

### A GENUINELY MULTIDISCIPLINARY JOURNAL

# CHEMPLUSCHEM

### CENTERING ON CHEMISTRY

# **Accepted Article**

Title: Herbicidal Ionic Liquids Containing the Acetylcholine Cation

Authors: Daria Czuryszkiewicz, Adam Maćkowiak, Katarzyna Marcinkowska, Andrzej Borkowski, Lukasz Chrzanowski, and Juliusz Pernak

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: ChemPlusChem 10.1002/cplu.201800651

Link to VoR: http://dx.doi.org/10.1002/cplu.201800651



# WILEY-VCH

www.chempluschem.org

# **FULL PAPER**

# Herbicidal Ionic Liquids Containing the Acetylcholine Cation

Daria Czuryszkiewicz,<sup>[a]</sup> Adam Maćkowiak,<sup>[a]</sup> Katarzyna Marcinkowska,<sup>[b]</sup> Andrzej Borkowski,<sup>[c]</sup> Łukasz Chrzanowski,<sup>[a]</sup> and Juliusz Pernak<sup>\*[a]</sup>

Abstract: This study presents a new group of herbicidal ionic liquids (HILs) based on a cation occurs commonly in nature - acetylcholine. The HILs were obtained with a high yield through ion exchange between acetylcholine chloride and potassium or sodium salts of selected acids with herbicidal activity. The results of the herbicidal activity measurement against common oilseed rape (Brassica napus L.) exceeded those of the commercial products. Spray solutions of the synthesized HILs revealed high surface activity and wetting properties which further manifested as higher herbicidal activity. The reduction of surface tension and low contact angles together with the specific action of acetylcholine allowed for better penetration of synthesized HILs into plant tissues. In addition, OECD 301F tests confirmed high mineralization of novel HILs. The simple transformation of commercial herbicides into acetylcholine HILs proved to be a very effective method of increasing their activity, and constitutes an interesting solution to the problem of weed infestation with the use of a substance commonly found in nature.

#### Introduction

The presence of weeds is one of the reasons responsible for the reduction of the yield of harvested crops. Those plants compete for access to light, water and mineral salts with arable crops, thus slowing their growth. Production of weeds seeds ensures their constant presence at the cultivated fields. In addition, they are characterized by very fast adaptation to a given cultivation technique. The weeds collected during harvest can also carry bacterial, viral or fungal diseases, and can thus be harmful to humans and animals.<sup>[1-6]</sup> Therefore application of herbicides is a common necessity with no other alternative. The most widespread substances with herbicidal activity from the group of growth regulators are potassium and sodium salts of: (2,4dichlorophenoxy)acetic acid (2,4-D), 2-(2,4acid (2,4-DP), dichlorophenoxy)propanoic 2-(4-chloro-2methylphenoxy)propanoic acid (MCPP-P), or (4-chloro-2methylphenoxy)acetic acid (MCPA). The aforementioned herbicides exhibit high toxicity, which combined with a long

[a]	MSc. D. Czuryszkiewicz, Eng. A. Maćkowiak,	
	PhD. Ł. Chrzanowski, Full Prof. J. Pernak*	
	Department of Chemical Technology	
	Poznan University of Technology	
	Berdychowo 4, Poznan 60-965, Poland	
	E-mail: juliusz.pernak@put.poznan.pl	
[b]	PhD. K. Marcinkowska	
	Institute of Plant Protection, National Research Institute	
	Węgorka 20, Poznan 60-318, Poland	
[c]	PhD. A. Borkowski	
	Faculty of Geology	
	University of Warsaw	
	Żwirki i Wigury 93, Warsaw 02-089, Poland	
	Supporting information for this orticle is given via a link at the av	~ d

Supporting information for this article is given via a link at the end of the document. persistence in the soil and the possibility of migration into the ground- and the surface-waters, allows them to be classified as substances with potential negative impact on the natural environment.<sup>[1,7-12]</sup> Ionic liquids (ILs) are chemical compounds with a melting point below 100 °C which have unique properties and applications as designable compounds. Thanks to the appropriate choice of the anion-cation pair, it is possible to obtain compounds characterized by the desired physicochemical properties and also biological activity.<sup>[13-18]</sup> At the beginning of the 21<sup>st</sup> century, the idea of herbicidal ionic liquids (HILs) was introduced.<sup>[7]</sup> This concept allows to look at the future of global agriculture with hope. The compounds obtained from the combination of a quaternary ammonium cation with a herbicidal anion may exhibit significantly higher effectiveness against weeds than those currently applied.[19,20] Moreover, ionic liquids are characterized by very low vapour pressure and relatively low flammability, which minimize the risk of fire or explosion.<sup>[21,22]</sup> Introduction of the organic cation of natural origin into the structure of HIL may result in lowering the toxicity of the anion.<sup>[7,23]</sup> Moreover, herbicidal ionic liquids may be applied at lower dose in comparison to the commercial substances.[5,7,11,13,17,24] Naturalderived compounds characterized by common accessibility, renewability and biodegradability are in scope of research by scientists around the world.<sup>[23,25]</sup> Choline-derivative-based ionic liquids are known in the literature.<sup>[26]</sup> Bio and readily biodegradable ILs also have been recognized.<sup>[27,28]</sup> In addition, a review of ILs was published as bioactive chemical tools for use in agriculture and the preservation of agricultural products. ILs were found to solve various problems and challenges, such as presence of weeds, harmful viruses, bacteria, and fungi, but also insects or rodent pests.<sup>[29]</sup> Acetylcholine occurs as a natural compound mainly in the human body, but also in plant tissues, with young leaves considered to be the place of its synthesis.<sup>[30-32]</sup> Acetylcholine (IUPAC name 2-acetyloxyethyl(trimethyl)azanium) is a white solid soluble in water, with a melting point of 148 °C. Acetylcholine may affect the growth and development of plants as well as the germination process. Similar to red light, it stimulates the adhesion of root tips to moist surfaces, and also enhances the ion permeability of the root. Acetylcholine influences leaf movements and stimulates ion absorption through leaf surfaces. Acetylcholine stimulates enzymes and can thus modify the metabolism of plants.<sup>[33,34]</sup> The aim of the study was to prepare new HILs, which could act as effective and environmentally friendly growth regulators with herbicidal activity. To achieve this goal, the acetylcholine cation was combined with popular, cheap and commercially available herbicidal acids. In addition to the synthesis of new HILs, this study also characterizes their physicochemical and biological properties.

### **Results and Discussion**

#### Synthesis

# **FULL PAPER**

Herbicidal ionic liquids (Table 1) were obtained *via* a two-step approach as follows: a neutralization reaction of selected herbicidal acid (Figure 1) in methanol by the potassium hydroxide, and the subsequent reaction of ion exchange of acetylcholine chloride (ACh). The reaction with iodosulfuron methyl was an exception for which the metathesis reaction with acetylcholine chloride was conducted. Commercially available iodosulfuron methyl sodium was used.



Figure 1. Structure of anions with herbicidal activity

The reaction acid-base and ion exchange shown in Figure 2.



A = Dicamba, 2,4-D, 2,4-DP, MCPP-P, MCPA, pelargonate, iodosulfuron methyl

Figure 2. Synthesis of ionic liquids with acetylcholine cation and herbicidal anions

All products were successfully purified with acetonitrile. Both the synthesis and purification processes were efficient, resulting in high yields in the range 88 - 98% (Table 1). Structures of obtained salts were confirmed by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy as well as elemental analysis and provided in the Electronic Supporting Information (ESI, Table S1 and Figure 4 - 17). Additionally, the halide level for all obtained salts determined by AgNO<sub>3</sub> test was below 500 ppm (above this value AgBr or AgCl precipitation is noticeable). As presented in Table 1, the salts **2**, **5** and **7** were solids. However, the values of their melting points (below 100 °C) allow them to be classified as ionic liquids. Compounds **1**, **3**, **4**, **6** were liquids at room temperature and may be classified to the group of room temperature ionic liquids (RTILs). The prepared ILs with acetylcholine cation are new compounds. Ionic liquids with

anions: Dicamba<sup>[13]</sup>, 2,4-D<sup>[5,35,36]</sup>, 2,4-DP<sup>[37]</sup>, MCPP<sup>[38]</sup>, pelargonate (Pel)<sup>[39]</sup> and iodosulfuron methyl (ISM)<sup>[40]</sup> are known in the literature.

Table 1. Obtained ionic liquids with acetylcholine cation						
IL	Short	Yield [%]	State <sup>[a]</sup>	Melting point [°C]		
1	[ACh][Dicamba]	97	Liquid	-		
2	[ACh][2,4-D]	88	Solid	95-97		
3	[ACh][2,4-DP]	98	Liquid	-		
4	[ACh]MCPP-P]	95	Liquid	-		
5	[ACh][MCPA]	99	Solid	90-91		
6	[ACh][Pel]	97	Liquid	-		
7	[ACh][ISM]	96	Solid	74-76		

[a] At 25 °C

#### **Physicochemical properties**

The solubility test was carried out for all obtained ILs (1 - 7) The physicochemical properties such as viscosity, density, refractive index were determined at 25 °C for the obtained RTILs (1, 3, 4). Measurements for **6** were not carried out due to too high viscosity and low clarity. The water content in all product, assayed by Karl-Fischer measurements before the physicochemical analyses, which amounted less than 500 ppm (Table S2 in ESI).

#### Solubility

The solubility of the obtained ILs was tested at 25 °C in common organic solvents selected in increasing order of the value of their Snyder polarity index and shown in Table 2.

Table 2. Solubility of the prepared ILs at 25 $^{\circ}\text{C}$										
IL	Water	Methanol	DMSO	Acetonitrile	Acetone	Isopropanol	Ethyl acetate	Chloroform	Toluene	Hexane
	9.0 <sup>[a]</sup>	6.6	6.5	6.2	5.1	4.3	4.3	4.1	2.3	0.0
ACh	+	+	±	-	-	+	-	+	-	-
1	±	+	+	-	+	+	-	±	-	-
2	-	+	+	-	-	+	-	-	-	-
3	-	+	-	+	+	±	+	+	-	-
4	-	+	±	+	+	±	+	+	-	-
5	+	+	+	±	±	+	-	+	-	-
6	+	+	-	-	-	-	-	-	-	-
7	+	+	+	±	+	-	-	±	-	-

[a] Snyder polarity index; + complete solubility;  $\pm$  limited solubility; - insoluble All the obtained ILs were insoluble in aprotic solvents possessing low polarity such as hexane and toluene. Most ILs are characterized by solubility in chloroform despite low polarity and

### **FULL PAPER**

aprotonicity, which may be associated with its high density. Most of the synthesized ILs were soluble in short-chain alcohols such as methanol and isopropanol. The exception was ILs 6, 7 with sulfonylurea and fatty acid (pelargonic acid) anions. The ion of choline ester has a favorable effect on the solubility of IL 1 in toluene and ethyl acetate as well as IL 2 in acetone compared to starting substrates. The acetyl group also has an influence on the solubility of IL 3. The IL with 2,4-D anion and the choline cation is dissolved in acetone, acetonitrile and water<sup>[36]</sup>, while acetylcholine IL comprising 2,4-D exhibits significantly lower affinity towards these solvents. The hydrophilic acetylcholine cation in the ILs structure causes an increase in the solubility of ILs 5, 6 and 7 in water in comparison to herbicidal acids. IL 6 has the most limited solubility - it dissolves only in the most polar protic solvents: methanol and water. IL 4 is characterized by the widest range of solubility in various diluents - it is insoluble only in water, toluene and hexane. The additional methyl group in ILs 3 and 4 in the substituent attached directly to the aromatic ring increases the solubility of these compounds in ethyl acetate. Solubility of the obtain ILs with acetylcholine cation depended on anions structures, physical and chemical properties of solvents. Methanol was a universal solvent for all of the obtained ILs.

#### Thermal analysis

The thermal stability and phase transition values are presented in Table 3.

 Table 3. Phase transitions and thermal stability of the prepared ILs, ACh and herbicidal acids

Compound	T <sub>g</sub> <sup>[a]</sup> [°C]	T <sub>c</sub> <sup>[b]</sup> [°C]	T <sub>m</sub> [c] [°C]	T <sub>onset 5%</sub> <sup>[d]</sup> [°C]	T <sub>onset 50%</sub> <sup>[e]</sup> [°C]
1	-5	-	-	178	204
2	-3	-	65	189	218
3	-2	-	-	184	216
4	-4	-	-	180	214
5	-11	58	91	183	215
6	-	-	-	188	211
7	26	-	54	177	244
ACh	-	78	132	180	237
Dicamba	-	102	111	201	239
2,4-D	-	128	138	181	229
2,4-DP	-	67	116	166	215
MCPP-P	-		97	159	204
MCPA	-	114	120	170	216
PelH	-	-13; 6	-8; 9	119	161
ISMNa <sup>[f]</sup>	139		-	208	393

Indications: [a] - glass transition temperature, [b] - crystallization temperature, [c] - melting point, [d] - decomposition temperature of 5% of the sample, [e] - decomposition temperature of 50% of the sample, [f] - amorphous state.

The melting point of the synthesized salts (1 - 7) did not exceed 100 °C, thus the obtained compounds may be classified as ionic liquids. The synthesized ILs were characterized by a wide glass transition temperature range, where the minimum occurred for IL 5 and it is -11 °C, and the maximum occurred for IL 7 (26 °C). The

glass transition temperature increased in the following order: MCPA < Dicamba < MCPP-P < 2,4-D < 2,4-DP < ISM. For the IL with pelargonate anion (6) no glass transition temperature, melting point and crystallization were noted. On the basis of the obtained results, it can be concluded that the introduction of the methyl group to the aromatic ring caused a decrease in the glass transition temperatures, which was observed for pairs of ILs 3, 4 and 2, 5. The inverse phenomenon was observed with the introduction of a methyl substituent to the ester group, which resulted in an increase of the glass transition temperatures (ILs 2, 3 and 4, 5). The crystallization temperature was only recorded for IL 5 (58 °C). The results of the thermal analysis carried out for the starting substrates revealed that the fusion of acetylcholine and herbicidal acids resulted in a significant change in their thermal characteristics. The obtained ILs 2, 5 and 7, which exhibited lower melting and crystallization temperatures in the analysed temperature range, underwent the respective phase transition at the lower temperatures compared to the starting materials.

Thermal stability of the obtained ILs revealed that they were stable up to 170 °C. The thermal stability increased in the following order considered of anions: Dicamba < Pel < MCPP-P < MCPA < 2,4-DP < 2,4-D < ISM. This dependence can be explained by the increase of nucleophilicity of the anion with which thermal stability decreases from 189 °C for 2 to 177 °C for 7.[41] The obtained ILs were degraded in a similar temperature range, which may indicate that the acetylcholine cation was preferentially degraded. The decomposition temperatures of individual herbicidal acids are very divergent, e.g. 119 °C for pelargonic acid, 170 °C for MCPA, and 208 °C for lodosulfuron methyl sodium. Comparing starting substrates and final products, it is concluded that the acetylcholine cation introduced into herbicidal acids increased the thermal stability of ILs with the anion derived from phenoxy acids (2 - 5) by 4-12% and the IL with pelargonate anion by 37%. In the case of ILs with anions derived from benzoic acid (1) and sulfonureas (7), it was noted that acetylcholine cation caused a reduction of thermal stability by 13% for 1 and 18% for 7. Due to the high thermal stability, the studied ILs can be used in agricultural formulations without the risk of decomposition of the active substance.

#### Viscosity

The temperature dependence of the viscosity of RTILs 1, 3, 4 in the range from 20 to 90  $^{\circ}$ C is presented in Table S3 and Figure 1 in ESI. The viscosity at 20  $^{\circ}$ C is shown in Table 4.

The decrease of viscosity with temperature increase should be noted. At 20 °C, viscosity values varied from 511.9 Pa·s (**4**) to 415.1 Pa·s (**3**). High viscosity values, above 400 Pa·s, are due to the presence of an additional carboxyl group in the cation that are able to form strong hydrogen bonds.<sup>[42]</sup> Analogues of the curves are the results of similar structures of obtained ILs which are phenoxy acids.<sup>[43]</sup> The ILs **2** and **4** have similar chemical structures, differing from each other by one substituent on the aromatic ring. The introduction of chlorine instead of the methyl group increases the viscosity by 20%. It may be due to the fact that chlorine atoms show stronger ion-ion interactions compared to the methyl group.<sup>[44]</sup> In addition, the presence of a halogen

## **FULL PAPER**

substituent in the aromatic ring may result in the formation of more hydrogen bonds, which also causes a rise in viscosity.<sup>[45]</sup>

The high viscosity of the prepared ILs is advantageous from the point of view of their storage and can be reduced as needed by increasing the temperature without the risk of changing the chemical structures. The exponential nature of the curve was obtained, which describes all RTILs. This characteristic behaviour of ILs has been described repeatedly in the literature.<sup>[46]</sup>

Table 4. Viscosity, density and refractive index selected ILs with acetylcholine cation at 20  $^\circ\text{C}$ 

IL	1	3	4
Viscosity [Pa·s]	430.4	415.1	511.9
Density [g·cm⁻³]	1.31	1.27	1.19
Refractive index	1.5406	1.5318	1.5199

#### Density

Density measurement was carried out for salts 1, 3 and 4 in the range from 20 to 90 °C. The density values at 20 °C are shown in Table 4. The dependence between density and temperature showed a linear character, which is characteristic for ILs. This phenomenon was most likely caused by a large temperature difference between their working temperature range and the critical temperature.[47,48] The density of the tested ILs at 20 °C ranged from 1.31 g·cm<sup>-3</sup> for **4** to 1.94 g·cm<sup>-3</sup> for **1**. At 90 °C the density value was the lowest for ILs 4 (1.14 g·cm<sup>-3</sup>), and highest for 1 (1.26 g·cm<sup>-3</sup>). All the collected values are given in ESI (Table S4). The tested compounds have higher density than water at 20 °C ranged from 30% for 4 to 95 % for 1. The cause of different values of studied ILs might be related with the degree of arranging in the space. IL 1 takes the least amount of space which results in the highest values of density. IL 4 has the lowest density of all compared ILs due to the presence of methyl group attached to aromatic ring which causes problems in proper arrangement in space. The chlorine atom in the anion may cause increased of symmetry of the molecule and the interactions ion-ion, leading to the decrease of the molar volume of the ILs. Obtained results confirmed the observations described in the literature that dicamba-based ILs were characterized by higher density values in comparison to phenoxyacids.<sup>39,45,49</sup> The measured density values decreased linearly with an increase in the temperature (Figure 2 in ESI), and the line describing this relationship was expressed by the equation y = ax + b, were a was equal to -0.0008 approximately and b varied from 1.21  $g \cdot cm^{-3}$  for **4** to 1.33  $g \cdot cm^{-3}$  for **1** (the correlation coefficients (R<sup>2</sup>) for all tested ILs amounted to at least 0.99 - see Table S5 in ESI). Heating the samples to 90 °C resulted in a reduction of density by approximately 0.12 g·cm<sup>-3</sup> for all tested ILs.

#### **Refractive indices**

Refractive indices measurement was carried out for ILs **1**, **3** and **4** in the temperature range from 20 to 90 °C. Figure 3 and Table S6 in ESI present the obtained results. The refractive index at 20 °C is shown in Table 4. The refractive index (RI) values depended on the structure of the cation and the anion comprising HILs.<sup>[50]</sup> The RI of ILs **1**, **3**, **4** at 20 °C ranged from 1.519 for **4** to 1.541 for **1**. The RI of a substance was higher if molecules were

more tightly packed, thus when the compound possessed a higher density.<sup>[51]</sup> Here the dependence between density and refractive indices can be observed.<sup>[52]</sup> Refractive indices presented for ILs **1**, **3**, **4** are correlated with their density. Similar to the density measurement, the temperature increase caused a linear decrease of the refractive indices and depended on the anion (Figure 3 in ESI). Linear regression can be described by the equation y = ax + b - see Table S7 in ESI).

#### Surface activity

By selecting the appropriate cations, some HILs can reduce both surface tension and contact angle.<sup>[36,43,53]</sup> In that case HILs could increase the contact area with the leaf cuticle. Such an ability renders the use additional surfactants, which potentially may cause unnecessary harm to the environment. The surface tension and contact angle tests were carried out for the spray solutions used in during greenhouse experiments – synthesized ILs were dissolved in a mixture of water and ethanol (1:1 v/v). The obtained values are provided in Figure 3 as well as in ESI – Table S8).



Figure 3. Surface tension and contact angle of spray solution of ILs 1 - 7

Surface tension values for all studied ILs were equal to approx. 33 [mN·m<sup>-1</sup>]. This phenomenon was caused by the presence of ethanol, which in small quantities may significantly decrease the surface tension values. Only the values of the tested parameter differ for 6, which is 26.83. Such deviation was caused by the presence of nonanoic anion which reduced the surface tension even more due to its amphiphilic properties. It is worth noticing that commercial products were characterised by higher surface tension (65-72 mN·m<sup>-1</sup>) than obtained ILs. Contact angle values for the synthesized ILs differ insignificantly. The highest value was obtained for 3 and the lowest for 6, because this IL has the lowest surface tension and affinity of the solute for the hydrophobic surface. It was previously established that lower surface tension and contact angle may result in better herbicidal activity.<sup>[37]</sup> Lower values of these properties allow for more efficient wetting of the leaf surface and thus easier absorption of the compound and penetration into the plant.

#### Octanol-water partition coefficient

This parameter is a thermodynamic measure of the tendency of the compound to preferentially distribute between water or non-

### **FULL PAPER**

aqueous phase.<sup>[54]</sup> Examination of this coefficient has particular importance for the environment. It allows to predict whether a given substance tends remain in the soil or if it will be more willing to migrate with water.<sup>[55]</sup> In case of herbicides, it is important to ensure that these compounds stay longer in soil, thus they should have higher affinity for octanol than for water. The values of the octanol-water partition coefficient depend strictly on the concentration<sup>[56]</sup>, therefore for this study the salts doses were equal to the doses used for studying the herbicidal activity. The obtained results were compared with the literature values for herbicidal acids<sup>[37,57-60]</sup>, and presented in Figure 4 and ESI - Table S9.



Figure 4. Values of logarithm of octanol-water partition coefficient of ILs 1-7, free herbicidal acids and iodosulfuron methyl sodium at 25  $^\circ\text{C}$ 

ILs 1, 3, 6 exhibit higher affinity for octanol whereas ILs 2, 4, 5 for the water phase. The highest value of octanol-water partition coefficient was measured for 6 (1.11 ± 0.07) and the lowest value for 5 (-1.38 ± 0.06). Structures of ILs 3 and 4 differ on the basis of the substituent in the aromatic ring, chlorine for 3 and methyl for 4. This results in a significant difference in affinity for the solvents. The presence of methyl group in the aromatic ring increases the affinity for water as represented by ILs 3 and 4. As expected, the long alkyl chain of IL 6 has a higher affinity for octanol. IL 7 has a higher affinity for octanol. ILs liquids 1, 3 and 7 were characterised by the octanol-water partition coefficient in the range 0 - 1. Such values were desirable for herbicide compounds. Values above 3 may cause a hazardous situation - e.g. excessive bioaccumulation, sorption to soil and toxicity toward fish.<sup>[61]</sup> Low values of the partition coefficient may have a harmful impact on the environment, as the herbicide together with pesticides can be easily washed out of plants and soil and can enter the groundwater. The low partition coefficient values may also cause difficulties in the penetration of the herbicide through the leaf membrane, which could make the substance useless.[62-64] Synthesized ILs have lower octanol-water partition coefficient than precursors - herbicidal acids. The exception was compound 7, in case of which the value was higher than iodosulfuron methyl by 1.57. ILs 1, 3, 6 and 7 were characterized by values of about 1, which was the most advantageous due to the ecology and applications of herbicides.

#### Biodegradability

Results of OECD 301 F test revealed high susceptibility of acetylcholine-based ionic liquids for microbial degradation. Previous experiments conducted with betaine and carnitinebased ILs of 2,4-D, MCPA, MCPP and Dicamba confirmed that strategy of incorporation of bio-based cations into the structure of HILs may have a positive effect on overall biodegradation efficiency.<sup>[65]</sup> The minimum positive result should be the reduction of effects associated with usually low biodegradation of synthetic cation. Thus its replacement with a bio-based cation should be beneficial. In the most desired scenario the bio-based cation should enhance the biodegradation rate of the herbicidal anion.<sup>[35]</sup> It should also be noted that the test was carried out with the use of activated sludge microorganisms and that the biodegradability of the studied compounds in agricultural soils may differ.<sup>[24]</sup> Furthermore, fully synthetic ILs may notably decrease the biodiversity of microbial populations on the example of phosphonium-based ILs<sup>[66]</sup> or ammonium-based ILs<sup>[67]</sup>, whereas HILs did not significantly impact the overall biodiversity<sup>[68]</sup> or did not exhibit mutagenic properties.<sup>[69]</sup> Acetylcholine is well known to not penetrate through lipid membranes, however it usually binds with ion channels present in the cell membrane. Such interaction between receptors of ion channel and acetvlcholine is responsible for opening of an ion channel and free ions can easily pass through it. Acetylcholine is actively participating in plants biochemistry therefore higher activity of acetylcholine-based herbicidal ILs might be associated with the biochemical behaviour of well-chosen cation which stimulates the transport of anions, however more research is needed to confirm this hypothesis. Results presented in Table 5.

 Table 5. Biodegradability of synthesized ILs with acetylcholine cation according to the OECD 301 F Test

IL	Biodegradation after 28 days [%]	Time window between 10% and 60% [days]
1	90	5
2	70	14
5	80	13

#### Herbicidal activity

The herbicidal efficacy of all the obtained ILs (1 - 7) has been evaluated with the use of oilseed rape. ILs were compared with their commercial equivalent (Figure 5 and in ESI - Table S10). It should be noted that all studied ILs exhibited high biological activity towards the tested plant, (Brassica napus L.) which was expressed as higher reduction of fresh weed weight compared to commercially available herbicides. Mean values for the reduction differed from 20% for 2 to 47% for 4. Acetylcholine pelargonate (6) had a 25-fold higher herbicidal activity compared to choline pelargonate.<sup>39</sup> The influence of the ester group is therefore significant. IL 1 showed no phytotoxic effects toward to the tested plants, 1 stimulated the growth of common oilseed rape, but to a lesser extent in comparison to the commercial agent by 25%. Acetylcholine cation favourably affected the herbicidal properties of products with the Dicamba anion, because it reduced their effect of pubic growth of weeds. These result indicated that the properly selected cation has a very significant effect on the

## **FULL PAPER**

biological activity of HILs. Ionic liquids with phenoxy-acid anions (2 - 5) showed high herbicidal activity, almost five times higher than commercial products. IL with sulfonureas anion (7) exhibited a high activity at a level of 37%, unlike the reference substance, which did not show phytotoxicity towards the tested plants. An additional advantage of the obtained ILs is the application of smaller doses of substances while maintaining higher herbicidal activity compared to commercial products. The obtain results allowed to classify ILs 1 - 7 as new HILs.



Figure 5. Herbicidal activity against oilseed rape of ILs 1 - 7

#### Conclusion

This study presents the general concept from a design of novel HILs with acetylcholine cation, through their synthesis and determination of physicochemical properties, to the final evaluation of their biological performance. The synthetized biobased HILs were obtained with high yields and easily purified. All of them belong to the group of ILs, four being room temperature ionic liquids (RTILs). The determined physicochemical properties, such as density, viscosity and refractive index, confirmed that the products exhibited characteristics typical for ILs. A linear decrease in density and refractive index in relation to temperature increase was observed, which indicates the absence of volatile impurities. The selected liquids were characterized by a viscosity of approx. 500 Pa·s, (at 20 °C) which is 500 000 times more viscous than water. A dependence was found between the rise of temperature and exponential decrease in viscosity. All synthesized HILs were thermally stable. The decomposition started between 170 - 190 °C, and the distribution of 50% of the content of the tested samples was in the range from 200 to 250 °C. In general, all obtained HILs were soluble in methanol, and in water, DMSO, acetonitrile, acetone, isopropanol, depending on the herbicidal anion. The synthesized HILs were insoluble in nonpolar solvents, specifically in hexane and toluene. The synthesized ILs examined for herbicidal activity against Brassica napus L., showed better efficiency in comparison to commercial preparations. It should be emphasized that the doses of herbicidal ionic liquids in g ha-1 were definitely lower than the doses of commercial preparations, which contain additional synthetic enhancers. In addition, the synthesized HILs contain the acetylcholine cation which is a naturally occurring compound and reduced the toxicity of the substances obtained. With longer use,

the synthesized HILs should be more environmentally friendly, due to the lower content of the herbicidal substance in the soil and therefore less toxicity. Spray solutions of the synthesized HILs revealed very good surface-activation and wetting properties which have significant effect on herbicidal activity. The reduction of surface tension and low values of contact angle allows the obtained HILs to easily penetrate into the plants leaves. The measurement octanol-water partition coefficient indicated that the synthesized HILs had a lower potential for bioaccumulation in the soil. An additional advantage of the synthesized acetylcholinebased HILs is associated with their rapid biodegradation, which confirms their environmental friendliness compared to commercially used herbicides. The presented results show the fundamental influence of the structure of synthesized HILs on biological properties and constitute a new contribution to the development of more environmentally friendly herbicides.

#### **Experimental section**

#### Materials

2-(2,4-Dichlorophenoxy)propanoic acid [2,4-DP] (purity 97%), (2,4-dichlorophenoxy)acetic [2,4-D] (purity 97%), 3,6-dichloro-2acid [Dicamba] (98%). methoxybenzoic 2-(4-chloro-2methylphenoxy) propanoic acid [MCPP-P] (purity 97%), (4-chloro-2-methylphenoxy)acetic acid [MCPA] (purity 97%) and iodosulfuron methyl sodium [ISMNa] (purity 97%) were obtained from CIECH Sarzyna (Nowa Sarzyna, Poland). Potassium hydroxide (purity 99%) and all solvents (methanol, acetonitrile, acetone, hexane, toluene, chloroform, isopropanol, DMSO and ethyl acetate) were purchased from Avantor (Gliwice, Poland). Acetylcholine chloride [ACh] (purity 99%) and pelargonic acid [PelH] (purity 96%) were purchased in Sigma-Aldrich (Poznan, Poland). Deionized water with a conductivity <0.1 µS·cm<sup>-1</sup>, from demineralizer HLP Smart 1000 (Hydrolab, Poland) was used for solubility and surface activity measurement. All reagents and solvents were used without further purification. Following commercial herbicides were used as the references: Dicamba 480 SL (480 g dicamba per 1 L, SL Sharda International Ltd., India), Aminopielik Standard 600SL (600 g 2,4-D per 1 L, Adama Polska, Warsaw, Poland), Chwastox Extra 300 SL (300 g MCPA per 1 L, CIECH Sarzyna, Nowa Sarzyna, Poland), VVH 86086 Devient Beloukha (Pel 3000 g per 1 L, Jade, Mérignac Cedex, France), Huzar 05 WG (ISMNa 7.5 g per 1 L, Bayer, Warsaw, Poland).

#### General

The studies were performed using a Varian XL300 spectrophotometer, at 300 MHz for <sup>1</sup>H NMR and 75 MHz for <sup>13</sup>C NMR. Deuterated methanol was used as the solvent, and tetramethylsilane was the reference. The elemental analyses (CHN) were performed by using Elementar Analyser Vario EL III at the Adam Mickiewicz University, Poznan (Poland). The water content was assayed by Karl-Fisher titration using a TitroLine KF Trace coulometric titrator (SI Analytics). The melting points were determined by using the Büchi Melting Point B-540 apparatus. The viscosity of the ILs was measured with a rheometer (Rheotec RC30-CPS) with cone-shaped geometry (C50–2). Density was

# **FULL PAPER**

determined by an Automatic Density Meter DDM2911 with the mechanical oscillator method. The density of the samples (approx. 2.0 cm<sup>3</sup>) was measured in the range of 20 - 90 °C controlled with a Peltier module. The apparatus was calibrated by using distilled water as the reference. After each series of measurements, the densimeter was washed with organic solvents (methanol and acetone) and dried with airflow. Viscosity was determined by using a rheometer (Rheotec RC30-CPS) with cone-shaped geometry (C50-2). The viscosity of the samples (approx. 1.5 cm<sup>3</sup>) was measured from 20 to 90 °C. The uncertainty of the viscosity measurement was estimated to be less than  $10^{-4}$  Pa·s. Refractive index was determined with an Automatic Refractometer J357 (Rudolph Research Analytical) with electronic temperature control.

#### Synthesis

Herbicidal ionic liquids with the acetylcholine cation were synthesized using a two-step approach. In the first step, the selected herbicidal acids were neutralized by potassium hydroxide in methanol. The solvent was then evaporated using a rotary vacuum evaporator. The obtained potassium salts of the selected acid were dried in a vacuum oven at 40 °C for 48 hours. Next, the previously obtained potassium salt of the selected acid or iodosulfuron methyl sodium was dissolved in methanol and mixed with acetylcholine chloride with 10% of stoichiometric excess. The reagent system was stirred in a water bath at 60 °C for 30 minutes. In the next step, the precipitated inorganic salt was filtered off and the solvent was subsequently evaporated. The obtained product was additionally purified through leaching with a portion of acetonitrile to remove the remaining inorganic impurities. The raw product was dried at 40 °C for 24 hours under reduced pressure. The obtained salts were stored in a vacuum desiccator over a drying agent.

#### Solubility

The solubility test was carried out based on the protocols described in Vogel's Textbook of Practical Organic Chemistry.<sup>[70]</sup> A 0.1 g sample of the substance was weighed into the vial, with an accuracy to the second decimal place, and then introduced into a specific volume of the solvent. All samples were thermostated at 20 °C. Depending on the solubility in the volume of solvent used, three types of behaviours were recorded: "soluble" applies to compounds that dissolved in 1 cm<sup>3</sup> of the solvent, "limited solubility" applies to compounds that dissolved in 3 cm<sup>3</sup> of the solvent, and "not soluble" applies to compounds that did not dissolve in 3 cm<sup>3</sup> of the solvent. The analyses was performed for ten organic solvents with a diverse polarity range, arranged in order of decreasing value of Snyder polarity index: deionized water (9.0), methanol (6.6), dimethyl sulfoxide (6.5), acetonitrile (6.2), acetone (5.1), ethyl acetate (4.3), isopropanol (4.3), chloroform (4.1), toluene (2.3) and hexane (0.0). The pH-value of water was 6.5.

#### Thermal analysis

The studies of thermal stability and temperature of phase transitions were performed using two methods: thermogravimetric analysis (TG) and differential scanning calorimetry (DSC). The

Mettler Toledo TG / DSC1 Star was used to conduct the TG. The analysis consisted of sampling a mass of 2 - 10 mg, which was heated from 40 to 500 °C at a constant rate of 10 °C/min under a nitrogen atmosphere. The Mettler Toledo TG / DSC1 Star was also used for DSC testing. The analysis consisted of sampling a mass of 2 - 10 mg, which was heated at a constant rate of 10 °C/min.

#### Surface activity

Interfacial surface tension was determined with the pendant drop method. The measurement of surface tension and contact angle was carried out for all synthetized compounds using DSA 100E analyser (Krüss, Germany, accuracy  $\pm$  0.01 mN·m<sup>-1</sup>) set at 25 °C (temperature controlled Fisherbrand FBH604 thermostatic bath, Fisher, with an accuracy of 0.1 °C). The test was conducted by preparing solutions of the active ingredients at the same concentration as spray solutions used in the greenhouse experiments. The surface tension ( $\gamma$  in mN·m<sup>-1</sup>) was calculated by analyzing the profile of the drop according to the Laplace equation. The determination of the contact angle was based on the sessile drop method, i.e., a drop of the spray solution is deposited on a hydrophobic surface (paraffin). During the measurement, a photo of the tested droplet was taken.

#### Octanol-water partition coefficient

The octanol-water partition coefficients (Kow) of new ILs were measured by the shake-flask method according to OECD guidelines.<sup>[71]</sup> For this test water saturated with octanol and octanol saturated with water were used. First, an aqueous solution of a particular IL (5 cm<sup>3</sup>) with the same concentration as the spray solution was prepared. Then, 5 cm<sup>3</sup> of octanol saturated with water was added and the system was vigorously stirred at 25 °C for 24 hours. After this time the solution was set aside to clarify the two phases. Then the concentration of active ingredient in the aqueous phase was analysed with UV/Vis spectrophotometer (based on formerly made calibration curves with plots of absorbance (at  $\lambda_{\text{max}}$  = 279 nm for MCPA and MCPP anion, at  $\lambda_{max}$  = 285 nm for 2,4-D anion, at  $\lambda_{max}$  = 283 for 2,4-DP anion, at  $\lambda_{max}$  = 274 nm for Dicamba anion, at  $\lambda_{max}$  = 235 nm for lodosulfuron methyl anion and at  $\lambda_{max}$  = 215 nm for pelargonic acid anion all measurements were done in triplicates.

#### **Biodegradability tests**

The test was performed according to standard OECD guideline for 301F test previously described in detail by Borkowski et al.  $^{[72]}$  and Choudhary et al.  $^{[73]}$ 

#### Herbicidal activity

The herbicidal activity of the synthesized ILs was assessed with the oilseed rape (*Brassica napus* L.). Plants were grown in 0.5 dm<sup>3</sup> plastic plots containing commercial peat-based potting material. Greenhouse conditions were: humidity of 60%, air temperature of 20  $\pm$ 2 °C and a photoperiod of 16/8 day/night hours. Within 10 days after emergence, the plants were thinned to five per pot and watered when necessary. All HILs were dissolved in a mixture of water and ethanol (1:1 v/v) in an amount corresponding to 400 g of the active substance (a.i.) per 1 hectare

# **FULL PAPER**

for ILs with MCPA, MCPP-P, 2,4-D, 2,4-DP anion, 200 g of the active substance (a.i.) per 1 hectare for IL with Dicamba anion, 3000 of the active substance (a.i.) per 1 hectare for IL with pelargonate anion and 7.5 g of the active substance (a.i.) per 1 hectare for IL with iodosulfuron methyl anion. The ILs were applied with a moving sprayer by using TEE Jet 1102, which was moving at a speed of 3.1 m/s over the weeds. The atomizer was located at a distance of 40 cm from the tops of the plants, and the liquid pressure was 0.2 MPa. After treatment, the plants were again placed in greenhouse under the environmental conditions defined previously. After a period of two weeks the plants were cut at a height of 2 mm from the soil and the mass was determined to the second decimal place. On the basis of the obtained results, the reduction of fresh plant mass was calculated in comparison to the mass of control objects.

#### Acknowledgements

This work was supported by the National Science, Poland (Grant 2017/25/B/ST5/01622).

Conflict of interest The authors declare no conflict of interest.

**Keywords:** acetylcholine • biodegradability • herbicides • ionic liquids • plant protection

- [1] N. C. Ellstrand, S. M. Hereida, J. A. Leak-Garcia, J. M. Heraty, J. C. Burger, L. Yao, S. Nohzadeh-Malakshah, C. E. Ridley, *Evol Appl.* 2010, 3, 494-504.
- [2] A. Mkindi, N. Mpumi, Y. Tembo, P. C. Stevenson, P. A. Ndakidemi, K. Mtei, R. Machunda, S. R. Belmain, *Ind. Crops Prod.* 2017 110, 113-122.
- [3] C.C. Vigueira, K.M. Olsen, A. L. Caicedo, *Heredity* 2013, *110*, 303-311.
- [4] R. Kordala-Markiewicz, H. Rodak, B. Markiewicz, F. Walkiewicz, A. Sznajdrowska, K. Materna, K. Marcinkowska, T. Praczyk, J. Pernak, *Tetrahedron* 2014, *70*, 4784-4789.
- [5] T. Praczyk, P. Kardasz, E. Jakubiak, A. Syguda, K. Materna, J. Pernak Weed Sci. 2012, 60, 189-194.
- [6] A. Westendorf, D. Benndorf, T. Pribyl, H. Harms, R. H. Müller, *Eng. Life Sci.* 2006, 6, 552-559.
- [7] J. Pernak, A. Syguda, D. Janiszewska, K. Materna, T. Praczyk, *Tetrahedron* 2011, 67, 4838-4844.
- [8] B. Schulz, K. Segobye, J. Exp Bot. 2016, 67, 3177-3179.
- [9] S. Ozdemir, F. M. Bekler, V. Okumus, A. Dündar, E. Kilinc, *Environ. Prog. Sustain. Energy.* 2012, 31, 544-552.
- [10] M. Kucharski, J. Sadowski, Prog. Plant Prot. 2014, 54, 5-12.
- [11] G. Ding, Y. Liu, B. Wang, D. Punyapitak, M. Guo, Y. Duan, J. Li, Y. Cao, *New J. Chem.* 2014, 38, 5590-5596.
- [12] E. Brillas, P. L. Cabot, R. M. Rodriguez, C. Arias, J. A. Garrido, R. Oliver, Appl. Catal. Environ. 2004, 51, 117-127.
- [13] O. A. Cojocaru, J. L. Shamshina, G. Gurau, A. Syguda, T. Praczyk, J. Pernak, R. D. Rogers, *Green Chem.* 2013, *15*, 2110-2120.
- [14] W. L. Hough, M. Smiglak, H. Rodríguez, R. P. Swatłowski, S. K. Spear, D. T. Daly, J. Pernak, J. E. Grisel, R. D. Carliss, M. D. Soutullo, J. H. Davis Jr., R. D. Rogers, *New J. Chem.* **2007**, *31*, 1429-1436.
- [15] P. Wasserscheid, T. Welton, (Eds.), Ionic Liquids in Synthesis, Wiley-VCH, 2008.
- [16] T. Welton, Biophys Rev. 2018, 10, 691-706.

- [17] R. L. Vekariya, J. Mol Liq. 2017, 227, 44-60.
- [18] C. D. S. Tomlin, *The Pesticide Manual, A World Compendium, 15<sup>th</sup> ed.*, British Crop Protection Council, Alton, Hampshire, **2009**.
- [19] J. Zhu, G. Ding, Y. Liu, B. Wang, W. Zhang, M. Guo, Q. Geng, Y. Cao, *Chem. Eng. J.* **2015**, *279*, 472–477.
- [20] Q. Wu, C. Liu, J. Yang, A. Guan, H. Ma, Pestic. Biochem. Physiol. 2017, 143, 246-251.
- [21] M. J. Earle, J. M. S. S. Esperança, M. A. Gilea, J. N. Canongia Lopes, L. P. N. Rebelo, K. R. Seddon, J. A. Widegren, *Nature* **2006**, *439*, 831–834.
- [22] R. Ludwig, Angew. Chem., Int. Ed. 2001, 40, 1808–1827.
- [23] F. E. Dayan, D. K. Owens, S. B. Watson, R. N. Asolkar, L. G. Boddy, Front. Plant Sci. 2015, 6, 1–11.
- [24] Ł. Ławniczak, K. Materna, G. Framski, A. Szulc, A. Syguda, Biodegradation 2015 26, 327–340.
- [25] J. Hulsbosch, D. E. De Vos, K. Binnemans, R. Ameloot, ACS Sustain. Chem. Eng. 2016, 4, 2917–2931.
- [26] J. Pernak, A. Syguda, I. Mirska, A. Pernak, J. Nawrot, A. Prądzyńska, S. T. Griffin, R. D. Rogers, *Chem. Eur. J.* 2007, *13*, 6817-6827.
- [27] J. Pernak, K. Czerniak, A. Biedziak, K. Marcinkowska, T. Praczyk, K. Erfurt, A. Chrobok, RSC Adv. 2016, 6, 52781-52789.
- [28] J. Pernak, K. Czerniak, M. Niemczak, Ł. Chrzanowski, Ł. Ławniczak, P. Fochtman, K. Macinkowska, T. Praczyk, *New J. Chem.* 2015, 39, 5715-5724.
- [29] A. Zajac, R. Kukawka, A. Pawlowska-Zygarowicz, O. Stolarska, M. Smiglak, Green Chem. 2018, 20, 4764-4789.
- [30] B. T. Green, S. T. Lee, K. D. Welch, D. Cook, *Res. Vet. Sci.* 2017, 115, 195-200.
- [31] R. T. R. Huckstepp, E. Llaudet, A.V. Gourine, PLOS One 2016, 11, 61-78.
- [32] G. R. Han, C. H. Jang, Colloid. Polym. Sci. 2015, 293, 2771-2779.
- [33] C. Wilson, M. D. Lee, J. G. McCarron, J. Phys. Chem. 2016, 594, 7267-7307.
- [34] A. Tretyn, E. R. Kendrick, Bot. Rev. 1991, 57, 33-73.
- [35] J. Niu, Z. Zhang, J. Tang, G. Tang, J. Yang, W. Wang, H. Huo, N. Jiang, J. Li, Y. Cao, *J. Agr. Food Chem.* **2018**, *66*, 10362-10368.
- [36] K. Marcinkowska, T. Praczyk, M. Gawlak, M. Niemczak, J. Pernak, Crop Prot. 2017, 98, 85-93.
- [37] M. Niemczak, A. Biedziak, K. Czerniak, K. Marcinkowska, *Tetrahedron* 2017, 73, 7315-7325.
- [38] J. Pernak, A. Luboiński, A. Łacka, T. Praczyk, New J. Chem. 2018, 42, 17259-17267.
- [39] J. Pernak, K. Czerniak, M. Niemczak, Ł. Ławniczak, D. K. Kaczmarek, A. Borkowski, T. Praczyk, ACS Sustain. Chem. Eng. 2018, 6, 2741-2750.
- [40] J. Pernak, M. Niemczak, J. L. Shamshina, G. Gurau, G. Głowacki, T. Praczyk, K. Marcinkowska, R. D. Rogers, J. Agric. Food Chem. 2015, 13, 3357-3366.
- [41] M. Niemczak, R. Giszter, K. Czerniak, K. Marcinkowska, F. Walkiewicz, *RSC Adv.* 2015, 5, 15487-15493.
- [42] M. Niemczak, T. Rzemieniecki, A. Biedziak, K. Marcinkowska, J. Pernak, *ChemPlusChem* 2018, 83, 529-541.
- [43] M. Niemczak, Ł. Chrzanowski, T. Praczyk, J. Pernak, New J. Chem. 2017, 41, 8066-8077
- [44] P. S. Kulkarni, L. C. Branco, J. G. Crespo, M. C. Nunes, A. Raymundo, C. A. M. Afonso, *Chem. Eur. J.* **2007**, *13*, 8478–8488.
- [45] B. Górska, L. Timperman, M. Anouti, J. Pernak, F. Béguin, *RSC Adv.* 2016, 6, 55144–55158.
- [46] G. Yu, D. Zhao, L. Wen, S. Yang, X. Chen, AIChE J. 2011, 58, 2885-2899.
- [47] J. Jacquemin, P. Husson, A. A. Padua, V. Majer, Green Chem. 2006, 8, 172-180.
- [48] M. Tariq, P. A. S. Forte, M. F. Costa Gomes, J. N. Canongia Lopes, L. P. N. Rebelo, *J. Chem. Thermodyn.* **2009**, *41*, 790-798.
- [49] S. Handy (ed.), Progress and Developments in Ionic Liquids, IntechOpen, 2017.

## **FULL PAPER**

- [50] S. Seki, S. Tsuzuki, K. Hayamizu, Y. Umebayashi, N. Serizawa, K. Takei, H. Miyashiro, *J. Chem. Eng.* 2012, 57, 2211-2216.
- [51] H. F. D. Almeida, J. A. Lopes-da-Silva, M. G. Freire, J. A. P. Coutinho J. Chem. Thermodyn. 2013, 57, 372-379.
- [52] A. P. Fröba, H. Kremer, A. Leipertz, J. Phys. Chem. B 2008, 112, 12420-12430.
- [53] J. Pernak, R. Giszter, A. Biedziak, M. Niemczak, R. Olszewski, K. Marcinkowska, T. Praczyk, J. Agric. Food Chem. 2017, 65, 260-269.
- [54] J. Sangter, Octanol-Water Partition Coefficients: Fundamentals and Physical Chemistry, Wiley Series in Solution Chemistry, 1997.
- [55] M. M. Moller, S. P. Waslk, *Environ. Sci. Technol.* **1985**, *19*, 522-529.
- [56] P. Jain, A. Kumar, Phys. Chem. Chem. Phys. 2016, 18, 1105-1113.
- [57] A. Sabljić, H. Güsten, H. Verhaar, J. Hermens, *Chemosphere* **1996**, *33*, 4489-4514.
- [58] T. Paszko, P. Muszyński, M. Materska, M. Bojanowska, M. Kostecka, I. Jackowska, *Environ. Toxicol. Chem.* 2016, 35, 271-286.
- [59] V. Cesio, L. Pareja, S. Niell, L.G. Asteggiante, B. Böcking, C. Garcia, G. Fernandez, A.R. Fernandez-Alba, H. Heinzen, *Critical Revision and Development Perspectives of Herbicide Residues Analysis in Agro Ecosystems, Herbicides and ENVIRONMENT*, (ed. A. Kortekamp), Intech, **2011**.
- [60] F. Spafiu, A. Mischie, P. Ionita, A. Beteringhe, T. Constantinescu, A.T. Balaban, ARKIVOC 2009, 2009, 174-194.
- [61] L. Ropel, L. S. Belveze, S. N.V. K. Aki, M. A. Stadtherr, J. F. Brennecke, *Green Chem.* 2005, 7, 83-90.
- [62] W.R. Carlile, Pesticide Selectivity, Health and the Environment, first ed., Cambridge University Press, 2006.
- [63] G. Tang, Y. Liu, G. Ding, W. Zhang, Y. Liang, C. Fan, H. Dong, J. Yang, D. Kong, Y. Cao, New J. Chem. 2017, 41, 8650-8655.

- [64] N. Lichiheb, E. Personne, C. Bedos, F. Van den Berg, E. Barriuso, Sci. Total Environ. 2016, 550,1022-1031.
- [65] J. Pernak, M. Niemczak, Ł. Chrzanowski, Ł. Ławniczak, P. Fochtman, K. Marcinkowska, T. Praczyk, *Chem-Eur. J.* 2016, 22, 12012-12021.
- [66] M. Sydow, M. Owsianiak, G. Framski, M. Woźniak-Karczewska, A. Piotrowska-Cyplik, Ł. Ławniczak, A. Szulc, A. Zgoła-Grześkowiak, H. J. Heipieper, Ł. Chrzanowski, *Ecotox. Environ. Safe.* **2018**, *147*, 157-164.
- [67] B. Markiewicz, A. Sznajdrowska, Ł. Chrzanowski, Ł. Ławniczak, A. Zgoła-Grześkowiak, K. Kubiak, J. Nawrot, J. Pernak, *New J. Chem.* 2014, 38, 3146-3153.
- [68] Ł. Ławniczak, A. Syguda, A. Borkowski, P. Cyplik, K. Marcinkowska, Ł. Wolko, T. Praczyk, Ł. Chrzanowski, J. Pernak, *Sci. Total Environ.* 2016, 563-564, 247-255.
- [69] A. Syguda, A. Gielnik, A. Borkowski, M. Woźniak-Karczewska, A. Parus, A. Piechalak, A. Olejnik, R. Marecik, Ł. Ławniczak, Ł. Chrzanowski, New J. Chem. 2018, 42, 9819-9827.
- [70] B. S. Furniss, A. J. Hannaford, P. W. G. Smith, A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5<sup>th</sup> ed. Wiley John & Sons Inc; 1989.
- [71] OECD, Product Properties Test Guidelines OPPTS 830.7550 Partition Coefficient (n-Octanol/Water), Shake Flask Method.
- [72] A. Borkowski, Ł. Ławniczak, T. Cłapa, D. Narozna, M. Selwet, D. Peziak, B. Markiewicz, Ł. Chrzanowski, *Ecotox. Environ. Safe* **2016**, *130*, 54-64.
- [73] H. Choudhary, J. Pernak, J. Shamshina, M. Niemczak, R. Giszter, Ł. Chrzanowski, T. Praczyk, K. Marcinkowska, O. Cojocaru, R. Rogers, ACS Sustain. Chem. Eng. 2017, 5, 6261–6273.

# **FULL PAPER**

# FULL PAPER



Acetylcholine as a component of herbicides. This study presents the synthesis of acetylcholine-based herbicidal ionic liquids and their physicochemical properties, such as: phase transitions, thermal stability, solubility, viscosity, density and refractive index. HILs exhibited superior physicochemical properties and biological activity compared commercial herbicides. Furthermore, synthesized HILs were readily biodegradable and had a low potential for bioaccumulation.

Daria Czuryszkiewicz, Adam Maćkowiak, Katarzyna Marcinkowska, Andrzej Borkowski, Łukasz Chrzanowski, Juliusz Pernak\*

Page No. – Page No.

Herbicidal Ionic Liquids Containing the Acetylcholine Cation