

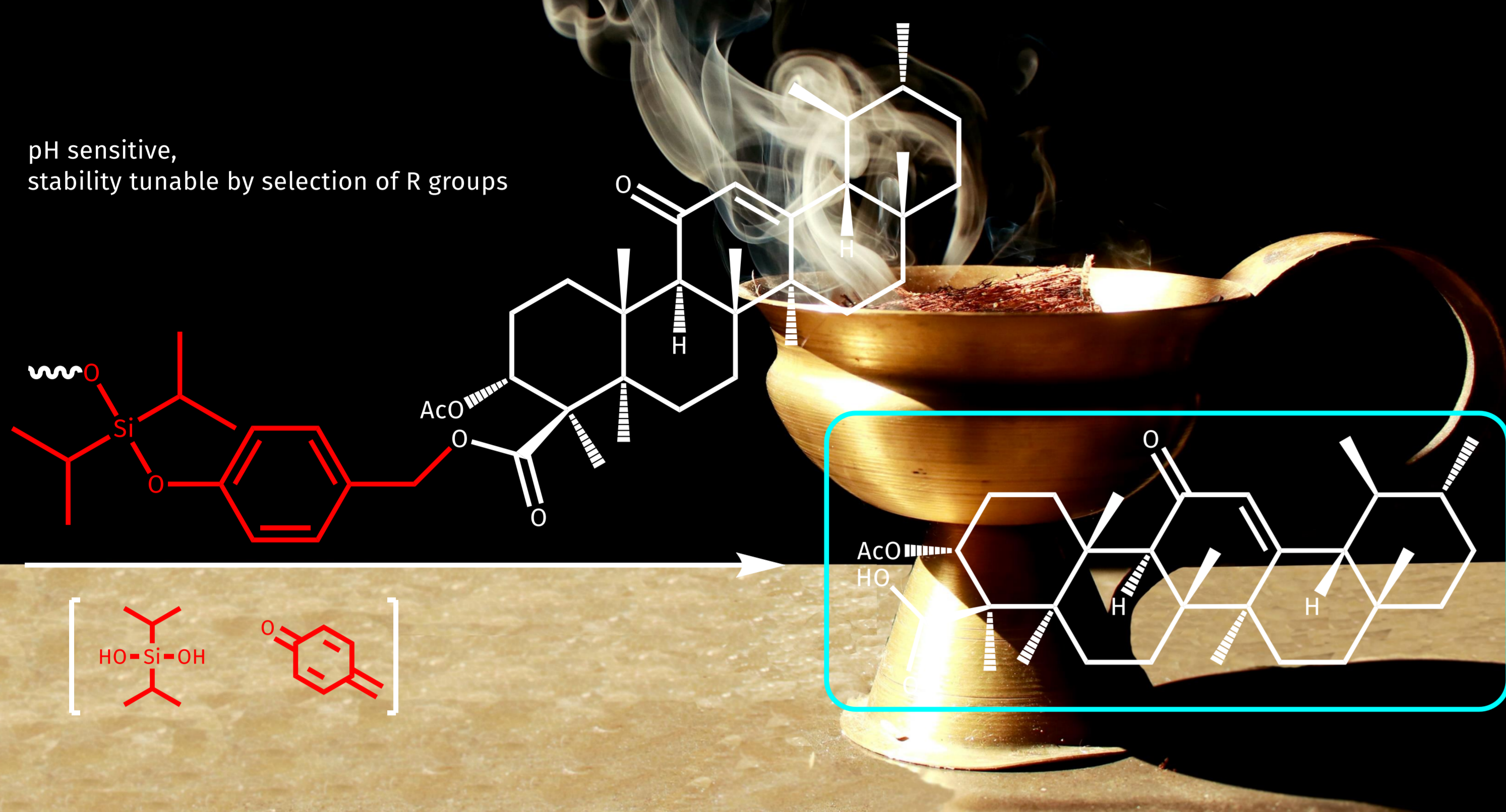
Linkerology®

2023 # 05 – Conjugation of Natural Products

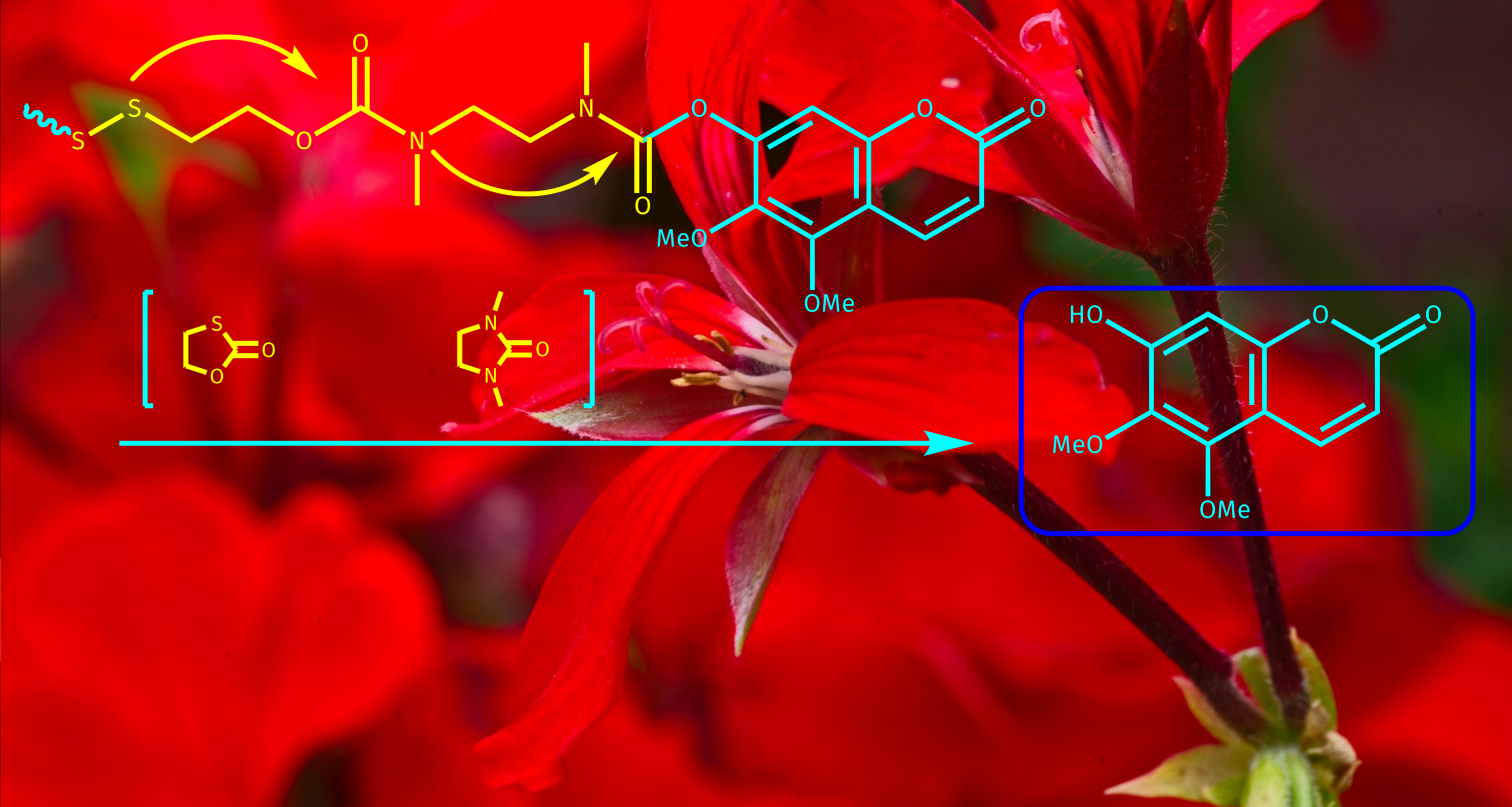


Examples how Natural Products can be Decorated with (Self-Immolative) Linkers

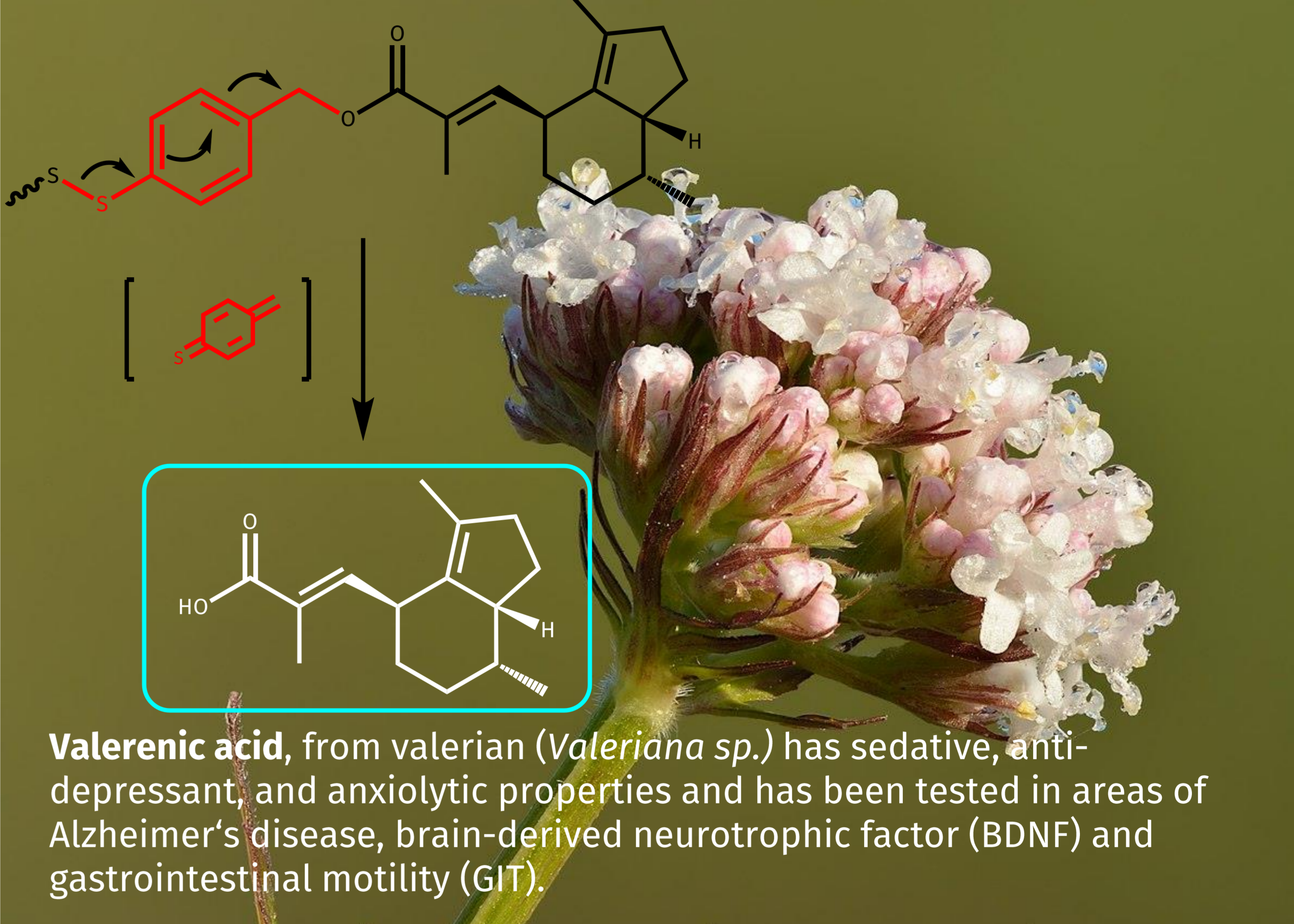
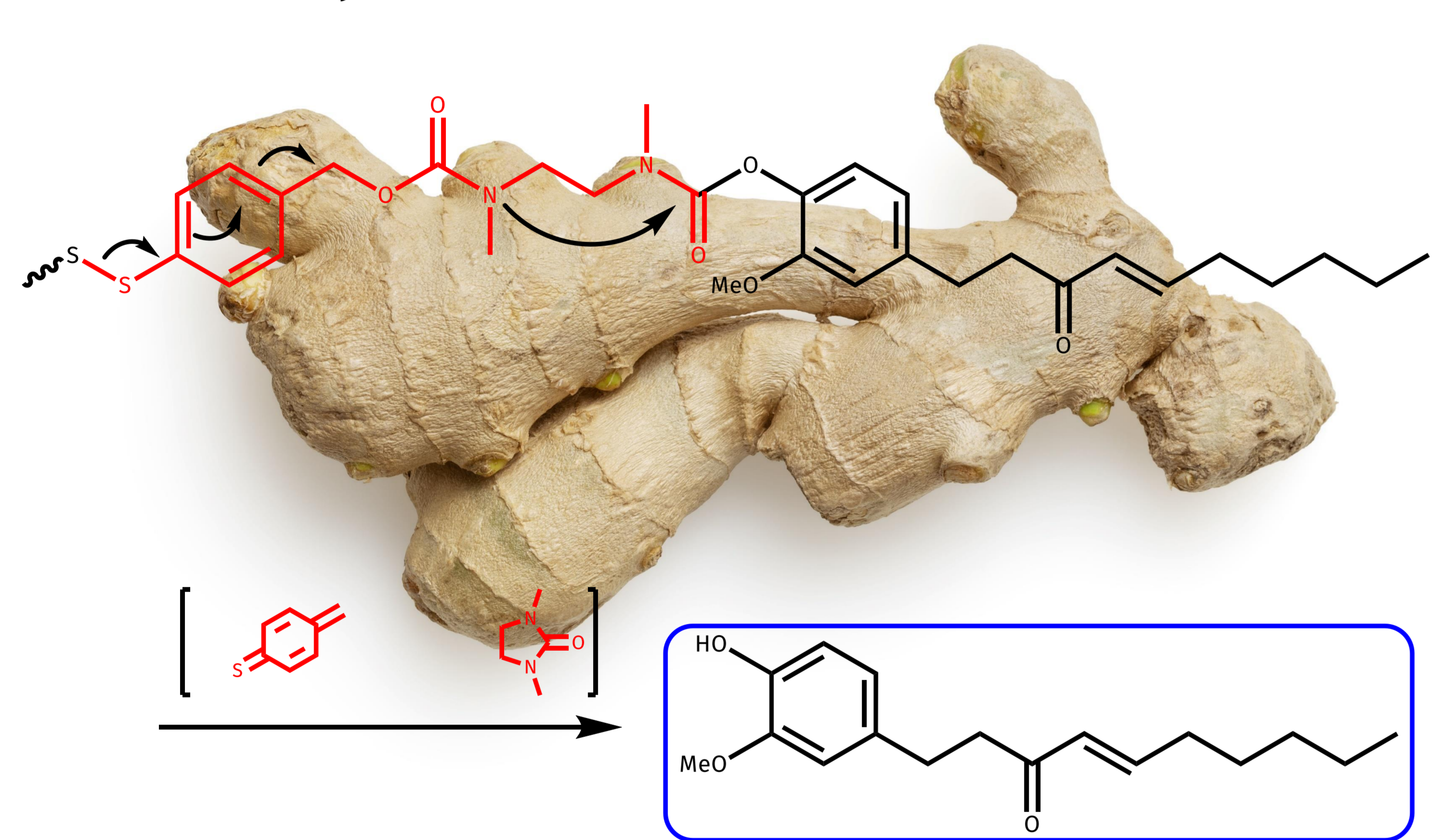
Boswellic acid, from the resin of incense tree (*Boswellia*) has anti-infectious and anti-oxidant properties and has been tested in areas of pancreatitis treatment.



Umckalin, is being isolated from the root of *Pelargonium sp.*, found in South-Africa and has anti-viral and anti-inflammatory properties and has been tested in the treatment of Covid-19.



6-Shogaol, from ginger (*Zingiber officinale*) has anti-inflammatory and anti-cancer properties and also tested in fields of immune response activation, obesity, and osteoarthritis.



Valerenic acid, from valerian (*Valeriana sp.*) has sedative, anti-depressant, and anxiolytic properties and has been tested in areas of Alzheimer's disease, brain-derived neurotrophic factor (BDNF) and gastrointestinal motility (GIT).

Linkerology® - Conceptual Overview

Carrier	Surface Treatment & Conjugation Chemistry	Cleavage	Fragmentation	Functionality of Natural Product
Metal surface	Affinity of sulfur to gold and silver	Enzymatic hydrolysis: • Val-Ala • Val-Cit • Phe-Lys • Gly-Phe-Leu-Gly • Ala-Leu-Ala-Leu • Cyclobutyl-Ala • Cyclobutyl-Cit • Glucuronic acid	<p><i>p</i>-Aminobenzyl <i>p</i>-Hydroxybenzyl</p> <p>Oxathiolone</p> <p>Dimethylimidazolidinone</p>	Primary & secondary amines Tertiary amines Alcohols Phenols Carboxylic acids
Metal oxide	Chelat formation			
Silicates	Affinity of silicon and oxygen	Reduction Acidic hydrolysis 	H ₂ N- R ₁ N- R ₂ HO- HO-C(=O)-	
Carbon: • Nanotubes • Fullerenes	Nitrenen addition via photoactivation of perfluoroarylazides			
Plastic polymers: • Teflon • Polyethylene • Polystyrene • Latex	Ammonia or acrylic acid plasma followed by amide bond formation			
Biopolymers: • Peptides • Proteins • Antibodies • Single Chain • Nanobodies • Camelids • Oligonucleotides • Aptamers	Thioether formation with maleimide Disulfide bond formation Acylation of Amines His-Tag acylation Click conjugation (CuCAAC, SPAAC, IEDDA) Enzyme supported conjugation: HaloTag® CLIP-Tag™ SNAP-Tag® Sequence dependent conjugation (Sortase)			

