# CAUGHT IN A MATRIX: X-RAY CRYSTALLOGRAPHY AND REACTIONS OF CLATHRATES

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## INTRODUCTION

This past July, *Science* reported the crystallographic structure of a cyclobutadiene derivative.[1] The paper marked the culmination of work by Mihail Barbiou, Makoto Fujita, and others to accommodate reagents in crystalline hosts and to monitor the subsequent reactions by X-ray crystallography.[1-13] This seminar provides an overview of the advances in crystals as hosts for reactions, discussing first the types of crystalline hosts and later the informational benefits of crystallography.

## TYPES OF CRYSTALLINE HOSTS

Crystalline frameworks used as hosts for reactions fall mainly into two categories: crystalline molecular cages[1-3] and porous metal-organic frameworks (MOFs).[4-11] The first type of framework, the crystalline molecular cage, confines reagents to closed cavities. To monitor reactions by crystallography, Fujita and coworkers initially enclathrated reagents inside coordination cages and crystallized these host-guest complexes.[2-3] Similarly, Barboiu and coworkers crystallized the precursor of 1,3-dimethylcyclobutadiene inside a framework of organic salts.[1] The reactions were monitored by single-crystal X-ray diffraction. The second type of crystalline framework, the porous MOF, permits reagents to flow through the matrix. One variation of the porous MOF lacks a confined reagent; the reagent is introduced after formation of the framework.[4-6] The second variation of the porous MOF contains one reagent embedded within the framework; a second reagent enters the matrix through the columnar pores.[7-11, 14] The reaction between the embedded and free reagents is a form of post-synthetic modification (PSM) of MOFs.[15] Crystalline frameworks, whether crystalline molecular cages or MOFs, have provided persistent, regular structures for monitoring reactions by X-ray crystallography.

## INFORMATION PROVIDED BY X-RAY CRYSTALLOGRAPHY

The crystallographic study of reactions within crystalline frameworks affords information unobtainable by spectroscopic analysis. Crystallography reveals details about the mobility, placement, and environment of substrates. Fujita observed the mobility or immobility of trapped substrates by single-crystal X-ray diffraction during his studies on photoreactions and imine formation.[2, 7-8]

Crystallography also showed steric effects on the regioselectivity of a Huisgen cycloaddition.[9] Coppens and coworkers studied the effects of pore size on the rate of a reaction within a matrix.[13] In addition to illustrating the placement and surroundings of enclathrated molecules, crystallography has revealed mechanistically significant structures, including those of transient species. For example, crystallographic analysis of an enclathrated salicylideneaniline confirmed the geometry of the photochromic species.[4] Although the geometry of the imine[7] and hemiaminal[8] were widely accepted before Fujita's crystallographic studies, this technique established the disputed structures of a cyclobutadiene derivative[1] and a labile organometallic intermediate.[3] These unstable species were kinetically persistent within the confines of a crystalline framework, signifying the ability of porous crystalline matrices to stabilize reactive intermediates. The crystallographic analysis of reactions of enclathrated species has provided details—from geometry to mobility constraints—which were beyond the scope of spectroscopy.

## CONCLUSION

By developing crystalline hosts as chambers for reactions, Fujita and others have demonstrated the potential of crystallography to monitor reactions, characterize intermediates, and visualize molecular dynamics within pores. The mechanistic information from crystallographic data could give insight into improved cavitand and MOF design. For instance, pore size could be optimized for a given reaction; or a binding group could be introduced to stabilize transient species. Fujita's work has laid the groundwork for future research.

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