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Solvent effects on ion pairing of tetra-*n*-butylammonium cyanide. A conductometric study

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Tetra-*n*-butylammonium cyanide (*n*-Bu_4NCN) is a commonly used reagent, for example, for the synthesis of nitriles. Recently *n*-Bu_4NCN has been used as the nucleophilic reagent in kinetic isotope effect studies of nucleophilic aliphatic substitution reactions. The present research concerns the aggregation status (dissociated ions, ion pairs, higher aggregates) and transport properties of *n*-Bu_4NCN in water, dimethyl sulfoxide (DMSO), and tetrahydrofuran (THF), at 25°C as studied by means of precision conductometry. These properties are of great importance since both non-polar and dipolar aprotic solvents are commonly used in the applications. In water as solvent the equilibrium constant for ion-pair formation, $K_p = 10.1$ and the limiting molar conductivity, $\Lambda_o = 102.4\,\mathrm{cm^2\,\Omega^{-1}\,mol^{-1}}$. The corresponding values for DMSO are $K_p = 1.98 \pm 0.19$ and $\Lambda_o = 34.59 \pm 0.03\,\mathrm{cm^2\,\Omega^{-1}\,mol^{-1}}$. These data imply that the degree of dissociation, in contrast to the expectations, is higher in DMSO than in water at the same salt concentration. In THF, the conductance as a function of concentration shows a minimum typical for solvents with low relative permittivity, indicating the formation of higher aggregates. The equilibrium constant for ion-pair formation and conductivity in THF is $K_p = 58.4 \times 10^3$ and $\Lambda_o = 9.81\,\mathrm{cm^2\,\Omega^{-1}\,mol^{-1}}$. Copyright © 2007 John Wiley & Sons, Ltd.

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Keywords: Conductometry; Ion pairs; Solvent effect; Tetra-*n*-butylammonium cyanide; DMSO; THF

INTRODUCTION

Tetra-*n*-alkylammonium cyanides are convenient sources of cyanide ions which exhibit high solubility in polar and non-polar aprotic solvents that are commonly used in organic synthesis. The tetra-*n*-alkylammonium cyanides are powerful nucleophiles and can also act as basic reagents.[1] These cyanides are also useful in mechanistic investigations. For instance, recent studies determining the transition-state structure of bimolecular nucleophilic aliphatic substitution reactions using kinetic isotope effects have employed tetra-*n*-butylammonium cyanide (*n*-Bu_4NCN) as the nucleophilic reactant.[2] It is well documented that electrolytes in solvents of low and moderately high relative permittivities can exist either as ion pairs, triple ions, quadruple ions, and higher aggregates.[3] Because the amount of aggregation has implications for the interpretation of kinetic data, we have undertaken an investigation of the aggregation of *n*-Bu_4NCN in tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), and water at 25°C using precision conductometry. The relative permittivity ε_r which is a main factor governing the extent of ionic aggregation, is 7.58, 46.68, and 78.30 for THF, DMSO, and water, respectively.[3,4] These solvents represent a selection of relatively low and high polarity solvents.

EXPERIMENTAL PROCEDURE

Materials

THF (Fluka, puriss, p.a. ≥ 99.5%) was distilled twice, first over potassium hydroxide and then over sodium and benzophenone. DMSO (Aldrich, anhydrous, 99.9%, <0.005% H_2O) was used as received. The *n*-Bu_4NCN (Fluka purum, >95.0%) was stored and handled in a glove box under nitrogen atmosphere. The conductivity, κ, of the Milli-Q water and DMSO was 3×10^{-6} and $1.6 \times 10^{-6}\,\Omega^{-1}\,\mathrm{cm^{-1}}$, respectively. It should be noted that THF purified as described is an excellent solvent for electrical conductance measurements. No corrections for the solvent conductivity had to be performed. The conductivity of THF was too low to be detected even with the advanced conductivity equipment described below. Solutions were prepared on a weight basis and converted to concentrations using the density of the solvent. For systems similar to the present, the difference between the density of the solution and the solvent amounts to at most a few tenths of a per cent within the concentration range here used to calculate the conductance parameters.

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Equipment

Conductivities were determined using a Leeds and Northrup 4666 conductivity bridge connected to a Princeton Applied Research Model 129A two-phase lock-in amplifier, a Hewlett Packard Model 201C audio oscillator, and an *hp* 11473 B balancing transformer. A 400 ml capacity conductometric cell,[5] fitted with platinized platinum electrodes to reduce the frequency dependence of the resistance, was used. The cell constant was found to be 0.056199 cm^{-1} with a standard deviation (SD) of 0.047%.

Conductivity measurements

An initial 300 ml portion of pure solvent was transferred to the cell and the resistance of the pure solvent was measured. Then, portions of an n-Bu_4NCN stock solution, usually 1–5 ml, were successively added using a calibrated Metrohm Herisau Dosimat E 535 burette or alternatively by means of an injection syringe in combination with differential weighing. After each addition, the cell solution was agitated by a magnetic stirrer. A certified mercury-in-glass thermometer, graduated to 0.01°C, was employed to determine the slowly changing temperature of the cell solution. At each concentration, the resistance of the cell solution was measured at three different frequencies, 2.0, 2.85, and 5.0 kHz, and extrapolated to infinite frequency to reduce, as far as possible, the relaxation effect. In practice, the extrapolated value was obtained from the equation of a least-squares plot of resistance *versus*. inverted frequency. To enable re-evaluation of resistances to 25.00°C, a temperature *versus*. resistance curve was recorded for each series of measurements at the highest n-Bu_4NCN concentration.

DATA EVALUATION

In the analysis of the experimental molar conductivity *versus*. concentration curve, the Fuoss-Hsia[6,7] and Fernandez-Prini[8] (FHFP) conductance equation

$$\Lambda = \Lambda_o - S \cdot c_i^{1/2} + E \cdot c_i \cdot \log c_i + J_1 \cdot c_i - J_2 \cdot c_i^{3/2} - K_p \cdot c_i \gamma^2 \Lambda \tag{1a}$$

for electrolytes subject to ion-pair formation was used. In this equation, c_i is the concentration of free ions, γ the mean molar activity coefficient, and K_p the thermodynamic equilibrium constant for ion-pair formation. The coefficients S and E are functions of the relative permittivity, ε_r, and viscosity, η, of the solvent, the limiting molar conductivity, Λ_o, and the temperature. The coefficients J_1 and J_2 depend, in addition, on the maximum distance between the charges in the ion pair, which was set equal to the Bjerrum radius, q, cf. References [9–11]. By rearranging the terms, Eqn (1a) can be written in the linear form as

$$y = \Lambda_o - K_p \cdot x \tag{1b}$$

K_p and Λ_o were iteratively calculated using Eqn (1b), the law of mass action for the equilibrium between free and paired ions and the Debye–Hückel equation for the mean molar activity coefficient of free ions (p. 229 in Reference [3]). The distance parameter involved in the Debye–Hückel equation was set equal to the Bjerrum radius. Constants used for the properties of the investigated solvent are given in Table 1.

Table 1. Density, relative permittivity, and viscosity for H_2O, DMSO, and THF measured at 25°C

	$d/g\,cm^{-3}$	ε_r	η/P	References
H_2O	0.99707	78.30	0.008903	[3]
DMSO	1.0958	46.68	0.01996	[4]
THF	0.88415	7.58	0.00460	[4]

RESULTS AND DISCUSSION

The Bjerrum theory for ion-pair formation states that the ion-pair association constant for a univalent electrolyte is given by

$$K_p = (4\pi N_A/1000)\int_a^q r^2 \exp\{-e^2/(\varepsilon_r k_B T r)\}\,dr \tag{2}$$

where a is the minimum, q the maximum, r the variable center-to-center distance between the ions in the ion pair, e the elementary charge, N_A Avogadros number, ε_r the relative permittivity, k_B Boltzmann's constant, and T is the absolute temperature. The maximum distance, the Bjerrum radius, q, corresponds to the state where the electrical potential energy between the ions in the ion pair is twice the thermal energy of the solvent molecules as described in

$$q = e^2/(2\varepsilon_r k_B T) \quad (1:1-\text{electrolyte}) \tag{3}$$

For the solvents H_2O, DMSO, and THF at 25°C eqn (3) yields $q = 358$, 600, and 3700 pm, respectively. Setting the minimum distance between the charges in the n-$Bu_4N^+CN^-$ ion pair equal to the sum of the radius, 494 pm of the n-Bu_4N^+ ion[3] and half the triple bond length, 58 pm, of the CN^- ion[12] affords $a = 552$ pm. This value exceeds the maximum distance possible for ion-pair formation in water. Accordingly, n-Bu_4NCN is expected to be unassociated in water.

n-Bu_4NCN in aqueous solution

The interpretation of the conductivity data for n-Bu_4NCN in aqueous solution is complicated by the hydrolysis of cyanide ion yielding hydrogen cyanide and hydroxide ion. However, the effect of hydroxide ions on the conductivity is significant only in the low concentration region. Values of K_p and Λ_0 were calculated by iteratively fitting the FHFP equation to the two, three, four, and so on, highest concentration points of the two series of measurements performed. In Fig. 1, K_p has been plotted as a function of the minimum concentration of n-Bu_4NCN in the interval. With increasing concentration the ion-pair formation constant asymptotically approaches $K_p = 10.1$, which corresponds to a degree of dissociation, $\alpha \sim 0.96$, at 5 mM. For n-Bu_4NI, Evans and Kay[13] report $K_p = 3.1 \pm 0.9$ ($\alpha \sim 0.987$ at this concentration) and 2.0 ± 3.4 ($\alpha \sim 0.992$). Hence, the assessed value of $K_p = 10$ for the n-Bu_4NCN ion-pair association constant appears to be most reasonable.

Using the same approach to estimate the limiting molar conductivity (Fig. 2) yields a value of $\Lambda_0 = 102.4\ cm^2\,\Omega^{-1}\,mol^{-1}$. Subtraction of the limiting molar conductivity reported[3] for the n-Bu_4N^+ ion, $\Lambda_0 = 19.4\ cm^2\,\Omega^{-1}\,mol^{-1}$, results in $\Lambda_0 = 83$ for the

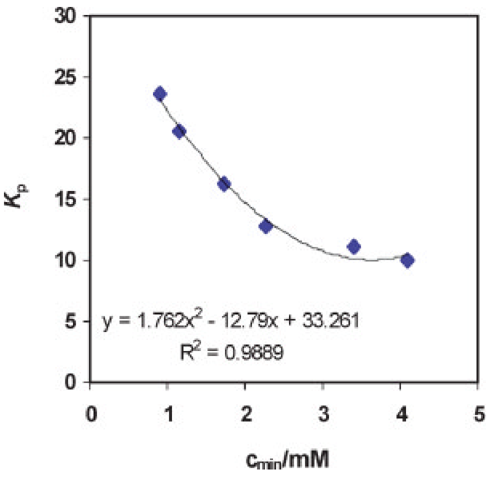

Figure 1. Dependence of K_p on the concentration interval for *n*-Bu$_4$NCN in H_2O at 25°C. The points represent the K_p-values calculated from the concentration interval spanning from the minimum concentration, C_{min}, to the maximal concentration of 0.0057 M. Also shown are the polynomial curve fitted to the K_p-values and its equation.

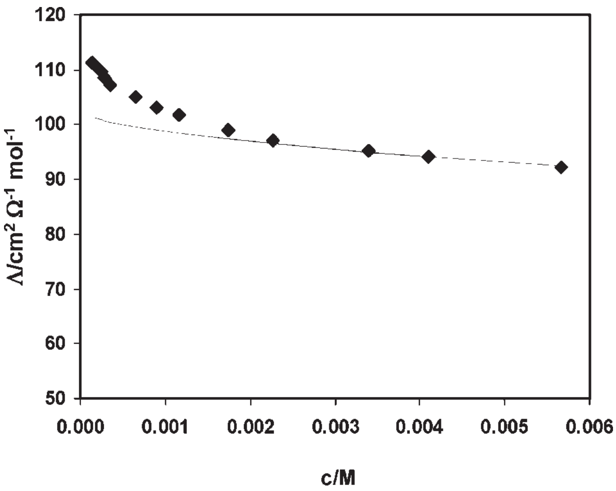

Figure 3. Dependence of the molar conductivity on the concentration of *n*-Bu$_4$NCN in H_2O at 25°C. The solid line represents the molar conductivity according to the FHFP equation when using $K_p = 10.1$ and $\Lambda_0 = 102.4\ \text{cm}^2\ \Omega^{-1}\ \text{mol}^{-1}$. The points represent the experimentally determined Λ-values.

cyanide ion which is in very good agreement with the value of $82\ \text{cm}^2\ \Omega^{-1}\ \text{mol}^{-1}$ reported by Falkenhagen.[14]

In Fig. 3 the concentration dependence of the experimentally determined Λ-values are depicted together with the molar conductivity assessed according to the procedure described above.

n-Bu$_4$NCN in DMSO

Despite the lower relative permittivity, $\varepsilon_r = 46.68$, as compared with water, $\varepsilon_r = 78.30$, the extent of ion pairing of *n*-Bu$_4$NCN is somewhat less than in the aqueous solution. The *x*–*y* plot in Fig. 4 exhibits an almost horizontal line, the slope of which corresponds to a K_p value of 1.98 ± 0.19 (SD). The line extrapolates to a value of the limiting molar conductivity of 34.59 ± 0.03 (SD) $\text{cm}^2\ \Omega^{-1}\ \text{mol}^{-1}$.

On the basis of the ion-pair formation constant, $K_p = 1.98$, and Bjerrum's eqn (2), the value 503 pm for the minimum distance, *a*, between the centers of charge of the *n*-Bu$_4$N$^+$ and CN$^-$ ions in the ion pair was calculated. This value is somewhat less than that estimated from the sum of the radius of the *n*-Bu$_4$N$^+$ ion, and half of a carbon-nitrogen triple bond length (552 pm).

n-Bu$_4$NCN in THF

In solvents of low relative permittivities, the observation of ion pairs is restricted to a narrow concentration range. This is due to noticeable formation of higher aggregates even at modest concentrations. According to a theory presented by Fuoss and Accascina,[15] the so-called critical concentration limit, c_o, for the

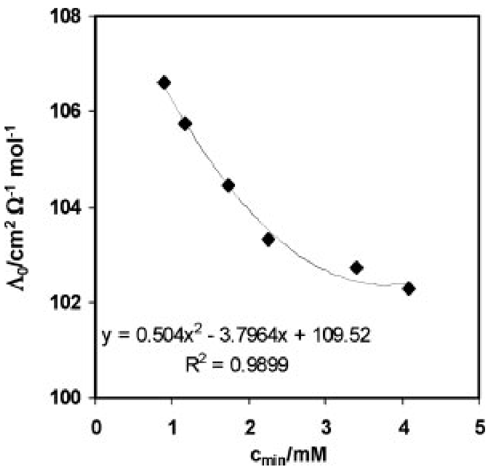

Figure 2. Dependence of Λ_0 on the concentration interval for *n*-Bu$_4$NCN in H_2O at 25°C. The points represent the Λ_0-values calculated from the concentration interval spanning from the minimum concentration, C_{min}, to the maximal concentration of 0.0057 M. Also shown are the polynomial curve fitted to the Λ_0-values and its equation.

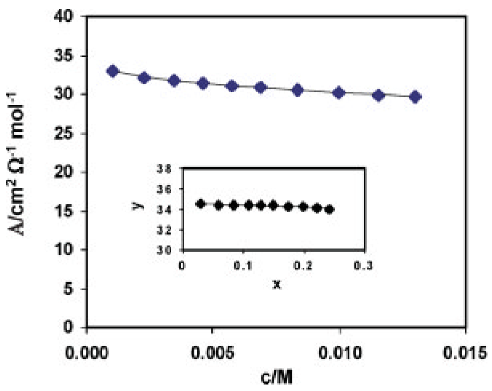

Figure 4. Molar conductivity of *n*-Bu$_4$NCN measured in DMSO at 25°C together with the molar conductivity according to the FHFP equation represented as a solid line. The inserted plot is the corresponding FHFP *x*–*y* plot yielding $K_p = 1.98$, $\Lambda_0 = 34.59\ \text{cm}^2\ \Omega^{-1}\ \text{mol}^{-1}$ according to the best fit.

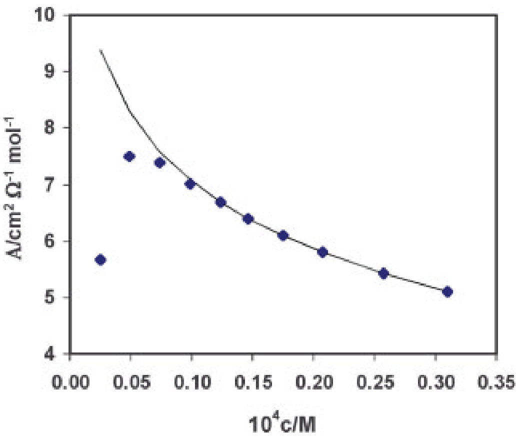

Figure 5. Molar conductivity of *n*-Bu_4NCN measured in THF at 25°C. The solid line represents the molar conductivity according to the FHFP equation fitted to the six points of the highest concentration. $K_p = 59.6 \times 10^3$; $\Lambda_0 = 10.71\ cm^2\ \Omega^{-1}\ mol^{-1}$.

Table 2. Equilibrium constants for ion-pair formation and limiting molar conductivity for some tetraphenylborates in THF (TAB = triisoamyl-*n*-butyl)[16]

Salt	$10^{-3}K_p$	$\Lambda_0/cm^2\ \Omega^{-1}\ mol^{-1}$
$TABBPh_4$	18.7	81.5
$LiBPh_4$	12.6	79.0
$NaBPh_4$	12.3	87.7
$KBPh_4$	41.7	97.2

formation of triple ions is a function of $e^2/\varepsilon k_B T$. For univalent electrolytes at 25°C, the expression derived reduces to

$$c_o = 3.2 \times 10^{-7} \varepsilon_r^3 \quad (4)$$

The critical concentration limit for ion-pair formation in THF thus equals 1.4×10^{-4} M. Therefore, the low concentration interval of 2–31 μM was investigated to determine K_p and Λ_0. The result is shown in Fig. 5. The four points of the lowest concentrations deviate significantly from the FHFP equation, which is fitted to the six points at the highest concentrations. The rationale for this behavior is probably adsorption of the electrolyte on the platinized platinum electrodes which have a large effective area. An adsorption effect of this kind has been observed earlier.[3]

A series of measurements in the concentration interval $(0.19–1.37) \times 10^{-4}$ M afforded an ion-pair association constant of 58.4×10^3 (as shown in the FHFP *x*–*y* plot in Fig. 6), in excellent agreement with $K_p = 59.6 \times 10^3$ obtained from the data found at low concentration, 2–31 μM in Fig. 5. This value is reasonable since it is of the same order of magnitude as the K_p reported for lithium, sodium, and potassium tetraphenylborate, and for triisoamyl-*n*-butylammonium tetraphenylborate in THF, that have been reported previously by Comyn *et al.*[16] (Table 2). The Λ_o value of $9.81\ cm^2\ \Omega^{-1}\ mol^{-1}$ is however of a remarkably smaller magnitude which indicates a considerably lower mobility of the ions of *n*-Bu_4NCN in the same solvent.

The minimum distance between the charges of the ions in the *n*-$Bu_4N^+CN^-$ ion-pair, $a = 586$ pm, calculated from Bjerrum's equation and $K_p = 58.4 \times 10^3$, appears most reasonable. It exceeds the radius of the *n*-Bu_4N^+ ion[3] by 92 pm, a plausible value for the "radius" of a solvated CN^- ion.

In the conductance graph shown in Fig. 6, the calculated curve according to the FHFP equation has been extrapolated from the ion/ion-pair range into the range exceeding the critical theoretical concentration, c_o, for triple-ion formation. The experimental points in this higher concentration range exceed the conductivity expected by FHFP theory. This behavior has previously been observed for tetra-*n*-butylammonium picrate in chlorobenzene,[17] $\varepsilon_r = 5.612$, and for sodium iodide in 1-octanol,[18] $\varepsilon_r = 9.85$. In both cases the introduction of a triple-ion association constant rendered a better agreement between the experimental points in the higher concentration range and the theoretical conductance curve.[17,18] However, the experimental data available in this study are not enough to make such a calculation meaningful.

In Fig. 7, the conductivity curve for *n*-Bu_4NCN in THF is shown for the concentration range 2×10^{-5}–0.12 M. The conductance

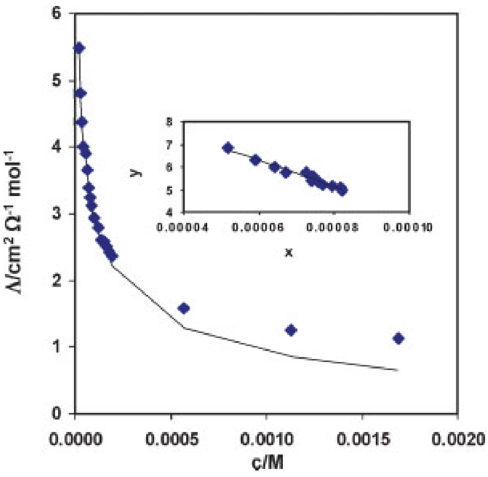

Figure 6. FHFP *x*–*y* plot and the molar conductivity of *n*-Bu_4NCN measured in THF at 25°C. The solid line represents the molar conductivity according to the FHFP equation extrapolated from the lower $(1.86–13.7) \times 10^{-5}$ M to the higher concentration range. $K_p = 58.4 \times 10^3$, $\Lambda_0 = 9.81\ cm^2\ \Omega^{-1}\ mol^{-1}$.

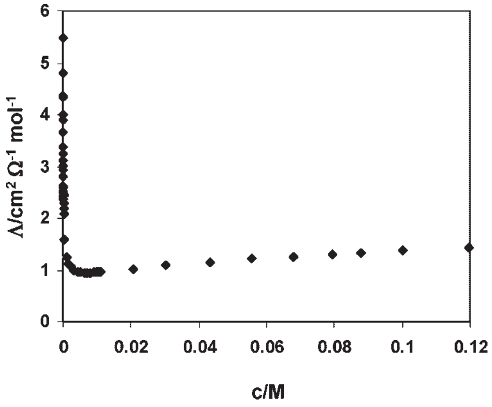

Figure 7. Molar conductivity of *n*-Bu_4NCN measured in THF at 25°C in the concentration range from 2×10^{-5} to 0.12 M

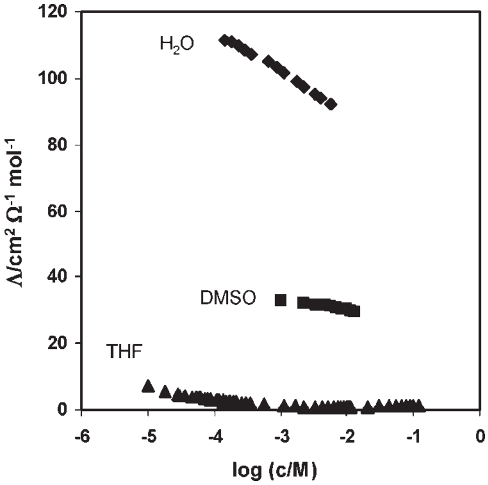

Figure 8. Molar conductivities for n-Bu$_4$NCN in H_2O, DMSO, and THF. Note that the points for *n*-Bu$_4$NCN in H_2O as solvent contain a contribution from OH^- ions

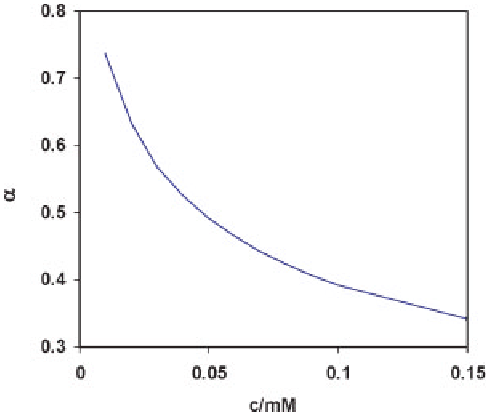

Figure 9. The degree of dissociation, α, of *n*-Bu$_4$NCN in THF. In this low concentration range the electrolyte is, in practice, completely dissociated in DMSO and H_2O.

curve shows a minimum, which is typical for electrolytes in solvents of low relative permittivity. This type of behavior has been observed, for instance, by Hughes *et al*. who in great detail discussed conductance data for several quaternary ammonium salts in benzene in terms of triple-ion formation.[19]

CONCLUDING REMARKS

An overall view of the conductivity data determined in the three solvents investigated is presented in Fig. 8. The extensive aggregation of *n*-Bu$_4$NCN in THF results in very low conductivity despite the low viscosity of this solvent compared with water and DMSO, as in Table 1.

In Fig. 9, the degree of dissociation, α, of *n*-Bu$_4$NCN in THF is shown as a function of concentration. The corresponding curves for *n*-Bu$_4$NCN in DMSO and water, not shown in this graph, are almost horizontal. The tendency of ion-pair formation in DMSO is very slight, slight in water and very strong in THF. For example, in a solution as dilute as 0.1 mM, ion pairs dominate over free ions in THF (approximately 60% of the ions are paired), while in DMSO *n*-Bu$_4$NCN is in practice completely dissociated. In aqueous solution at this concentration, approximately 0.1% of the ammonium cyanide exists as ion pairs.

Acknowledgements

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REFERENCES

[1] a) See, e.g., A. Brändström, *Preparative Ion Pair Extraction*, Apotekarsocieteten, Stockholm, **1976**; b) A. Brändström, in *Adv. Phys. Org. Chem.* **1977**, *15*, 267–330; c) H. Kobler, K. -H. Schuster, G. Simchen, *Justus Liebiegs Ann. Chem.* **1978**, 1946; d) D. A. White, M. M. Baizer, *J.Chem.Soc., Perkin Trans. I* **1973**, 2230.
[2] a) Y. Fang, Y. Gao, P. Ryberg, J. Eriksson, M. Kolodziejska-Huben, A. Dybala-Defraktyka, S. Madhavan, R. Danielsson, P. Paneth, O. Matsson, K. Westaway, *Chem. Eur. J.* **2003**, *9*, 2696; b) Y. -R. Fang, S. MacMillar, J. Eriksson, M. Kolodziejska-Huben, A. Dybala-Defratyka, P. Paneth, O. Matsson, K. C. Westaway, *J. Org. Chem.* **2006**, *71*, 4742.
[3] R. A. Robinson, R. H. Stokes, *Electrolyte Solutions, 2nd edn*, Dover Publications INC, Mineola, New York, **2002**.
[4] J. A. Riddick, W. B. Bunger, *Techniques of Chemistry, Organic Solvents*, Vol. II, Wiley-Interscience, New York, **1970**.
[5] H. M. Daggett, Jr E. J. Bair, C. A. Kraus, *J. Am. Chem. Soc.* **1951**, *73*, 799.
[6] R. M. Fuoss, K. L. Hsia, *Proc. Natl. Acad. Sci. USA* **1967**, *57*, 1550.
[7] R. M. Fuoss, K. L. Hsia, *Proc. Natl. Acad. Sci. USA* **1968**, *58*, 1818.
[8] R. Fernandez-Prini, *Trans. Faraday Soc.* **1969**, *65*, 3311.
[9] J. C. Justice, *Electrochim. Acta* **1971**, *16*, 701.
[10] P. Beronius, *Acta Chem. Scand.* **1976**, *A30*, 115.
[11] W. H. Lee, R. J. Wheaton, *J. Chem. Soc., Faraday Trans. 2.* **1979**, *75*, 1128.
[12] G. Aylward, T. Findlay, *SI Chemical Data, 4th edn*, Wiley, Brisbane, **1998**.
[13] D. F. Evans, R. L. Kay, *J. Phys. Chem.* **1966**, *70*, 366.
[14] H. Falkenhagen, *Theorie der Elektrolyte*, S. Hirzel Verlag, Stuttgart, **1971**, p. 195.
[15] R. M. Fuoss, F. Accascina, *Electrolytic Conductance*, Interscience, New York, **1959**.
[16] J. Comyn, F. S. Dainton, K. J. Ivin, *Electrochim Acta* **1968**, *13*, 1851.
[17] P. Beronius, T. Lindbäck, *Acta Chem. Scand. A* **1979**, *33*, 397.
[18] P. Beronius, L. Pataki, *Acta Chim. Acad. Sci. Hung.* **1980**, *103*, 17.
[19] E. D. Hughes, C. K. Ingold, S. Patai, Y. Pocker, *J. Chem. Soc.* **1957**, 1206.