METAL ION TRANSPORT THROUGH BULK LIQUID MEMBRANE MEDIATED BY CATIONIC LIGAND SURFACTANTS

Eva SVOBODOVÁ[1], Radek CIBULKA[2], František HAMPL[3,*], Jan ŠMIDRKAL[4] and František LIŠKA[5]

Department of Organic Chemistry, Institute of Chemical Technology, Prague, Technická 5, 166 28 Prague 6, Czech Republic; e-mail: [1] svobodoe@vscht.cz, [2] cibulkar@vscht.cz, [3] hamplf@vscht.cz, [4] smidrkal@sas.upenn.edu, [5] liskaf@vscht.cz

Received December 20, 2004
Accepted February 21, 2005

A series of *N*,*N*,*N*-trialkyl-2-(hydroxyimino)-2-(pyridin-2-yl)ethan-1-aminium nitrates **3a**–**3h** and *N*,*N*,*N*-trialkyl-4-(hydroxyimino)-4-(pyridin-2-yl)butan-1-aminium nitrates **3i**–**3l** representing cationic surfactants with a powerful 1-(hydroxyimino)-1-(pyridin-2-yl)alkyl chelating subunit were prepared as potential selective metal ion extractants. Their extraction ability was tested in transport of Cu^{2+}, Ni^{2+}, Co^{2+}, and Pd^{2+} through a bulk liquid membrane. The introduction of the cationic group into the extractant molecule increases the selectivity and facilitates the metal ion transport as shown by comparing the transports carried out with ligand surfactants **3** and lipophilic alkyl pyridin-2-yl ketoximes **2**. The efficiency and selectivity of the metal ion transport mediated by ligand surfactants **3** depends predominantly on their structure and lipophilicity, i.e. on the number and length of hydrophobic alkyl chains and on the length of the spacer connecting the chelating moiety with the cationic head group of the surfactant.

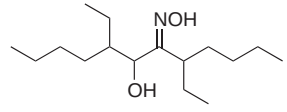
Keywords: Ligands; Liquid membranes; Metal ion transport; Oximes; Pyridine derivatives; Surfactants; Copper; Palladium; Quaternary ammonium salts; Extractions.

Important industrial processes like hydrometallurgy, recovery of precious metals, waste water treatment, and isolation and separation of radionuclides utilize solvent extraction[1] or metal ion transport through liquid membrane[1b,2].

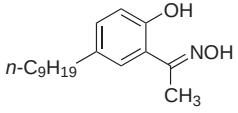
Liquid membrane stands for an organic solvent immiscible with water separating source and receiving aqueous phases. Metal ion transport through liquid membrane from the source phase into receiving phase is mediated by a lipophilic ligand dissolved in the membrane. So far, three types of liquid membranes differing in the thickness of organic layer and mutual positions of all phases have been described[2b–2f]: bulk, supported, and emulsion liquid membranes. From the theoretical point of view, metal ion transport through liquid membrane provides a useful tool for the inves-

tigation of interactions between metal ions and ligands at the aqueous/organic interface, which enables exploring and characterizing the strength and selectivity of host–guest interactions and other features as well as studying the principles of specific metal ion transport and partitioning in living systems[1b,2d].

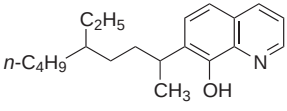
Numerous metal ion carriers derived for example from crown ethers and their aza analogues (azacrowns, cyclens and cyclams), lariate ethers, and calixarenes have been reported in countless papers over the years (see, e.g., reviews[2b,2d,2f,3a–3c] and several recently published papers[3d–3i]). Various ligands of much simpler structures have been designed for industrial applications. Clearly, both the efficiency and selectivity of these extractants are usually lower compared to the above-mentioned ligands tailored often as selective cation receptors. Oximes of α-hydroxyketones, e.g. LIX 63 (lit.[4]), oximes of *o*-hydroxyacetophenones, e.g. LIX 84 (lit.[5]), 7-alkyl-8-hydroxyquinolines, e.g. Kelex 100 (lit.[6]), and dialkyl phosphates, e.g. sodium bis(2-ethylhexyl)phosphate[7] (D2EHPA) can be given as examples of industrial extractants. Tetraazadiol **1** prepared by Menger[8] seems to be one of the most efficient Cu^{2+} carriers so far reported.



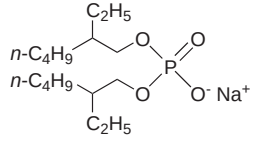
LIX 63



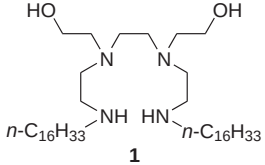
LIX 84



Kelex 100



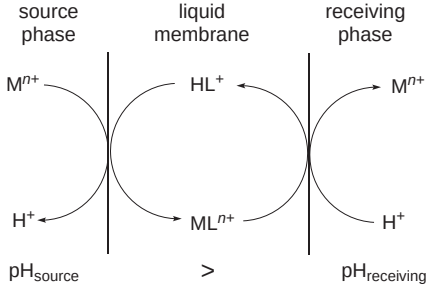
D2EHPA



1

To disclose the mechanism of metal ion transfer across the aqueous/organic interface as well as the factors governing this process, Tondre and co-workers investigated complexation and metal ion transport in micelles and microemulsions[6a,9]. In several cases[6a,9e] they observed remarkable differences in the rates of various metal ion extraction by the same ligand. Similar kinetic selectivity has been reported for lipophilic alkyl pyridin-2-yl ketoximes **2** and Cu^{2+}, Co^{2+}, and Ni^{2+} ions in micelles of cetyltrimethylammonium bromide[10].

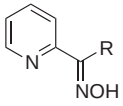
Despite its potential, the focus on surfactant-like metal ion carriers has been low so far. Only a few examples of lipophilic ligands possessing an ionic head group have been reported[1b,2d]. The ionic head group in these ligand surfactants is usually formed by protolytic reactions. Ligands comprising amino[8,11] and carboxylic[12] functions serve as examples. If these types of ligands are employed in metal ion transport through liquid membrane, the uphill transport (i.e. transport against the concentration gradient) and the shuttle effect (i.e. transport of more than stoichiometric amount of the metal ion) can be observed. There are two essential prerequisites for successful uphill transport (Scheme 1): (i) metal ion transport from the source phase is compensated by proton counter-transport from the receiving phase; the constant difference in pH values of the source and receiving phases is a driving force of the process, (ii) an ionizable function participates in coordination to metal ion.



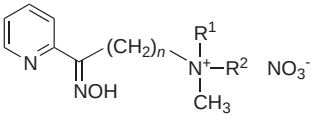
SCHEME 1

N,*N*,*N*-Trialkyl-ω-(hydroxyimino)-ω-(pyridin-2-yl)alkan-1-aminium salts **3** possessing a cationic head group and 1-(hydroxyimino)-1-(pyridin-2-yl)-alkyl chelating subunit are other examples of ligand surfactants. Originally, we have synthesized ethan-1-aminium salts **3a**–**3c** (R^1 = CH_3, R^2 = alkyl C_8–C_{12}) to serve as ligands for metallomicellar hydrolytic catalysts[13a]. In pilot experiments, we have also examined their ability to extract metal ions from aqueous phase into organic solvents; two-chain salts **3f** and **3h** were

involved in this study as well[13b]. The efficiency of the carrier **3f** in Cu^{2+} transport through liquid membrane was comparable to that of Menger's "magic" tetraazadiol **1**.



2	R
a	CH_3
b	*n*-C_3H_7
c	*n*-C_6H_{13}
d	*n*-C_8H_{17}
e	*n*-$C_{10}H_{21}$
f	*n*-$C_{12}H_{25}$



3	*n*	R^1	R^2
a	1	CH_3	*n*-C_8H_{17}
b	1	CH_3	*n*-$C_{10}H_{21}$
c	1	CH_3	*n*-$C_{12}H_{25}$
d	1	CH_3	*n*-$C_{16}H_{33}$
e	1	*n*-C_6H_{13}	*n*-C_6H_{13}
f	1	*n*-C_8H_{17}	*n*-C_8H_{17}
g	1	*n*-$C_{10}H_{21}$	*n*-$C_{10}H_{21}$
h	1	*n*-$C_{16}H_{33}$	*n*-$C_{16}H_{33}$
i	3	*n*-C_6H_{13}	*n*-C_6H_{13}
j	3	*n*-C_8H_{17}	*n*-C_8H_{17}
k	3	*n*-$C_{10}H_{21}$	*n*-$C_{10}H_{21}$
l	3	*n*-$C_{12}H_{25}$	*n*-$C_{12}H_{25}$

Promising results of our preliminary transport experiments with ethanaminium salts[13b] **3a**–**3c**, **3f**, and **3h** encouraged us to perform more detailed and systematic investigation of the extraction ability in a series of *N*,*N*,*N*-trialkyl-ω-(hydroxyimino)-ω-(pyridin-2-yl)alkan-1-aminium salts **3**. We considered the ligand surfactants **3** to be prospective metal ion carriers: their amphiphilic nature allows them to orient themselves on the phase interface and penetrate with their chelating subunit into aqueous phase as shown schematically in Fig. 1. Protonation of nitrogen atom of pyridine fa-

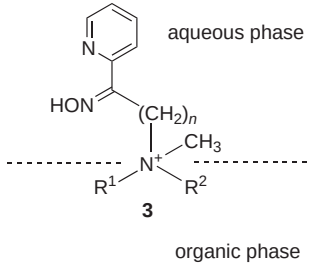


FIG. 1
Expected orientation of the ligand surfactants **3** at the aqueous/organic interface

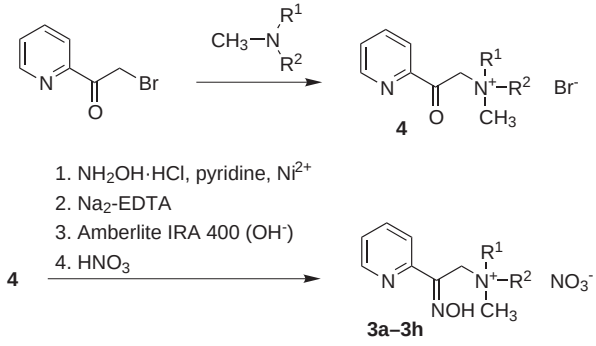
cilitates metal ion release at the liquid membrane/receiving phase interface and allows counter-transport of protons.

This paper is focused on the influence of the quaternary ammonium moiety structure and the length of the spacer between the ionic head group and the chelating function on the extraction ability of cationic ligand surfactants. Besides, the efficiency of lipophilic alkyl pyridin-2-yl ketoximes **2** in metal ion transport through liquid membrane was examined as well. These experiments served as a reference in the evaluation of the influence of the cationic head group in the molecule of the carrier on the metal ion transport rate and selectivity.

RESULTS AND DISCUSSION

*Syntheses of Metal Ion Carriers **2** and **3***

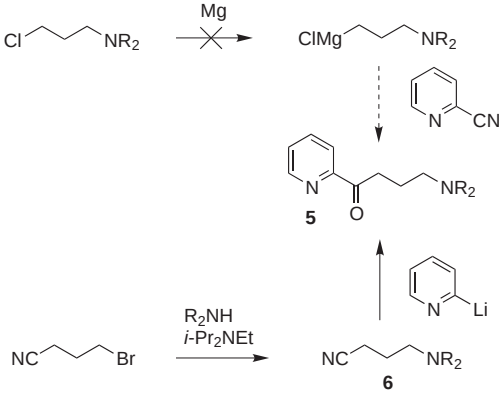
The new ethanaminium ligands **3d**, **3e**, and **3g** employed in this study were prepared using the described procedure[13b]: 2-(bromoacetyl)pyridine and corresponding lipophilic tertiary amines afforded quaternary 2-oxo-2-(pyridin-2-yl)ethan-1-aminium salts **4**. Salts **4** were transformed to ligand surfactants **3d**, **3e**, and **3g** by the reaction with hydroxylamine utilizing the stabilizing effect of Ni^{2+} ions[13b] followed by anion exchange (Scheme 2).



SCHEME 2

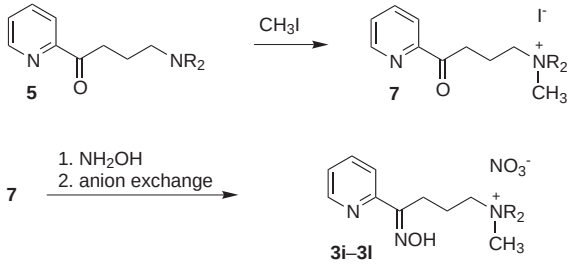
Two synthetic routes for the preparation of ketones **5**, the key intermediates in the synthesis of butanaminium ligands **3i**–**3l**, were considered. The first involved the addition of the 3-(dialkylamino)propylmagnesium halide to pyridine-2-carbonitrile, the other the addition of (pyridin-2-yl)lithium to 4-(dialkylamino)butanenitriles **6** (Scheme 3). Although the addition of 3-(dialkylamino)propylmagnesium chlorides to pyridine-2-carbonitrile seemed to be the method of choice (various 4-(dialkylamino)butan-2-ones

have been prepared using the procedure[14]), the preparation of lipophilic 3-(dialkylamino)propylmagnesium chlorides (R = n-C_6H_{13} and higher homologues) failed in our hands. The alternative pathway, i.e. the addition of (pyridin-2-yl)lithium to nitriles **6**, afforded ketones **5**. Nitriles **6** were prepared from commercially available 4-bromobutanenitrile and corresponding dialkylamines in the presence of the Hünig base[15] (Scheme 3).



SCHEME 3

Quaternization of ketones **5** with methyl iodide followed by the reaction of salts **7** with hydroxylamine and anion exchange in the obtained iodides **8** afforded the desired ligand surfactants **3i**–**3l** in good yields (Scheme 4). The reverse order of these reactions, i.e. the reaction of ketones **5** with hydroxylamine followed by quaternization of the obtained oximes, led to complex mixtures of products. Dichloromethane was found to be a satisfactory solvent for quaternization of amino group in lipophilic ketones **5**. The reaction time in this case (tens of hours) can be reduced to 10 min when the reaction is performed in microwave oven using toluene as a solvent. The iodides **8** were converted to nitrates **3i**–**3l** to prevent air oxidation of iodide ion during the metal ion transport experiments. The anion exchange using Amberlite IRA 400 gave higher yields (ligands **3i**–**3k**) than that performed with silver nitrate (ligand **3l**).



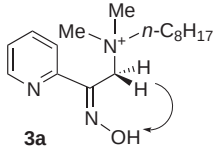
SCHEME 4

All the prepared salts **3** were of uniform configuration since only one set of signals was found in their ^{1}H and ^{13}C NMR spectra. In the case of ethanaminium salt **3a**, irradiation of methylene protons at C-1 affords NOE transferred to proton of the hydroxyimino group thus giving evidence of *E* configuration at the C=N bond (Fig. 2). We assume that all the other investigated salts **3** were of the same configuration since the chemical shifts of corresponding heteroaromatic protons were practically the same. It is known[16] that chemical shifts of heteroaromatic protons in alkyl or aryl pyridin-2-yl ketoximes are strongly influenced by the C=N bond configuration – the differences in chemical shifts of the corresponding heteroaromatic protons in *E* and *Z* isomers being up to 0.28 ppm (lit.[16a]).

Alkyl pyridin-2-yl ketoximes **2** were prepared from pyridine-2-carbonitriles analogously to the described procedure[10a].

Transport of Metal Ions

The extraction ability of the prepared metal ion carriers **2** and **3** was examined in transport of metal ions through bulk liquid membrane. The transport cell used (Fig. 3) was constructed to follow the design of apparatus described elsewhere[2a–2c,8]. Chloroform layer (70 ml) containing the tested ligand **2** or **3** (70 μmol) was used as the liquid membrane which separated the source (50 ml, pH 4.6) and the receiving (25 ml, pH 1.0) phases. The experiments were initiated by charging the apparatus with the source phase containing the total metal ion amount to be transported (250 μmol). The 2:1 ratio of the source and receiving phase volumes was chosen to keep a substantial part of the transport experiment under uphill conditions (assuming negligible accumulation of the metal ion in the membrane, the uphill transport starts at the moment when one third of the metal ion amount has been transferred into receiving phase). During the transport experiments, the metal ion content was monitored in all the phases – source and receiving, and in the membrane. To get a better insight into the trends



3a

FIG. 2
NOE of salt **3a**

of the structure/transport ability relationship, the results of our previously performed experiments with ligand surfactants[13b] **3a**–**3c**, **3f**, and **3h** were also included in the discussion given below.

Rigorous analysis of the obtained metal ion concentration vs time data in all the phases is rather complex and lies beyond the scope of this work. Exact mathematical model should take into consideration – besides the metal ion transport from the source into receiving phase – also the non-productive proton transport from the receiving into source phase and the distribution of the ligand between the membrane and aqueous phases, which can be significant especially in transport experiments involving ligands of lower lipophilicity. Therefore, we needed simple and readily available criteria allowing a comparison of the transport effectivity of the investigated ligands. In our opinion, the amount of metal ion transferred from the source phase into membrane (shown as the percentage of the total metal ion amount in the experiment) during the first 24 h of the transport can be considered as a plausible approximation of the initial transport rate across this interface. The metal ion amount transferred into receiving phase during this period is an approximation of the initial overall metal ion transport rate which can serve as a measure of the ligand efficiency.

Cu^{2+} Transport

No Cu^{2+} transport occurred in the absence of the carrier. All the investigated types of ligands mediated uphill transport of Cu^{2+} with the only exception of ligand **3a** (no transport occurred). The transport rates in experi-

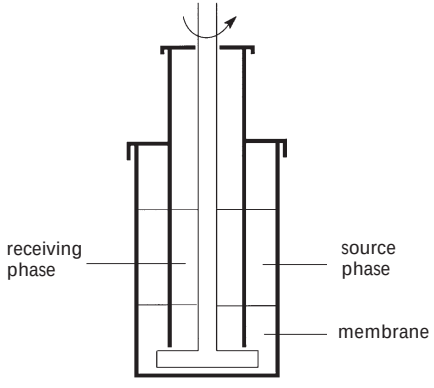


FIG. 3
Transport cell

ments mediated by short-chain ligands **2a** and **3i** were very low. The stoichiometry of Cu^{2+} complexes with similar types of ligands was reported to be both 1:1 (lit.[17a–17c]) and 1:2 (lit.[17b,17d,17e]). Taking into consideration any of possible stoichiometries (both 1:2 and 1:1) the occurrence of the shuttle effect in all transports is unquestionable (Table I). The course of the Cu^{2+} transports mediated by ligands **3e** and **3k** (Fig. 4) can be given as typical examples. In all cases, the rates of the Cu^{2+} transfer across both interfaces were similar since no substantial accumulation of the metal ion in the membrane was observed.

It is generally known[1–3] that lipophilicity of the ligand influences significantly its transport or extraction ability. Therefore, we plotted the observed initial Cu^{2+} transfer rate into membrane as well as the initial overall transport rate against log *P* values (logarithm of the partition coefficient between octan-1-ol and water) for all the investigated ligands (Fig. 5). Values of log *P* were calculated using a software package Pallas 1.2 (lit.[18]).

All the investigated carriers (two chain ammonium salts with monomethylene spacer **3e**–**3h**, two chain salts with trimethylene spacer **3i**–**3l**, and alkyl pyridin-2-yl ketoximes **2**) exhibit similar dependences of the initial Cu^{2+} transfer rate into membrane as well as the dependence of the initial overall transport rate on their lipophilicity. In transports mediated by alkyl pyridin-2-yl ketoximes **2**, the Cu^{2+} extraction from the source phase is somewhat faster than its release from the membrane into receiving phase.

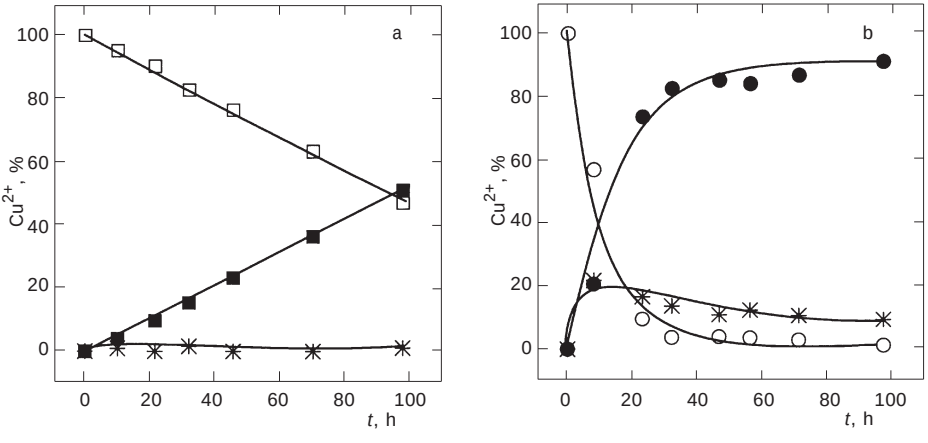


FIG. 4
The course of the Cu^{2+} transport mediated by ligand **3e** (a) and **3k** (b). Cu^{2+} content in the source phase (empty symbols), receiving phase (full symbols), and in the membrane (asterisks) is given as a percentage of the total Cu^{2+} amount charged into transport cell

TABLE I
Cu^{2+} transport mediated by ligands **2** and **3**

Ligand	log *P*	Cu^{2+} amount in aqueous phases after 24 h, %[a]		Cu^{2+} amount in receiving phase after 100 h, %[a]
		source phase	receiving phase	
2a	0.83	88	7	69[b]
2b	2.03	40	57	81
2c	3.56	36	38	88
2d	4.58	39	38	82
2e	5.60	44	34	87
2f	6.62	61	20	86
3d	5.47	43	34	51
3e	2.87	90	10	94
3f	4.91	21	70	84
3g	6.95	41	54	97
3i	3.21	94	3	17[c]
3j	5.33	38	51	94
3k	7.37	10	74	90
3l	9.41	42	42	85

[a] Relative to initial amount. [b] After 600 h. [c] After 200 h.

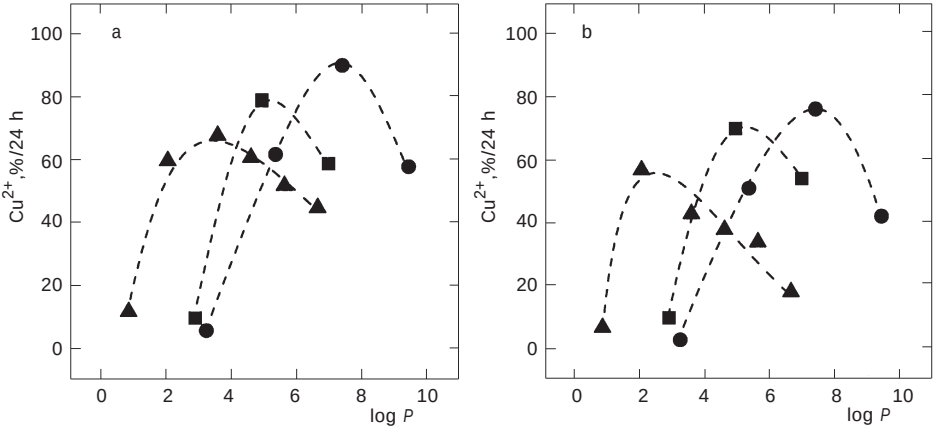


FIG. 5
Initial Cu^{2+} transfer rate from the source phase into membrane vs lipophilicity of the ligand (log *P*) (a). Overall transport rate vs lipophilicity of the ligand (log *P*) (b). Ligands: **3e**–**3g** (■), **3i**–**3l** (●), **2** (▲). The dashed lines should only help the eyes to follow the points

Nevertheless, even in these cases the maximum Cu^{2+} accumulation in the membrane in the initial phase of the experiment did not exceed 20% of the total metal ion amount. For each structural type, the carrier efficiency vs log *P* profile shows a marked optimum (Fig. 5). This optimum lipophilicity increases when going from ketoximes **2** to salts **3i**–**3l** possessing trimethylene spacer. The maximum observed Cu^{2+} transport rate increases in the same order. A comparison of the most efficient ligands from each series of homologues (ethanaminium salt **3f**, butanaminium salt **3k**, and propyl pyridin-2-yl ketoxime **2b**) clearly demonstrates that the presence of the quaternary ammonium group in the carrier molecule increases the rate of the metal ion transport. Apparently, the presence of cationic head group in the ligand molecule facilitates its adsorption on the interface in proper orientation for the metal ion withdrawal from the source phase or for its release into receiving phase. Of the two chain monomethylene ligands **3e**–**3h** and trimethylene ligands **3i**–**3l**, the most efficient Cu^{2+} carriers were salts **3f** and **3k**. Most likely, the higher efficiency of ligand **3k** compared with that of ligand **3f** is a consequence of its longer spacer between the quaternary nitrogen and pyridine moiety. It is reasonable to assume that higher flexibility of the chelating function at the interface and the possibility of its deeper penetration into aqueous phase facilitates the complexation and decomplexation at the source phase–membrane and membrane–receiving phase interfaces.

In the case of salts **3**, a question also appeared about the influence of the number of lipophilic alkyl chains attached to quaternary nitrogen on the transport efficiency. A comparison of the rates of Cu^{2+} transport mediated by two chain salt **3f** (the most efficient two chain carrier with monomethylene spacer) and by analogous single chain salt **3d** of similar lipophilicity (Table I) provides evidence of higher efficiency of two chain ligands.

Other Metal Ion Transport

Majority of transport experiments performed with ligands **2** and **3** did not show detectable changes of the Ni^{2+} and Co^{2+} content in the source phase. The only exceptions were single chain decyl and dodecyl salts **3b** and **3c** which slowly transported Ni^{2+} ions into receiving phase[13b]. Interestingly, the more lipophilic dodecyl ligand **3c** is a worse Ni^{2+} carrier than the decyl salt **3b**. Slow Ni^{2+} transport occurred also in the case of short-chain ligands **2a**–**2c**. Similarly to salts **3b** and **3c**, the Ni^{2+} transport rate decreases with the ligand lipophilicity (Table II).

What is the source of the observed selectivity in metal ion transport mediated by ligands **2** and **3**? While Cu^{2+} usually forms square-planar complexes, the metal ions that are not transported (Co^{2+} and Ni^{2+}) have octahedral coordination sphere. As drawn schematically in Fig. 6, lipophilic chelating ligands in square-planar complexes can be arranged at the interface in such a way that all hydrophobic alkyl chains are oriented into organic phase. On the other hand, this is not possible for lipophilic ligands forming octahedral complexes. Therefore, the formation of octahedral complex at aqueous/organic interface is disfavoured although under normal circumstances (i.e. in homogeneous solutions) ligands possessing

TABLE II
Ni^{2+} transport mediated by ligands **2** and **3**

Ligand	log *P*	Ni^{2+} amount in aqueous phases after 24 h, %[a]		Ni^{2+} amount in receiving phase after 100 h, %[a]
		source phase	receiving phase	
2a	0.83	77	10	29
2b	2.03	94	4	21
2c	3.56	78	8	8
3b	2.41	90	10	59[b]
3c	3.43	94	6	28[b]

[a] Relative to initial amount. [b] After 200 h.

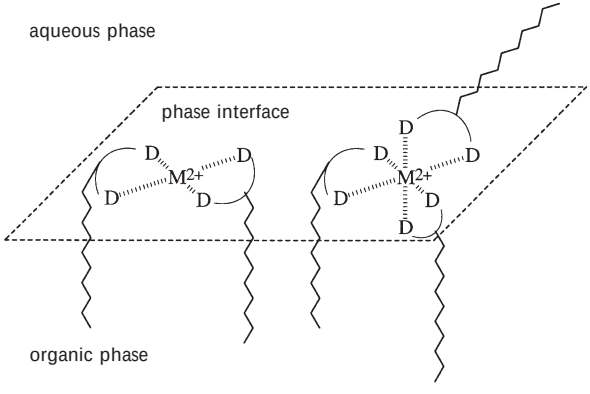


FIG. 6
Arrangement of the square-planar and octahedral metal ion complexes with lipophilic ligands at the aqueous/organic interface

1-(hydroxyimino)-1-(pyridin-2-yl)alkyl chelating unit readily form stable complexes of NiL_3 stoichiometry[19]. The orientation of hydrophobic alkyl chains of the ligand disadvantaging the formation of Ni^{2+} complexes at the aqueous/organic interface explains also the above-mentioned order of the Ni^{2+} transport rates mediated by ligands **2a**–**2c**, **3b**, and **3c**.

To verify this hypothesis we decided to test our carriers **3** in palladium transport. In addition to the fact that palladium forms square-planar complexes, it is worthy of attention for its scarcity and high price. Surprisingly, only a small number of papers dealing with Pd^{2+} transport through liquid membrane has been published so far[20].

In our preliminary experiments with Pd^{2+} transport we employed salts **3f** and **3k**, the most successful Cu^{2+} carriers. The first experiments were carried out with ligand **3f** under the same conditions as the above-mentioned Cu^{2+}, Co^{2+}, and Ni^{2+} transports. However, the results were disappointing: Pd^{2+} was accumulated in the membrane only (ca. 30% of the total metal amount) but no metal was detected in the receiving phase. Only after increasing the hydrochloric acid concentration in the receiving phase (to 5 mol l^{-1}), the transfer of Pd^{2+} ions across the membrane-receiving phase interface occurred[13b]. Most likely, the Pd^{2+} transfer from the membrane depends on sufficient concentration of chloride anions in the receiving phase due to the formation of $[PdCl_4]^{2-}$. To verify this hypothesis we performed Pd^{2+} transport using a 4.9 M NaCl solution in 0.1 M HCl as a receiving phase (i.e. we kept the same total concentration of chlorides as in the previous case). As expected, both the initial Pd^{2+} transfer rate into membrane and the initial overall rate of the transport did not differ significantly in both cases. Comparable results were obtained with the Pd^{2+} transport mediated by ligand **3k** under the same conditions (Table III).

TABLE III
Pd^{2+} transport mediated by ligands **2** and **3**

Ligand	Pd^{2+} amount in aqueous phases after 24 h, %[a]		Pd^{2+} amount in receiving phase after 100 h, %[a]
	source phase	receiving phase	
3f[b]	42	27	57
3k[b]	15	55	71
3f[c]	21	47	74
3k[c]	41	25	70

[a] Relative to initial amount. [b] 5 M HCl as a receiving phase. [c] 4.9 M solution of NaCl in 0.1 M HCl.

Conclusion

Comparison of transport experiments performed with ligands **2** without ionic head group and ligands **3** possessing a quaternary ammonium moiety demonstrates that ligand surfactants are promising agents in metal ion extractions from aqueous solutions into organic solvents. The results of the transport experiments provide evidence of both the lipophilic part of the ligand (i.e. the number and length of the hydrophobic alkyl chain) and the distance between the charged head group and the chelating unit strongly influencing the efficiency of the metal ion carrier and their usefulness in designing new ligand surfactants for metal ion extractions. Obviously, a successful extractant of this type should contain a flexible spacer allowing deeper penetration of the chelating unit into aqueous phase. Considering the lipophilic part of the molecule, two short hydrophobic alkyl chains seem to be more useful than one long chain providing the same lipophilicity. Most likely, two chain ligand surfactant molecules are able to arrange more favourably at the phase interface than the single-chain ones as a consequence of the hydrophilic/lipophilic balance[21].

Generally, the selectivity of metal ion extractions with lipophilic ligands is controlled predominantly by the stability of the resulting complex. Nevertheless, this is not the case of ligand surfactants whose mobility at the interface is restricted. Depending on the complex stoichiometry some coordination sites in the coordination sphere of the metal ion might be inaccessible to donor atoms of the ligand. This circumstance can be utilized in designing new metal ion extractants with enhanced selectivity.

EXPERIMENTAL

General

Temperature data are uncorrected. NMR spectra were recorded on Varian Gemini 300 (300.08 MHz for ^{1}H) and Bruker AMX3 400 (400.13 MHz for ^{1}H and 125.77 MHz for ^{13}C) spectrometers. Chemical shifts are given in ppm relative to an internal standard tetramethylsilane (δ 0.0), coupling constants, *J*, are given in Hz. Infrared spectra (ν in cm^{-1}) were taken on an FTIR spectrometer Nicolet 740. TLC analyses were carried out on DC Alufolien Kiesegel 60 F_{254} (Merck). Preparative column chromatography was performed on silica gel Kieselgel 60 0.040–0.063 mm (Merck). Elemental analyses were performed on a Perkin–Elmer 240 analyser.

Chemicals

All solvents were purified by standard procedures. Dihexylamine (purum), dioctylamine (purum), didecylamine (purum), *N*-ethyldiisopropylamine (purum), 4-bromobutanenitrile

(purum), butyllithium (2.5 M solution in hexane), hydroxylamine (purum), and 2-acetylpyridine (purum) were obtained from Aldrich, 2-bromopyridine (purum) and methyl iodide (purum) were products of Fluka. $Cu(NO_3)_2$ and $Ni(NO_3)_2$ (analytical grade), and other auxiliary chemicals and solvents were obtained from Lachema Brno. Didodecylamine[22], dihexadecylamine[22], *N*-methyldihexylamine[22], *N*-methyldioctylamine[22], *N*-methyldidecylamine[22], *N*-methyldihexadecylamine[22], *N*,*N*-dimethylhexadecylamine[13a], and 2-(bromoacetyl)pyridine hydrobromide[13a] were prepared using the described procedures.

Alkyl Pyridin-2-yl Ketoximes (**2**). General Procedure

Aqueous solution of hydroxylamine (50%) or aqueous solution of hydroxylamine hydrochloride and potassium carbonate were added in several portions to a stirred refluxing solution of ketone in ethanol until the starting compound was completely converted to oxime. The conversion of the reaction was monitored by TLC with eluent chloroform–methanol 100:1. After evaporation of solvents, the obtained crude oxime was purified by crystallization from ethanol–water or by column chromatography.

Methyl pyridin-2-yl ketoxime (**2a**). Yield 80%, m.p. 122–123 °C (lit.[10b] 120–122 °C). ^{1}H NMR ($CDCl_3$): 2.41 s, 3 H (CH_3); 7.26 dd, 1 H, ^2J(5,4) = ^2J(5,6) = 6.6 (H-5); 7.68 td, 1 H, ^2J(4,3) = ^2J(4,5) = 7.7, ^3J(4,6) = 1.7 (H-4); 7.84 d, 1 H, ^2J(3,4) = 7.9 (H-3); 8.64 d, 1 H, ^2J(6,5) = 4.4 (H-6).

Propyl pyridin-2-yl ketoxime (**2b**). Yield 62%, m.p. 46–49 °C (lit.[23] 48 °C). ^{1}H NMR ($CDCl_3$): 0.98 t, 3 H, ^2J(3′,2′) = 7.7 (CH_3); 1.63 qi, 2 H, ^2J(2′,1′) = ^2J(2′,3′) = 7.7 (O=CCH$_2$C**H**$_2$); 2.98 t, 2 H, ^2J(1′,2′) = 7.7 (O=CCH$_2$); 7.26 m, 1 H (H-5); 7.69 ddd, 1 H, ^2J(4,3) = ^2J(4,5) = 7.7, ^3J(4,6) = 1.7 (H-4); 7.80 dd, 1 H, ^2J(3,4) = 8.2, ^3J(3,5) = 1.1 (H-3); 8.63 dd, 1 H, ^2J(6,5) = 4.9, ^3J(6,4) = 1.1 (H-6).

Hexyl pyridin-2-yl ketoxime (**2c**). Yield 90%, m.p. 71–75 °C. ^{1}H NMR ($CDCl_3$): 0.87 t, 3 H, ^2J(6′,5′) = 5.9 (CH_3); 1.30 m, 6 H ((CH_2)$_3$); 1.58 qi, 2 H, ^2J(2′,1′) = ^2J(2′,3′) = 7.8 (HON=CCH$_2$C**H**$_2$); 2.98 t, 2 H, ^2J(1′,2′) = 7.7 (HON=CC**H**$_2$); 7.26 m, 1 H (H-5); 7.69 ddd, 1 H, ^2J(4,3) = ^2J(4,5) = 8.0, ^3J(4,6) = 1.5 (H-4); 7.8 d, 1 H, ^2J(3,4) = 7.8 (H-3); 8.62 d, 1 H, ^2J(6,5) = 3.3 (H-6). For $C_{12}H_{18}N_2O$ (206.3) calculated: 69.87% C, 8.79% H, 13.58% N; found: 69.94% C, 9.08% H, 13.52% N.

Octyl pyridin-2-yl ketoxime (**2d**). Yield 45%, m.p. 38–42 °C (lit.[10a] 38–40 °C). ^{1}H NMR ($CDCl_3$): 0.86 t, 3 H, ^2J(8′,7′) = 6.7 (CH_3); 1.25 m, 10 H ((CH_2)$_5$); 1.57 qi, 2 H, ^2J(2′,1′) = ^2J(2′,3′) = 7.5 (HON=CCH$_2$C**H**$_2$); 2.97 t, 2 H, ^2J(1′,2′) = 7.8 (HON=CC**H**$_2$); 7.26 m, 1 H (H-5); 7.67 ddd, 1 H, ^2J(4,3) = ^2J(4,5) = 7.6, ^2J(4,6) = 1.7 (H-4); 7.80 d, 1 H, ^2J(3,4) = 7.9 (H-3); 8.62 d, 1 H, ^2J(6,5) = 4.7 (H-6).

Decyl pyridin-2-yl ketoxime (**2e**). Yield 92%, m.p. 52–54 °C. ^{1}H NMR ($CDCl_3$): 0.87 t, 3 H, ^2J(10′,9′) = 7.0 (CH_3); 1.24 m, 14 H ((CH_2)$_7$); 1.57 qi, 2 H, ^2J(2′,1′) = ^2J(2′,3′) = 7.7 (HON=CCH$_2$C**H**$_2$); 2.98 t, 2 H, ^2J(1′,2′) = 7.9 (HON=CC**H**$_2$); 7.26 ddd, 1 H, ^2J(5,4) = 8.0, ^2J(5,6) = 4.9, ^3J(5,3) = 1.2 (H-5); 7.68 ddd, 1 H, ^2J(4,3) = ^2J(4,5) = 7.9, ^3J(4,6) = 1.9 (H-4); 7.80 dd, 1 H, ^2J(3,4) = 8.0, ^3J(3,5) = 1.0 (H-3); 8.62 dd, 1 H, ^2J(6,5) = 4.7, ^3J(6,4) = 1.7 (H-6). For $C_{16}H_{26}N_2O$ (262.4) calculated: 73.24% C, 9.99% H, 10.68% N; found: 73.40% C, 10.50% H, 10.32% N.

Dodecyl pyridin-2-yl ketoxime (**2f**). Yield 75%, m.p. 59–63 °C (lit.[10b] 58–63 °C). ^{1}H NMR ($CDCl_3$): 0.87 t, 3 H, ^2J(12′,11′) = 6.6 (CH_3); 1.24 m, 18 H ((CH_2)$_9$); 1.57 qi, 2 H, ^2J(2′,1′) = ^2J(2′,3′) = 7.6 (HON=CCH$_2$C**H**$_2$); 2.97 t, 2 H, ^2J(1′,2′) = 7.7 (HON=CC**H**$_2$); 7.25 ddd, 1 H, ^2J(5,4) = 8.0, ^2J(5,6) = 4.9, ^3J(5,3) = 1.1 (H-5); 7.67 ddd, 1 H, ^2J(4,3) = ^2J(4,5) = 7.7, ^3J(4,6) =

1.8 (H-4); 7.80 dd, 1 H, $^2J(3,4)$ = 8.2, $^3J(3,5)$ = 1.1 (H-3); 8.62 dd, 1 H, $^2J(6,5)$ = 5.2, $^3J(6,4)$ = 1.4 (H-6).

N,N-Dialkyl-2-(hydroxyimino)-*N*-methyl-2-(pyridin-2-yl)ethan-1-aminium Nitrates (**3d**–**3h**). General Procedure

Aqueous solution of nickel nitrate (1.3 mol l^{-1}) was mixed with pyridine and ethanol (1:2:2 v/v). A blue Ni^{2+} complex of pyridine appeared immediately. Salt **4** (2 mol/mol Ni^{2+}) and hydroxylamine hydrochloride (4 mol/mol Ni^{2+}) were added and the reaction mixture was stirred at 60 °C for 45 h. Pyridine was removed in vacuo and the residue was dissolved in 50% aqueous ethanol. Then Na_2-EDTA dihydrate (6 mol/mol Ni^{2+}) was added to this solution and stirred at 60 °C for 3 h. The solid was filtered off and washed with 50% aqueous ethanol. The filtrate was extracted with chloroform, the extract dried with anhydrous sodium sulfate and the solvent was evaporated. The crude product was dissolved in methanol and then treated with Amberlite IRA 400 (OH^-), neutralized with nitric acid, evaporated and purified by column chromatography or crystallization.

N-Hexadecyl-2-(hydroxyimino)-N,N-dimethyl-2-(pyridin-2-yl)ethan-1-aminium nitrate (**3d**). Nitrate **3d** was prepared from the salt **4d** (0.900 g, 2.12 mmol) and hydroxylamine hydrochloride (0.870 g, 12.45 mmol) in the presence of $Ni(NO_3)_2$ (1.55 mmol). Column chromatography with eluent chloroform–methanol–acetone–water 15:5:5:1. Pure product was obtained as a yellow viscous liquid (0.750 g, 76%). ^{1}H NMR ($CDCl_3$): 0.88 t, 3 H, $^2J(16'',15'')$ = 6.5 (CH_3); 1.27 m, 26 H (($CH_2)_{13}$); 1.87 m, 2 H ($N^+CH_2C\mathbf{H}_2$); 3.18 s, 6 H (N^+CH_3); 3.46 m, 2 H (N^+CH_2); 4.82 s, 2 H ($N^+C\mathbf{H}_2C$=NOH); 7.28 m, 1 H (H-5′); 7.71 dd, 1 H, $^2J(4',3')$ = $^2J(4',5')$ = 6.8 (H-4′); 8.10 d, 1 H, $^2J(3',4')$ = 7.7 (H-3′); 8.52 d, 1 H, $^2J(6',5')$ = 4.9 (H-6′). ^{13}C NMR ($CDCl_3$): 14.1 (C-16″); 22.6 (C-15″); 23.3 (C-14″); 24.3 (C-13″); 26.4 (C-12″); 26.5 (C-11″); 29.0 (C-10″); 29.1 (C-9″); 29.3 (C-8″); 29.4 (C-7″); 29.5 (C-6″); 29.6 (C-5″); 29.7 (C-4″); 31.9 (C-3″); 43.1 (N^+CH_3); 52.1 (C-2″); 53.7 (C-1); 58.3 (C-1″); 120.9 (C-5′); 124.3 (C-4′); 137.2 (C-3′); 149.4 (C-2′); 146.4 (C-6′); 152.2 (C=NOH). For $C_{25}H_{46}N_4O_4$ (466.7) calculated: 64.35% C, 9.94% H, 12.01% N; found: 63.78% C, 10.06% H, 11.74% N.

N,N-Dihexyl-2-(hydroxyimino)-N-methyl-2-(pyridin-2-yl)ethan-1-aminium nitrate (**3e**). Nitrate **3e** was prepared from the salt **4e** (2.000 g, 4.92 mmol) and hydroxylamine hydrochloride (2.040 g, 29.52 mmol) in the presence of $Ni(NO_3)_2$ (3.69 mmol). Column chromatography with eluent chloroform–methanol 10:1. Pure product was obtained as a yellow viscous liquid (0.900 g, 46%). ^{1}H NMR ($CDCl_3$): 0.87 m, 6 H (CH_3); 1.29 m, 12 H (($CH_2)_3$); 1.77 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.09 s, 3 H (N^+CH_3); 3.29 m, 4 H ($N^+(CH_2)_2$); 4.79 s, 2 H ($N^+C\mathbf{H}_2C$=NOH); 7.38 dd, 1 H, $^2J(5',4')$ = $^2J(5',6')$ = 4.5 (H-5′); 7.71 dd, 1 H, $^2J(4',3')$ = $^2J(4',5')$ = 7.5 (H-4′); 8.08 d, 1 H, $^2J(3',4')$ = 4.4 (H-3′); 8.50 d, 1 H, $^2J(6',5')$ = 3.9 (H-6′). ^{13}C NMR ($CDCl_3$): 13.8 (C-6″); 22.8 (C-5″); 25.9 (C-4″); 31.1 (C-3″); 49.9 (N^+CH_3); 51.4 (C-2″); 56.4 (C-1); 63.9 (C-1″); 121.0 (C-5′); 124.2 (C-4′); 137.1 (C-3′); 146.4 (C-2′); 148.3 (C-6′); 152.6 (C=NOH). For $C_{20}H_{36}N_4O_4$ (396.5) calculated: 60.58% C, 9.15% H, 14.13% N; found: 59.90% C, 9.23% H, 14.43% N.

2-(Hydroxyimino)-N-methyl-N,N-dioctyl-2-(pyridin-2-yl)ethan-1-aminium nitrate (**3f**). Nitrate **3f** was prepared from the salt **4f** (1.045 g, 2.22 mmol) and hydroxylamine hydrochloride (0.309 g, 4.44 mmol) in the presence of $Ni(NO_3)_2$ (1.11 mmol). Crystallization from ethanol–ether afforded **3f** as a white solid (0.221 g, 29%), m.p. 81–83 °C. ^{1}H NMR (DMSO-d_6): 0.87 t, 6 H, $^2J(8'',7'')$ = 6.5 (CH_3); 1.20 m, 20 H (($CH_2)_5$); 1.69 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 2.93 s, 3 H (N^+CH_3); 3.22 t, 4 H, $^2J(1'',2'')$ = 8.2 ($N^+(CH_2)_2$); 4.70 s, 2 H ($N^+C\mathbf{H}_2C$=NOH); 7.50 dd, 1 H,

^2J(5′,4′) = 7.3, ^2J(5′,6′) = 5.2 (H-5′); 7.95 m, 2 H (H-3′, H-4′); 8.63 d, 1 H, ^2J(6′,5′) = 4.4 (H-6′). ^{13}C NMR ($CDCl_3$): 14.0 (C-8″); 22.6 (C-7″); 22.8 (C-6″); 26.3 (C-5″); 29.0 (C-4″); 31.6 (C-3″); 49.5 (N^+CH_3); 52.8 (C-2″); 55.7 (C-1); 62.6 (C-1″); 121.1 (C-5′); 126.4 (C-4′); 137.1 (C-3′); 141.3 (C-2′); 142.8 (C-6′); 152.6 (C=NOH). For $C_{24}H_{45}N_5O_7$ (515.7) calculated: 55.91% C, 8.79% H, 13.58% N; found: 55.10% C, 8.32% H, 13.56% N.

N,N-Didecyl-2-(hydroxyimino)-N-methyl-2-(pyridin-2-yl)ethan-1-aminium nitrate (**3g**). Nitrate **3g** was prepared from the salt **4g** (4.200 g, 8.20 mmol) and hydroxylamine hydrochloride (2.540 g, 36.60 mmol) in the presence of $Ni(NO_3)_2$ (6.10 mmol). Column chromatography with eluent chloroform–methanol 10:1. Pure product was obtained as a yellow viscous liquid (3.680 g, 88%). ^{1}H NMR ($CDCl_3$): 0.87 m, 6 H (CH_3); 1.27 m, 28 H ($(CH_2)_7$); 1.83 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.14 s, 3 H (N^+CH_3); 3.37 m, 4 H ($N^+(CH_2)_2$); 4.81 s, 2 H ($N^+C\mathbf{H}_2C$=NOH); 7.28 m, 1 H (H-5′); 7.68 dd, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.7 (H-4′); 8.13 d, 1 H, ^2J(3′,4′) = 8.2 (H-3′); 8.48 d, 1 H, ^2J(6′,5′) = 3.8 (H-6′). ^{13}C NMR ($CDCl_3$): 14.1 (C-10″); 22.6 (C-9″); 23.0 (C-8″); 23.7 (C-7″); 26.3 (C-6″); 6.8 (C-5″); 29.2 (C-4″); 31.8 (C-3″); 50.3 (N^+CH_3); 52.1 (C-2″); 55.8 (C-1); 63.9 (C-1″); 21.2 (C-5′); 24.1 (C-4′); 37.0 (C-3′); 145.8 (C-2′); 148.1 (C-6′); 152.7 (C=NOH). For $C_{28}H_{52}N_4O_4$ (508.5) calculated: 66.14% C, 10.31% H, 11.02% N; found: 67.04% C, 10.50% H, 11.32% N.

N,N-Dihexadecyl-2-(hydroxyimino)-N-methyl-2-(pyridin-2-yl)ethan-1-aminium nitrate (**3h**). Nitrate **3h** was prepared from the salt **4h** (1.134 g, 1.49 mmol) and hydroxylamine hydrochloride (0.410 g, 5.88 mmol) in the presence of $Ni(NO_3)_2$ (0.75 mmol). Column chromatography with eluent chloroform–methanol 100:5. Crystallization from petroleum ether afforded **3h** as a white solid (0.220 g, 22%), m.p. 93–94 °C. ^{1}H NMR ($CDCl_3$): 0.88 t, 6 H, ^2J(16″,15″) = 6.6 (CH_3); 1.25 m, 52 H ($(CH_2)_{13}$); 1.79 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.08 s, 3 H (N^+CH_3); 3.26 m, 2 H (N^+CH_2); 3.38 m, 2 H (N^+CH_2); 4.79 s, 2 H ($N^+C\mathbf{H}_2$C=NOH); 7.29 m, 1 H (H-5′); 7.70 td, 1 H, ^2J(4′,3′) = 8.2, ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 1.7 (H-4′); 8.11 d, 1 H, ^2J(3′,4′) = 8.2 (H-3′); 8.49 d, 1 H, ^2J(6′,5′) = 4.4 (H-6′). ^{13}C NMR ($CDCl_3$): 14.1 (C-16″); 22.5 (C-15″); 22.7 (C-14″); 26.2 (C-13″); 27.4 (C-12″); 29.1 (C-11″); 29.2 (C-10″); 29.3 (C-9″); 29.4 (C-8″); 29.5 (C-7″); 29.5 (C-6″); 29.6 (C-5″); 29.7 (C-4″); 31.9 (C-3″); 49.7 (N^+CH_3); 53.4 (C-2″); 57.0 (C-1); 62.0 (C-1″); 121.4 (C-5′); 125.0 (C-4′); 137.4 (C-3′); 149.4 (C-2′); 149.6 (C-6′); 152.6 (C=NOH). For $C_{40}H_{76}N_4O_4$ (677.1) calculated: 70.96% C, 11.31% H, 8.27% N; found: 70.94% C, 10.80% H, 8.27% N.

N,N-Dialkyl-4-(hydroxyimino)-*N*-methyl-4-(pyridin-2-yl)butan-1-aminium Nitrates (**3i**–**3l**). General Procedure

Aqueous solution of hydroxylamine (50%) was added in several portions to a stirred refluxing solution of salt **7** in ethanol until the starting ketone **7** was completely converted to oxime **8**. The conversion of the reaction was monitored by TLC with eluent chloroform–methanol–acetone–water 15:5:5:1. After evaporation of solvents, the obtained crude iodide **8** was purified by column chromatography with eluent chloroform–methanol–acetone–water 15:5:5:1 and then converted to nitrate **3**.

Anion exchange, method A: Saturated solution of iodide **8** in methanol was passed through a column packed with Amberlite IRA 400 (OH^- form, five-fold excess of OH^- to **8**). The resulting solution of quaternary ammonium hydroxide was neutralized with dilute nitric acid (1:1). Evaporation of solvents afforded the nitrate **3**.

Anion exchange, method B: Equal volumes of aqueous solution of silver nitrate (0.2 mol l^{-1}) and a solution of iodide **8** in dichloromethane (0.04 mol l^{-1}) were vigorously stirred at room

temperature overnight. Then, silver iodide was filtered off and a saturated aqueous solution of Na_2-EDTA was added to the filtrate. This mixture was vigorously stirred overnight. Organic phase was washed with water and dried with anhydrous magnesium sulfate. Evaporation of dichloromethane afforded the nitrate **3**.

N,N-Dihexyl-4-(hydroxyimino)-N-methyl-4-(pyridin-2-yl)butan-1-aminium nitrate (**3i**). Oxime **3i** was prepared from ketone **7i** (0.620 g, 1.31 mmol). Method *A* was used for anion exchange. Pure product was obtained as a white solid (0.465 g, 84%), m.p. 55–60 °C. ^{1}H NMR ($CDCl_3$): 0.84 t, 6 H, ^2J(6″,5″) = 6.3 (CH_3); 1.23 m, 12 H ((CH_2)$_3$); 1.60 m, 4 H (N^+($CH_2C\mathbf{H}_2$)$_2$); 2.09 m, 2 H (HON=C$CH_2C\mathbf{H}_2$); 3.05 t, 2 H, ^2J(3,2) = 6.6 (HON=CC$\mathbf{H}_2$); 3.09 s, 3 H (N^+CH_3); 3.22 m, 4 H (N^+(CH_2)$_2$); 3.42 m, 2 H ($C\mathbf{H}_2N^+$(C_6H_{13})$_2$); 7.24 m, 1 H (H-5′); 7.66 td, 1 H, ^2J(4′,3′) = 8.3, ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 1.7 (H-4′); 7.97 d, 1 H, ^2J(3′,4′) = 8.3 (H-3′); 8.52 d, 1 H, ^2J(6′,5′) = 4.9 (H-6′); 10.95 s, 1 H (NOH). ^{13}C NMR ($CDCl_3$): 13.7 (C-6″); 19.4 (C-5″); 20.8 (C-4″); 22.0 (C-3″); 22.2 (C-2″); 25.7 (C-2); 30.9 (N^+CH_3); 48.3 (C-3); 60.7 (C-1); 61.7 (C-1″); 120.7 (C-5′); 123.5 (C-4′); 136.3 (C-3′); 148.4 (C-6′); 153.6 (C-2′); 156.2 (HON=C). For $C_{22}H_{40}N_4O_4$ (424.6) calculated: 62.24% C, 9.50% H, 13.20% N; found: 61.97% C, 9.82% H, 12.97% N.

4-(Hydroxyimino)-N-methyl-N,N-dioctyl-4-(pyridin-2-yl)butan-1-aminium nitrate (**3j**): Oxime **3j** was prepared from ketone **7j** (3.085 g, 5.81 mmol). Method *A* was used for anion exchange. Pure product was obtained as a yellow solid (2.145 g, 77%), m.p. 60–64 °C. ^{1}H NMR ($CDCl_3$): 0.86 t, 6 H, ^2J(8″,7″) = 7.1 (CH_3); 1.21 m, 20 H ((CH_2)$_5$); 1.58 m, 4 H (N^+($CH_2C\mathbf{H}_2$)$_2$); 2.08 m, 2 H (HON=C$CH_2C\mathbf{H}_2$); 3.03 t, 2 H, ^2J(3,2) = 6.6 (HON=CC$\mathbf{H}_2$); 3.09 s, 3 H (N^+CH_3); 3.21 m, 4 H (N^+(CH_2)$_2$); 3.41 m, 2 H ($C\mathbf{H}_2N^+$(C_8H_{17})$_2$); 7.23 m, 1 H (H-5′); 7.67 t, 1 H, ^2J(4′,5′) = 7.7 (H-4′); 7.97 d, 1 H, ^2J(3′,4′) = 8.3 (H-3′); 8.52 d, 1 H, ^2J(6′,5′) = 4.9 (H-6′). ^{13}C NMR ($CDCl_3$): 13.8 (C-8″); 19.3 (C-7″); 20.7 (C-6″); 22.0 (C-5″); 22.3 (C-4″); 26.1 (C-3″); 28.8 (C-2″); 31.4 (C-2); 48.3 (N^+CH_3); 52.7 (C-3); 60.7 (C-1); 61.6 (C-1″); 120.7 (C-5′); 123.4 (C-4′); 136.3 (C-3′); 148.3 (C-6′); 153.5 (C-2′); 156.5 (HON=C). For $C_{26}H_{48}N_4O_4$ (480.7) calculated: 64.97% C, 10.07% H, 11.66% N; found: 64.66% C, 10.53% H, 11.09% N.

N,N-Didecyl-4-(hydroxyimino)-N-methyl-4-(pyridin-2-yl)butan-1-aminium nitrate (**3k**). Oxime **3k** was prepared from ketone **7k** (2.044 g, 3.48 mmol). Method *A* was used for anion exchange. Pure product was obtained as a white solid (1.490 g, 80%), m.p. 75–77 °C. ^{1}H NMR ($CDCl_3$): 0.87 t, 6 H, ^2J(10″,9″) = 6.6 (CH_3); 1.23 m, 28 H ((CH_2)$_7$); 1.60 m, 4 H (N^+($CH_2C\mathbf{H}_2$)$_2$); 2.09 m, 2 H (HON=C$CH_2C\mathbf{H}_2$); 3.04 t, 2 H, ^2J(3,2) = 6.1 (HON=CC$\mathbf{H}_2$); 3.09 s, 3 H (N^+CH_3); 3.22 m, 4 H (N^+(CH_2)$_2$); 3.42 m, 2 H ($C\mathbf{H}_2N^+$($C_{10}H_{21}$)$_2$); 7.23 td, 1 H, ^2J(5′,4′) = 2.2, ^2J(5′,6′) = 5.0 (H-5′); 7.66 td, 1 H, ^2J(4′,3′) = 7.7, ^2J(4′,5′) = 1.7 (H-4′); 7.97 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.52 d, 1 H, ^2J(6′,5′) = 5.5 (H-6′); 11.02 s, 1 H (NOH). ^{13}C NMR ($CDCl_3$): 14.1 (C-10″); 19.7 (C-9″); 20.9 (C-8″); 22.3 (C-7″); 22.6 (C-6″); 26.3 (C-5″); 29.1 (C-4″); 29.3 (C-3″); 29.4 (C-2″); 31.8 (C-2); 48.5 (N^+CH_3); 52.8 (C-3); 61.1 (C-1); 61.7 (C-1″); 120.9 (C-5′); 123.6 (C-4′); 136.4 (C-3′); 148.3 (C-6′); 153.8 (C-2′); 156.5 (HON=C). For $C_{30}H_{56}N_4O_4$ (536.8) calculated: 67.13% C, 10.52% H, 10.44% N; found: 66.92% C, 10.74% H, 10.65% N.

N,N-Didodecyl-4-(hydroxyimino)-N-methyl-4-(pyridin-2-yl)butan-1-aminium nitrate (**3l**). Oxime **3l** was prepared from ketone **7l** (2.775 g, 4.32 mmol). Method *B* was used for anion exchange. Pure product was obtained as a white solid (0.400 g, 16%), m.p. 65–68 °C. ^{1}H NMR ($CDCl_3$): 0.87 t, 6 H, ^2J(12″,11″) = 6.5 (CH_3); 1.24 m, 36 H ((CH_2)$_9$); 1.59 m, 4 H (N^+($CH_2C\mathbf{H}_2$)$_2$); 2.08 m, 2 H (HON=C$CH_2C\mathbf{H}_2$); 3.03 t, 2 H, ^2J(3,2) = 6.6 (HON=CC$\mathbf{H}_2$); 3.08 s, 3 H (N^+CH_3); 3.20 m, 4 H (N^+(CH_2)$_2$); 3.41 m, 2 H ($C\mathbf{H}_2N^+$($C_{12}H_{25}$)$_2$); 7.21 t, 1 H, ^2J(5′,4′) = 7.4, ^2J(5′,6′) = 5.0 (H-5′); 7.63 t, 1 H, ^2J(4′,3′) = 7.7 (H-4′); 7.94 d, 1 H, ^2J(3′,4′) = 8.0 (H-3′); 8.50 d, 1 H, ^2J(6′,5′) = 4.4 (H-6′); 11.02 s, 1 H (NOH). ^{13}C NMR ($CDCl_3$): 14.1 (C-12″); 19.7 (C-11″); 20.9

(C-10″); 22.3 (C-9″); 22.7 (C-8″); 26.3 (C-7″); 29.1 (C-6″); 29.3 (C-5″); 29.4 (C-4″); 29.5 (C-3″, C-2″); 29.6 (C-3); 31.9 (C-2); 48.5 (N^+CH_3); 61.1 (C-1); 61.7 (C-1″); 120.9 (C-5′); 123.6 (C-4′); 136.4 (C-3′); 148.6 (C-6′); 153.8 (C-2′); 156.5 (HON=C). For $C_{34}H_{64}N_4O_4$ (592.9) calculated: 68.88% C, 10.83% H, 9.45% N; found: 68.22% C, 11.13% H, 9.56% N.

N,N-Dialkyl-*N*-methyl-2-oxo-2-(pyridin-2-yl)ethan-1-aminium Bromides (**4**)

Bromides **4** were prepared using the previously described procedure[13a]. The differences from this procedure (concerning isolation and purification only) are given below.

N-Hexadecyl-N,N-dimethyl-2-oxo-2-(pyridin-2-yl)ethan-1-aminium bromide (**4d**). Salt **4d** was prepared from hexadecyldimethylamine (1.150 g, 4.23 mmol) and 2-(bromoacetyl)pyridine hydrobromide (4.89 g, 17.78 mmol). Crude product was purified by column chromatography with eluent chloroform–methanol 100:15. Pure product was obtained as a yellow viscous liquid (0.950 g, 53%). ^{1}H NMR ($CDCl_3$): 0.87 m, 3 H (CH_3); 1.26 m, 26 H ($(CH_2)_{13}$); 1.70 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.74 s, 6 H (N^+CH_3); 3.86 m, 2 H (N^+CH_2); 5.76 s, 2 H (N^+CH_2C=O); 7.58 m, 1 H (H-5′); 7.91 dd, 1 H, ^2J(4′,5′) = ^2J(4′,3′) = 7.1 (H-4′); 8.03 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.68 d, 1 H, ^2J(6′,5′) = 4.5 (H-6′).

N,N-Dihexyl-N-methyl-2-oxo-2-(pyridin-2-yl)ethan-1-aminium bromide (**4e**). Salt **4e** was prepared from dihexylmethylamine (2.600 g, 12.83 mmol) and 2-(bromoacetyl)pyridine hydrobromide (14.320 g, 51.33 mmol). Crude product was purified by column chromatography with eluent chloroform–methanol–acetone–water 15:5:5:1. Pure product was obtained as a yellow viscous liquid (3.820 g, 78%). ^{1}H NMR ($CDCl_3$): 0.87 t, 6 H, ^2J(6″,5″) = 6.8 (CH_3); 1.31 m, 12 H ($(CH_2)_3$); 1.66 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.68 s, 3 H (N^+CH_3); 3.78 m, 2 H (N^+CH_2); 3.96 m, 2 H (N^+CH_2); 5.69 s, 2 H (N^+CH_2C=O); 7.59 dd, 1 H, ^2J(5′,4′) = ^2J(5′,6′) = 6.8 (H-5′); 7.92 dd, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.6 (H-4′); 8.03 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.68 d, 1 H, ^2J(6′,5′) = 3.3 (H-6′).

N-Methyl-N,N-dioctyl-2-oxo-2-(pyridin-2-yl)ethan-1-aminium bromide (**4f**). Salt **4f** was prepared from methyldioctylamine (5.180 g, 20.00 mmol) and 2-(bromoacetyl)pyridine hydrobromide (6.720 g, 24.09 mmol). Crude product was purified by column chromatography with eluent chloroform–methanol–acetone–water 35:5:5:1. Pure product was obtained as a yellow viscous liquid (4.32 g, 46%). ^{1}H NMR ($CHCl_3$): 0.84 t, 6 H, ^2J(8″,7″) = 6.6 (CH_3); 1.24 m, 20 H ($(CH_2)_5$); 1.69 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.66 s, 3 H (N^+CH_3); 3.76 m, 2 H (N^+CH_2); 3.91 m, 2 H (N^+CH_2); 5.63 s, 2 H (N^+CH_2C=O); 7.50 dd, 1 H, ^2J(5′,4′) = 7.8, ^3J(5′,6′) = 4.7 (H-5′); 7.91 dd, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.6 (H-4′); 8.03 d, 1 H, ^2J(3′,4′) = 8.3 (H-3′); 8.67 d, 1 H, ^2J(6′,5′) = 5.0 (H-6′).

N,N-Didecyl-N-methyl-2-oxo-2-(pyridin-2-yl)ethan-1-aminium bromide (**4g**). Salt **4g** was prepared from didecylmethylamine (2.580 g, 8.28 mmol) and 2-(bromacetyl)pyridine hydrobromide (6.080 g, 21.64 mmol). Crude product was purified by column chromatography with eluent chloroform–methanol 10:1. Pure product was obtained as a yellow viscous liquid (5.400 g, 90%). ^{1}H NMR ($CDCl_3$): 0.87 t, 6 H, ^2J(10″,9″) = 7.1 (CH_3); 1.23 m, 28 H ($(CH_2)_7$); 1.66 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 3.68 s, 3 H (N^+CH_3); 3.80 m, 2 H (N^+CH_2); 3.95 m, 2 H (N^+CH_2); 5.68 s, 2 H (N^+CH_2C=O); 7.60 m, 1 H (H-5′); 7.91 dd, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.4 (H-4′); 8.05 d, 1 H, ^2J(3′,4′) = 6.3 (H-3′); 8.69 d, 1 H, ^2J(6′,5′) = 3.9 (H-6′).

N,N-Dihexadecyl-N-methyl-2-oxo-2-(pyridin-2-yl)ethan-1-aminium bromide (**4h**). Salt **4h** was prepared from dihexadecylmethylamine (2.870 g, 5.60 mmol) and 2-(bromacetyl)pyridine hydrobromide (2.300 g, 8.25 mmol). Crude product was purified by column chromatography with eluent chloroform–methanol 10:1. Pure product was obtained as a yellow viscous

liquid (1.290 g, 32%). ^{1}H NMR ($CDCl_3$): 0.87 m, 6 H (CH_3); 1.30 m, 52 H ($(CH_2)_{13}$); 1.70 m, 4 H ($N^+(CH_2CH_2)_2$); 3.67 s, 3 H (N^+CH_3); 3.80 m, 2 H (N^+CH_2); 3.94 m, 2 H (N^+CH_2); 5.66 s, 2 H ($N^+CH_2C{=}O$); 7.59 dd, 1 H, ^2J(5′,4′) = ^2J(5′,6′) = 6.4 (H-5′); 7.91 dd, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.8 (H-4′); 8.03 d, 1 H, ^2J(3′,4′) = 7.8 (H-3′); 8.68 d, 1 H, ^2J(6′,5′) = 4.9 (H-6′).

4-(Dialkylamino)-1-(pyridin-2-yl)butan-1-ones (**5**). General Procedure

A solution of 2.5 M butyllithium in hexane (10.0 mmol) was added dropwise at –25 °C under nitrogen within 20 min to a stirred solution of 2-bromopyridine (10.1 mmol) in ether (85 ml). The obtained dark-red solution was cooled to –78 °C and stirred for 5 min. Then, a solution of butanenitrile **6** (7.6 mmol) in ether (15 ml) was added dropwise. After stirring at –78 °C (2 h) and at ambient temperature (4 h), the reaction mixture was quenched with 1 M hydrochloric acid (150 ml). Organic layer was washed with water (5 × 150 ml). Aqueous phase was alkalinized with potassium carbonate and then extracted with ether (9 × 100 ml). The combined organic layers were dried with anhydrous magnesium sulfate. Evaporation of solvents afforded crude product which was purified by column chromatography.

4-(Dihexylamino)-1-(pyridin-2-yl)butan-1-one (**5i**). Ketone **5i** was prepared from 2-bromopyridine (1.600 g, 10.13 mmol) and nitrile **6i** (1.905 g, 7.55 mmol). Gradient elution with dichloromethane–methanol from 100:1 to 10:1. Pure product was obtained as a reddish viscous liquid (0.950 g, 39%). ^{1}H NMR ($CDCl_3$): 0.86 t, 6 H, ^2J(6″,5″) = 6.6 (CH_3); 1.24 m, 12 H ($(CH_2)_3$); 1.39 m, 4 H ($N(CH_2CH_2)_2$); 1.89 qi, 2 H, ^2J(2,1) = ^2J(2,3) = 7.3 ($COCH_2CH_2$); 2.40 t, 4 H, ^2J(1″,2″) = 7.4 ($N(CH_2)_2$); 2.51 t, 2 H, ^2J(1,2) = 7.4 ($CH_2N(C_6H_{13})_2$); 3.22 t, 2 H, ^2J(3,2) = 7.4 (CH_2CO); 7.45 ddd, 1 H, ^2J(5′,4′) = 7.7, ^2J(5′,6′) = 4.7, ^3J(5′,3′) = 1.1 (H-5′); 7.82 td, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 2.2 (H-4′); 8.03 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.67 d, 1 H, ^2J(6′,5′) = 4.9 (H-6′). ^{13}C NMR ($CDCl_3$): 13.9 (C-6″); 21.3 (C-5″); 22.5 (C-4″); 26.6 (C-3″); 27.1 (C-2); 31.7 (C-2″); 35.4 (C-3); 53.3 (C-1); 53.8 (C-1″); 121.5 (C-5′); 126.8 (C-4′); 136.6 (C-3′); 148.7 (C-6′); 153.5 (C-2′); 201.6 (C=O). IR ($CHCl_3$): 1696 (CO).

4-(Dioctylamino)-1-(pyridin-2-yl)butan-1-one (**5j**). Ketone **5j** was prepared from 2-bromopyridine (3.685 g, 23.32 mmol) and nitrile **6j** (5.625 g, 18.23 mmol). Gradient elution with dichloromethane–methanol from 100:1 to 1:1. Pure product was obtained as a reddish viscous liquid (3.905 g, 55%). ^{1}H NMR ($CDCl_3$): 0.84 t, 6 H, ^2J(8″,7″) = 6.6 (CH_3); 1.22 m, 20 H ($(CH_2)_5$); 1.35 m, 4 H ($N(CH_2CH_2)_2$); 1.85 qi, 2 H, ^2J(2,1) = ^2J(2,3) = 7.4 ($COCH_2CH_2$); 2.35 t, 4 H, ^2J(1″,2″) = 7.4 ($N(CH_2)_2$); 2.47 t, 2 H, ^2J(1,2) = 7.4 ($CH_2N(C_8H_{17})_2$); 3.19 t, 2 H, ^2J(3,2) = 7.1 (CH_2CO); 7.41 td, 1 H, ^2J(5′,4′) = 7.7, ^2J(5′,6′) = 4.4, ^3J(5′,3′) = 1.1 (H-5′); 7.78 td, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 1.7 (H-4′); 8.00 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.64 d, 1 H, ^2J(6′,5′) = 4.4 (H-6′). ^{13}C NMR ($CDCl_3$): 14.0 (C-8″); 21.5 (C-7″); 22.6 (C-6″); 26.9 (C-5″); 27.6 (C-2); 29.3 (C-4″); 29.5 (C-3″); 31.8 (C-2″); 35.5 (C-3); 53.4 (C-1); 54.0 (C-1″); 121.6 (C-5′); 126.8 (C-4′); 136.7 (C-3′); 148.8 (C-6′); 153.6 (C-2′); 201.7 (C=O).

4-(Didecylamino)-1-(pyridin-2-yl)butan-1-one (**5k**). Ketone **5k** was prepared from 2-bromopyridine (3.205 g, 20.28 mmol) and nitrile **6k** (5.615 g, 15.40 mmol). Gradient elution with dichloromethane–methanol from 100:3 to 10:1. Pure product was obtained as a reddish viscous liquid (1.560 g, 23%). ^{1}H NMR ($CDCl_3$): 0.86 t, 6 H, ^2J(10″,9″) = 6.9 (CH_3); 1.23 m, 28 H ($(CH_2)_7$); 1.50 m, 4 H ($N(CH_2CH_2)_2$); 1.97 qi, 2 H, ^2J(2,1) = ^2J(2,3) = 7.4 ($COCH_2CH_2$); 2.56 m, 4 H ($N(CH_2)_2$); 2.66 m, 2 H ($CH_2N(C_{10}H_{21})_2$); 3.25 t, 2 H, ^2J(3,2) = 6.9 (CH_2CO); 7.45 ddd, 1 H, ^2J(5′,4′) = 7.7, ^2J(5′,6′) = 4.4, ^3J(5′,3′) = 1.1 (H-5′); 7.81 td, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 1.7 (H-4′); 8.01 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.65 d, 1 H, ^2J(6′,5′) = 5.5 (H-6′). ^{13}C NMR ($CDCl_3$): 13.9 (C-10″); 20.0 (C-9″); 22.5 (C-8″); 25.6 (C-7″); 27.2 (C-6″);

29.1 (C-5″); 29.3 (C-2); 29.3 (C-4″); 29.4 (C-3″); 31.7 (C-2″); 35.1 (C-3); 52.6 (C-1); 53.3 (C-1″); 121.5 (C-5′); 126.9 (C-4′); 136.6 (C-3′); 148.7 (C-6′); 153.2 (C-2′); 201.0 (C=O).

4-(Didodecylamino)-1-(pyridin-2-yl)butan-1-one (**5l**). Ketone **5l** was prepared from 2-bromopyridine (2.310 g, 14.60 mmol) and nitrile **6l** (3.550 g, 8.40 mmol). Gradient elution with dichloromethane–methanol from 100:3 to 1:1. Pure product was obtained as a reddish viscous liquid (2.530 g, 60%). ^{1}H NMR ($CDCl_3$): 0.88 t, 6 H, ^2J(12″,11″) = 6.7 (CH_3); 1.25 m, 36 H ((CH_2)$_9$); 1.68 m, 4 H (N($CH_2C\mathbf{H}_2$)$_2$); 2.12 m, 2 H ($COCH_2C\mathbf{H}_2$); 2.80 m, 6 H (N(CH_2)$_3$); 3.31 t, 2 H, ^2J(3,2) = 6.6 (CH_2CO); 7.47 ddd, 1 H, ^2J(5′,4′) = 7.4, ^2J(5′,6′) = 4.9, ^3J(5′,3′) = 1.3 (H-5′); 7.82 td, 1 H, ^2J(4′,3′) = ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 1.7 (H-4′); 8.00 dd, 1 H, ^2J(3′,4′) = 7.7, ^3J(3′,5′) = 1.1 (H-3′); 8.65 dd, 1 H, ^2J(6′,5′) = 5.5, ^3J(6′,4′) = 1.7 (H-6′). ^{13}C NMR ($CDCl_3$): 14.0 (C-12″); 22.6 (C-11″); 27.0 (C-10″); 29.1 (C-9″); 29.2 (C-8″); 29.4 (C-7″, C-6″); 29.4 (C-5″, C-4″, C-3″); 29.5 (C-2); 31.8 (C-2″); 34.8 (C-3); 52.0 (C-1); 52.9 (C-1″); 121.6 (C-5′); 127.2 (C-4′); 136.8 (C-3′); 149.0 (C-6′); 153.0 (C-2′); 200.6 (C=O).

4-(Dialkylamino)butanenitriles (**6**). General Procedure

A solution of 4-bromobutanenitrile (20.0 mmol), dialkylamine (20.3 mmol), and *N*-ethyldiisopropylamine (20.1 mmol) in ethanol (125 ml) was refluxed for 100 h. After cooling the reaction mixture and evaporation of the solvents, the residue was dissolved in dichloromethane (150 ml), washed with 2 M hydrochloric acid (8 × 100 ml) and then vigorously stirred with a saturated solution of potassium carbonate (120 ml) for 2 h. Organic layer was dried with anhydrous magnesium sulfate. Evaporation of the solvent afforded crude product which was purified by column chromatography.

4-(Dihexylamino)butanenitrile (**6i**). Nitrile **6i** was prepared from 4-bromobutanenitrile (3.050 g, 20.61 mmol), dihexylamine (3.880 g, 20.93 mmol), and *N*-ethyldiisopropylamine (2.675 g, 20.69 mmol). Gradient elution with petroleum ether–ethyl acetate from 100:30 to 2:1. Pure product was obtained as a yellow viscous liquid (4.070 g, 78%). ^{1}H NMR ($CDCl_3$): 0.86 t, 6 H, ^2J(6′,5′) = 6.6 (CH_3); 1.25 m, 12 H ((CH_2)$_3$); 1.36 t, 4 H, ^2J(2′,1′) = 6.6 (N($CH_2C\mathbf{H}_2$)$_2$); 1.72 qi, 2 H, ^2J(3,2) = ^2J(3,4) = 6.6 ($NCCH_2C\mathbf{H}_2$); 2.33 t, 4 H, ^2J(1′,2′) = 7.1 (N(CH_2)$_2$); 2.38 t, 2 H, ^2J(4,3) = 7.1 ($C\mathbf{H}_2$N(C_6H_{13})$_2$); 2.45 t, 2 H, ^2J(2,3) = 6.6 ($NCCH_2$). ^{13}C NMR ($CDCl_3$): 14.0 (C-6′); 14.7 (C-2); 22.6 (C-5′); 23.8 (C-4′); 27.1 (C-3′); 27.2 (C-3); 31.8 (C-2′); 52.3 (C-4); 54.1 (C-1′); 120.0 (C-1). For $C_{16}H_{32}N_2$ (252.4) calculated: 76.13% C, 12.78% H, 11.10% N; found: 74.58% C, 12.86% H, 11.24% N.

4-(Dioctylamino)butanenitrile (**6j**). Nitrile **6j** was prepared from 4-bromobutanenitrile (4.435 g, 36.72 mmol), dioctylamine (8.980 g, 37.19 mmol), and *N*-ethyldiisopropylamine (4.750 g, 36.75 mmol). Gradient elution with petroleum ether–ethyl acetate from 100:30 to 1:1. Pure product was obtained as a yellow viscous liquid (6.525 g, 58%). ^{1}H NMR ($CDCl_3$): 0.87 t, 6 H, ^2J(8′,7′) = 6.6 (CH_3); 1.26 m, 20 H ((CH_2)$_5$); 1.39 qi, 4 H, ^2J(2′,1′) = 7.1, ^2J(2′,3′) = 6.6 (N($CH_2C\mathbf{H}_2$)$_2$); 1.74 qi, 2 H, ^2J(3,2) = 6.6, ^2J(3,4) = 7.1 ($NCCH_2C\mathbf{H}_2$); 2.35 t, 4 H, ^2J(1′,2′) = 7.7 (N(CH_2)$_2$); 2.40 t, 2 H, ^2J(4,3) = 7.1 ($C\mathbf{H}_2$N(C_6H_{13})$_2$); 2.47 t, 2 H, ^2J(2,3) = 6.6 ($NCCH_2$). ^{13}C NMR ($CDCl_3$): 13.4 (C-8′); 13.9 (C-2); 22.1 (C-7′); 23.3 (C-6′); 26.7 (C-5′); 26.9 (C-3); 28.8 (C-4′); 29.0 (C-3′); 31.3 (C-2′); 51.7 (C-4); 53.5 (C-1′); 118.9 (C-1). For $C_{20}H_{40}N_2$ (308.6) calculated: 77.85% C, 13.07% H, 9.08% N; found: 77.19% C, 13.06% H, 9.44% N.

4-(Didecylamino)butanenitrile (**6k**). Nitrile **6k** was prepared from 4-bromobutanenitrile (3.560 g, 24.05 mmol), didecylamine (7.160 g, 24.06 mmol), and *N*-ethyldiisopropylamine (3.120 g, 24.14 mmol). Gradient elution with petroleum ether–ethyl acetate from 4:1 to 1:1. Pure product was obtained as a yellow viscous liquid (6.693 g, 76%). ^{1}H NMR ($CDCl_3$): 0.86 t,

6 H, ^2J(10′,9′) = 6.6 (CH_3); 1.25 m, 28 H ((CH_2)$_7$); 1.38 m, 4 H (N($CH_2C\mathbf{H}_2$)$_2$); 1.73 qi, 2 H, ^2J(3,2) = 6.6, ^2J(3,4) = 7.1 ($NCCH_2C\mathbf{H}_2$); 2.34 t, 4 H, ^2J(1′,2′) = 7.7 (N(CH_2)$_2$); 2.39 t, 2 H, ^2J(4,3) = 7.1 ($C\mathbf{H}_2N(C_{10}H_{21})_2$); 2.47 t, 2 H, ^2J(2,3) = 6.6 ($NCCH_2$). ^{13}C NMR ($CDCl_3$): 14.1 (C-10′); 14.7 (C-2); 22.8 (C-9′); 24.0 (C-8′); 27.3 (C-7′); 27.6 (C-6′); 29.4 (C-5′); 29.7 (C-4′, C-3′); 29.8 (C-3); 32.0 (C-2′); 54.2 (C-1′); 54.4 (C-4); 119.9 (C-1). For $C_{24}H_{48}N_2$ (364.7) calculated: 79.05% C, 13.27% H, 7.68% N; found: 78.79% C, 13.58% H, 7.67% N.

4-(Didodecylamino)butanenitrile (**6l**). Nitrile **6l** was prepared from 4-bromobutanenitrile (2.895 g, 19.56 mmol), didodecylamine (6.900 g, 19.51 mmol), and *N*-ethyldiisopropylamine (2.540 g, 19.65 mmol). Elution with petroleum ether–ethyl acetate 5:1. Pure product was obtained as a yellow viscous liquid (4.985 g, 61%). ^{1}H NMR ($CDCl_3$): 0.88 t, 6 H, ^2J(12′,11′) = 6.6 (CH_3); 1.27 m, 36 H ((CH_2)$_9$); 1.39 qi, 4 H, ^2J(2′,1′) = ^2J(2′,3′) = 6.9 (N($CH_2C\mathbf{H}_2$)$_2$); 1.76 qi, 2 H, ^2J(3,2) = ^2J(3,4) = 6.6 ($NCCH_2C\mathbf{H}_2$); 2.36 t, 4 H, ^2J(1′,2′) = 7.4 (N(CH_2)$_2$); 2.42 t, 2 H, ^2J(4,3) = 7.1 ($C\mathbf{H}_2N(C_{12}H_{25})_2$); 2.49 t, 2 H, ^2J(2,3) = 6.5 ($NCCH_2$). ^{13}C NMR ($CDCl_3$): 14.1 (C-12′); 14.8 (C-2); 22.7 (C-11′); 23.8 (C-10′); 27.1 (C-9′); 27.5 (C-8′); 29.3 (C-7′); 29.6 (C-6′, C-5′); 29.6 (C-4′, C-3′); 29.7 (C-3); 31.9 (C-2′); 52.4 (C-4); 54.1 (C-1′); 120.0 (C-1). For $C_{28}H_{56}N_2$ (420.8) calculated: 79.93% C, 13.41% H, 6.66% N; found: 79.98% C, 13.71% H, 6.60% N.

N,N-Dialkyl-*N*-methyl-4-oxo-4-(pyridin-2-yl)butan-1-aminium Iodides (**7**).
General Procedure

Method A: A solution of ketone **5** (2.0 mmol) and methyl iodide (15.3 mmol) in toluene (50 ml) was heated under stirring at 90 °C in a microwave reactor (Synthewave 402, Prolabo) for 10 min. Evaporation of the solvent afforded the crude product.

Method B: A solution of ketone **5** (2.0 mmol) and methyl iodide (15.3 mmol) in dichloromethane (50 ml) was stirred at ambient temperature for 78 h. Evaporation of the solvent afforded the crude product. The obtained salts **7** were used for the preparation of target ligands **3** without any purification.

N,N-Dihexyl-N-methyl-4-oxo-4-(pyridin-2-yl)butan-1-aminium iodide (**7i**). Salt **7i** was prepared from ketone **5i** (0.700 g, 2.11 mmol) and methyl iodide (1.0 ml, 16 mmol) using method *A*. Yield 0.620 g (62%). ^{1}H NMR ($CDCl_3$): 0.87 t, 6 H, ^2J(6″,5″) = 6.6 (CH_3); 1.33 m, 12 H ((CH_2)$_3$); 1.77 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 2.14 qi, 2 H, ^2J(2,1) = 8.2, ^2J(2,3) = 6.6 ($COCH_2C\mathbf{H}_2$); 3.34 s, 3 H (N^+CH_3); 3.45 m, 6 H ($N^+(CH_2)_2$, CH_2CO); 3.59 m, 2 H ($C\mathbf{H}_2N^+(C_6H_{13})_2$); 7.48 ddd, 1 H, ^2J(5′,4′) = 2.8, ^2J(5′,6′) = 4.9, ^3J(5′,3′) = 1.1 (H-5′); 7.83 td, 1 H, ^2J(4′,3′) = 7.7, ^2J(4′,5′) = 1.7 (H-4′); 7.98 d, 1 H, ^2J(3′,4′) = 8.2 (H-3′); 8.65 d, 1 H, ^2J(6′,5′) = 4.9 (H-6′).

N-Methyl-N,N-dioctyl-4-oxo-4-(pyridin-2-yl)butan-1-aminium iodide (**7j**). Salt **7j** was prepared from ketone **5j** (3.480 g, 8.95 mmol) and methyl iodide (1.2 ml, 19 mmol) using method *A*. Yield 3.08 g (65%). ^{1}H NMR ($CDCl_3$): 0.86 t, 6 H, ^2J(8″,7″) = 6.3 (CH_3); 1.37 m, 20 H ((CH_2)$_5$); 1.75 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 2.15 qi, 2 H, ^2J(2,1) = 7.3, ^2J(2,3) = 6.6 ($COCH_2C\mathbf{H}_2$); 3.35 s, 3 H (N^+CH_3); 3.46 m, 6 H ($N^+(CH_2)_2$, CH_2CO); 3.60 m, 2 H ($C\mathbf{H}_2N^+(C_8H_{17})_2$); 7.49 ddd, 1 H, ^2J(5′,4′) = 1.7, ^2J(5′,6′) = 5.5, ^3J(5′,3′) = 1.1 (H-5′); 7.84 td, 1 H, ^2J(4′,3′) = 7.7, ^2J(4′,5′) = 1.7 (H-4′); 7.99 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.66 d, 1 H, ^2J(6′,5′) = 4.4 (H-6′).

N,N-Didecyl-N-methyl-4-oxo-4-(pyridin-2-yl)butan-1-aminium iodide (**7k**). Salt **7k** was prepared from ketone **5k** (1.550 g, 3.49 mmol) and methyl iodide (3.0 ml, 48 mmol) using method *B*. Yield 2.044 g (99%). ^{1}H NMR ($CDCl_3$): 0.85 t, 6 H, ^2J(10″,9″) = 6.6 (CH_3); 1.24 m, 28 H ((CH_2)$_7$); 1.77 m, 4 H ($N^+(CH_2C\mathbf{H}_2)_2$); 2.15 m, 2 H ($COCH_2C\mathbf{H}_2$); 3.08 m, 2 H (CH_2CO); 3.34 s, 3 H (N^+CH_3); 3.45 m, 6 H ($N^+(CH_2)_2$); 3.58 m, 2 H ($C\mathbf{H}_2N^+(C_{10}H_{21})_2$); 7.49 td, 1 H,

^2J(5′,4′) = 1.1, ^2J(5′,6′) = 4.4 (H-5′); 7.84 td, 1 H, ^2J(4′,3′) = 7.7, ^2J(4′,5′) = 1.7 (H-4′); 7.98 d, 1 H, ^2J(3′,4′) = 7.7 (H-3′); 8.65 d, 1 H, ^2J(6′,5′) = 3.9 (H-6′).

N,N-Didodecyl-N-methyl-4-oxo-4-(pyridin-2-yl)butan-1-aminium iodide (**7l**). Salt **7l** was prepared from ketone **5l** (2.445 g, 4.88 mmol) and methyl iodide (4.5 ml, 72 mmol) using method *B*. Yield 2.775 g (88%). ^{1}H NMR ($CDCl_3$): 0.88 t, 6 H, ^2J(12″,11″) = 6.7 (CH_3); 1.26 m, 36 H ((CH_2)$_9$); 1.78 m, 4 H ($N^+(CH_2CH_2)_2$); 2.17 m, 2 H ($COCH_2CH_2$); 3.03 t, 2 H, ^2J(3,2) = 7.0 (CH_2CO); 3.36 s, 3 H (N^+CH_3); 3.48 m, 4 H ($N^+(CH_2)_2$); 3.63 m, 2 H ($CH_2N^+(C_{12}H_{25})_2$); 7.50 td, 1 H, ^2J(5′,4′) = 7.4, ^2J(5′,6′) = 4.2, ^3J(5′,3′) = 1.4 (H-5′); 7.84 ddd, 1 H, ^2J(4′,3′) = 7.7, ^2J(4′,5′) = 7.7, ^3J(4′,6′) = 1.7 (H-4′); 7.99 dd, 1 H, ^2J(3′,4′) = 7.1, ^3J(3′,5′) = 1.1 (H-3′); 8.66 d, 1 H, ^2J(6′,5′) = 4.7 (H-6′).

Transport Experiments

A glass tube (48 mm and 44.5 mm were the external and internal diameters, respectively) was immersed coaxially into a cylindrical glass vessel (internal diameter 57 mm) beneath the surface of the chloroform layer (70 ml), thus separating two aqueous phases: the source phase (50 ml) and the receiving phase (25 ml). The chloroform layer (liquid membrane) was stirred slowly (60 rpm) by a mechanical stirrer keeping the phase interfaces motionless (Fig. 3). The cell was thermostatted at 25 ± 0.5 °C. The source phases were 5.0×10^{-3} M aqueous solutions of $Cu(NO_3)_2$, $Ni(NO_3)_2$ and $Co(NO_3)_2$, and 5.0×10^{-3} M $PdCl_2$ in 2.0×10^{-2} M aqueous NaCl. Acetate buffer (5.0×10^{-1} mol l^{-1}, pH 4.7) was used to adjust pH of the source phases. The receiving phase was 0.1 M HCl (Cu^{2+}, Co^{2+}, and Ni^{2+}), 5.0 M HCl (Pd^{2+}), or 4.9 M NaCl in 0.1 M HCl (Pd^{2+}). In all cases, the concentration of the carrier in chloroform membrane was 1.0×10^{-3} mol l^{-1}.

Concentration of Cu^{2+}, Co^{2+}, and Ni^{2+} ions in source and receiving phases and in chloroform membrane was determined spectrophotometrically using sodium diethyldithiocarbamate trihydrate[8]. The absorbance was measured with a Hewlett–Packard HP8452 spectrophotometer. Concentration of Pd^{2+} in all phases was determined spectrophotometrically using pyridine-2-carbaldoxime[24].

The authors thank the Prague Institute of Chemical Technology and Ministry of Education, Youth and Sports of the Czech Republic (grant No. 223100001) for financial support of this project.

REFERENCES

1. a) Rydberg J., Musikas C., Choppin G. R.: *Principles and Practices of Solvent Extraction*. Dekker, New York 1992; b) Moyer B. A. in: *Comprehensive Supramolecular Chemistry* (G. W. Gokel, Ed.), Vol. 1, p. 377. Elsevier, Oxford 1996; c) Chmielewski A. G.: *Hydrometallurgy* **1997**, *45*, 333.
2. a) Noble R. D., Way J. D.: *Liquid Membranes: Theory and Applications, ACS Symp. Ser. 347*. ACS, Washington DC 1987; b) Araki T., Tsukube H.: *Liquid Membranes: Chemical Applications*. CRC Press, Boca Raton 1990; c) Noble R. D., Stern S. A.: *Membrane Separation Technology: Principles and Applications*. Elsevier, Amsterdam 1995; d) de Jong F., Visser H. C. in: *Comprehensive Supramolecular Chemistry* (D. N. Reinhoudt, Ed.), Vol. 10, p. 13. Elsevier, Oxford 1996; e) Bartsch R. A., Way J. D.: *Chemical Separations with Liquid*

Membranes, ACS Symp. Ser. 64. ACS, Washington DC 1996; f) Yang X. J., Fane A. G., Soldenhoff K.: *Ind. Eng. Chem. Res.* **2003**, *42*, 392, and references therein.

3. a) Visser H. C., Reinhoudt D. N., de Jong F.: *Chem. Soc. Rev.* **1994**, 75; b) Bradshaw J. S., Izatt R. M.: *Acc. Chem. Res.* **1997**, *30*, 338; c) Lumetta G. J., Rogers R. D., Gopalan A. S.: *Calixarenes for Separations, ACS Symp. Ser. 757*. ACS, Washington DC 2000; d) Tsukube H., Shinoda S., Uenishi J., Hiraoka T., Imakoga T., Yonemitsu O.: *J. Org. Chem.* **1998**, *63*, 3884; e) Kim J. K., Kim J. S., Shul Y. G., Lee K. W., Oh W. Z.: *J. Membr. Sci.* **2001**, *187*, 3; f) Song H. C., Chen Y. W., Yao J. H., Xu Z. L., Lee S. C., Izatt R. M., Zhang X. X., Nelson E. G., Lamb J. D., Savage P. B., Bradshaw J. S.: *Inorg. Chim. Acta* **2001**, *317*, 174; g) Ulewicz M., Walkowiak W., Jang Y. C., Aguilar J. C., de San Miguel E. R., de Gyves J., Bartsch R. A., Kim M.: *Talanta* **2001**, *54*, 1195; i) Kim J. S., Bartsch R. A.: *Anal. Chem.* **2003**, *75*, 2276, and references therein.
4. a) Mikucki B. A., Osseo-Asare K.: *Solvent Extr. Ion Exch.* **1986**, *4*, 503; b) Yamashita K., Kakoi T., Kosaka H., Goto M., Nakashio F.: *Sep. Sci. Technol.* **1998**, *33*, 369, and references therein.
5. a) Kralj D., Breembroek G. R. M., Witkamp G. J., vanRosmalen G. M., Brecevic L.: *Solvent Extr. Ion Exch.* **1996**, *14*, 705; b) Lee J. C., Jinki P., Jin T., Youn I. J., Chung H. S.: *Sep. Sci. Technol.* **1999**, *34*, 1689, and references therein.
6. a) Ismael M., Tondre C.: *Langmuir* **1992**, *8*, 1039; b) Ashrafizadeh S. N., Demopoulos G. P., Rovira M., Sastre A. M.: *Sep. Sci. Technol.* **1998**, *33*, 1145; c) Aguilar J. C., Sanchez-Castellanos M., de San Miguel E. R., de Gyves J.: *J. Membr. Sci.* **2001**, *19*, 107, and references therein.
7. a) Zhang B., Gozzelino G., Dai Y.: *J. Membr. Sci.* **2002**, *210*, 103; b) Bhandare A. A., Argekar A. P.: *J. Membr. Sci.* **2002**, *201*, 233, and references therein.
8. Menger F. M., Lee J. J.: *J. Org. Chem.* **1993**, *58*, 1909.
9. a) Tondre T., Hebrant M.: *J. Mol. Liq.* **1997**, *72*, 279; b) Son S. G., Hébrant M., Tecilla P., Scrimin P., Tondre C.: *J. Phys. Chem.* **1992**, *96*, 11072; c) Tondre C., Hébrant M.: *J. Phys. Chem.* **1992**, *96*, 11079; d) Hebrant M., Tondre C.: *Colloids Surf., A* **1994**, *83*, 293; e) Tondre C., Canet D.: *J. Phys. Chem.* **1991**, *95*, 4810.
10. a) Hampl F., Liska F., Mancin F., Tecilla P., Tonellato U.: *Langmuir* **1999**, *15*, 405; b) Cibulka R., Hampl F., Martinů T., Mazáč J., Totevová S., Liška F.: *Collect. Czech. Chem. Commun.* **1999**, *64*, 1159.
11. a) Nakatsuji Y., Kobayashi H., Okahara M.: *J. Org. Chem.* **1986**, *51*, 3789; b) Kimura E., Dalimunte C. A., Yanshita A., Machida R.: *J. Chem. Soc., Chem. Commun.* **1985**, 1041, and references therein.
12. a) Fyles T. M.: *J. Chem. Soc., Faraday Trans. 1* **1986**, *82*, 617; b) Fyles T. M.: *J. Membr. Sci.* **1985**, *24*, 229; c) Bartsch R. A., Yang I. W., Jeon E. G., Walkowiak W., Cherewicz W. A.: *J. Coord. Chem.* **1992**, *27*, 75, and references therein.
13. a) Cibulka R., Dvořák D., Hampl F., Liška F.: *Collect. Czech. Chem. Commun.* **1997**, *62*, 1342; b) Cibulka R., Hampl F., Šmidrkal J., Jr., Liška F.: *Tetrahedron Lett.* **1999**, *40*, 6849.
14. a) Marxer A.: *Helv. Chim. Acta* **1941**, *24*, 209; b) Perine T. D.: *J. Org. Chem.* **1953**, *18*, 1356; c) Gautier J.-A., Miocque M., Duclos J. P.: *Bull. Soc. Chim. Fr.* **1969**, 4356; d) Sadet J., Rumpf P.: *Bull. Soc. Chim. Fr.* **1973**, *6*, 2016.
15. van Esch J. H., Damen M., Feiters M. C., Nolte R. J. M.: *Rec. Trav. Chim. Pays-Bas* **1994**, *113*, 186.

16. a) Holzer W., von Philipsborn W.: *Magn. Reson. Chem.* **1989**, *27*, 511; b) Cibulka R., Hampl F., Kotoučová H., Mazáč J., Liška F.: *Collect. Czech. Chem. Commun.* **2000**, *65*, 227.
17. a) Meek T. L., Cheney G. E.: *Can. J. Chem.* **1965**, *43*, 64; b) Lees G., Holmes F., Underhill A. E.: *J. Chem. Soc. A* **1971**, 999; c) Hoskins B. F., Vince D. G.: *Aust. J. Chem.* **1972**, *25*, 2039; d) Liu C. H., Liu Ch. F.: *J. Am. Chem. Soc.* **1961**, *83*, 4169; e) Bucci R., Carunchio V., Magri A. D., Magri A. L.: *J. Therm. Anal.* **1984**, *29*, 679.
18. *Pallas 1.2*. CompuDrug Chemistry, Ltd, Budapest 1994.
19. a) Orama M., Saarinen H., Korvenranta J.: *Acta Chem. Scand.* **1989**, *43*, 407; b) Orama M., Saarinen H.: *Acta Chem. Scand.* **1998**, *52*, 1209.
20. a) Uheida A., Zhang Y., Muhammed M.: *J. Membr. Sci.* **2004**, *241*, 289; b) Lachowicz E., Rozanska B., Teixidor F., Meliani H., Barboiu M., Hovnanian N.: *J. Membr. Sci.* **2002**, *210*, 279; c) Alizadeh N., Salimi S., Jabbari A.: *Sep. Purif. Technol.* **2002**, *28*, 173, and references therein.
21. Myers D.: *Surfaces, Interfaces and Colloids: Principles and Applications*, p. 237. VCH Publishers, Inc., Weinheim 1991.
22. a) Ralston A. W., Reck R. A., Harwood H. J., DuBrow P. L.: *J. Org. Chem.* **1948**, *13*, 186; b) Hoerr C. W., Harwood H. J., Ralston A. W.: *J. Org. Chem.* **1946**, *11*, 199.
23. Engler C., Majmon H.: *Ber. Dtsch. Chem. Ges.* **1891**, *24*, 2536.
24. Pflaum R. T., Wehking M. W., Jensen R. E.: *Talanta* **1964**, *11*, 1193.