Carboxylic Esters as Radical Leaving Groups: a New and Efficient Gas-phase Synthesis of Benzofurans

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Flash vacuum pyrolysis (FVP) of *o*-allyloxycinnamate esters gives benzofurans in high yield, *via* cyclisation of a phenoxyl radical and subsequent cleavage of the carboxylic ester function; coumarins are obtained by FVP of the corresponding phenols.

Intramolecular free-radical attack on aromatic systems under flash vacuum pyrolysis (FVP) conditions usually leads to oxidative cyclisation, in which regeneration of the benzenoid system provides the driving force for the final elimination.¹ In seeking to extend these ideas to alkene systems for which this driving force is diminished (Scheme 1) we required an efficient radical leaving group (Z) to compensate and also to ensure selectivity. We now report that the carboxylic ester function ($Z = CO_2R$) fulfils these criteria, and show how the methodology can be applied to a simple, versatile, and efficient synthesis of the benzofuran ring system.

The radical precursors 1-8 were easily made in two steps from salicylaldehyde derivatives, by sequential Wittig reaction (or Knoevenagel condensation) and O-allylation‡





Scheme 2 Reagents: i, CH₂=CHCH₂Br, K₂CO₃, dimethylformamide; ii, Ph₃P=C(R²)CO₂R¹, CH₂Cl₂ or R²CH₂CO₂Me

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[‡] All new compounds were characterised by their spectra and by elemental analysis (solids) or accurate mass measurement (liquids).

(Scheme 2). These steps could be carried out in either order, and overall yields were often in excess of 80%. Because of the low reactivity of 2-hydroxyacetophenone, the precursor **9** was made by Wadsworth-Emmons reaction of the 2-benzyloxy derivative.

Flash vacuum pyrolysis of the phenoxyl radical precursors 1–9 at 650 °C (10^{-2} to 10^{-3} Torr) gave the benzofurans 10–18 respectively as the major product in each case (Table 1). Yields are generally in the range 60–90% and chromatography is not normally required in the workup. The loss of the carboxylic ester function (CO₂R¹) on cyclisation takes place quantitatively and with total specificity (Scheme 3) even in potentially competitive situations¹ [*e.g.* formation of 12, 13 and 17 where no cleavage of methyl radicals (R²) was observed]. In addition, there are no complications of hydrogen transfer and rearrangement processes in this series, which often limit the synthetic potential of phenoxyl radicals in the gas phase.² Thus, no hydrogen-transfer products were detected from the methyl-substituted precursors 3, 4 and 9, and the regiospecific formation of the 2,5-disubstituted



Scheme 3

Table 1 Yields of benzofurans 10-18 obtained by pyrolysis

Precursor	Product	R ²	R ³	Yield (%)
1	10	Н	н	68
2	11	Н	Cl	60
3	12	Me	н	75
4	13	Me	Cl	85
5	14	CO ₂ Me	н	95
6	15	CN	н	52
7	16			39
8	17			88
9	18			67



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product 13 confirms the absence of spiro-type rearrangements. From a synthetic point of view, the pyrolysis conditions are sufficiently mild to be compatible with most functional groups (R^3 etc.), and the method provides a simple, three-step route to benzofurans from salicylaldehydes, which complements our earlier gas-phase synthesis of dibenzofurans.³

In cases where the lower yields are obtained, coumarins are major by-products, and these may be formed by alcohol ($R^{1}OH$) elimination from the parent phenol (Scheme 4). Indeed we have found tht FVP of these compounds at 750 °C is a particularly facile means of accomplishing this transformation which avoids the use of high-boiling solvents.⁴ Yields of the coumarins **19–23** were in the range 75–96%.

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