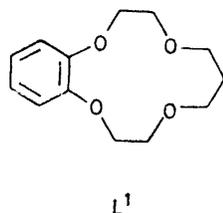


Complexation and Solvent Extraction of Lithium Salts with 2,3,6,7,9,10-Hexahydro-5H-1,4,8,11-benzotetraoxacyclotridecin (Benzo-13-crown-4)

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Solubility measurements were conducted in order to compare the affinity towards lithium salts of several 12- to 16-membered ring 'crown' ethers. The 13-membered ring benzo-13-crown-4 (L^1) was found to be the most effective complexing agent for lithium among the investigated macrocyclic ethers. The effect of counter ions on the solubility was found to be $\text{OH}^- < \text{Cl}^- < \text{ClO}_4^- \approx \text{SCN}^- < \text{picrate}$. The benzene and the methylene chloride solutions of L^1 extract lithium salts selectively from aqueous solutions. In the latter solvent the selectivity factor $\gamma(\text{Li}^+/\text{M}^{n+})$ was found to be 2.5, 44, 216, and 355 for Na^+ , K^+ , Mg^{2+} , and Ca^{2+} respectively. Hydrogen-1 n.m.r. measurements for the solutions of the lithium complexes of L^1 indicate that a planar conformation of the quadridentate macrocyclic ring seems to be favoured in the complexed L^1 . The 1 : 1 complexes have been found to be dominant in all investigated solvent systems. However, in methylene chloride and in nitromethane the 2 : 1 'sandwich' type complexes could also be detected. The stability constants of the complexes were found to increase in order of decreasing donicity of the solvent media.

THE use of macrocyclic ethers as complexing agents and ionophores of alkali and alkaline-earth metals has been extensively investigated.¹⁻⁹ Preferential complexation of lithium by small 12- and 14-membered ring 'crown' ethers has previously been reported by several investigators.^{1,3-5} The (1,1,2) cryptand, having two 12- and one 14-membered macrocyclic ring, acts also as a selective complexing agent for lithium.¹⁰ However, the use of this cryptand as an ionophore is precluded on kinetic and solubility grounds. Acyclic quadridentate amido-ethers, introduced as ionophores by Simon *et al.*,¹¹ preferentially complex lithium,¹² when their molecular structure is such that their four oxygen atoms tend to form a 'cavity' of a size comparable with that of the 13- to 14-membered rings in crown ethers. Equilibrium constants of formation and stoichiometry of such lithium complexes in various solvents were recently investigated in this laboratory.¹³



Preferential complexation of lithium ions by the 13-membered macrocyclic polyether, benzo-13-crown-4 (L^1), is discussed in the present paper.

EXPERIMENTAL

The macrocyclic ethers were synthesized according to the general procedures given by Pedersen.¹ Ethylene glycol and 1,3-dibromopropane (Fluka, purum) were used as starting materials for the preparation of L^1 . Sodium hydride (Fluka, AG) (1 mol dm^{-3}) was added to 1 l of ethylene glycol. The reaction mixture was cooled to 5 °C and 1,3-dibromopropane (1 mol dm^{-3}) was added dropwise to the

stirred reaction mixture. Stirring was continued for 20 h at room temperature. The 1,8-dihydroxy-3,7-dioxaoctane thus formed was distilled *in vacuo* (105 °C, 0.2 Torr) † and treated in benzene solution with a 20% molar excess of thionyl chloride in the presence of an equivalent amount of pyridine. The reaction mixture was refluxed for 18 h and the dichloride formed was distilled *in vacuo* (74 °C, 0.2 Torr). The dichloride was then treated with catechol in n-butanol in the presence of an equivalent amount of $\text{Li}[\text{OH}]$. The reaction mixture was neutralized with concentrated HCl and extracted with chloroform. The chloroform solution was washed with aqueous 5% $\text{K}[\text{OH}]$ and with water and dried over $\text{Mg}[\text{SO}_4]$. The solvent was evaporated off. Compound L^1 was distilled *in vacuo* (90 °C, 5×10^{-2} Torr) and recrystallized from n-heptane. Pure L^1 , m.p. 53 °C, was thus obtained in 25% yield (with respect to catechol).

2,3,5,6,8,9-Hexahydro-1,4,7,10-benzotetraoxacyclododecin (L^2), 7,8,16,17-tetrahydro-6H,15H-dibenzo[b,i]-[1,4,8,11]tetraoxacyclotetradecin (L^3), 2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxacyclopentadecin (L^4), and 6,7,9,10,17,18,20,21-octahydrodibenzo[b,k][1,4,7,10,13,16]hexaoxacyclo-octadecin (L^5) were purified as described elsewhere.¹⁴

Deuteriated solvents (Merck, 99.9%) for n.m.r. experiments were dried for 48 h on 4A molecular sieves before use.

Benzene (Frutarom, AnalaR) was distilled over sodium and stored over 4A molecular sieves.

Methylene chloride (Frutarom, AnalaR) was washed with three aliquots of water, dried over $\text{Ca}[\text{SO}_4]$, distilled, and stored over molecular sieves. A 1 : 1 mixture of dichloroethane (Fluka) and tricresyl phosphate (B.D.H.) for the extraction experiments was used without further purification.

The compound $\text{Li}[\text{SCN}]$ was prepared from equivalent amounts of $\text{Ba}[\text{SCN}]_2$ and $\text{Li}_2[\text{SO}_4]$ in aqueous solution. The solution was filtered, evaporated to dryness in a rotavapor, and $\text{Li}[\text{SCN}]$ was dried for 48 h in high vacuum (10^{-4} Torr) at 90 °C. Thermal gravimetric analysis of samples of the dried salts proved that absolutely dry anhydrous salts were thus obtained.

Solutions were prepared under a blanket of dry argon.

† Throughout this paper: 1 Torr = (101 325/760) Pa.

Absence of traces of water was checked by gas chromatography with a 'para pack' type Q column.

The solubility of lithium salts in benzene and in methylene chloride solutions of crown ethers was determined by stirring them for 48 h (under dry argon) with an excess of dry solvent. Solutions were filtered under a blanket of dry argon, the solvent was distilled off, and the residue dissolved in water (10 cm³). Dry benzene or methylene chloride (1 l) was used for solubility determinations in the absence of 'crown'.

An atomic absorption spectrometer (Varian 1200) was used for the determination of the concentration of Li⁺, Na⁺, K⁺, Ca²⁺, and Mg²⁺ in aqueous solutions.

Concentrations of picrate in the solutions were determined spectroscopically on a Cary-15 spectrophotometer.

The ¹H n.m.r. spectra were recorded at 270 MHz on a Bruker WH-270 spectrometer operating in the Fourier-transform mode, using sample tubes of 5-mm outside diameter. Tetramethylsilane served as internal reference. All chemical shifts are given in p.p.m. relative to SiMe₄.

RESULTS AND DISCUSSION

Dry Li[SCN] was dissolved in benzene and in methylene chloride solutions of several 'crown' ethers having 12- to 15-membered rings. Inspection of the results summarized in Table 1 reveals that benzo-13-crown-4

TABLE 1

Complexation (expressed as values of [salt]/[crown ether] of Li[SCN] by 12- to 15-membered ring crown ethers in benzene and in methylene chloride solutions at 25 °C

Solvent	Ligand				
	None [LiSCN]/ mol dm ⁻³	L ²	[LiSCN]/[L ¹] L ¹	[LiSCN]/[L ³] L ³	L ⁴
Benzene	1.0 × 10 ⁻⁵	0.12	0.66	0.26	
Methylene chloride	1.6 × 10 ⁻⁵	0.14	0.75	0.25	0.17

* Crown concentrations are 3 × 10⁻² mol dm⁻³.

(L¹) is the most efficient complexing agent of the investigated compounds. Experiments involving extraction of lithium picrate from its aqueous solutions lead to a similar conclusion (Table 2). Apparently the 12-

TABLE 2

Extraction of lithium picrate with 0.025–0.05 mol dm⁻³ solutions of crown ethers in tricresyl phosphate-ethylene chloride (1 : 1) from the initially 1 × 10⁻⁴–10⁻⁵ mol dm⁻³ solutions of picrate in 0.1 mol dm⁻³ Li[OH] at 25 °C

Extraction % (based on picrate) 10 ⁻² K _{ex} *	Ligand					
	None	L ²	L ¹	L ³	L ⁴	L ⁵
	7	18	89	82	50	58
		0.41	15.1	9.3	2.0	5.7

* Extraction constant (see ref. 9), K_{ex} = [Li⁺, L, picrate]_{org.}/([M⁺]_{H₂O}[picrate]_{H₂O}[L]_{org.}).

membered ring of L² is too small to accommodate a lithium ion in such a way that its four oxygen atoms may co-ordinate with the complexed lithium without straining the ring. The difference in the complexing power of L¹ and L³ must be partially attributed to the lower basicity

of two of the oxygen atoms of the latter crown ether. However, extraction experiments conducted by Pedersen with the hydrogenation product of a derivative of L³, bis(butylcyclohexyl)-14-crown-4, revealed that although it complexes lithium preferentially, its complexing power is fairly limited.^{1b} For the 14-membered crown ethers the ratio, *F*, of the diameter of the lithium ion to the hole diameter of the crown, was estimated^{1,15} as 0.80–0.89. On the other hand, inspection of molecular models leads to an estimated value of *F* ca. 1.0 for the Li⁺–L¹ system. The fit between the size of the lithium ion and the hole diameter of L¹ is consistent with results of n.m.r. measurements that indicate that for the Li⁺–L¹ systems the complexation constants of the 1 : 1 complexes are several orders of magnitude higher than those of the 1 : 2 complex (see Table 6). When the hole size of the crown ether is smaller than the diameter of the complexed ion,

TABLE 3

Extractions with solutions of L¹ (0.03 mol dm⁻³) in methylene chloride and in benzene from the solutions of alkaline-earth and alkali-metal thiocyanates (1 mol dm⁻³) in water

Cation	Benzene		Methylene chloride	
	10 ⁴ [salt] _{org.} / mol dm ⁻³	γ(Li ⁺ / M ⁿ⁺) *	10 ⁴ [salt] _{org.} / mol dm ⁻³	γ(Li ⁺ / M ⁿ⁺) *
Li ⁺	9.9	1	11.0	1
Na ⁺	4.2	2.4	4.4	2.5
K ⁺	0.23	43	0.25	44
Mg ²⁺	0.044	202	0.051	216
Ca ²⁺	0.028	354	0.031	355

* Selectivity factor = [Li⁺]_{org.}/[Mⁿ⁺]_{org.}

a 1 : 2 sandwich type complex may be favoured,^{1,4} although some exceptions to such behaviour were noted.¹⁵

Preferential complexation by L¹ of the small lithium ion is expected on geometric grounds. Indeed, extraction experiments summarized in Table 3 show that in

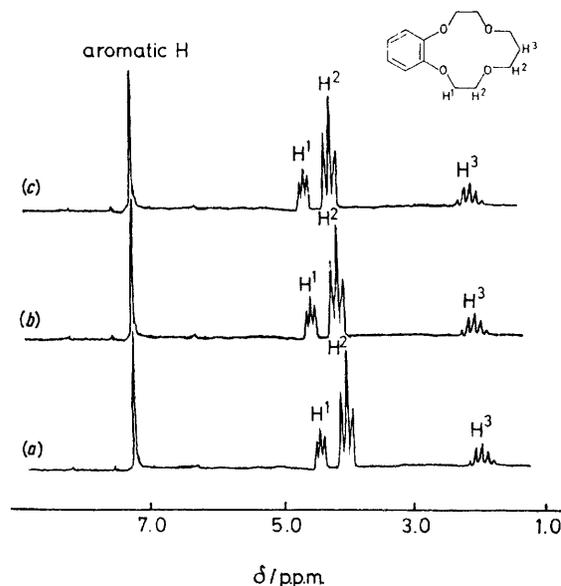


FIGURE 1 Hydrogen-1 n.m.r. spectra of 10⁻² mol dm⁻³ solutions of L¹ in nitromethane in the presence of Li[ClO₄]. Free ligand (a), [LiClO₄] : [L¹] = 1 : 2 (b), and [LiClO₄] : [L¹] = 1 : 1 (c)

spite of the strong hydration of lithium ions they are preferentially extracted from aqueous solutions. The

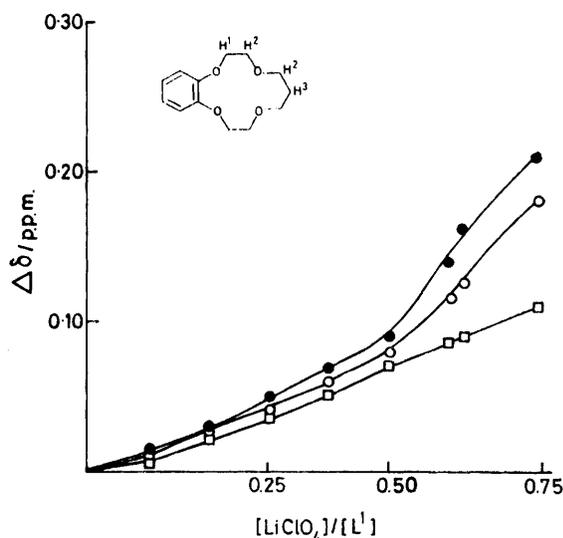


FIGURE 2 Increments of chemical shifts of proton signals of L¹ in methylene chloride against [LiClO₄]:[L¹] ([L¹] = 10⁻³ mol dm⁻³). H¹ (●), H² (○), and H³ (□). Full lines correspond to the computed points

high selectivity for Li⁺ (diameter, $D = 1.2 \text{ \AA}$) compared to Mg²⁺ ($D = 1.35 \text{ \AA}$) may also be affected by the very strong hydration of the bivalent Mg²⁺ ion.

Experiments conducted with dry lithium hydroxide, chloride, perchlorate, and thiocyanate indicated that

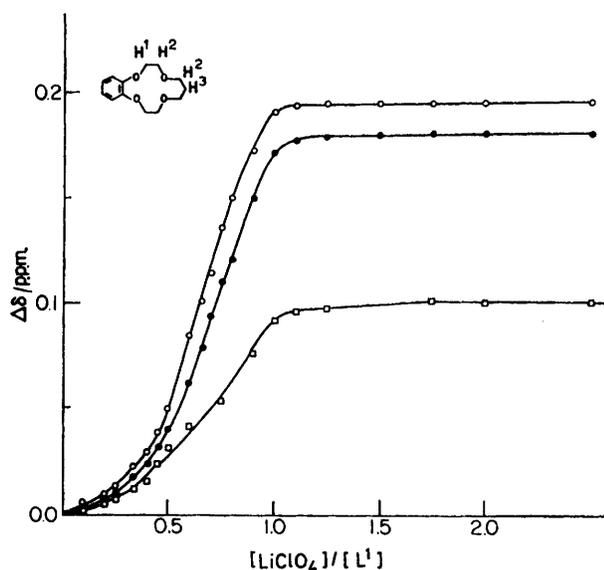


FIGURE 3 Increments of chemical shifts of proton signals of L¹ in nitromethane against [LiClO₄]:[L¹] ([L¹] = 10⁻² mol dm⁻³). H¹ (○), H² (●), and H³ (□). Full lines correspond to the computed points

their solubility in 0.03 mol dm⁻³ solutions of L¹ in benzene increases in this order. The ratio of the respective solubilities is 1 : 7 : 18 : 18.5.

Nuclear Magnetic Resonance Measurements.—Complexation of Li[ClO₄] with L¹ in methylene chloride, nitromethane, and acetonitrile was investigated by n.m.r. 'titrations'. Hydrogen-1 n.m.r. spectra of L¹ in nitromethane solutions containing various amounts of Li[ClO₄] are shown in Figure 1. Changes in the chemical

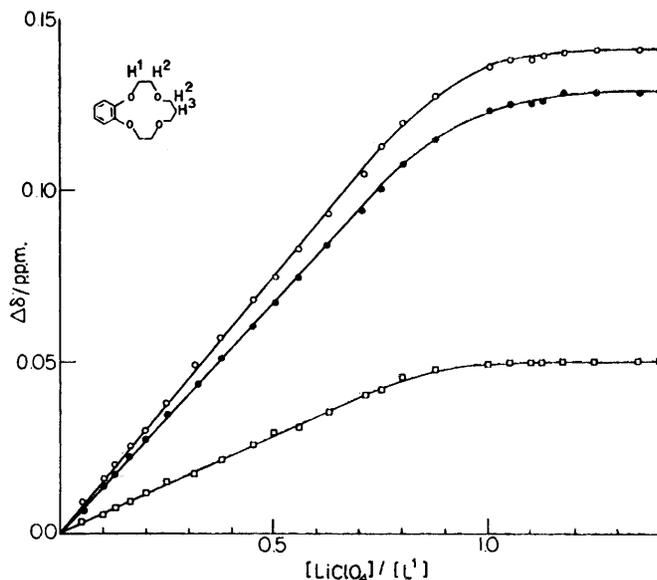
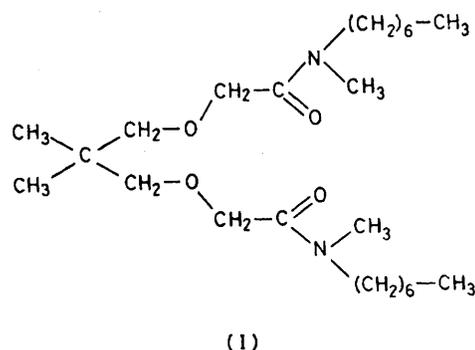


FIGURE 4 Increments of chemical shifts of proton signals of L¹ in acetonitrile against [LiClO₄]:[L¹] ([L¹] = 10⁻² mol dm⁻³). H¹ (○), H² (●), and H³ (□). Full lines correspond to the computed points

shifts of the protons of L¹, due to changes in the [LiClO₄]:[L¹] ratio, are depicted in Figures 2, 3, and 4 for the methylene chloride, nitromethane, and acetonitrile systems respectively. At room temperature the exchange of the complexed lithium between L¹ molecules is fast on the n.m.r. time scale. Deflections of the experimental points at [LiClO₄]:[L¹] *ca.* 0.5 : 1 seem to indicate that in methylene chloride and in nitromethane



the 1 : 2 sandwich type complexes may also be formed. Only the 1 : 1 complex seems to be formed in acetonitrile (Figure 4). The ¹H n.m.r. 'titration' curves provide no indication for the formation of a dilithium 2 : 1 complex similar to the 2 : 1 complex of lithium with tetraoxacyclohexadecane in CHCl₃ observed by Dale and Krane^{3a} or

to the dilithium complex of a quadridentate amido-ether in nitromethane [see (I)] recently investigated in this laboratory.¹³ The presence of small amounts of water induces a very small shift (0.01–0.02 p.p.m.) in the position of the chemical shifts of the L¹ protons. However, a significant effect of traces of water is noted in the

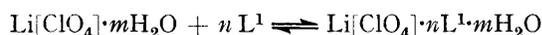
complexing site) after complexation are much smaller than those of protons H¹ and H² (of methylene groups adjacent to the oxygen atoms). The effect of complexation on the respective chemical shifts of H¹ and H² calls for comment; the basicity of oxygen atoms adjacent to an aromatic ring is lower than that of those of

TABLE 4

Chemical shifts of crown-ether protons in methylene chloride in the presence of Li[ClO₄] and its hydrates. [L¹] = 10⁻³ mol dm⁻³

System	[LiClO ₄] : [crown]	H ¹		H ²		H ³	
		δ/p.p.m.	10 ² Δδ/ p.p.m.	δ/p.p.m.	10 ² Δδ/ p.p.m.	δ/p.p.m.	10 ² Δδ/ p.p.m.
Li[ClO ₄]	0.5 : 1	4.42	9	4.00	8	1.97	7
Li[ClO ₄]·H ₂ O		4.39	5	3.97	3	1.94	4
Li[ClO ₄]·3H ₂ O		4.37	3	3.95	1	1.92	2
Li[ClO ₄]	0.75 : 1	4.54	21	4.10	18	2.01	11
Li[ClO ₄]·H ₂ O		4.47	13	4.04	10	1.98	6
Li[ClO ₄]·3H ₂ O		4.42	8	4.00	6	1.95	3
Li[ClO ₄]·H ₂ O	1 : 1	4.52	18	4.10	16	2.02	10
Li[ClO ₄]·3H ₂ O		4.46	12	4.04	10	1.98	6

presence of Li[ClO₄] (see Table 4). Obviously, the equilibrium reactions of the type¹⁶ shown below are shifted to the left in comparison with the analogous equilibrium reactions involving anhydrous Li[ClO₄].



Calculation of Equilibrium Constants.—Values of the intrinsic chemical shifts of the complexes and the values of the corresponding equilibrium constants were calculated by a computer iteration procedure from the experi-

an aliphatic ether.¹ The interaction of the complexed lithium must, therefore, be stronger with the latter than with the former oxygen atoms. Nevertheless, it may be seen from Table 5 that chemical shifts of H¹ are more affected by complexation than those of H². This behaviour may be explained by assuming that the macrocyclic ring of L¹ deviates less from planarity in the complexed than in the uncomplexed species. Such a conclusion is based on the following argument: when a methylene group, close to an aromatic ring, deviates

TABLE 5

The intrinsic chemical shifts of the protons of L¹ (relative to SiMe₄)

Solvent	System	δ/p.p.m.			
		H ¹	H ²	H ³	H _{Ar}
Methylene chloride	L ¹ *	4.33	3.92	1.90	7.10
	L ¹ ·Li[ClO ₄]	4.45 ± 0.05	4.02 ± 0.05	2.00 ± 0.03	7.12 ± 0.01
	L ¹ ·Li[ClO ₄]	4.63 ± 0.05	4.16 ± 0.05	2.16 ± 0.03	7.12 ± 0.01
Nitromethane	L ¹ *	4.38	4.09	2.03	7.15
	L ¹ ·Li[ClO ₄]	4.45 ± 0.05	4.15 ± 0.05	2.07 ± 0.03	7.17 ± 0.01
	L ¹ ·Li[ClO ₄]	4.60 ± 0.02	4.27 ± 0.02	2.12 ± 0.01	7.17 ± 0.01
Acetonitrile	L ¹ *	4.36	4.10	2.04	7.15
	L ¹ ·Li[ClO ₄]	4.52 ± 0.03	4.24 ± 0.05	2.09 ± 0.02	7.16 ± 0.01

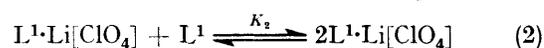
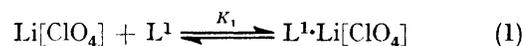
* Directly measured values.

mentally determined chemical shifts (Figures 2–4). Solid lines in the graphs represent values calculated from the extrapolated intrinsic chemical shifts and the equilibrium constants given in Table 6. The procedure described by Reuben and co-workers¹⁷ for conditions of fast exchange between free ligand and its bonded states was used for the mathematical analysis of the experimental data. The saturation parameter, *S*, which determines the reliability of the computed values for weak complexes,^{17,18} could be maintained within the required limits of 0.2 ≤ *S*_{*i*} ≤ 0.8. The extrapolated intrinsic chemical shifts are summarized in Table 5.

Aromatic protons are essentially unaffected by complexation. The chemical shifts of H³ (far apart from the

from planarity, the inductive deshielding effect of the aromatic ring is partially cancelled by shielding due to the cloud of the π electrons, hence when a more planar configuration of the macrocyclic ring is induced by complexation, a downfield shift is expected for the methylenic protons close to the aromatic ring.

Equilibrium constants of complexation defined by equations (1) and (2) are given in Table 6.



The complexation of L¹ in acetonitrile was treated as a 1 : 1 case. Treatment of this system as a 2 : 1 case

defined by the two equilibria¹⁷ [equations (1) and (2)], yields $K_2 = 0.9 \pm 0.5 \text{ dm}^3 \text{ mol}^{-1}$. Such a result for K_2 cannot be regarded as significant (the value of K_1 being the same as in the 1 : 1 case).

The complexation of L^1 in methylene chloride and in nitromethane was treated as the 2 : 1 cases. For the methylene chloride system the n.m.r. measurements yield a rough estimate only of the value of K_1 . It must

TABLE 6
Stability constants of the $\text{Li}[\text{ClO}_4]-L^1$ complexes

Solvent	ϵ	D.N.*	$K_1/$ $\text{dm}^3 \text{ mol}^{-1}$	$K_2/$ $\text{dm}^3 \text{ mol}^{-1}$
CH_2Cl_2	9.1		$10^5 ?$	50 ± 10
CH_3NO_2	35.9	2.7	$ca. 10^3$	18 ± 2
CH_3CN	38.0	14.1	250 ± 60	

* Donor numbers according to Gutmann (ref. 19).

be noted, however, that solubility measurements summarized in Table 1 for the methylene chloride system also yield $K_1 \approx 5 \times 10^4 \text{ dm}^3 \text{ mol}^{-1}$, if one assumes that the solubility of the free salt is not affected by the presence of the complex.

Inspection of the tabulated equilibrium constants clearly indicates that they depend strongly on the donicity of the solvent,¹⁹ but are unrelated to the dielectric constants (ϵ).

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