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Reaction of α,β-Unsaturated and α-Phenyl Acetals with Epoxides, Promoted by Lithium-Potassium Mixed Base LICKOR: Synthesis of Homoallyl Alcohols

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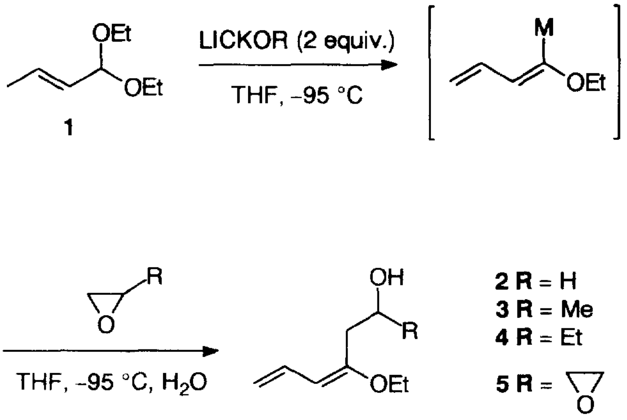
Abstract. Acetals **1**, **7** and **8**, in the presence of the mixed metal base LICKOR, undergo deprotonation and elimination reactions, affording enol ethers intermediates. Further hydrogen-metal exchange at the α-vinyl site of elimination products gives α-metalated species that yield, by reaction with epoxides, homoallyl alcohols. Experimental procedures are given for the conversion of the unsaturated species into the corresponding carbonyl compounds. α-Substituted ethoxy diene **4** is also an useful intermediate for a one-pot synthesis of 2,6-disubstituted tetrahydro-4*H*-pyran-4-one **19**.

The stoichiometric mixture of butyllithium and potassium *tert*-butoxide ("Schlosser's reagent" LICKOR) proved to be particularly suited for selective metal-hydrogen exchange at resonance active sites, *i.e.* at allylic and benzylic positions.[1] Schlosser's base metalates unbranched olefins, and the reaction is always typo- and regioselective: only proton abstraction occurs without traces of addition products and only metalation at allylic position takes place in alkenes also having vinylic hydrogens. Consistently with these findings we have reported that α,β-unsaturated acetals react with the LICKOR base, undergoing to 1,4-elimination process that yields 1-alkoxy-1,3-dienes.[2,3] An analogous pathway it has been observed for α-phenyl acetals that, upon metalation at the benzylic position and β-elimination, afford enol ethers.[4] These derivatives can be further metalated at the α-vinyl site giving a vinylpotassium intermediate which reacts with various electrophiles, yielding the corresponding α-substituted terms. Owing to the presence of the vinyl ether function, hydrolysis under mild acidic conditions leads to carbonyl compounds, according to an ***umpolung***[5] approach that allows starting acetals to be considered as masked acyl anions.

In the present paper we report the progress of our investigations on the reactivity of acetals with electrophiles, in the presence of *sec*-butyllithium complexed with potassium *tert*-butoxide (LICKOR base).

RESULTS AND DISCUSSION

As shown in Scheme 1, 1,1-diethoxybut-2-ene **1** in the presence of 2 equivalents of LICKOR reagent (THF, −95 °C) gives α-metalated 1-ethoxybuta-1,3-diene which reacts with epoxides as electrophiles to afford, after ring opening, homoallyl alcohols. Compounds **2** and **3** have been previously synthesised: reaction yields were 70% and 80%, respectively.[2c]



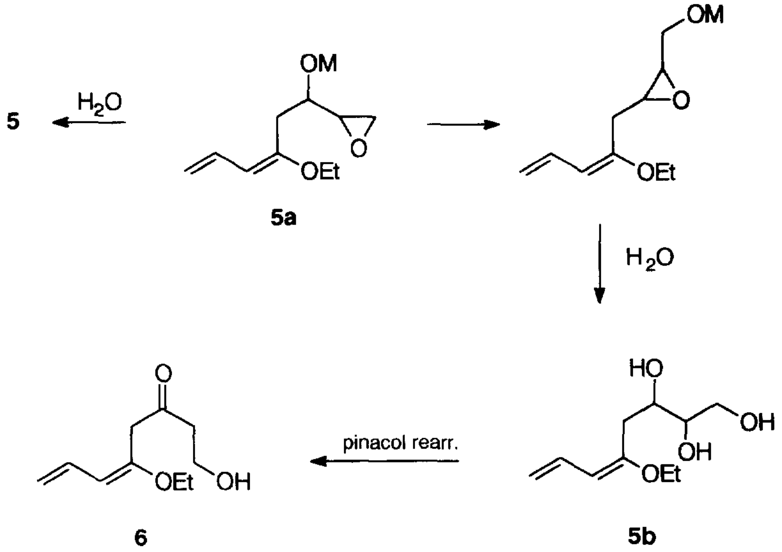
Scheme 1 LICKOR-promoted reaction of acetal 1 and epoxides: synthesis of α-substituted ethoxy dienes

Table 1 Homoallyl Alcohols Obtained from Acetals 1, 7 and 8 with Epoxides, in the Presence of LICKOR Reagent[a]

Substrate	Epoxide	Product	Yield[b] (%)
1	1,2-Epoxibutane	**4**	65
1	1,3-Butadiene diepoxide	**5**	55[c]
7	Ethylene oxide[d]	**9**	68
7	Propylene oxide[d]	**10**	50
8	Ethylene oxide[d]	**11**	93
8	Propylene oxide[d]	**12**	93

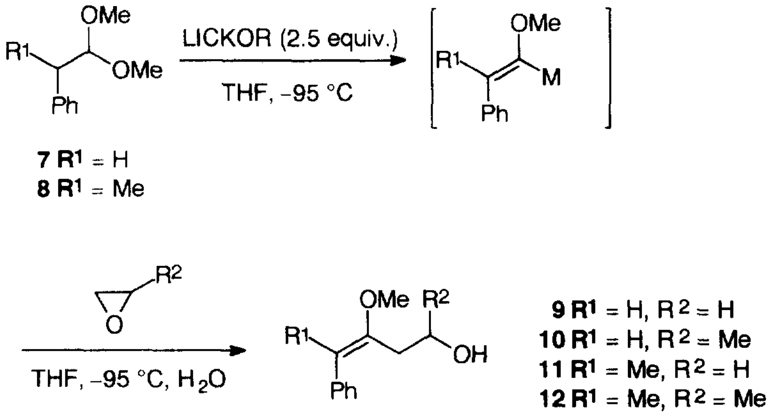
[a] Acetal (2.5 mmol), *s*-BuLi (5.0 mmol), *t*-BuOK (5.0 mmol), if not otherwise stated, epoxide (2.7 mmol), (ethylene oxide was bubbled into the reaction mixture until red purple color was discharged), THF (10 mL), T = −95 °C. [b] Yield of purified product. [c] Ketone **6** was also isolated (18% yield). [d] LICKOR reagent, 2.5 equiv. with respect to the substrate.

Here we report in addition the synthesis of homoallyl alcohols **4** and **5**, obtained using 1,2-epoxybutane and 1,3-butadiene diepoxide as electrophiles (Table 1). As a matter of fact, with 1,3-butadiene diepoxide, two products, **5** and **6**, are obtained. In particular, compound **5** is formed by nucleophilic substitution reaction on only one epoxide ring, while ketone **6** probably results from ring closure and opening induced by intramolecular nucleophilic attack of alkoxide **5a**. Subsequent hydrolysis, during aqueous workup, produces intermediate glycol **5b** which undergoes pinacol rearrangement to afford ketone **6** (Scheme 2).



Scheme 2 Suggested mechanistic pathway that leads to ketone **6** during aqueous workup of the reaction mixture of **1** with 1,3-butadiene diepoxide

In Scheme 3 are shown the products obtained by reaction of 1,1-dimethoxy-2-phenylethane **7** and 1,1-dimethoxy-2-phenylpropane **8** with epoxides as an electrophile, in the presence of 2.5 equivalents of LICKOR base in THF at −95 °C. The reaction with the Schlosser's reagent is initiated by hydrogen-metal exchange at the benzylic site which induces 1,2-elimination reaction to the corresponding methyl vinyl ethers. Subsequent α-metalation[6,7] of these intermediates gives homoallyl alcohols **9–12** by reaction with epoxides (Table 1).

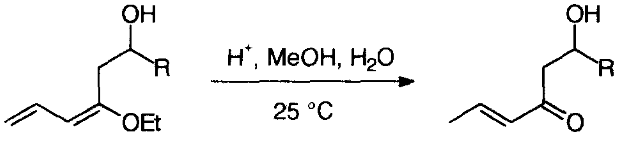


Scheme 3 LICKOR-promoted reaction of acetals **7** and **8** and epoxides: synthesis of α-substituted vinyl ethers

It is noteworthy that in experiments carried out starting from acetal **7** in the presence of 2.5 equivalents of *sec*-butyllithium, and not adding potassium *tert*-butoxide, (*E*)-3-methyl-1-phenylpent-1-ene was isolated (60%) as the only reaction product after the addition of the electrophile. This compound comes from a substitution reaction by organolithium reagent on intermediate vinyl ether obtained through 1,2-elimination reaction.[8] This results confirms that lithium-potassium mixed reagents are endowed with a strong basic properties and poor nucleophilicity.[1]

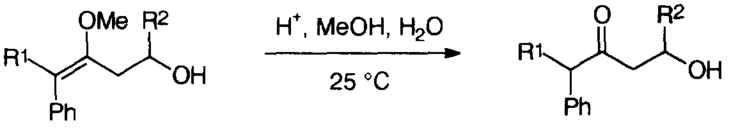
α-Substituted ethoxy dienes **2–6**, and enol ethers **9–12** exist in an *E*-configuration. The double bond configuration for elimination products **2–6** and **9** and **10** has been deduced from the J_{trans} coupling constants in the ^{1}H-NMR spectra of the corresponding unsubstituted derivatives that were obtained by quenching the reaction with water and not adding the electrophile. The *E*-configuration of alcohols **11** and **12** has been assigned on the analogy of (*E*)-1-methoxy-2-phenylpropene, where irradiation of the olefinic hydrogen atom gives rise to an Overhauser enhancement of the signal assigned to the hydrogens of the Ph and OMe groups which indicates the *E*-configuration. Moreover, irradiation of Me allyl hydrogen atoms caused a NOE of the signal assigned to the aromatic hydrogens. (*E*)-1-methoxy-2-phenylpropene was the product of the reaction of **7** with 2.5 equivalents of LICKOR base, when it was quenched with water in the absence of the electrophile.

Alcohols **2–5**, and **9–12** can be converted into carbonyl compounds by mild acidic treatment, according to the reactions reported in Schemes 4 and 5.[2d–e,7] The results are reported in Table 2.



13 **R** = Me
14 **R** = Et

Scheme 4 Aqueous hydrolysis of α-substituted alkoxy dienes into β-hydroxy enones



15 **R¹** = H, **R²** = H
16 **R¹** = H, **R²** = Me
17 **R¹** = Me, **R²** = H
18 **R¹** = Me, **R²** = Me

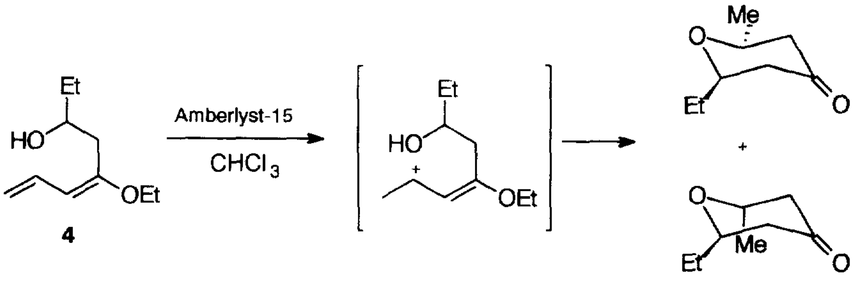
Scheme 5 Aqueous hydrolysis of α-substituted enol ethers into β-hydroxy ketones

Table 2 **Carbonyl Compounds Obtained from Homoallyl Alcohols 3, 4 and 9–12**[a]

Substrate	Product	Yield[b] (%)
3	**13**	55
4	**14**	58
9	**15**	78
10	**16**	99
11	**17**	87
12	**18**	84

[a] Substrate (2.5 mmol), catalyst (0.02 N HCl), solvent (MeOH : H_2O, 4 : 1; 25 mL), T = 25 °C. [b] Yield of purified product.

Moreover, when ethoxy diene **4** was dissolved in chloroform, and stirred for 2h at 25 °C in the presence of a catalytic amount of Amberlyst-15, a mixture of *cis* and *trans* 2-ethyl-6-methyltetrahydro-4*H*-pyran-4-one **19** was isolated (80%). Unlike hydrolysis, in chloroform solution, the absence of polar protic solvent, drives the reaction to proceeds through an intramolecular S_N cyclization process, as shown in Scheme 6. The two isomers were not separated, and the *cis* : *trans* ratio (55 : 45) was deduced by GC analysis. Cyclization reaction proceeds trough the pathway shown in Scheme 6 rather than through intermediate α,β-unsaturated ketone **14**: enone **14** is not isolable even when the reaction is quenched by filtration of the acidic catalyst and neutralisation before completion. Moreover, the absence of the cyclic enol ether 4-ethoxy-6-ethyl-2-methyl-2,3-dihydro-2*H*-pyran is probably due to hydrolysis, which readily takes place under not-anhydrous reaction conditions.[2c] *cis*-2-Ethyl-6-methyltetrahydro-4*H*-pyran-4-one was established to be the major component in the isomeric mixture (lower retention time in the GC spectrum), on the analogy of 2,6-dimethyltetrahydro-4*H*-pyran-4-one.[2c] In that case the *cis* : *trans* ratio was determined on the basis of both GC and ^{1}H-NMR analyses, and the *cis*-isomer showed the lower GC retention time. The relative position of the substituents attached to C-2 and C-6 is not deducible on the base of the ^{1}H-NMR spectrum of **19**, as the resonance patterns of 2-H, 3-H and 6-H, 5-H are confused.[13]



Scheme 6 Acid catalysed intramolecular cyclization of diene **4** to tetrahydro-4*H*-pyran-4-one **19**

EXPERIMENTAL SECTION

Flasks and all the equipment used for the generation and reactions of metalated alkoxy dienes were flame dried under argon. The temperature of acetone-liquid nitrogen slush bath is consistently indicated as –95 °C, and "room temperature" as 25 °C. Anhydrous THF was obtained by distillation over sodium wire after persistence of the blue color of sodium diphenylketyl.[9] *s*-BuLi (1.4 M solution in cyclohexane) was purchased from Aldrich. *t*-BuOK, obtained from Merck, was sublimated *in vacuo* (0.1 Torr) prior to the reaction. All commercially available chemicals were reagent grade and were used without further purification. α,β-Unsaturated acetal **1** has been synthesised according to the literature method.[10] The synthesis of homoallyl alcohols **2** and **3** have been previously reported.[2c] ^{1}H-NMR spectra were recorded at 60 or 300 MHz in $CDCl_3$ solution, using TMS as internal standard. Coupling constants (*J*) are measured in hertz, and coupling patterns are described by abbreviation: s (singlet), d (doublet), t (triplet), q (quartet), p (pentuplet), hex (hexuplet), bs (broad singlet). ^{13}C-NMR were recorded at 75 MHz in $CDCl_3$ solution. A cross linked methyl silicone capillary column (12.5 m × 0.2 mm × 0.33 mm film thickness; oven temperature = 70 → 250 °C, 2 °C/min; flow rate (He) 5 mL/min) was used for GC-MS spectra, that were obtained at a 70 eV ionisation potential. Preparative column chromatography was carried out on Merck silica gel 60 with diethyl ether–light petroleum ether (bp 30–60 °C) as an eluant.

LICKOR-Promoted Synthesis of Homoallyl Alcohols 4 *and* 5

t-BuOK (0.56 g, 5.0 mmol) was added to 10 mL of anhydrous THF at 25 °C. The suspension was cooled to –95 °C and acetal **1** (0.36 g, 2.5 mmol) was added. After 15 min, *s*-BuLi (1.4 M solution in cyclohexane, 3.57 mL, 5.0 mmol) was added dropwise with stirring to the solution. After a few seconds the solution turned purple and was stirred at –95 °C for 2 h. After the addition of a suitable epoxide (2.7 mmol) the color was discharged. The reaction mixture was kept 2 h at –95 °C and was then treated with a THF solution of H_2O (5 mL). The mixture was poured into water, the organic phase was separated, and the aqueous phase extracted with diethyl ether (3 × 25 mL). The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated to give crude products. Further purification of the products was carried out by means of chromatography on a SiO_2 column.

(E)-5-Ethoxyocta-5,7-dien-3-ol (**4**). Colorless oil, Et_2O : light petroleum ether, 30 : 70. δ_H (60 MHz; $CDCl_3$) 1.10 (3 H, t, *J* = 6.0 Hz), 1.38 (5 H, m), 2.35 (2 H, d, *J* = 6.0 Hz), 2.52 (1 H, bs), 3.70 (3 H, m), 4.85 (1 H, dd, *J* = 10.0, 1.9 Hz), 5.02 (1 H, dd, *J* = 15.8, 1.9 Hz), 5.40 (1 H, d, *J* = 10.0 Hz), 6.45 (1 H, dt, *J* = 15.8, 10.0 Hz); MS m/z (relative intensity) 170 (M^+, 12%), 97 (24), 84 (23), 68 (42), 66 (100). Anal. Calc. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.7; H, 10.55%.

(E)-1,2-Epoxy-5-ethoxyocta-5,7-dien-3-ol (**5**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (300 MHz; $CDCl_3$) 1.30 (3 H, t, *J* = 6.0 Hz), 2.35 (1 H, bs), 2.55 (1 H, *J* = 14.0, 6.0 Hz), 2.65 (1 H, dd, *J* = 14.0, 7.0 Hz), 2.73 (1 H, dd, *J* = 5.2, 3.0 Hz), 2.79 (1 H, dd, *J* = 5.2, 4.0 Hz), 3.05 (1 H, td, *J* = 4.0, 3.0 Hz), 3.75 (1 H, m), 3.77 (2 H, q, *J* = 6.0 Hz), 4.85 (1 H, dd, *J* = 10.0, 1.9 Hz), 5.02 (1 H, dd, *J* = 15.8, 1.9 Hz), 5.40 (1 H, d, *J* = 10.0 Hz), 6.45 (1 H, dt, *J* = 15.8, 10.0 Hz); δ_C (75 MHz, $CDCl_3$) 14.4, 35.5, 44.6, 54.6,

62.5, 69.7, 102.9, 112.2, 132.0, 155.2; MS m/z (relative intensity) 184 (M^+, 15%), 97 (25), 69 (67), 68 (100), 45 (28), 66 (77), 55 (48). Anal. Calc. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.0; H, 8.85%.

(E)-5-Ethoxy-1-hydroxyocta-5,7-dien-3-one (**6**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 1.15 (3 H, t, J = 6.0 Hz), 2.40 (2 H, t, J = 6.0 Hz), 2.53 (1 H, bs), 3.15 (2 H, s), 3.70 (4 H, m), 4.85 (1 H, dd, J = 10.0, 1.9 Hz), 5.02 (1 H, dd, J = 15.8, 1.9 Hz), 5.40 (1 H, d, J = 10.0 Hz), 6.45 (1 H, dt, J = 15.8, 10.0 Hz); MS m/z (relative intensity) 184 (M^+, 18%), 97 (14), 73 (100), 69 (35), 66 (33), 57 (37), 55 (50); ν_{max}/cm^{-1} (neat) 3400, 1717, 1630.

***LICKOR-Promoted Synthesis of Homoallyl Alcohols* 9–12**

A solution of *s*-BuLi (1.4 M solution in cyclohexane, 4.5 mL, 6.25 mmol) was evaporated under reduced pressure.[11] Precooled (–95 °C) THF (10 mL), acetal **7** or **8** (2.5 mmol) and sublimed *t*-BuOK (0.70 g, 6.25 mmol) were consecutively added with stirring at –95 °C. After 3 h at –95 °C a suitable epoxide (2.7 mmol) was added (ethylene oxide was bubbled in excess, until the purple color of the reaction mixture was discharged), the reaction mixture was kept 1 h at –50 °C, and was then quenched with a THF solution of H_2O (5 mL). The procedure proceeds afterwards as above described for compounds **4** and **5**. When cyclohexane solvent was not evaporated from the solution of *s*-BuLi, the metalating power of LICKOR reagent decreased, and metalation at the α-vinyl site did not take place. Starting from acetal **7**, (*E*)-1-methoxy-2-phenylethene was recovered as the only reaction product, regardless of the added electrophile.

(E)-3-Methoxy-4-phenylbut-3-en-1-ol (**9**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 2.40 (2 H, t, J = 6.0 Hz), 2.63 (1 H, bs), 3.55 (3 H, s), 3.65 (2 H, t, J = 6.0 Hz), 5.50 (1 H, s), 7.05 (5 H, m); MS m/z (relative intensity) 178 (M^+, 55%), 115 (100), 102 (26), 76 (33), 91 (72). Anal. Calc. for $C_{11}H_{14}O_2$: C, 74.12; H, 7.92. Found: C, 74.05; H, 8.0%.

(E)-4-Methoxy-5-phenylpent-4-en-2-ol (**10**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 1.12 (3 H, d, J = 6.0 Hz), 2.40 (2 H, d, J = 6.0 Hz), 2.50 (1 H, bs), 3.55 (3 H, s), 3.95 (1 H, m), 5.50 (1 H, s), 7.05 (5 H, m); MS m/z (relative intensity) 192 (M^+, 12%), 148 (17), 116 (100), 115 (58), 91 (22). Anal. Calc. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.5; H, 8.3%.

(E)-3-Methoxy-4-phenylpent-3-en-1-ol (**11**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 1.70 (3 H, s), 2.15 (2 H, t, J = 6.0 Hz), 2.50 (1 H, bs), 3.50 (3 H, s), 3.60 (2 H, t, J = 6.0 Hz), 6.9 (5 H, m); MS m/z (relative intensity) 192 (M^+, 51%), 161 (25), 131 (38), 129 (100), 91 (40). Anal. Calc. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 75.5; H, 8.45%.

(E)-4-Methoxy-5-phenylhex-4-en-2-ol (**12**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 0.95 (3 H, d, J = 6.0 Hz), 1.8 (3 H, s), 2.10 (2 H, d, J = 6.0 Hz), 2.55 (1 H, bs), 3.45 (3 H, s), 3.80 (1 H, m), 7.05 (5 H, m); MS m/z (relative intensity) 206 (M^+, 14%), 131 (23), 130 (100), 115 (46), 91 (28). Anal. Calc. for $C_{13}H_{18}O_2$: C, 75.68; H, 8.80. Found: C, 75.25; H, 8.75%.

Acid-Catalysed Conversion of α-Substituted Ethoxy Dienes and of α-Substituted Enol Ethers into Carbonyl Compounds

Ethoxy diene **3–5** or enol ether **9–12** (2.5 mmol) was dissolved in 25 mL of aqueous methanolic (1 : 4) 0.02 N HCl and stirred at 25 °C. The reaction was followed by TLC, until the disappearance of the spot corresponding to the reagent (2–4 h). After this time the solution was neutralised with 5% aqueous $NaHCO_3$, evaporated under vacuum to half the volume, and then extracted with Et_2O (3 x 20 mL). The organic phase was washed with brine (2 x 20 mL) and dried. After evaporation of the solvent the residue was purified by column chromatography.

2-Hydroxyhept-5-en-4-one (**13**). Colorless oil, Et_2O : light petroleum ether, 60 : 40. δ_H (60 MHz; $CDCl_3$) 1.05 (3 H, d, *J* = 6.0 Hz), 1.85 (3 H, dd, *J* = 6.0, 1.9 Hz), 2.45 (2 H, d, *J* = 6.0 Hz), 2.90 (1 H, bs), 3.95 (1 H, hex, *J* = 6.0 Hz), 5.85 (1 H, dq, *J* = 15.8, 1.9 Hz), 6.70 (1 H, dq, *J* = 15.8, 6.0 Hz) (lit.[12]); MS m/z (relative intensity) 113 (M^+– Me, 1%), 87 (8), 84 (7), 71 (7), 69 (100); ν_{max}/cm^{-1} (neat) 3450, 1667, 1633. Anal. Calc. for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 66.0; H, 9.5%.

6-Hydroxyoct-2-en-4-one (**14**). Colorless oil, Et_2O : light petroleum ether, 70 : 30. δ_H (60 MHz; $CDCl_3$) 0.90 (3 H, t, *J* = 6.0 Hz), 1.30 (2 H, p, *J* = 6.0 Hz),1.85 (3 H, dd, *J* = 6.0, 1.9 Hz), 2.45 (2 H, d, *J* = 6.0 Hz), 2.80 (1 H, bs), 3.95 (1 H, p, *J* = 6.0 Hz), 5.85 (1 H, dq, *J* = 15.8, 1.9 Hz), 6.7 (1 H, dq, *J* = 15.8, 6.0 Hz); MS m/z (relative intensity) 124 (M^+ – H_2O, 10%), 113 (9), 84 (10), 69 (100), 57 (11); ν_{max}/cm^{-1} (neat) 3450, 1668, 1623. Anal. Calc. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 68.1; H, 10.0%.

4-Hydroxy-1-phenylbutan-2-one (**15**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 2.50 (2 H, t, *J* = 6.0 Hz), 3.05 (1 H, bs), 3.60 (2 H, s), 3.65 (2 H, t, *J* = 6.0 Hz), 7.05 (5 H, s); MS m/z (relative intensity) 164 (M^+, 12%), 91 (56), 73 (100), 65 (33); ν_{max}/cm^{-1} (neat) 3450, 1710; Anal. Calc. for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.85; H, 7.45%.

4-Hydroxy-1-phenylpentan-2-one (**16**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$), 0.95 (3 H, d, *J* = 6.0 Hz), 2.20 (2 H, d, *J* = 6.0 Hz), 2.65 (1 H, bs), 3.65 (2 H, s), 3.85 (1 H, hex, *J* = 6.0 Hz), 7.05 (5 H, s); MS m/z (relative intensity) 178 (M^+, 10%), 91 (100), 87 (48), 65 (42); ν_{max}/cm^{-1} (neat) 3450, 1710. Anal. Calc. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.3; H, 7.95%.

1-Hydroxy-4-phenylpentan-3-one (**17**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 0.95 (3 H, d, *J* = 6.0 Hz), 2.1 (2 H, t, *J* = 6.0 Hz), 2.35 (1 H, bs), 3.35 (2 H, t, *J* = 6.0 Hz), 3.55 (1 H, q, *J* = 6.0 Hz), 6.95 (5 H, bs); MS m/z (relative intensity) 178 (M^+, 6%), 105 (100), 77 (38), 73 (87); ν_{max}/cm^{-1} (neat) 3500, 1700. Anal. Calc. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.5; H, 7.85%.

5-Hydroxy-2-phenylhexan-3-one (**18**). Colorless oil, Et_2O : light petroleum ether, 50 : 50. δ_H (60 MHz; $CDCl_3$) 0.95 (3 H, d, *J* = 6.0 Hz), 1.15 (3 H, d, *J* = 6.0 Hz), 2.15 (2 H, d, *J* = 6.0 Hz), 3.25 (1 H, bs), 3.45 (1 H, q, *J* = 6.0 Hz), 3.75 (1 H, hex, *J* = 6.0 Hz), 7.05 (5 H, s); MS m/z (relative intensity) 192 (M^+, 3%), 105

(100), 87 (49), 77 (50), 59 (25); ν_{max}/cm^{-1} (neat) 3500, 1710. Anal. Calc. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.05; H, 8.4%.

Acid-Catalysed Cyclization of 4 into 2,6-Disubstituted Tetrahydro-4H-pyran-4-one (19)

(*E*)-5-Ethoxyocta-5,7-dien-3-ol (0.42 g, 2.5 mmol) was dissolved in a $CHCl_3$ (50 mL) suspension of Amberlyst-15 (4.6 mequiv. × g^{-1}; 0.15 g) under stirring at 25 °C. After 2 h the resin was filtered off, and the reaction mixture was treated with K_2CO_3, filtered and concentrated *in vacuo* to afford crude 2-ethyl-6-methyltetrahydro-4*H*-pyran-4-one **19**. The product was purified by column chromatography, as a mixture of *cis* and *trans* isomers (55 : 45), that were not separated. δ_C (75 MHz, $CDCl_3$) 9.5, 9.6, 20.6, 21.9, 27.1, 29.2, 46.4, 47.0, 48.2, 49.3, 67.8, 73.0, 73.4, 78.1, 207.6; MS (*cis*, retention time = 2.45 min) m/z (relative intensity) 142 (M^+, 16%), 113 (31), 83 (32), 71 (69), 69 (34), 57 (34), 56 (100); MS (*trans*, retention time = 2.72 min) m/z (relative intensity) 142 (M^+, 11%), 113 (31), 83 (13), 71 (100), 69 (51), 56 (51); ν_{max}/cm^{-1} (neat) 1710. Anal. Calc. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.15; H, 10.0%.

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