The use of proline derivatives, and related α-functionalized secondary amine organocatalysts, in organic reactions has received extensive consideration over the last two decades. [1]–[3] In this work, a novel primary β-amino amide structural framework was synthesised, generating a series of novel organocatalysts which were applied in the challenging ketone-ketone cross aldol reaction towards substituted oxindoles. Following a comprehensive study, the optimum catalyst 8 provided an enantioselective strategy for the synthesis of 3,3-disubstituted-2-oxindole derivatives’, a privileged scaffold possessing a potent anti-cancer, anti-HIV and other biological properties, [4] in up to 99% yield, 52% ee and >99% dr.

Direct infusion ESI-MS detection of intermediate species (MW 433.2 and MW 286.2), and a screen of structurally similar catalysts were used to propose the catalytic cycle of the optimum catalytic system in the aldol reaction of isatin 1 with ketone 2.