## Synthesis of a Nor-Neolignan from Krameria Ramosissima

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**Abstract**: The synthesis of the norneolignan  $\underline{2}$ , isolated from *Krameria ramosissima*, is described. It proceeds in seven steps from *trans*-anethol in an overall yield of 14%. The key step involves arylation of the benzofuranone  $\underline{5}$  by 2.4,6-trimethoxyphenyllead triacetate  $\underline{8}$ .

2-Arylbenzofurans of type  $\mathbf{1}$  are mostly found in two taxonomically different families, the Leguminosae and the Krameriaceae. Their biological activities, particularly of some of them as phytoalexins, has prompted interest in their synthesis. Of the reported syntheses<sup>1</sup> only one, involving copper (I) acetylide substitution of an *ortho*-iodophenol, is a relatively general method<sup>2</sup>. We recently reported<sup>3</sup> that 2-aryl-3(2H)-benzofuranones can be produced in good to high yields from 3(2H)-benzofuranones by *C*-arylation using aryllead(IV) triacetates<sup>4</sup> 2-Aryl -3(2H)-benzofuranones are seen as precursors to the 2-arylbenzofurans  $\mathbf{1}$ .



In this letter we describe the total synthesis of the naturally occuring nor-neolignan  $\underline{2}$ , recently isolated from the roots of a Mexican shrub, *Krameria ramosissima*, which are used to make medicinal tea effective against diarrhoea and mild fevers. This shrub is the source of a range of 2-arylbenzofurans<sup>5</sup>, one of which is 2-(2,4,6-trimethoxyphenyl)-5-(E)-propenylbenzofuran  $\underline{2}$  that we have now synthesised in 14% overall yield from *trans*-anethole  $\underline{3}$ .

5-(E)-Propenyl-3(2H)-benzofuranone  $\underline{4}$  (m.p. 113-115 °C) was produced in 60% yield by Friedel-Crafts acylation of *trans*-anethole followed by base-catalysed cyclisation. Reaction of the lithium anion of  $\underline{4}$  with allyl cyanoformate at -78 °C gave the  $\beta$ -keto-ester  $\underline{5}$  (60%, m.p. 116-117.5 °C). Arylation of  $\underline{5}$  was carried out under the previously described conditions<sup>3</sup> using 2,4,6-trimethoxyphenyllead triacetate  $\underline{8}$  to give the arylated product  $\underline{6}$ (85%, m.p. 114 -116 °C). Deallyloxycarbonylation of  $\underline{6}$  using Tsuji's palladium-catalysed method<sup>6</sup> afforded the 2-arylbenzofuranone  $\underline{7}$  (81%, m.p. 124-125.5 °C). Due to the steric hindrance, this compound exists only under the ketonic form as shown by the NMR spectrum (<sup>1</sup>H-NMR :  $\delta$  C<sub>2</sub>-H 5.99 ppm, <sup>13</sup>C-NMR ·  $\delta$  C<sub>2</sub> 79.58, C<sub>3</sub> 197.89 ppm), whereas compounds with no or one *ortho*-substituent<sup>3</sup> exist only as enols [ for example,  $\underline{1}$  : R =



6-CH<sub>3</sub>O, R' = OH, Ar = 2-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>, <sup>1</sup>H-NMR :  $\delta$  (enolic OH). 11.72 ppm, 100%, <sup>13</sup>C-NMR :  $\delta$  C<sub>2</sub> 191.62, C<sub>3</sub> 196.66 ppm]. Reduction of <u>7</u> with a large excess of sodium borohydride and acid-catalysed dehydration gave the 2-arylbenzofuran <u>2</u> (56% from <u>7</u>, m.p. 138.5-140 °C, lit.<sup>5</sup> 139-140 °C)

In conclusion the preparation of 5-(E)-propenyl-2(2,4,6-trimethoxyphenyl)-3(2H)-benzofuran illustrates the generality of our approach towards the synthesis of 2-arylbenzofuranones and its interest for the synthesis of a large range of substituted 2-arylbenzofurans, particularly containing double bonds.

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## **References:**

- 1. Meyer, M.; Deschamps, C.; Molho, D. Bull Soc. Chim Fr 1991, 91-99 and references therein
- 2. McKittrick, B.A.; Scannell, R T; Stevenson, R.T. J. Chem. Soc., Perkin Trans 1 1982, 3017-3020 and references therein.
- Barton, D.H.R.; Donnelly, D.M.X; Finet, J.P.; Guiry, P.J.; Kielty, J.M Tetrahedron Lett 1990, <1, 6637-6641
- 4. Kozyrod, R.P; Pinhey, J.T. Aust J Chem. 1985, 38, 1155-1161 and references therein.
- Achenbach, H.; Gross, J.; Dominguez, X A.; Star, J.V., Salgado, F. Phytochemistry, 1987, 26, 2041-2043.
  Turii L. Near, M. Sharara, L. L. Ora, Chan. 1985, 50, 2416 2417.
- 6 Tsuji, J; Nisar, M.; Shimizu, J. J. Org Chem, 1985, 50, 3416-3417.

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