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[A006]

Novel synthesis of 6-chloroindoxyl-1,3-diacetate (Salmon)

Alexander Balbuzano-Deus[1], Juan C. Rodríguez-Domínguez[1],*, Anais Fernández Villalobo[1]
Miguel López-López[1] and Gilbert Kirsch[2],**

1. Departamento de Química, Centro de Química Farmacéutica, Calle 200 y 21, Atabey, Playa, CP: 11600, Ciudad de la Habana, Cuba. *E-mail: jcrdchem@yahoo.com

2. Laboratoire d´Ingénierie Moléculaire et Biochimie Pharmacologique, 1, Boulevard Arago, 57070, Metz, France. **E-mail: kirsch@sciences.univ-metz.fr

Nowadays the chromogenic substrates are very used for the quality control of different products such as water and food among others. These type of compounds are present as a component of some diagnostic media and allow to carry out the identification of different harmful bacteria. The enzimes excreted by the bacteries produce the *lisis* of the glycosidic linkage of the substrate showing a blue or magenta coloration [1]. One of these bacteria is the *E. Coli* that is identified by the 6-chloro-3-indolyl-b-D-glucuronide cyclohexylamine salt (**Fig.1**), among others[2,3], which present an indolic moiety as the aglycon part.

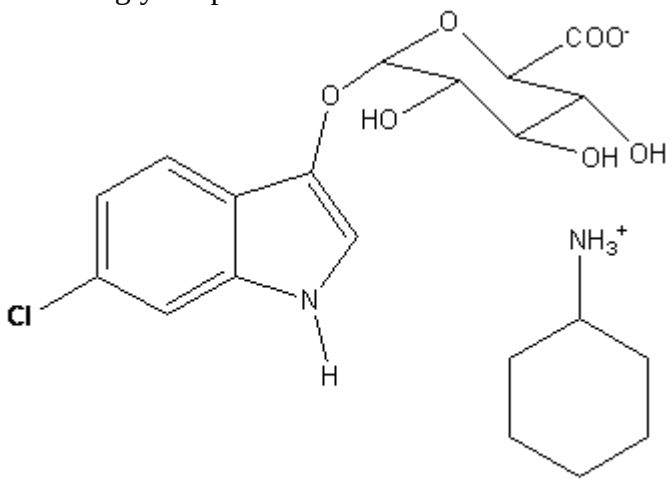
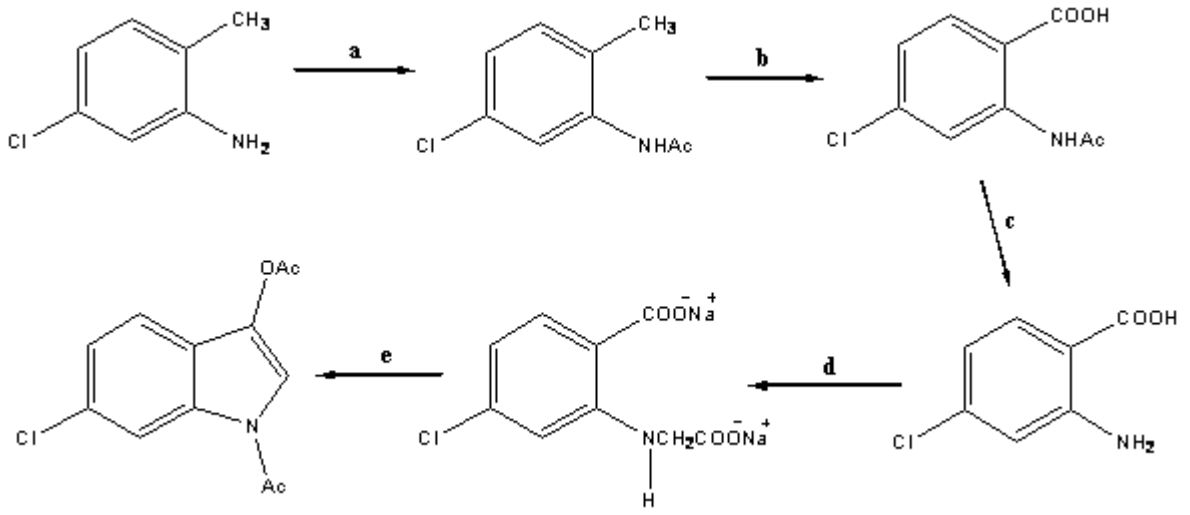


Fig.1
6-chloro-3-indolyl-β-D-glucuronide cyclohexylamine salt

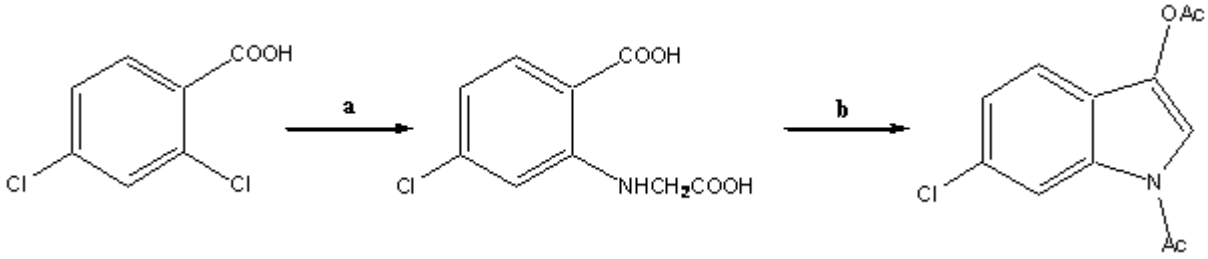
The indolic part of the chromogenic substrate has to be prepared by chemical synthesis and the more stable and commonly employed derivative is 6-chloroindoxyl -1,3- diacetate (Salmon) synthesized by Roth and Ferguson[3] from the commercially available 5-chloro-2-methyl aniline according to the **Scheme 1**.

This procedure involves five steps of synthesis. A long time of reaction is required for the amino-alkylation, and the overall yield of the diacetate is 12%.



Scheme 1

a) Ac_2O, AcOH, smooth reflux, 0.5 h; **b)** $KMnO_4$, 80-85^oC, 1.5 h; **c)** HCl, 80^oC, 8 h- NaOAc, 58.3% (two steps); **d)** $ClCH_2COONa$, 60^oC, 72 h, 43%; **e)** Ac_2O, NaOAc, reflux and after 5^oC for 24h, 47.6%.



Scheme 2

a) H_2NCH_2COOH, Cu, K_2CO_3, DMF, 1h reflux, 82%; **b)** Ac_2O, NaOAc, reflux and after 5^oC for 24 h, 61.5%.

We have developed a new, very short procedure **(Scheme 2)** to access to the 6-chloroindoxyl-1,3-diacetate in only two steps. Shortening of the reaction time and decreasing the number of steps, enhanced the overall yield to about 50 %. Every step of the process was carried out with reproducible results and a very good purity of the intermediate and the final product.

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