EXTRACTION OF SELECTED ORGANIC BASES FROM WATER INTO CHLOROFORM BY MEANS OF THE COBALTACARBORANE ANION

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Received November 20, 1997
Accepted April 22, 1998

The cobaltacarborane anion labelled with ^{60}Co was used to study the solvent extraction and stability of its ion associates with a series of organic nitrogen base cations or quaternary salts, some of which are psychoactive. The aqueous phase was 0.1 M HCl, the organic phase was chloroform. The extraction constants of the ion associates were calculated. A method was devised for competitive extraction of ion associates with additional dye anions which are used in the extraction-photometric determination of selected bases.

Key words: Extraction; Ion associates; Cobaltacarborane anion; Boranes; Carboranes; Amines; Quaternary ammonium salts; Alkaloids.

The cobaltacarborane anion, $[Co(\eta^5\text{-}1,2\text{-}C_2B_9H_{11})_2]^-$, henceforth X^-, was first used by Kyrs and coworkers[1] for the separation of alkali metals. The assets of this anion include a good chemical and radiation[2] stability, owing to which it has found application mainly in the separation of nuclear fission products[3–5]. Polar nitrobenzene was largely employed as the separating organic phase, not only for the separation of alkali metals and alkaline earths but also for lanthanoids (Tc, ref.[6], and Pd, ref.[7]). Metal cations were also frequently coordinated by suitable donor reagents, organic bases in particular[3–5]. The separation of ion associates in which X^- is associated with an organic cation was rarely examined. The studies included determination of the solubility of a series of ion associates of X^- with organic nitrogen base cations[8] and extraction-radioanalytical determination of the purity/stability of a benzimidazole-based cytostatic drug[9]. The present paper is a continuation of our earlier studies where monosulfonated and disulfonated dyes forming ion pairs with base cations were utilized for the quantitation of organic bases using an extraction-spectrophotometric technique[10,11]. In this work, radiometric indication of the equilibrium concentration of X^- labelled with ^{60}Co was used.

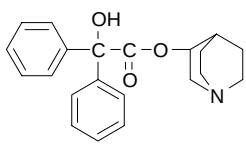
EXPERIMENTAL

Chemicals and Apparatus

Cesium cobaltacarborane labelled with ^{60}Co, $Cs[^{60}Co(\eta^5\text{-}1,2\text{-}C_2B_9H_{11})_2]$ (henceforth CsX), was synthesized in the Nuclear Research Institute in Rez. The radiochemical purity of the compound was checked by gamma spectroscopy at a total activity of 7.4 MBq.

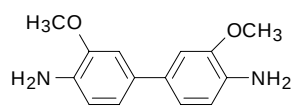
The stock solution was prepared by dissolving a known amount of CsX in 0.1 M HCl so that the resulting concentration lay within the range from $1.2 \cdot 10^{-5}$ to $5.6 \cdot 10^{-4}$ mol l^{-1} and activity was from 10 to 380 Bq ml^{-1}. A stock solution of CsX in 0.1 M citrate buffer at pH 4.00 for the investigation of competitive extraction was prepared similarly.

The following bases or quaternary salts were employed: propane-1,3-diamine, hexane-1,6-diamine, diethylamine, triethylamine, triethanolamine, aniline, *N*,*N*-diethyl-1,4-phenylenediamine, 1,4-phenylenediamine, diphenylamine, *N*-(1-naphthyl)ethanamine, pyridine, 2,2′-bipyridine, piperidine, hexadecylpyridinium bromide, quinoline, 3,3′-dimethoxybenzidine, 4,7-diphenyl-1,10-phenanthroline, hexadecyltrimethylpyridinium bromide, 1-(1′-phenylcyclohexyl)piperidine (PCP), ephedrine, quinuclidin-3-one, quinuclidin-3-yl benzilate (BZ), codeine, ethylmorphine, morphine, cocaine, physostigmine, scopolamine, lysergic diethylamide (LSD), methyltriphenylphosphonium iodide, tetraphenylarsonium chloride. These substances were products of the companies Aldrich, Merck, Ferak (Germany), Fluka, Loba (U.K.), Lachema (Czech Republic), SPOFA (Czech Republic), and Military Factory 072 Zemianske Kostol'any (Slovak Republic). Known amounts of the bases/quaternary salts were dissolved in 0.1 M HCl so that the concentration of their stock solutions was from 0.2 to 5 mmol l^{-1}.

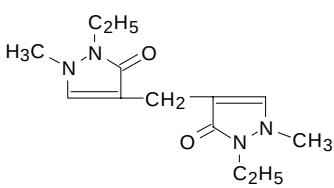


quinuclidin-3-yl benzilate

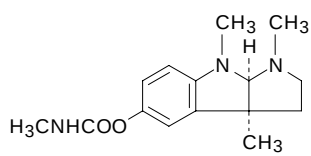
quinuclidin-3-one



3,3'-dimethoxybenzidine



diantipyrinylmethane



physostigmine

When examining the competitive extraction, BZ or PCP ($c_{base} = 7.5 \cdot 10^{-5}$ mol l^{-1}) was dissolved in 0.1 M citrate buffer at pH 4.00. Bromoxylene Blue, Xylenol Blue, and Bromothymol Blue (Merck) served as the competitive anions. Chloroform was obtained from Lachema Brno and used as received.

All chemicals were of analytical grade purity.

The gamma activity of the solutions containing ^{60}Co was measured with a well-type NaI(Tl) detector interfaced to an NA 3601 Gamaautomat (TESLA Liberec, Czech Republic). The radiochemical purity of the CsX was checked by means of a 4096-channel spectrometer (Silena, Italy) equipped with a Ge detector. A Spekol-11 single-beam spectrophotometer (Zeiss, Jena) served the spectrophotometric measurements within the 350–550 nm region.

Procedures

Solvent extraction was performed using ground-glass test tubes. The volumes of the organic and aqueous phases were 4 ml each, temperature 20 ± 1 °C. The extraction time was 1 h for practical reasons, although preliminary experiments showed that 10 min was sufficient for establishing the equilibrium. After agitating, 2 ml aliquots of either phase were taken and measured on the Gamaautomat for a time which was long enough to ensure that the mean square error of each activity measurement of the sample was below 5%.

The regression straight line equations were calculated for the experimental points in Figs 1–3, the regression coefficients being determined by the ADSTAT package.

Except for the experiments aimed at examining the dependences on the organic phase composition, all the measurements were performed with chloroform. The aqueous phase was 0.1 M HCl; citrate buffer of the same concentration (pH 4.00) was used when studying the competitive extraction.

After establishing the absorption maximum and absorbance, an aqueous solution of non-labelled CsX, c = 0.5 mmol l^{-1}, was prepared. The dependence of the ion-associate formation on pH was investigated over the region of pH 1.0–6.0 (step 0.5). Volumes of 0.1 ml of the base and of the CsX solutions were added to a test tube and the mixture was diluted to 2.0 ml with the 0.1 M citrate buffer. If the effect of the CsX concentration on the extraction recovery was to be studied, 0.1 ml of the base solution was mixed gradually with 0.02 to 0.2 ml of the CsX solution, and the mixture was diluted to 2.0 ml with the citrate buffer. The calibration dependence of the solution absorbance on the base concentration, $A = f([B^+])$, was established for a sample set prepared by mixing 0.1 ml to 1 ml of the base solution (step 0.1 ml) with 0.1 ml of the CsX solution and diluting with the citrate buffer to 2.0 ml. The blank solution contained 0.1 ml of CsX and 1.9 ml of the citrate buffer. All the mixtures were extracted with 2.0 ml of chloroform for 4 min.

RESULTS AND DISCUSSION

Effect of Organic Phase Composition

Ten solvents were tested as the organic phase. For practical reasons, PCP served as the model base (Table I). Chloroform, benzene, toluene, and tetrachloromethane were found to be suitable solvents. 1,2-Dichloroethane and 1,1,2,2-tetrachloroethane were acceptable, whereas octane, octan-1-ol, cyclohexane, and Freon 113 were not because organic bases studied were either low-soluble in both phases or (the alcohols) gave rise to parasitic extractable components. Since chloroform was used in our previous work dealing with the extraction of ion associates[10,11], we employed this solvent in the present work as well, although the use of benzene, toluene, and tetrachloromethane or, maybe, 1,2-dichloroethane and 1,1,2,2-tetrachloroethane, is also possible.

Effect of Base Concentration

In 0.1 M HCl, neutral bases – with a few exceptions (diphenylamine, physostigmine) – are converted virtually quantitatively into their protonized forms, denoted B^+. This symbol will also be used for quaternary salt cations. Hexane-1,6-diamine, 3,3′-dimethoxybenzidine, and *N*,*N*-diethyl-1,4-phenylenediamine are even doubly protonized, giv-

ing the species B^+ and B^{2+}, but since ion associates with cations whose charge is higher than +1 are extractable to a substantially lower degree, the (B^{2+},2 X^-) associates were assumed not to be extracted[12].

Figures 1 and 2 show plots of the logarithm of the distribution ratio of X^- (measured only radiometrically) *versus* logarithm of the starting concentration of the protonized form, for all of the bases B^+ or quaternary salts studied. The ions B^+ form the ion associates (B^+,X^-) with the anions X^-, and the ion associates are extracted:

$$[B^+] + [X^-] \rightarrow [(B^+,X^-)];\ K_{ass} = [(B^+,X^-)]/[B^+][X^-] \qquad (1)$$

$$[(B^+,X^-)] \rightarrow [(B^+,X^-)]_{OR};\ K_D = [(B^+,X^-)]_{OR}/[(B^+,X^-)]\ . \qquad (2)$$

For the distribution of X^-, we have:

$$D_X = [(B^+,X^-)]_{OR}/[(B^+,X^-)] + [X^-] = K_D\,K_{ass}[B^+]/K_{ass}[B^+] + 1. \qquad (3)$$

The square brackets denote equilibrium concentrations, the subscript OR refers to the organic phase, concentrations without any subscript refer to the aqueous phase. If the concentration of X^- in the aqueous phase is substantially higher than that of the ion associate, the $K_{ass}[B^+]$ product can be disregarded compared with unity, and we have

$$D_X = K_D\,K_{ass}[B^+], \qquad (4)$$

TABLE I
Effect of organic phase composition (c_{PCP} = 0.625 mmol l^{-1}, c_X = 0.141 mmol l^{-1})

Organic phase	log D_x	Note
Chloroform	0.00	
Benzene	–0.01	
Toluene	0.02	
CCl_4	–0.06	
Cyclohexane	–0.72	voluminous precipitate at the interface, loss of activity
1,2-Dichloroethane	0.37	organic phase hazy
1,1,2,2-Tetrachloroethane	0.06	organic phase hazy
Octan-1-ol	2.03	extracts also in the absence of base
Octane	–0.80	voluminous presipitate at the interface, loss of activity
Freon 113	–0.90	voluminous precipitate at the interface, loss of activity

hence, Figs 1 and 2 will display the dependences $D_X = f(\log [B^+])$ with a slope of unity. The $K_D K_{ass}$ products then can be calculated from them (Table II) as the intercept of the log D_X values for log $[B^+] = 0$. The protonation constants were taken from refs[13–15].

The data in Table II enable us to compare the extractability of the bases or quaternary salts studied in general and some structurally related bases in particular, and thus to study the effect of the structure of the base or quaternary salt on the extractability of the ion associate. This is well seen, for instance, in the following pairs or groups: triethanolamine–triethylamine, diphenylamine–diethylamine–*N*-(1-naphthyl)ethanamine, aniline–*N*,*N*-diethyl-1,4-phenylenediamine, pyridine–quinoline–2,2′-bipyridine–hexadecylpyridinium bromide, morphine–codeine–ethylmorphine.

Some bases and quaternary salts (Table II) form with X^- ion associates which are very low-soluble in the aqueous phase alone and very well extractable into the organic phase. As a consequence, the D_X values are very low until the equimolar concentration (with respect to the base or quaternary salt) is reached (*i.e.*, as long as the B^+ to X^- molar concentration ratio is lower than unity), and very high after the equimolar concentration is exceeded. The $K_D K_{ass}$ value will be well measurable in this group only if

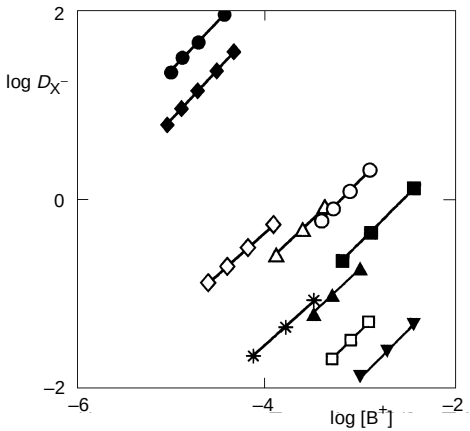


FIG. 1
Effect of starting concentration of protonized base on the distribution of the cobaltacarborane anion between 0.1 M HCl and chloroform; $[X^-]$ = 14.0 to 65.8 μmol l^{-1}. Base (regression coefficient): ▼ hexane–1,6-diamine (0.98), ❒ triethanolamine (0.92), ▲ aniline (0.99), * diphenylamine (0.99), ■ 3,3′-dimethoxybenzidine (0.99), ❍ diethylamine (0.99), Δ quinuclidin-3-one (0.99), ✧ morphine (0.99), ◆ codeine (0.99), ● ethylmorphine (0.99)

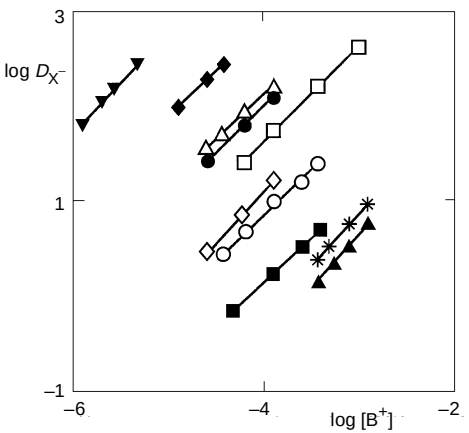


FIG. 2
Effect of starting concentration of protonized base on the distribution of the cobaltacarborane anion between 0.1 M HCl and chloroform; $[X^-]$ = 12.0 to 65.8 μmol l^{-1}. Base: ▲ piperidine, * pyridine, ■ ephedrine, ❍ scopolamine, ✧ *N*,*N*-diethyl-1,4-phenylenediamine, ❒ triethylamine, ● *N*-(1-naphthyl)ethanamine, Δ quinoline, ◆ 2,2′-bipyridine, ▼ 4,7-diphenyl-1,10-phenanthroline. Regression coefficient invariably 0.99

TABLE II
log K_D and K_{ass} values for extraction from 0.1 M HCl to $CHCl_3$

Base	log K_D K_{as}	pK_{BH^+}	p$K_{BH_2^+}$
Propane-1,3-diamine	[a]	10.47	8.49
1,4-Phenylenediamine	[a]	6.08	3.29
Hexane-1,6-diamine	1.03	10.93	9.83
Triethanolamine	1.53	7.96	
Aniline	2.28	4.63	
Diphenylamine	2.43	0.79	
3,3′-Dimethoxybenzidine	2.56	9.66[b]	3.63[b]
Diethylamine	3.20	10.49	
Quinuclidin-3-one	3.3	8.74[c]	
Piperidine	3.7	11.12	
Morphine	3.7	8.21	
Pyridine	3.9	5.25	
Ephedrine	4.1	10.1	
Scopolamine	4.8	9.68[d]	
N,*N*-Diethyl-1,4-phenylenediamine	5.0	6.08[e]	3.29[e]
Triethylamine	5.6	11.0	
Codeine	5.9	8.21	
N-(1-Naphthyl)ethanamine	6.0	4.11[f]	
Quinoline	6.2	4.90	
Ethylmorphine	6.4	8.21	
2,2′-Bipiridine	6.8	4.35	–0.52
Quinuclidin-3-yl benzilate	7.5[i]	8.74	
4,7-Diphenyl-1,10-phenanthroline	7.7	4.86[g]	
1-(1′-Phenylcyclohexyl)piperidine	7.9[i]	7.98	
Triphenylmethylphosphonium iodide	[j]		
Cocaine	[j]	8.41	
Tetraphenylarsonium chloride	[j]		
Hexadecylpyridinium bromide	[j]		
Hexadecyltrimethylammonium bromide	[j]		
Physostigmine	[j]	1.76	
LSD	[j]	7.68	

[a] Not determined, D_X value too low; [b] benzidine; [c] BZ; [d] hyoscyamine; [e] 1,4-phenylenediamine; [f] 2-naphthylamine; [g] 1,10-phenanthroline; [h] antipyrine; [i] obtained with a new CsX reagent of a higher activity, to be published; [j] insoluble ion associate (see text).

the starting concentrations of X^- or B^+ are suitably reduced, that is, if we have the labelled compound CsX with a specific activity at least 2 orders of magnitude higher.

Competitive Extraction

The carrier system (B^+,X^-) can be employed to examine the stability and/or distribution of the non-radioactive ion associate (B^+,L^-) where HL is a suitable monobasic acid forming a more or less extractable competitive system. This can be, for instance, a colour reagent used to determine bases by extraction spectrophotometry[10,11]. In addition to Eqs (*1*) and (*2*), we have:

$$[B^+] + [L^-] \rightarrow [(B^+,L^-)];\ K'_{ass} = [(B^+,L^-)]/[B^+][L^-] \qquad (5)$$

$$[(B^+,L^-)] \rightarrow [(B^+,L^-)]_{OR1};\ K'_D = [(B^+,L^-)]_{OR}/[(B^+,L^-)]\ , \qquad (6)$$

wherefrom

$$[B^+] = [(B^+,L^-)]/K'_{ass}[L^-] \qquad (7a)$$

and

$$[B^+] = [(B^+,L^-)]_{OR}/K'_D\,K'_{ass}[L^-]\ . \qquad (7b)$$

Introducing into Eq. (*4*), we obtain

$$D_X = K_D\,K_{ass}[(B^+,L^-)]_{OR}/K'_D\,K'_{ass}[L^-]\ , \qquad (8)$$

hence, the dependence $D_X = f(\log [L^-])$ has a slope of –1. This can be seen in Fig. 3, showing the dependence of log D_X on log $[L^-]$ in citrate buffer at pH 4.00 for BZ and PCP, where the slopes are -1 ± 0.2.

If $D_X = 1$ in Eq. (*8*) (50% extraction of X), then

$$K'_D\,K'_{ass} = K_D\,K_{ass}[(B^+,L^-)]_{OR}/[L^-]\ . \qquad (9)$$

Thus, for the particular system shown in Fig. 3, the $K'_D\,K'_{ass}$ product can be determined if the $K_D\,K_{ass}$ product is known and if B^+ is present virtually solely in the organic phase as the ion associates $(B^+,X^-)_{OR}$ and $(B^+,L^-)_{OR}$. The calculated values of the $K'_D\,K'_{ass}$ products are given in Table III.

Spectrophotometry of CsX Solutions

The molar absorptivity of the aqueous solution of dicarbollide was determined at its absorption maximum, 370 nm; the value was 6 530 l mol^{-1} cm^{-1}. The chloroform extracts of the ion associates with dicarbollide did not exhibit any marked peak in the visible region (Fig. 4). Additional measurements of chloroform extracts of the associates were made at 380 nm. The dependence of the formation of the ion associates on pH of the aqueous phase is shown in Fig. 5. The course of the extraction process was similar for all of the bases studied; the optimum pH value was 1.8. Constant extraction

TABLE III
$K_D' K_{ass}'$ products for extraction from citrate buffer (pH 4.00) into chloroform

Reagent	$\log K_D' K_{as}'$	
	PCP	BZ
Bromothymol Blue	5.2	5.3
Bromoxylenol Blue	5.3	5.3
Xylenol Blue	4.4	4.6

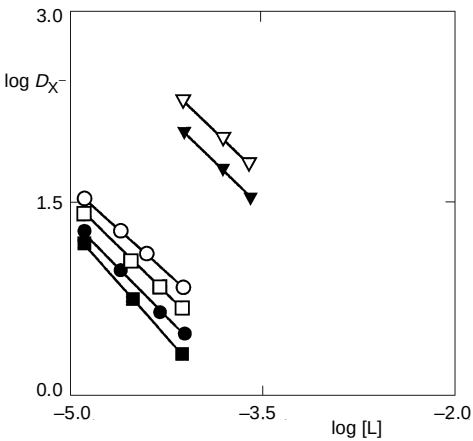


FIG. 3
Effect of starting concentration of competitive reagent [L^-] on the distribution of the cobaltacarborane anion between citrate buffer (pH 4.00) and chloroform; c_X = 67.6 μmol l^{-1}. Full symbols: BZ, open symbols: PCP. ❒, ■ Bromothymol Blue; ○, ● Bromoxylenol Blue; ∇, ▼ Xylenol Blue

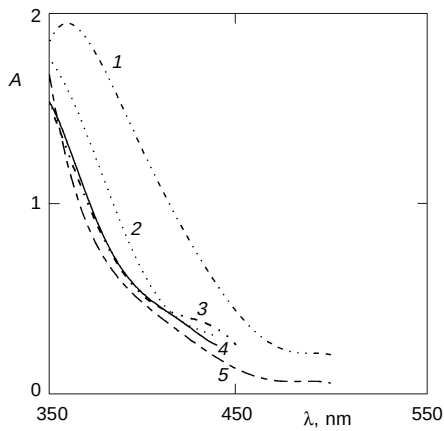


FIG. 4
Spectra of aqueous solution (*1*) of cesium cobaltacarborane and chloroform extracts of (B^+,X^-) ion pairs in the visible region. Base: *2* PCP, *3* ethylmorphine, *4* codeine, *5* ephedrine

yields of the ion associates in the chloroform phase were achieved in 10 min. When investigating the $A = f([X^-])$ dependence, an increase in the dicarbollide concentration was accompanied not only by an increase in the ion-associate extraction yield but also by an increase in the absorbance of the blank solution up to 0.4. Therefore, the dicarbollide concentration $[X^-] = 0.5$ mmol l^{-1} was used when measuring the calibration curves. The molar absorptivities of the ion associates in chloroform were calculated by linear regression of the calibration dependences $A = f([B^+])$. The spectrophotometric parameters are given in Table IV. Due to the absorbances of the blank solutions, high limits od detection and determination were obtained.

CONCLUSIONS

This work proved the possibility of obtaining information concerning the formation of ion associates with a suitable anion and their distribution between aqueous and organic phases by the radiometric method. The cations of the ion associates formed from ni-

TABLE IV
Results of spectrophotometric measurements

Parameter	Base			
	PCP	ethylmorphine	codeine	ephedrine
ε^a, l mol^{-1} cm^{-1}	13 500	13 000	12 200	10 800
$L_D{}^b$, μg ml^{-1}	3.19	5.16	5.41	4.24
$L_Q{}^c$, μg ml^{-1}	7.62	12.63	13.08	10.47

[a] Molar absorptivity of ion associate with dicarbollide at 370 nm; [b] limit of detection; [c] limit of determination.

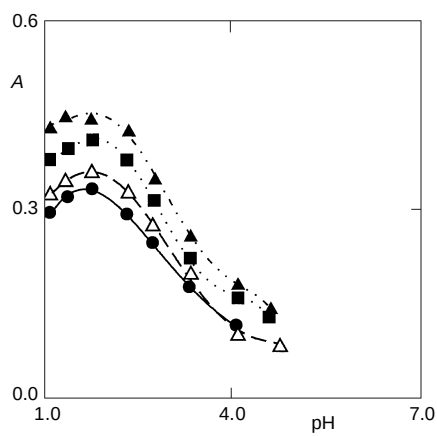


FIG. 5
Absorbances of chloroform extracts of ion associates of protonized bases with the cobaltacarborane anion at 380 nm in dependence on pH of the aqueous phase. ▲ PCP, ■ ethylmorphine, Δ codeine, ● ephedrine

trogen bases or quaternary salts can be grouped in a series according to the increasing solubility of the associate in the organic phase. In addition to some alkaloids, the psychoactive substances quinuclidin-3-yl benzilate and 1-(1′-phenylcyclohexyl)piperidine were also examined.

The proposed competitive extraction method makes it possible to determine the base radiometrically and compare the results with those obtained by the conventional spectrophotometric method.

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