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### AN IMPROVED METHOD FOR THE SELECTIVE HYDROLYSIS OF 1-ACETYL-5-BROMO-4-CHLOROINDOXYL ACETATE TO 1-ACETYL-5-BROMO-4-CHLOROINDOXYL

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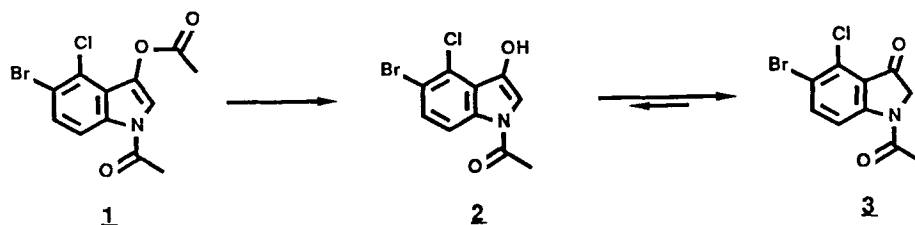
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AN IMPROVED METHOD FOR THE SELECTIVE HYDROLYSIS OF  
 1-ACETYL-5-BROMO-4-CHLOROINDOXYL ACETATE TO  
 1-ACETYL-5-BROMO-4-CHLOROINDOXYL

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Derivatives of 5-bromo-4-chloroindoxyl have been found to be especially useful as staining indicators.<sup>1</sup> Commercially available 1-acetyl-5-bromo-4-chloroindoxyl acetate (1)<sup>2</sup> is hydrolyzed to 1-acetyl-5-bromo-4-chloroindoxyl (2), and is then derivatized to the appropriate substrate.



Literature procedures for this hydrolysis include the use of refluxing aqueous ethanol in the presence of sodium sulfite<sup>3</sup> and sodium in methanol.<sup>4</sup> The efficiency of the latter method is low (56% yield). The production of large amounts of blue dye via the former procedure, even when run under a nitrogen atmosphere, led to the development of the present procedure which affords high yields of 2 with minimal production of dye. Replacement of sodium sulfite with the more powerful anti-oxidant sodium hydrosulfite inhibits dye formation, and the use of one equivalent of sodium bicarbonate induces rapid hydrolysis. Excess sodium bicarbonate catalyzes indigo production and should be avoided.

## EXPERIMENTAL SECTION

1-Acetyl-5-bromo-4-chloroindoxyl (3).- A mixture of 3.51 g (10 mmol) of 1, 0.84 g (10 mmol) of sodium bicarbonate, and 3.50 g (20 mmol) of sodium hydrosulfite in 200 ml each of ethanol and water under a nitrogen atmosphere was heated at reflux until TLC monitoring indicated the reaction was complete (<15 min). Upon cooling and the addition of 100 ml of water, 3 was collected and washed with water. After drying in vacuo, 2.88 g (87%) of dull white to pale blue-green tinted solid was obtained. MS(FD): M+ 287/289

Anal. Calcd. for C<sub>10</sub>H<sub>7</sub>BrClNO<sub>2</sub>: C,41.63; H,2.45; Br,27.69; Cl,12.29; N,4.85  
Found: C,41.87; H,2.53; Br,27.66; Cl,12.33; N,4.86

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