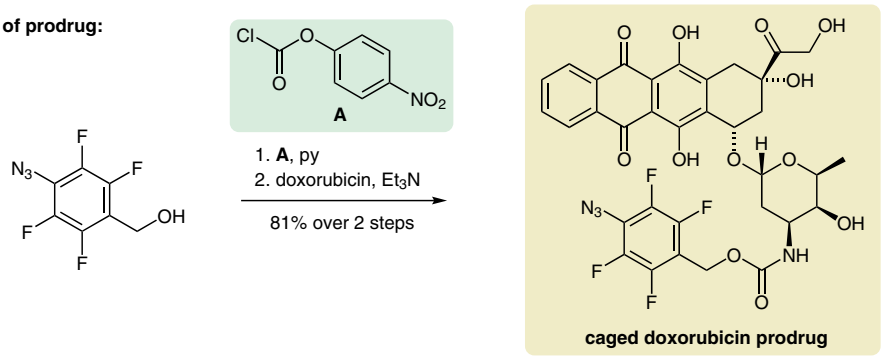
J. GENG*, Y. ZHANG, Q. GAO, K. NEUMANN, H. DONG, H. PORTER, M. POTTER, H. REN, D. ARGYLE, M. BRADLEY* (UNIVERSITY OF EDINBURGH, UK AND THE SHENZHEN INSTITUTE OF ADVANCED TECHNOLOGY, P. R. OF CHINA)

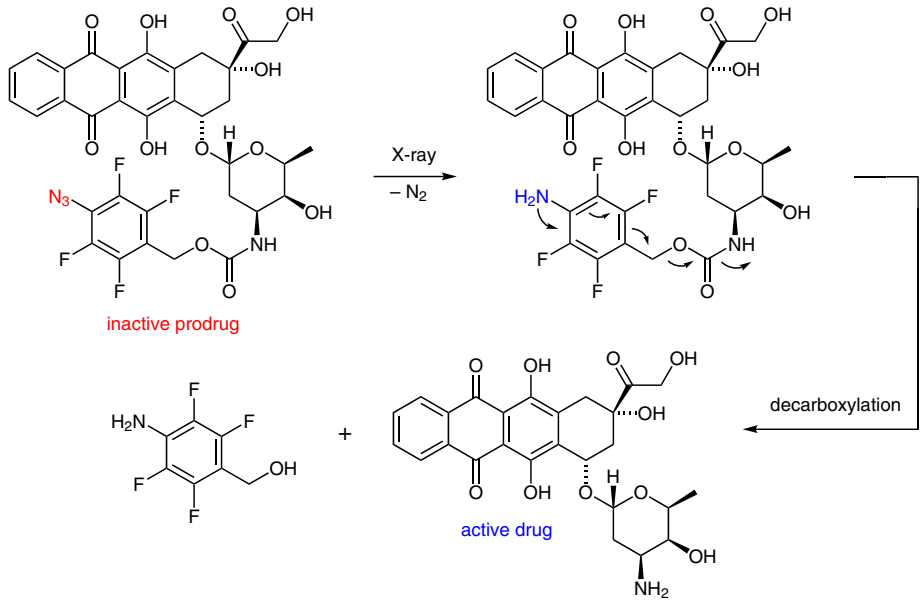
Switching on Prodrugs Using Radiotherapy
Nat. Chem. **2021**, *13*, 805–810, DOI: 10.1038/s41557-021-00711-4.

X-ray Irradiation Promoted Activation of Prodrugs

Synthesis of prodrug:



Prodrug activation by X-ray irradiation:



Significance: Activating an anticancer prodrug with clinical doses of ionizing radiation could enable localized release of a drug at the tumor site and potentially eliminate the global systemic toxicity of conventional chemo-radiotherapy. In a tumor-bearing mice model, the combination of caged prodrug and X-ray treatment not only inhibited tumor growth but also reduced doxorubicin-induced heart toxicity.

Comment: The caged doxorubicin prodrug was synthesized in two steps, by following a reported procedure (*Bioconjugate Chem.* **2018**, *29*, 324). Decaging of doxorubicin was achieved using X-ray irradiation (from 0 to 60 Gy) through radical reduction of the tetrafluorophenyl azide followed by 1,6-self-immolation linker cleavage.

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Synfact of the Month