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ALKYLATION OF THE 2-HYDROXYPYRIDINE ANION IN IONIC LIQUID MEDIA

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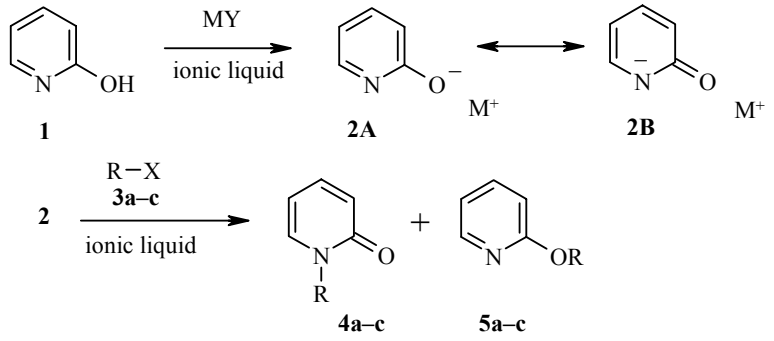
The alkylation reaction of the ambident 2-hydroxypyridine anion was examined in ionic liquid media. Ionic liquids increase the alkylation reaction rate in comparison with molecular liquids, as well as the level of impact on the reaction rates of the counter ion and/or additives, and the distribution of isomers of the reaction products in trans- formations of the ambident 2-hydroxypyridine anion.

Keywords: ambident anion, 2-hydroxypyridine, ionic liquids, alkylation.

Ionic liquids (ILs) have become an increasingly popular medium for transformations of organic compounds during the last decade and replace step-by-step molecular liquids – conventional organic solvents [1-17]. Among the numerous organic reactions performed in ionic liquids little attention is paid to transformations of ambident ions in ILs. A few published communications [18-26] signalize the increase in the reaction rates in ILs but do not allow us to foresee at present whether the selectivity of the reactions of ambident anions would change in the media of ILs as compared with that in molecular liquids.

In the course of the systematic investigation of ambident ions concerning their benefits in media of ILs [23-26], regularities of the alkylation reaction of the ambident 2-hydroxypyridine anion **2** are discussed in the present communication considering different alkylation reagents **3** and various ILs **6**, **7**.

Scheme 1



M = K, Na, Li, Ag; Y= H, Bu, OH, OMe, CO_3^{2-};

3 $\mathbf{a_1}$ X = Cl, $\mathbf{a_2}$ X = Br, $\mathbf{a_3}$ X = I, $\mathbf{a_4}$ X = Ts; **3– 5 a** R= *n*-Bu, **b** R = $PhCH_2$, **c** R = CH_2=$CHCH_2$

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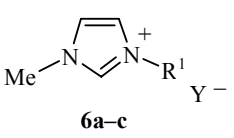
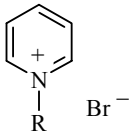
2-Hydroxypyridine anion **2** forms two isomeric products in its reactions with electrophilic reagents – N-substituted (**4**) and O-substituted (**5**) derivatives [27-30]. Particularities of the chosen solvent, the impact of the cation connected with the substrate anion, and other factors influencing the transformation rates, as well as the regioselectivity of reactions in these alkylation reactions performed in non-conventional solvents, ILs, are discussed.

In order to assess the rate and regioselectivity of the alkylation of 2-hydroxypyridine anion in ILs, the following imidazolium **6a**–**c** and pyridinium **7a,b** salts with alkyl groups of various length were used.



6a–c



7a,b

6 a R^1 = Me, Y = Ts; **b** R^1 = Bu, Y = Br; **c** R^1 = Bu, Y = Ts;

7 a R = C_7H_{15}, **b** R = *n*-Bu

We have alkylated 2-hydroxypyridine salts by *n*-butyl halides, 3-chloro-1-propene (allyl chloride), and benzyl chloride. The reaction pathway was followed by gas chromatography (GC). Joint gas chromatography – mass spectrometry (GC/MS), together with the characterization of isolated individual compounds by ^{1}H NMR spectra and the data of elemental analyses, have served to prove the structures of the alkylation products obtained.

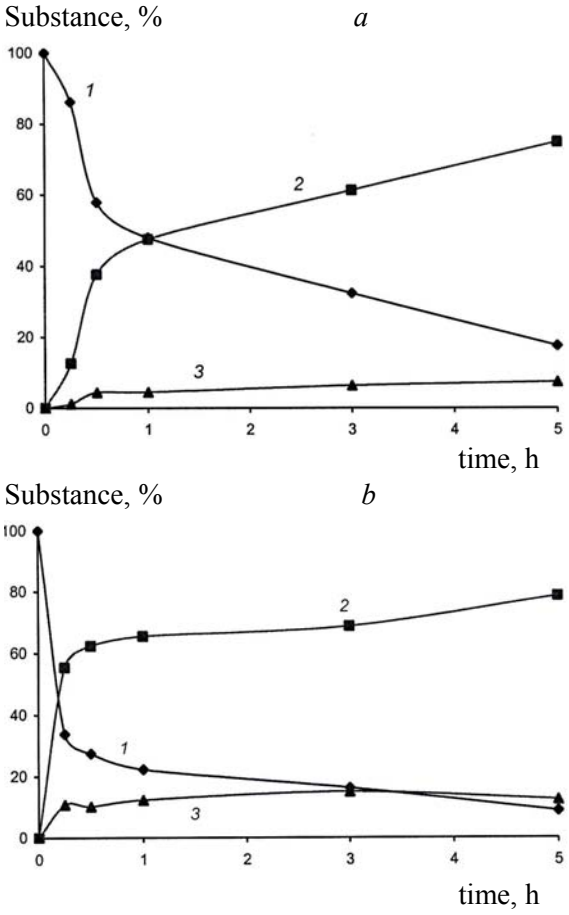


Fig. 1. Alkylation of 2-hydroxypyridine potassium salt with 1-iodobutane in (**7a**) at: *a* – 25°C; *b* – 80°C: *1* – 1-iodobutane; *2* – 1-butyl-2-pyridone; *3* – 2-butoxypyridine.

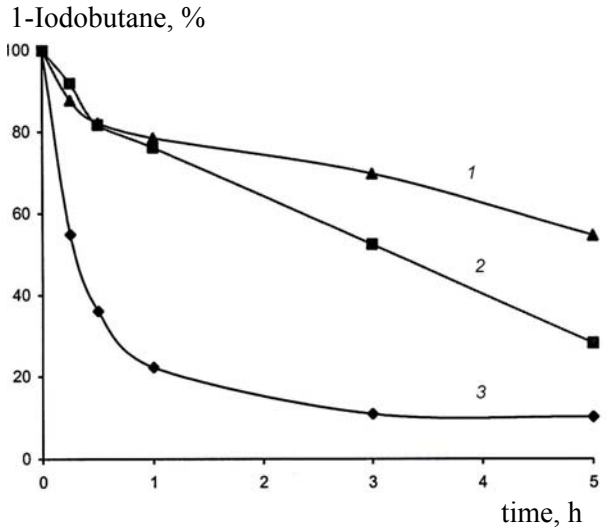


Fig. 2. Alkylation of 2-hydroxypyridine potassium salt with 1-iodobutane at 65°C in: *1* – N,N-dimethylformamide; *2* – tetrahydrofuran; *3* – **7a.**

Alkylation of 2-hydroxypyridine potassium salt in IL media proceeds rapidly (Fig. 1*a*, *b*). A good conversion degree (73%) is reached in the medium of 1-heptylpyridinium bromide (**7a**) at 80°C for 0.5 h, a conversion of 80% being obtained during 5 h at room temperature. 1-Butyl-2-pyridone (**4a**) and 2-butoxypyridine (**5a**) were formed in both cases; the yield and reaction rate increased with temperature (Fig. 1*a*, *b*)

ILs as a solvent cause the augmentation of the reaction rates in these transformations in comparison with molecular liquids. The results of such a comparison are presented in Fig. 2, where the reaction rate in the IL **7a** is compared with the rates in solvents most frequently used for similar alkylation reactions – N,N-dimethyl-formamide and tetrahydrofuran. These results look very promising for ILs.

Alkali metal salts (K, Na, Li) of 2-hydroxypyridine enter the alkylation reactions mainly at the nitrogen atom, resulting in the formation of 1-alkyl-2-pyridones (**4**), the alkylation rates of Li salts being considerably lower than those of sodium or potassium salts. The alkylation reaction of the silver salt results in the formation of a larger fraction of 2-alkoxypyridines (**5**) – the product of O-alkylation. All the reaction mixtures of the mentioned silver salts are heterogeneous at the beginning, and they turn homogeneous during the reaction course (~ 15 min). Four different ILs were examined in order to obtain some information on the impact of the structure of ILs themselves on the pathway of the alkylation reactions (Table 1).

The data presented above (Table 1) confirm that IL solvents affect both the alkylation reaction rates (conversion) of 2-hydroxypyridine anion and the distribution of isomers in the product mixture.

The type of substrate cation in IL media, the alkyl group and leaving group of the alkylating reagent, and the type of cation and anion of the used IL itself all affect the substrate conversion rate. The last decreases in the row of substrate cations K > Na > Li (Table 1, entries 1–3, 5–7, 9–11, 15–17, 19–21, 23–25, 27–29, 35–37, 39–41, 45–47, 49–51, 57–59, 61–63). Hence, a weaker electrostatic interaction between a cation and anion in the substrate molecule facilitates alkylation of the ambident anion – the harder lithium cation hinders the alkylation rate more than the softer potassium cation. The silver cation does not fall within the mentioned row because the specific interaction between it and the alkylating reagent (alkyl halide or tosylate) becomes predominant. Its impact on the substrate conversion becomes especially favorable in the case of butyl iodide or butyl tosylate (Table 1, entries 26, 34, 48, 56). It was noticed that the alkylation of the 2-hydroxypyridine silver salt proceeds only slightly, if at all, in ionic liquids having tosylate or other sulfonate anion (Table 1, entries 4, 8, 12, 18, 44).

The type of the alkyl group and the leaving group influence the reagent conversion rate. Reagents with benzyl or allyl groups have higher conversion than those with saturated alkyl groups without any possible conjugation, as it is shown by comparison of the conversion of benzyl, allyl, and butyl chlorides (Table 1, entries 15-17 and 19-21 *vs* 9-11; entries 35-37 and 39-41 *vs* 31; entries 57-59 and 61-63 *vs* 53). This phenomenon can be seen even better if registered in time (Fig. 3).

TABLE 1. Ratio of Isomers in the Alkylation Reactions of 2-Hydroxypyridine Salts **2** in Different Ionic Liquids

Entry	Reaction conditions			Conversion of the substrate **3**, %*	Compound in the product mixture after alkylation, %*	
	IL	Reagent **3**	M in the salt **2**		**4**	**5**
1	2	3	4	5	6	7
1	**6a**	BuI	K	62.8	85.9	14.1
2			Na	38.1	87.9	12.1
3			Li	5.7	80.2	19.8
4			Ag	6.5	6.0	94.0
5		BuBr	K	42.1	90.6	9.4
6			Na	23.1	94.4	5.6
7			Li	1.6	100.0	0.0
8			Ag	0.0	0.0	0.0
9		BuCl	K	11.4	92.4	7.6
10			Na	9.4	88.8	11.2
11			Li	1.4	100.0	0.0
12			Ag	0.0	0.0	0.0
13		BuOTs	K	92.9	83.1	16.9
14			Ag	18.1	10.3	89.7
15		$PhCH_2Cl$	K	25.8	59.4	40.6
16			Na	19.0	53.8	46.2
17			Li	8.1	70.3	29.7
18			Ag	5.0	0.0	100.0
19		$CH_2=CHCH_2Cl$	K	90.8	97.3	2.7
20			Na	81.1	96.5	3.5
21			Li	2.1	100.0	0.0
22			Ag	23.4	0.0	100.0
23	**6b**	BuI	K	28.4	83.5	16.5
24			Na	33.2	89.6	10.4
25			Li	0.5	0.0	100.0
26			Ag	20.6	19.5	80.5
27		BuBr	K	63.3	70.5	29.5
28			Na	25.3	77.6	22.4
29			Li	0.3	0.0	100.0
30			Ag	45.1	15.6	84.4
31		BuCl	K	22.9	83.5	16.5
32			Ag	0.0	0.0	0.0
33		BuOTs	K	84.2	79.8	20.2
34			Ag	43.8	20.6	79.4
35		$PhCH_2Cl$	K	70.7	90.8	9.2
36			Na	28.2	88.8	11.2
37			Li	4.3	73.5	26.5
38			Ag	47.2	14.5	85.5
39		$CH_2=CHCH_2Cl$	K	89.2	95.2	4.8
40			Na	76.7	94.3	5.7
41			Li	14.0	0.0	100.0
42			Ag	65.7	23.7	76.3
43	**6c**	BuBr	K	48.1	87.4	12.6
44			Ag	1.1	0.0	100.0

TABLE 1. (continued)

1	2	3	4	5	6	7
45	**7a**	BuI	K	82.5	91.0	9.0
46			Na	54.6	76.5	23.5
47			Li	0.6	100.0	0.0
48			Ag	96.4	20.9	79.1
49		BuBr	K	17.1	80.1	19.9
50			Na	7.6	57.6	42.4
51			Li	6.5	100.0	0.0
52			Ag	34.7	48.0	52.0
53		BuCl	K	6.4	88.3	11.7
54			Ag	0.8	87.4	12.6
55		BuOTs	K	47.0	81.3	18.7
56			Ag	60.1	11.1	88.9
57		$PhCH_2Cl$	K	87.3	94.0	6.0
58			Na	81.4	92.3	7.7
59			Li	4.7	24.3	75.7
60			Ag	92.0	68.9	31.1
61		$CH_2=CHCH_2Cl$	K	85.1	96.4	3.6
62			Na	76.3	92.5	7.5
63			Li	15.1	51.8	48.2
64			Ag	96.0	51.0	49.0

* After stirring at 25°C for 5 h, and determined by GC, with accuracy ±5%.

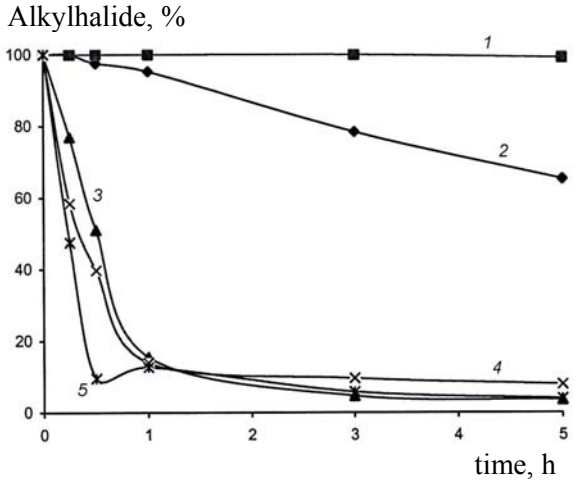


Fig. 3. Alkylation of 2-hydroxypyridine silver salt with different alkylating reagents (in **7a** at 25°C): *1* – 1-chlorobutane; *2* – 1-bromobutane; *3* – 1-iodobutane; *4* – benzyl chloride; *5* – allyl chloride.

The observation alludes that the ionization of the C–X bond following S_N1 substitution is more favorable than the bimolecular (S_N2) pathway in IL media. The auspicious influence of the leaving group corresponds to the row Bu–I > > Bu–Br > Bu–Cl in every separate IL, albeit the conversion values hardly differ between various ILs. This fact drives one to the assumption that sufficiently strong hydrogen bonds might exist between ILs and reagent molecules in the investigated reactions similar to those existing in protic solvents.

The possibility of IL to form hydrogen bonds is discussed in the literature and has been experimentally proved, at least between the C(2)–H bond and a substrate molecule in solutions of 1,3-dialkyl imidazolium salts. The contributory influence of the silver ion on the ionization of the R–X bond can be observed only with butyl iodide and butyl bromide, provided that the ILs used do not contain a sulfonate anion. In the latter case, the conversion of the silver salt takes place only slightly, if at all (Table 1, entries 4, 8, 26, 30, 44, 48, 52). The tosylate anion seems to be a better leaving group than the bromide anion in the reagent molecule Bu–X in some cases (Table 1, entry 13 *vs* 5; 33 *vs* 27; 55 *vs* 49) and worse in others (Table 1, entry 43 *vs* 27). Accordingly, in the examples observed, the influence is less significant by comparison with the dominance of the IL structure.

Regarding the structure of ILs, it should be mentioned that the conversion of the 2-hydroxypyridine anion is higher in ILs with 1-alkylpyridinium cation than with the 1,3-dialkylimidazolium cation (for example, Table 1, entry 45 *vs* 1 and 23 or 57 *vs* 15 and 35). The difference can be seen more convincingly when the comparison is made in time (Fig. 4).

The difference observed might be caused hydrogen bonding between the C(2)–H bond of imidazolium cycle and the ambident anion, as mentioned above, which could decrease the reactivity of the latter. To prove this hypothesis, further experiments are in progress in our laboratory using ILs with a substituted C(2) atom. The impact of the IL anion manifests itself in the disturbing influence of the sulfonate anion on the conversion of the silver salt as well as in higher conversion rates in the medium of 1,3-dialkyl- imidazolium tosylate by comparison with the same in 1,3-dialkylimidazolium bromide (Table 1, entries 1–22 *vs* 23–42), the tosylate anion influence being more favorable.

The distribution of isomers in the mixture of reaction products in ILs markedly favors the N-alkylation direction. Always more N-alkylpyridones (**4**) than the products of O-alkylation – 2-alkoxypyridines (**5**) – were formed in IL media than in molecular solvents. The formation of O-alkylated products (**5**) in the examined ILs is substantially promoted by the silver ion and slightly promoted by the lithium ion in the substrate molecule. Benzyl and allyl groups in the reagent molecule are also advantageous for O-alkylation in comparison with the butyl group; the iodide anion as a leaving group is much more favorable than the bromide, chloride, or tosylate anion. As to the structure of the ILs, more O-alkylation product forms in ILs with the 1-alkylpyridinium cation than with the 1,3-dialkylimidazolium one. It was difficult to find any effect of the IL anion on the ratio of isomers in the product mixture.

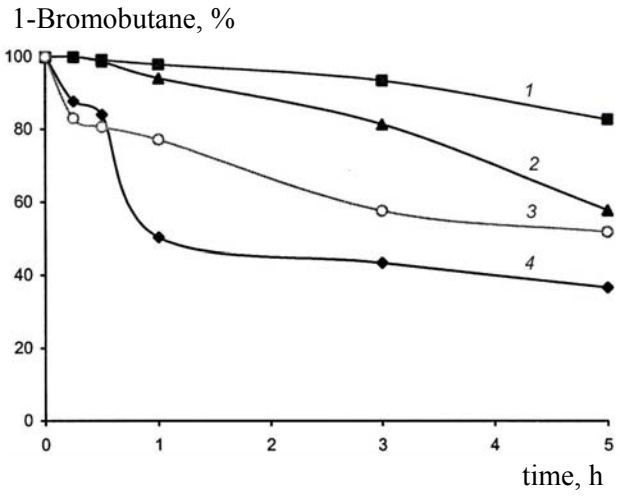
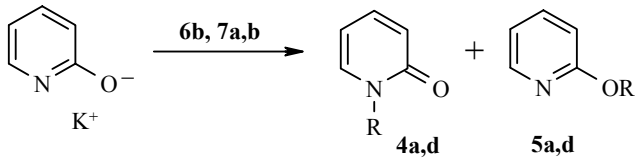


Fig. 4. Alkylation of 2-hydroxypyridine potassium salt with 1-bromobutane in different ionic liquids (at 25°C) in: *1* – **7a**; *2* – **6a**; *3* – **6c**; *4* – **6b**.

ILs are quaternary ammonium salts and therefore they might also serve as alkylating reagents in the reactions investigated, as formerly noticed in the alkylation reactions of indole or nitrite anions [24–26]. Such a parasitic reaction takes place slowly at room temperature, the N-alkylation product being the dominant one. The latter is also the major product in the alkylation reaction at elevated temperature (65°C), and the fraction of the O-alkylation product diminishes sharply in this case (Table 2). Fortunately, the fraction of the alkylation products created by ILs themselves is quite small in the general mixture of products and does not exceed 3%.

Scheme 2



6b, 7a, b – ionic liquids; **4, 5 a** R = *n*-Bu; **d** R = C_7H_{15}

As quaternary ammonium salts, ILs quite are frequently highly hygroscopic materials. We have performed special experiments to clarify the influence of the presence of protic solvents in ILs on the course of the alkylation reactions investigated. Small amounts of water or methanol were purposely added to the alkylation reaction mixture. The presence of water decreased the conversion rate, and its influence increased with rising concentration of water in the reaction mixture. One can presume that water might induce the hydrolysis of the 2-hydroxypyridine salt into 2-hydroxypyridine, which cannot enter the alkylation reaction any more. This appears possible because the molar concentration of water exceeds that of the mentioned salt by 1.5 times. The addition of methanol (weaker acid) does not lead to such a disastrous aftereffect, the conversion degree remaining practically the same in the presence or absence of methanol. It is worth mentioning that the presence of protic solvents in the reaction mixture in ILs does not change the ratio of product isomers (Table 3). One can presume, therefore, that ILs have a dominant role on the regioselectivity of alkylation reactions in the mixtures with molecular liquids.

The unexpected decreased influence of the substrate cation (M) on the distribution of N- *vs* O-alkylation products in comparison with the situation in molecular liquids (organic solvents) [27–29] could be explained by the ILs leveling effect. An exchange reaction might take place between the substrate cation (M) and the bulky hard cation of the IL. As a result, a loose ion pair is formed between the ambident 2-hydroxypyridine anion and the bulky IL cation, and any specific cation–anion interaction between the substrate ions is diminished or even fully abolished, which explains the IL leveling effect.

TABLE 2. Ratio of alkylation products of the 2-hydroxypyridine potassium salt by ionic liquids themselves

Entry	IL	Alkyl group R in ILs and in products	Temp., °C	Content of the substance in the product mixture, %*	
				4	**5**
1	**6b**	Bu	25	87.4	12.6
2	**6b**	Bu	80	93.2	6.8
3	**7a**	C_7H_{15}	25	89.8	10.2
4	**7a**	C_7H_{15}	80	97.8	2.2
5	**7b**	Bu	25	66.4	33.6
6	**7b**	Bu	80	98.9	1.1

* Without any other alkylating reagent after 6 h.

TABLE 3. Influence of protic solvents on the ratio of alkylation products of 2-hydroxypyridine sodium salt

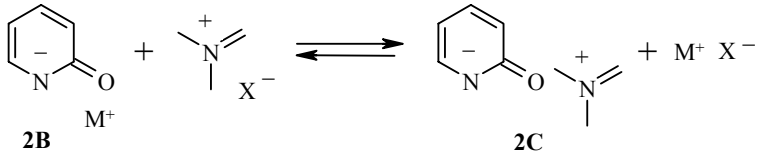
Entry	Sodium salt **2** preparation procedure*	Conversion of iodobutane **3a**, %*[2]	Compound in the product mixture after alkylation, %*[2]	
			4a	**5a**
1	NaH	54.6	76.5	23.5
2	NaH + H_2O	19.9	87.7	12.3
3	NaH + H_2O	12.0	87.4	12.6
4	$NaOCH_3$	92.2	90.6	9.4
5	$NaOCH_3$ + CH_3OH	99.7	90.6	9.4
6	$NaOCH_3$ + CH_3OH	96.5	91.2	8.8

* Entry 2 – 0.46; 3 – 1.58, 5 – 0.083, 6 – 0.26 mmol / 1 mmol IL.

*[2] In the reaction of 2-hydroxypyridine sodium salt with 1-iodobutane in IL **7a** at 25°C.

The mentioned ion exchange causes a decrease in the specific interaction even of the silver cation with the 2-hydroxypyridine anion, wich makes the well-known effect of the silver ion very much less powerful in ILs in comparison with molecular liquids such as N,N-dimethylformamide [28, 29].

Scheme 3



2B **2C**

EXPERIMENTAL

^{1}H NMR spectra were registered on a Varian Mercury BB (200 MHz) instrument in DMSO-d_6, internal standard TMS.

Gas chromatographic (GC) analyses were carried out on a Hewlett Packard 5890 instrument using a flame ionization detector with a hydrogen flow rate of 30 ml/min, air flow rate of 300 ml/min, and helium flow rate of 25 ml/min. A DB-5MS (30 m × 0.25 mm) column was used, injection temperature was 250°C, and the temperature regime of analyses was as follows: starting temperature 50°C (1 min), then 10°C/min up to 250°C, and final temperature 250°C (for 10 min). GC/MS analyses were performed with a Shimadzu GC 2010 gas chromatograph connected with Shimadzu QP 2010 mass spectrometer, EI ionization with energy 70 eV, distribution in splitless injector 1:30, and using automatic injector OAC 20i. The sample volume for all the analyses was 1 μl.

Ionic liquids 1,3-dimethylimidazolium *para*-toluenesulfonate (**6a**), 1-butyl-3-methylimidazolium bromide (**6b**), 1-butyl-3-methylimidazolium *para*-toluenesulfonate (**6c**), N-heptylpyridinium bromide (**7a**), and N-butylpyridinium bromide (**7b**) were prepared according to the procedures described [30, 31]. Other reagents were purchased from Aldrich and used without further purification. Solvents were purchased from Aldrich and also used without further purification. 1-Butyl-2-pyridone (**4a**), 2-butoxypyridine (**5a**), 1-benzyl-2-pyridone (**4b**), and 2-benzyloxypyridine (**5b**) were prepared according to [32], and 1-allyl-2-pyridone (**4c**), and 2-allyl-oxypyridine (**5c**) – according to [33, 34].

1-Butyl-2-pyridone (**4a**) **and 2-Butoxypyridine** (**5a**). A. *Alkylation in ionic liquids***.** 2-Hydroxypyridine (200 mg, 2.10 mmol), IL **6b** (920 mg, 4.20 mmol), and KOH (236 mg, 4.20 mmol) were mixed together under argon and stirred for 0.5 h at room temperature. 1-Bromobutane (575 mg, 4.20 mmol) was added to the stirred mixture. Samples (~ 1 mg) were taken from the mixture after definite time intervals (0.25, 0.5, 1, 3, and 5 h), treated with diluted (1:1) HCl, and extracted with ether (3 × 5 ml). The joint extract was analyzed by GC, 1-butyl-2-pyridone and 2-butoxypyridine being used as reference materials (Table 1 and Figs. 1, 3, 4).

Other 2-hydroxypyridine derivatives 4, **5** (Table 1 and Figs. 1, 3, 4) were obtained and other experiments were performed in a similar way. Bases KOH, MeONa, NaH, BuLi, and Ag_2CO_3 were used for preparation of the corresponding salts of 2-hyd-roxypyridine. The alkylating reagents 1-chlorobutane, 1-bromobutane, 1-iodobutane, benzyl chloride, and 3-chloro-1-propene (allyl chloride) were used for 2-hydroxy- pyridine alkylation at room temperature (25°C) and at 80°C. Structures of the products were initially confirmed by ^{1}H NMR analyses. ^{1}H NMR analyses for **4a**,**b**, **5a**,**b** correspond to the literature data [32]; for **4c**, **5c** – to [33, 34]. 1-Heptyl-2-pyridone (**4d**) and 2-heptyloxypyridine (**5d**) were obtained in a way similar to the described one [32]. ^{1}H NMR spectrum, δ, ppm (*J*, Hz) for **4d**: 7.63 (1H, dd, *J* = 2.0, *J* = 6.6, H-4); 7.34 (1H, ddd, *J* = 1.9, *J* = 6.6, *J* = 9.9, H-6); 6.33 (1H, d, *J* = 9.9, H-3); 6.16 (1H, td, *J* = 1.6, *J* = 6.6, H-5); 3.85 (2H, t, *J* = 7.5, $NC\underline{H}_2$); 1.69 (2H, m, $NCH_2–C\underline{H}_2$); 1.19 (8H, s, $(CH_2)_4$); 0.82 (3H, t, *J* = 7.5, CH_3); for **5d**: 8.15 (1H, ddd, *J* = 0.9, *J* = 2.1, *J* = 5.1, H-6); 7.68 (1H, ddd, *J* = 2.1, *J* = 7.1, *J* = 8.4, H-4); 6.90 (1H, ddd, *J* = 1.0, *J* = 5.1, *J* = 7.1, H-5); 6.75 (1H, d, *J* = 8.3, H-3); 4.25 (2H, t, *J* = 7.5, $OC\underline{H}_2$); 1.75 (2H, m, $OCH_2–C\underline{H}_2$); 1.35 (8H, s, $(CH_2)_4$); 0.92 (3H, t, *J* = 7.3, CH_3). The experiments were subsequently followed by GC analyses, the GC/MS being used for further confirmation of signals of chromatography. Every measurement was repeated 3–5 times.

B. *Alkylation in organic solvents*. 2-Hydroxypyridine (200 mg, 2.10 mmol) was dissolved in anhydrous THF (9 ml). The solution was slowly added to a KOH suspension (236 mg) in THF (5 ml) at room temperature. After that the mixture was stirred at 65°C for 15 min. A solution of butyl iodide (773 mg, 4.20 mmol) in anhydrous THF (5 ml) was added to the 2-hydroxypyridine potassium salt solution at room temperature, and the mixture was stirred at 65°C. The samples (~ 1 mg) were taken from the mixture after definite time intervals (0.25, 0.5, 1, 3, 5 h), treated with aqueous ammonium chloride, and extracted with diethyl ether (3 × 5 ml). Each joint extract was analyzed by GC.

The reaction was run also in N,N-dimethylformamide solution in a very similar way. All the results obtained were presented in Fig. 2.

C. *Alkylation by ionic liquids themselves*. 2-Hydroxypyridine (200 mg, 2.10 mmol), KOH (236 mg, 4.20 mmol), and N-butylpyridinium bromide (**7b**, 903 mg, 4.20 mmol) were stirred at 25°C for 6 h. Samples (~ 1 mg) were taken from the mixture and extracted with ether (3 × 5 ml). The joint extract was analyzed by GC, the 1-butyl-2-pyridone and 2-butoxypyridine being used as reference materials. The results obtained are compiled in Table 2, entry 5.

The experiments with other ILs at 25 and 80°C and analyses of the results were made in a similar way, the results being presented in Table 2.

D. *Alkylation in ionic liquids in the presence of protic solvents*. 2-Hydroxypyridine (200 mg, 2.10 mmol), N-heptylpyridinium bromide (**7a**, 1.08 g, 4.20 mmol), and NaH (168 mg of 60% dispersion in mineral oil; 4.20 mmol) were stirred at 25°C for 15 min. Butyl iodide (773 mg, 4.20 mmol) and water (120 mg, 6.65 mmol) were added, and the mixture was stirred at 25°C for 5 h. A sample (~ 1 mg) was taken from the mixture and extracted with ether (3 × 5 ml). The joint extract was analyzed by GC 1-butyl-2-pyridone and 2-butoxypyridine being used as reference materials. The results obtained are compiled in Table 3, entry 3.

The experiment with a different amount of water (Table 3, entry 2) was made in a similar way. Sodium ethoxide was used for sodium salt preparation (Table 3, entries 4–6) in three other experiments, and methanol was added instead of water (Table 3, entries 5, 6) in these experiments, the isolation procedure and GC analyses being the same as mentioned above.

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