NOVEL CARRIER MOLECULES: LIPOPHILIC AMMONIUM YLIDES FOR MEMBRANE TRANSPORT OF METAL PICRATES

Vladimír KRÁL[a], Juraj KOUDELKA[a], Helena MOHYLOVÁ[b] and David ŠAMAN[a]

[a] *Institute of Organic Chemistry and Biochemistry,*
Czechoslovak Academy of Sciences, 166 10 Prague 6
[b] *Bateria, 274 01 Slaný*

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The novel artifcial carriers have been synthesized by introduction of lipophilic group of pyrrolidinomalonaldehyde and N-imidazolylmalonaldehyde. These stable dipolar synthetic carriers were used for transport of metal picrates through a liquid membranes. The cation specificity of the transport was determined by the means of atomic absorption spectroscopy. Carrier properties of ylides were compared with N,N-dimethyldodecylamine N-oxide and DB18C6. The formation of complexes of ylides with some inorganic salts by the means of NMR spectroscopy, X-ray and potentiometric measurement of K_s have been studied.

The transport of cationic substrates by membrane carriers is of great importance in chemistry, biology and separation science. A variety of polyether[1], polyamine[2], and polyamide[3] macrocycles have been shown to be excellent carriers for the transport of metal cations[4] and aminoacid ester salts.

Crown ethers which contain nitrogen donor atoms in the macrocycle, form stable and selective complexes and exhibit characteristic transport properties especially for some ammonium cations and heavy metal cations[1,5].

At present a lot of effort is aimed to design and synthesis of carriers with specific binding properties, i.e. for Cd^{2+} (ref.[1]), new armed macrocyclic host molecules[6-8] and to mimic (Na^+, K^+)-ATPase.

The relationship between K_s of the complex carrier–cation and the ability of the carrier to mediate cation flux in H_2O–$CHCl_3$–H_2O liquid membrane has been already described[9].

Generally, the transport of the cation strongly decreases when K_s is too small or too high in comparison with the desired optimum value.

The low K_s value results in low uptake of cations from source phase, and hence in low membrane concentration of cation–carrier complex. High K_s value, on the other hand, results in accumulation of the cation–carrier complex in membrane, but little partitioning of the cation in the receiving phase.

Among the different transport mechanisms, facilitated diffusion, or carrier-mediated transport, consists of the transfer of a substrate across membrane with the assistance of a carrier molecule (Fig. 1). The carrier is a transport catalyst, which strongly increases the rate of passage of the substrate with respect to its free diffusion. The active species is carrier–substrate supermolecule[10].

The mechanism of transport of ionic species across membrane have been the subject of numerous investigations, both in a biological and a chemical context[11,12], with the condition that it is diffusion limited. The quantitative description of the macrocycle-mediated separation of cations in liquid membranes as a function of system parameters (constants of extraction, distribution coefficients, aqueous phase macrocycle-cation and anion-cation interaction constants, membrane geometry) was presented by American authors[13].

We report here about binding and transporting properties of a new series of stabilized lipophilic nitrogen ylides. The transport ability of these compounds was compared with that of dibenzo 18-crown-6 and also with similar dipolar compound – N,N-dimethyldodecylamin N-oxide. These synthetic carriers were used for the transport of metal picrates through a liquid membranes. One of the initial motivations of our work was the fact that stabilized ammonium and sulphonium ylides form equimolar complexes with a number of anorganic salts[14,15].

RESULTS AND DISCUSSION

While macrocycle mediated flux of salts $M^{n+}X_n$ is based on interaction of M^{n+} with a macrocycle, dipolar carriers used by us interact both with cation and anion.

We wanted to obtain deeper insight in the character of the interactions and the structure of the formed complex of ylides with anorganic salts.

For the study we used ^{1}H NMR and ^{13}C NMR spectroscopy, potentiometric determination of the values of the stability of the studied complexes and X-ray spectroscopy.

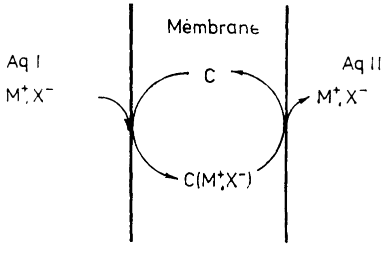


FIG. 1

Liquid membrane system for transport of salts M guest cation, X co-transported anion, C carrier

NMR *Results*

Nitrogen and sulphur ylides stabilized in carbanion center by two formyl groups represent stable compounds[14,15]. It is possible to study their complexation by the means of NMR spectroscopy[16]. We have used trimethylammoniodiformyl methylide (*I*) as a model compound. The complex formation of compound *I* with alkali, magnesium and silver perchlorates was probed by using spin–spin coupling constants and ^1H and ^{13}C chemical shifts. Concentration and temperature dependence of chemical shifts were applied to study the thermodynamics of the complexes[16]. Lithium, magnesium and silver perchlorates induce nonlinear, whereas sodium perchlorate linear dependence of the shift on concentration.

NMR results lead us to conclusion that studied complexes are by no means very strong because the complexation was not completed even at cation/ylide molar ratio 10. Solving the structure of the complexes of salts with ylide we were interested in following facts: conformation of the ylide; if there was any change of conformation with respect to the change free ylide–complexed ylide; binding center for anion and cation.

Spatial arrangement and charge distribution of compound *I* calculated in quantum chemical study was in good agreement with the arrangement in crystal lattice[18].

Theoretical study of equimolar complex of ylide *I* with sodium perchlorate also predicts that Na binds in the place of highest electron density. This is at the oxygen atoms of the formyl groups (a delocalization of the charge of ylide carbon to oxygens of formyl groups occurs) without any change in the conformation of ylide. This prediction was confirmed by X-ray analysis[16].

Transport

Here we report on cation-binding and transporting properties of a new series of stabilized lipophilic ylides (*IV*–*VIII*). The novel artificial carriers have been synthesized by introduction of lipophilic group at pyrrolidinomalonaldehyde[19], and N-imidazolylmalonaldehyde[20]. These stable dipolar synthetic carriers were used for transport of metal picrates through a bulk liquid membrane. The metal ion transport was studied using double cylindrical glass cell open at one end. The ammonium ylides could be also used for organic anions – they have binding center for anion-coulombic interaction with quaternary ammonium group.

Prediction of the effectiveness of a compound for membrane transport can be done on the basis of the value of K_s of the respective carrier with the compound which should be transported. For K_s values too low is the transport reduced owing to the slow uptake of the salt to organic phase. In such way only small amount of the complex is formed. On the other hand, the salt can be easily released from the complex to the receiving phase. For high K_s values the transport of the salt to organic phase is easy, but the release of the salt to receiving phase is worse as the complex is too strong. The K_s values of studied compounds are presented in Table I. Generally we can say that these values are lower than the ones optimal for the transport. For these ylides it is important to have a long hydrocarbon chain as the concomitant insolubility in the aqueous phase protects the liquid membrane system from degradation.

For our compounds ion uptake can be the rate-determining due to the low K_s values. It was find for 18-crown-6 that ion release was rate determining and the concentrtion of the metal (potassium) picrate in the organic phase was much higher.

We were interested especially in the effectivity of the transport with respect to charge distribution, namely with respect to the distance of positive and negative charges at the study of dipolar carriers mediated transport. Except of ylides *III*, *IV*, *VII*, and *VIII* (positive charge at quaternary nitrogen, negative charge delocalized on malonaldehyde anion) we have also studied the transport at N,N-dimethyldodecylamine N-oxide (*IX*), too, (positive and negative charges localized on neighboring atoms). The results (Table II, Table III) suggest that the effectivity of the transport decreases with increasing distance of positive and negative charges and also with the delocalization of the charge on more atoms.

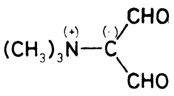
Interactions of ylides with salts were repeatedly studied[14,15,17,21]. For our compounds, it can be supposed from ^{1}H NMR (ref.[16]) and from quantum chemical study[17] that cation is bound to the place with highest electron density – oxygen atoms of formyl groups, and the anion is bound to the metal cation and at the same time to the quaternary ammonium group. X-Ray study of the complex *I* with $NaClO_4$ has confirmed the supposed arrangement[16].

TABLE I

The values of the constant of formation K_s for ylides *I*–*VIII* and aminoxide *IX* with NaCl (25°C, in water)

Compound	K_s	Compound	K_s
I	14·1[a]	*VII*	17·8
III	19·4	*VIII*	12·9
IV	20·9	*IX*	17·0
V	28·x		

[a] For $NaClO_4$ the value of K_s is 7·5.



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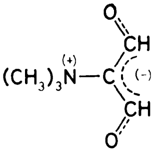
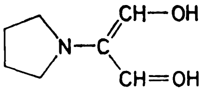
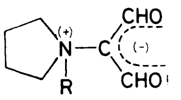
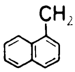


Ia

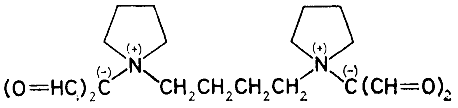


II



III, R = 

IV, R = $CH_3(CH_2)_{16}CH_2$



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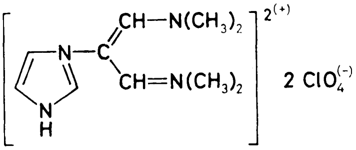
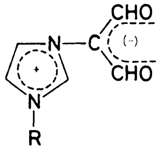
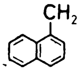
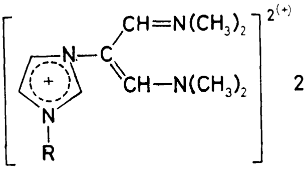


VI

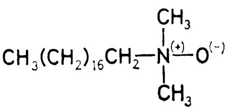


VIII, R = $CH_3(CH_2)_{16}CH_2$

VII, R = 

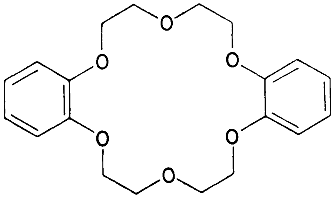


VIIIa



$CH_3(CH_2)_{16}CH_2-\overset{CH_3}{\underset{CH_3}{N^{(+)}}}-O^{(-)}$

IX



X

CONCLUSIONS

As the kinetics of the transport through the membrane for compounds *III* and *IV* and *VII* and *VIII* differ only slightly (as we found from preliminary experiments) and also with respect to higher stability of ylides *III* and *IV* we have measured the kinetics of the transport NaPi at the compounds *III* and *IV*, resp., as well as selectivity of the transport of MPi. The found values were compared to those aminooxide *IX* and also with that of DB18C6 (*X*).

The results are presented at Tables I–III and in Fig. 2 and Fig. 3. It was found that the most effective carrier was the compound *IX*, where positive and negative

TABLE II

Transport of the compound *IV* against the gradient of the concentration. Liquid membrane: 5 ml of 1 mM solution of *IV* in chloroform; outer phase: 5 ml of solution of NaPi; inner phase: 5 ml of solution of NaPi

Time h	Outer phase conc. of NaPi		Inner phase conc. of NaPi	
	10^{-5} mol l^{-1}	%	10^{-5} mol l^{-1}	%
	pH 9·15		pH 7·28	
0	5·379	49·68	5·448	50·32
1	5·448	52·00	5·030	48·00
2	5·724	54·96	4·690	45·04
5	6·345	60·93	4·069	39·07
7	6·621	64·87	3·586	35·13
9	6·966	69·18	3·103	30·82
	pH 7·00		pH 6·00	
0	5·517	50·00	5·517	50·00
1	5·517	50·00	5·517	50·00
2	5·724	51·55	5·379	48·45
6	6·275	58·90	4·379	41·10
8	6·621	61·93	4·070	38·07
	pH 9·15		pH 6·28	
0	5·480	49·82	5·520	50·18
1	5·586	53·63	4·830	46·37
2	5·931	59·30	4·070	40·70
3	6·137	64·03	3·448	35·97
4	6·758	72·60	2·551	27·40

charges are concentrated on neighboring atoms. Effectivity of transport decreases with increasing delocalization of the charge.

TABLE III

Selectivity of the transport for ylides *III*, *IV*, aminoxide *IX* and crown *X* (conc. in receiving phase after 24 h, relating to Na^+ in %)

Carrier	pH	Mixture A					Mixture B				
		Li	Na	K	Rb	Cs	Na	Ag	Cd	Cu	Pb
hIII	7	0	100	23	0·5	0	100	10	0	23	3
	9	2	100	15	0·5	0	100	21	0	18	3
IV	7	0	100	19	0·4	0	100	10	0	26	6
	9	1	100	21	0·7	0	100	2	0·3	23	6·5
IX	7	0·1	100	21	0·5	0	100	8	0	14	0
	9	0·2	100	16	1	0	100	12	0	27	0
X	7	—	—	—	—	—	100	11	0	0	64
	9	0	100	253	600	633	100	3	0	24	0

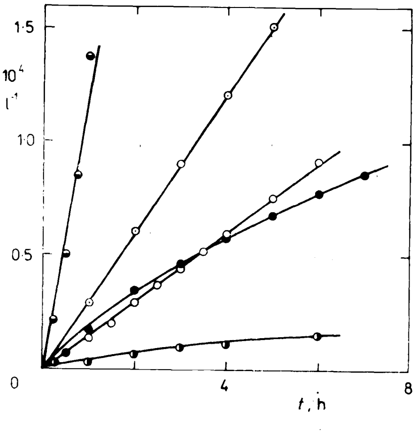


FIG. 2

The concentration of Na^+ ion in the receiving phase as a function of time and a carrier (source phase: $1·5 . 10^{-2}$—$1·5 . 10^{-3}$M NaPi, pH 7; receiving phase: pH 7). ◑ no carrier; ○ *III*, ● *IV*; ◒ *IX*, ⊙ *X*

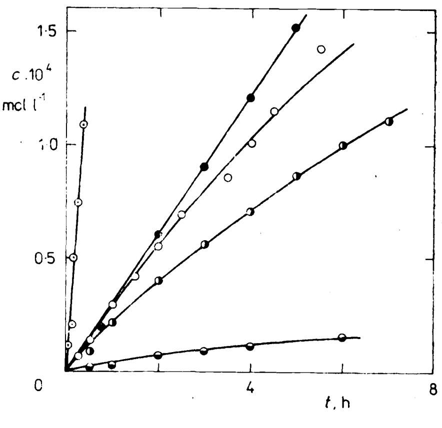


FIG. 3

The concentration of Na^+ ion in the receiving phase as a function of time and a carrier (source phase: $1·5 . 10^{-2}$—$1·5 . 10^{-3}$M NaPi, pH 7; receiving phase: pH 9). ◒ no carrier; ○ *III*; ◑ *IV*; ⊙ *IX*; ● *X*

We have found strong dependence of transport on pH at all types of dipolar carriers. At higher pH is the transport of NaPi quicker.

Analogical phenomenon was observed by Japan authors at N^+—N^- carbonyl stabilized ylides[22].

We have used this fact at the measurement against the gradient of concentration. At the arrangement, where both the receiving and source phases were of the same concentration of NaPi (app. $7 . 10^{-5}$M NaPi – suitable for UV detection of the kinetics), but of the different pH, we have found that NaPi was transferred to the phase with higher value of pH. This fact was not observed at DB18C6. The reason is the dependence of degree of interaction of the dipolar carrier with the transported salt on pH. The results are given in Fig. 2 and Fig. 3.

The selectivity of the transport of the picrate mixture was studied by the means of atomic absorption (mixture A: MPi, M = Li, Na, K, Rb, Cs; mixture B: MPi, M = Na, Ag, Cu, Cd, Pb), starting concentration $1 . 10^{-3}$M MPi.

Selectivity of the transport is given by interaction of metal M^{n+} with oxygens in malonaldehyde anion. These, according to quantum chemical results, carry the prevailing part of negative charge[23]. From hard-soft theory, it can be concluded that oxygen strongly interacts with Na^+, and the transport of Cu^{2+} is probably affected by easy formation of the complexes of β-dicarbonyl compounds with this cation.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried over phosphorous pentoxide at 25°C/27 Pa for 24 h. ^1H NMR spectra were taken on the FT NMR spectrometer Varian XL-200 (200 MHz) and the CW NMR spectrometer Tesla BS-467 (60 MHz) in $CDCl_3$ with tetramethylsilane as an internal standard. IR spectra were measured on a Zeiss UR-20 spectrometer in chloroform; wavenumbers are given in cm^{-1}. Mass spectra were measured on ZAB-EQ, VG analytical. Atomic absorption spectra were taken on Perkin-Elmer 1380 instrument.

Trimethylammoniumdiformyl methylide (*I*) was prepared according ref.[14], pyrrolidonmalonaldehyde (*II*) according ref.[19] and trimethinium salt according ref.[20]. N,N-Dimethyldodecylamin N-oxide was purchased from fy Aldrich.

Transport Experiments

The transport of ions (salts) across the $CHCl_3$ membrane was studied using the double cylindrical cell (see Fig. 4), which consisted of a 30 ml membrane phase ($CHCl_3$ containing 1 mmol of carrier), stirred at 150 r.p.m. by a magnetic stirrer at 22°C interfaced to both 5 ml source phase (aqueous layer I containing metal picrate in concentration $5 . 10^{-5}$ mol l^{-1}), buffered at pH 7 (tris) and to 20 ml receiving phase (aqueous layer II) buffered at pH 7—9 (tris). At a certain intervals 2 ml sample was taken from the receiving phase and concentration of picrate was determined by UV spectroscopy and concentration of the metal cations by atomic absorption spectroscopy (an average of three measurements, an error 5%). Blank experiments (no carrier present at $CHCl_3$ phase) were performed to demonstrate the absence of membrane leakage.

The carrier resides in the $CHCl_3$ layer with no sign (TLC) of decomposition or migration into aqueous layers.

1-Naphthylmethylpyrrolidiniodiformyl Methylide (*III*)

To pyrrolidinomalonaldehyde (1·41 g, 10 mmol) in methanol (5 ml) potassium methoxide (0·71 g, 10 mmol) was added and the mixture evaporated in vacuo to dryness. Then acetonitrile (20 ml) and 1-bromomethylnaftalene (2·21 g, 10 mmol) were added. The mixture was stirred for 24 h, the course of the reaction being monitored by the TLC. After evaporation of the solvent the solid rest was dissolved with stirring in potassium carbonate (10 ml) and the product was extracted to the 5 : 1 mixture of methylene chloride–ethanol. The product was purified by chromatography in methylene chloride–ethanol 10 : 1 mixture. The yield of *III* was 2·50 g (89%), m.p. 117–125°C. Mass spectrum, *m*/*z*: 281 (M^+). ^1H NMR spectrum: 1·91 m, 4 H (CH_2CH_2); 2·95 m, 4 H (2 CH_2N); 5·22 s, 2 H (CH_2Ar); 7·35–8·08 m, 7 H (arom); 8·64 s, 2 H (CHO). IR spectrum: 2 776 sh, (CHO); 1 717, 1 662 (C=O); 1 582 (C=C); 1 462 sh, 1 472 sh, 1 482 (CH_2); 1 597, 1 387, 1 396, sh (ring). For $C_{18}H_{19}NO_2$ (281·3) calculated: 76·84% C, 6·81% H, 4·98% N; found: 76·64% C, 6·90% H, 4·77% N.

Octadecylpyrrolidiniodiformyl Methylide (*IV*)

Pyrrolidinomalonaldehyde (0·705 g, 5 mmol) was dissolved in methanol (10 ml), DMF (15 ml) and potassium methoxide (0·426 g, 6 mmol) was added. Methanol was evaporated in vacuo. Octadecylbromide (2·0 g, 6 mmol) and benzene (5 ml) were added. The mixture was stirred for 24 h at room temperature. The reaction mixture was concentrated and for purification the same procedure as for *III* was used. The yield of product *IV* was 1·417 g (72%), m.p. 73–74°C. Mass spectrum, *m*/*z*: 393 (M^+). ^1H NMR spectrum: 0·82 t, 3 H (CH_3, $J = 6{\cdot}0$); 1·23 m, 32 H ($(CH_2)_{16}$); 1·75 m, 4 H (CH_2CH_2); 3·33 m, 2 H ($NCH_2(CH_2)_{16}$); 3·93 m, 4 H (NCH_2); 8·73 s, 2 H (CHO). IR spectrum: 2 774 (C—H); 2 936, 2 863 (CH_2); 1 649, 1 585 (O—CH—C—CH—O); 1 469 (CH_2). For $C_{25}H_{47}NO_2$ (393·6) calculated: 76·28% C, 12·04% H, 3·56% N; found: 76·16% C, 12·17% H, 3·46% N.

3-(1-Naphthylmethyl)imidazoliniumdiformyl Methylide (*VII*)

Perchlorate *VI* (2·92 g, 10 mmol) was dissolved in absolute acetonitrile (20 ml) and potassium hydrogencarbonate (2 g) and then 1-(bromomethyl)naphthalene (2·21 g, 10 mmol) were added.

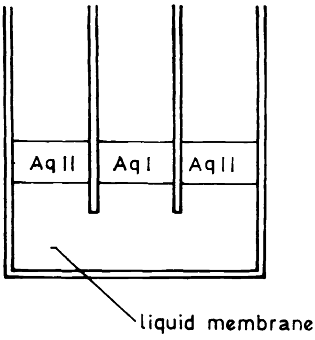


FIG. 4
Scheme of the measuring cell

The reaction mixture was stirred for 24 h, then the solvent evaporated and potassium hydrogen carbonate (2 g) and water (20 ml) added. The mixture was heated at 80°C for 2 h, evaporated to dryness and the product was extracted to the methylene chloride–ethanol (5 : 1) mixture and then purified on silica gel in methylene chloride–ethanol 10 : 1. The yield of ylide *VII* was 2·31 g (83%), m.p. 188–191°C. Mass spectrum, *m/z*: 278 (M^+). ^1H NMR spectrum: 5·92 s, 2 H (CH_2Ar); 7·25–8·10 m, 10 H (aromatic and heteroaromatic H); 8·57 bs, 2 H (CHO). IR spectrum: 2 780 sh (CHO); 1 680 (C═O); 1 616, 1 599 (C═C); 1 481 (CH_2). For $C_{17}H_{14}N_2O_2$ (278·3) calculated: 73·36% C, 5·07% H, 10·07% N; found: 73·19% C, 5·02% H, 10·12% N.

3-Octadecylimidazoliniumdiformyl Methylide (*VIII*)

This compound was prepared in analogous way as *VII*, using octadecyl bromide (3·33 g,10 mmol) as alkylating agent. The yield of ylide *VIII* was 2·695 g (69%), m.p. 216–219 C. Mass spectrum, *m/z*: 390 (M^+). ^1H NMR spectrum: 0·85 t, 3 H (CH_3, $J = 6·1$); 1·22 m, 32 H ($(CH_2)_{16}$); 3·20 s, 2 H (CH_2N); 8·00 bs, 1 H (CH, imidazole, position 4); 8·82 s, 2 H (CHO); 9·07 ks, 1 H (CH, imidazole, position 2); 9·58 bs, 1 H (CH, imidazole, position 5). IR spectrum: 2 750 sh (CHO); 1 632, 1 590 (OCH—CH—CHO); 1 551, 1 486 sh (ring); 1 467 (CH_2); 1 384 sh (CH_3). For $C_{24}H_{42}N_2O_2$ (390·6) calculated: 73·79% C, 10·84% H, 7·17% N; found: 73·67% C, 10·71% H, 7·20% N.

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