Chromatographic enrichment of calcium isotopes with 18-crown-6 bound to a macroporous solid support

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<u>Abstract</u> Calcium isotopes were enriched in chromatography columns containing 18-crown-6 bound to a solid support. The solid support consisted of polystyrene divinylbenzene to which the crown was bound with a short tether of the structure -CH_2OCH_2-. Separation coefficients for the chemical exchange reaction ranged from 0.0021 to 0.0034 for the ^{44}Ca-^{40}Ca isotope pair. The presence of dimethylsulfoxide (DMSO) in the fluid phase was found to increase the separation coefficient. This increase was accompanied by additional mass transfer resistance. Higher calcium concentrations in the fluid phase also led to increased separation coefficients. Increases in calcium concentrations in the fluid phase resulted in substantial increases in separative power and reductions in theoretical stage heights and stage residence times. The calcium capacity of the column was decreased by the presence of DMSO and increased by increases in the fluid phase concentration.

INTRODUCTION

Calcium isotopes were first enriched in a macrocycle containing chromatography column by Heumann and Schiefer (ref. 1). They reported large calcium isotope effects with [222] cryptand bound to a polystyrene divinylbenzene solid support. The elution technique of chromatography was used in that work to determine separation factors. Later the same chemical system was examined using the displacement technique of chromatography with the purpose of evaluating column performance (ref. 2). A reaction rate limitation was found to preclude the use of this system for any practical application to the separation of calcium isotopes.

Calcium chemical exchange with dicyclohexano 18-crown-6 in a liquid-liquid extraction system was known to exhibit a similarly large isotope effect and was also known to undergo rapid exchange (ref. 3). Thus a program to study polymer-bound 18-crown-6 was initiated. No column packings were commercially available. Polymer-bound crowns were originally obtained from R. A. Bartsch (ref. 4) for investigation of chemical features such as separation coefficients and binding constants (ref. 5). While these available materials were suitable for determining chemical features, they were not suitable for extended use in a practical continuous process. In the work described in this paper the thrust has been altered from investigation of chemical features such as separation coefficients and heterogeneous binding strengths to establishing mass transfer related features of more interest to chromatography. The emphasis is thus more on column and packing performance including stage heights, band velocities, stage residence times, and separative powers.


COLUMN AND PACKING

Glass columns 5.0 mm in diameter, jacketed, and maintained at 20 °C were used. Column packed lengths were 29.2 cm (Runs 1, 2, and 6) and 19.1cm for remaining runs. The solid support was high crosslinked polystyrene divinylbenzene. This material was chloromethylated by R. A. Bartsch at Texas Tech University.

The synthesis of the crown-tether combination and the subsequent attachment of the tether to the solid support were performed at Mound Laboratory by D. L. Jones and L. P. Parts. Figure 1 illustrates the structure of the polymer-bound 18-crown-6. The crown content of the packing was determined by elemental analysis to be 0.53 mmole/dry gram of packing.
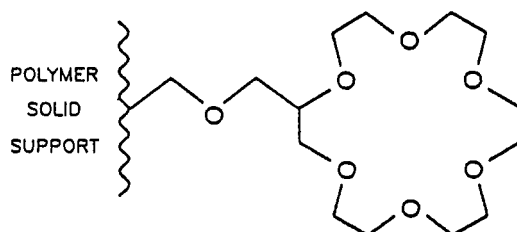

Figure 1. Polymer-bound 18-crown-6 and tether.

The solid support was somewhat fragile and fracturing caused fines to accumulate with handling. Pressure drops across the columns were high for Runs 1,2, and 6, ranging from 200 to 300 psig. After column Runs-1,2 and 6 were performed, the packing was refined and approximately one-third of the packing was removed. The remaining packing, now free of fines, was loaded into a smaller column. Pressure drop over this shorter column ranged from 0-20 psig for Runs-3,4,7, and 8.

COLUMN OPERATION

The breakthrough technique was used in the column experiments. Feed solutions consisted of a 70/30 methanol/chloroform mixture with 0.2% by volume of water and calcium chloride. In the case of Runs 6, 7, and 8, 2%, 2%, and 4% by volume of dimethylsulfoxide (DMSO), respectively, were added. Procedures for sample analysis have been previously described (ref. 2). At the conclusion of each column experiment, all calcium was removed from the column and the total quantity determined to obtain the column capacity. Measurement of the void fraction of the column was accomplished by two different methods. First, the ratio of superficial velocity to band velocity of a non-absorbed chromophore was measured. Second, the isotope ratios of the recovered calcium from the completed column runs were measured. From these, the void fraction was obtained from material balances. The two methods yielded an average void fraction of 0.66.

The breakthrough curves and isotope enrichment profiles obtained for two of the column runs are shown in Figure 2. The breakthrough curves shown are sharp and typical of those found for all of the column runs. It can be observed that the breakthrough for Run-8 with DMSO occurred more quickly than for Run-4, with all other conditions being equal. This was a consequence of a reduced solid phase capacity. The isotopic enrichments at the front of the enrichment bands were typically greater in Runs 1-4, without the added DMSO than with DMSO, as illustrated in the two enrichment profiles shown. Further, the slopes of the isotope enrichment profiles were steeper with DMSO than without DMSO. This was a consequence of the longer theoretical stage heights with DMSO. Steady state conditions were achieved for both the breakthrough curves and the enrichment profiles in all experiments. That was an essential condition for the validity of the determination of the separation coefficient.
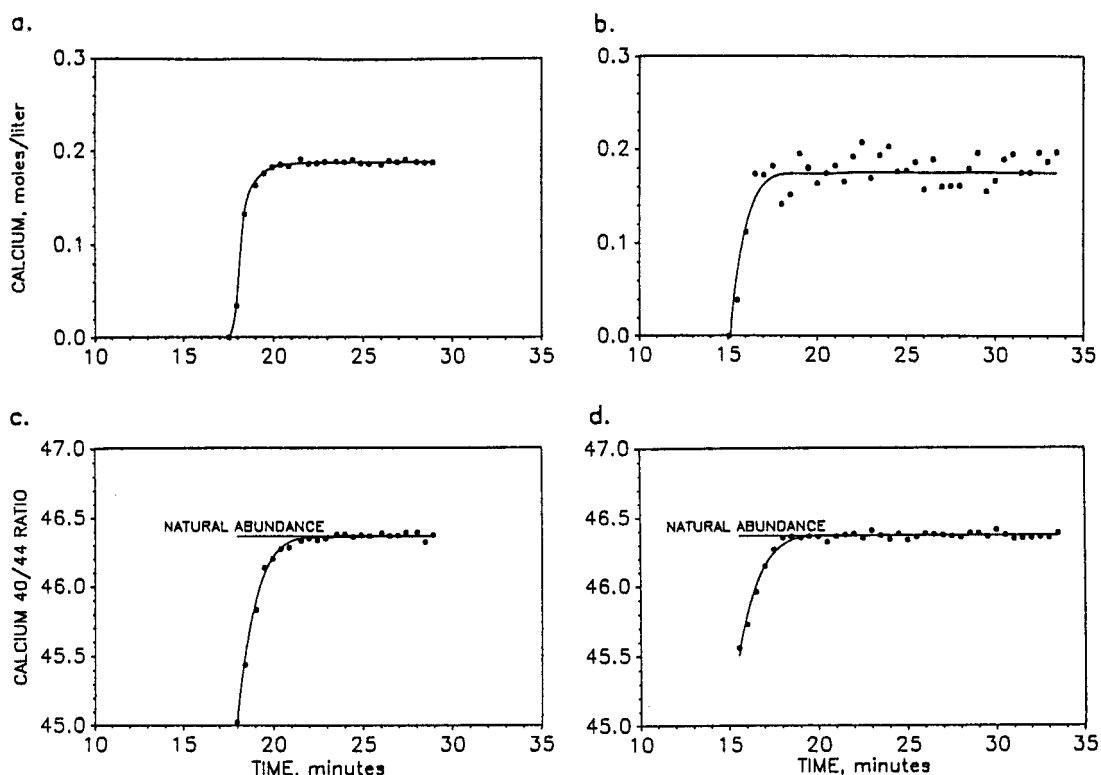
Figure 2. Breakthrough curves a) Ca eluted for Run-4 without DMSO, and b) Ca eluted for Run-8 with DMSO. Isotope ratios c) $^{40}Ca/^{44}Ca$ for Run-4 without DMSO, and d) $^{40}Ca/^{44}Ca$ for Run-8 with DMSO.

EQUILIBRIUM PROPERTIES

Separation coefficient

The chromatographic enrichment of calcium isotopes proceeds according to the chemical exchange reaction:

$$^{40}Ca^{2+}_{(fluid)} + \,^{44}CaL^{2+}_{(solid)} \rightleftharpoons \,^{44}Ca^{2+}_{(fluid)} + \,^{40}CaL^{2+}_{(solid)} \qquad 1.$$
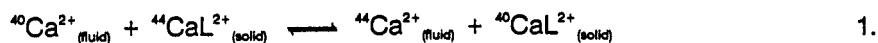
where L represents 18-crown-6 bound to a solid support. The separation coefficient, e, for this exchange reaction is defined as K-1, where K is the equilibrium coefficient of Reaction-1. The computation of the separation coefficient has been previously described (ref. 2). Table 1 shows the separation coefficients obtained under various operating conditions.

Binding strength

The complexation and decomplexation of calcium proceeds according the reaction:

$$Ca^{2+}_{(fluid)} + L^{2+}_{(solid)} \rightleftharpoons CaL^{2+}_{(solid)} \qquad 2.$$

Heterogeneous binding constants are not reproducible from one packing to another. The greatest stability occurs with very low crosslinked microporous gel type solid supports. The maximum level of complexation in very low crosslinked polymer supports found was 87% of crown complexed for the ligand-tether combination shown in Figure 1 and the fluid phase compositions described above (ref. 5). The much lower degree of complexation attained with macroporous packings is attributed to inaccessibility of some of the polymer-bound crown. The precise reasons for this inaccessibility

have not yet been determined. The fraction of crown complexed at steady state conditions is shown in Table 1.

TABLE 1. Summary of operating conditions and performance for chromatography columns containing polymer-bound 18-crown-6.

Column Runs:	Fluid phase without DMSO				Fluid with DMSO		
	1	2	3	4	6	7	8
Fluid Phase [Ca] Concentration, $\underline{M}$	0.103	0.101	0.101	0.200	0.101	0.101	0.201
Flow Rate, cc/min	0.05	0.05	0.2	0.2	0.05	0.2	0.2
Band Velocity, mm/min	1.3	1.7	7.8	10.1	1.8	8.4	11.4
Crown Complexed, %	24	24	22	24	20	19	16
Separation Coefficient for (40-44 pair), $\varepsilon \times 10^4$	22	21	22	33	32	33	34
HETP, mm	1.6	1.7	2.6	1.8	4.3	4.9	3.8
Stage Residence Time, sec	36	30	10.1	5.4	71	17.5	9.9
Separative Power, (40-44 pair), gm/liter-year	2.8	3.5	10.0	63	3.2	12.2	33

The calcium capacity of the column is an essential factor in the separative power as will be seen below. The column capacity was measured by recovering all calcium from the column after each run. It is a composite of the fluid phase concentration and the solid phase calcium content. The average calcium concentration is the total capacity of both fluid phase and solid phase divided by the column packed volume. The average concentration can be expressed as:

$$C_{avg} = v[Ca]_{fluid} + Ca_{solid} \qquad\qquad 3.$$

where v is the void fraction of the column, and C_{avg} is the unit volume capacity of the column.

Dimethylsulfoxide   DMSO has a strong influence on the separation coefficient at low calcium concentrations as can be seen in Table 1. The chemical exchange reaction shown in Reaction-1 is actually an exchange between a fluid phase calcium-DMSO complex and the solid phase calcium-crown complex. Approximately stoichiometric quantities of DMSO were used in the preparation of the fluid phase feed solution assuming the formation of a tri-DMSO calcium complex. The calcium-DMSO complex was first reported by Franklin and Owen who constructed a ternary diagram for the $CaCl_2$-DMSO-water system and identified a compound with the composition of $CaCl_2 \cdot 3H_2O \cdot 3DMSO$ (ref. 6). Further, Tokmatov et. al. isolated and identified the $CaCl_2 \cdot 3DMSO$ compound in phase studies of the $CaCl_2$-DMSO-hexamethylenetetramine ternary system (ref. 7).

Calcium concentration   Calcium concentration in the fluid phase has an influence on the separation coefficient as shown in Table 1. The higher separation coefficient in Run-4 compared to Runs 1-3 was attributed to differences in the coordination sphere of the calcium at higher concentrations. Since DMSO forms a complex with calcium in the fluid phase, the coordination sphere is unchanged with calcium concentration and the separation coefficient remains unchanged.

COLUMN PERFORMANCE

The overall column performance depends both upon equilibrium features and mass transfer features. The kinetics of the exchange are described by band velocity, height equivalent of a theroetical plate (HETP), and stage residence time. When the equilibrium features of column capacity and separation coefficient are combined with mass transfer features, the separative power is obtained.

Theoretical stage heights

Theoretical stage heights were calculated from the isotope enrichment profiles according to the method previously reported (ref. 2). Several general observations can be made from Table 1 regarding HETPs. The presence of DMSO yields much longer HETPs. This is attributed to mass transfer resistance introduced by the formation of the fluid phase calcium-DMSO complex. Somewhat less strong influences are higher flow rates leading to longer HETPs and higher concentrations leading to shorter HETPs. The latter relationship indicates more rapid mass transfer solely as a consequence of higher calcium concentration.

Stage residence time

The stage residence time is given by $T_{res} = (HETP)/2B$ where B is the band velocity. In the cryptand work previously reported, the stage residence time was constant and independent of flow rate over widely varying flow rates (ref. 2). In Table 1 the stage residence time is shown to decrease with increasing flow rate and to decrease with increasing concentration. This contrasts with the cryptand work where stage residence time was constant with increasing flow rate. It can also be observed that the residence time for DMSO containing systems is slightly less than twice that of comparable non-DMSO systems, again illustrating the mass transfer resistance introduced by the DMSO.

Separative power

The equilibrium characteristics and mass transfer characteristics can be combined to give a measure of the power of a separating device or of a unit volume of an enrichment band in a chromatography column. The separative power, δU, is defined:

$$\delta U = \frac{\epsilon^2 \overline{C} B}{4(HETP)} \qquad\qquad 5.$$

with the variables as defined above. The units on separative power are mass/time-volume. Thus, the larger the separative power, the smaller will be the volume of a band needed to perform a given separation. It is convenient to rearrange this expression to the following:

$$\delta U = \frac{\epsilon^2 \overline{C}}{8 T_{res}} \qquad\qquad 6.$$

Referring to Table 1, it is evident that Run-4 with high flow, high concentration and no DMSO yields the greatest separative power. Within the ranges of operating conditions studied, some general observations can be made. Increased flow rates lead to shorter stage residence times. This relationship is not a direct one, however, since increasing flow rates also increase stage heights. The fluid phase calcium concentration has the greatest influence on separative power. Increasing concentrations increase the column capacity and also reduce the stage residence time. In the case of the non-DMSO work, a substantial increase in the separation coefficient was also obtained. All of these contributed to the large increase in separative power. The stage residence time of 5.4 seconds associated with this column run is, however, too slow to form the basis of a separations process.

CONCLUSIONS

The breakthrough technique was used to determine separation coefficients, theoretical stage heights, stage residence times and separative powers under varying fluid phase compositions, calcium concentrations, and flow rates. The use of dimethylsulfoxide (DMSO) in the fluid phase conferred an increase in the separation coefficient, but introduced additional mass transfer resistance not present in identical systems without DMSO. Increases in calcium concentration in the fluid phase led to substantial increases in separative power and reductions in stage heights and residence times. Increases in flow rate in general resulted in larger separative powers and smaller stage residence times.

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