

components as respect of phases), from one phase into another phase. The phases thus differ from one another in one or more physical and/or chemical characteristics, or in other differentiating properties. Such term specifically encompasses, but is not limited to, the transfer of one material from a first liquid component into a second liquid component that is distinct from and immiscible with such first liquid component. Such term further encompasses any transfer of material from one phase component to another based on differences in size, shape, mass, density, solubility, volatility, permeability, diffusion rate, charge distribution, mass/charge ratio, binding affinity, adsorption/absorption potential, and/or reactivity between such respective phase components.

[0035] The term "spontaneous" as used herein refers to a process that proceeds under internal force(s) and requires no external force(s) or intervention. A spontaneous process is not limited by any specific time frame, i.e., it may occur instantaneously or over a relatively long period of time.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] Figures 1A-1D illustrate a wide variety of generalized reaction processes for forming macrocyclic compounds.

[0037] Figure 2 is a graph of intensity as a function of average oligomer length, showing shifts in oligomer distributions when different concentrations of extraneous oligomerization byproduct are introduced to the reaction system.

[0038] Figure 3 shows a high-performance liquid chromatograph (HPLC) of the products produced by reaction of benzaldehyde and pyrrole in an absolute ethanol solution without oligomerization control.

[0039] Figures 4A and 4B show HPLC chromatographs of the products produced by reaction of benzaldehyde and pyrrole in a solution containing a precipitating solvent and oligomerization control additive species.

[0040] Figure 4A shows a HPLC of the products produced by reaction of benzaldehyde and pyrrole in a solution containing 50% methanol and 50% water by volume.

[0041] Figure 4B shows a HPLC of the products produced by reaction of benzaldehyde and pyrrole in a solution containing methanol and water at a volume ratio of 3:5 with about 0.014 g/ml NaCl.



[0083] By selecting the appropriate oligomerization control additive(s), reacting solvent(s), co-solvent(s), and/or separation additive(s), one can readily adjust the product distribution of the oligomerization and/or cyclization reactions and improve the production yield of the macrocyclic compound.

[0084] For example, Figure 3 is a HPLC chromatograph for the products formed by reacting benzaldehyde and pyrrole (which are used to form tetraphenylporphyrinogen) in absolute ethanol (which functions as a precipitating solvent for selectively precipitating the non-polar tetraphenylporphyrinogen so formed), without any oligomerization control. The lack of oligomerization control in such reaction results in formation of a wide variety of reaction products, as indicated by the Gaussian distribution. Majority of such reaction products were linear extended oligomers that were formed and precipitated out of the reaction solution concurrently with the tetraphenylporphyrinogen, with only a small amount of tetraphenylporphyrinogen (as represented by the peak at 29.153), approximately less than 1%.

[0085] By reacting benzaldehyde and pyrrole in a reaction composition that comprises ethanol (i.e., the precipitating solvent) and water (i.e., the oligomerization control additive) at a volumetric ratio of 1:1, approximately 30% of the reaction products were tetraphenylporphyrinogen as mixed with undesired oligomers. Figure 4A is a HPLC chromatograph for the products formed by reacting benzaldehyde and pyrrole in a reaction composition that comprises methanol (i.e., a different precipitating solvent) and water (i.e., the oligomerization control additive) at a volumetric ratio of 1:1. About 75% of the reaction products were tetraphenylporphyrinogen (as represented by the peak at 29.261). Figure 4B is a HPLC chromatograph for the products formed by reacting benzaldehyde and pyrrole in a reaction composition that contained about 37.5% by volume of methanol (i.e., the precipitating solvent), 62.5% by volume of water (i.e., the oligomerization control additive), and 0.014 g/ml of NaCl (i.e., the separation additive). The reaction composition used in Figure 4B contained a higher concentration of oligomerization control additive for more effective modulation of the oligomerization reactions, and the separation additive NaCl functioned to further adjust the solvent strength of the reaction composition for more selective separation of the macrocyclic compound. Consequently, the production yield of the tetraphenylporphyrinogen (as represented by the peak at 29.004) was further improved to about 85%. Addition of water in the synthesis of non-polar porphyrinogens is completely opposite to the teachings of the conventional wisdom, which advocates removal of water instead, and it surprisingly and unexpectedly improves the production yield of the non-polar porphyrinogen (e.g., tetraphenylporphyrinogen) by almost a hundred fold.