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ESR10 (BAS)

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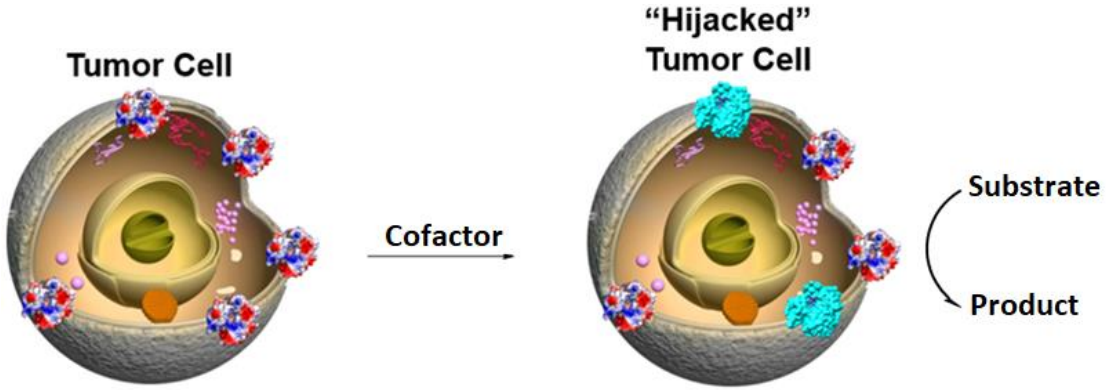
Meeting 2
Edinburgh, 3rd February 2020

Innovative Training Networks (ITN) – Marie Skłodowska-Curie Actions
H2020-MSCA-ITN-2017 (THERACAT-765497)

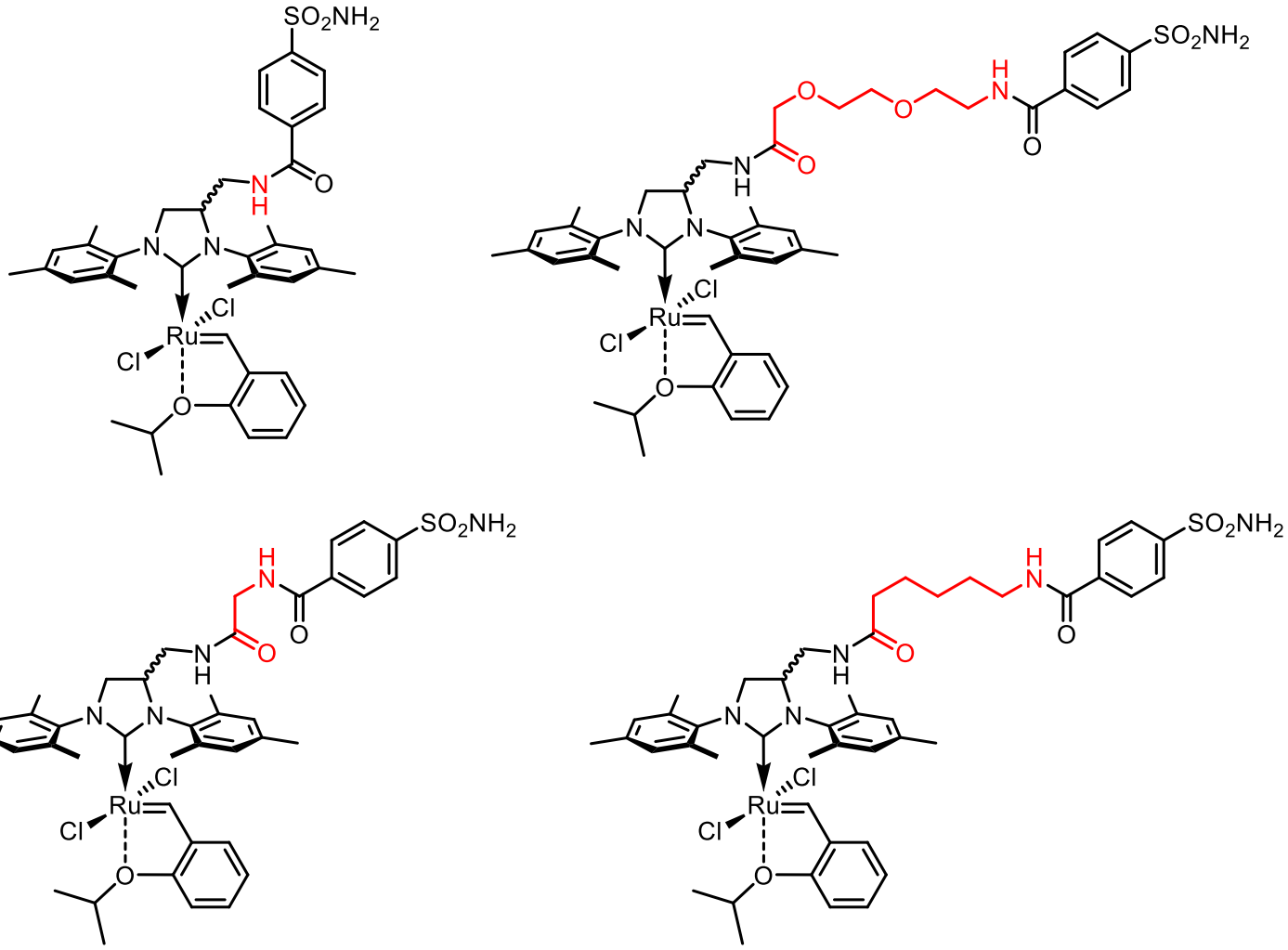
Due to the fact that cancer cells overexpress the enzymes, it was decided to synthesize specific cofactors for in vivo catalysis:




1. Identify metathesis catalyst activated upon binding to hCA IX.
2. Uncage cargo (fluorophore or drug) by ring-closing metathesis.
3. Fluorophore- and/or drug-release by ring-closing metathesis on the surface of cancer cell overexpressing hCA IX.
4. (Alternative approach) All of the above for other bioorthogonal reactions (e.g. deallylation).

# Results obtained (cofactors)

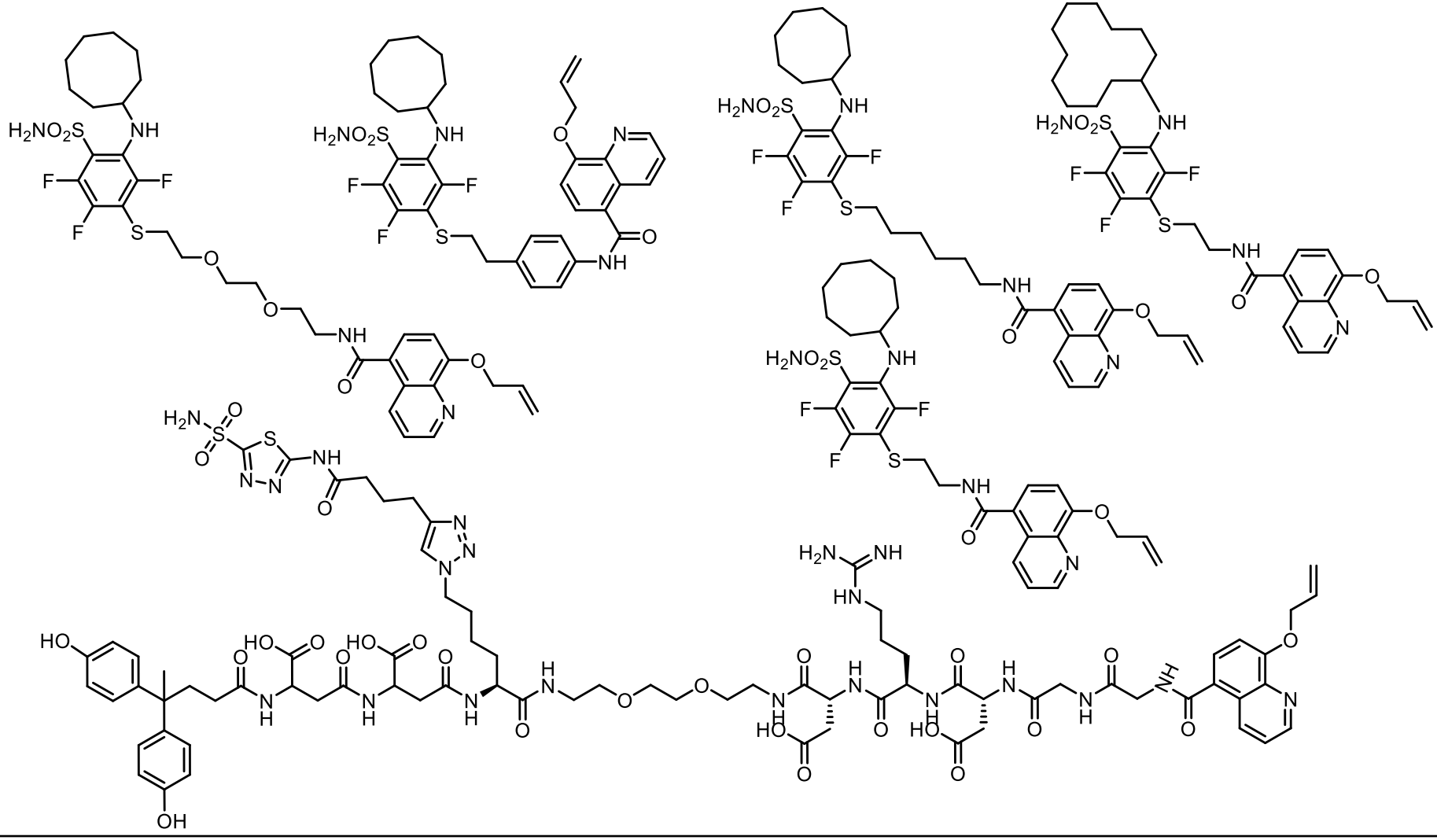
4 metathesis cofactors for hCAII/hCAIX for *in vivo* application were obtained:



# Results obtained (cofactors)



6 deallylation cofactors for hCAII/hCAIX for *in vivo* application were obtained:



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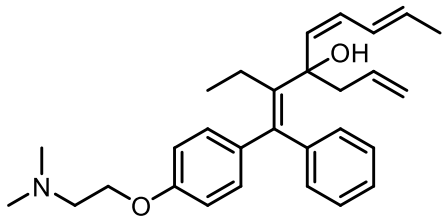
# Results obtained (substrates)



3 new prodrugs for release under metathesis conditions were synthesized.

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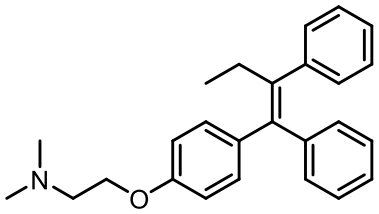
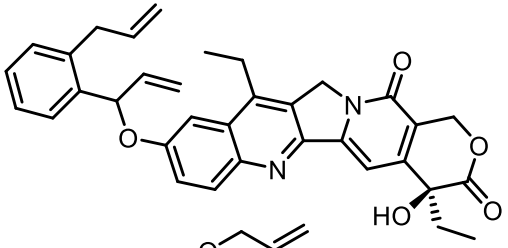



Tamoxifen (selective estrogen receptor modulator for breast cancer treatment)

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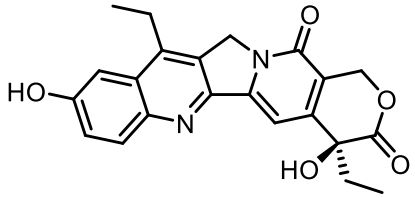
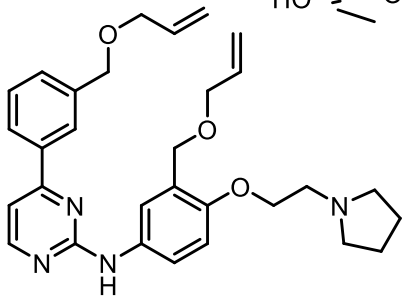



SN-38 (DNA topoisomerase inhibitor – colon cancer and small-cell carcinoma)

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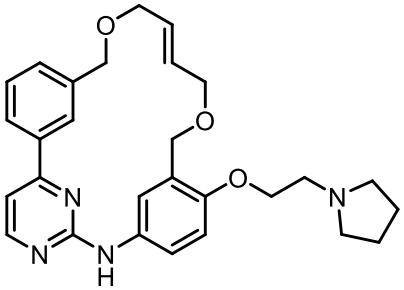
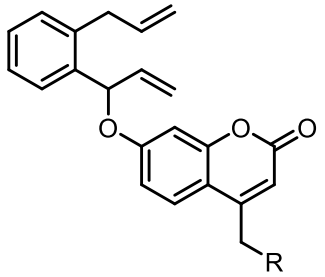



Pacritinib (Janus kinase inhibitor – in clinical trials)

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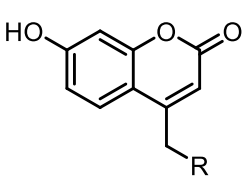


For initial tests on cells, a number of profluorophores with different polarity were obtained (R = -H, -COOH, $NMe_3Br$)

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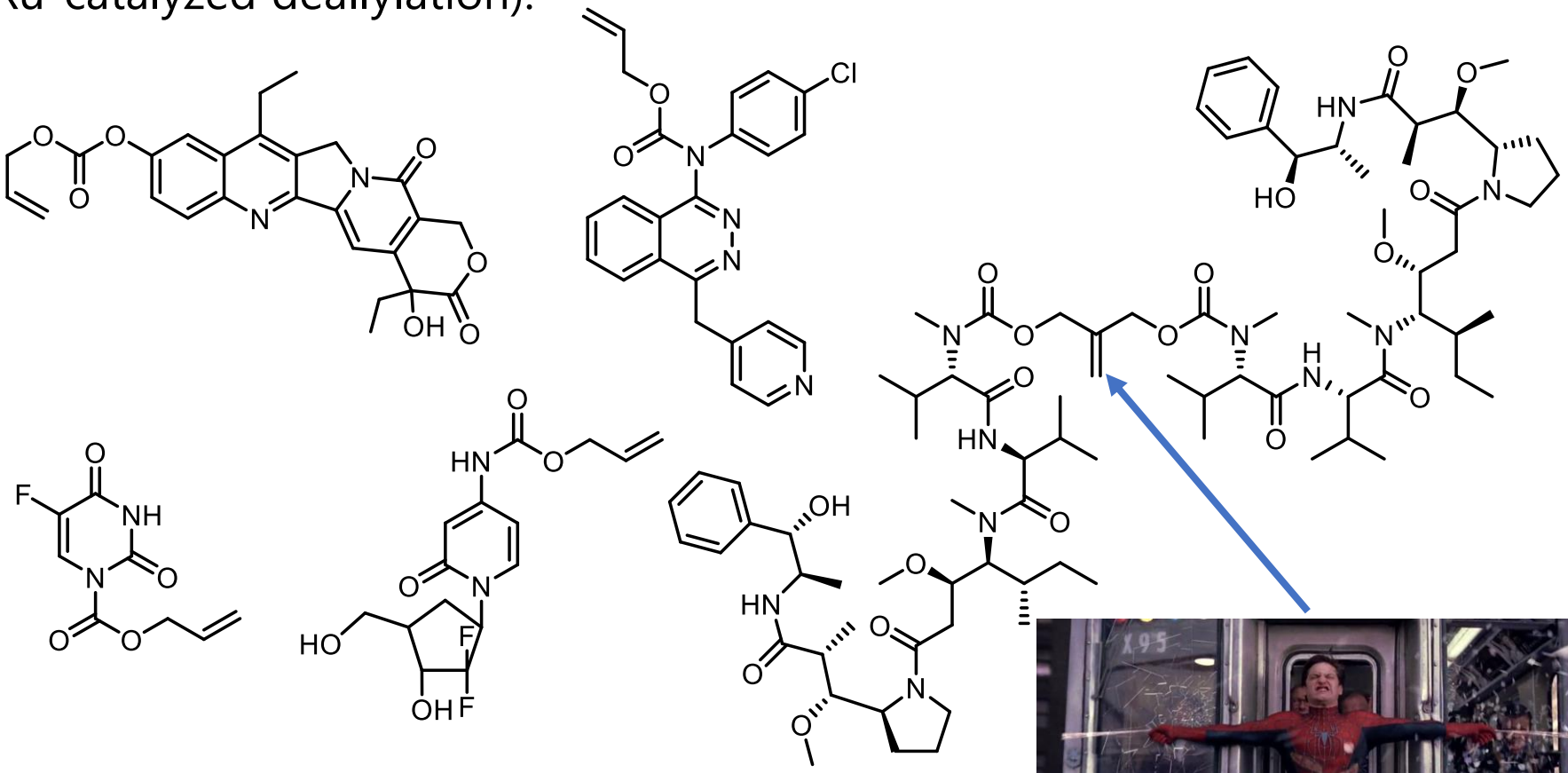
# Results obtained (substrates)

The following prodrugs were prepared for an alternative part of the project (Ru-catalyzed deallylation):



Courses:

- Current topics in organometallic and biomimetic chemistry (Sept – Dec 2019, UniBas)
- Organic Chemistry Research Seminar (Sept – Dec 2019, UniBas)

Trainings:

- "Writing to Be Published" (Oct 2019, UniBas)
- "Out of the Box! Visualize Your Science“ (Nov 2019, UniBas)

# Communication and dissemination



Talks:

- 2 Progress reports at research seminars
- Annual talk in the framework of the university program

Conferences:

- NCCR Molecular System Engineering Site Visit (poster session), Basel, Switzerland