Solubility of *p*-t-butylcalix[n]arenes (n=4,6,8) in Supercritical Carbon Dioxide and their Correlation with Pseudo-Solubilities from Supercritical Fluid Extraction

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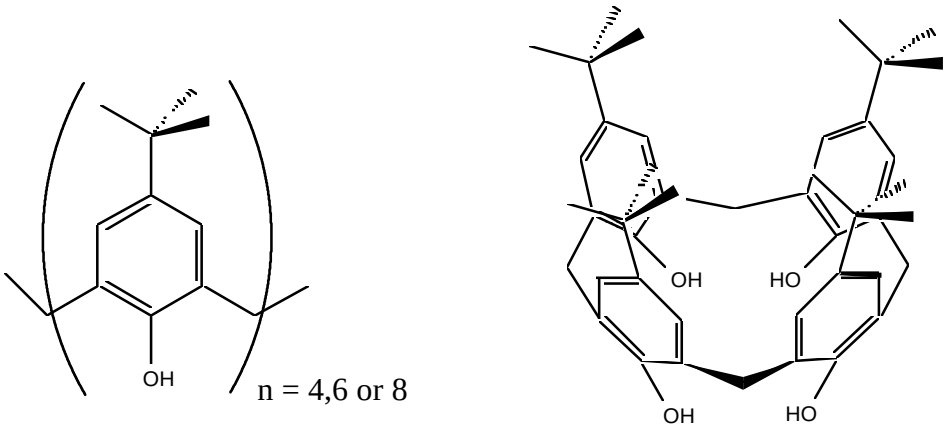
Abstract

In previous work [1] the solubility of the *p*-t-butylcalix[n]arenes, n=4, 6, 8, has been measured in supercritical carbon dioxide under a variety of conditions using a static solubility cell. The measurements showed large increases in solubility of the calixarenes with increases in pressure (density) and temperature. A comparison of these results with measurements made with a commercially available analytical SFE unit showed less than 10% deviation between the two sets of data over a common range of conditions. The SFE unit allows measurements to be made over a significantly wider range than is currently available using the solubility cell. An anomaly observed in the IR spectrum of p-t-butylcalix[4]arene after removal of the solid from the solubility cell is believed to be a result of formation of a CO_2/calixarene inclusion complex. Preliminary investigations of this phenomenon are reported herein.

Introduction:

Calixarenes are macrocyclic oligo-phenols formed by cyclo-oligomerisation of a 4-substituted phenol and formaldehyde; the most readily obtained are those where the 4 substituent is a t-butyl group and the macrocycle contains 4,6 or 8 phenolic units [2,3] (Figure 1). The calixarenes derive their name from the Greek word “calix” meaning bowl, which is the shape adopted by the smallest member of the family, calix[4]arene, in the solid state [2]. This cone conformation is stabilised by extensive hydrogen bonding between the hydroxyl groups on the “lower” rim. The larger calixarenes adopt nearly planar structures though all the *p*-t-butylcalixarenes are conformationally mobile in solution [3,4].



p-t-butylcalix[4]arene

Figure 1. General structure of the *p*-t-butylcalixarenes and the cone conformation of *p*-t-butylcalix[4]arene.

A characteristic of the p-t-butylcalixarenes is their low solubility in common organic solvents, with p-t-butylcalix[4]arene being the least soluble. This insolubility was a major hindrance to the elucidation of the calixarene structure, though an increase in calixarene size or functionalisation of the lower rim usually increases solubility [2]. The varying cavity size and the ease of functionalisation of the lower rim has allowed the calixarenes to be used for molecular recognition. They have shown the ability to recognise metal ions, especially alkali metals, [2] and to form inclusion complexes with small organic

molecules, both charged and neutral [2,5,6]. These complexes can exist in both the solution and solid phases. Some host molecules are so tightly bound that strong heating under vacuum for a period of days is required for full removal of the guest (e.g., the toluene:p-t-butylcalix[4]arene complex [7]) while other complexes only last a few minutes at atmospheric conditions (e.g., the chloroform:p-t-butylcalix[8]arene adduct [2])

Our interest in calixarenes is their potential use as chelating agents in supercritical fluids for the selective extraction of metals such as the lanthanides and actinides from minerals, so an understanding of the solubility behaviour of the calixarenes in supercritical carbon dioxide (our fluid of choice) is required. We report herein a comparison of two experimental procedures for measurement of the solubility of the three important p-t-butylcalix[n]arenes, n=4, 6 and 8 and the first study into a possible CO_2:calixarene inclusion complex.

Materials

p-t-Butylcalix[4]arene [7], p-t-butylcalix[6]arene [8] and p-t-butylcalix[8]arene [9] were synthesised by literature methods. Toluene (AR grade, Shell Australia) was fractionally distilled and dried to remove water.

Experimental

A Hewlett-Packard 7680 Supercritical Fluid Extractor (SFE) with 7 mL extraction thimbles was used to perform the solubility measurements with anaerobic grade CO_2 (Air Liquide, 99.99% stated purity) as the solvent (Fig. 2). The SFE equipment was controlled through Hewlett-Packard ChemStation software running on a PC.

Approximately 10 mg of the calixarene was placed in the extraction thimble with glass fibre filter papers (Macherey Nagel) at each end to stop any powder blocking the frits in

the end caps. The calixarene was then statically extracted (dissolved) at the set conditions (Table I) for 10 minutes and then flushed with 1.5 thimble-volumes of CO_2 to move the dissolved material to the solid bed trap filled with silica packing. The trapped calixarene was then washed from the silica packing with toluene into a 1.5 mL vial containing 0.1 mL of an anthracene standard in toluene.

		Extraction Temperature (°C)			
Pressure (bar)	40	50	60	70	80
150	0.78	0.7	0.6	0.51	0.45
200	0.84	0.78	0.72	0.66	0.6
250	0.88	0.83	0.79	0.74	0.69
300	0.91	0.87	0.83	0.79	0.75

Table I. SFE fluid conditions and densities (g/mL) used for the solubility measurements conducted in the SFE.

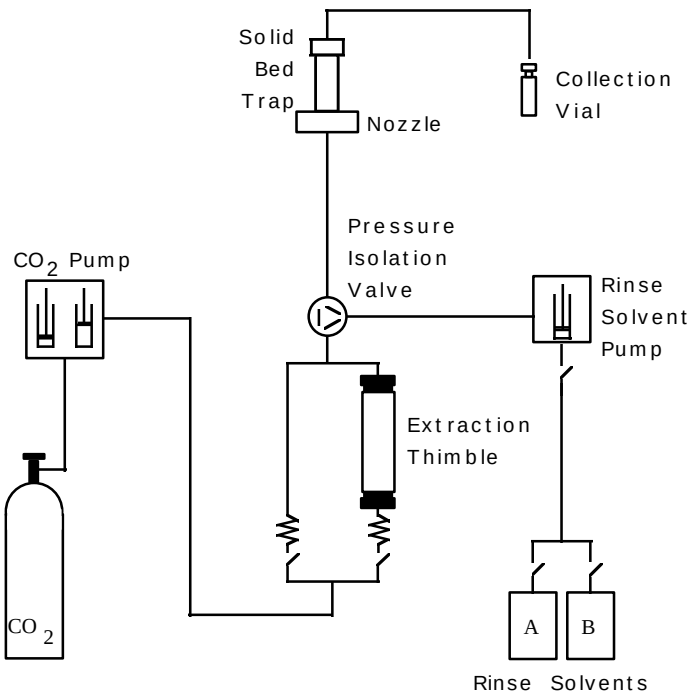


Figure 2. Schematic diagram of the SFE apparatus used with solid bed analyte trapping.

The concentration of the calixarene in the toluene was determined by HPLC (Hewlett-Packard 1090 Series II instrument) using a Hypersil BDS C18 column (125 x 4 mm, 5µm particle size); a mobile phase of acetonitrile:ethyl acetate:acetic acid 80:19.9:0.1, and UV detection at 278 nm for the calixarene and 376 nm for the anthracene standard. A calibration curve was constructed to determine the concentration of the collected calixarene. Triplicates for each concentration on the calibration curve had a relative standard deviation (R.S.D.) of 2.1% or lower. The solubilities of the extracted calixarene were calculated from peak area by the use of this calibration curve.

Infra-red spectroscopy of the calixarenes was conducted by the KBr disc method with a Bio-Rad FTS 45 spectrometer. The IR spectra were taken over the range from 4000 to 400 cm^{-1} at a resolution of 0.125 cm^{-1}. Thermogravimetric analysis was conducted on a Rigaku Thermoflex PTC-10A instrument. Solid state ^{13}C NMR (75.5 MHz) spectra were measured on a Bruker AM 300 spectrometer, while solution ^{1}H NMR (500 MHz) and ^{13}C NMR (125.8 MHz) spectra were recorded on a Bruker ARX 500 instrument.

Results and Discussion

In a previous paper [1] we reported the solubility behaviour of p-t-butylcalix[4]arene, p-t-butylcalix[6]arene and p-t-butylcalix[8]arene in supercritical carbon dioxide These measurements were conducted over the pressure range of 100 - 200 bar for temperatures of 40, 50 and 60 °C using a solubility cell at the Thermophysical Division of N.I.S.T in Boulder, Colorado. These results showed the solubility of all three calixarenes rose with an isothermal increase in density and with an isobaric increase in temperature, with p-t-butylcalix[4]arene exhibiting a solubility 10 times that of the hexamer and octamer. All three calixarenes exhibited the highest solubility at the maximum pressure and temperature used with the cell (200 bar and 60 °C). Table II lists the maximum solubilities obtained for the three calixarenes at the given conditions.

	p-t-butylcalix[4]arene	p-t-butylcalix[4]arene	p-t-butylcalix[4]arene
40 °C	1.59E-05	3.58E-06	1.76E-06
50 °C	1.84E-05	3.12E-06	2.26E-06
60 °C	1.64E-05	1.82E-06	1.86E-06

Table II. Solubilities of the three *p*-t-butylcalixarenes at the given conditions measured using a spectroscopic solubility cell.

In order to extend the temperature and pressure range over which measurements could be made, a commercial analytical supercritical fluid extraction apparatus was used to conduct solubility measurements. The intention was that results obtained from the SFE unit would be compared with the N.I.S.T. solubility data and a calibration factor derived. The use of an SFE unit addresses an issue with the use of *in situ* electronic absorption spectroscopy in the solubility cell, i.e., the assumption that the oscillator strength of the analyte is the same in CO_2 and the solvent used to make the standards. Rice et al [11] have shown that the extinction coefficient at the peak maxima of some analytes is dependent on the density of the fluid with changes of 170% over the density range of 0.3 to 0.9 g/mL. The SFE method does not rely on the direct spectrophotometric measurement of the analyte in the fluid as the extracted analyte concentrate can be analysed by UV spectrophotometry in the same solvent as the calibration standards. In this case HPLC with UV detection was used as it separated the calixarene from the trap rinse solvent, toluene, to allow accurate determination of the concentration.

A series of solubility curves for p-t-butylcalix[4]arene between 150 bar and 300 bar at temperatures of 40, 50, 60, 70, and 80 °C were determined. The maximum solubility for p-t-butylcalix[4]arene obtained over the experimental range was 3.3×10^{-5} mol/L at 80 °C and a density of 0.69 g/mL. The solubility measurements for p-t-butylcalix[4]arene over the studied temperature and density ranges are shown in Fig. 3. The solubility was measured at each temperature and pressure in triplicate and had a R.S.D. of less than

5%. This is slightly higher than the 3.5% R.S.D. obtained for the solubility cell data. A probable contributing factor to this decreased precision is the reduced temperature and pressure control in the SFE unit.

Compared to the data from the solubility cell, the solubilities obtained from the SFE unit were consistently lower, though qualitatively similar over the common studied range. This apparent lower solubility may be due to the uncertainty in the volume of the SFE extraction thimble and associated tubing. This is currently being investigated. A calibration factor of 0.86 was derived from the average ratio of N.I.S.T. and SFE data across the temperature range 40 to 60 °C. The scaled SFE solubility values differed by less than 3% at 40 °C but this deviation rose at the higher temperatures (lower densities) used. This increasing deviation from the N.I.S.T. data at lower densities was a general trend observed over the range of mutually studied conditions.

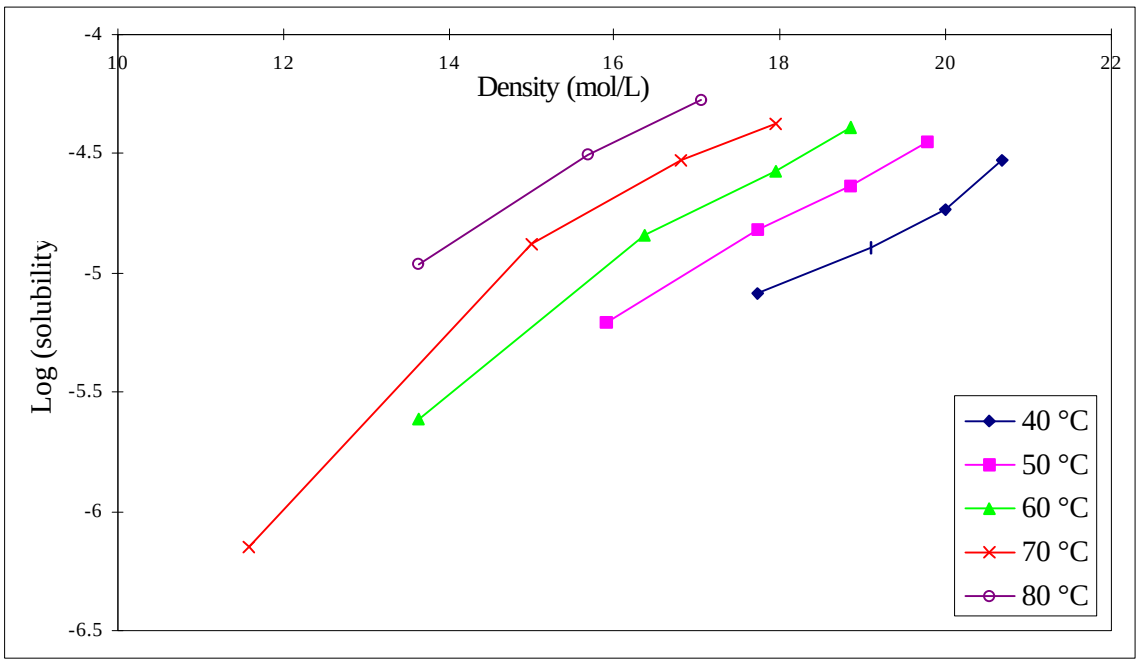


Figure 3. Solubility curves for *p*-t-butylcalix[4]arene obtained from the use of an SFE.

During the initial solubility measurements at the N.I.S.T., an infra-red spectrum was run on a sample of p-t-butylcalix[4]arene removed from the spectroscopic cell immediately

after completion of the analysis to determine if any reactions were occurring between the calixarene and the carbon dioxide. It was thought that a carbonate ester could form at the lower rim of the calixarene. The spectrum showed an additional absorption compared to p-t-butylcalix[4]arene, at approximately 2330 cm^{-1}. Due to the known inclusion chemistry of the calixarenes and the close proximity of this absorbance to that of gaseous carbon dioxide it was thought that the calixarene may be forming an inclusion complex with the carbon dioxide. Solution ^{1}H and ^{13}C NMR spectra after exposure to supercritical carbon dioxide within the lifetime of the complex as shown by infra-red studies showed no change, indicating that the carbon dioxide was not reacting with the phenolic hydroxyl groups. The absorption maximum at 2333 cm^{-1} is red shifted by 26 cm^{-1} from the centre of the absorption peaks of CO_2 gas at 2349 cm^{-1}. The peak showed no rotational fine structure indicating the molecule is rotationally hindered and the P and R branches had collapsed into the single Q branch. This behaviour is similar to surface adsorbed carbon dioxide which also shows a peak red shifted by around 10-20 cm^{-1} with no rotational structure [12]. Work carried out by Keresztury *et al.* [13] has also shown that the spectrum of CO_2 gas trapped in a solid matrix exhibits a red shift and a single Q branch with no rotational structure.

Further studies have shown that the formation of the complex is density dependent with low densities (<0.60 g/mL) giving rise to a very weak absorption peak at 2333 cm^{-1} which is only short lived. The SFE conditions under which maximum formation of the complex was observed were 40 °C, a density of 0.91 g/mL (the highest density obtainable) and a formation/reaction time of 60 minutes. Longer times showed no detectable increase in the absorption peak area. Infra-red studies of the larger calixarenes showed no absorption band at near 2333 cm^{-1}, indicating there is no stable solid complex formed with the carbon dioxide.

Thermogravimetric analysis (TGA) was used to determine both the mass of CO_2 lost over time and the molar ratio of CO_2 to calixarene. The mass loss curve was logarithmic in shape with constant mass being achieved after approximately 45 minutes and the IR spectrum showing no evidence of any residual carbon dioxide present. The mass loss indicated a molar ratio of CO_2 to calixarene of between 0.6 and 0.7 for the original material. Attempts to obtain crystals of the CO_2 adduct suitable for a determination of the structure by X-ray crystallography were unsuccessful due to their rapid efflorescence on removal from the CO_2.

Solid state ^{13}C NMR was used to look for any structural differences the CO_2 may have caused. After exposure of the p-t-butylcalix[4]arene to supercritical carbon dioxide a series of spectra were taken over a period of two weeks to firstly see if a peak attributable to carbon dioxide could be detected and to see if any structural changes to the molecule had occurred. While none of the spectra showed any peaks attributable to carbon dioxide, the spectrum had changed markedly from that of unexposed p-t-butylcalix[4]arene. The spectrum showed marked band broadening compared to that of p-t-butylcalix[4]arene before exposure to the supercritical carbon dioxide. This is indicative of the formation of a very fine powder which is consistent with observations of the crystals crumbling to powder upon touching.

Conclusion

The use of a commercial SFE for conducting solubility measurements over an expanded range of conditions has shown promise though the measurements are not as precise as those obtained from the solubility cell. Comparison of the SFE data to those obtained from the solubility cell has shown good agreement at high densities with a decrease in accuracy and precision at lower densities. With further refinement of this technique, it is hoped that accurate solubility data can be measured with an SFE unit which will allow accurate extraction efficiencies to be calculated. Initial investigations of an anomalous IR

peak in the spectrum of p-t-butylcalix[4]arene after exposure to supercritical carbon dioxide have shown carbon dioxide molecules are included in the crystal lattice.

Acknowledgments

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