Tetrahedron 67 (2011) 4838–4844

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Ionic liquids with herbicidal anions

Juliusz Pernak [a,*], Anna Syguda [a], Dominika Janiszewska [a], Katarzyna Materna [a], Tadeusz Praczyk [b]

[a] Department of Chemical Technology, Poznan University of Technology, Poznan 60-965, Poland
[b] Institute of Plant Protection—National Research Institute, Poznan 60-318, Poland

ARTICLE INFO

Article history:
Received 14 February 2011
Received in revised form 14 April 2011
Accepted 5 May 2011
Available online 12 May 2011

Keywords:
Ionic liquids
Herbicides
Toxicity
MCPA
Surface activity

ABSTRACT

Ionic liquids with herbicidal anions (named herbicidal ionic liquids—HILs) were synthesized and characterized. The combination of two active chemicals as the [cation][anion] form in a single moiety reduced the number of additional chemicals required per application. HILs ([cation][MCPA]) exhibited higher biological activity than currently used salts of MCPA, and involved pesticides of a multidirectional activity ([plant growth regulator][MCPA]). Acute toxicity of HILs could be controlled by appropriate selection of cation type. These salts had chemical and thermal stability, and showed substantially lower water solubility than starting herbicides, thus reducing soil and groundwater mobility.

1. Introduction

Derivatives of phenoxy acids have been commercialized as synthetic herbicides since the 1940s and they are still commonly used in weed control. The most important are 2,4-dichlorophenoxyacetic acid (2,4-D, first described by Zimmerman and Hitchcock[1]) and 4-chloro-2-methylphenoxyacetic acid (MCPA, herbicidal activity reported by Slade[2]). The available, on-the-market herbicides utilizing 2,4-D or MCPA contain these active substances in several forms, including acids, sodium, and potassium salts, primary, secondary, and tertiary ammonium salts, and esters. Esters are more active in comparison with acids and salts. However, they have the disadvantage of being very volatile.

Members of the phenoxy family of herbicides are presented in Fig. 1. Ammonium forms of MCPA and 2,4-D available on the market are presented in Table 1.[3] Recently, the tertiary ammonium salts derived from herbicidal carboxylic acids and certain trialkylamines or heteroarylamines were described in a patent application by Dow Agrosciences LLC.[4]

The high application potential of ionic liquids (ILs) inspired us to obtain salts containing the phenoxy family of herbicides in the anion. ILs are substances composed exclusively of ions, which form phases that are liquids below 100 °C.[5–10] The generality of this definition requires a specific identification of ILs, generally on the basis of NMR spectroscopy. For example, considering ammonium ILs, the chemical shifts in proton signals were observed for protons localized adjacent to the quaternary nitrogen atom. The substitution of a small anion $[Cl]^-$ for a large one $[NTf_2]^-$ resulted in proton signal shifts of as much as 0.53 ppm.[11]

ILs as compounds with unique properties have found different applications.[12] Their toxicity and ecotoxicity have been studied intensively.[13,14] The literature reports have given rise to the series of ILs generations. The evaluation of these compounds proceeds very quickly from the first generation (ILs with unique tunable physical properties) to the second generation (ILs with targeted chemical properties combined with selected physical properties), to the third generation (ILs with targeted biological properties combined with chosen physical and chemical properties).[15,16]

2. Results and discussion

Ammonium, phosphonium, pyridinium, imidazolium, morpholinium, and piperidinium salts containing herbicidal anions—MCPA, 2,4-D, and MCPP-P, were synthesized by the metathesis reaction in water or in organic solvents with a high yield. Scheme 1 presents the synthesis of ammonium salts with an MCPA anion. Several examples are presented in Table 2. The structures of cations are shown in Scheme 2. All synthesized salts are waxes with a melting point below the boiling point of water. The above-mentioned new salts may, in some cases, be considered as ionic liquids. They are stable in air and in contact with water and popular organic solvents. These ILs can be made anhydrous by heating at 80 °C in vacuo and storing them over P_4O_{10}. The water content was determined to be less than 500 ppm by coulometric Karl–Fischer titration. The purities of synthesized salts were determined by HPLC analysis and ranged from 96.5 to 98.8%.

* Corresponding author. Tel.: +48 61 665 3682; fax: +48 61 665 3649; e-mail address: juliusz.pernak@put.poznan.pl (J. Pernak).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.05.016

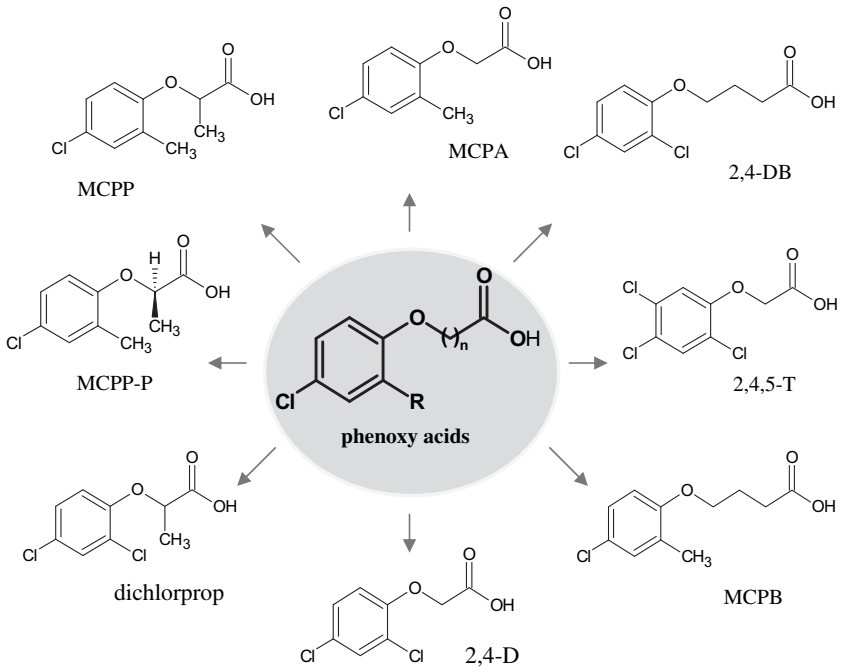
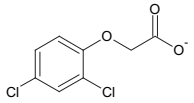
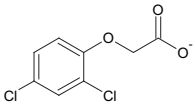
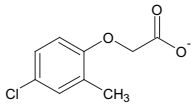
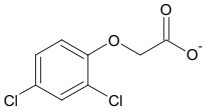
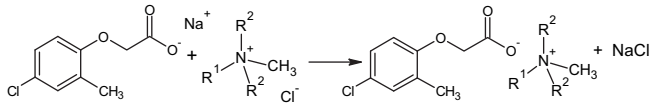


Fig. 1. Structures of phenoxy herbicides.

Table 1
Commercial ammonium salts with 2,4-D and MCPA

Ammonium	Anion (herbicide)	Cation
Primary		$H_3N^+CH(CH_3)_2$
Secondary		$H_2N^+(CH_3)_2$
		$H_2N^+(CH_2CH_2OH)_2$ $H_2N^+(CH_3)_2$
Tertiary		$HN^+[CH(CH_3)_2]_3$ $HN^+(CH_2CH_2OH)_3$ $HN^+[CH_2CH(OH)CH_3]_3$



Scheme 1. Synthesis of ammonium HILs with MCPA anion.

The obtained ILs were thermally stable with decomposition temperatures above 200 °C (Table 2). Selection of the cation determined hydrophobicity or hydrophilicity of the ILs. Limited solubility in water was observed when using large cations with long alkyl substituents. The synthesized salts were soluble in DMSO and alcohols (methanol, ethanol, and propanol). Moreover, **N-1**, **N-2**, and **N-3** were soluble in acetone and chloroform, and **N-4** was soluble in water.

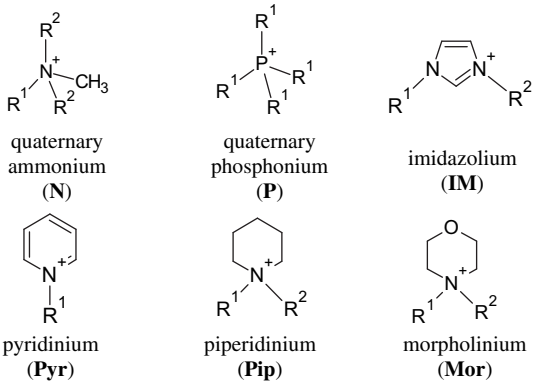
Table 2
The prepared ILs

IL	Cation			Anion	Yield [%]	T_g[a] [°C]	T_m[b] [°C]	$T_{onset5\%}$[c] [°C]	T_{onset} [°C]
	Structure	R^1	R^2						
N-1	N	Tallow[d]	CH_3	MCPA	92	—	80	212	265
N-2	N	CH_3	Tallow[d]	MCPA	99	—	90	210	377
N-3	N	CH_3	$C_{10}H_{21}$	MCPA	95	−51	—	205	285
N-4	N	$ClCH_2CH_2$	CH_3	MCPA	96	−8	—[e]	200	245
P-1	P	C_4H_9	—	2,4-D	88	−44	—	260	288
P-2	P	C_4H_9	—	MCPA	89	—	—	305	325
P-3	P	C_8H_{17}	—	MCPP-P	85	−61	10	307	350
IM-1	IM	CH_3	C_4H_9	MCPP-P	99	−39	6	252	270
Pyr-1	Pyr	$C_{12}H_{25}$	—	2,4-D	77	—	−34	260	285
Pyr-2	Pyr	$C_{12}H_{25}$	—	MCPA	94	−57	−31	200	230
Pyr-3	Pyr	$C_{16}H_{33}$	—	MCPA	96	—	6.5	200	250
Pip-1	Pip	CH_3	C_3H_7	MCPA	86	—	Solid[f]	230	260
Mor-1	Mor	CH_3	C_4H_9	MCPA	87	—	Solid[g]	220	245

[a] T_g—glass transition temperature.
[b] T_m—melting point.
[c] $T_{onset5\%}$—decomposition temperature.
[d] Hydrogenated tallow (alkyl chain distribution $C_{12}H_{25}$—1, $C_{14}H_{29}$—4, $C_{16}H_{33}$—31, $C_{18}H_{37}$—64%).
[e] Crystallized from acetone, monohydrate 95–96 °C.
[f] 39–42 °C.
[g] 77–79 °C.

The synthesized ILs were characterized by ^1H and ^{13}C NMR spectroscopy and elemental analysis. In the ^1H NMR spectra proton chemical shifts were observed for the protons located around the quaternary nitrogen atom. The substitution of the chloride anion for the herbicidal anion caused the chemical shift to increase by 0.5 ppm. The ^{13}C NMR spectra of these ILs indicated no significant variation in the carbon signals.

The synthesized ionic liquids (**N-1**, **N-2**, and **N-3**) were not hygroscopic in contrast to the initial chlorides and showed high viscosity at room temperature. On the other hand, **N-4**, obtained from the starting material of chlormequat chloride, proved to be highly hygroscopic. The chemical structure of **N-4** monohydrate was corroborated by crystallographic analysis and is presented in Fig. 2. **N-4** is stable in aqueous solution. The transition of **N-4** to esterquat was not observed (Scheme 3).



Scheme 2. Structure of cations of the prepared salts.

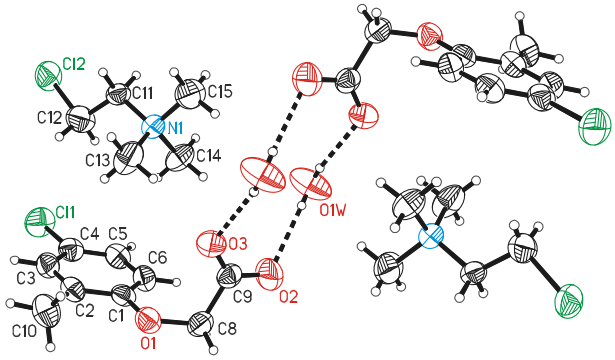
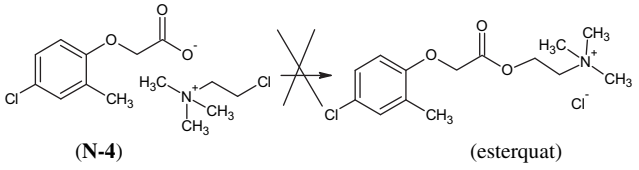


Fig. 2. The crystal structure of a centrosymmetric dimer of 2-chloroethyltrimethylammonium (4-chloro-2-methylphenoxy)acetate—(N-4) monohydrate. The hydrogen bonds have been indicated as the dashed lines.



Scheme 3.

The type of cation was decisive for surface activity of the HILs (Table 3). **N-1**, **N-2**, and **N-3** can be considered as novel surface active compounds effectively decreasing surface tension and having good wetting properties.

Table 3
The CMC, surface tension (γ_{CMC}), surface excess Γ_{max}, area per molecule A_{min}, and contact angle (CA) of aqueous solution of HILs, at 25 °C

HIL	CMC (mmol L^{-1})	γ_{CMC} (mN m^{-1})	$\Gamma_{max}\times10^{6}$ (mol m^{-2})	$A_{min}\times10^{19}$ (m^2)	*CA* (°)
N-1	0.083	34.9	17.12	9.699	67.2
N-2	3.163	28.0	196.6	0.084	40.6
N-3	0.251	26.2	5.143	3.228	33.2
N-4	6.612	40.0	12.85	1.292	87.2

Some synthesized ILs were tested in numerous field experiments conducted from 2007 to 2009 in winter wheat, spring wheat, and spring barley. The biological activity of **N-1**, applied at doses of 400 or 500 g MCPA ha^{-1}, was similar to that of MCPA-salt used at the dose of 900 g ha^{-1} or MCPA-ester at the dose of 600 g ha^{-1}. **N-1** was very effective against oilseed rape volunteers (*Brassica napus*), larkspur (*Consolida regalis*) and field pennycress (*Thlaspi arvense*), but in the case of mayweed (*Matricaria inodora*) **N-1** was more effective (Table 4). In other experiments **N-1** gave excellent control of fat-hen (*Chenopodium album*), shepherd's-purse (*Capsella bursa pastoris*), red deadnettle (*Lamium purpureum*), and creeping thistle (*Cirsium arvense*) in spring wheat and in spring barley. We found a profitable influence of **N-1** on the quantity and quality of winter wheat yield (Table 5). **N-4** showed herbicidal activity as well as plant growth inhibition effect. Efficacy of control of oilseed rape volunteers, field pennycress and field pansy (*Viola arvensis*) was similar to results obtained with a tank mixture of MCPA-salt-+chlormequat chloride used at recommended doses (900 g ha^{-1} and 1450 g ha^{-1}, respectively). In others experiments conducted in 2009, **N-4** was very effective against cornflower (*Centaurea cyanus*), fat-hen, field forget-me-not (*Myosotis arvense*) and spurge (*Euphorbia helioscopia*). **N-4** also caused the shortening of wheat stems, thus increasing crop resistance to lodging.

Table 4
Weed control in winter wheat by different forms of MCPA

Treatments	Dose of MCPA (g ha^{-1})	*Brassica napus* (%)	*Consolida regalis* (%)	*Thlaspi arvense* (%)	*Matricaria indora* (%)
N-1	200	86	54	75	40
N-1	400	100	91	100	75
N-1	500	100	93	100	78
MCPA (salt)	900[a]	100	96	100	56
MCPA(ester)	600[a]	100	95	100	62

[a] The dose recommended in Poland.

Table 5
Influence of different forms of MCPA on the yield of winter wheat

Treatments	Dose of MCPA (g ha^{-1})	Yield (t ha^{-1})	Weight of 1000 grains (g)	Protein (%)	Gluten (%)
Untreated check	0	7.40	37.79	11.12	25.95
N-1	200	8.28	38.24	11.31	27.87
N-1	400	8.23	37.64	11.12	27.48
N-1	500	7.88	38.66	10.87	26.95
MCPA (salt)	900[a]	7.81	39.30	11.08	27.33
MCPA (ester)	600[a]	7.80	39.78	11.03	27.12
LSD (5%)		1.47	2.16	0.90	2.60

[a] The dose recommended in Poland.

The results show that the synthesized salts are active as herbicides. They can be considered as a new group ILs—herbicidal ionic liquids (HILs).

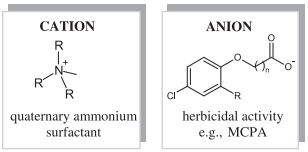
The high surface activity permitted a reduction in the contact angle of the spray solution and allowed for a closer contact between a new form of MCPA and a plant. Hence, the surface properties of the droplet improved wetting, spreading, and retention time and promoted a change in the diffusion coefficient of the HILs and their mobility.

HILs, being ionic compounds, have low volatility. At moderate temperatures, the vapor pressure over a particular compound was so low that it was difficult to establish. Recently it was demonstrated that ILs could be distilled at very low pressures and high temperatures but not all compounds were stable under the very harsh conditions.[15]

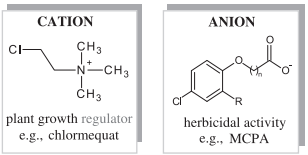
HILs may be considered as an extension to the third generation of ILs (i.e., those containing active pharmaceutical ingredients),[16,17] and are subsequently termed phytopharmaceutical ionic liquids.

A large cation in quaternary ammonium HILs, e.g., didecyldimethylammonium, resulted in liquids that were poorly soluble in water. Activity of the cation can be divided into two distinct subgroups:

- the structure of HILs resulting from the combination of hydrophobic cation with herbicide:



- the structure of a hydrophilic HIL:



The four examined quaternary ammonium HILs, of which **N-1**, **N-2**, and **N-3** represent the first group and **N-4** represents the second group.

In addition, we synthesized esterquat (Scheme 3), which the cation in the crystal structure is presented in Fig. 3. This compound showed herbicidal activity but no plant growth regulating activity.

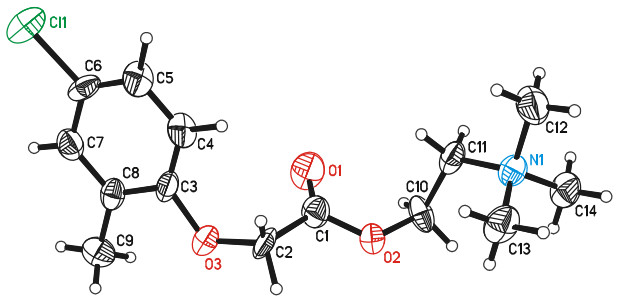


Fig. 3. One of three symmetry-independent cations in the crystal structure of (4-chloro-2-methylphenoxy)-2-acetoxyethyltrimethylammonium.

The type of cation determined the toxicity level (Table 6). The acute oral toxicity data allow the conclusion that **N-2** can be included to the Category 5, and the representative of the second group (**N-4**) to the Category 4, in line with the guidelines of the Globally Harmonized System of Classification and Labeling of Chemicals (GHS). GHS categories were integrated in the GHS Acute Toxicity scheme from which the appropriate elements relevant to transport, consumer, worker, and environment protection can be selected. Substances are assigned to one of the five toxicity categories on the basis of LD_{50} (oral, dermal) or LC_{50} (inhalation). Category 1, the most severe toxicity category, has cut-off values currently used primarily by the transport sector for classification for packing groups. Category 5 is for chemicals, which are of relatively low acute toxicity but which, under certain circumstances, may cause a hazard to susceptible populations.[18] Our results proved that it is possible to design non-toxic HILs by taking advantage of the data on effective and widely used herbicides. It was found that the toxicity of the parent compound MCPA could be reduced via inclusion into a HIL.

Table 6
Acute oral LD_{50} for rats of quaternary ammonium HILs

HIL	Category GHS[a]	LD_{50} (mg kg^{-1})
N-1	4	300–2000
N-2	5	> 2000
N-3	4	300–2000
N-4	4	300–2000

[a] Globally Harmonized System of Classification and Labeling of Chemicals; rat LD_{50} value for MCPA 962-1470, for ester (MCPA 2-ethylhexyl) 1300–1800 and for chlormequat chloride 270 mg kg^{-1}, respectively.[3]

3. Conclusion

We synthesized herbicidal ionic liquids (HILs) with additional pesticidal and surfactant properties. Synthesis of HILs was possible via a simple metathesis reaction that proceeds rapidly in water with an insignificant thermal effect and high efficiency.

The combination of two active chemicals in the form [cation][anion] in a single moiety will reduce the number of additional chemicals, such as adjuvants or surfactants, required per application. HILs as [cation][MCPA] exhibited higher biological activity than currently used MCPA in the form of sodium or potassium salts. HILs as [plant growth regulator][MCPA] involved pesticides with more than one type of activity.

These novel forms of phenoxy acids possess reduced volatility and drift during and after application. No damage is expected to plants neighboring the area in which HILs are used and the associated risk for the operator is restricted. Hydrophobic HILs had substantially lower water solubility than starting herbicides, thus minimizing soil and groundwater mobility.

Moreover, acute toxicity of HILs can be controlled by appropriate selection of cation type. It is possible to obtain forms of MCPA that are less toxic than caffeine, aspirin, and citric acid. Additionally, the risk of adverse effects of HILs on the environment is reduced, because they will not react with the metal ions in the soil. Hence, HILs could be applied at lower rates, have lower inherent toxicity and thus a lower impact on human health and the environment than the parent herbicide.

In summary, our results proved that the old phenoxy herbicides can be transformed, using new tricks, into modern plant protection products—herbicidal ionic liquids.

4. Experimental section

4.1. General

^{1}H NMR spectra were recorded on a Mercury Gemini 300 spectrometer operating at 300 MHz with tetramethylsilane as the internal standard. ^{13}C NMR spectra were obtained with the same instrument at 75 MHz. CHN elemental analyses were performed at A. Mickiewicz University, Poznan (Poland). The water content was determined by using an Aquastar volumetric Karl–Fischer titration with Composite 5 solution as the titrant and anhydrous methanol as solvent.

HPLC analysis—HPLC Merck Hitachi LaChrom, detector DAD with LED matrix, column: symmetry C18, Waters (250×4.6 mm, 5 μm), mobile phase: isocratic elution; 50:50 (acetonitrile: 40 mM phosphate buffer pH=3.55), temperature of column, 40 °C, time of analysis: 15 min, wavelength: 218 nm, injection volume: 10 μL.

4.2. Preparation of ammonium HILs with MCPA anion

In a round-bottom flask equipped with dropping funnel and reflux condenser 0.01 mol of (4-chloro-2-methylphenoxy)acetic acid, 40 mL of distilled water and 0.011 mol of 10% aqueous solution of NaOH was heated at 50 °C until the mixture became a clear solution. Then a stoichiometric amount of quaternary ammonium

chloride was added and the mixture was stirred for 30 min at room temperature. The product deposited as the bottom layer, which was separated. Then it was dissolved in 50 mL of chloroform. The organic phase was washed with distilled water until no chloride was present in water. After removal of chloroform the product was dried under reduced pressure at 60 °C for 24 h.

*4.2.1. Hydrogenated tallowtrimethylammonium (4-chloro-2-methylphenoxy)acetate (**N-1**) (chain distribution $C_{12}H_{25}$—1, $C_{14}H_{29}$—4, $C_{16}H_{33}$—31, $C_{18}H_{37}$—64%).* ^{1}H NMR ($CDCl_3$) δ ppm=0.88 (t, J=6.7 Hz, 3H), 1.26 (m, 28H), 1.59 (q, J=7.3 Hz, 2H), 2.21 (s, 3H), 3.14 (s, 9H), 3.22 (t, J=8.5 Hz, 2H), 4.34 (s, 2H), 6.71 (d, J=8.6 Hz, 1H), 7.02 (dd, $J^{1,2}$=2.5 Hz, $J^{1,3}$=8.8 Hz, 1H), 7.04 (d, J=2.5 Hz, 1H); ^{13}C NMR δ ppm=14.1, 16.4, 22.7, 23.1, 26.3, 29.32, 29.35, 29.52, 29.59, 29.66, 29.72, 31.9, 53.0, 66.6, 68.3, 112.7, 124.2, 126.1, 128.4, 129.9, 155.8, 173.4.

*4.2.2. Di(hydrogenated tallow)dimethylammonium (4-chloro-2-methylphenoxy)acetate—(**N-2**) (chain distribution $C_{12}H_{25}$—1, $C_{14}H_{29}$—4, $C_{16}H_{33}$—31, $C_{18}H_{37}$—64%).* ^{1}H NMR ($CDCl_3$) δ ppm=0.88 (t, J=6.7 Hz, 6H), 1.24 (m, 49H), 1.57 (q, J=6.9 Hz, 4H), 2.23 (s, 3H), 3.21 (s, 6H), 3.28 (t, J=8.5 Hz, 4H), 4.41 (s, 2H), 6.76 (d, J=8.7 Hz, 1H), 6.98 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.6 Hz, 1H), 7.03 (d, J=2.6 Hz, 1H); ^{13}C NMR δ ppm=13.9, 16.3, 22.46, 22.50, 26.1, 29.0, 29.17, 29.20, 29.30, 29.41, 29.47, 29.51, 31.7, 50.6, 63.0, 68.8, 112.7, 123.7, 125.8, 128.2, 129.7, 156.2, 172.6.

*4.2.3. Didecyldimethylammonium (4-chloro-2-methylphenoxy)-acetate—(**N-3**).* 1H NMR (CDCl3) δ ppm=0.88 (t, J=6.7 Hz, 6H), 1.25 (m, 28H), 1.57 (q, J=6.9 Hz, 4H), 2.24 (s, 3H), 3.12 (s, 6H), 3.21 (t, J=8.5 Hz, 4H), 4.41 (s, 2H), 6.75 (d, J=8.8 Hz, 1H), 7.00 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.8 Hz, 1H), 7.04 (d, J=2.6 Hz, 1H); ^{13}C NMR δ ppm=14.0, 16.3, 22.5, 22.52, 26.1, 29.06, 29.12, 29.26, 29.30, 31.7, 51.1, 63.3, 68.4, 112.7, 124.1, 126.0, 128.4, 129.9, 156.1, 173.1. Elemental analysis calcd (%) for $C_{31}H_{56}ClNO_3$ (526.23): C 70.75, H 10.73, N 2.66; found: C 70.54, H 10.52, N 2.98.

*4.2.4. Tetrabutylphosphonium (2,4-dichlorophenoxy)acetate (**P-1**).* ^{1}H NMR ($CDCl_3$) δ ppm=0.95 (t, J=7.0, 12H), 1.46 (m, 16H), 2.28 (m, 8H), 4.50 (s, 2H), 6.93 (d, J=8.8 Hz, 1H), 7.08 (dd, $J^{1,2}$=2.7 Hz, $J^{1,3}$=9.0 Hz, 1H), 7.28 (d, J=2.5 Hz, 1H); ^{13}C NMR δ ppm=13.2 (d, J^{CP}=1.0 Hz), 18.3 (d, J^{CP}=47.2 Hz), 23.4 (d, J^{CP}=9.0 Hz), 23.7 (d, J^{CP}=15.5 Hz), 69.1, 114.8, 122.3, 124.1, 127.1, 129.0, 153.8, 171.3. Elemental analysis calcd (%) for $C_{24}H_{41}O_3PCl_2$ (M=479.52): C 60.11, H 8.64; found: C 60.31, H 8.43.

*4.2.5. Tetrabutylphosphonium (4-chloro-2-methylphenoxy)acetate (**P-2**).* ^{1}H NMR (CDCl3) δ ppm=0.95 (t, J=5.8 Hz, 12H), 1.46 (m, 16H), 2.25 (s, 3H), 2.28 (m, 8H), 4.44 (s, 2H), 6.78 (d, J=8.5 Hz, 1H), 7.03 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.6 Hz, 1H), 7.04 (d, J=2.6 Hz, 1H); ^{13}C NMR δ ppm=13.1 (d, J^{CP}=1.0 Hz), 16.1, 18.5 (d, J^{CP}=47.5 Hz), 23.4 (d, J^{CP}=4.8 Hz), 23.7, (d, J^{CP}=15.2), 68.5, 112.7, 123.6, 125.6, 128.2, 129.5, 156.1, 172.3. Elemental analysis calcd (%) for $C_{25}H_{44}O_3PCl$ (M=459.11): C 65.40, H 9.68; found: C 65.21, H 9.75.

*4.2.6. Tetraoctylphosphonium (+)–(R)-2-(4-chloro-2-methylphenoxy)-propionate—(**P-3**).* ^{1}H NMR ($CDCl_3$) δ ppm=0.88 (t, J=6.6 Hz, 12H), 1.27 (m, 40H), 1.42 (q, J=5.6 Hz, 8H), 1.60 (d, J=6.9 Hz, 3H), 2.20 (t, J=2.7 Hz, 8H), 2.24 (s, 3H), 4.42 (q, J=6.7 Hz, 1H), 6.83 (d, J=8.8 Hz, 1H), 6.97 (dd, $J^{1,2}$=2.7 Hz, $J^{1,3}$=8.7 Hz, 1H), 7.02 (d, J=2.7 Hz, 1H); ^{13}C NMR δ ppm=13.8, 16.3, 18.3, 18.9, 19.4, 21.6 (d, J^{CP}=4.8 Hz), 22.3, 28.7, 30.6 (d, J^{CP}=14.5), 31.4, 76.5, 113.3, 123.3, 125.7, 128.1, 129.5, 156.0, 176.3. Elemental analysis calcd (%) for $C_{42}H_{78}ClO_3P$ (M=697.62) C 72.32, H 11.27; found: C 72.48, H 11.07.

*4.2.7. 3-Butyl-1-methylimidazolium (+)-(R)-2-(4-chloro-2-methylphenoxy)propionate—(**IM-1**).* ^{1}H NMR (DMSO-d_6) δ ppm=0.88 (t, J=7.3 Hz, 3H), 1.24 (sex, J=7.4 Hz, 2H), 1.41 (d, J=6.8 Hz, 3H), 1.72 (q, J=5.5 Hz, 2H), 2.12 (s, 3H), 3.84 (s, 3H), 4.15 (t, J=7.1 Hz, 2H), 4.24 (q, J=6.7 Hz, 1H), 6.73 (d, J=8.8 Hz, 1H), 7.02 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.8 Hz, 1H), 7.10 (d, J=2.7 Hz, 1H), 7.77 (d, J=1.7 Hz, 1H), 7.84 (d, J=1.3 Hz, 1H), 9.65 (s, 1H); ^{13}C NMR δ ppm=13.3, 16.0, 18.8, 19.3, 31.5, 35.6, 48.4, 76.0, 113.4, 122.2, 122.3, 123.6, 125.8, 127.8, 129.3, 137.2, 156.0, 173.9. Elemental analysis calcd (%) for $C_{18}H_{25}ClN_2O_3$ (M=352.90) C 61.27, H 7.14, N 7.94; found: C 61.56, H 6.89, N 8.32.

*4.2.8. 1-Dodecylpyridinium (2,4-dichlorophenoxy)acetate (**Pyr-1**).* ^{1}H NMR ($CDCl_3$) δ ppm=0.87 (t, J=6.7 Hz, 3H), 1.21 (m, 18H), 1.86 (q, J=7.7 Hz, 2H), 4.46 (s, 2H), 4.67 (t, J=7.4 Hz, 2H), 6.87 (d, J=8.8 Hz, 1H), 7.08 (dd, $J^{1,2}$=2.7 Hz, $J^{1,3}$=8.7 Hz, 1H), 7.24 (d, J=2.5 Hz, 1H), 8.00 (t, J=7.1 Hz, 2H), 8.39 (t, J=7.8 Hz, 1H), 9.09 (t, J=5.5 Hz, 2H); ^{13}C NMR δ ppm=14.1, 22.6, 26.1, 29.1, 29.3, 29.4, 29.51, 29.56, 31.6, 31.8, 61.9, 68.6, 114.5, 122.5, 124.8, 127.4, 128.1, 129.3, 144.7, 144.8, 153.2, 172.1. Elemental analysis calcd (%) for $C_{25}H_{35}O_3NCl_2$ (M=468.51): C 64.09, H 7.54, N 2.99; found: C 63.98, H 7.82, N 3.11.

*4.2.9. 1-Dodecylpyridinium (4-chloro-2-methylphenoxy)acetate (**Pyr-2**).* ^{1}H NMR ($CDCl_3$) δ ppm=0.87 (t, J=6.7 Hz, 3H), 1.24 (m, 18H), 1.92 (q, J=7.4 Hz, 2H), 2.19 (s, 3H), 4.44 (s, 2H), 4.76 (t, J=7.4 Hz, 2H), 6.77 (d, J=8.8 Hz, 1H), 6.99 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.8 Hz, 1H), 7.01 (d, J=2.6 Hz, 1H), 7.98 (t, J=7.1 Hz, 2H), 8.34 (t, J=7.7 Hz, 1H), 9.35 (d, J=5.8 Hz, 2H); ^{13}C NMR δ ppm=14.1, 16.4, 22.6, 26.1, 29.0, 29.24, 29.31, 29.44, 29.51, 31.8, 61.8, 68.7, 112.7, 123.9, 125.9, 128.0, 128.2, 129.7, 144.4, 145.1, 156.0, 173.2. Elemental analysis calcd (%) for $C_{26}H_{38}ClNO_3$ (M=448.04): C 69.70, H 8.55, N 3.13; found C 69.95, H 8.82, N 2.98.

*4.2.10. 1-Hexadecylpyridinium (4-chloro-2-methylphenoxy)acetate (**Pyr-3**).* ^{1}H NMR ($CDCl_3$) δ ppm=0.88 (t, J=6.7 Hz, 3H), 1.25 (m, 26H), 1.88 (q, J=6.6 Hz, 2H), 2.20 (s, 3H), 4.43 (s, 2H), 4.72 (t, J=7.4 Hz, 2H), 6.76 (d, J=8.5 Hz, 1H), 7.00 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.6 Hz, 1H), 7.01 (d, J=2.6, 1H), 7.97 (t, J=7.1 Hz, 2H), 8.33 (t, J=7.8 Hz, 1H), 9.26 (d, J=5.5 Hz, 2H); ^{13}C NMR δ ppm=14.1, 16.4, 22.7, 26.1, 29.03, 29.29, 29.34, 29.48, 29.55, 29.59, 29.63, 31.8, 31.9, 61.9, 68.7, 112.7, 123.9, 125.9, 128.0, 128.2, 129.8, 144.4, 145.0, 156.0, 173.2. Elemental analysis calcd (%) for $C_{30}H_{46}ClNO_3$ (M=504.14): C 71.47, H 9.20, N 2.78; found C 71.05, H 8.98, N 2.48.

*4.2.11. 1-Methy-1-propylpiperydinium (4-chloro-2-methylphenoxy)-acetate (**Pip-1**).* ^{1}H NMR (DMSO-d_6) δ ppm=0.90 (t, J=7.3 Hz, 3H), 1.51 (sex, J=5.8 Hz, 2H), 1.63 (q, J=4.9 Hz, 2H), 1.70 (q, J=5.0 Hz, 4H), 1.74 (t, J=3.9 Hz, 4H), 2.16 (s, 3H), 2.99 (s, 3H), 3.29 (t, J=6.0 Hz, 2H), 4.20 (s, 2H), 6.72 (d, J=8.6 Hz, 1H), 7.08 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.6 Hz, 1H), 7.13 (d, J=2.6 Hz, 1H); ^{13}C NMR δ ppm=10.7, 14.7, 16.1, 19.3, 20.8, 47.1, 59.9, 63.7, 68.2, 113.1, 122.7, 126.0, 128.0, 129.5, 156.2, 171.3. Elemental analysis calcd (%) for $C_{18}H_{28}ClNO_3$ (M=341.92): C 63.23, H 8.27, N 4.10; found C 63.62, H 8.01, N 4.32.

*4.2.12. 4-Butyl-4-methylmorpholinium (4-chloro-2-methylphenoxy)-acetate (**Mor-1**).* ^{1}H NMR (DMSO-d_6) δ ppm=0.94 (t, J=7.3 Hz, 3H), 1.32 (sex, J=7.3 Hz, 2H), 1.65 (q, J=4.1 Hz, 2H), 2.16 (s, 3H), 3.14 (s, 3H), 3.42 (t, J=4.4 Hz, 2H), 3.48 (t, J=7.6 Hz, 4H), 3.91 (t, J=4.5 Hz, 4H), 4.21 (s, 2H), 6.72 (d, J=8.8 Hz, 1H), 7.08 (dd, $J^{1,2}$=2.8 Hz, $J^{1,3}$=8.8 Hz, 1H), 7.14 (d, J=2.8 Hz, 1H); ^{13}C NMR δ ppm=13.6, 16.1, 19.3, 22.8, 46.0, 58.9, 59.8, 63.5, 68.2, 112.9, 122.6, 125.8, 127.8, 129.3, 155.9, 171.1. Elemental analysis calcd (%) for $C_{18}H_{28}ClNO_4$ (M=357.92): C 60.40, H 7.90, N 3.91; found C 60.12, H 8.05, N 4.01.

*4.2.13. (2-Chloroethyl)trimethylammonium (4-chloro-2-methylphenoxy)acetate (**N-4**).* Preparation: 0.01 mol of (4-chloro-2-methylphenoxy)acetic acid, 30 mL of distilled water and 0.01 mol of NaOH were placed in round-bottom flask. The

mixture was heated at 50 °C until the solution became clear. Then a stoichiometric amount of chlormequat chloride dissolved in 20 mL of distilled water was added. The mixture was stirred for 24 h. Water was evaporated and product was treated with 30 mL of anhydrous acetone, the precipitate was filtered off and acetone was removed on rotary evaporator. The obtained product, (2-chloroethyl)trimethylammonium (4-chloro-2-methylphenoxy)acetate—(**N-4**), was dried at 60 °C under reduced pressure and crystallized from acetone.

^{1}H NMR (DMSO-d_6) δ ppm=2.13 (s, 3H), 3.20 (s, 9H), 3.83 (t, J=6.9 Hz, 2H), 4.11 (t, J=6.9 Hz, 2H), 4.17 (s, 2H), 6.69 (d, J=8.6 Hz, 1H), 7.07 (dd, $J^{1,2}$=2.4 Hz, $J^{1,3}$=8.6 Hz, 1H), 7.12 (d, J=2.0 Hz, 1H); ^{13}C NMR δ ppm=16.1, 36.5, 52.6, 64.8, 68.2, 113.0, 122.7, 125.9, 127.9, 129.5, 156.1, 170.9. Elemental analysis calcd (%) for $C_{14}H_{21}Cl_2NO_3$ (322.23): C 52.18, H 6.57, N 4.35; found: C 52.37, H 6.80, N 4.45.

4.2.14. (4-Chloro-2-methylphenoxy)-2-acetoxyethyltrimethylammonium iodide—(esterquat). Preparation: 0.9 mol of thionyl chloride was carefully added dropwise to 0.33 mol of (4-chloro-2-methylphenoxy)acetic acid, and mixed in a round-bottomed flask, equipped with a magnetic stirring bar, a reflux condenser, and an addition funnel. Following the addition thionyl chloride, the mixture was heated at 80 °C for 60 min. Then excess of thionyl chloride was removed by distillation in atmospheric pressure, and product was distilled under reduced pressure (boiling point 165–167 °C at 19 hPa). Yield of (4-chloro-2-methylphenoxy)acethyl chloride preparation was 90%.

Deanol (0.28 mol) in 150 mL chloroform was stirred with a stoichiometric amount of (4-chloro-2-methylphenoxy)acethyl chloride. A reacting vessel was cooled with ice, and after 10 min the precipitate was filtered, washed with chloroform and dried. Yield of (4-chloro-2-ethylphenoxy)-2-acetoxyethyldimethylammonium hydrochloride preparation was 98% (melting point 152–154 °C).

The solution of triethylamine (0.035 mol) in chloroform (100 mL) was slowly added to a stirred suspension with a stoichiometric amount of (4-chloro-2-ethylphenoxy)-2-acetoxyethyldimethylammonium hydrochloride in chloroform (250 mL). The mixture was stirred until became clear. After that chloroform was evaporated under reduced pressure, and 100 mL of hexane was added. Triethylamine hydrochloride (produced) was filtered off and washed by hexane. The filtrate was placed in a separator funnel and washed with 50 mL distilled water, and hexane from organic phase was removed by evaporated. The obtained product was liquid, yield of (2-dimethylamino)ethyl-[(4-chloro-2-methylphenoxy)]acetate preparation was 82%.

Methyl iodide (0.03 mol) was added into a round-bottomed flask, which contained a vigorously stirred mixture of 30 mL hexane and 0.028 mol of (2-dimethylamino)ethyl-[(4-chloro-2-methylphenoxy)]acetate. The reaction mixture was stirred at room temperature for 60 min, after that 10 mL of ethyl acetate was added. The precipitate was filtered, washed with hexane and dried at 50 °C under reduced pressure and crystallized from acetone. Yield of (4-chloro-2-methylphenoxy)-2-acetoxyethyltrimethylammonium iodide preparation was 63% (melting point 120 °C).

^{1}H NMR (DMSO-d_6) δ ppm=2.20 (s, 3H), 3.16 (s, 9H), 3.75 (t, J=4.5 Hz, 2H), 4.58 (t, J=4.5 Hz, 2H), 4.90 (s, 2H), 6.96 (d, J=8.8 Hz, 1H), 7.20 (dd, $J^{1,2}$=2.6 Hz, $J^{1,3}$=8.6 Hz, 1H), 7.26 (d, J=2.6 Hz, 1H); ^{13}C NMR δ ppm=15.7, 52.9, 58.5, 63.5, 65.0, 113.2, 124.5, 126.3, 128.4, 130.0, 154.4, 168.1. Elemental analysis calcd (%) for $C_{14}H_{21}O_3NClI$ (413.67): C 40.64, H 5.13, N 3.39; found: C 40.18, H 5.36, N 3.15.

4.3. Thermal analysis

Differential scanning calorimetry (DSC) was performed on a Mettler Toledo Stare TGA/DSC1 unit (Leicester, UK) under nitrogen. Samples between 5 and 15 mg were placed in aluminum pans and were heated from 25 to 110 °C at a heating rate of 10 °C min^{-1} and cooled at a cooling rate of 10 °C min^{-1} to −100 °C.

Thermogravimetrical analysis was performed on a Mettler Toledo Stare TGA/DSC1 unit (Leicester, UK) under nitrogen. Samples between 2 and 10 mg were placed in alumina pans and were heated from 30 °C to 500 °C with a heating rate of 10 °C min^{-1}.

4.4. Crystal structure

The crystals of 2-chloroethyltrimethylammonium (4-chloro-2-methylphenoxy)acetate (**N-4**) monohydrate and (4-chloro-2-methylphenoxy)-2-acetoxyethyltrimethylammonium iodide were grown. The sample for the single-crystal X-ray analysis was a chip cut off a bigger crystal. The reflection intensities were measured on a four-circle KUMA KM4-CCD diffractometer and the structure was solved by direct methods[19] and refined by full-matrix least squares. The H-atoms were located from the molecular geometry and their isotropic thermal parameters were calculated as 1.5 and 1.2 times of the U_{eq} of their methyl, and ethylene and arene carriers, respectively, except for the water H-atoms for which the coordinates and U_{iso} were refined. The full list of details has been deposited with the Cambridge Crystallographic Database Centre as a supplementary publication No. CCDC 755950 and 768723 for 2-chloroethyltrimethylammonium (4-chloro-2-methylphenoxy)acetate (**N-4**) monohydrate and (4-chloro-2-methylphenoxy)-2-acetoxyethyltrimethylammonium iodide, respectively—copies can be obtained on request from the Cambridge Crystallographic Database Centre.

4.5. Surface activity

Surface tension measurements were carried out by the use of a DSA 100 analyzer (Krüss, Germany, accuracy ±0.01 mN m^{-1}), at 25 °C. The surface tension was determined using the shape drop method. Basically, the principle of this method is to form an axisymmetric drop at the tip of a needle of a syringe. The image of the drop (3 μL) is taken from a CCD camera and digitized. The surface tension (γ in mN m^{-1}) is calculated by analyzing the profile of the drop according to the Laplace equation. Temperature was controlled using a Fisher brand FBH604 thermostatic bath (Fisher, Germany, accuracy ±0.1 °C). The values of the critical micelle concentration (CMC) and the surface tension at the CMC (γ_{CMC}) were determined from the intersection of the two straight lines drawn in low and high concentration regions in surface tension curves (γ-log C curves) using a linear regression analysis method.

4.6. Acute oral toxicity study

Wistar rats (symbol lmp: WIST, stado outbred) used in these studies originated from a culture in the Medical Institute of Work in Lodz/Poland and were kept in cages of the conventional type. Before the study, the animals were quarantined for a minimum 5 days and observed daily during this period. The animals were marked individually. During quarantine and the experiments, the animals were kept in a conditioned room of the following parameters: temperature 21–22 °C, relative air humidity 40–75%, and artificial illumination 12 h light/12 h darkness. Rats were kept in cages with plastic bottom and wired superstructure, with the dimensions of 58×37×21 cm (length×width×height). The animals were kept in cages individually (in the observation study—the rats received a dosage of 2000 or 300 mg kg^{-1} b.w.) or 4 rats per cage (in the main study—the dose of 300 mg kg^{-1} b.w.). UV-sterilized wooden shavings were used as litter. Each cage was equipped with a label containing information on name of test material, study code, used dose, start date, and planned ending date of the experiment, sex, and animal numbers. The rats were given standard granulated GLM fodder and tap water *ad libitum*.

The day before the start of the experiment, about 18–19 h before administration of the test material, the animals were left with no food, but water was still available. The food was given again 3 h following administration of the material.

In the preliminary experiment, one female was given the tested material in the form of a water solution, at the dose of 2000 mg kg^{-1} b.w. and, then, to another one female at the dose of 300 mg kg^{-1} b.w. The material was administered as a single dose using a metal intragastric catheter. The total of 0.5 mL solution was given per 100 g rat b.w.

In the main experiment following the preliminary study, the materials were administered to five female rats (including the one from the preliminary experiment) at the dose of 300 mg kg^{-1} b.w. The preparation for administration, administration procedure, and the administered volume corresponded to those used in the preliminary experiment.

4.7. Herbicidal activity

HILs were tested in field experiments performed in 2007–2009 at Experimental Station in Winna Gora and Trzebnica (Poland) in winter and spring wheat and in spring barley.

Cereals were cultivated according to agricultural practice. Plot size was 16.5 m^2. The experimental design was a randomized block with four replications. HILs and standard products were applied at the end of tillering stage of crop. All treatments were applied using a small plot spraying equipment with XR 11,003 flat-fan nozzle with a water volume of 270 L ha^{-1} and an operating pressure of 0.3 MPa. The standard products were herbicides containing MCPA as sodium salt (Chwastox Extra 300 SL—300 g MCPA per 1 l) and as 2-ethylhexyl ester (Chwastox AS 600 SL—600 g MCPA per 1 l). Both products are marketed in Poland by Organika-Sarzyna.

Weed control was evaluated visually 4 weeks after herbicide applications, comparing the weeding with separate weed species on each plot treated with the herbicide with the weeding on relevant untreated plot. The efficacy of herbicides has been presented in percent, where 100% indicates complete destruction, 0%—lack of herbicide efficacy. Moreover the following measurements were performed: yield of grains, weight of 1000 grains, weight of 1 hL, content of protein and gluten, and length of wheat stems (in experiments with **N-4** only).

Acknowledgements

This work was supported by the Foundation for Polish Science, academic grants for professors, MISTRZ Programme, 2009 edition.

References and notes

1. Zimmerman, P. W.; Hitchcock, A. E. *Contrib. Boyce Thompson Inst.* **1942**, *12*, 321–343.
2. Slade, R. E.; Templeman, W. G.; Sexton, W. A. *Nature (London)* **1945**, *155*, 497–498.
3. Tomlin, C. D. S. *The Pesticide Manual, a World Compendium*; British Crop Protection Council: Alton Hampshire, 2006.
4. WO 2008/106118, 2008.
5. Rogers, R. D.; Seddon, K. R. *Science* **2003**, *302*, 792–793.
6. Rogers, R. D.; Seddon, K. R. *Ionic Liquids as Green Solvents: Progress and Prospects, ACS Symposium Series 856*; American Chemical Society: Washington D.C, 2003.
7. Stark, A.; Seddon, K. R. In *Kirk-othmer Encyclopaedia of Chemical Technology*; Seidel, A., Ed.; John Wiley & Sons,: New Jersey, 2007; 26, pp 836–920.
8. Chowdhury, S.; Mohan, R. S.; Scott, J. L. *Tetrahedron* **2007**, *63*, 2363–2389.
9. Wasserscheid, P.; Welton, T. *Ionic Liquids in Synthesis*; Wiley-VCH: Weinheim, 2008.
10. Olivier-Bourbigou, H.; Magna, L.; Morvan, D. *Appl. Catal., A* **2010**, *373*, 1–56.
11. Pernak, J.; Syguda, A.; Mirska, I.; Pernak, A.; Nawrot, J.; Prądzyńska, A.; Griffin, S. T.; Rogers, R. D. *Chem.—Eur. J.* **2007**, *13*, 6817–6827.
12. Plechkova, N. V.; Seddon, K. R. *Chem. Soc. Rev.* **2008**, *37*, 123–150.
13. Pham, T. P. T.; Cho, C. W.; Yun, Y. S. *Water Res.* **2010**, *44*, 352–372.
14. Petkovic, M.; Seddon, K. R.; Paulo, L.; Rebelo, N.; Pereira, C. S. *Chem. Soc. Rev.* **2011**, Advance Article doi:10.1039/C004968A.
15. Earle, M. J.; Esperanca, J. M. S. S.; Gilea, M. A.; Lopes, J. N. C.; Rebelo, L. P. N.; Magee, J. W.; Seddon, K. R.; Widegren, J. A. *Nature* **2006**, *439*, 831–834.
16. Hough, W. L.; Smiglak, M.; Rodriguez, H.; Swatloski, R. P.; Spear, S. K.; Daly, D. T.; Pernak, J.; Grisel, J. E.; Carliss, R. D.; Soutullo, D. M.; Davis, J. H.; Rogers, R. D. *New J. Chem.* **2007**, *31*, 1429–1436.
17. Hough, W. L.; Rogers, R. D. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 2262–2269.
18. United Nations (UN) *Globally Harmonized System of Classification and Labelling of Chemicals (GHS) Revision 1* New York and Geneva, to be found under; United Nations, 2005; http://www.unece.org/trans/danger/publi/ghs/ghs_rev01/01files_e.html.
19. Sheldrick, G. M. *Program for Crystal Structure Determination and Refinement from Diffractometer Data, SHELXL-93*; University of Göttingen: Göttingen, 1993.