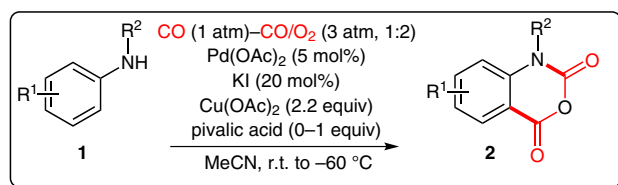
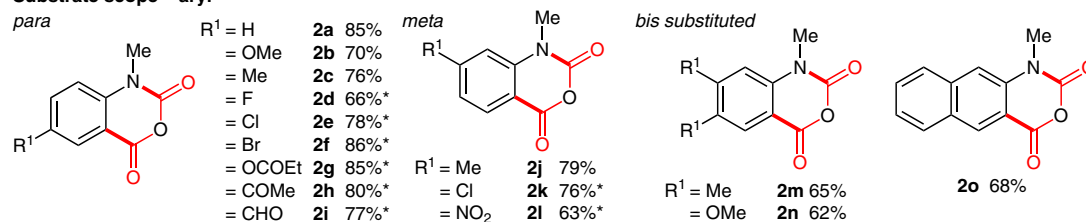


Isatoic Anhydrides via C–H Activation

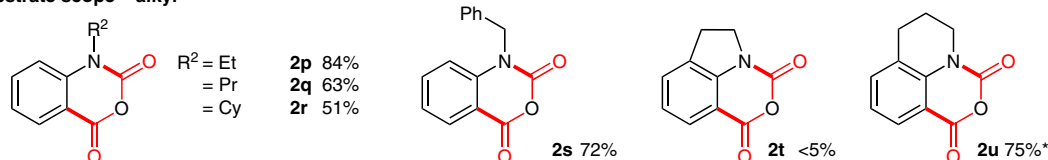


*Starred examples were run with pivalic acid (1 equiv):

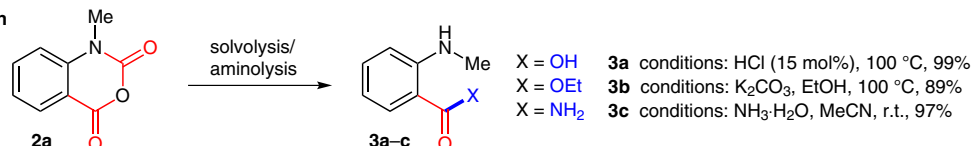
Substrate scope – aryl



Substrate scope – alkyl



Derivatization



Significance: Reported is the synthesis of isatoic anhydrides **2** via the carbonylation of substituted anilines **1** utilizing a C–H activation procedure. Optimization studies demonstrated the beneficial effects of potassium iodide and the importance of oxidant and solvent choice. A substrate-scope screen showed that electron-rich anilines were the most reactive (**2a–c**). However, electron-deficient anilines proved useful substrates with the addition of pivalic acid and increased pressure (**2d–i**). In the case of **2a**, a catalytic procedure [with respect to Cu(OAc)₂] using oxygen as the terminal oxidant was demonstrated, affording the desired isatoic anhydride in marginally reduced yield. Derivatization of **2a** to the *ortho*-amino acid **3a**, ester **3b**, and primary amide **3c** was reported.

Comment: Isatoic anhydrides are useful reagents for the preparation of anthranilic acid derivatives and various heterocycles alike (see Review below). Traditionally these heterocycles have been prepared via various multi-step sequences, for example from the anthranilic acids themselves (E. C. Wagner, M. F. Fegley *Org. Synth.* **1947**, *27*, 45) or via oxidation of phthalimides. The current report is attractive for several reasons, including circumventing the need for regioselective pre-functionalization and employing readily available anilines **2** as starting material.

Review: G. M. Coppola *Synthesis* **1980**, 505–536.