

ALKYLATION OF THE AMBIDENT INDOLE ION IN IONIC LIQUIDS

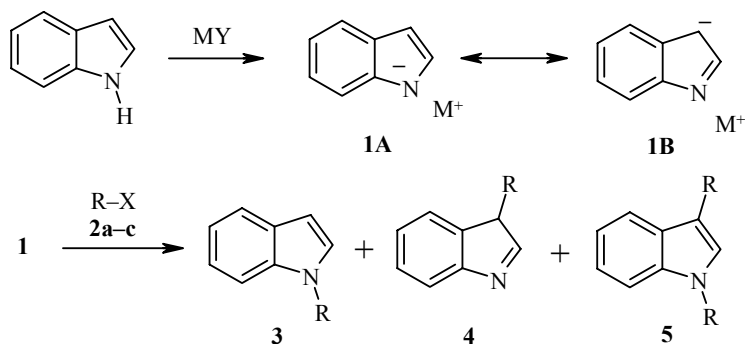
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Alkylation of the ambident indole anion in ionic liquids has been investigated. The reaction rate is greater in ionic liquids than in organic solvents. The polarity of certain ionic liquids has been determined to be located between methanol and acetonitrile.

Keywords: ambident anion, indole, ionic liquids, alkylation.

Conversions of ambident anions in ionic liquids (IL) have been little investigated in organic synthesis [1-11], in spite of the great interest of chemists in these solvents during the past 20 years [12-31]. Only a few conversions of ambident anions of heterocyclic compounds are reported in the literature [1-5]. The poor availability of information does not permit generalizations on rules for such reactions and the forecasting of their results.

The ambident anion of indole (**1**) forms several products in alkylation reactions, *viz.* the N-substituted compound 1-alkylindole **3**, the C-substituted compound 3-alkylindole **4**, and the N,C-disubstituted compound 1,3-dialkylindole **5** [32-34]. The rate of the alkylation reaction and the distribution of isomers in the mixture of products **3-5** depend on various factors, the properties of the solvents used, the form and charge of the cation, the structure of the alkylating agent, etc. [32-34]. The overall effect of these factors is considered in reactions which are carried out in molecular liquids (organic solvents), and a difference in their influence has

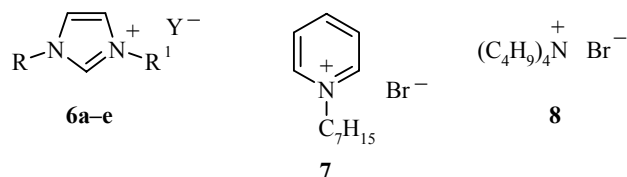


Y a = OMe, **b** Y = Bu, **c** Y = Me; **1 a** M = Na, **b** M = Li, **c** M = MgI;
2-5 a R = *n*-C₄H₉, **b** R = PhCH₂, **c** R = CH₂=CHCH₂;
2a₁ X = Cl, **a₂** X = Br, **a₃** X = I

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been noted [35-38]. In a medium of ionic liquids the influence of these factors is only touched upon in several studies [5, 6, 8-11], consequently in the present report factors influencing the rate of alkylation and the ratio of isomers of products on alkylation of various indole salts in ionic liquids will be considered in more detail. Comparison of them with reactions in molecular liquids (organic solvents) will be carried out.

Imidazolium **6a-e**, pyridinium **7**, and tetrabutylammonium **8** salts with alkyl groups of various length were used as solvents in order to assess the rate and regioselectivity of alkylation in ionic liquids.



6 a R = R¹ = Me, Y = OTs; **b** R = Me, R¹ = Bu, Y = Br; **c** R = Bu, R¹ = CH₂CH₂CH₂SO₃;
d R = Et, R¹ = Me, Y = MeSO₃; **e** R = Me, R¹ = Bu, Y = OTs

In the ionic liquids used the structure of the cation and anion determines the overall polarity of a medium of these solvents. At the present time the polarity of a solvent is described with the aid of Reichardt constants, which have been determined for many organic solvents [39, 40], including several ionic liquids [39]. It also includes the possible influence of forming a hydrogen bond between the solvent and reactants on the direction of the reaction. The formation of such a hydrogen bond in a medium of ionic liquids is widely disputed, especially in examples using C(2)-unsubstituted imidazolium salts [20, 39].

In the ionic liquids used by us imidazolium salts **6** form the strongest hydrogen bond with the reactants and pyridinium salts **7** the weakest. Tetrabutylammonium salts **8** in practice do not form hydrogen bonds [20, 39]. In imidazolium **6** and pyridinium **7** salts the cations are aromatic heterocycles with a conjugated system of π -electrons. Consequently they offer to partners in the alkylation reaction (and to the transition state of this reaction) not only because of the electrostatic interaction of the positive and negative charges of their ions, but also an additional donor-acceptor type of interaction of the π -system of electrons. The latter interconnection has no place in the case of tetrabutylammonium salt **8**. The anions of the ionic liquids used differ little. These stable anions are bromide and sulfonates. In the case of the *p*-toluenesulfonate (tosylate) anion of **6a,e** it is possible that the anion interacts with partners of the alkylation reaction, using their own system of π -electrons.

We alkylated indole salts **1** with 1-butyl halides, 3-chloropropene (allyl chloride), and benzyl chloride. The alkyl group was chosen with the aim of assisting the mechanism of the S_N2 (1-butyl group) or S_N1 (benzyl or allyl group) reaction. Halogen atoms in the 1-butyl halides varied in their electronegativity and polarizability. The progress of the reaction was followed by gas chromatography.

In order to assess the influence of the cation of the ambident anion in indole salts, we compared magnesium, lithium, and sodium cations. The Grignard reagent was used to obtain indolylmagnesium iodide, butyllithium for indolyl lithium, and sodium methylate for indolyl sodium. The metal cations were selected with the aim of gradually weakening the interconnection between the cation and indole anion, however the strongest interconnection (tightest ion pair) might have been expected in the case of the indolylmagnesium iodide salt (**1c**).

Alkylation of all three indole salts leads to a mixture of products of N- and C-alkylation **3-5** in a medium of ionic liquids as also in organic solvents. The observed regularities of alkylation reactions in ionic liquids differed from the regularities of reactions in organic solvents only quantitatively. These differences are best of all considered in the case of magnesium salt **2c**, and in the present report they are discussed most widely. Alkylation of the indole magnesium salt in ionic liquids occurs with more difficulty (more slowly) than

the alkylation of lithium or sodium salts, but fairly rapidly at increased temperature (Fig. 1). At 80°C conversion of the magnesium salt achieves results analogous to the results of alkylation of indolyl lithium and indolyl sodium at room temperature. The conversion was 55% in 5 h. The observed slow progress of the reaction in the case of magnesium salt **2c** compared with the progress of the reaction with lithium and sodium salts **2a,b** is explained by the fact that C-alkylation occurs as a thermodynamically controlled reaction, which is slower than the kinetically controlled N-alkylation reaction.

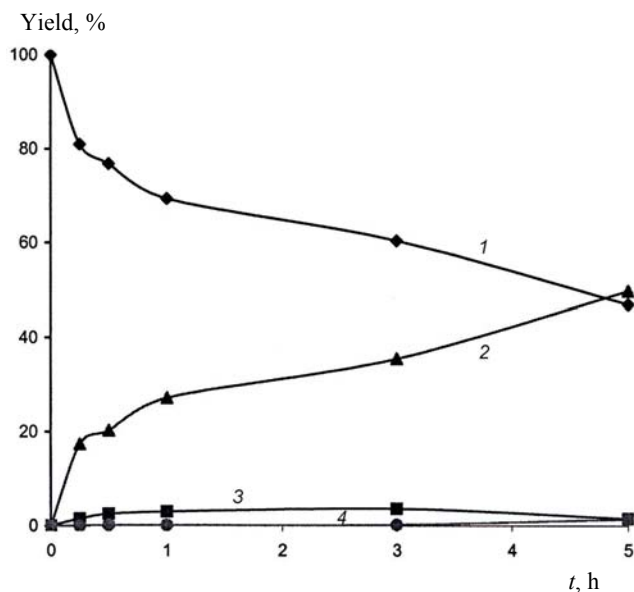


Fig. 1. Alkylation of indolylmagnesium iodide with 1-iodobutane in **7a** at 80°C: 1 – indole; 2 – 3-buty lindole; 3 – 1-buty lindole; 4 – 1,3-dibuty lindole, %.

The results confirm the suggestion that the N,C-dialkylation product **5** is formed through the C-monoalkylation product **4**, and not through the N-alkyl product **3** [5, 32].

The correlated results (Table 1) indicate that the metal cation of the ambident indole anion, the leaving alkyl groups in the alkylating reagent, and the kind of the cation and anion in the ionic liquid, influence the conversion and distribution of isomers in the products of the reaction mixture.

Conversion increased in the series Mg < Li < Na (Table 1; expt. 1-6, 10-15, 19-21, 31-48). The regioselectivity of alkylation (ratio of N- and C-alkylation products) is determined mainly by the metal cation mentioned. Since the indole anion forms a tighter ion pair with magnesium ion than with lithium ion, and particularly with sodium ion [33], in the case of indolyl sodium (**1a**) the product of N-alkylation **3** is formed in larger amount in a medium of ionic liquids (Table 1; expt. 3, 6, 9, 12, etc.). Lithium cation also assists formation of significant amounts of N-alkylation product **3** (Table 1; expt. 2, 5, 8, 11, 14, 20, 23, 26, 32, 35, 38, 41, 44, 47, 53, 56). For example, on alkylating with 1-butyl iodide or allyl chloride in ionic liquids which contain bromide anion, the lithium indole salt **2b** gives more C-alkylation product **4** and correspondingly N,C-dialkylation product **5**, than the sodium salt **1a** (Table 1; expt. 17, 29, 50, 62). In its turn indolylmagnesium iodide **1c** forms more C-alkylation product **4** (90%), since access of reactant to the nucleophilic center of the ambident anion, the nitrogen atom, is blocked (Table 1; expt. 1, 4, 7, etc.). Development of what is going on in time the best of all is reflected in Fig. 2, which confirms the fact that the alkylation reaction of magnesium salt **1c** at 80°C is practically finished after 3 h.

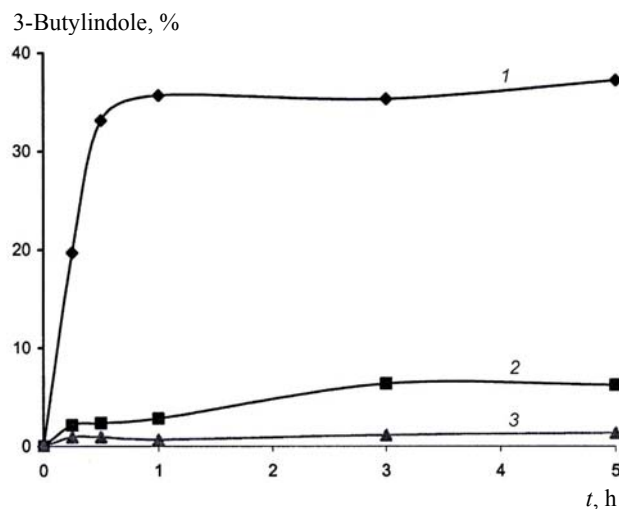


Fig. 2. Rate of formation of C-alkylation product, 3-butyldole (**4**) in the alkylation of indole salt with 1-bromobutane in **6a** at 80°C with cations: 1 – MgI; 2 – Li; 3 – Na.

The conversion and distribution of isomers in an ionic liquid medium is significantly influenced by the kind of the leaving group X and the alkyl radical R in the structure of the reactant R-X. A higher conversion is observed with alkylating agents containing a benzyl or allyl group than with agents containing a butyl group. A similar picture was observed in molecular liquids. This is best seen on considering the process with time (Fig. 3).

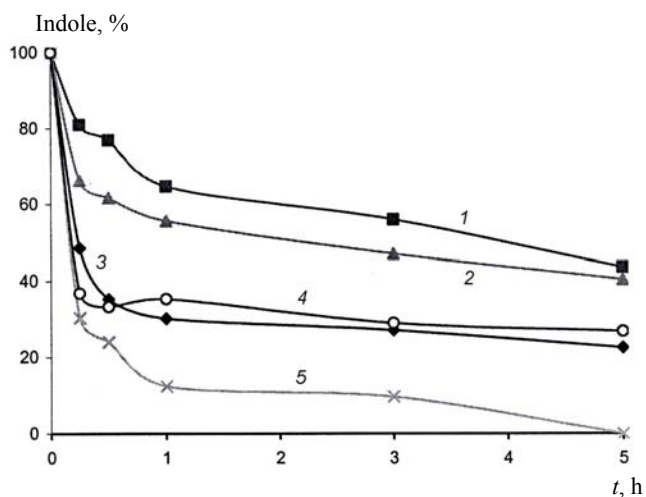


Fig. 3. Alkylation of indolylmagnesium iodide with different alkylating agents (25°C, **6b**): 1 – 1-chlorobutane; 2 – 1-bromobutane; 3 – 1-iodobutane; 4 – allyl chloride; 5 – benzyl chloride.

Benzyl chloride gives the most N,C-dialkylation **5** product (Table 1, expt. 25, 58), allyl chloride as the reactant forms more C-alkylation **4** product (Table 1, expt. 13, 28, 61). This is not contradictory if it is considered that, in accordance with ideas proposed in the literature [5, 32], the 1,3-dialkylated product **5** is formed by alkylating 3-alkylindole **4**, and not 1-alkyl product **3**.

TABLE 1. Distribution of Isomers in the Alkylation of Indole in Ionic Liquids*

Experiment	Reaction conditions		Conversion of indole, (%)	Compounds in product mixture after alkylation, %			Mixture of C-alkylation products 4 + 5 , %		
	Ionic liquid	Reactant		Salt 1	N-Alkylindole 3	C-Alkylindole 4		N,C-Dialkylindole 5	
1	2	3	5	6	7	8	9		
1	6a	BuI	1c	54.3	6.4	91.2	2.4	93.6	
2				67.0	76.2	17.4	6.4		23.8
3				72.9	88.4	6.8	4.8		11.6
4				57.6	25.9	67.7	6.4		74.1
5				58.3	91.8	5.5	2.7		8.2
6				84.0	96.7	1.4	1.9		3.3
7				21.4	4.6	95.4	0.0		95.4
8				19.4	96.0	3.9	0.0		3.9
9				12.7	99.8	0	0.2		0.2
10				26.4	41.0	37.1	21.9		59.0
11	80.0	82.3	17.7	0.0	17.7				
12	98.4	100	0.0	0.0	0.0				
13	61.1	7.4	84.2	8.4	92.6				
14	79.9	62.4	17.1	20.5	37.6				
15	96.1	93.4	1.0	5.6	6.6				
16	77.4	0.0	97.5	2.5	100.0				
17	66.0	28.5	63.9	7.6	71.5				
18	61.1	93.0	5.9	1.1	7.0				
19	59.4	1.4	96.0	2.6	98.6				
20	65.7	73.1	10.2	16.7	26.9				
21	71.8	97.9	1.6	0.5	2.1				
22	56.3	13.4	73.1	13.5	86.6				
23	49.3	95.6	0.0	4.4	4.4				
24	27.1	100	0	0	0				
25	98.7	0.0	4.7	95.3	100.0				
26	86.2	97.5	2.5	0.0	2.5				
27	79.3	98.5	1.5	0	1.5				
28	73.1	0.0	88.3	11.7	100.0				
29	69.2	26.2	57.1	16.7	73.8				
30	56.5	92.6	5.6	1.8	7.4				
31	76.4	1.8	93.8	4.4	98.2				
32	79.5	78.9	18.7	2.4	21.1				
33	83.8	80.4	15.0	4.6	19.6				
34	82.7	11.3	86.9	1.8	88.7				

TABLE 1. (continued)

1	2	3	4	5	6	7	8	9
35			1b	84.3	89.4	9.0	1.6	10.6
36			1a	89.5	94.9	3.3	1.8	5.1
37	6d	BuI	1c	69.6	21.0	75.8	3.2	79.0
38			1b	83.9	78.7	8.4	12.9	21.3
39			1a	100.0	94.7	0.0	5.3	5.3
40		BuBr	1c	60.7	2.9	94.4	2.7	97.1
41			1b	88.4	90.4	3.7	5.9	9.6
42			1a	100.0	98.4	0.0	1.6	1.6
43	6e	BuI	1c	87.0	35.6	57.5	6.9	64.4
44			1b	97.5	71.5	6.1	22.4	28.5
45			1a	99.0	89.3	7.4	3.3	10.7
46		BuBr	1c	32.5	39.7	54.0	6.3	60.3
47			1b	82.7	92.4	2.8	4.8	7.6
48			1a	92.0	99.0	0.5	0.5	1.0
49	7	BuI	1c	74.3	1.4	95.9	2.7	98.6
50			1b	55.9	36.3	54.6	9.1	63.7
51			1a	5.4	100	0	0	0
52		BuBr	1c	22.9	2.5	97.5	0.0	97.5
53			1b	15.8	90.9	7.5	1.6	9.1
54			1a	11.5	100	0	0	0
55		BuCl	1c	33.1	0.0	100.0	0.0	100.0
56			1b	3.6	77.8	16.2	6.0	22.2
57			1a	2.4	100	0	0	0
58		PhCH ₂ Cl	1c	100.0	6.2	0.0	93.8	93.8
59			1b	63.3	33.9	66.1	0.0	66.1
60			1a	48.8	95.8	4.2	0.0	4.2
61		CH ₂ =CHCH ₂ Cl	1c	55.9	0.0	95.1	4.9	100.0
62			1b	51.6	23.1	67.3	9.6	76.9
63			1a	14.3	100	0	0	0
64	8	BuBr	1c	90.6	1.1	96.2	2.7	98.9
65			1b	84.3	88.5	11.5	0.0	11.5
66			1a	96.5	100.0	0.0	0.0	0.0

*After stirring for 5 h at 25°C (Na, Li) and at 80°C (MgI), determined by gas chromatography with a precision of ±5%.

When assessing the role of the leaving group it should be noted that both the amount of C-alkylation product **4**, and also the product of N,C-alkylation **5** in medium **6b** falls in the sequence of reagents used BuI > BuBr > BuCl, which corresponds to the order of reaction of alkyl halides in polar protic solvents (Table 1, expt. 16, 19, 22). In other ionic liquids such as **6a** and **7** the activity series falls in the opposite way, BuCl > BuBr > BuI (Table 1, expt. 1, 4, 7, 49, 52, 55). This observation compels consideration of the change of form of the interaction between ionic liquids and the reaction participants and/or the transition state. In medium **6b** this looks like a substitution reaction in polar protic solvents and in **6a** or **7** this is more a reminder of an alkylation process in polar aprotic solvents, such as acetonitrile. In the first case the Reichardt constant (E_T^N), which characterizes the overall polarity of solvents, for ionic liquid **6b** is in reality close to the corresponding Pirto constant (E_T^N for **6b** is 0.614; for methanol 0.654; for 1-propanol 0.600 [40]). For the two other ionic liquids mentioned the Reichardt constant is, regrettably, not known. For organic solvents they are known, *viz.* for acetonitrile 0.460, and for N,N-dimethylformamide 0.400 [20].

The structure of the ionic liquid itself influences the course of the alkylation reaction. The conversion of indole anion is usually greater in ionic liquids with 1,3-dialkylimidazolium cation (for example, Table 1, expt. 16 and 49; 19 and 52; 22 and 55). Here it is worth mentioning that the 1,3-dialkylimidazolium salt forms its own strong hydrogen bonds with reactants using the C(2)-H bond of the imidazolium cation. Comparison of the influence of certain imidazolium salts shows that when assessing them the effect of the anion of the ionic liquid should also be considered, as this is at least reflected in the rate of conversion of substrate (Fig. 4).

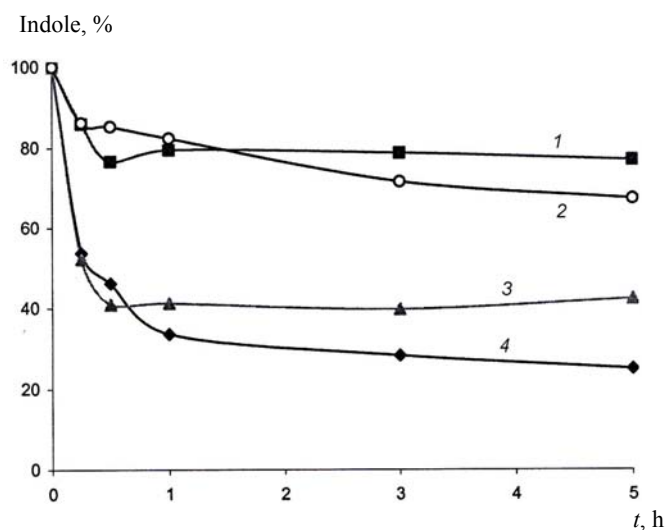


Fig. 4. Alkylation of indolylmagnesium iodide with 1-bromobutane in various ionic liquids (at 80°C): 1 – **7**; 2 – **6e**; 3 – **6a**; 4 – **6b**.

When assessing the role of the anion of an ionic liquid we note that ionic liquids with a bromide anion provide a higher conversion than tosylate or mesylate anions. For example, indolylmagnesium iodide achieves a higher conversion of substrate on reaction with butyl iodide in a medium of **6b** than in **6a** (Table 1, expt. 1 and 16). In ionic liquids with tosylate anion, in their turn, a larger amount of N-alkylation product **3** is formed than in an ionic liquid with a bromide anion (Table 1, expt 1, 4, 10, 43, 46).

As is evident from Fig. 4 the rate of conversion of indolylmagnesium iodide **1c** in the alkylation reaction with butyl bromide is less in **6a** than in **6b**. The conversion is greater with aliphatic mesylates than with aromatic tosylates (Table 1, expt 1, 4, 37, 40, 46). Comparing the effect on the alkylation reaction of ionic

liquids with sulfonate and sulfate anions **6a,c-e**, the biggest conversion was successfully obtained using the bipolar ionic liquid 3-[3-butyl-1-imidazolium]propan-1-sulfonate (**6c**) (Table 1, expt. 31, 34 as against 1, 4, 37, 40, 46), in which the disposition of cation and anion in space is fixed. However it is seen that ionic liquids with aliphatic anions **6c,d** assist conversion better than the solvents, ionic liquids, containing aromatic anions **6a,e** (Table 1, expt. 31, 34, 37, 40 against 1, 4, 43, 46). Consequently the alkylation reaction occurs more rapidly in ionic liquids not containing aromatic anions.

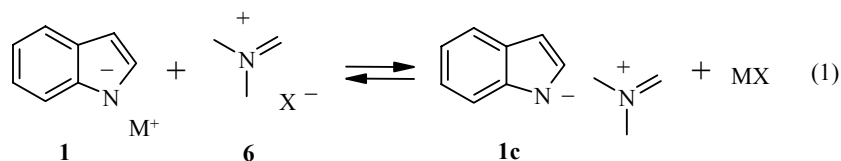
A change in the structure of the cation of the ionic liquids gives a greater possibility of increasing the rate of the alkylation reaction under study. If the ionic liquid contains an imidazole ring then the amount of C-alkylation product **4** increases in the following order of reactants BuI > BuBr > BuCl. On comparing the aliphatic ionic liquid **8** with the aromatics **6b** and **7**, we see that in the first case the conversion is greater than in the two others (Table 1, expt. 19, 52, 64). The observation obliges us to think that the interaction of the hydrogen bonds formed by the cation of the ionic liquid and/or the system of π -electrons between the ionic liquid and the transition state of the alkylation reaction delays conversion of the substrate somewhat.

The length of the alkyl chain in the cation of the ionic liquid and also the hydrophobicity of this cation influence the rate of conversion of substrate and the distribution of isomers in the product mixture. In a medium of compounds **6a** and **6e** the conversion in the alkylation of indolylmagnesium iodide with butyl bromide was reduced with increasing length of the alkyl chain. Meanwhile, in the ratio of isomers the butyl group in the cation of the ionic liquid provides greater formation of the N-alkylation product **3** than the short methyl group (Table 1, expt. 4 and 46). This effect enables understanding of the leveling effect of the ionic liquids mentioned later in the text.

The rate of alkylation of indole salts and the distribution of isomers in the product mixture in ionic liquids is markedly different from the results of conversion in molecular liquids. The rate of the investigated alkylation reaction in ionic liquids is far more rapid than in molecular solvents, i.e. in the usual organic solvents, in spite of the fact that the overall polarity of an ionic liquid is approximately equal to the polarity of propanol, acetonitrile, and other polar solvents, judging by the value of the Reichardt constant. Comparison of the rate of alkylation in organic solvents (THF 48 h, toluene 6-8 days [33], and hexamethylphosphotriamide (HMPT) 15 h [33]) and in ionic liquids (~5 h) clearly points in favor of the latter.

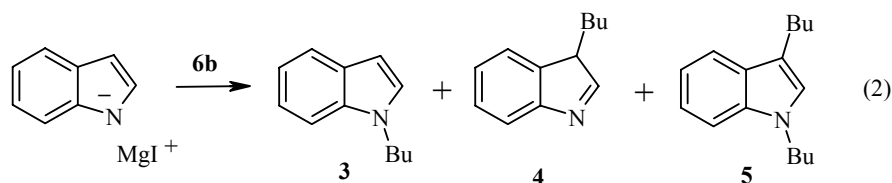
In our experiments in ionic liquids the concentrations of substrate and reagent used were 0.7 and 1.4 M respectively. They differed little from the concentrations of substrate and reagent in alkylation reactions in organic solvents described in the literature, which were 0.89 and 0.89 M in N,N-dimethylformamide and 0.89 and 0.89 M in tetrahydrofuran [34]. However it is impossible to forget that in a medium of ionic liquid the interactions both between molecules of ionic liquids, substrate, and reagent, and also between ionic liquids and the reaction transition state, differ significantly from the interactions in organic solvents. Ion-ion and ion-dipole interactions dominate in ionic liquids and are stronger than ion-dipole and dipole-dipole interactions in the case of organic solvents.

Regarding the ratio of isomers of reaction products, the product of the kinetically controlled reaction is formed more in ionic liquids than in organic solvents. Ionic liquids significantly reduce the specific interaction of metal cation with its ambident anion, i.e. the influence of this cation is leveled out. The effect of such leveling is even observed when the specific interaction of ambident anion with metal cation is expressed very

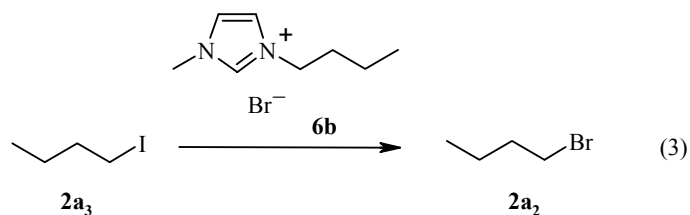


clearly, as for example the interaction between magnesium cation and indole anion. The effect of leveling may be explained by the active interchange of ions between the ionic liquid and the substrate, which reduces the effect of the opposite ion on the ambident anion.

The alkylation of indole salts is, regrettably, accompanied by side reactions. Firstly, ionic liquids themselves serve as alkylating reagents like other quaternary ammonium salts. This parasitic alkylation reaction occurs in small yield ($\leq 3\%$) at room temperature, but the yield grows at increased temperature (8%).



Another side reaction is linked with the change in structure of the reagent in the course of the alkylation reaction. On adding the alkylating reactant to the ionic liquid (in two-molar excess) replacement occurs of the halogen atom in it by the anion of the ionic liquid. The influence of this undesirable reaction also grows with increased temperature (Table 2).



It is not worth denying or replacing the side reactions mentioned as a result of which a mixture of products is formed in ionic liquids. Separation of these mixtures requires additional work and reduces the preparative yields of the reaction products.

TABLE 2. Replacement of Halogen Atom Between Ionic Liquid and Butyl Halide

Ionic liquid	Reaction conditions		Composition of product mixture			
	T, °C	Time, h	Reactant*	Amount, %	Product	Amount, %
6a	80	0.5	Bu-I	9.6	Bu-OTs	0.4
	80	5	Bu-I	98.1	Bu-OTs	1.9
6b	25	0.5	Bu-I	96.5	Bu-Br	6.2
	25	5	Bu-I	86.7	Bu-Br	23.6
	80	0.5	Bu-I	38.0	Bu-Br	62.0
	80	5	Bu-I	31.4	Bu-Br	68.6
	70	0.5	Bu-Cl	91.3	Bu-Br	8.7
	70	5	Bu-Cl	65.3	Bu-Br	34.1

* Ratio of reactant–indole anion, 2:1.

EXPERIMENTAL

The ionic liquids 1,3-dimethylimidazolium *p*-toluenesulfonate (**6a**), 1-butyl-3-methylimidazolium bromide (**6b**), 1-butyl-3-methylimidazolium *p*-toluenesulfonate (**6e**), and 1-heptylpyridinium bromide (**7**) were obtained by the known method of [41, 42]. 1-Ethyl-3-methylimidazolium methanesulfonate was purchased from Solvent-Innovation, and the other reactants from Aldrich. All were used without further purification. Solvents were dried and distilled before use. 1-Butylindole (**3a**) was synthesized according to the method of [43], 3-butylindole (**4a**) according to [44], 1,3-dibutylindole (**5a**) according to [32]. 1-Benzylindole (**3b**), 3-benzylindole (**4b**), 1,3-dibenzylindole (**5b**), 1-allylindole (**3c**), 3-allylindole (**4c**), and 1,3-diallylindole (**5c**) were obtained by the method of [34].

Analyses by gas chromatography were carried out on a Hewlett Packard 5890 instrument using a flame-ionization detector with flow rates of hydrogen 30, compressed air 300, and helium 25 ml/min. A DB-5MS column was used, injector temperature 250°C. The temperature regimen for analysis was established at initial temperature 50°C (1 min), then increasing (10°C/min) to 250°C, final temperature 250°C (for 10 min). The GC/MS analyses were taken on a Shimadzu GC 2010 apparatus with a QP 2010 mass spectrometer, energy of ionizing electrons 70 eV, division ratio of carrier gas in injector 1:30, and a OAC 20i automatic injector was used. Sample volume was 1 µl for all analyses.

The NMR spectra were taken on a Varian Mercury BB (200 MHz) spectrometer in DMSO, internal standard was TMS.

3-(3-Butyl-1-imidazolio)propane-1-sulfonate (6c). 1-Butylimidazole (3.00 g, 24 mmol) was dissolved in dry ethyl methyl ketone (150 ml) and 1,3-propane sulfone (2.93 g, 24 mmol) was added to the solution. The mixture was heated at 85-90°C for 3 h, then cooled, and the solid filtered off. After crystallization from a mixture of ethanol–water, 1:1, colorless crystals of compound **6c** were obtained of mp 175-176°C. Yield was 3.14 g (53%). NMR spectrum, δ , ppm (*J*, Hz): 9.18 (1H, s, CH); 7.78 (2H, d, *J* = 2.9, 2CH); 4.28 (2H, t, *J* = 6.6, CH₂); 4.15 (2H, t, *J* = 6.6, CH₂); 2.38 (2H, t, *J* = 6.6, CH₂); 2.07 (2H, m, CH₂); 1.76 (2H, m, CH₂); 1.23 (2H, m, CH₂); 0.88 (3H, t, *J* = 7.3, CH₃).

Alkylation of Indolylmagnesium Iodide with 1-Bromobutane in Ionic Liquid 6b. Dry diethyl ether (3 ml) was poured onto activated by iodine magnesium (0.06 g, 2.26 mmol) and a solution of iodomethane (0.14 ml, 2.05 mmol) in dry diethyl ether (3 ml) was added dropwise at a rate providing steady boiling of the mixture. A solution of indole (0.20 g, 1.71 mmol) in dry diethyl ether (3 ml) was added to the reacted suspension, and the mixture stirred at 25°C for 0.5 h. The diethyl ether was removed from the reaction with a stream of argon. Ionic liquid **6b** (0.75 g, 3.42 mmol) and 1-bromobutane (0.47 g, 3.42 mmol) were added to the obtained mixture of indolylmagnesium iodide, and the mixture was then stirred and heated at 80°C. Samples (1 mg), taken from the mixture after definite periods of time (0.25, 0.5, 1, 3, and 5 h), were shaken with 5% NH₄Cl, and extracted with diethyl ether (3×5 ml). The diethyl ether solution was dried over MgSO₄. The obtained extract was analyzed by gas chromatography.

Alkylation of indolyllithium with alkylating agents in ionic liquids was carried out analogously, only when obtaining the indole salt butyllithium was used with diethyl ether as solvent.

Alkylation of indolylsodium with alkylating agents in ionic liquids was carried out analogously. When obtaining indole salts sodium methylate was used with methanol as solvent.

The other indole derivatives **3-5** were obtained analogously. 1-Chlorobutane, 1-bromobutane, 1-iodobutane, benzyl chloride, and 3-chloro-1-propene (allyl chloride) were used as agents for alkylating indole salts at room temperature (25°C) and at 80°C. Structures of products were confirmed by GC/MS and NMR spectra. The progress of experiments was followed by gas chromatography. Each measurement was repeated three times. The results are correlated in Table 1 and are reflected in Figs. 1-4.

Alkylation of Indolylmagnesium Iodide by an Ionic Liquid. Dry diethyl ether (3 ml) was added to activated by iodine magnesium (0.06 g, 2.26 mmol) and a mixture of methyl iodide (0.14 ml, 2.05 mmol) in dry

diethyl ether (3 ml) was added dropwise so that steady boiling of the mixture was provided. A solution of indole (0.20 g, 1.71 mmol) in dry diethyl ether (3 ml) was added to the reacted suspension and the mixture stirred at 25°C for 0.5 h. The diethyl ether was removed from the reaction mixture with a stream of argon. Ionic liquid **6b** (0.75 g, 3.42 mmol) was added to the residue of indolylmagnesium iodide, and the mixture obtained was stirred and heated at 80°C for 6 h. Samples (1 mg), taken from the mixture, were extracted with diethyl ether (3×5 ml). The extracts obtained were analyzed by gas chromatography.

Replacement of Halogen Atoms in the Reactant. 1-Iodobutane (0.84 g, 4.56 mmol) was added to ionic liquid **6b** (0.50 g, 2.28 mmol). The mixture was stirred at various temperatures (Table 2) for 0.5 or 5 h. Samples (1 mg) taken from the mixture at the end of the reaction were extracted with petroleum ether (3×5 ml). The obtained extract was analyzed by gas chromatography (Table 2).

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