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## A NEW ONE STEP PREPARATION OF PICROPODOPHYLLONE FROM PODOPHYLLOTOXIN

C. ANJANA MURTHY AND K. M. LOKANATHA RAI  
Department of Chemistry, University of Mysore,  
Manasa Gangotri, Mysore 570 006 India.

DURING our studies on the synthesis of analogues of podophyllotoxin (I), a lignan antitumor<sup>1,2</sup> and cytotoxic spindle poison<sup>3</sup>, we required picropodophyllone (II), a cis ketolactone, an isomer of the trans ketolactone, podophyllotoxone (III). The known method of preparing picropodophyllone (II) is a two-step process, the first by isomerizing podophyllotoxin I by bases to the picropodophyllin<sup>4</sup> (IV) and then oxidiz-

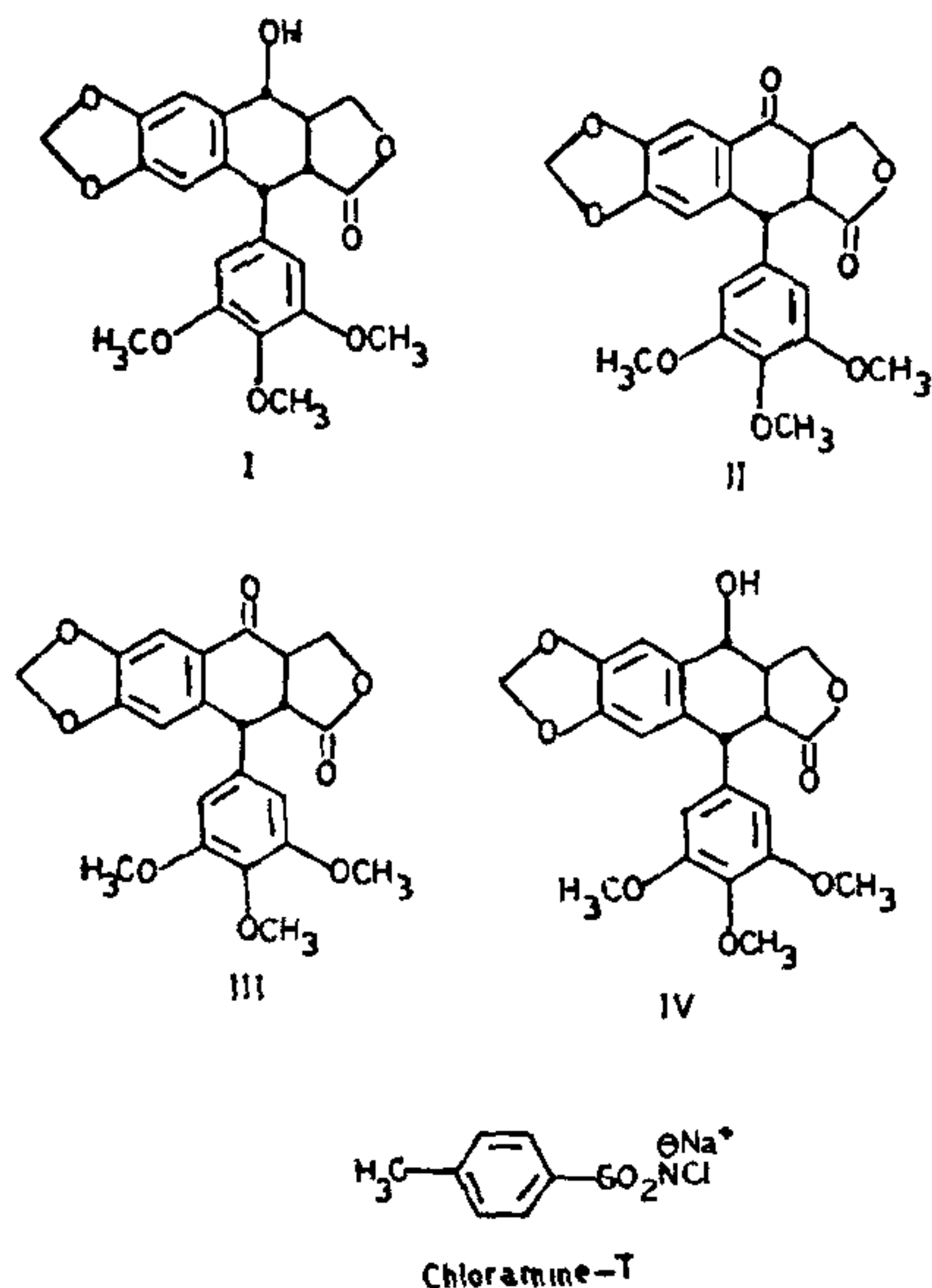
ing the hydroxy lactone (IV) to the ketolactone (II) by manganese dioxide<sup>5</sup>. Though the yield in first step is very good, it was very low in the second step.

We had earlier<sup>6</sup> used successfully, chloramine-T (trihydrate) in nonaqueous medium such as dimethyl sulphoxide and dioxan to oxidize some benzylic alcohols such as benzyl alcohol, benzoin, and furoin and therefore we considered utilizing both the base properties and the oxidizing ability of chloramine-T, to convert the podophyllotoxin (I) to picropodophyllone (II). We report here the successful conversion of podophyllotoxin to picropodophyllone with a very much improved yield of the desired product in a single step, using DMSO as nonaqueous medium.

The product obtained in the above reaction was identical with the product obtained by the two-step synthesis in mp<sup>5</sup>; COTLC in 5 different solvent systems and products showed no change in mixed m.p.

In a typical experiment a mixture of podophyllotoxin (I) (0.5 g) and chloramine-T trihydrate (1 g) was kept stirred in dry DMSO (50 ml) at 60-65°C for 30 hr. The reaction mixture was diluted with water (Ca 100 ml) and then with 10% NaOH (Ca 50 ml) and stirred well and extracted into ether. The ether layer was successively washed with water and dried over sodium sulphate. The solid residue obtained after evaporation of ether was purified by column chromatography using chloroform: acetone (7:1) yield of the product: (0.27, 54%); mp 151-152°C (lit<sup>5</sup> mp 153-154°C).

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