

## De novo $sp^3$ carbon-carbon and carbon-heteroatom bond-forming reactions via catalytic functionalization of native functional groups



Timeline | 09/2022 to 08/2025



ICIQ People | [R. Martín Research Group](#)



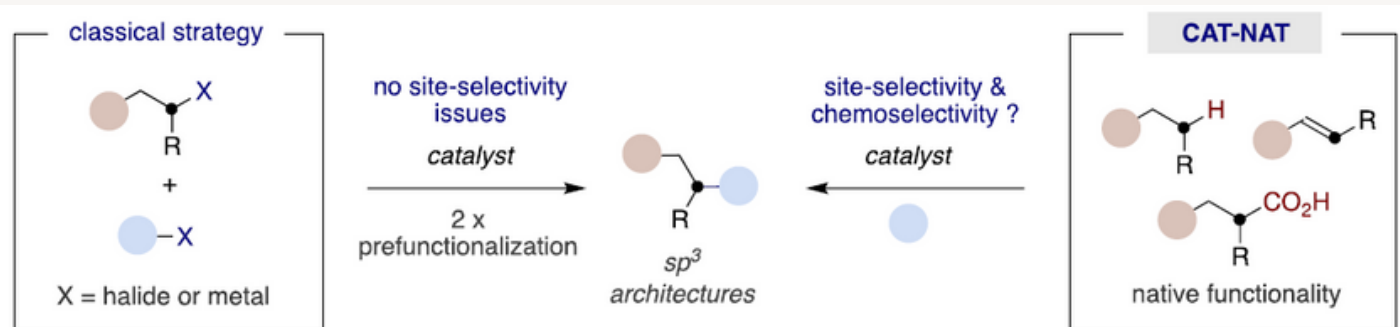
Budget | 387.200 €



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### SUMMARY

Although cross-coupling reactions have become one of the pillars of modern chemical synthesis, the ability to forge  $sp^3$  architectures from naturally-occurring entities or chemical feedstocks with improved flexibility, practicality, predictable site-selectivity, preparative utility and stereocontrol still remains a major challenge in catalytic endeavours. The successful realization of this goal will contribute to create new logics of organic synthesis when rapidly and reliably building up molecular architectures from simple precursors in both basic and applied research. This is particularly important when building up  $sp^3$  linkages in an efficient and catalytic manner, given that an increase of  $sp^3$  character in drug candidates improve several molecular attributes that ultimately contribute to clinical success, including solubility, molecular shape (3D-structure) or substrate recognition, among others. **CAT-NAT** offers a series of catalytic methodologies for forging  $sp^3$  linkages by harnessing native functional groups such as  $sp^3$  C-H bonds, aliphatic carboxylic acids, aliphatic alcohols, alpha olefins and CC bonds as adaptive handles for bond-construction, without losing sight the mechanistic implications of these processes. The multidisciplinary nature of the project is illustrated by the merger of organic synthesis, organometallic catalysis and light-induced processes for streamlining the synthesis of valuable structures in the drug discovery pipeline, even in the context of late-stage functionalization, such as carboxylic acids, nitrogen containing heterocycles or fluorinated molecules, among others. In addition, this project will also offer a new enabling technique for the catalytic valorization of  $N_2O$ , a greenhouse gas with much greater warming potential than  $CO_2$ , and its conversion to added-value chemicals. Preliminary results demonstrate the feasibility of many of the tasks delineated in **CAT-NAT**, constituting a valuable entry point for building up  $sp^3$  architectures in a tunable, controllable and general fashion. Given the prospective potential of the technologies included in this proposal, we expect that **CAT-NAT** will not only provide new dogmas in retrosynthetic analysis by fundamentally altering the way  $sp^3$  architectures are made, but also a *à la carte* technique that industrial and academic chemists can make use of when building up densely functionalized backbones from simple and available precursors.



Building up  $sp^3$  linkages by harnessing native functionality

