

ISATOGENS VIII: THE REACTION OF 2(2-PYRIDYL)ISATOGEN WITH LEUCINE AND VALINE

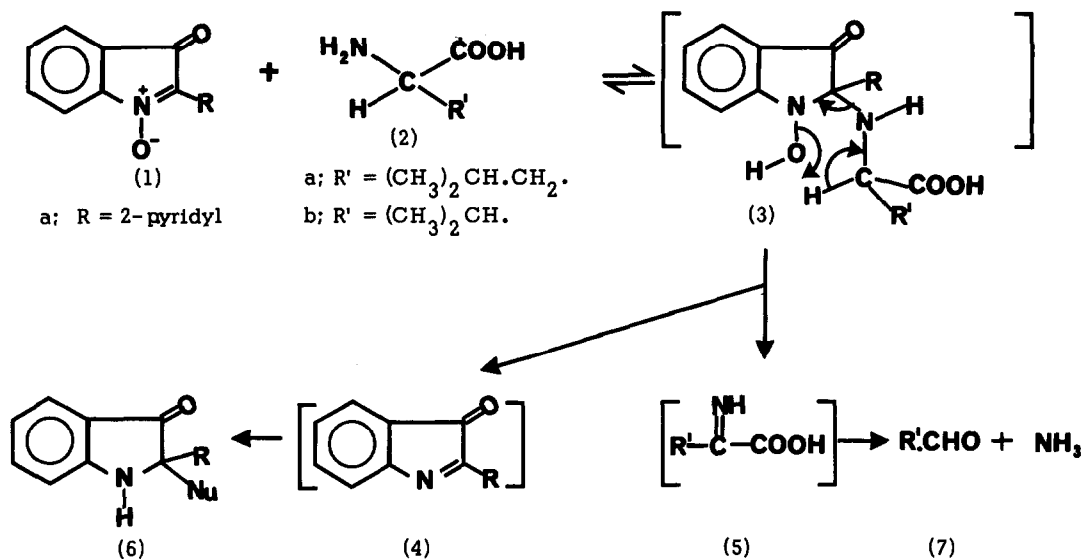
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In the search for a possible chemical basis for the biological activity of isatogens it has already been shown that isatogens (1) readily undergo nucleophilic attack, and are also oxidising agents comparable with the naturally occurring quinones.<sup>1,2</sup> We now report the initial results of our study of the reaction between 2(2-pyridyl)isatogen (1a) and the  $\alpha$ -amino acids leucine (2a) and valine (2b). Our results indicate that isatogens, like ninhydrin<sup>3a</sup> and isatin,<sup>3b</sup> oxidatively deaminate and decarboxylate  $\alpha$ -amino acids giving aldehydes (7) and isatogen reduction products (6). The neutral form of the amino acid<sup>4</sup> functions as a weak nucleophile attacking the isatogen at the 2-position. The intermediate transition complex (3) has not been isolated but is analogous to the isolable adduct formed when 2(2-pyridyl)isatogen reacts with piperidine.<sup>5</sup> The intermediate complex can readily break down by a 6-centre rearrangement to 2(2-pyridyl)indolone (4) and an  $\alpha$ -imino carboxylic acid (5). The indolone rapidly forms the labile ethanol and water adducts (6; Nu = OEt, OH)<sup>6</sup>, whilst the unstable imino acid undergoes hydrolysis and decarboxylation to the aldehyde (7a or 7b). The transfer of oxygen from an N-oxide nitrogen atom under these conditions has not previously been reported although Russell<sup>7</sup> has reported a similar oxygen transfer from a nitro group.

In these reactions equimolar amounts of the isatogen (1a) and the L- $\alpha$ -amino acid in 50% aqueous ethanol were heated under reflux. The reactions were followed by t.l.c., after 10 min. both isatogen and amino acid were shown to be absent. The following amounts of products were recovered; indolone adducts (6), 90%, aldehydes (7), 86% (g.l.c.), ammonia, 70% (titrimetry).



Other  $\alpha$ -amino acids also reacted with the isotropin (1a) under these conditions but the reactions were usually slower, isoleucine (10 mins.), alanine (15 mins), phenylalanine and histidine (30 mins.), glycine and tryptophan (60-70 mins). All these reactions gave indolone adducts (t.l.c.) and ammonia usually accompanied by tarry or oily products. These and related reactions are being studied in more detail and the results will be reported at a later date. Neither N-acetyl leucine nor proline reacted with the isotropin even after several hours, indicating that a nucleophilic amino group is essential for the reaction and that steric factors are important in the reaction.

#### References.

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