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Towards the Total Synthesis of Clerodin. Part II.

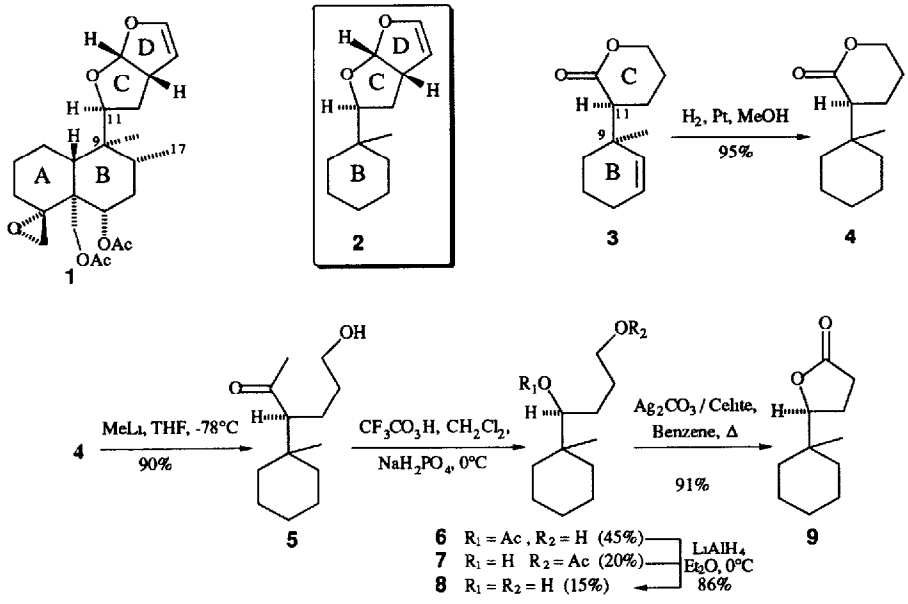
H. Bouchard, J. Soulié and J.Y. Lallemand*.

Laboratoire de Synthèse Organique, Ecole Polytechnique,
91128 Palaiseau, France

Key Words clerodin, Antifeedant, Claisen rearrangement, furo-furan, orthoester

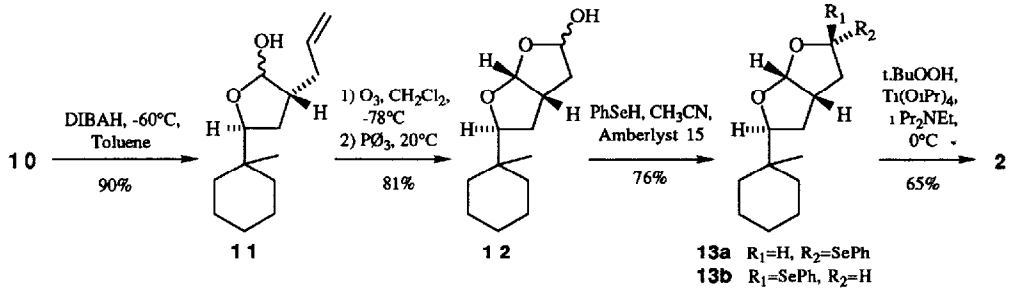
Abstract *In a model study aimed at the total synthesis of clerodin* **1**, *the tricyclic furo-furan moiety* **2** *was prepared This approach was based on a stereoselective Claisen rearrangement between a cyclohexenol and a cyclic orthoester*

Many natural compounds related to the general structure of clerodin **1** display interesting antifeedant activities against various insects and larvae [1] In an approach [2] towards the total synthesis of **1**, we designed a strategy consisting of the early construction of the C-9/C-11 bond via a Claisen rearrangement [3] With this aim in mind, we present here a convenient access to the furo-furan model **2** [4], compatible with our strategy



The starting material was compound **3**, a key intermediate in our approach towards clerodin synthesis [5] (preceeding paper) Transformation of this lactone into the furo-furan system was studied with hydrogenated compound **4** Opening of the lactone **4** with MeLi provided the methyl-ketone derivative **5** Introduction of the required oxygen atom at C-11 was achieved through a Baeyer-Villiger oxidation, reaction of methyl-ketone **5**

with trifluoroperacetic acid giving, along with starting material **5** (8%), the secondary acetate **6** (45%), the primary acetate **7** (20%) and the diol **8** (15%) Other peracids were tried (mCpBA, perbenzoic acid and peracetic acid under various conditions) however these failed to react with the rather hindered ketone **5** Reduction of the crude mixture ($LiAlH_4$, ether, 86%) gave diol **8** which was selectively converted into the γ-lactone **9** with Fétizon's reagent [6] Compound **9** was then alkylated (LDA, HMPA-THF, -78°C) with allyl bromide to give lactone **10** which was smoothly reduced (DIBAH, -60°C) to the lactol **11** Following the procedure of Ley *et al* [7], ozonolysis of the terminal olefin in **11** and treatment with excess triphenylphosphine provided the bicyclic lactols **12** as an inseparable mixture



Final conversion of lactol **12** into the desired furo-furan model was then completed in two steps Phenyl selenylation of the lactol led to the separable selenyl derivatives **13a** and **13b** (ratio 2 1), which underwent an oxidation-elimination step to afford model **2** [8] As we reported earlier [9], Ley's strategy, using the oxidation of the corresponding phenylsulphide lactol, gave only poor yields in this case

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References and Notes .

1 T A Van Beek and Ae de Groot,*Recl Trav Chim Pays-Bas*, **1986**, *105* , 513

2 H Bouchard and J Y Lallemand,*Tetrahedron Lett* , **1990**, *31* , 5151

3 This general approach has been discussed in the preceeding paper

4 All new compounds were fully characterized by their IR, ^1H NMR, ^{13}C NMR and MS

5 Compound **3** ^1H NMR (200 MHz, $CDCl_3$, ppm) 1 15 (s, 3H), 1 48-2 05 (m, 10H), 2 40 (dd, J = 7 8 and 11 4 Hz, 1 H), 4 20 (m, 2H), 5 59(m, 2H), ^{13}C NMR (50 3 MHz, $CDCl_3$, ppm) 18 6, 20 9, 22 3, 24 3, 24 6, 30 9, 36 7, 48 1, 67 5,125 8, 135 0, 172 3

6 M Fétizon, M Golfier and J-M Louis, *Tetrahedron* , **1975**, *31*, 171

7 S V Ley, D Santafianos, W M Blaney and M S J Simmonds, *Tetrahedron Lett* , **1988**, *29* , 2179

8 Compound **2** ^1H NMR (200 MHz, $CDCl_3$, ppm) 0 87 (s, 3H), 1 06-1 61 (m, 11H), 1 77 (dd, J = 8 3 and 11 2 Hz, 1H), 3 50 (bt, J = 6 4 Hz, 1H), 3 78 (dd, J = 4 9 and 10 9 Hz, 1H), 4 80 (t, J = 2 6 Hz, 1H), 6 04 (d, J = 6 1 Hz, 1H), 6 43 (bt, J = 2 4 Hz, 1H), ^{13}C NMR (50 3 MHz, $CDCl_3$, ppm) 18 6, 21 6 (2), 26 4, 31 2, 34 1, 34 7, 35 0, 46 2, 86 3, 102 4, 109 0, 146 1,

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