Significance: The first Brønsted acid catalyzed enantioselective indole aza-Claisen rearrangement for the generation of optically enriched 3-amino-2-substituted indoles is reported. An arene CH–O interaction is proposed to synergistically activate and stereo-induce as a second point of interaction (two-point interaction). Several allylic moieties are compatible with the reaction conditions. Electron-donating and -withdrawing groups did not affect the efficiency. Yet, aliphatic substituents significantly lowered the stereoselectivity. The obtained products can be transformed into the corresponding 3-aminooxindoles, which are substrates for the synthesis of many biologically active small molecules.

Comment: The proposed two-point interaction was modeled on a B3LYP/6-31G(d) level. CH–O and NH–O interactions organize the adduct in a way that one 9-anthracene unit blocks the si face of the substrate inducing the allyl shift on the re face leading to the observed enantiomer. Other interactions such as edge-to-face CH–π interaction between the R² group and the second 9-anthracene unit as well as CH–O interaction between the R² group and the phosphate are also proposed. A synthetic derivative confirmed the absolute configuration by X-ray crystallography to be in accordance with the calculations. The aza-Claisen rearrangement to obtain chiral indole alkaloids is currently under investigation.