Z.-H. GUAN,\* M. CHEN, Z.-H. REN (NORTHWEST UNIVERSITY, XI'AN, P. R. OF CHINA) Palladium-Catalyzed Regioselective Carbonylation of C-H Bonds of N-Alkyl Anilines for Synthesis of Isatoic

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## Isatoic Anhydrides via C-H Activation

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

Substrate scope - aryl

Substrate scope – alkyl

Derivatization solvolvsis/ X = OH3a conditions: HCl (15 mol%), 100 °C, 99% aminolysis X = OEt**3b** conditions:  $K_2CO_3$ , EtOH, 100 °C, 89%  $X = NH_2$ 3c conditions: NH<sub>3</sub>·H<sub>2</sub>O, MeCN, r.t., 97% 3a-c

**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)<sub>2</sub>] 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.

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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 prefunctionalization and employing readily available anilines 2 as starting material.

Review: G. M. Coppola Synthesis 1980, 505-536.

Category

Synthesis of **Heterocycles** 

**Key words** 

carbonylation palladium aniline C-H activation

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