Base Catalysed Aromatic Claisen Rearrangement of 3-Hydroxyphenyl Allyl Ethers

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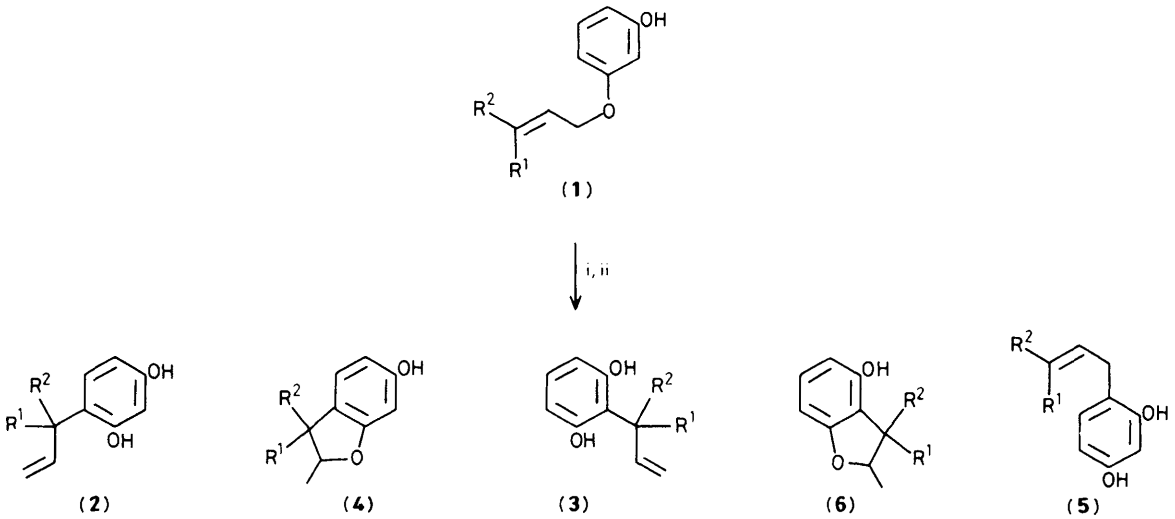
The 3-hydroxyphenyl allyl ethers (**1a**—**d**) have been shown to undergo rearrangement in refluxing aqueous methanolic potassium hydroxide in the presence of oxygen, whereas no reaction occurs in the absence of base and oxygen, and the products formed are the result of accelerated [3,3] sigmatropic processes in which moderate regioselection is operating; evidence is presented for the process being radical rather than anion mediated.

The aromatic Claisen rearrangement responds to catalysis by a wide range of Lewis acids, Brönsted acids, and transition metals.[1] During our studies into catalysed Claisen rearrangements of unsymmetrically substituted substrates we have demonstrated that good regioselectivity can be obtained in the Lewis acid catalysed reaction.[2] Despite interest in its aliphatic counterpart[3] base catalysis of the aromatic Claisen rearrangement has received less attention although an example has been reported in a guanine derivative,[4] and recently Buchi has reported the promotion of a Claisen rearrangement in a



a; $R^1 = R^2 = H$
b; $R^1 = H, R^2 = Me$
c; $R^1 = Me, R^2 = H$
d; $R^1 = R^2 = Me$

Scheme 1. *Reagents and conditions:* i, $MeOH/H_2O$ (1 : 1), KOH (5 equiv.), reflux, 6 days; ii, H_3O^+.

dianionic substrate.[5] Although 2-hydroxyphenyl allyl ethers, which are stable in the absence of added base, undergo rearrangement in refluxing ethanolic sodium ethoxide, the major products are not those expected from simple Claisen rearrangement but result instead from initial [2,3] sigmatropic rearrangement followed by [3,3] sigmatropic rearrangement of the intermediate.[6] In the light of these results, it was of interest to us to determine whether deprotonation of 3-hydroxyphenyl allyl ethers (**1**) would be capable of both increasing the rate of Claisen rearrangement and directing the regiochemistry due to the increased electron donating ability of the oxyanion. We now report our observations on the base promoted rearrangements of such substrates.

It was found that 3-allyloxyphenol (**1a**), on refluxing in aqueous methanolic potassium hydroxide, underwent rearrangement to produce 4-allyl-1,3-dihydroxybenzene (**2a**) [δ 6.95 (1H, d, *J* 7.5 Hz, H^5), 6.40 (1H, dd, *J* 7.5 Hz, *J*′ 2.5 Hz, H^6), 6.38 (1H, d, *J* 2.5 Hz, H^2] and 2-allyl-1,3-dihydroxybenzene (**3a**) [δ 6.98 (1H, t, *J* 7.5 Hz, H^5), 6.43 (2H, d, *J* 7.5 Hz, H^4, H^6)] in 31 and 17% isolated yields respectively, with 28% recovery of starting material (Scheme 1). Although an extended reflux period (6 days) was necessary to achieve this conversion, (**1a**) was found to be stable for indefinite periods at this temperature in the absence of added base. In addition, methylating the hydroxy group of (**1a**) removed the accelerative effect of the potassium hydroxide. It is noteworthy that this moderate accelerative effect was not observed if atmospheric oxygen was rigorously excluded; extending the reaction period in the presence of base but absence of oxygen resulted in slow degradation of (**1a**) with no identifiable products being formed.

Similarly, the monoallyl ethers (**1b**,**c**,**d**), whilst stable in refluxing aqueous methanol, underwent rearrangement on addition of potassium hydroxide (5 equiv.). Reactions were allowed to proceed for 144 h. and consistently gave good material recovery (*ca.*70% or greater after chromatography) (Scheme 1).† In each case the major products from rearrangement of (**1a**—**d**) possessed a 4-alkyl substituent, either as the initial rearrangement products (**2**) or dihydrobenzofurans (**4**) (Table 1) [*e.g.* (**4d**), δ 1.07 (3H, s), 1.28 (3H, s), 1.37 (3H, d, *J* 7.5 Hz), 4.40 (1H, q, *J* 7.5 Hz), 5.10 (1H, s, removable with D_2O), 6.32 (1H, d, *J* 7.5 Hz), 6.37 (1H, dd, *J* 7.5 Hz, *J*′ 2.5 Hz), 6.92 (1H, d, *J* 7.5 Hz)] indicating the same regioselectivity as that observed in the acid catalysed processes.

Table 1. Products from rearrangement of (**1a**—**d**).

Substrate	Products: % yield					Other products: % yield
	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	
(**1a**)	31	17	—	—	—	Starting material: 28
(**1b**)	62	—	11	—	11	Starting material: 8
(**1c**)	45	—	7	—	5	Starting material: 33
(**1d**)	12	—	34	22	9	1,3-Dihydroxybenzene: 2

The rate of rearrangement of the *E*-crotyl ether (**1b**) was marginally faster than that of the *Z*-crotyl ether (**1c**) and rearrangement of a mixture of the two geometric isomers for 6 days led to solely *Z*-isomer in recovered starting material. This result is in keeping with the rearrangement proceeding *via* a chair-like transition state, and has been observed previously in thermal rearrangements.[7] In the rearrangement of (**1d**) the 4-substituted product (**5d**) was also observed [22%, partial n.m.r. data: δ 1.78 (6H, br.s), 3.28 (2H, d, *J* 7.5 Hz), 5.28 (1H, br.t, *J* 7.5 Hz)], probably resulting from a second sterically favoured [3,3] rearrangement of the dienone intermediates from either, or both, of the two Claisen rearrangement pathways.[8] The minor products of reaction possessed 2-alkyl substituents either as the allylated products (**3c**—**d**) or dihydrobenzofurans (**6c**—**d**) [*e.g.*(**6d**), δ 1.22 (3H, s), 1.38 (3H, d, *J* 7.5 Hz), 1.47 (3H, s), 4.38 (1H, q, *J* 7.5 Hz), 4.83 (1H, s, removeable with D_2O), 6.23 (1H, d, *J* 7.5 Hz), 6.40 (1H, d, *J* 7.5 Hz), 6.97 (1H, t, *J* 7.5 Hz)].

The lack of base catalysed rearrangements in the absence of oxygen was a consistent observation in all of the substrates studied. The mixtures did not darken during reaction, no oxidised or dimeric materials were detected in the crude

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† All novel compounds isolated gave spectroscopic and analytical data in accord with their assigned structures.

product mixtures, and material recovery after chromatography was good. It may be that rearrangement proceeds *via* phenoxyl radicals, generated by air oxidation of the phenoxide anion,[9] rather than anionic intermediates themselves. Preferential oxidation of the methanol solvent by the radical species present,[10] or involvement of the rearranged radical as a propagator in a radical chain process,‡ would explain the absence of polymerization. In support of this, addition of excess of the hindered phenol 4-4′-thiobis(6-t-butyl-*o*-cresol) as a competing radical trap caused the base accelerative effect to removed, whereas addition of 1 equiv. of potassium ferricyanide[11] to the basic reaction mixture increased the reaction rate at the expense of material recovery.

In conclusion, substrates (**1a**—**d**) undergo base catalysed Claisen rearrangement in the presence of oxygen, possibly *via* phenoxyl radicals. The accelerative effect and regioselectivity are in accord with, but lower than, those observed under acid catalysed conditions on substrates having similar substitution patterns.

We thank the S.E.R.C. and Fisons Plc. for financial support (to A.J.O.).

Received, 8th July 1987; Com. 973

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‡ We thank a referee for suggesting this second possibility.

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