**PROGRESS REPORT, YEAR 3 (2017 to 2018)**
**PRF Grant # 54862 UR 4**
**Title: Employing γ-cyclodextrin to mediate photo-heterodimerization of alkenes in the solid state**
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**1. SCIENTIFIC SUMMARY** The third year of research supported by ACS-PRF resulted in exploration of two different groups of alkenes for homo- and heterodimerization: (a) extended and cross conjugated diene systems (dibenzylidene acetones), and unsymmetrical chalcones (phenyl styryl ketones). These new class of photosubstrates were explored to understand the excited-state photocycloaddition (PCA) characteristics of the alkenes. In both cases native efficiency of PCA is significantly lower in solution phase and solid state, and several PCA products are possible. Complexing the photoreactants to γ-cyclodextrin (γ-CD) increases PCA efficiency resulting formation of a single product. Investigation of the photochemical and photophysical features of the host-guest complex, evaluation of its association constants experimentally, and computational analysis of the complex structures provided insight into the nature of weak interactions involving aromatic groups and excited state reactivity of such alkenes.

**2. SUMMARY OF PRODUCTS:** Three students were supported partly by the PRF grant to be involved in this grant. Four publications, four conference presentations, one talk, and two major federal grants were submitted based on the findings generated from last year's work.

## 3. DETAILED SCIENTIFIC REPORT

### 3.1. Photocycloaddition of cross-conjugated chalcones:

This year we explored photocycloaddition (PCA) of a cross-conjugated diene system – the dibenzalidine acetones (Figure 1). Photochemistry of this substrate has not been previously explored and the findings from this work were of fundamental and applied significance. Due to the presence of the cross-conjugated chromophore several questions regarding its excited state reactivity were unclear. Irradiation of the alkene in homogeneous organic solutions all yielded isomerization products. Similarly, photoreactivity of the substrate in solid state either did not yield any significant conversion at all or resulted in a mixture of at least 6 different products. The reactants were then subject to γ-CD complexation and studied for its PCA.

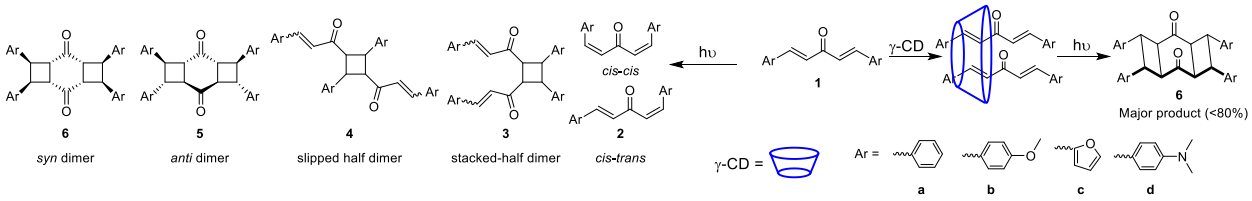


**Figure 1.** Structure of photosubstrates explored. Their photoreactivity in presence and absence of γ-cyclodextrin host.

As with previously explored cinnamic acid and naphthyl acrylic acid photosubstrates (please see reports for year 1 and year 2), substrates shown in figure 1 underwent efficient complexation as indicated by formation of chalky off-yellow slurry. Irradiation of the complex for 36 hrs resulted in more than 85% conversions. All photosubstrates except **1d** yielded a single major product. The photoproduct was isolated using preparative HPLC and analyzed NMR spectroscopy (proton, carbon, and NOESY). Analysis of spectral characteristics of all compounds suggested dimeric product structure. However, several stereochemically equivalent structures were attributed to the spectral data. Therefore, in order to resolve ambiguity, single crystal of the compounds were obtained and analyzed using X-Ray diffractometry (figure 2). The product was ascertained to be a stacked *syn* H-H dimer arrangement.

To better understand a mechanistic aspect of PCA, we subject the complex of $1a_2$@ γ-CD to time-dependent conversion. This revealed that the product forms in a single step instead of dimerization of one part of the molecule followed by the other part. This was further conformed by computational analysis of

‡ Data not displayed in this document. Pls refer to published work

the FMOs of the complex‡. Furthermore, host-guest characteristics of the molecule were deduced using isothermal titration calorimetry of the complex‡ formation and energy-optimized structure of the complex. Considering the several possible products in this reaction and formation of a single product with such high efficiency indicates that there is a strong affinity for the molecule to engage in π-π interaction. This was further reinforced by the analysis of geometry optimized structure of 1:2 host-guest complex obtained using ONIOM HF wB97XD/631++G(2d,2p)/Auto:PM6.

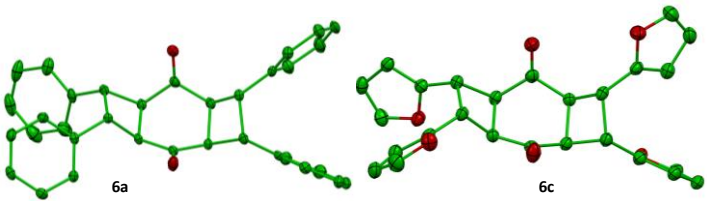


**Figure 2.** Single crystal XRD structure major products from reaction of **1a** and **1c** in γ-CD.

We tested the reaction and its product selectivity within γ-CD with three other compounds. Other than the N,N-dimethyl derivative, other compounds yielded similar stereo- and regioselectivity and reaction conversions. In case of **1d**, it was unclear if the lack of PCA was due to supramolecular control (1:1 complex which was preferred over 1:2) or photochemical inertness due to quenching of excited state by the amino group.‡ Investigation of Job's plot extended irradiation of the compound revealed that the lack of PCA was due to supramolecular factors and not electron transfer quenching. We also explored the cross-dimerization reaction between alkenes. However, the product mixtures contained numerous product and we are currently engaged in resolving the mixtures and isolating them for characterization.

### 3.2. Photocycloaddition of unsymmetrical chalcones

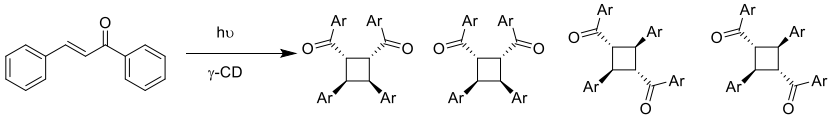


**Figure 2.** Structure of photosubstrates explored. Their photoreactivity in presence and absence of γ-cyclodextrin host.

We are currently exploring cavitand-influenced photochemistry of unsymmetrical chalcones. In this work, we are currently investigating the influence of charge-transfer substituents on the styryl and phenyl sides of the chalcone and affect molecular alignment to observe product selectivity. Substituents explored thus far includes various combinations of nitro and methoxy, cyano and methyl, chloro and methoxy, and trifuloromethyl and methoxy groups. The compounds were synthesized which took significant amount of time and resources. Now we are exploring the photochemistry of these compounds. It is expected that by next year the work will yield results that affords insight into the nature of charge transfer interactions and magnitude of such interactions in molecular alignment.

## 4. SCHOLARLY PRODUCTIVITY

This year, I have total of five publications. Four of those publications are direct result of work supported by ACS-PRF: (1) *Organic & Biomolecular Chemistry*, 2018, (In Press) DOI: 10.1039/C8OB01966E. (2) *Anticancer Research* 2018, 38(8), 4469-4474. (3) Journal of Pain Research 2018, 11, 1075 - 1085. **(4)** *Israel Journal of Chemistry*, 2018, 58, 3-4, 264 – 275. Support from ACS PRF has been gratefully acknowledged in these publications. In addition, four conference presentations, one talk, and two federal grant (DoD, NIH) were submitted based on the data generated from the PRF grant. *Students supported by the grant were co-authors in all four of the publications, talks, and conference presentations.*

## 5. FUTURE DIRECTION

Currently the PRF is third and final year according to original grant duration. However, I had requested an extension of grant duration due to availability of residual funds, which was generously granted. We plan to continue our investigation of the unsymmetrical chalcones within the macrocyclic cavitand. Findings from this work will be applied towards designing strategies for molecular alignment which can find applications in construction of liquid crystals, LED devices, and thermally labile polymers.

‡ Data not displayed in this document. Pls refer to published work