## AN APPROACH TO THE SYNTHESIS OF PSEUDOMONIC ACIDS

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<u>Abstract</u>:- The synthesis of the cis-fused  $\gamma$ -lactone 2,7-dioxabicyclo-[4,3,0] non-4-en-8-one (3) by two routes is reported. Its stereoselective conversion to a key intermediate for pseudomonic acid synthesis is described.

Interest in the antibiotic activity of the pseudomonic acids<sup>1</sup> (e.g. acid A; 1) has prompted considerable interest in the synthesis of this group of bacterial metabolites.<sup>2</sup> In a recent communication<sup>3</sup> the use of the lactone (2) was envisaged and the viability of the proposed Claisen transposition and further elaboration was verified on a model carbocyclic analogue. This work prompts us to report our results employing the isomeric lactone (3) which was synthesised by the following two routes.

Treatment of the hydroxylactone<sup>4</sup> (4) with lithiotetrahydropyranyloxypropyne gave, after lactonisation of the initially-formed hydroxyacid, the acetylenic lactone (5; 51%). Partial catalytic hydrogenation (Lindlar) gave the corresponding (Z,Z)-diene (95%) treatment of which in methanol with Amberlite IR-120 gave the hydroxydienelactone (6; 91%). Intramolecular acid-catalysed Michael addition using methanesulphonic acid then gave the required

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cis-fused lactone (3; 48%) m.p.  $71 - 72^{\circ}$ , together with the triene dehydration product (7).



In a second route from the readily-available dihydropyran, reaction with phenylselenenyl chloride in aqueous triethylamine/ tetrahydrofuran gave the adduct (8; 70%). This was converted by a Wittig reaction into the conjugated hydroxyester (9) which was cyclised by methanolic sodium methoxide to the pyran (10; 80% overall). Conversion to the selenoxide (ozone)<sup>5</sup> and elimination led to an ester which was hydrolysed (0.15M KOH/MeOH/H<sub>2</sub>O) to the corresponding acid (11; 81% overall). Phenylselenolactonisation (PhSePF<sub>6</sub>/CH<sub>2</sub>Cl<sub>2</sub>)<sup>6</sup> produced the lactone (12; 77%) oxidation of which with hydrogen peroxide and consequent elimination then led to lactone (3) identical with that obtained as above.

Reaction of this lactone (3) with dimethyl sodiomalonate in tetrahydrofuran in the presence of  $Pd(Ph_3P)_4$  effected stereoselective  $S_N 2'$  transposition<sup>7</sup> with the production of the required cis-disubstituted acid (13; 80%). Further elaboration of this intermediate is now in train.





Confirmatory analytical and spectroscopic data were obtained for all the above new compounds.

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