194. A Case of Highly Diastereoselective Addition to Unsymmetrical Ketones: *lk*-Addition[1]) of (2-Alkenyl)triphenoxytitanium Derivatives

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(19.VII.82)

Summary

(2-Butenyl)-, (4-methyl-2-pentenyl)-, and (2-heptenyl)triphenoxytitanium (**2a–c**) add to dialkyl, alkyl aryl-, and alkinyl aryl ketones to give high yields of tertiary homoallylic alcohols (**5–12**), which are diastereomerically enriched up to 98%. Configurational assignment by degradation of two of the products to olefins **15** and **18** – through β-hydroxy acids **13** and **16** and β-lactones **14** and **17** – leads to the proposal of a general mechanism and of a specification of the relative topicity *lk* of the process *(Scheme 5)*. The allylic Ti-compounds **2** can serve as d^2-reagents (see the d^2-synthon **II** and the aldol-type structures **1**).

A) Introduction. – The stereoselective synthesis of β-hydroxy-carbonyl compounds **1** from two precursors corresponding to the a^1- and d^2-synthons **I** and **II** has attracted much recent interest[3]) *(Scheme 1)*. On examination of the numerous contributions in this field (reviewed extensively in [2] [6] [7] [8] [9]) no reports are found about diastereoselective C,C-bond formations with generation of tertiary alcohols of type **1** (R^3 *and* $R^4 \neq H$)[4]). We think that this is not surprising, mainly for three reasons. *i)* There is less synthetic need: tertiary alcohols and ethers are not as ubiquitous in macrolide and ionophore target molecules as are secondary ones[5]). *ii)* There is a chemical problem: the aldol addition to ketones leading to products of type **1**, is more readily reversible than the addition to aldehydes[6]).

[1]) Following our recent proposal [1] the relative configuration *R*,R** is termed *l* (like), *R*,S* u* (unlike), the relative topicity *Re*,Re** [2] is termed *lk* (like), *Re*,Si* ul* (unlike).

[2]) Part of the projected Ph. D. thesis of *L. W.*, ETH Zürich.

[3]) This is also true of other processes in which two trigonal centres are joined with formation of two new asymmetric C-atoms [2], such as the nitroaldol [3] [4] and the *Michael* addition [2] [3] [5].

[4]) In contrast, β-hydroxy-carbonyl derivatives persubstituted in the α-position have been obtained diastereoselectively by aldol-type reactions [10] [11] as well as by alkylation of reagents corresponding to 3-hydroxy-carbonyl-d^2 synthons [12] [13] [14].

[5]) Different routes have been chosen if the construction of such centres was necessary in the course of syntheses of complex natural products [15].

[6]) Li-Enolates derived from α-heterosubstituted carboxylic acids can exhibit high kinetic diastereoselectivity in additions of ketones [11] [16].

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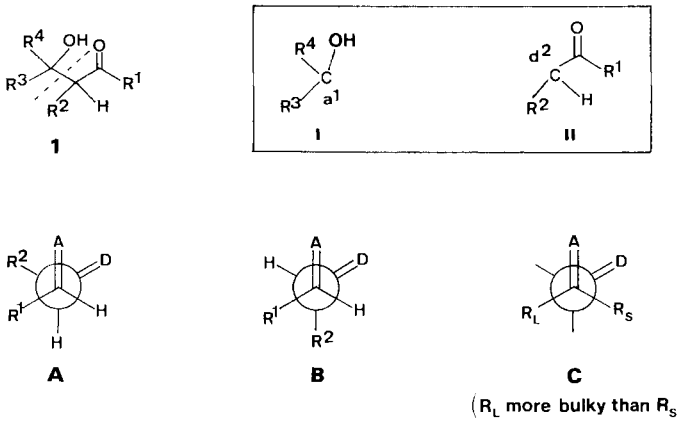
Scheme 1[a])



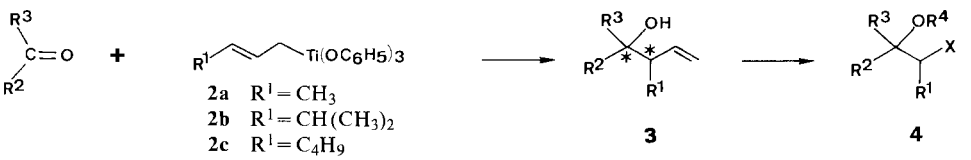
[a]) A = Acceptor, D = donor, L = large, S = small.

iii) There is a problem of stereoselectivity: whatever effects cause the kinetic preference of the approach with a *gauche*-relationship between the donor group and the – smaller – H-atom of the acceptor molecule in processes **A** and **B** [2] [4] [5] [6] [7] [8] [9], less pronounced effects are expected with ketones in case of approach **C** ($A = O$, $R_S \neq H$).

In the course of our investigation of allylic organotitanium reagents [17] we have now discovered some remarkably stereoselective additions to ketones, see *Scheme 2*. Since a C, C-double bond is synthetically equivalent to a carbonyl group, the Ti-reagents **2** correspond to the d^2-synthon **II**. Other possible conversions (**3** → **4**) outlined in *Scheme 2* show that reagents **2** can also correspond to d^3-synthons.

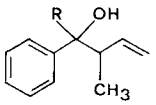
B) Additions of (2-butenyl)-, (4-methyl-2-pentenyl)- and (2-heptenyl)triphenoxytitanium (*2a–c*) to ketones and determination of the diastereoselectivity. – Solutions of the allylic Ti-reagents **2** were prepared as described in [17] for **2a**: allylic *Grignard* compounds obtained from the corresponding halides and *Rieke* magnesium in tetrahydrofuran (THF) were combined with stock solutions of chlorotriphenoxy-

Scheme 2[a])

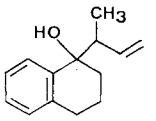


[a]) X in **4** may be $CH(OH)CH_3$ (hydration of the double bond), $COCH_3$ (hydration/oxidation), $COOR^5$ (ozonolysis or other cleavages), CH_2CH_2OH (hydroboration), CH_2COR^5 (hydroboration/oxidation).

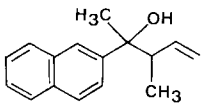
Scheme 3



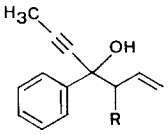
5a R = H (85% ds) [17]
5b R = CH_3 (83–92% ds)
5c R = C_2H_5 (74% ds)
5d R = $CH(CH_3)_2$ (55% ds)
5e R = $C(CH_3)_3$ (> 97% ds)



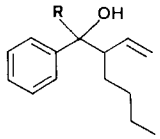
6 (65% ds)



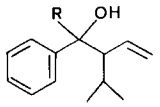
7 (> 97% ds)



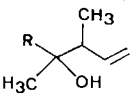
8a R = CH_3 (72% ds)
8b R = $CH(CH_3)_2$ (77% ds)
8c R = C_4H_9 (77% ds)



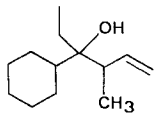
9a R = H (93% ds)
9b R = CH_3 (87% ds)



10a R = H (> 97% ds)
10b R = CH_3 (87% ds)



11a R = C_6H_{13} (hexyl) (70% ds)
11b R = C_6H_{11} (cyclohexyl) (87% ds)
11c R = *t*-C_4H_9 (96% ds)



12 (60% ds)

titanium[7]) in the same solvent. *In situ* addition of ketones at low temperature, warming up overnight and workup furnished the homoallylic alcohols **5**–**12** in good-to-excellent chemical yields (70–90%) (see *Scheme 3*[8])). The composition of the product mixtures was determined by capillary gas chromatography. We did not detect more than two isomers. The NMR. spectra clearly show that diastereomeric

[7]) Since the addition to aldehydes was most diastereoselective with the triphenoxy derivative [17], we did not test other OR-groups in the present investigation.

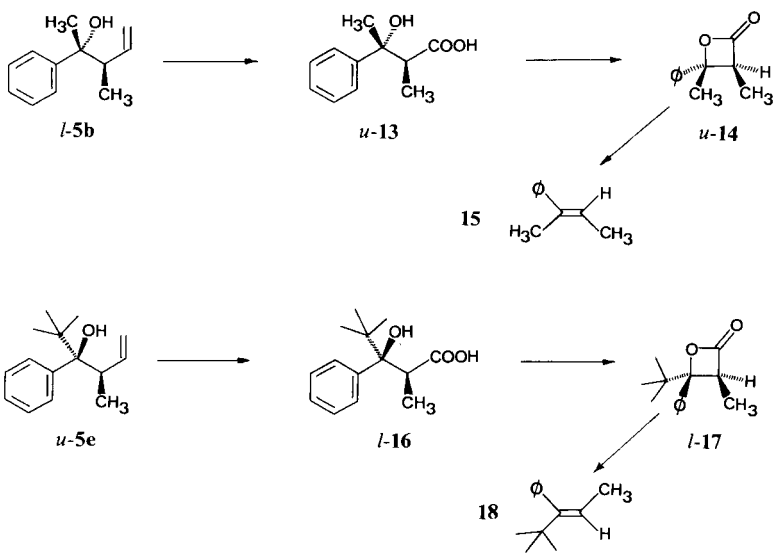
[8]) The reaction leading to **5b** was carried out several times, so that a range of yields (see *Exper. Part*) and of diastereoselectivities can be given which is probably representative of the uncertainty of the numbers given in all other cases as well.

pairs of enantiomers[8]) of the products **5–12** with a terminal, monosubstituted double bond are formed, and not the constitutional isomers with a disubstituted double bond and only one asymmetric C-atom. These latter isomers are undoubtedly the more stable ones, thus the additions leading to the products **5–12** must be kinetically controlled. We assume that kinetic control determines not only the constitutional selectivity, but also the configurational one[10]) (see *Scheme 3*, diastereoselectivity =% ds [11]). Inspection of the ds-values shows that selectivities above 90% are obtained if the difference in steric bulkiness of the groups attached to the carbonyl C-atom is sufficiently large. In three cases addition to benzaldehyde and to acetophenone occurs with similar selectivity (**5a/5b**, **9a/9b** and **10a/10b**). On the other hand, alkyl aryl ketones exhibit decreasing selectivity as the alkyl group gets larger, see propiophenone (→ **5c**), isobutyrophenone (→ **5d**) and α-tetralone (→ **6**), only to jump up to >97% ds with pivalophenone (→ **5e**). A similar relation is observed with aliphatic ketones (→ **11a–c** and **12**); the addition to an acetylenic ketone (→ **8a–c**) shows only a *ca.* 3:1-selectivity.

Thus, a variety of tertiary, homoallylic alcohols of type **3** is now available in a diastereomeric purity sufficient for many synthetic purposes.

C) Degradation of the homoallylic alcohols *5b* and *5e* to β-hydroxy-acids *13* and *16* and configurational assignment by correlation. – Next, the (relative) configuration of the products **5–11** had to be assigned. The determination of the configuration[8]) of **5b** and **5e** is demonstrated in *Scheme 4*.

Scheme 4



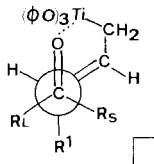
[9]) If configurations are indicated in the *formulae*, only one enantiomer of the racemic mixture is shown throughout this paper.

[10]) Occasionally, we observed configurational isomerization to a *ca.* 1:1-mixture during transformation of the products **5–12** (see *Exper. Part*).

Lemieux-Rudloff oxidation[11]) [18] with potassium permanganate and sodium periodate in dioxane/water with careful control of the pH (*ca.* 7) furnished the *β*-hydroxy acids **13** (60%) and **16** (52%), respectively. These were cyclized to the *β*-lactones **14** and **17**, respectively, with benzenesulfonyl chloride/pyridine, conditions which are known to cause cyclization with retention of configuration at the carbinol centre [19]. The lactone **14** derived from acetophenone has been previqusly obtained in diastereomerically pure form [19] [20]. Decarboxylation of **14** leads to the olefin **15** of (*E*)-configuration, determined by us using the ^{1}H-NMR. shift-increment method [21]. Since it can be considered as well-established that the decarboxylation of *β*-lactones occurs with retention of configuration [19] [22] [23], the *l*-configuration is assigned to our adduct **5b**. The *t*-butyl-substituted lactone **17** was decarboxylated to give a single olefin (**18**), the ^{1}H-NMR. spectrum of which was identical with that of the isomer to which the (*Z*)-configuration was previously assigned [24]. From these results we conclude that **5b** has the *l*- and **5e** the *u*-configuration[8]).

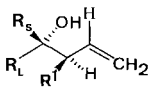
The conversions of **5b** and **5e**, products of type **3**, to carboxylic acids **13** and **16**, respectively, proves not only the configuration by chemical correlation, but also demonstrates the synthetic equivalence of *tertiary* homoallylic alcohols with aldol-type compounds (see **II** in *Scheme 1*, and *Scheme 2*).

Scheme 5



D

lk-approach if $R_L > R_S$



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Product	**5a**	**5b**	**5c**	**5d**	**5e**	**6**
R_L	C_6H_5	C_6H_5	C_6H_5	C_6H_5	$C(CH_3)_3$	C_6H_4
R_S	H	CH_3	C_2H_5	$CH(CH_3)_2$	C_6H_5	$(CH_2)_3$
Configuration	*l*	*l*	*l*	*l*	*u*	*l*

Product	**7**	**8a**	**8b**	**8c**	**9a**	**9b**
R_L	$C_{10}H_7$	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5
R_S	CH_3	$C\equiv C-CH_3$	$C\equiv C-CH_3$ ($R^1=CHMe_2$)	$C\equiv C-CH_3$ ($R^1=C_4H_9$)	H ($R^1=C_4H_9$)	CH_3 ($R^1=C_4H_9$)
Configuration	*l*	*l*	*l*	*l*	*l*	*l*

Product	**10a**	**10b**	**11a**	**11b**	**11c**	**12**
R_L	C_6H_5	C_6H_5	C_6H_{13}	C_6H_{11}	t-C_4H_9	C_6H_{11}
R_S	H ($R^1=CHMe_2$)	CH_3 ($R^1=CHMe_2$)	CH_3	CH_3	CH_3	C_2H_5
Configuration	*l*	*l*	*u*	*u*	*l*	*u*

[11]) The alternative method, ozonization with subsequent *Jones* oxidation did not work with **5b**.

D) Generalization and discussion. – *The relative topicity of the reaction.* Although we were not able to obtain NMR. spectra of the allylic Ti-reagents **2**, which might have been suitable for configurational assignment, we assume that they all have the thermodynamically more favorable (*E*)-configuration as shown in *Scheme 2*.

Thus, the previously observed addition of the (2-butenyl)titanium reagent **2a** to aldehydes [17] and the two correlated present cases of addition of **2a** to acetophenone and pivalophenone are compatible with an approach as indicated in **D** (*Scheme 5*, compare also **B** and **C** in *Scheme 1*), with the titanium coordinated to the carbonyl O-atom and the smaller group R_S in a *pseudo*-1,3-diaxial relationship with the vinylic H-atom [2]. If this picture holds generally and if the reasonable assessments about the relative bulkiness of groups are made as shown in *Scheme 5* [25], all but four of the above combinations of ketones and allylic organotitanium reagents would have to be specified as *lk*.

Except for **5a**, **5b**, and **5e**, and until proved definitively, the configurational assignments made here, must be considered tentative.

We thank *R. Hähner*, *M. Huser*, and *R. Kölliker* for carrying out some of the experiments, *D. Manser* for determining the elemental compositions of the new compounds. Financial support by the *Sandoz AG* (Basel) is gratefully acknowledged.

Experimental Part

1. General remarks. – Tetrahydrofuran (THF) and ether were purified by distillation from either $LiAlH_4$(LAH) or potassium benzophenone. Hexamethylphosphoric triamide (HMPT) was vacuum-distilled over CaH_2. Butyllithium (BuLi) in hexane *(Metallgesellschaft AG)* was standardized using the diphenylacetic acid method [26]. The reactions in which anhydrous conditions had to be maintained, were over CaH_2. Butyllithium (BuLi) in hexane *(Metallgesellschaft AG)* was standardized using the diphenylacetic acid method [26]. The reactions in which anhydrous conditions had to be maintained, were carried out in a dry Ar-atmosphere; the glassware was dried overnight at 140°. Capillary GC: *Carlo Erba HRGC Fractovap* series *4160* using a *Pluronic L-64* column (20 m). For flash column-chromatography, *Merck* silica gel *60* (230–400 mesh) was used. Diastereomeric selectivity (% ds) was determined by GC. prior to any purification. Melting points (m.p.) were determined using a *Büchi 510* apparatus and are not corrected. – ^{1}H-NMR. were measured in $CDCl_3$ on a *Varian EM-390* (90 MHz); chemical shifts are given in δ [ppm] relative to tetramethylsilane (TMS) as internal reference; multiplicities as *s* (singlet), *d* (doublet), *qa* (quadruplet), *m* (multiplet), br. (broad); coupling constants (*J*) in Hz. – ^{13}C-NMR. were recorded on a *Varian CFT-20* (chemical shifts in δ [ppm] with TMS-signal at 0.00 ppm as the internal standard). – Mass spectra (MS.) were obtained on a *Hitachi-Perkin-Elmer RMU-6M*. For most compounds one does not observe M^+ but only the fragment-ion (in most cases base peak), originating from breaking the bond between the two asymmetric centres.

2. Starting materials. – *Preparation of phenyl propinyl ketone.* 1-Bromopentene was reacted in anh. ether with 2 mol-equiv. of butyllithium (BuLi). Addition of 1 mol-equiv. benzaldehyde furnished 1-phenyl-2-butyn-1-ol [27] which was oxidized to the ketone [28] by treatment with manganese dioxide in acetone. Overall yield: 63%, b.p. 97°/0.7 Torr.

Preparation of 1-bromo-2-hepten. Following a suggestion by *Sharpless et al.* [29a], the dilithio derivative [29b] of 2-propynol (propargyl alcohol) was generated in THF/HMPT 5:1 and butylated. Catalytic reduction with H_2, $Pd/BaSO_4$ in anh. MeOH *(Fluka puriss.)*/3% quinoline afforded the corresponding olefin [30] which gave after treatment with PBr_3 (*Fluka, purum*, freshly distilled) and

a catalytic amount of pyridine *(Fluka, puriss.)* in EtOH *(Fluka, puriss.)* 1-bromo-2-hepten in an overall yield of 30%, b.p. 61–62°/12 Torr.

Preparation of 1-bromo-4-methyl-2-penten. Vinylmagnesium bromide [31] was added to 2-methylpropanol to yield 5-methyl-1-penten-3-ol which gave exclusively the rearranged bromide on treatment with PBr_3 [32]; overall yield: 50%.

Preparation of (2-butenyl)magnesium bromide, (2-heptenyl)magnesium bromide, and (4-methyl-2-pentenyl)magnesium bromide. These *Grignard* reagents were prepared as described [17] using *Rieke* magnesium. Their concentration was determined by titration with EtOH using the indicator *N*-phenyl-1-naphthylamine [33].

Chlorotriphenoxytitanium was prepared as reported in [17] and stored as a THF-solution (0.25–0.5 M).

3. General method for the addition of substituted allyltriphenoxytitanium to aldehydes and ketones [17]. – Under Ar-atmosphere 4 mmol of chlorotriphenoxytitanium was cooled to −80°. To the red solution 4 mmol of *Grignard* reagent was added. The color changed immediately to dark brown-red. After warming up slowly to −30° within 1–2 h, the electrophile (*ca.* 0.7 mol-equiv.) was added at −100°. The solution was allowed to reach r.t. overnight. After hydrolysis with sat. neutral aq. KF-solution, the reaction mixture was extracted several times with ether. The organic layer was washed three times with 2N NaOH and twice with sat. aq. NaCl-solution, dried (Na_2SO_4) and evaporated to give the crude alcohol which was purified by flash-chromatography to yield analytically pure samples.

2-Methyl-1-phenyl-3-buten-1-ol (**5a**). From **2a** and benzaldehyde; yield 94%. – ^{1}H-NMR.: 0.83 and 0.95 (2 *d*, J=7, 3 H, H_3C–C(2), diastereomeric ratio 85:15); 2.25–2.55 (*m*, 1 H, H–C(2)); 2.8 (br. *s*, 1 H, OH); 4.25 and 4.42 (2 *d*, J=7, H–C(1), diastereomeric ratio 85:15); 4.8–5.2 (*m*, 2 H, 2 H–C(4)); 5.45–6.0 (*m*, 1 H, H–C(3)); 7.15:7.5 (*m*, 5 H, arom. H).

$C_{11}H_{14}O$ (162.23) Calc. C 81.44 H 8.70% Found C 81.40 H 8.63%

3-Methyl-2-phenyl-4-penten-2-ol (**5b**). From **2a** and acetophenone; yield 85–96%. – ^{1}H-NMR.: 0.95 (*d*, J=7, 3 H, H_3C–C(3)); 1.5 (*s*, 3 H, 3 H–C(1)); 2.05 (*s*, 1 H, OH); 2.4–2.75 (*m*, 1 H, H–C(3)); 4.9–5.2 (*m*, 2 H, 2 H–C(5)); 5.5–5.9 (*m*, 1 H, H–C(4)); 7.1–7.5 (*m*, 5 H, arom. H).

$C_{12}H_{16}O$ (175.26) Calc. C 81.77 H 9.15% Found C 81.70 H 8.98%

4-Methyl-3-phenyl-5-hexen-3-ol (**5c**). From **2a** and propiophenone; yield 85%. – ^{1}H-NMR.: 0.55–0.9 (*m*, 3 H–C(1) and H_3C–C(4) of minor diastereomer); 1.00 (*d*, J=7, H_3C–C(4) of major diastereomer); 1.7–2.1 (*m*, 3 H, OH and 2 H–C(2)); 2.4–2.8 (*m*, 1 H, H–C(4)); 4.9–5.25 (*m*, 2 H, 2 H–C(6)); 5.45–6.1 (*m*, 1 H, H–C(5)); 8.15–7.5 (*m*, 5 H, arom. H).

$C_{13}H_{18}O$ (190.29) Calc. C 82.06 H 9.53% Found C 82.03 H 9.44%

2,4-Dimethyl-3-phenyl-5-hexen-3-ol (**5d**). From **2a** and 2-methyl-1-phenyl-1-propanone (isobutyrophenone); yield 79%. – ^{1}H-NMR.: 0.7–1.1 (*m*, 9 H, 3 H–C(1), H_3C–C(2), H_3C–C(4)); 1.73 and 1.9 (2 *s*, OH, diastereomeric ratio 55:45); 2.1–2.5 (*m*, 1 H, H–C(4)); 2.7–3.15 (*m*, 1 H, H–C(2)); 4.95–5.3 (*m*, 2 H–C(6)); 5.5–6.0 (*m*, 1 H, H–C(5)); 7.1–7.5 (*m*, 5 H, arom. H).

$C_{14}H_{20}O$ (204.31) Calc. C 82.30 H 9.87% Found C 81.93 H 9.83%

2,2,4-Trimethyl-3-phenyl-5-hexen-3-ol (**5e**). From **2a** and 2,2-dimethyl-1-phenyl-1-propanone (pivalophenone); yield 72%. – ^{1}H-NMR.: 0.73 (*d*, J=7, 3 H, H_3C–C(4)); 0.8–1.35 (*m*, 9 H, 3 H_3C–C(2)); 1.85 (*s*, 1 H, OH); 3.0–3.4 (*m*, 1 H, H–C(4)); 4.95–5.3 (*m*, 2 H, 2 H–C(6)); 5.97–6.42 (*m*, 1 H, H–C(5)); 7.2–7.6 (*m*, 5 H, arom. H). – ^{13}C-NMR.: 18.35, 27.30, 39.40, 44.88, 81.96, 113.67, 126.07, 126.54, 127.34, 142.73, 145.46 (diastereomerically pure).

$C_{15}H_{22}O$ (218.34) Calc. C 82.52 H 10.16% Found C 82.50 H 9.99%

1-(3-Buten-2-yl)-1,2,3,4-tetrahydro-1-naphthol (**6**). From **2a** and 1,2,3,4-tetrahydro-1-naphthalenon (*α*-tetralone); yield 86%. – ^{1}H-NMR.: 0.77 and 1.15 (2 *d*, J=7, 3 H, 3 H–C(1′), diastereomeric ratio 65:35); 1.65–1.95 (*m*, 4 H, 2 H–C(2), 2 H–C(3)); 1.95–2.2 (br. *s*, 1 H, OH); 2.6–3.1 (*m*, 3 H, 2 H–C(4), H–C(2′)); 4.8–6.3 (*m*, 3 H, 2 H–C(4′), H–C(3′)); 7.0–7.7 (*m*, 4 H, arom. H).

$C_{14}H_{18}O$ (202.30) Calc. C 83.12 H 8.97% Found C 83.02 H 8.84%

3-Methyl-2-(2-naphthyl)-4-penten-2-ol (**7**). From **2a** and methyl 2-naphthyl ketone; yield 92%. – ^{1}H-NMR.: 0.92 (*d*, *J* = 7, 3 H, H_3C–C(3)); 1.70 (*s*, 3 H, 3 H–C(1)); 2.28 (*s*, 1 H, OH); 3.38 (*m*, 1 H, H–C(3)); 5.05–5.35 (*m*, 2 H, 2 H–C(5)); 5.7–6.2 (*m*, 1 H, H–C(4)); 7.2–8.0 (*m*, 7 H, arom. H).

$C_{16}H_{18}O$ (226.32) Calc. C 84.91 H 8.02% Found C 84.78 H 8.03%

3-Methyl-4-phenyl-1-hepten-5-yn-4-ol (**8a**). From **2a** and 1-phenyl-2-butyn-1-one; yield 93%. – ^{1}H-NMR.: 0.88 and 1.08 (2 *d*, *J* = 7, 3 H, H_3C–C(3), diastereomeric ratio 70:30); 1.90 and 1.94 (2 *s*, 3 H, 3 H–C(7)); 2.25–2.6 (*m*, 1 H, H–C(3)); 2.65 (*s*, 1 H, OH); 4.85–5.2 (*m*, 2 H, 2 H–C(1)); 5.6–6.2 (*m*, 1 H, H–C(2)); 7.15–7.75 (*m*, 5 H, arom. H).

$C_{14}H_{16}O$ (200.28) Calc. C 83.96 H 8.05% Found C 83.80 H 8.22%

4-Phenyl-3-(2-propyl)-1-hepten-5-yn-4-ol (**8b**). From **2b** and 1-phenyl-2-butyn-1-one; yield 88% (partial separation of the diastereomers by chromatography). – ^{1}H-NMR. of major diastereomer: 0.68 (*d*, *J* = 6, 3 H, H_3C–CH–C(3)); 0.93 (*d*, *J* = 6, 3 H, H_3C–CH–C(3)); 1.35–1.8 (*m*, 1 H, H_3C–C*H*–C(3)); 1.85 (*s*, 3 H, 3 H–C(7)); 2.25 (*d* × *d*, *J* = 10.5 and 2.5, 1 H, H–C(3)); 2.65 (br., 1 H, OH); 5.0–5.4 (*m*, 2 H, 2 H–C(1)); 5.8–6.3 (*m*, 1 H, H–C(2)); 7.2–7.8 (*m*, 5 H, arom. H). – ^{1}H-NMR. of minor diastereomer: 0.83 (*d*, *J* = 2, 3 H, H_3C–CH–C(3)); 0.90 (*d*, *J* = 2, 3 H, H_3C–CH–C(3)); 1.90 (*s*, 3 H, 3 H–C(7)); 2.05–2.30 (*m*, 2 H, H–C(3), CH_3CH–C(3)); 2.33 (*s*, 1 H, OH); 4.65–5.15 (*m*, 2 H, 2 H–C(1)); 5.5–5.95 (*m*, 1 H, H–C(3)); 7.25–7.7 (*m*, 5 H, arom. H).

$C_{16}H_{20}O$ (228.34) Calc. C 84.16 H 8.83% Found C 83.98 H 8.69%

3-Butyl-4-phenyl-1-hepten-5-yn-4-ol (**8c**). From **2c** and 1-phenyl-2-butyn-1-one; yield 87%. – ^{1}H-NMR.: 0.6–1.5 (*m*, 9 H, C_4H_9–C(3)); 1.88 and 1.93 (2 *s*, 3 H, 3 H–C(7)); 2.15–2.55 (*m*, 1 H, H–C(3)); 2.73 (*s*, 1 H, OH); 4.7–5.5 (*m*, 2 H, 2 H–C(1)); 5.5–6.1 (*m*, 1 H, H–C(2)); 7.25–7.75 (*m*, 5 arom. H).

$C_{17}H_{22}O$ (242.35) Calc. C 84.25 H 9.15% Found C 84.20 H 9.11%

2-Ethenyl-1-phenyl-1-hexanol (**9a**). From **2c** and benzaldehyde; yield 87%. – ^{1}H-NMR.: 0.65–0.95 (*m*, 3 H, 3 H–C(6)); 0.95–1.4 (*m*, 6 H, 2 H–C(5), 2 H–C(4), 2 H–C(3)); 2.1–2.5 (*m*, 2 H, H–C(2), OH); 4.35 (*d*, *J* = 7.5, 1 H, H–C(1)); 4.95–5.3 (*m*, 2 H, 2 H–C(2′); 5.35–5.85 (*m*, 1 H, H–C(1′)); 7.15–7.4 (*m*, 5 H, arom. H).

$C_{14}H_{20}O$ (204.31) Calc. C 82.30 H 9.87% Found C 82.21 H 9.85%

3-Ethenyl-2-phenyl-2-heptanol (**9b**). From **2c** and acetophenone; yield 89%. – ^{1}H-NMR.: 0.7–0.9 (*m*, 3 H, 3 H–C(7)); 0.9–1.4 (*m*, 6 H, 2 H–C(6), 2 H–C(5), 2 H–C(4)); 1.53 (*s*, 3 H, 3 H–C(1)); 2.1 (*s*, 1 H, OH); 2.1–2.4 (*m*, 1 H, H–C(3)); 5.0–5.3 (*m*, 2 H, 2 H–C(2′)); 5.4–5.8 (*m*, 1 H, H–C(1′)); 7.2–7.55 (*m*, 5 H, arom. H).

$C_{15}H_{22}O$ (218.34) Calc. C 82.52 H 10.16% Found C 82.41 H 10.21%

1-Phenyl-2-(2-propyl)-3-buten-1-ol (**10a**). From **2b** and benzaldehyde; yield 91%. – ^{1}H-NMR.: 0.83 (*d*, *J* = 7, 6 H, 2 H_3C–C(2′)); 1.1–1.7 (*m*, 1 H, H–C(2′)); 2.05–2.35 (*m*, 2 H, H–C(2), OH); 4.55–4.7 (*m*, 1 H, H–C(1)); 5.0–5.4 (*m*, 2 H, 2 H–C(4)); 5.6–6.0 (*m*, 1 H, H–C(3)); 7.25–7.4 (*m*, 5 H, arom. H). – ^{13}C-NMR.: 17.62, 21.83, 27.68, 58.88, 74.71, 119.79, 126.85, 127.54, 128.27, 135.84, 143.11 (diastereomerically pure).

$C_{13}H_{18}O$ (190.29) Calc. C 82.06 H 9.53% Found C 81.93 H 9.55%

2-Phenyl-3-(2-propyl)-4-penten-2-ol (**10b**). From **2b** and acetophenone; yield 90%. – ^{1}H-NMR.: 0.62 (*d*, *J* = 7, 3 H, 3 H–C(1′)); 0.73 (*d*, *J* = 7, 3 H, 3 H–C(3′)); 1.42 and 1.53 (2 *s*, 3 H, 3 H–C(1), diastereomeric ratio 85:15); 1.7–2.1 (*m*, 1 H, H–C(2′)); 2.1 (*s*, 1 H, OH); 2.1–2.25 (*m*, 1 H, H–C(3)); 4.7–5.35 (*m*, 2 H, 2 H–C(5)); 5.5–6.05 (*m*, 1 H, H–C(4)); 7.15–7.6 (*m*, 5 H, arom. H).

$C_{14}H_{20}O$ (204.31) Calc. C 82.30 H 9.87% Found C 82.24 H 9.77%

3,4-Dimethyl-1-decen-4-ol (**11a**). From **2a** and 2-octanone; yield 98%. – ^{1}H-NMR.: 0.75–1.9 (*m*, 20 H); 2.1–2.45 (*m*, 1 H, H–C(3)); 4.9–5.2 (*m*, 2 H, 2 H–C(1)); 5.6–6.1 (*m*, 1 H, H–C(2)).

$C_{12}H_{24}O$ (184.31) Calc. C 78.20 H 13.12% Found C 78.06 H 13.02%

2-Cyclohexyl-3-methyl-4-penten-2-ol (**11b**). From **2a** and cyclohexyl methyl ketone; yield 93%. – ^{1}H-NMR.: 0.9–2.0 (*m*, 18 H); 2.2–2.6 (*m*, 1 H, H–C(3)); 4.9–5.2 (*m*, 2 H, 2 H–C(5)); 5.7–6.15 (*m*, 1 H, H–C(4)).

$C_{12}H_{22}O$ (182.31) Calc. C 79.06 H 12.16% Found C 79.01 H 11.98%

2,2,3,4-Tetramethyl-5-hexen-3-ol (**11c**). From **2a** and 3,3-dimethyl-2-butanone; yield 60%. – ^{1}H-NMR.: 1.00 (*s*, 9 H, 3 H_3C–C(2)); 1.15 (*d*, *J* = 7, 3 H, H_3C–C(4)); 1.17 (*s*, 3 H, H_3C–C(3)); 2.4–2.8 (*m*, 1 H, H–C(4)); 4.95–5.2 (*m*, 2 H, 2 H–C(6)); 5.65–6.15 (*m*, 1 H, H–C(5)).

$C_{10}H_{20}O$ (156.27) Calc. C 76.86 H 12.90% Found C 76.67 H 13.04%

3-Cyclohexyl-4-methyl-5-hexen-3-ol (**12**). From **2a** and cyclohexyl ethyl ketone; yield 76%. – ^{1}H-NMR.: 0.75–1.95 (*m*, 20 H); 0.92 and 1.04 (2 *d*, *J* = 7, H_3C–C(4), diastereomeric ratio 40:60); 2.3–2.7 (*m*, 1 H, H–C(4)); 4.9–5.2 (*m*, 2 H, 2 H–C(6)); 5.6–6.2 (*m*, 1 H, H–C(5)).

$C_{13}H_{24}O$ (196.34) Calc. C 79.53 H 12.32% Found C 79.57 H 12.20%

3-Hydroxy-2-methyl-3-phenylbutanoic acid (**13**). To a solution of 931 mg (5.28 mmol) **5b** in 75 ml dioxane *(Fluka, puriss.)* and 225 ml H_2O were added 350 mg $NaHCO_3$, 8.94 g (41.8 mmol) $NaIO_4$, and 112 g (0.71 mmol) $KMnO_4$. The purple solution was stirred for 1 h. Since the $KMnO_4$ was consumed after 1 h as indicated by the change of the color from purple to red, the same amount of $KMnO_4$ was added as above. After three more hours, the reaction mixture was worked up with ether. The acid **13** could be separated by extraction with sat. K_2CO_3-solution and reacidification with phosphoric acid. – Yield of **13** 615.5 mg (3.17 mmol, 60%). This reaction was done repeatedly, and in some cases partial epimerization occurred. – ^{1}H-NMR.: 1.18 (*d*, *J* = 7, 3 H, H_3C–C(2)); 1.43 (*s*, 3 H, 3 H–C(4)); 2.95 (*qa*, *J* = 7, 1 H, H–C(2)); 6.6–7.2 (br., 2 H, OH and COOH); 7.2–7.5 (*m*, 5 H, arom. H).

2-Methyl-3-phenyl-3-butanolid (**14**). A solution of 188 mg (0.97 mmol) **13** in 4 ml pyridine *(Fluka, purum)* was cooled to 0°–5° and 250 µl (1.95 mmol) of benzenesulfonyl chloride were added. The mixture was stirred well and placed in the refrigerator (+ 5°) overnight. The workup consisted of pouring the reaction mixture on to five volumes of crushed ice and extracting several times with ether. The combined ethereal layers were washed with sat. $NaHCO_3$-solution and H_2O and after drying ($MgSO_4$), the ether was evaporated at reduced pressure. Yield 140 mg (0.79 mmol, 82%) of lactone **14** as yellow oil. – ^{1}H-NMR.: 1.42 (*d*, *J* = 8, 3 H, H_3C–C(2)); 1.75 (*s*, 3 H, 3 H–C(4)); 3.65 (*d*, *J* = 8, 1 H, H–C(2)); 7.15–7.5 (*m*, 5 H, arom. H).

(E)-2-Phenyl-2-butene (**15**). The crude lactone **14** (140 mg) was heated in a *Kugelrohr* oven to 140–160° at atmospheric pressure. After 30 min the product was destilled at reduced pressure to give 97 mg (0.60 mmol, 76%) of **15**. The olefin structure was confirmed by ^{1}H-NMR. spectroscopy, applying the increment method [31], and by comparison with literature data [19] [20]. – ^{1}H-NMR.: 1.76 (*d*, *J* = 7, 3 H, 3 H–C(4)); 2.02 (*s*, 3 H, 3 H–C(1)); 5.82 (*qa*, *J* = 7, 1 H, H–C(3)).

3-Hydroxy-2,4,4-trimethyl-3-phenylpentanoic acid (**16**). Obtained as described for **13**; yield 52%. – ^{1}H-NMR.: 0.8–1.1 (*m*, 12 H, 3 H_3C–C(4), H_3C–C(2)); 3.37 (*qa*, *J* = 6, 1 H, H–C(2)); 7.1–7.5 (*m*, 6 H, arom. H, OH and COOH).

2,4,4-Trimethyl-3-phenyl-3-pentanolid (**17**). This compound was prepared in 84% yield as described for **14**, m.p. 79–81° (from petroleum ether). – ^{1}H-NMR.: 0.9–1.15 (*m*, 12 H, 3 H_3C–C(4), H_3C–C(2)); 3.88 (*qa*, *J* = 7.5, 1 H, H–C(2)); 6.85–7.65 (*m*, 5 H, arom. H).

(E)-4,4-Dimethyl-3-phenyl-2-penten (**18**). The olefin **18** was obtained in 80% yield by heating the recrystallized lactone **17** to 140–160° (*cf.* the preparation of **15**). The structure was confirmed by comparison of the ^{1}H-NMR. spectrum with data in [24]. – ^{1}H-NMR.: 1.03 (*s*, 9 H, 3 H_3C–C(4)); 1.28 (*d*, *J* = 6, 3 H, 3 H–C(1)); 5.63 (*qa*, *J* = 6, 1 H, H–C(2)); 6.9–7.45 (*m*, 5 H, arom. H).

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