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# BENZONORBORNADIENE DERIVATIVES AND REACTIONS

## THERAPEUTICS

Biorthogonal release reactions based on benzonornadiene derivatives that are highly stable and release cargo molecules for use in drug delivery systems.

### TECHNOLOGY TYPE

Drug Delivery  
Small Molecules  
Oncology

### STAGE OF DEVELOPMENT

- Preliminary experiments have validated the reaction of benzonornadiene with tetrazine releasing a cargo molecule.

- Next steps involve demonstrating proof of principles for potential applications.

### IP PROTECTION

U.S. utility patent filed.

PCT filed.

### LEARN MORE

Reference Numbers: U-6141,  
U-6456

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### TECHNOLOGY SUMMARY

Biorthogonal dissociative reactions boast diverse potential applications in chemical biology and drug delivery. Specific cargo molecules within cells are released when benzonornadienes react with tetrazines to release amines from carbamate leaving groups. These carrier molecules are highly stable at physiological conditions, but react rapidly with tetrazines and near-quantitatively release cargo molecules such as drugs and optical reporters. The reactions are designed to take place without interfering with the existing cell chemistry and could serve a number of different purposes including DNA sequencing, cell imaging, drug delivery systems, and reaction protection groups.

### FEATURES AND BENEFITS

- Allows use in cells, tissue samples, and in vivo.
- Increases reaction rate.
- Facilitates complete release of cargo molecules.
- Eliminates need for metal catalyst.
- Reduces toxicity.

### RECENT PUBLICATIONS

Xu, M., Tu, J., Franzini, R. (2017). Rapid and efficient tetrazine-induced drug release from highly stable benzonornadiene derivatives. *Chemical Communications*. 53:6271-6274. doi: [10.1039/C7CC03477E](https://doi.org/10.1039/C7CC03477E).

Xu, M., Galindo-Murillo, R., Cheatham, T. E., & Franzini, R. M. (2017). Dissociative reactions of benzonornadienes with tetrazines: scope of leaving groups and mechanistic insights. *Organic & Biomolecular Chemistry*. 15(46): 9855-9865. doi: [10.1039/c7ob02191g](https://doi.org/10.1039/c7ob02191g).

### INVENTOR PROFILE

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