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Cyclodextrin-promoted Diels Alder reactions of a polycyclic aromatic hydrocarbon under mild reaction conditions

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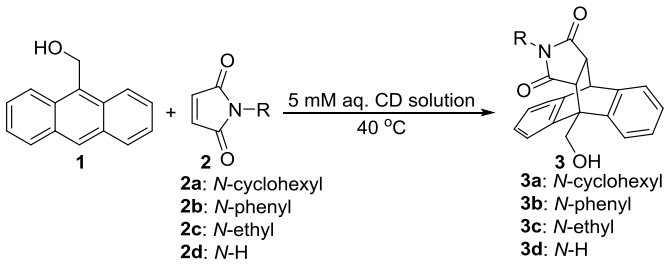
ABSTRACT

Reported herein is the effect of cyclodextrins on the rates of aqueous Diels Alder reactions of 9-anthracenemethanol with a variety of *N*-substituted maleimides. These reactions occurred under mild reaction conditions (aqueous solvent, 40 °C), and were most efficient for the reaction of *N*-cyclohexylmaleimide with a methyl-β-cyclodextrin additive (94% conversion in 24 hours). These results can be explained on the basis of a model wherein the cyclodextrins bind the hydrophobic substituents on the maleimides and activate the dienophile via electronic modulation of the maleimide double bond. The results reported herein represent a new mechanism for cyclodextrin-promoted Diels Alder reactions, and have significant potential applications in the development of other cyclodextrin-promoted organic transformations. Moreover, the ability to deplanarize polycyclic aromatic hydrocarbons (PAHs) under mild conditions, as demonstrated herein, has significant applications for PAH detoxification.

Cyclodextrins are torus shaped cyclic oligoamyloses, with the size of the interior cavity determined by the number of repeating amylose units. The ability of cyclodextrins to form host-guest complexes with hydrophobic guests occurs as a result of their hydrophobic interiors, whereas their relatively hydrophilic exteriors enable them to be used in mostly aqueous environments.[1] Once host-guest complexes form, the guests can undergo cyclodextrin-mediated catalysis;[2] such catalysis has been reported for sigmatropic rearrangements,[3] for Diels-Alder reactions,[4] and for a variety of other organic transformations.[5] Cyclodextrins have also been used for a number of applications based on their ability to form host-guest complexes, including the solubilization of pharmaceutically active compounds,[6] the extraction of polycyclic aromatic hydrocarbons (PAHs) from contaminated sediments,[7] soil,[8] and water,[9] and the promotion of proximity-induced energy transfer.[10]

Previous research in our group has focused on the development of cyclodextrin-based systems for the detection of a wide variety of aromatic toxicants in multiple complex environments via cyclodextrin-promoted energy transfer from the toxicants to high quantum yield fluorophores.[11] We have also reported the ability of cyclodextrins to extract aromatic toxicants, in particular PAHs, from complex oils, including motor oil, vegetable oil, and vacuum pump oil, as well as oil collected directly from an oil spill site.[12] This dual function system of extraction followed by detection has significant applications in oil spill remediation efforts.

Much of the toxicity of PAHs is related to their highly planar structures, which enable the PAHs to intercalate in DNA and form covalent, carcinogenic adducts.[13] Converting the PAHs to non-planar products using chemical transformations disrupts this facile intercalation and limits their ability to form carcinogenic adducts. Reported herein is the ability of cyclodextrins to promote such transformations for one PAH, 9-anthracenemethanol (compound **1**), via its Diels-Alder reactions with *N*-substituted maleimides. Mechanistic investigations demonstrate that the rate enhancements achieved in the presence of cyclodextrin rely on cyclodextrin-induced activation of the maleimide double bond via binding of the hydrophobic substituents to promote the reaction and achieve substantial rate accelerations.



Equation 1. Cyclodextrin-catalyzed aqueous Diels Alder reactions of 9-anthracenemethanol **1** with *N*-substituted maleimides **2**.

The conversion of compound **1** to its corresponding Diels Alder adduct **3** was calculated after various time intervals under standard reaction conditions (5 mM aqueous cyclodextrin, 40 °C) (Equation 1). The percent conversion of each reaction was calculated based on the following equation: