Synthesis of Naturally Occurring 5-Allyl-2-aryl-7-methoxybenzofuran and 2-Aryl-5-(3-hydroxypropyl)-7-methoxybenzofurans†

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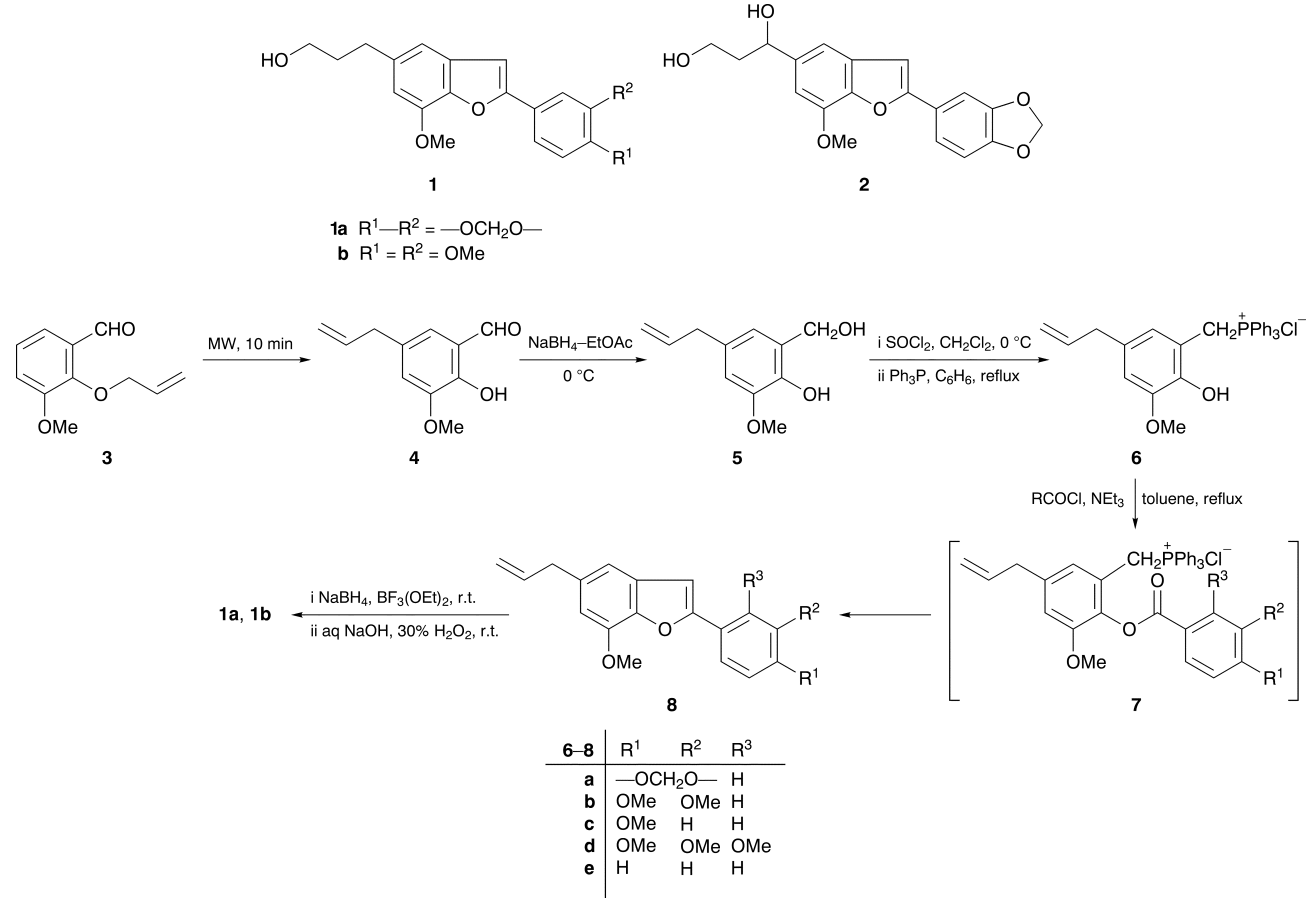
A convenient and general procedure is described for the synthesis of 5-allyl-2-aryl-7-methoxybenzofurans (**8a**–**e**) from 2-allyloxy-3-methoxybenzaldehyde (**3**). The compounds **8a** and **8b** on hydroboration followed by oxidation provide the naturally occurring benzofurans (**1a** and **1b**).

A few compounds, containing the 2-arylbenzofuran nucleus (**1a**, **1b**, **2** and **8a**), have been isolated from plants.[2–4] Egonol (**1a**) and homoegonol (**1b**) were isolated[2,3] from the seeds of *Styrax japonicum* and *Styrax officinalis L.* respectively, while (±)-machicendiol **2** was isolated[4] from the leaf extracts of *Machilus glaucescens*, which are used for the treatment of asthma, rheumatism and ulcers. These compounds are also reported for their cytostatic activity against human leukemic HL-60 cells.[5]

In view of the natural occurrence and valuable biological activities associated with **1a**, **1b** and **2**, several methods have been developed for their synthesis.[7–9,11] Four approaches are known[7–9,11] for egonol **1a** and one [8,9] each for homoegonol **1b** and neolignan **8a**.

We report herein a convenient, general approach (Scheme 1) for the synthesis of egonol **1a**, homoegonol **1b** and neolignan **8a**, starting from 2-allyloxy-3-methoxybenzaldehyde[13] **3**. When a solution of aldehyde **3** in *N*,*N*-dimethylaniline was irradiated in a microwave oven for 10 min, 5-allyl-2-hydroxy-3-methoxybenzaldehyde **4** was obtained in 65% yield along with minor amount (15%) of 2-allyl-6-methoxyphenol. The aldehyde **4** on reduction with sodium tetrahydroborate in ethyl acetate solution, gave the benzyl alcohol **5** as a thick liquid in 76% yield. Reaction of **5** with thionyl chloride in methylene chloride, followed by treatment with triphenylphosphine in benzene solution yielded the phosphonium salt **6**, which on reaction with benzoyl chlorides in toluene solution, in the presence of triethylamine, furnished the 2-arylbenzofurans (**8a**–**e**) in 60–89% yields *via* the intermediacy of phosphonium salts **7a**–**e**.



6–8	R^1	R^2	R^3
a	—OCH_2O—		H
b	OMe	OMe	H
c	OMe	H	H
d	OMe	OMe	OMe
e	H	H	H

Scheme 1

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†Dedicated to Professor Dr Dieter Seebach on the occasion of his 60th birthday.

The present work thus describes the total synthesis of neolignan **8a** and the related compounds **8b**–**e**. Conversion of 2-arylbenzofuran **8a** into egonol **1a** has already been reported[8] in the literature using the hydroboration approach. The compound **8b** on similar reaction provided homoegonol **1b**, mp 121 °C (lit.,[3] mp 120–122 °C) in 70% yield, which is another natural product.

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Techniques used: IR, ^{1}H NMR, elemental analyses, TLC and column chromatography

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