If a search for exoplanet life were mounted today, the likely focus would be to detect oxygen (or ozone) in the atmosphere of a water-bearing rocky planet orbiting roughly 1AU from a G-type star. This appropriately conservative and practical default is necessary in large part because biological input on the question of where and how to look for life has progressed little beyond a purely empirical reliance on the example of terrestrial biology. However, fundamental physical and chemical considerations may impose significant yet universal constraints on biological potential. The liquid water + oxygen paradigm will be considered as an example, with a focus on the question, “is liquid water a prerequisite for life?”. Life requires a solvent to mediate interactions among biological molecules. A key class of these interactions is molecular recognition with high specificity, which is essential for high fidelity catalysis and (especially) information processing. For example, to correctly reproduce a string consisting of 600,000 units of information (e.g., 600 kilobases, equivalent to the genome of the smallest free living terrestrial organisms) with a 90% success rate requires specificity $> 10^7:1$ for the target molecule vs. incorrect alternatives. Such specificity requires (i) that the correct molecular association is energetically stabilized by at least 40 kJ/mol relative to alternatives, and (ii) that the system is able to sample among possible states (alternative molecular associations) rapidly enough to allow the system to fall under thermodynamic control and express the energetic stabilization. We argue that electrostatic interactions are required to confer the necessary energetic stabilization vs. a large library of molecular alternatives, and that a solvent with polarity and dielectric properties comparable to water is required for the system to sample among possible states and express thermodynamic control. Electrostatic associations can be made in non-polar solvents, but the resulting complexes are too stable to be “unmade” with sufficient frequency to confer thermodynamic control on the system. Such considerations suggest that water, or a solvent with properties very like water, is necessary to support high-fidelity information processing – a feature that must be common to all biology – and can therefore be considered a critical prerequisite for life.