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Triisobutylaluminium promoted reductive rearrangement of substituted vinyl ethers to homologous alcohols

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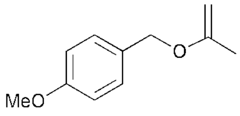
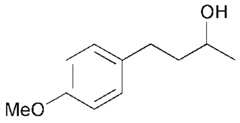
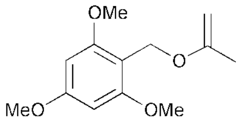
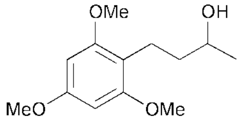
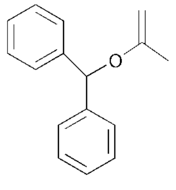
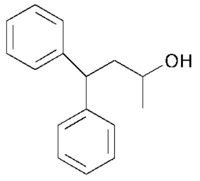
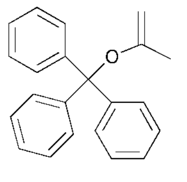
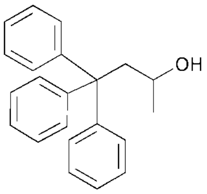
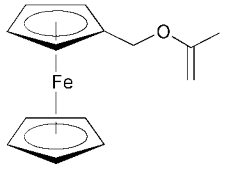
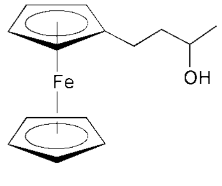
Substituted vinyl ethers carrying electron-donating groups in the ether moiety undergo smooth oxygen to carbon rearrangement with triisobutylaluminium to afford chain extended alcohols.

Lewis acid promoted oxygen to carbon rearrangements of vinyl acetals have received considerable attention as synthetically useful procedures.[1] For example, we have developed efficient methodology for the preparation of carbocycles by the reductive rearrangement of carbohydrate based vinyl acetals using TIBAL (triisobutylaluminium) as the Lewis acid.[2] We recently reported[3] that unsaturated *C*-aryl glycosides (hex-5-eno-pyranosides) such as **1**, also undergo the analogous TIBAL promoted rearrangement into carbocycles, provided that the aryl moiety is sufficiently electron-donating in nature in order to stabilise the carbocationic centre of the proposed intermediate **2** (Scheme 1). It is noteworthy that **1** is however no longer a vinyl acetal but a cyclic benzyl vinyl ether. Given that the Lewis acid promoted rearrangement of acyclic vinyl acetals[4] and allyl benzyl ethers[5] has been reported, we reasoned that an acyclic variant of **1** should also undergo a Lewis acid promoted rearrangement. Therefore, as part of our evaluation of the wider scope of the TIBAL promoted reductive rearrangement, we herein report the first application of this process to the rearrangement of acyclic *non-carbohydrate* based systems.

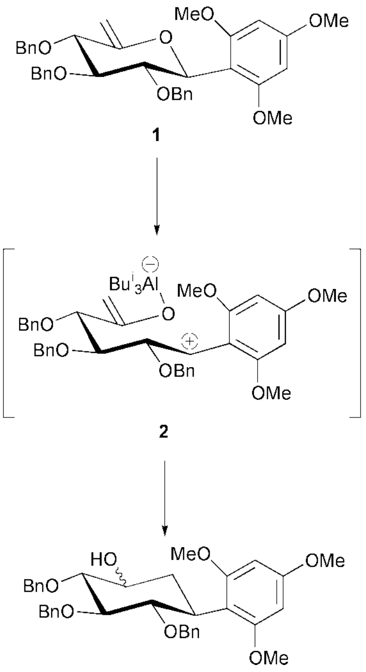
The substituted vinyl ethers **4** were readily prepared by standard acetylation of the starting alcohols **3** and methylenation using the Tebbe reagent (Scheme 2).

The substituents were chosen in order to stabilise the proposed carbocation intermediate and therefore favour rearrangement over the known competitive hydroalumination–elimination process[3] which would afford **3**. The TIBAL promoted reductive rearrangements† of **4** proceeded smoothly (64–70%) for electron-rich aromatic derivatives **4a** and **4b**

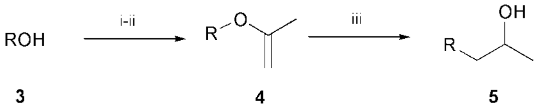
Table 1 Reaction of substituted vinyl ethers with TIBAL

Substituted vinyl ether	Product	Yield (%)
 **4a**	 **5a**	64
 **4b**	 **5b**	70
 **4c**	 **5c**	87
 **4d**	 **5d**	35[a]
 **4e**	 **5e**	60[a]

[a] **3d** (15%) and **3e** (10%)—the products of the competitive cleavage process *via* hydroalumination–elimination[3] were also isolated.



Scheme 1



Scheme 2 *Reagents and conditions*: i, Ac_2O, pyridine (for **3a**,**b**); AcCl, Et_3N (for **3c**,**e**); AcBr, AcOH, NH_3, toluene (for **3d**); ii, 2.0 equiv. Tebbe reagent, 4.0 equiv. pyridine, THF, −45 °C to rt; iii, 5.0 equiv. TIBAL (1 M in toluene).†

(Table 1). The related non-reductive rearrangement of benzyl vinyl ethers has been reported as a side-reaction to Claisen rearrangements under radical[6] or forcing thermal conditions.[7] The TIBAL promoted rearrangement of diphenylmethyl isopropenyl ether (**4c**) proceeded in excellent yield. In the case of triphenylmethyl isopropenyl ether (**4d**), TIBAL rearrangement was indeed observed, although in only 35% yield, probably due to steric hindrance. Finally, the ferrocenylmethyl isopropenyl ether (**4e**) underwent smooth TIBAL promoted rearrangement to afford 4-ferrocenylbutan-3-ol (**5e**)‡ in 60% yield.

In summary, substituted vinyl ethers carrying electron-donating groups in the ether moiety undergo smooth TIBAL promoted rearrangement to afford chain extended alcohols. This approach constitutes a simple three step homologation procedure for benzylic alcohols, carrying electron-donating substituents in the aromatic nucleus and other alcohols bearing adjacent electron-donating groups and furthermore illustrates the more *general* nature of the TIBAL induced rearrangement.

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Notes and references

† *Typical procedure*: TIBAL (1 M in toluene, 5 equiv.) was added to a stirred solution of starting material **4** in dry toluene (1 mL/100 mg), at 0 °C under argon. The cooling bath was then removed and the reaction mixture was allowed to warm to room temperature. After *ca*. 2 h (as indicated by TLC), the reaction mixture was cooled to 0 °C and distilled water was added dropwise until no further gas evolution was observed. The reaction mixture was then filtered (Celite®) and washed with EtOAc. The organic phase was then diluted with distilled water and extracted twice with EtOAc. The organic layers were then combined, dried ($MgSO_4$), filtered and the solvent was removed *in vacuo*. Purification of the residue by flash chromatography (cyclohexane–EtOAc) afforded pure **5**.

‡ *Selected data* for **5e**: δ_H(400 MHz; $CDCl_3$) 1.26 (d, 3H, *J* 6.3, CH_3), 1.57 (br s, 1H, OH), 1.63–1.78 (m, 2H, $FnCH_2CH_2$), 2.42 (ddd, 1H, *J* 14.5, 9.6 and 6.6, $FnCH_aH_b$), 2.51 (ddd, 1H, *J* 14.5, 9.6 and 6.2, $FnCH_aH_b$), 3.86 (m, 1H, CHOH), 4.10–4.12 (m, 4H, 4 × HCp), 4.15 (5H, s, 5 × HCp); δ_C(100 MHz; $CDCl_3$) 23.6 (CH_3), 25.7 ($FnCH_2$), 40.4 ($FnCH_2CH_2$), 67.1 (2 × CCp), 67.8 (CHOH), 67.8 (CCp), 68.0 (CCp), 68.4 (5 × CCp), 88.7 ($CCpCH_2$); *m/z* (CI, NH_3) 276 (100%, M + 18); (calc. for $C_{14}H_{18}OFe$: C, 65.14; H, 7.03; found: C, 65.07; H, 7.19%).

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