Optical Control of Phosphatidic Acid Signaling

Significance: Phosphatidic acids (PA) are signaling lipids that are directly implicated in the modulation of the mTOR and Hippo pathways, which are cell growth enhancing and suppressing, respectively. The authors developed photoswitchable PA that contain azobenzene groups in their tails. These photolipids were found to selectively activate the mTOR and inhibit the Hippo pathways in their bent cis form.

Comment: The synthesis of dAzoPA, one of the photoswitchable PA, containing azobenzene groups in both its tails, began from previously reported photolipid Azo-LPA (J. Am. Chem. Soc. 2020, 142, 10612). Subsequent DCC-promoted acylation with FAAzo4 and deprotection with TFA furnished the desired photolipid. cis-dAzoPA was shown to substantially increase levels of phosphorylated p70-S6 kinase, a key downstream target of mTOR.