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Peracetylated Sugar Derivatives Show High Solubility in Liquid and Supercritical Carbon Dioxide

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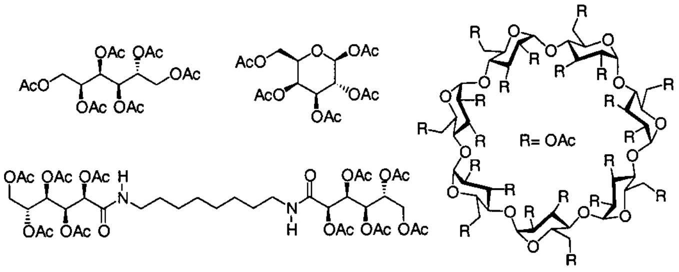
ABSTRACT



Acetylated sugars derivatives exhibit high solubility in liquid and supercritical carbon dioxide ($scCO_2$). Peracetylated sorbitol and β-D-galactose are soluble under mild conditions in $scCO_2$, high pressures are required to dissolve peracetylated β-cyclodextrin, and peracetoxyalkyl chains impart CO_2-solubility to amides.

Over the past several years there has been intense interest in the use of supercritical carbon dioxide ($scCO_2$) as an environmentally friendly solvent for laboratory and industrial applications.[1] However, a critical factor in limiting the use of $scCO_2$ is its weak solvent strength relative to that of organic liquids. This hurdle has led to the investigation of CO_2-philic groups that enhance the solubility of $scCO_2$ insoluble derivatives. Currently the most widely used class of $scCO_2$ solubilizing groups are perfluorinated ester or ether derivatives.[2] While these CO_2-philes have found widespread application in surfactants and additives, their use is limited by prohibitive cost, lack of availability in bulk quantity, and environmental and biological persistence.

From a theoretical analysis[3] of the origin of fluoroalkane CO_2-philicity we proposed that similarly electronegative oligocarbonate and oligoester derivatives would make useful substitutes, as demonstrated by the high CO_2 solubility of poly(ether-carbonate).[4] We have also observed that the addition of acetate side chains to silicone dramatically increased its CO_2 solubility,[5] and others have noted the remarkable solubility of poly(vinyl acetate) in CO_2 relative to that of other nonfluorous homopolymers.[6] All of these examples are based on polymeric derivatives that, while useful, did not fulfill our search for a nonfluorinated small

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molecule derivative that could be attached to a given compound to increase its solubility in CO_2. An alternative approach to constructing molecular subunits with multiple ester functionalities could involve the acetylation of oligohydroxyl derivatives.[7] A ready source of multihydroxylated compounds is the family of mono-, di-, and oligosaccharides. These can be readily converted to their peracetylated derivatives (Figure 1), which should have a density of electronegative groups (and hence CO_2 solubility) similar to that of perfluorohydrocarbons.

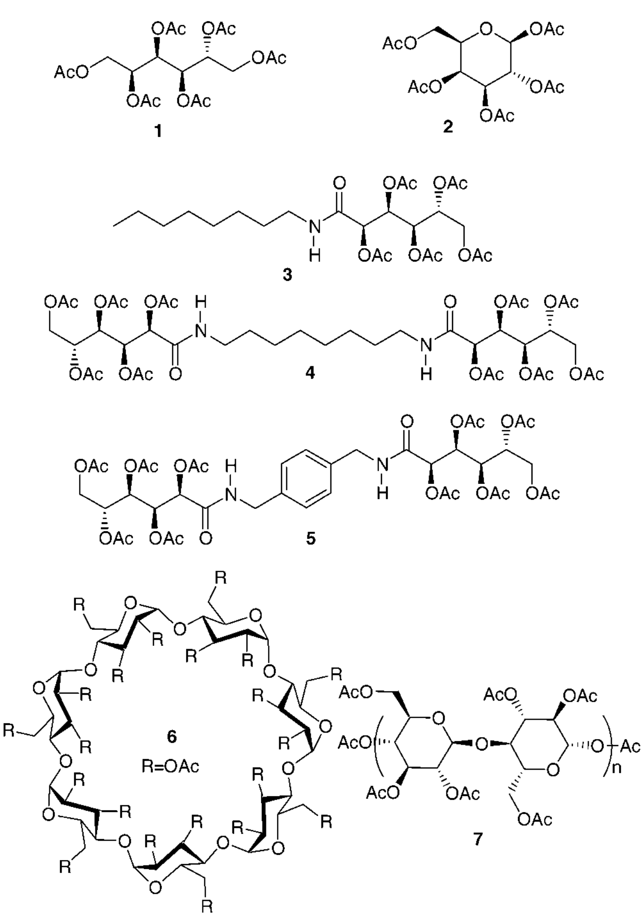

Figure 1. Peracetylated sugar derivatives tested for solubility in carbon dioxide.

To test our hypothesis we determined the CO_2 solubility of commercially available sorbitol hexaacetate (**1**) and β-D-galactose pentaacetate (**2**).[8] These materials were combined with liquid CO_2 at subcritical ($T < 304$ K) and supercritical ($T > 304$ K) temperatures in a high-pressure, windowed, variable-volume cell. The high-pressure single-phase solutions were gradually expanded until a second phase appeared. If the second phase was not a solid, the system was further expanded until particles of **1** and **2** appeared at the three-phase pressure. At lower pressures CO_2-rich vapor coexisted with the solid phase of **1** or **2**. Upon removal of the CO_2 the final form of the solid obtained was also noted. The results (summarized in Table 1 and Figure 2) indicate that both **1** and **2** are soluble in CO_2 at low pressures and both exhibit three-phase equilibria. The modest increase in the two-phase pressure over a broad range in concentration of **2** in CO_2 is characteristic of highly CO_2-soluble compounds.[6,9] At 5 wt %, phase behavior results for **1** and **2** were nearly identical. Whereas sorbitol hexaacetate (**1**) was recovered as a powder at the end of the experiment, β-D-galactose pentaacetate (**2**)

Table 1. Phase Behavior of Acetylated Sugars in Liquid ($T < 304$ K) and $scCO_2$ ($T > 304$ K)

acetyl sugar	% (wt)	T (K)	3-phase pressure (MPa)	2-phase pressure (MPa)	state after CO_2 venting
1	5	298	3.58	6.34^a	powder
1	5	313	4.48	8.98^a	powder
2	5–25	298	5.17	Figure 2^a	foam
2	5–25	313	8.27	Figure 2^a	foam
3	1	298	5.51	6.55^a	powder
4	2	298		37.22^b	powder
4	2	323		37.91^b	powder
4	2	343		42.74^b	powder
5	1	298		37.91^b	powder
5	1	338		41.36^b	powder
5	1	353		41.42^b	powder
6	2–30	298	5.52	Figure 2^a	foam
6	2–30	313	8.27	Figure 2^a	foam
7	1	448	insol	insol	

^{a} Bubble point pressure. ^{b} Cloud point pressure

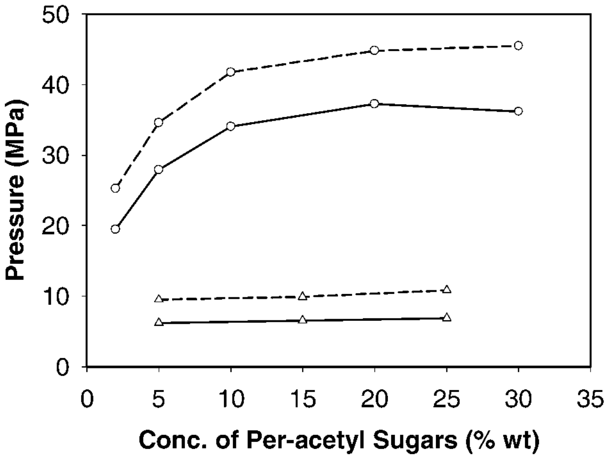

Figure 2. Phase diagrams for the solubility of acetylated sugars **2** (△) and **6** (○) in CO_2 at 298 K (solid line) and 313 K (dashed line). The area above each of the curves represents a single-phase region.

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(7) While this work was in progress a related strategy was reported. Wallen, S. L; Raveendran, P.; Blatchford, M. A.; Schoenbachler, L. K.; Dawson, E. D. 223rd National Meeting of the American Chemical Society, Orlando, FL, April 19–22, 2002.

(8) Compounds **1**, **2**, **6**, and **7** were purchased from Aldrich and used without further purification.

formed a fragile foam with a fibrillar morphology and a density of 0.09 g/mL.

Encouraged by the low pressures required to dissolve **1** and **2** in dense CO_2, we prepared a series of test compounds in which CO_2-insoluble amides were functionalized by peracetoxy alkyl chains (analogous to the frequently used perfluorinated alkyl esters) to assess any improvement in solubility. In particular, the peracetylated amides of D-gluconic acid with 1-octylamine, 1,8-diaminooctane, and 1,4-aminomethylbenzene (compounds **3**, **4**, and **5**, respectively)[10,11] were prepared by ring-opening reaction of the amine with gluconolactone followed by peracetylation with acetic anhydride. Phase behavior results (Table 1**)** demonstrate that each of the amides exhibited CO_2 solubility. While compound **3** was readily soluble in CO_2 at 298 K, compounds **4** and **5** were less soluble in CO_2, exhibiting high bubble point pressures at supercritical temperatures. Even though compounds **4** and **5** were initially insoluble in CO_2 at 298 K, a single phase could be obtained at elevated temperature and pressure, and a cloud point was eventually determined by cooling to 298 K followed by expansion until a second phase appeared.

Another challenging test was the cyclic heptasaccharide, β-cyclodextrin. This molecule contains 21 hydroxyl groups surrounding a central cavity. The peracetylated derivative, β-cyclodextrin heneicosaacetate (**6**), showed outstanding solubility in liquid and $scCO_2$ over a very broad range of compositions (Table 1 and Figure 2). The two-phase boundary for this peracetylated heptasaccharide (**6**) was observed at higher pressures compared to the peracetylated monosaccharide (**2**) because of the increase in molecular weight. However, **6** was more soluble than the much smaller functionalized amides **4** and **5**, because of the absence of the highly CO_2-phobic amide group. As the CO_2 was evacuated from the top of the cell at the end of the experiment, the β-cyclodextrin heneicosaacetate (**6**) formed a fragile, fibrillar foam with a density of 0.06 g/mL.

The limit of this strategy was reached with the attempted dissolution of cellulose triacetate (CTA) **7** ($n \approx 180$) in CO_2. CO_2 is known to permeate CTA membranes, which is partially attributable to the CO_2-philicity of CTA.[12] Although CTA is plasticized[9] in the presence of CO_2 the high molecular weight ($\sim$103,000) of peracetylated polysaccharide rendered it completely insoluble in CO_2 over a range of temperatures (298−448 K) and pressures up to 52 MPa. This is not surprising given the large increase in pressure required to dissolve **6** compared to **2** (Figure 2).

In summary, these results represent a significant step in the design of nonfluorous CO_2-philic agents. High solubility in $scCO_2$ can be achieved with a range of peracetylated sugars, from monosaccharides to cyclodextrin. This strategy will permit not only the construction of simple and biodegradable CO_2-additives but also a unique opportunity to investigate host−guest interactions in $scCO_2$.

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(10) The unacetylated precursors to compound **3**, **4**, and **5** were prepared according to: Fuhrhop, J. H.; Boettcher, C. *J. Am. Chem. Soc.* **1990**, *112*, 1768.

(11) **Typical Peracetylation Procedure and Selected Data for 3−5.** To a stirred suspension of the unacetylated precursor (1 mmol) in acetic anhydride (5 mL/g of the substance) was added freshly fused anhydrous zinc chloride (20 mmol), the mixture was warmed slightly to get a homogeneous solution, and stirring continued for 1 h. The reaction mixture was quenched ice water and extracted with dichloromethane. The organic layer was concentrated, and the crude product was purified by column chromatography over silica gel to yield 80−95% of the peracetylated derivative**.** **Compound 3.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.044 (t, J = 5.0 Hz, 1H), 5.673 (t, J = 5.5, 1H), 5.441 (dd, J = 4.5 Hz, 6.5 Hz, 1H), 5.288 (d, J = 6.0 Hz, 1H), 5.035 (m, 1H), 4.312 (dd, J = 4.0 Hz, 12.5 Hz, 1H), 4.126 (dd, J = 5.5 Hz, 12.5 Hz, 1H), 3.235 (m, 1H), 2.197 (s, 1H), 2.105 (s, 3H), 2.088 (s, 3H), 2.048 (s, 6H), 1.476 (m, 2H), 1.278 (m, 10H), 0.084 (t, J = 6.5, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.59, 169.85, 169.62, 169.17, 165.85, 71.68, 69.39, 69.09, 68.73, 61.54, 39.54, 31.74, 29.38, 29.14, 26.79, 22.60, 20.73, 20.67, 20.41, 14.14. HRMS (FAB) calcd for $C_{24}H_{40}NO_{11}$ $(M + H)^+$ 518.2601, found 518.2603. **Compound 4.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.130 (t, J = 5.0 Hz, 2H), 5.647 (t, J = 5.5, 2H), 5.423 (dd, J = 4.5 Hz, 6.5 Hz, 2H), 5.263 (d, J = 5.5 Hz, 2H), 5.023 (m, 2H), 4.311 (dd, J = 4.0 Hz, 12.5 Hz, 2H), 4.119 (dd, J = 5.5 Hz, 12.5 Hz, 2H), 3.229 (m, 4H), 2.182 (s, 6H), 2.093 (s, 6H), 2.075 (s, 6H), 2.036 (s, 12H), 1.468 (m, 4H), 1.263 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.60, 169.83, 169.82, 169.64, 169.19, 165.93, 71.67, 69.37, 69.05, 68.73, 61.54, 39.41, 29.24, 28.89, 26.53, 20.69, 20.63, 20.44, 20.37, 18.93. HRMS (FAB) calcd for $C_{40}H_{61}N_2O_{22}$ $(M + H^+)$ 921.3716 found 921.3716. **Compound 5.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.209 (s, 4H), 6.402 (t, J = 5.5 Hz, 1H), 5.686 (t, J = 5.5, 2H), 5.439 (dd, J = 4.5 Hz, 6.5 Hz, 2H), 5.332 (d, J = 5.5 Hz, 2H), 5.040 (m, 2H), 4.462 (dd, J = 6.0 Hz, 14.5 Hz, 2H), 4.358 (dd, J = 6.0 Hz, 14.5 Hz, 2H), 4.306 (dd, J = 4.0 Hz, 12.5 Hz, 2H), 4.117 (dd, J = 5.0 Hz, 12.5 Hz), 2.127 (s, 3H), 2.086 (s, 3H), 2.073 (s, 3H), 2.043 (s, 3H), 1.964 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.61, 169.83, 169.68, 169.18, 166.13, 137.05 128.11, 71.63, 69.40, 68.98, 68.78, 61.54, 43.02, 20.71, 20.65, 20.63, 20.32. HRMS (FAB) calcd for $C_{40}H_{53}N_2O_{22}$ $(M + H^+)$ 913.3090 found 913.3091.

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