ONE-POT ROUTE TO VINYL-2,3-DIHYDROBENZOFURANS

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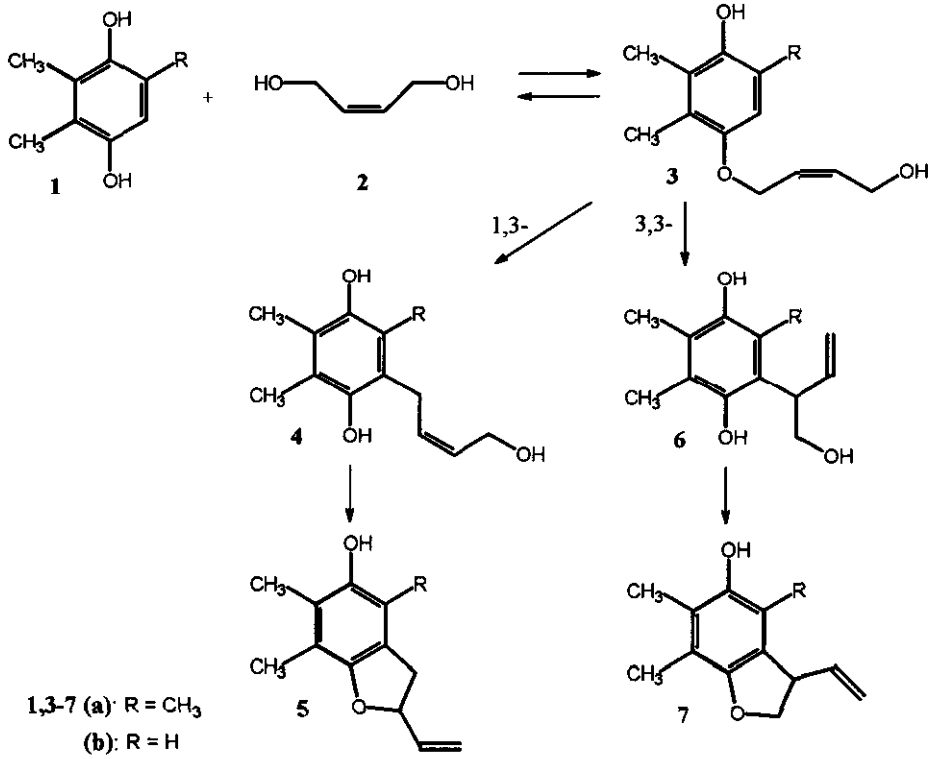
Abstract - *A one-pot approach to the title compounds (5) and (7) has been developed by employing 1,3- and 3,3-rearrangements of in situ generated allyl aryl ethers followed by cyclization.*

Sigmatropic rearrangement provides an efficient and selective method for constructing C-C bonds and has increasingly been employed in synthesis.[1-4] Our general interest in the mechanism of sigmatropic shifts prompted us to investigate the rearrangement of allyl aryl ethers generated *in situ* from hydroquinone (**1**) and (*Z*)-2-butene-1,4-diol (**2**) (Scheme 1).



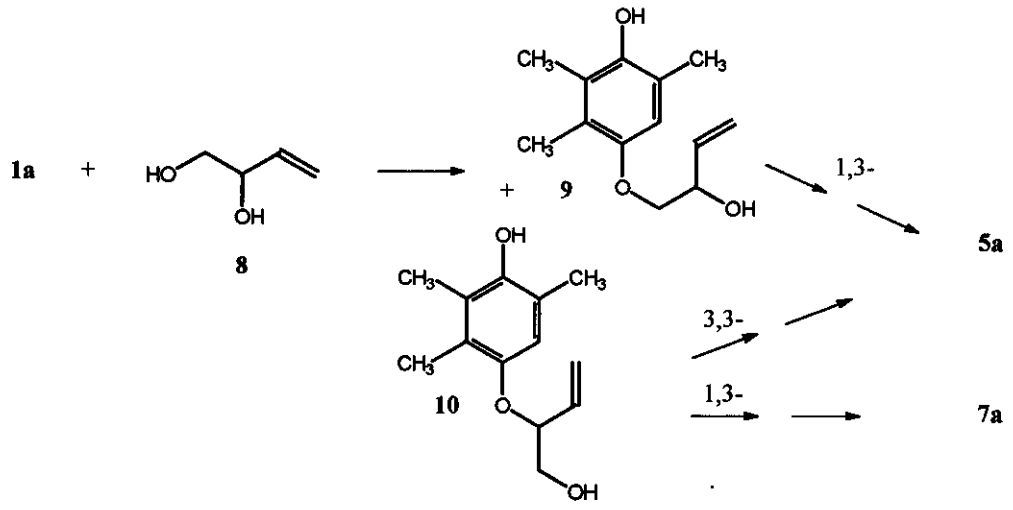
Scheme 1

Compounds (**1a**) and (**2**) on heating in toluene at 70 °C in the presence of *p*-toluenesulfonic acid, were found to give rise to a mixture of products (**5a**) and (**7a**), which was readily separated by recrystallization (hexane, 37% and 23% isolated yield, respectively). The same result was achieved from the reaction of **1b** and **2** , and **5b** and **7b** were the isolated products.

Reasonable pathways leading to the formation of **5** and **7** would likely involve the initial acid-catalyzed formation of ether (**3**), followed by competing 1,3- and 3,3-sigmatropic migrations. The resulting hydroquinones (**4**) and (**6**) then underwent acid-catalyzed cyclization to afford **5** and **7** , respectively.

The ratio of products (**5**) and (**7**) was dependent upon reaction temperature. At lower temperature (50 °C) the 1,3-shift was heavily favoured (ratio 5:1), whereas in boiling toluene the 3,3- (Claisen) rearrangement became more competitive (ratio 1:2).

A 3:2 mixture of **5a** and **7a** was also isolated from the acid-catalyzed reaction of **1a** and 3-butene-1,2-diol (**8**) (Scheme 2). Here, the 1,3-shift on the initially formed ether (**9**) and the 3,3-rearrangement of the isomeric ether (**10**) with subsequent cyclizations furnished **5a** , whereas 1,3-shift on **10** led to the formation of **7a** through cyclization of intermediate (**6a**).



Scheme 2

ACKNOWLEDGEMENTS

Financial support from EGIS Pharmaceutical Work (Budapest) and Hungarian OTKA Foundation are gratefully acknowledged.

EXPERIMENTAL

Melting points were determined on a Büchi apparatus and are uncorrected. Ir spectra were obtained with a Spectromom 2000 Spectrophotometer. ^{1}H-Nmr spectra measurements were carried out using a JEOL-FX-100 spectrometer. All signals are expressed as δ-values ppm downfield from TMS used as an internal standard. Ms spectra were obtained on a JEOL 01SG-2 spectrometer. Hplc analyses were performed on a Du Pont 830 instrument equipped with UV detector; stationary phase: Partisil 5 (250 x 4.6 mm), eluent n-hexane-CH_2Cl_2-dioxane 49:49:2.

5-Hydroxy-4,6,7-trimethyl-2-vinyl-2,3-dihydrobenzofuran (5a) and 5-Hydroxy-4,6,7-trimethyl-3-vinyl-2,3-dihydrobenzofuran (7a). A mixture of **1a** (10.0 g, 66.7 mmol), **2** (20.0 g, 277 mmol) and 2.0 g of *p*-toluenesulfonic acid hydrate in 400 ml of dry toluene was stirred at 70°C for 16 h under argon. After cooling, water (150 ml) and EtOAc (200 ml) were added, the organic layer was separated and washed with brine, dried ($MgSO_4$) and concentrated. The residue was filtered through a short column and then crystallized from n-hexane to give **5a** (5.1 g, 37.4%, colorless crystals). The hexane solution was concentrated and the residue was recrystallized from n-hexane to yield **7a** (3.13g, 23.1%, colorless needles).

Compound **5a**. mp 130-135°C. Tlc: (hexane-acetone 5:2) R_f= 0.64. Hplc: R_t= 6.0 min. Ir (KBr): 3430 cm^{-1} (OH). ^{1}H-Nmr ($CDCl_3$): 2.12 (9H, s, $3CH_3$), 3.15 (2H, m, CH_2), 4.31 (1H, br s, OH), 5.20 (1H, m, CH-O), 5.05-6.20 (3H, m, $CH=CH_2$). Ms: m/z 205 (M^++1, 16), 204 (M^+, 100), 189 (M^+-15, 86), 177 (M^+-27, 18).

Compound **7a**. mp 87-88°C. Tlc (hexane-acetone 5:2): R_f= 0.69. Hplc: R_t= 6.45 min. Ir (KBr): 3450 cm^{-1} (OH). ^{1}H-Nmr ($CDCl_3$): 2.11 (9H, s, $3CH_3$), 3.95 (1H, m, CH), 4.20 and 4 45 (2H, m, CH_2-O), 4.43 (1H, br s, OH), 5.05-6.20 (3H m, $CH=CH_2$). Ms: m/z 205 (M^++1, 14), 204 (M^+, 100), 189 (M^+-15, 72), 177 (M^+-27, 22).

5-Hydroxy-6,7-dimethyl-2-vinyl-2,3-dihydrobenzofuran (5b) and 5-Hydroxy-6,7-dimethyl-3-vinyl-2,3-dihydrobenzofuran (7b). A mixture of **1b** (5.0 g, 36 mmol), **2** (10.0 g, 138 mmol) and 1.0 g of (1**R**)-(-)-10-camphorsulfonic acid monohydrate in 50 ml of dry toluene was stirred at 100°C for 24 h under argon. After cooling, water was added and the toluene phase was separated. The aqueous phase was extracted with EtOAc and the combined organic phases were washed with brine and dried ($MgSO_4$). Evaporation of the solvents *in vacuo* gave a mixture of isomers which was separated by chromatography to yield **5b** (1.2 g, 17 5%) and **7b** (0.8 g,11.7%).

Compound **5b**. mp 125°C (hexane). Tlc (hexane-acetone 5:2): R_f= 0.56. Ir (KBr): 3440 cm^{-1} (OH). ^{1}H-Nmr ($CDCl_3$): 2.10 (6H, s, $2CH_3$), 3.15 (2H, m, CH_2), 4.62 (1H, br s, OH), 5.15 (1H, m, CH-O), 5.80-6.25 (3H, m, $CH=CH_2$), 6.50 (1H, s, aromatic-H). Ms: m/z 191 (M^++1, 18), 190 (M^+, 100), 175 (M^+-15, 90), 160 (M^+-30, 16).

Compound **7b**. mp 118°C (hexane). Tlc (hexane-acetone 5:2): R_f= 0 59. Ir (KBr): 3450 cm^{-1} (OH). ^{1}H-Nmr ($CDCl_3$) 2.12 (6H, s, $2CH_3$), 3.90 (1H, m, CH), 4.30 (3H, m, CH_2-O and OH), 4.90-6.15 (3H, m, $CH=CH_2$), 6.50 (1H, s, aromatic-H). Ms: m/z 191 (M^++1, 16), 190 (M^+, 100), 175 (M^+-15, 92), 160 (M^+-30, 18).

Reaction of 1a with 3-butene-1,2-diol (8). A mixture of **1a** (3.5 g, 23 mmol), **2** (10.0 g, 139 mmol) and 2.0 g of (1**R**)-(-)-10-camphorsulphonic acid monohydrate in 100 ml of dry toluene was stirred at 70°C for 17 h. After cooling, the reaction mixture was poured into ice/water The organic layer was separated and washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The resultant oily residue was purified by column chromatography to afford a 3.2 mixture of **5a** and **7a** (1.6 g, 34%).

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Received, 30th August, 1993