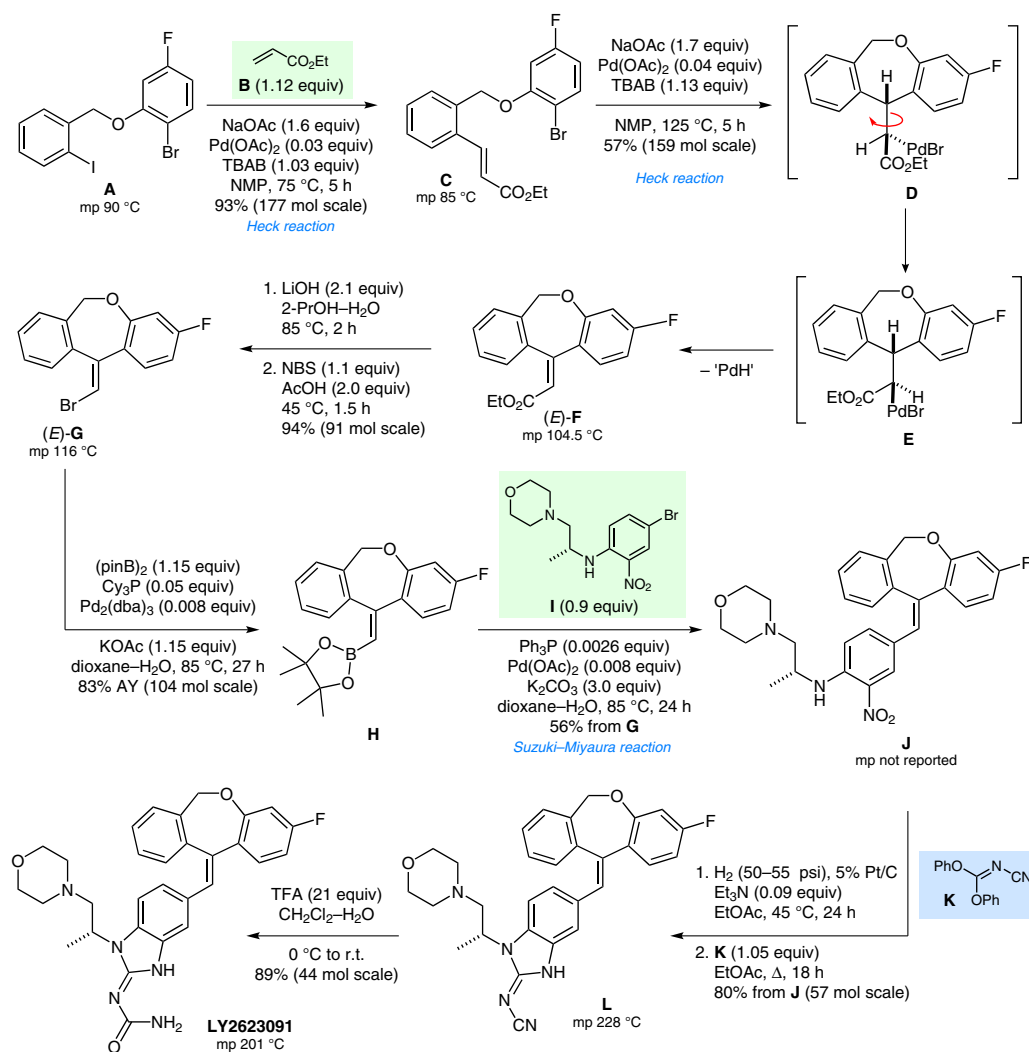


Synthesis of LY2623091



Significance: LY2623091 is a mineralocorticoid receptor antagonist that was of interest for the treatment of resistant hypertension. The kilogram-scale synthesis depicted features two sequential Heck reactions to construct the (E)-dihydrodibenzo[b,e]oxepine ring system. Note the clean retention of stereochemistry in the conversion of (E)-F into bromoalkene (E)-G.

Comment: An investigation of the conversion of **A** into (E)-F through a one-pot, double Heck reaction revealed that the first Heck reaction (**A** → **C**) was fast and occurred at 60 °C whereas the second Heck reaction [**C** → (E)-F] required a much higher temperature (145 °C) owing to iodide acting as a catalyst poison. Better yields and stereoselectivity were obtained in the two-pot process shown.