the position of all hydrogens was precisely determined, including those in cyclohexane.

In this fragment of ^1H , ^1H COSY spectra, it is easy to see two different signals from protons belonging to the carbon number 7 of the cyclic ring. The positions of these two protons, marked with numbers Ha-7 and Hb-7, are different and this is clearly visible in ^1H , ^1H COSY spectroscopy. These protons show two separate, dissimilar signals: δ [ppm] = 0.95 (m, 1H, Ha-7) and 2.18 (d, $J = 11.7$ Hz, 1H, Hb-7). In an analogous way two-dimensional techniques differentiate also two other pairs of protons of the cyclic ring:

– Ha-3 and Hb-3 (belonging to the carbon number 3): δ [ppm] = 0.86 (td, $J^{1,3} = 12.4$ Hz, $J^{1,2} = 3.1$ Hz, 1H, Ha-3) and 1.67 (m, 1H, Hb-3);

– Ha-4 and Hb-4 (belonging to the carbon number 4): δ [ppm] = 0.98 (m, 1H, Ha-4) and 1.65 (m, 1H, Hb-4).

Below is presented a description of complete two-dimensional spectra of quaternary ammonium salt with a (1R,2S,5R)-(-)-menthoxy-methyl substituent: butyldimethyl[(1R,2S,5R)-(-)-menthoxy-methyl]ammonium chloride [28]: ^1H NMR (2D NMR) (CDCl_3 , 25 °C): δ [ppm] = 0.81 (d, $J = 6.9$ Hz, 3H, H9 or H10), 0.86 (td, $J = 12.4$ Hz, $J = 3.1$ Hz, 1H, Ha-3), 0.92 (d, $J = 6.5$ Hz, 3H, H1), 0.93 (d, $J = 6.9$ Hz, 3H, H9 or H10), 0.95 (m, 1H, Ha-7), 0.98 (m, 1H, Ha-4), 0.99 (t, $J = 7.4$ Hz, 3H, H18), 1.32 (m, 1H, H5), 1.42 (m, 1H, H2), 1.42 (m, 2H, H17), 1.65 (m, 1H, Hb-4), 1.67 (m, 1H, Hb-3), 1.68 (m, 2H, H16), 2.07 (sept. d, $J = 6.9$ Hz, $J = 2.4$ Hz, 1H, H8), 2.18 (d, $J = 11.7$ Hz, 1H, Hb-7), 3.36 (s, 3H, H13 or H14), 3.37 (s, 3H, H13 or H14), 3.51 (m, 2H, H15), 3.59 (td, $J = 10.6$ Hz, $J = 4.2$ Hz, 1H, H6), 4.98, 4.94 (d, $J = 6.9$ Hz, 2H, AB system).

Chemical shifts

^1H and ^{13}C NMR spectra indicated notable differences in the chemical shifts depending on the anion used. These chemical shifts are evident for the protons and the carbons localized adjacent to the quaternary nitrogen atom. It is caused mainly by the steric effect of electron clouds and changing of electrostatic interactions between ionic charges. For instance, the ^1H NMR spectra of the alkylimidazolium chlorides and the other alkylimidazolium salts [formula (II)] indicate different chemical shifts for the imidazolium ring protons and methylene protons adjacent to the oxygen atoms. A strong anion effect was evident. The substitution of the $[\text{Cl}]^-$ anion with $[\text{ClO}_4]^-$, $[\text{Ace}]^-$, $[\text{I}]^-$, $[\text{BF}_4]^-$, $[\text{PF}_6]^-$, $[\text{Tf}_2\text{N}]^-$, and $[\text{CF}_3\text{COO}]^-$ resulted in changes in the imidazolium ring electron density. A shift of 2.07 ppm between the $[\text{Cl}]^-$ salt and the $[\text{PF}_6]^-$ salt in the case of the HC12 group, exemplifies the dramatic effect of the change in electron density resulting from changing the anion. Whereas the value of the chemical shift for proton numbered HC9 amounts to 0.46 ppm,

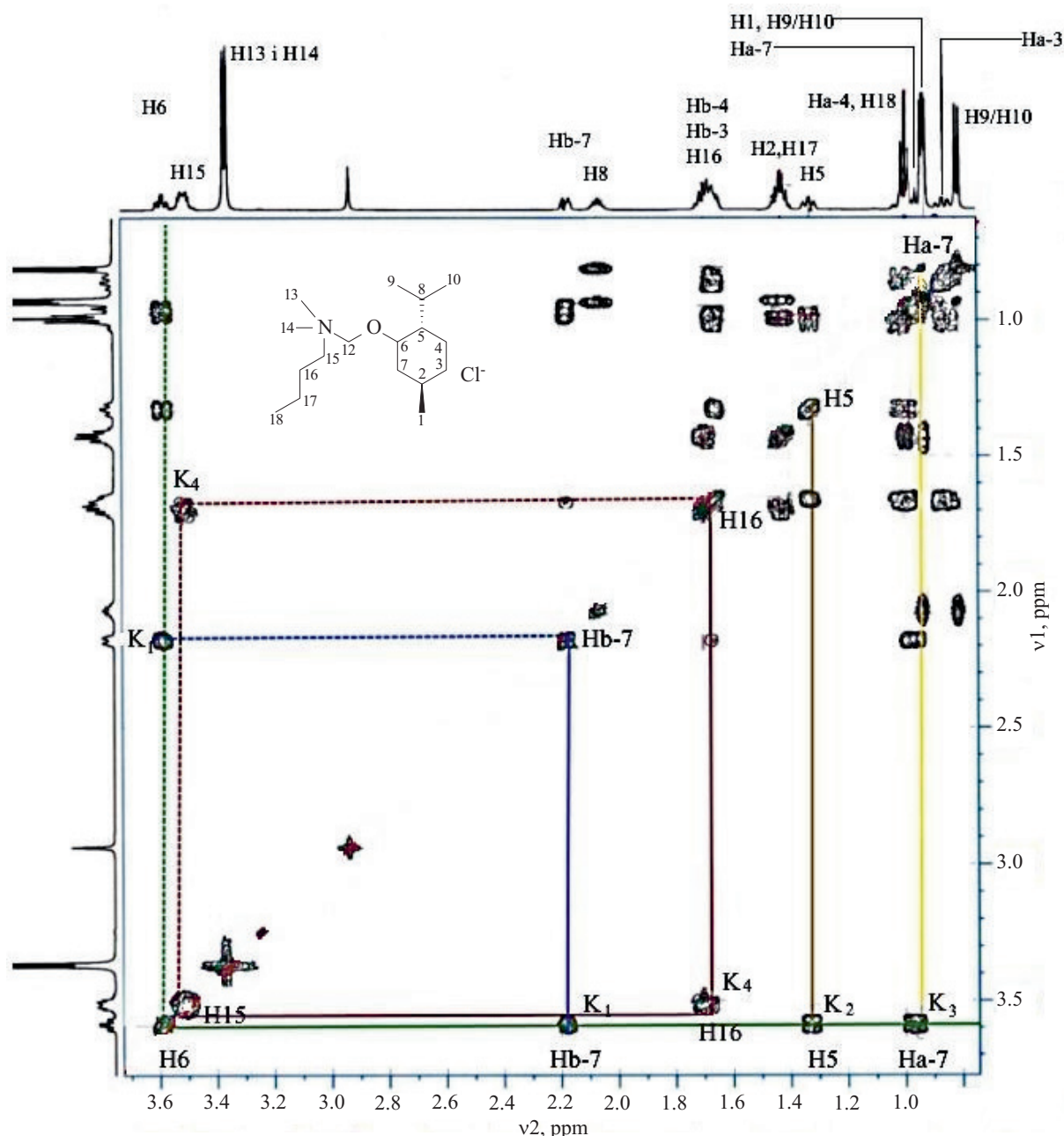


Fig. 2. A fragment of ^1H , ^1H COSY spectrum of butyldimethyl[(1*R*,2*S*,5*R*)-(-)-menthoxyethyl]ammonium chloride

also for hexafluorophosphate. For other protons, adjacent to the oxygen atom: H_3C_{10} , HC_{11} , H_2C_{13} and HC_6 , the chemical proton signal shifts are as much as 0.22 ppm. For an illustration of the chemical shifts depending on the anion used, a part of ^1H NMR of 1-[(1*R*,2*S*,5*R*)-(-)-menthoxyethyl]-3-methylimidazolium salts is presented in Figure 3.

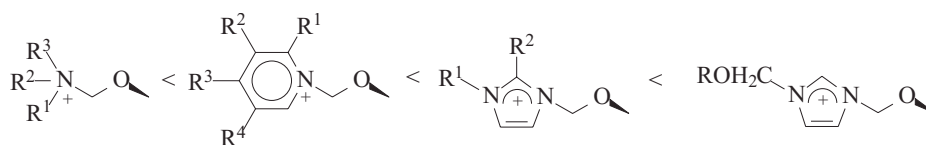
The spectrum shows these chemical shifts evident for the protons located adjacent to the quaternary nitrogen atom. Comparing the differences between the values of the chemical shifts, the anions can be ordered according to their increasing shielding capacities as follows: $[\text{Cl}]^- < [\text{I}]^- < [\text{CF}_3\text{COO}]^- < [\text{Ace}]^- < [\text{ClO}_4]^- < [\text{BF}_4]^- < [\text{Tf}_2\text{N}]^- < [\text{PF}_6]^-$.

The most pronounced shielding abilities were noted for the $[\text{PF}_6]^-$ and $[\text{Tf}_2\text{N}]^-$ anions. These anions' increasing

shielding capacities are identical for other synthesized groups of salts.

As was already mentioned, the ^{13}C NMR spectra indicated also notable differences in the chemical shifts depending on the anion used. These shifts were most evident for carbon C12; the differences between corresponding $[\text{Cl}]^-$ and $[\text{Tf}_2\text{N}]^-$ salts ranged from 1.5 to 3 ppm. The alkyl group substitution in position 3 of the imidazolium ring also affected the shifts, e.g., 1.5 ppm for CH_3 but 3 ppm for C_2H_5 or C_3H_7 .

Comparing the differences between the values of the chemical shifts in NMR for the same anions: $[\text{Cl}]^-$ and $[\text{PF}_6]^-$, the quaternary ammonium salts, depending on the amine used, can be ordered according to their increasing shielding capacities as follows:



As shown above the most increasing shielding capacities appear in quaternary alkoxyethylimidazolium salts. For those chiral salts a chemical proton shift of nearly 3 ppm between the [Cl]⁻ salt and the [PF₆]⁻ salt has been noticed. Similar results have been noticed for 1-alkylimidazolium salts, but there a shift of 2 ppm for the same anions has been observed.

A few examples of differences in the chemical shifts depending on the anion used, in the ¹H NMR spectra, are

already shown in the literature for other ionic liquids: choline ionic liquids [32, 33] and dialkoxyethylimidazolium ionic liquids [34]. These shifts were most evident for imidazolium derivatives (2 ppm). Even though the compounds in the article mentioned above [34] and those presented in this study contain the same substituent in the imidazolium ring: alkoxyethyl, the differences in the chemical shifts are about 1 ppm bigger for menthol derivatives (for carbon number C12). Additionally, the

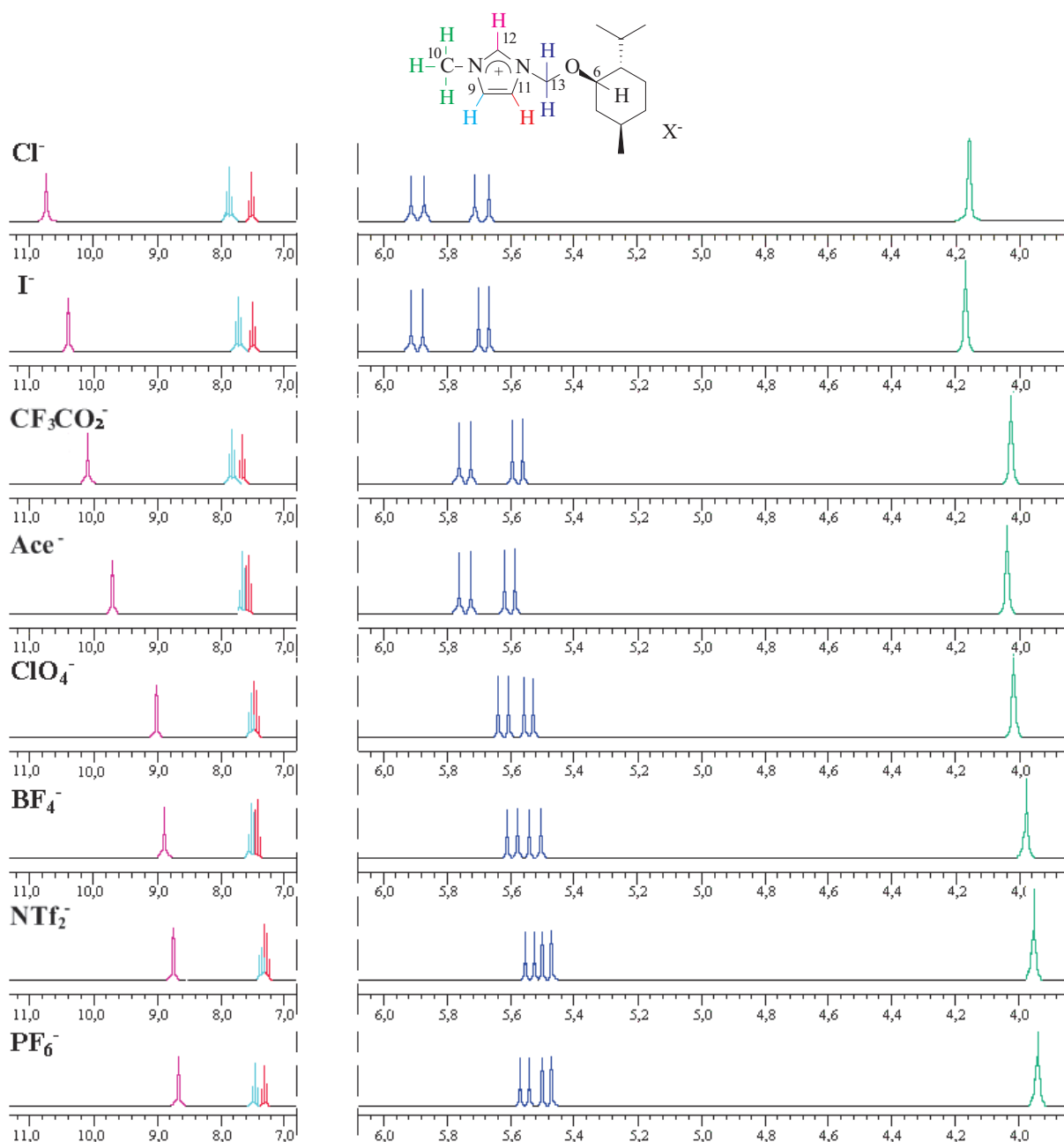


Fig. 3. Differences in the chemical shifts in ¹H NMR spectrum of 1-[(1R,2S,5R)-(-)-menthoxyethyl]-3-methylimidazolium salts

cited works mention that in ^{13}C NMR spectrum no alterations in the carbon signal shifts were seen.

CONCLUSIONS

The chiral ionic liquids discussed here present new potential media for enantioselective organic chemistry, including enantioselective polymer chemistry. NMR spectroscopy (including two-dimensional spectra) of new chiral ionic liquids was discussed in detail. In ^1H NMR characteristic diastereotopic protons of the CH_2 group (AB spin system) which links menthol and amine derivatives are observed for all the presented compounds. ^1H and ^{13}C NMR spectra indicated notable differences in the chemical shifts depending on the anion used. The most pronounced shielding abilities were noted for the $[\text{PF}_6]^-$ and $[\text{Tf}_2\text{N}]^-$ anions. These anions' increasing shielding capacities are identical for other synthesized groups of salts. Also, the quaternary ammonium salts, depending on the amine used, were ordered according to their increasing shielding capacities. The quaternary alkoxyethylimidazolium salts have the most increasing shielding capacities. For those chiral salts a chemical proton shift of nearly 3 ppm between the $[\text{Cl}]^-$ salt and the $[\text{PF}_6]^-$ salt has been noticed.

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