Iodosulfuron-methyl-based herbicidal ionic liquids comprising alkyl betainate cation as an example of incorporation of adjuvant into chemical structure of herbicide to reduce environmental impact

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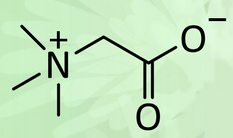
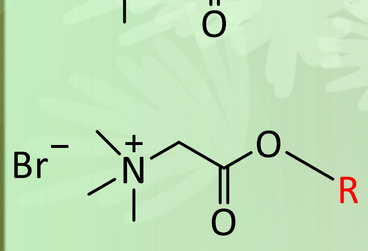
Ionic liquids (ILs) are compounds, which consist exclusively of ions and occur in liquid state at 100°C. Their properties can be easily adjusted by the modification of cation's and anion's structure, for example, the length of alkyl chain, exhibit a siginificant impact on the biological activity of such compounds. ILs are used in various industries including pharmacy, agrochemistry, but the most popular application refers to their utilization as catalysts and solvents. This group of organic compounds is characterised by high thermal stability, low combustibility and very low vapour pressure. The following properties allow to classify ILs as compounds safe in use, which is consistent with trend of sustainable development as well as principles of *green chemistry*.

Herbicidal ionic liquids (HILs) belong to the 3rd generation of ILs, which possess herbicidal activity. Herbicide in that form turns out to be more active and more susceptible to biodegradation compared to the parent active ingredient. Moreover, its easier to optimize surface activity of their spray solutions, which directly affect mobility in groundwater or soil and improve biological activity.

Iodosulfuron methyl (ISM) is a plant protection product that is widely applied to control monocotyledonous and dicotyledonous weeds, like rapeseed or white mustard in cereal cultivation. It was described for the first time in 1999, and one year later introduced to the market as active ingredient. ISM is characterised by numerous advantages such as: low application rate (approx. 10-20 g per ha), low toxicity (LD_{50}, rat, oral = 2678 mg/kg) and good availability, which makes it an interesting source of anion for the synthesis of ILs.

Firstly, (2-alkyloxy-2-oxoethyl)trimethylammonium (alkyl betainate) bromides were synthesized *via* the O-alkylation reaction of glycine betaine (in a zwitterionic form) and an appropriate linear 1-bromoalkane in acetonitrile at 82 °C. After evaporation of the solvent, the crude product was washed three times with 15 cm^3 of ethyl acetate to eliminate unreacted 1-bromoalkane and dried under vacuum (5-10 mbar) at 50 °C for 24 h. Next, the appropriate alkyl betainate bromide (0.1 mol) was dissolved in 15 cm^3 methanol. Next, a 2% molar excess of the sodium salt of iodosulfuron-methyl, dissolved in 15 cm^3 of methanol, was added to perform the ion exchange reaction. The reaction mixture was stirred at 50 °C for 15 minutes and then cooled to 0 °C. Subsequently, the precipitated inorganic salt was filtered off and the solvent was evaporated from the filtrate. The obtained products were additionally purified through leaching with a small portion (10-15 cm^3) of acetone (1-12) or a mixture of acetone:acetonitrile 1:1 (v:v) (13) to remove the traces of inorganic impurities as well as the excess reactant. Finally, the obtained products were dried at 40 °C for 24 h under reduced pressure.

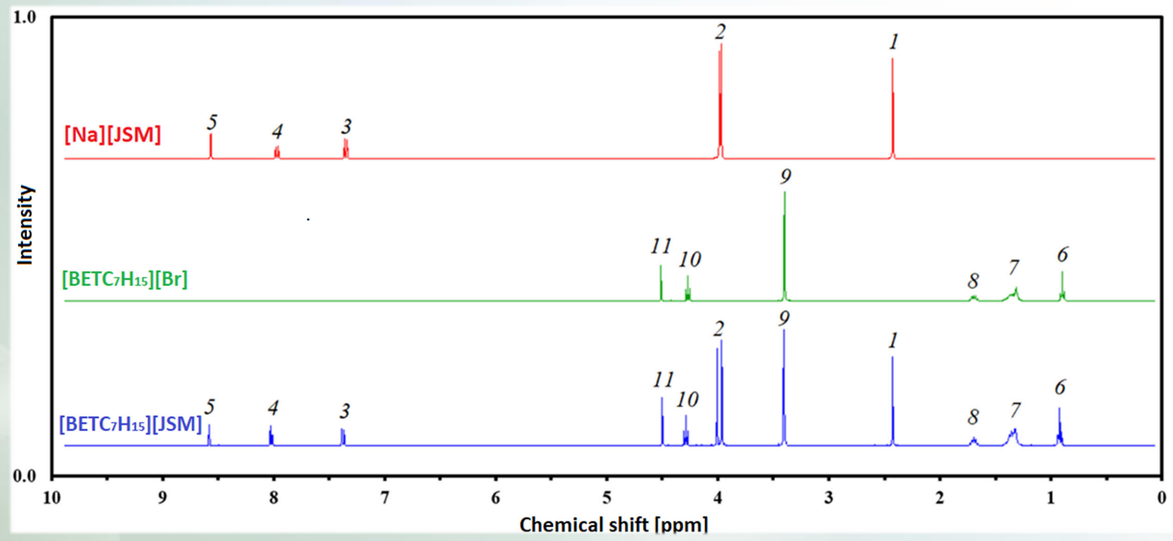




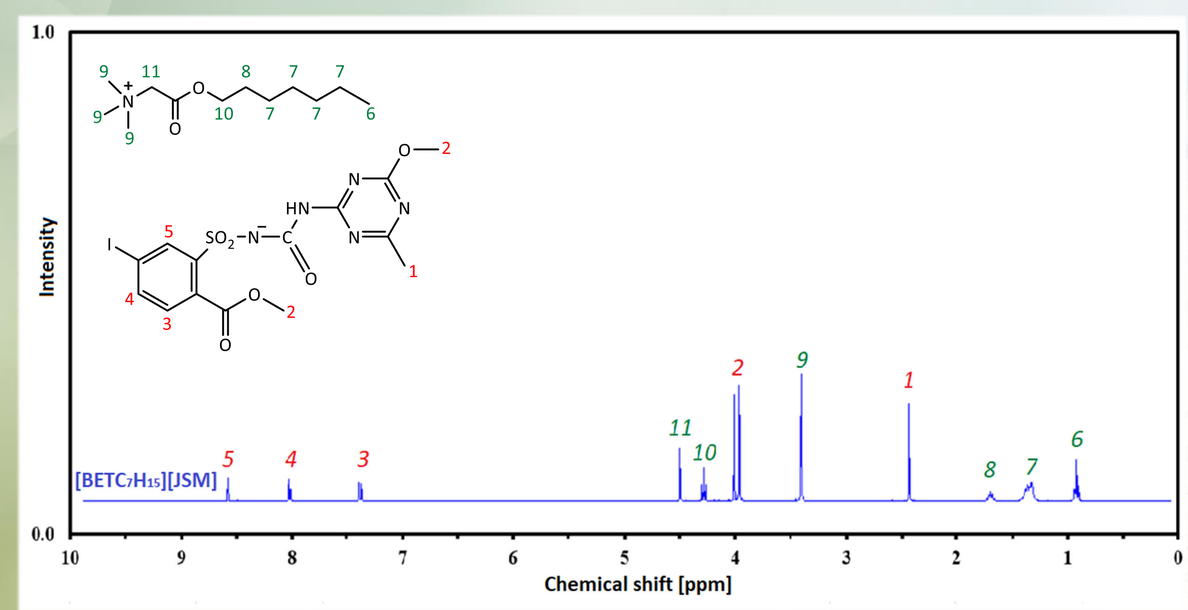
Salt	R	Yield (%)	Melting point (°C)	IL	Yield (%)	Melting point (°C)
P1	C_2H_5	87	154-156	1	92	91-93
P2	C_3H_7	92	106-108	2	98	51-52
P3	C_4H_9	95	99-101	3	95	66-68
P4	C_5H_{11}	92	129-131	4	97	72-74
P5	C_6H_{13}	89	110-112	5	98	54-56
P6	C_7H_{15}	93	103-105	6	96	52-54
P7	C_8H_{17}	94	93-95	7	97	71-73
P8	C_9H_{19}	90	92-94	8	98	76-78
P9	$C_{10}H_{21}$	92	103-105	9	98	74-76
P10	$C_{12}H_{25}$	95	99-101	10	94	80-81
P11	$C_{14}H_{29}$	90	110-112	11	99	81-83
P12	$C_{16}H_{33}$	91	102-104	12	96	83-84
P13	$C_{18}H_{37}$	88	115-117	13	97	98-99

Structures of all compounds were confirmed by IR, ^1H and ^{13}C NMR spectroscopy. There is no residual peaks from organic impurities on the attached NMR spectrum, which proves high purity of synthesized compounds.

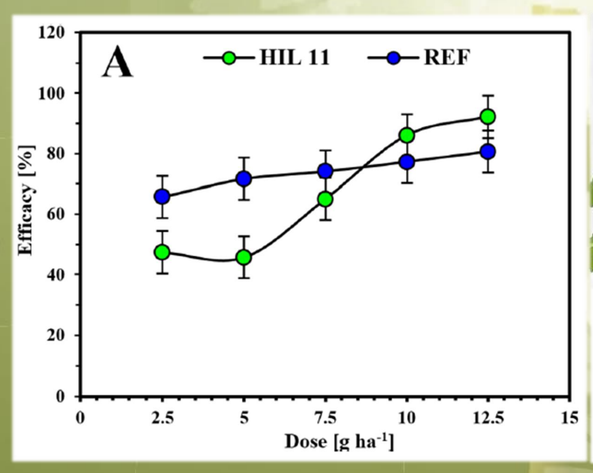
Comparison of ^1H NMR spectrum of precursors and product

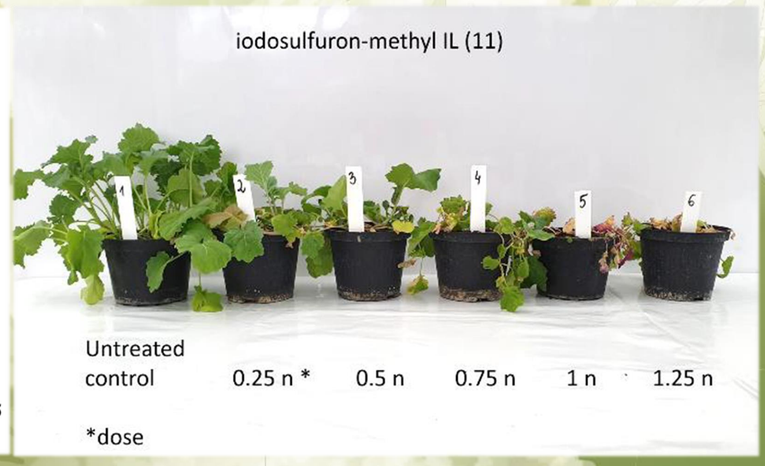


^1H NMR spectrum of iodosulfuron-methyl hexyl betainate

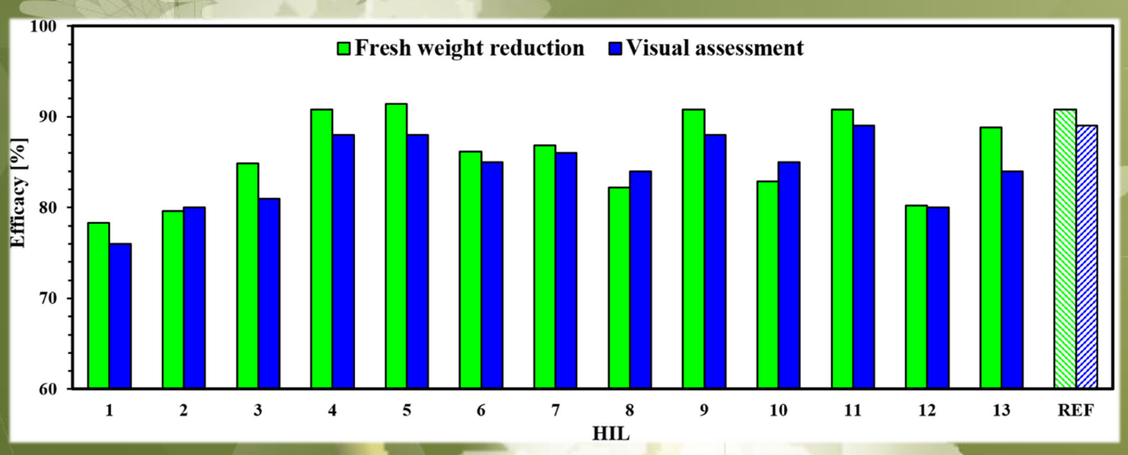


Dose response of iodosulfuron-methyl tetradecyl betainate

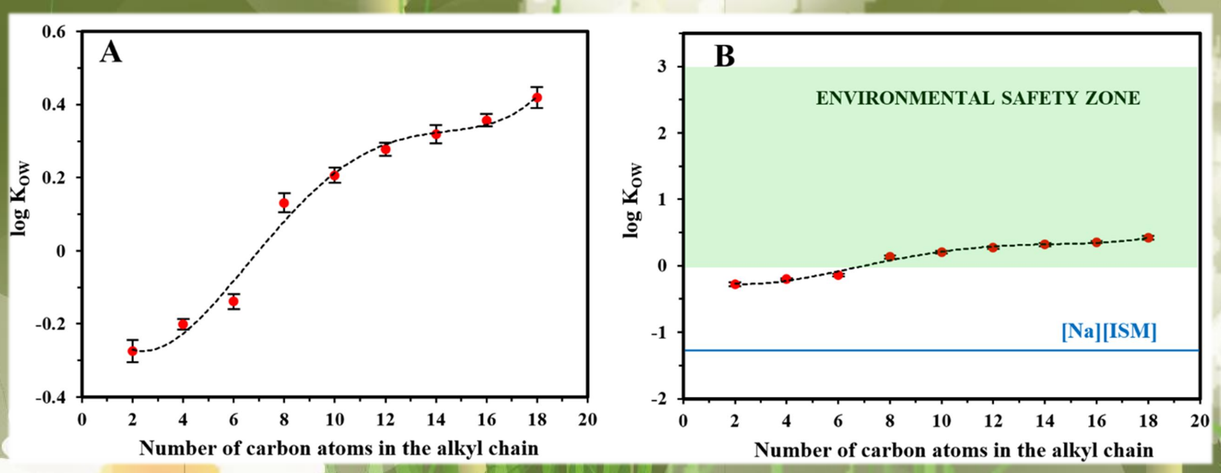




Herbicidal activity versus rapeseed:



Lipophilicity of the obtained compounds:



The values of the logarithm of the octanol-water partition coefficient increased with the elongation of alkyl chain. The majority of the obtained compounds was characterised by values in a range from 0 to 3, which means, that risk of their migration into groundwater after application or the possibility of their bioaccumulation in the environment is extremely low.

Summary

- In the course of this research, 13 new biobased ILs synthesized from a raw material of plant origin (glycine betaine) has been effectively used for efficient protection against weeds.
- The products were obtained with high yields from 92% to 99% and their structures were confirmed by various spectroscopic methods.
- Examination of octanol-water partition coefficient revealed, that the majority of obtained compounds was characterised by low risk of migration into groundwater and lack of risk of their bioaccumumulation in the environment occur.
- The majority of the obtained compounds were characterized by the same biological effectiveness as commercial product containing sodium salt of iodosulfuron-methyl. This means, that the alkyl betainate cation is able to act as an effective adjuvant, which eliminates utilization of external additives or efficacy enhancers.
- Among the synthesized compounds, the salt containing a tetradecyl substituent was found to exhibit the greatest efficacy. After its application at the recommended dose or higher by 25%, the fresh weight reduction of the tested plants was superior to that of the preparation containing the sodium salt.
- The part of this experiment was described recently in: Niemczak M. et al., Iodosulfuron-Methyl-Based Herbicidal Ionic Liquids Comprising Alkyl Betainate Cation as Novel Active Ingredients with Reduced Environmental Impact and Excellent Efficacy. J. Agric. Food Chem. 2020, 68, 13661–13671. (https://doi.org/10.1021/acs.jafc.0c05850).

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