Alternative synthetic approaches to biologically active indeno[1,2-*c*]isoquinoline-5,11-diones

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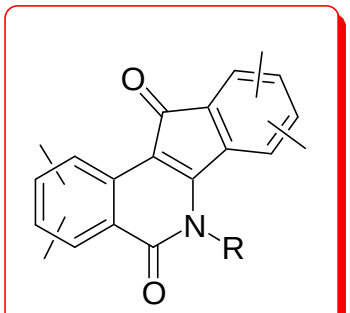
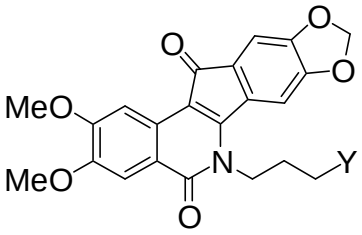
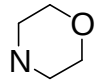
Indenoisoquinolinediones are a class of non-camptothecin topoisomerase I poisons that display marked cytotoxic properties and for some of them, potent antitumor activities in xenograft models. Indotecan and indimitecan have been demonstrated to inhibit topoisomerase I enzymes by intercalating between the DNA base pairs





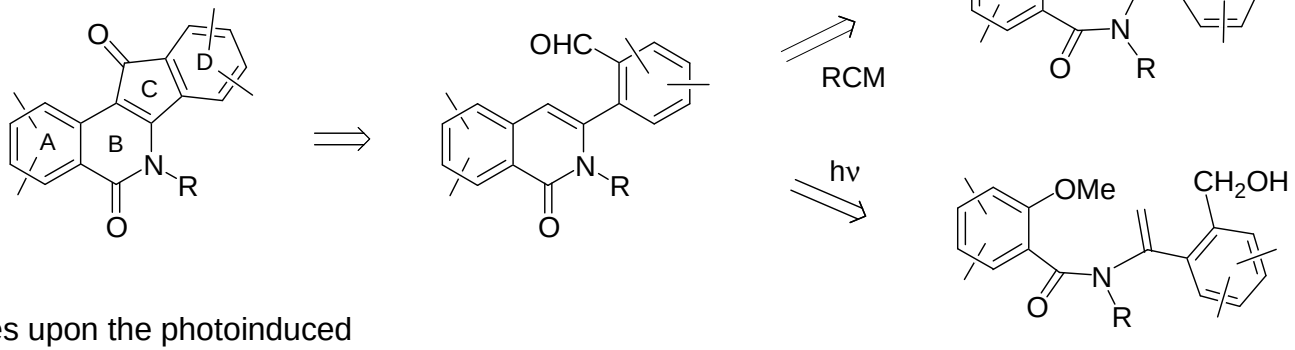
Indotecan (NCS 724998) Y = 

Indimitecan (NCS 725776) Y = 

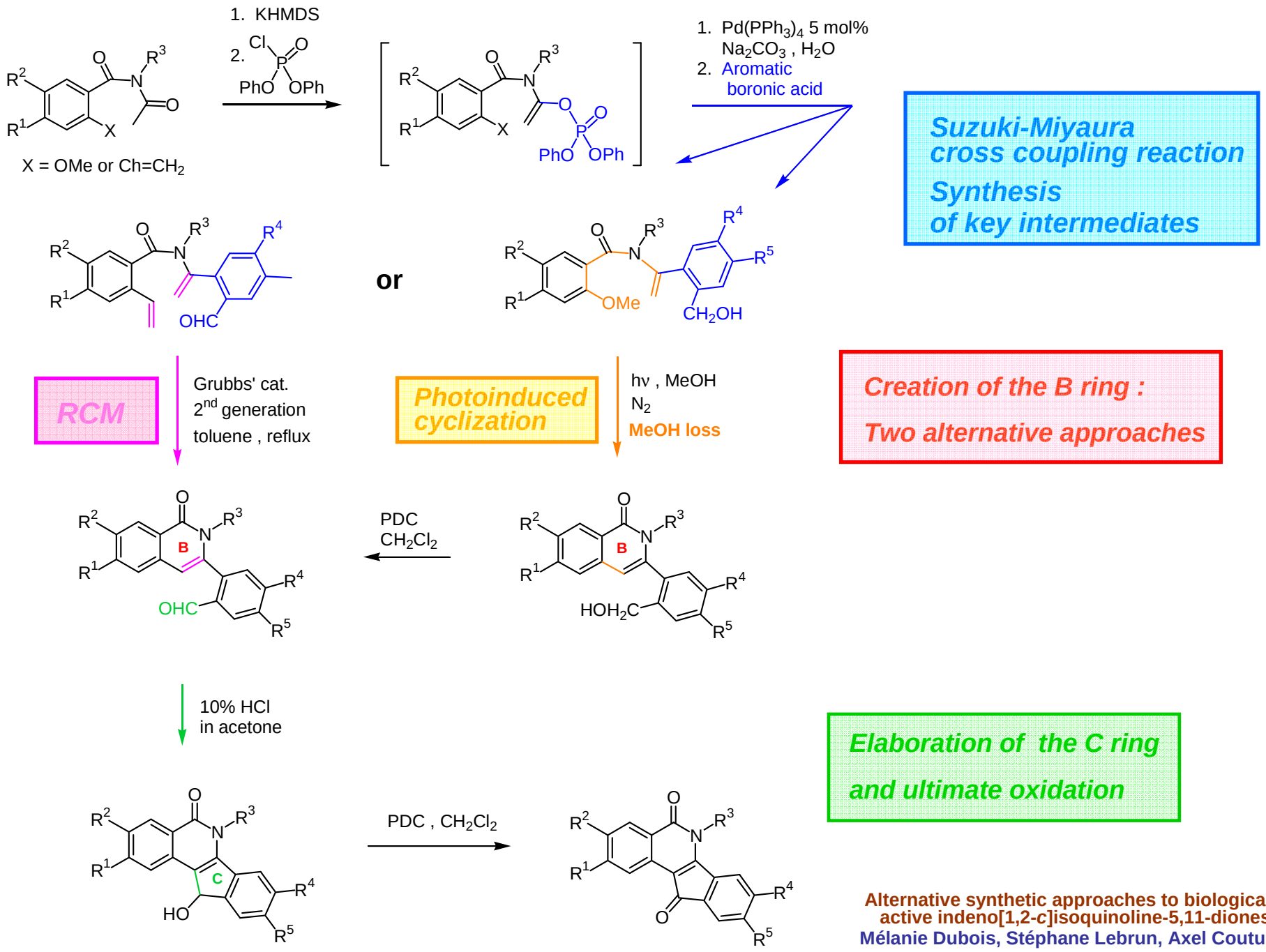
Retrosynthetic analysis

We have developed two alternative synthetic approaches:

•The first one is based upon the ring-closing metathesis (RCM) of styrenic enamides



* The second approach hinges upon the photoinduced cyclization of 6-π electron aromatic enamides



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