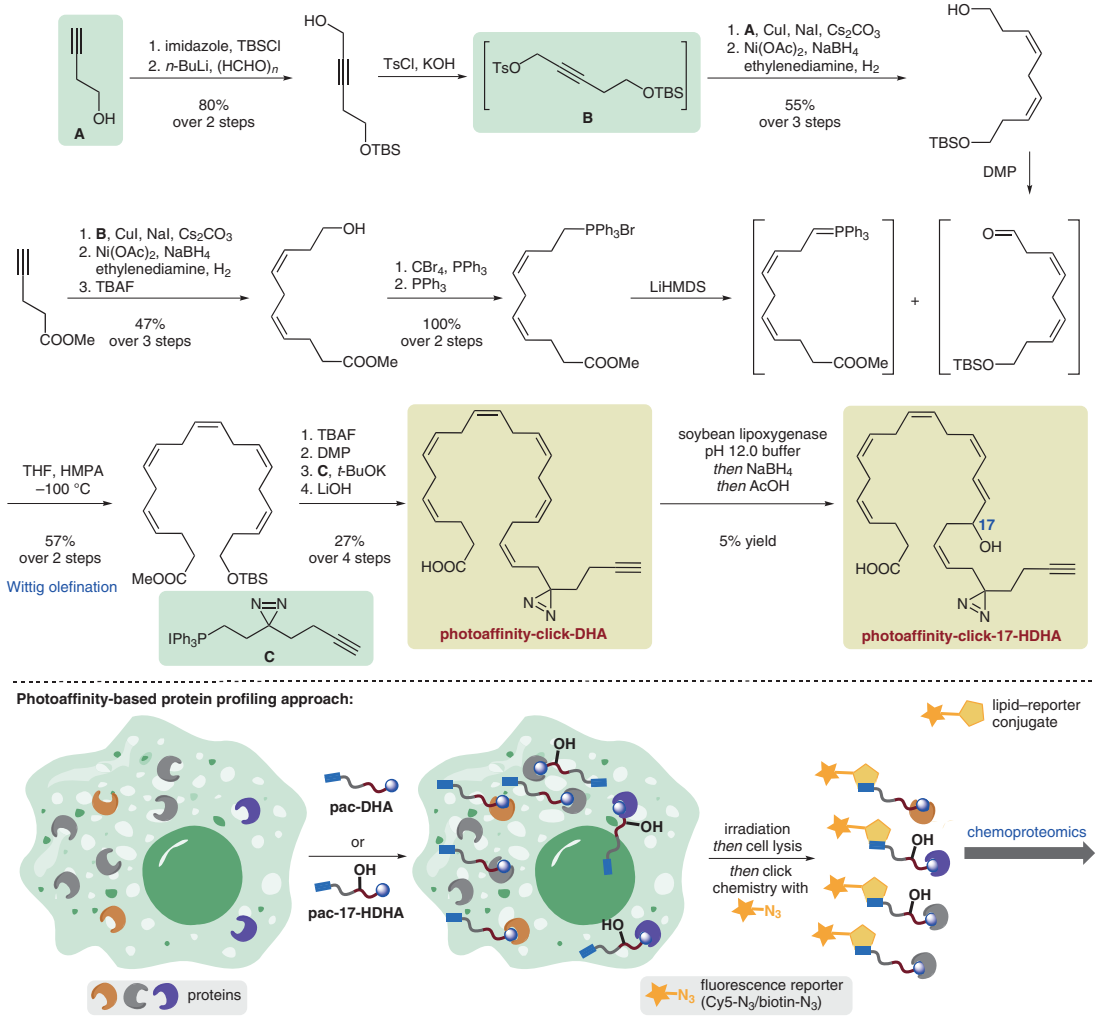
M. VAN DER STELT* ET AL. (LEIDEN UNIVERSITY AND ONCODE INSTITUTE, THE NETHERLANDS)

Comparative Photoaffinity Profiling of Omega-3 Signaling Lipid Probes Reveals Prostaglandin Reductase 1 as a Metabolic Hub in Human Macrophages

*J. Am. Chem. Soc.* **2022**, *144*, 18938–18947, DOI: 10.1021/jacs.2c06827.

# Photoaffinity Lipid Probes Decipher Docosahexanoic Acid Target




**Significance:** Docosahexanoic acid (DHA) is an omega-3-polyunsaturated fatty acid (PUFA) and an endogenous signaling lipid with anti-inflammatory properties. However, its biological mechanism in the resolution of inflammation is poorly understood. Here, the authors developed two bio-orthogonal photoaffinity-click (pac) probes, pac-DHA and its 17-hydroxy metabolite pac-17-HDHA, to identify their targets in human macrophages.

**Comment:** The authors synthesized the PUFAs using Wittig olefination as a key reaction. Photoaffinity-based protein profiling revealed prostaglandin reductase 1 as the lipid-binding partner, which metabolizes 17-oxo-DHA – a metabolite of 17-HDHA. The authors also found that 17-oxo-DHA reduces the formation of pro-inflammatory lipids in human macrophages and neutrophils.

**SYNFACTS Contributors:** Dirk Trauner, Tufan K. Mukhopadhyay
Synfacts 2023, 19(01), 0085 Published online: 16.12.2022
**DOI:** 10.1055/s-0042-1751775; **Reg-No.:** T00523SF



**Category**

Innovative Drug Discovery and Development

**Key words**

omega-3 fatty acids

bio-orthogonal lipid probes

Wittig olefination

Synfact of the Month