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Stereoselective Synthesis of β-Ketoesters from Prop-2-yn-1-ols

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ABSTRACT: The activation of allylic prop-2-yn-1-ols by the $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ catalyst in the presence of carboxylic acids leads to unsaturated β-ketoesters in one step. The utilization of optically active prop-2-yn-1-ols provides a new stereoselective access to optically active β-ketoesters with retention of configuration at the propargylic carbon. © 1997 Elsevier Science Ltd.

β-Ketoesters have been shown to be valuable organic intermediates for the access to heterocycles such as furanones, imidazoles and oxazinones due to the presence of their reactive carbonyl group.[1] Their ketonic group has been involved in the Wittig reaction to give allylic esters,[2] and its reduction in the presence of enzymes has led to optically pure monoesters of 1,2-diols,[3] which is an alternative route to that recently opened *via* the enantioselective hydrogenation of carbonates.[4] β-Ketoesters are also acylating reagents,[5] operating under mild conditions, especially useful for peptide synthesis.[6] In the presence of a Lewis acid, α-unsaturated β-ketonic esters undergo highly regio- and stereoselective Diels-Alder reactions with 1,3-dienes to afford cyclohexene derivatives bearing geminal ketonic and ester functionalities.[7]

β-Ketoesters are usually prepared by esterification of β-ketoalcohols with anhydrides[8] or acyl chlorides,[9] or reaction of carboxylates with α-chloroketones.[10] They have also been obtained by hydration of prop-2-ynyl carboxylates in the presence of mercury(II)[11] or gold(III)[12] salts. The hydrolysis of dioxolium salts also provides ketoesters in good yields.[13] The palladium(II)-catalyzed oxidation of allyl acetate by hydrogen peroxide selectivity gives 3-acetoxypropan-2-one.[14] The selective copper(I)[15] or palladium/copper[16]-catalyzed cross-coupling of α-alkoxystannanes with acyl chlorides also offer efficient syntheses of β-ketoesters.

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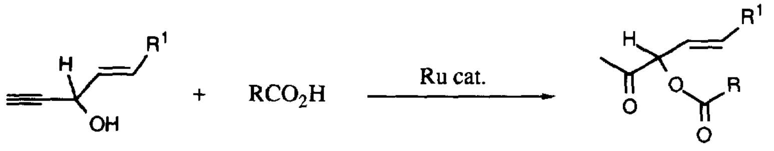
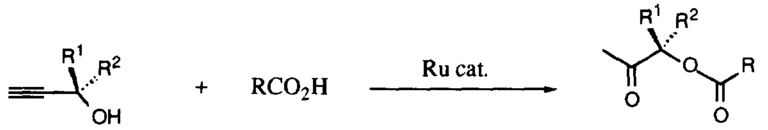
We have already reported the one-step synthesis of β-ketoesters from simple terminal alk-2-yn-1-ols[6,17] such as propargyl alcohol or 2-methylbut-3-yn-2-ol, and carboxylic acids catalyzed by ruthenium complexes. We now report i) the development of this catalytic synthesis towards the formation of ketonic allylic esters from unsaturated (1-ethynyl) alcohols (equation 1), ii) the preparation of optically enriched terminal prop-2-yn-1-ols and their use for the stereoselective preparation of optically active β-ketoesters *via* ruthenium-catalyzed addition of carboxylic acids (equation 2).



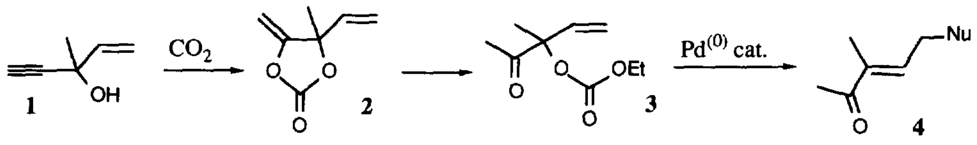
Equation 1



Equation 2

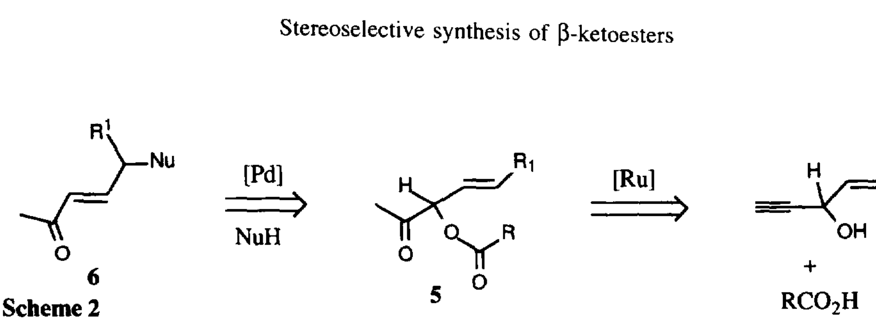
RUTHENIUM-CATALYZED SYNTHESIS OF 2-OXOPENT-4-EN-3-YL ESTERS FROM PENT-1-EN-4-YN-3-OLS

3-Methyl-2-oxopent-4-en-3-yl ethyl carbonate **3** has been shown to be useful for the stereoselective preparation of conjugated enones **4** *via* palladium-catalyzed allylation of nucleophiles[18] (Scheme 1). The carbonate **3** resulted from the ring-opening of the cyclic carbonate **2** which was obtained from the unsaturated prop-2-yn-1-yl alcohol **1** and CO_2. Unfortunately, the preparation of such cyclic carbonates was efficient only from tertiary alcohols so that the secondary derivatives of type **3** ($MeCOC\mathit{H}(CH=CH_2)Y$), with an allylic leaving group Y= OCO_2R, could not be reached by this route.



Scheme 1: Palladium-catalyzed nucleophilic substitution of carbonates

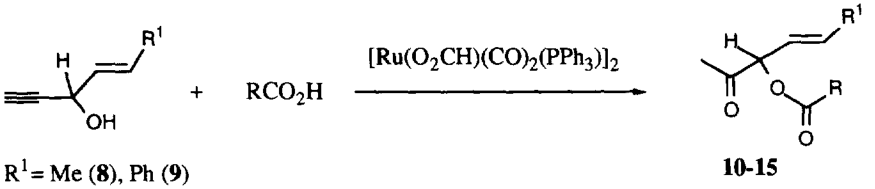
We have thus considered the possible obtention of such derivatives (Y= OCOR)*via* the ruthenium-catalyzed activation of alkenyl prop-2-yn-1-ols **1**. The addition of carboxylic acid could lead to β-ketoesters of type **5** and provide a solution to the preparation of but-3-en-2-ones **6** without substituent at the olefinic C(3) carbon atom *via* palladium-catalysis (Scheme 2).



6 5

Scheme 2

The alkenyl prop-2-yn-1-ols **7**, **8** and **9** were first prepared in 60, 85 and 85% respective yields, upon reaction of lithium acetylide with acrolein, crotonaldehyde and *trans*-cinnamaldehyde, respectively, at 80 °C in tetrahydrofuran followed by quenching with a saturated ammonium chloride solution.[19] The reaction of a variety of carboxylic acids with the 1-alkenyl prop-2-yn-1-ols **8-9** in the presence of 0.5 mol% of the binuclear ruthenium complex $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$,[20] led to the formation of the unsaturated β-ketoesters **10-15**. Thus, when 10 mmol of carboxylic acid (acetic, diphenylacetic, pivalic and benzoic acid), 10 mmol of alkenyl propynols **8** and **9**, and 0.05 mmol of ruthenium catalyst were heated in toluene (10 mL) at 80-110 °C (equation 3), the complete transformation of the alkynol was achieved after 15-20 h and the esters **10-15** were isolated by distillation under reduced pressure in 50-70% yield (Table 1).



R^1= Me (**8**), Ph (**9**)

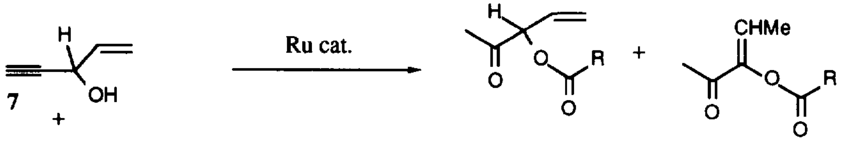
10-15

Equation 3

Table 1. Ruthenium-catalyzed synthesis of unsaturated β-ketoesters **10-15**

Acid	Alkynol	Conditions	Ester		Yield (%)
CH_3CO_2H	**8**	80 °C / 33 h	R= R^1= Me	**10**	65
$PhCO_2H$	**8**	80 °C / 20 h	R= Ph, R^1= Me	**11**	68
Ph_2CHCO_2H	**8**	110 °C / 15 h	R= $CHPh_2$, R^1= Me	**12**	68
CH_3CO_2H	**9**	80 °C / 15 h	R= Me, R^1= Ph	**13**	47
$PhCO_2H$	**9**	80 °C / 16 h	R= R^1= Ph	**14**	63
Me_3CCO_2H	**9**	80 °C / 16 h	R= ^{t}Bu, R^1= Ph	**15**	55

From pent-1-en-4-yn-3-ol **7**, two types of esters were obtained, depending on the reaction conditions (equation 4). Thus, the addition of pivalic acid to **7** led to compounds **16a** and **17a** in a ratio **16a/17a** : 80/20 with an overall yield of 25% after 44 h at 80 °C, whereas the same reaction carried out at 110 °C for 20 h gave 51% of the esters **16a** and **17a** in a ratio **16a/17a** : 15/85. The reaction with diphenylacetic acid was even more selective as it gave only **16b** at 80 °C and only **17b** at 110 °C, both in 65% isolated yields after 14 and 20 h of reaction, respectively.



RCO_2H R= Me_3C (**a**), Ph_2CH (**b**) **16a-b** **17a-b**

Equation 4

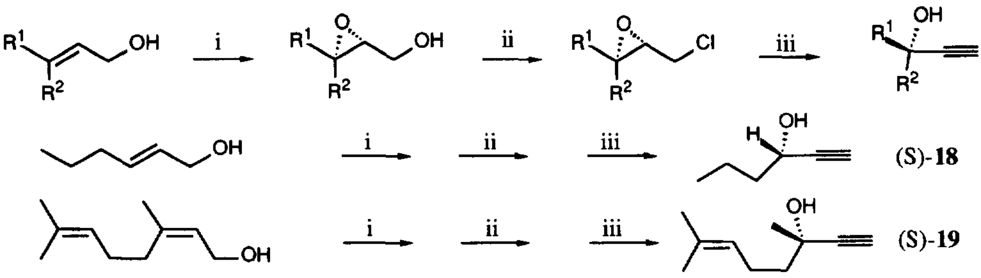
These results show that the formation of the allylic esters **16a-b** is favoured at 80 °C and the vinyl esters **17a-b** are preferentially produced at higher temperature. The transformation of **16** into **17** may result from a thermal sigmatropic rearrangement but we have shown that without ruthenium catalyst the conversion of **16b** into **17b** at 110 °C was only 40% after 14 h of heating, whereas it was complete in the catalytic reaction with 0.5 mol% of ruthenium catalyst. It is noteworthy that ketoesters of type **17** have already been prepared by acylation of biacetyl[7c] and used as Diels-Alder dienophiles.[7]

PREPARATION OF OPTICALLY ACTIVE β-KETOESTERS

We had already shown that the ruthenium-catalyzed addition of carboxylic acids to sterically hindered steroids containing the geminal ethynyl and hydroxy groups attached to a rigid cyclic skeleton, stereoselectively led to β-ketoesters. The study of the stereoselectivity of this catalytic transformation applied to optically active tertiary and secondary prop-2-yn-1-ols containing only one chiral carbon centre, not involved in a rigid cyclic structure, required the preparation of such acetylenic alcohols. We investigated the preparation of optically active propargylic alcohols according to two methods : i) a catalytic synthesis based on the *asymmetric epoxidation* of allylic alcohols, ii) an *enzymatic process* based on the stereoselective hydrolysis of propynyl acetates.

The *Sharpless epoxidation* of allylic alcohols[22] is one of the rare methods which make possible the access to tertiary optically active propargylic alcohols in three steps with satisfactory enantioselectivity according to Scheme 3.[23] This method applied to (*E*)-hex-2-en-1-ol and geraniol led to the alcohols (S)-(-)-**18** and (S)-(-)-**19** in 58 and 77% yields, respectively. Their absolute configurations were deduced from literature data,[22,23c] and their enantiomeric excesses determined by ^1H NMR from the corresponding Mosher esters, were respectively 78 and 65%.

The *enzymatic resolution* of tertiary acetylenic acetates, especially with one trifluoromethyl group as substituent of the propargylic carbon has been shown to give optically active prop-2-yn-1-ols.[24] The enantioselective hydrolysis of secondary prop-2-ynyl acetates in the presence of a lipase also provided an efficient method to produce optically active secondary prop-2-yn-1-ols.[25]



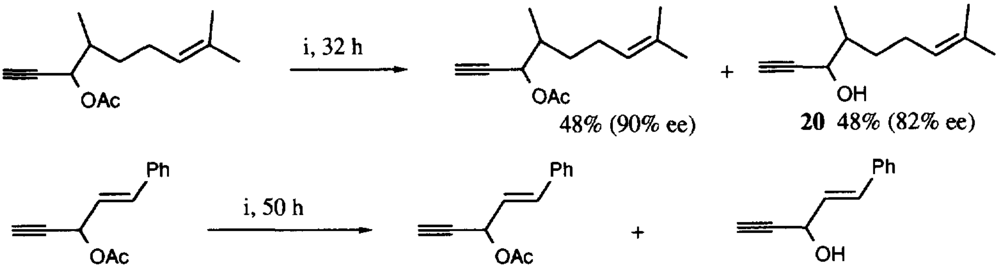
(S)-18

(S)-19

i) Bu^tOOH, $Ti(OPr^i)_4$ / (L)-(+)-diisopropyltartrate, molecular sieve 4Å, CH_2Cl_2, -25 °C ;
ii) PPh_3, CCl_4, $NaHCO_3$, reflux ; iii) BuLi, - 30 °C

Scheme 3. Preparation of optically active prop-2-yn-1-yl alcohols *via* enantioselective epoxidation of allylic alcohols

We have attempted the enzymatic hydrolysis of prop-2-yn-1-ylic acetates with enzymes (*Candidae Cylindracea Lipase, Pseudomonas Fluorescens Lipase, Lipozyme*) and shown that the porcine pancreatic lipase (PPL) gave the best results and made possible the preparation of the optically active alcohols **20** and (-)-**9** with enantiomeric excesses of 82 and 100%, respectively (Scheme 4).



48% (90% ee) | **20** 48% (82% ee)

46% (66% ee) | (-)-**9** 43% (100% ee)

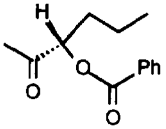
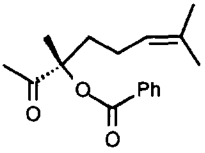
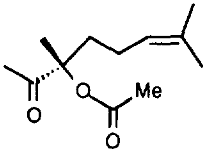
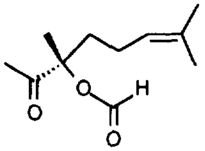
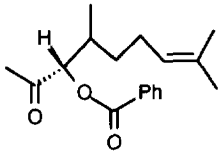
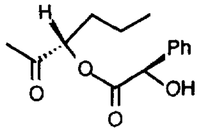
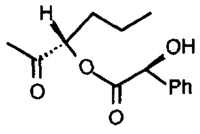
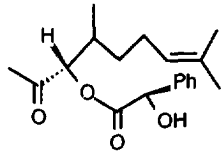
i) PPL, phosphate buffer 0.1 M, pH= 7, room temperature $[\alpha]_D$ = -12 ((c= 2.1, $CHCl_3$, 20 °C)

Scheme 4. Preparation of optically active pro-2-yn-1-ylic alcohols *via* enzymatic hydrolysis of propynylic acetates

RUTHENIUM-CATALYZED PREPARATION OF OPTICALLY ENRICHED β-KETOESTERS

In a preliminary communication,[21a] we have previously established that the concomitant ruthenium-catalyzed transformations of geminal ethynyl and hydroxy groups of steroids, into acetyl and ester functions *via* addition of carboxylic acids, took place with retention of configuration at the asymmetric C(17) centre. We have now studied the stereoselectivity of this reaction starting from the acyclic optically active prop-2-yn-1-ols **18-20**.

Table 2. Preparation of the optically active β-ketoesters **21-28**

run	Acid	Alkynol	ee (%)	Ester		Yield (%)	de (%)
1	$PhCO_2H$	(S)-**18**	78		(+)-**21**	73	
2	$PhCO_2H$	(S)-**19**	65		(-)-**22**	83	
3	$MeCO_2H$	"	"		(-)-**23**	74	
4	HCO_2H	"	"		(+)-**24**	65	
5	$PhCO_2H$	**20**	82		(+)-**25**	98	
6	(R)-$PhCH(OH)CO_2H$	(S)-**18**	78		(-)-**26**	54	74
7	(S)-$PhCH(OH)CO_2H$	"	"		(+)-**27**	68	75
8	(R)-$PhCH(OH)CO_2H$	**20**	82		(-)-**28**	61	76

Thus, the addition of a variety of achiral carboxylic acids to the propynylic alcohols **18-20** in toluene in the presence of 0.5 mol% of the binuclear $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ catalyst precursor, led to optically active β-ketoesters in good chemical yields (Table 2 - runs 1-5). The transformation of the secondary acetylenic alcohols **18** and **20** was performed at 80 °C and gave the esters **21** and **25** in 73 and 98% isolated yields, respectively. From the tertiary propynol **19**, a higher reaction temperature of 100 °C was required to obtain a complete conversion in less than 30 h, and the optically active β-ketoesters **22-24** were collected in 83, 74 and 65% yields, respectively.

The addition of the optically pure (R)- and (S)-mandelic acids made possible the preparation of the ketoesters **26** and **27** containing two asymmetric centres from the alcohol **18**, and the ester **28** with three stereocentres from the alkynol **20** (Table 2). By ^{1}H NMR, it was possible to determine the amount of each diastereoisomer and calculate the diastereoisomeric excess. Thus, starting from the propynol (S)-**18** (ee= 78%), the corresponding ketonic (R)- and (S)-mandelates were formed with diastereoisomeric excesses of 74 and 75%, respectively, whereas the addition of (R)-mandelic acid to **20** (82% ee) led to the ester **28** with a diastereoisomeric excess of 76%. These results show that the catalytic reaction is stereoselective with acyclic optically active prop-2-yn-1-ols and takes place without significant racemization as shown by the optical purity of the esters compared to the enantiomeric purity of the starting chiral alkynols. It demonstrates that it is possible to obtain optically active β-ketoesters from acyclic optically active prop-2-yn-1-ols and carboxylic acids in the presence of $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ as catalyst precursor.

CONCLUSION

The addition of carboxylic acids to prop-2-yn-1-ols, catalyzed by the binuclear $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ complex provides an efficient one-step synthesis of β-ketoesters. α-Alkenyl-β-keto esters are readily accessible from alkenyl acetylenic alcohols in good yields, and the presence of the unsubstituted double bond in pent-1-en-4-yn-3-ol **7** offers the possibility to obtain β-keto-α-enol esters. The use of optically active propargylic alcohols, prepared *via* enantioselective epoxidation of allylic alcohols and enzymatic resolution of propargylic acetates, has allowed the stereoselective preparation of optically active β-ketoesters with retention of configuration.

EXPERIMENTAL

All experiments were carried out in dry Schlenk tubes under an inert atmosphere of nitrogen. Hexane and pentane were distilled over calcium hydride, tetrahydrofuran, toluene and ether were distilled over sodium/benzophenone. Column chromatography was performed on Merck silicagel 30-60 μm. ^{1}H and ^{13}C NMR spectra were recorded on a Brucker AM 300 WB at 300 MHz and at 75 MHz, respectively with TMS as the internal standard. IR spectra were recorded on a Nicolet 205 FTIR-spectrometer and mass spectra were obtained at 70 eV with a high resolution spectrometer VARIAN MAT 311 by "Le Centre de Mesures Physiques de l'Ouest", Rennes, France. Elemental analyses were performed by "Le Service de Microanalyses du C.N.R.S.", Lyon, France.

Typical preparation of propargylic alcohols ***7-9*** *:*

Acetylene (200 mmol) was dissolved in dry THF (100 ml), cooled at -80 °C, and a solution of n-BuLi (1.6 M in hexanes - 150 mmol) was added dropwise.[19] The mixture was stirred at -80 °C for 15 min and a solution of aldehyde or ketone (150 mmol) was added dropwise and stirred for 15 min at -80 °C. A saturated aqueous NH_4Cl solution was slowly added and the mixture was warmed up to room temperature followed by addition of diethylether. The aqueous layer was extracted twice with diethylether and the combined organic phases were dried over $MgSO_4$ and concentrated.

pent-4-en-1-yn-3-ol (7). Obtained from acetylene (300 mmol) in THF (200 ml), n-BuLi (250 mmol) and acrolein (200 mmol) as a colourless liquid (9.01 g, 55%) after distillation at 30 °C under 20 mm Hg ; IR ν/cm^{-1} 3400 (OH), 3300 (≡C-H), 3100 (=C-H), 2130 (C≡C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 6.0-5.9 (m, 1 H, =CH), 5.45 (dt, 1 H, ^3J= 17.1 Hz, ^2J= 1.3 Hz, $=CH\underline{H}_{trans}$), 5.20 (dt, 1 H, ^3J= 10.2 Hz, ^2J= 1.3 Hz, $=CH\underline{H}_{cis}$), 4.85 (m, 1 H, $C\underline{H}OH$), 2.97 (s, 1 H, OH), 2.55 (s, 1 H, ≡CH). Anal. calcd. for C_5H_6O : C, 73.15 ; H, 7.37. Found : C, 73.07 ; H, 7.38.

(E)-hex-4-en-1-yn-3-ol (8). Obtained from acetylene (150 mmol) in THF (70 ml), n-BuLi (125 mmol) and crotonaldehyde (100 mmol) as a colourless oil (6.35 g, 71%) after distillation at 30-35 °C under 20 mm Hg ; IR ν/cm^{-1} 3395 (OH), 3297 (≡C-H), 2123 (C≡C), 1666 and 1644 (C=C), 965 ((*E*)-CH=CH) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 5.92-5.52 (m, 2 H, CH=CH), 4.78 (d, 1 H, ^3J= 5.0 Hz, $C\underline{H}$-OH), 2.51 (d, 1 H, ^4J= 2.1 Hz, HC≡), 1.67 (d, 3 H, ^3J= 6.5 Hz, Me) Anal. calcd. for C_6H_8O : C, 74.97 ; H, 8.39. Found : C, 75.12 ; H, 8.35.

(E)-5-phenylpent-4-en-1-yn-3-ol (9). Obtained from acetylene (100 mmol) in THF (50 ml), n-BuLi (75 mmol) and *trans*-cinnamaldehyde (60 mmol) as a white solid (7.043 g, 85%) after crystallization (diethylether/pentane). IR ν/cm^{-1} 3395 (OH), 3310 (≡C-H), 2120 (C≡C), 1590 (C=C), 970 ((*E*)-C=C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 7.28 (m, 5 H, Ph), 6.72 (dd, 1 H, ^3J= 15.8 Hz, ^4J= 0.9 Hz , $CH=C\underline{H}Ph$), 6.23 (dd, 1 H, ^3J= 15.8 Hz, ^3J= 5.9 Hz, $C\underline{H}=CHPh$), 4.99 (d, 1 H, J= 5.7 Hz, $C\underline{H}$-OH), 2.56 (d, 1 H, ^4J= 2.1 Hz, HC≡), 2.26 (s, 1 H, OH) ; Anal. calcd. for $C_{11}H_{10}O$: C, 83.52 ; H, 6.37. Found : C, 83.70 ; H, 6.38.

General procedure for the synthesis of the racemic β-oxopropyl esters ***10-17***.

Propargylic alcohol (10 mmol) was added to a mixture of carboxylic acid (10 mmol), $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.05 mmol) and anhydrous toluene (10 ml). The mixture was stirred and heated at 80-110 °C and the reaction was monitored by GC or TLC. The mixture was diluted with diethylether (20 ml), washed with a saturated aqueous $NaHCO_3$ solution (15 ml). The aqueous layer was extracted with ether and the combined organic phases were dried over $MgSO_4$ and evaporated. The products were purified by column chromatography over silica gel or by distillation.

2-oxohex-4-en-3-yl acetate (10). Obtained from **8** (7.5 mmol), acetic acid (10 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.038 mmol) in anhydrous toluene (10 ml) after 33 h at 80 °C as a yellow oil (0.700 g, 65%) after a bulb-to-bulb distillation (Kugelrohr) at 150 °C under 0.5 mm Hg ; IR ν/cm^{-1} 1754 (C=O), 1733 (C=O), 1602 (C=C), 1236 (C-O) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 5.96 (dq, 1 H, ^3J= 14.8 Hz, ^3J= 6.6 Hz, $CH=C\underline{H}Me$), 5.56 (d, 1 H, ^3J= 8.1 Hz, $C\underline{H}COMe$), 5.45 (ddq, 1 H, ^3J= 14.8 Hz, ^3J= 8.0 Hz, ^4J= 1.6 Hz, $C\underline{H}=CHMe$), 2.13 (s, 3 H, MeCO), 2.11 (s, 3 H, MeCO), 1.74 (dd, 3 H, ^3J= 6.6 Hz, ^4J= 1.2 Hz, $CH=CH\underline{Me}$) ; ^{13}C NMR δ (75.5 MHz, $CDCl_3$) 202.77 (s, $Me\underline{C}O$), 170.06 (q, $^2J_{CH}$ = 3.2 Hz, Me CO_2), 134.09 (dm, $^1J_{CH}$ = 149.4 Hz, $CH=\underline{C}HMe$), 122.82 (dm, $^1J_{CH}$ = 159.0 Hz, $\underline{C}H=CHMe$), 79.82 (d, $^1J_{CH}$ = 154.8 Hz, $\underline{C}HCOMe$), 25.86 (q, $^1J_{CH}$ = 128 Hz, $CO\underline{Me}$), 20.56 (q, $^1J_{CH}$ = 130 Hz, $\underline{Me}CO_2$), 17.95 (qd, $^1J_{CH}$ = 127 Hz, $^2J_{CH}$ = 6.1 Hz, $CH=CH\underline{Me}$) ; HRMS calcd. for $C_6H_9O_2$ ($M^{+\bullet}$- $COCH_3$) 113.060. Found 113.060.

2-oxohex-4-en-3-yl benzoate (11). Obtained from **8** (7.5 mmol), benzoic acid (7.5 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.038 mmol) in anhydrous toluene (10 ml) after 20 h at 80 °C as a yellow oil (1.120 g, 68%) after a bulb-to-bulb distillation (Kugelrohr) at 150 °C under 1.5 mm Hg ; IR ν/cm^{-1} 1734 (C=O), 1719 (C=O), 1673 (C=C), 1609 (C=C), 1272 (C-O) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 8.10-7.41 (m, 5 H, Ph), 6.11-5.99 (m, 1 H, $CH=C\underline{H}Me$), 5.66-5.56 (m, 2 H, $C\underline{H}COMe$ + $C\underline{H}=CHMe$), 2.22 (s, 3 H, COMe), 1.79 (dd, 3 H, ^3J= 6.6 Hz, ^4J= 1.2 Hz, $CH=CH\underline{Me}$). Anal. calcd. for $C_{13}H_{14}O_3$: C, 71.54 ; H, 6.47. Found : C, 70.91 ; H, 6.51. HRMS calcd. for $C_{11}H_{11}O_2$ (M^+ - CH_3CO) 175.076. Found 175.077.

2-oxohex-4-en-3-yl diphenylacetate (12). Obtained from **8** (7.5 mmol), diphenylacetic acid (7.5 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol% - 0.038 mmol) in anhydrous toluene (10 ml) after 15 h at 110 °C as a brown oil (1.410 g, 61%) ; IR ν/cm^{-1} 1732 (C=O), 1637 (C=C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 7.34 - 7.10 (m, 10 H, Ph), 5.80 -5.79 (m, 1 H, $CH=C\underline{H}Me$), 5.42-5.35 (m, 2 H, $C\underline{H}=CHMe$ + $C\underline{H}COMe$), 5.06 (s, 1 H, $C\underline{H}Ph_2$), 2.00 (s, 3 H, COMe), 1.66 (dd, 3 H, ^3J= 6.6 Hz, ^4J= 1.0 Hz, Me). Anal. calcd. for $C_{20}H_{20}O_3$: C, 77.90 ; H, 6.54. Found : C, 77.98 ; H, 6.48.

5-phenyl-2-oxopent-4-en-3-yl acetate (13). Obtained from **9** (6.3 mmol), acetic acid (6.3 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.032 mmol) in anhydrous toluene (10 ml) after 15 h at 80 °C as a brown oil (0.649 g, 47%) after column chromatography over silica gel with hexane/ether mixtures as eluent ; IR ν/cm^{-1} 1738 (C=O), 1620 (C=C), 1238 (C–O), 970 ((*E*)-C=C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 7.42 - 7.22 (m, 5 H, Ph), 6.82 (d, 1 H, ^3J= 15.9 Hz, CH=C$\underline{H}$Ph), 6.16 (dd, 1 H, ^3J= 15.9 Hz ; ^3J= 7.8 Hz ; C$\underline{H}$=CHPh), 5.61 (dd, 1 H, ^3J= 7.8 Hz ; ^4J = 1.1 Hz ; C$\underline{H}$COMe), 2.23 (s, 3 H, MeCO), 2.19 (s, 3 H, COMe). HRMS calcd. for $C_{11}H_{11}O_2$ (M^+- CH_3CO) 175.076. Found 175.076.

5-phenyl-2-oxopent-4-en-3-yl benzoate (14). Obtained from **9** (6.3 mmol), benzoic acid (6.3 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.032 mmol) in anhydrous toluene (10 ml) after 16 h at 80 °C as an orange oil (1.109 g, 63%) after column chromatography over silica gel with hexane/ether mixtures as eluent ; IR ν/cm^{-1} 1721 (C=O), 1677 (C=O), 1610 (C=C), 1273 (C-O), 970 ((*E*)-C=C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 8.19-7.27 (m, 10 H, Ph), 6.91 (d, 1 H, ^3J= 15.9 Hz, CH=C$\underline{H}$Ph), 6.31 (dd, 1 H, ^3J= 7.5 Hz, ^3J= 15.9 Hz, C$\underline{H}$=CH-Ph), 5.86 (dd, 1 H, ^3J= 7.5 Hz, ^4J= 1.1 Hz, C$\underline{H}$COMe), 2.30 (s, 3 H, COMe). Anal. calcd. for $C_{18}H_{16}O_3$: C, 77.12 ; H, 5.75. Found : C, 77.30 ; H, 5.69.

5-phenyl-2-oxopent-4-en-3-yl pivalate (15). Obtained from **9** (6.3 mmol), pivalic acid (6.3 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.032 mmol) in anhydrous toluene (10 ml) after 16 h at 80 °C as a brown oil (0.893 g, 55%) after column chromatography over silica gel with hexane/ether mixtures as eluent ; IR ν/cm^{-1} 1729 (C=O), 1680 (C=O), 1610 (C=C), 1148 (C=O), 970 ((*E*)-C=C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 7.49-7.18 (m, 5 H, Ph), 6.73 (d, 1 H, ^3J= 15.9 Hz, CH=C$\underline{H}$Ph), 6.12 (dd, 1 H, ^3J= 15.9 Hz, ^3J= 7.44 Hz, C$\underline{H}$= CHPh), 5.50 (dd, 1 H, ^3J= 7.4 Hz, ^4J= 1.2 Hz, C$\underline{H}$-CH=CHPh) , 2.15 (s, 3 H, COMe), 1.23 (s, 9 H, Me_3C). HRMS calcd. for $C_{16}H_{20}O_3$ (M^+) 260.141. Found 260.140.

2-oxopent-4-en-3-yl pivalate (16a) and 2-oxopent-3-en-3-yl pivalate (17a). Obtained from **7** (8.5 mmol), pivalic acid (10 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.043 mmol) in anhydrous toluene (6 ml) after 20 h at 110 °C as a yellow oil (0.800 g, 51%) after a bulb-to-bulb distillation (Kugelrohr) at 100 °C under 0.5 mm Hg ; IR ν/cm^{-1} 1758 (C=O), 1691 (C=O), 1652 (C=C). HRMS calcd. for $C_{10}H_{16}O_3$ (M^+) 184.110. Found 184.111.

(*16a*) : ^{1}H NMR δ (300 MHz, $CDCl_3$) 5.93-5.74 (m, 1 H, C$\underline{H}$=CH_2), 5.51-5.34 (m, 3 H, CH=C$\underline{H_2}$ and C$\underline{H}$COMe), 2.14 (s, 3 H, COMe), 1.28 (s, 9 H, Me_3C).

(*17a*) : ^{1}H NMR δ (300 MHz, $CDCl_3$) 6.51 (q, 1 H, ^3J= 7.1 Hz, C=C$\underline{H}$Me), 2.26 (s, 3 H, COMe), 1.72 (d, 3 H, ^3J= 7.1 Hz, C=CH$\underline{Me}$), 1.32 (s, 9 H, Me_3C).

2-oxopent-4-en-3-yl diphenylacetate (16b). Obtained from **7** (8.5 mmol), diphenylacetic acid (10 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.043 mmol) in anhydrous toluene (10 ml) after 14 h at 80 °C as a white solid (0.927 g, 37%) after crystallization (dichloromethane/pentane) ; m. p. 96-98 °C ; IR ν/cm^{-1} 1743 (C=O), 1718 (C=O), 1617 (C=C) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 7.39 - 7.25 (m, 10 H, Ph), 5.90-5.79 (m, 1 H, C$\underline{H}$=CH_2), 5.52 (dt, 1 H, ^3J= 6.6 Hz, J= 1.1 Hz, C$\underline{H}$COMe), 5.41 (dt, 1 H, $^3J_{trans}$= 17.3 Hz, ^4J= 1.1 Hz, CH=CH$\underline{H}_{trans}$), 5.39 (dt, 1 H, $^3J_{cis}$= 10.5 Hz, ^4J= 1.1 Hz, CH=CH$\underline{H}_{cis}$), 5.17 (s, 1 H, $Ph_2C\underline{H}$), 2.08 (s, 3 H, COMe).

2-oxopent-3-en-3-yl diphenylacetate (17b). Obtained from **7** (9.7 mmol), diphenylacetic acid (10 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%. 0.049 mmol) anhydrous toluene (10 ml) after 17 h at 110 °C as a white solid (1.870 g, 65%) after crystallization (dichloromethane/pentane) ; m. p. 86-89 °C ; IR ν/cm^{-1} 1747 (C=O), 1675 (C=O), 1652 (C=C), 973 ((*E*)-CH=CH) ; ^{1}H NMR δ (300 MHz, $CDCl_3$) 7.42 - 7.25 (m, 10 H, Ph), 6.52 (q, 1 H, ^3J= 7.0 Hz, C=C$\underline{H}$Me), 5.28 (s, 1 H, $Ph_2C\underline{H}$), 2.25 (s, 3 H, COMe), 1.59 (d, 3 H, ^3J= 7.0 Hz, C=CH$\underline{Me}$). Anal. calcd. for $C_{19}H_{18}O_3$: C, 77.58; H, 6.17. Found : C, 77.79; H, 6.36. HRMS calcd. for $C_{19}H_{18}O_3$ (M^+) 294.126. Found 294.125.

Synthesis of optically active propargylic alcohols via enantioselective epoxidation.

L(+)-Diethyltartrate (0.6 mmol) and $Ti(O^iPr)_4$ (0.5 mmol) were stirred for 15 min at -20 °C under inert atmosphere in dry dichloromethane (35 ml) containing 4 Å molecular sieves (1 g). ^{t}-BuOOH (3 M in isooctane - 20 mmol) was added over a period of 5 min and the mixture was stirred for 0.5 h. A solution of allylic alcohol (10 mmol) in dry dichloromethane (5 ml) was slowly added at -20 °C. The mixture was stirred for 5 h at a temperature located in the range [-20/-15 °C], and then at room temperature for 1 h. This mixture was then poured at 0 °C into a solution of $FeSO_4 \cdot 7\ H_2O$ (12 mmol), tartaric acid (6 mmol) in an overall volume of 10 ml of distilled water. The mixture was vigorously stirred for 10 min and the aqueous layer was extracted with diethylether. The combined organic phases were stirred with NaOH (0.3 N, 1 ml) at 0 °C for 1 h. The mixture was diluted with water (5 ml) and the aqueous layer was extracted with diethylether (2x5 ml). The combined organic phases were dried over $MgSO_4$ and evaporated. The epoxyalcohol was isolated and characterized (IR, NMR, $[\alpha]_D$). It was then treated with 1.2 equiv.of triphenylphosphine and $NaHCO_3$ in refluxing CCl_4 to give the chlorinated oxirane. A solution of chlorooxirane (2.65 mmol) in dry THF (3 ml) was added dropwise at - 30 °C to a solution of n-BuLi (1.6 M in hexanes - 7.95 mmol) in dry THF (10 ml) under inert atmosphere. The mixture was stirred at - 30 °C for 1 h. A saturated aqueous NH_4Cl solution (10 ml) was slowly added and the mixture was warmed to room temperature. After addition of diethylether, the aqueous layer was extracted with CH_2Cl_2 (2x10 ml). The combined organic phases were dried over $MgSO_4$ and distillated.

(3S)-Hex-1-yn-3-ol (18).[22] IR ν/cm^{-1} 3369 (OH), 3306 (≡C-H), 2108 (C≡C) ; ^1H NMR δ (300 MHz, $CDCl_3$) 4.37 (td, 1 H, ^3J= 6.6 Hz, ^4J= 2.1 Hz, $C\underline{H}(OH)$), 2.10 (d, 1 H, ^4J= 2.1 Hz, HC≡), 2.10 (s, 1 H, OH), 1.42–1.78 (m, 4 H, CH_2), 0.94 (t, 3 H, ^3J= 7.3 Hz, CH_3). Anal. calcd. for $C_6H_{10}O$: C, 73.43 ; H, 10.27. Found : C, 73.25 ; H, 10.41. $[\alpha]_D$ = - 13.4 (c= 1.05, $CHCl_3$, 20 °C) ; ee = 78% (determined by ^1H NMR of the Mosher ester and by ^1H NMR with $Eu(hfc)_3$ as chiral shift reagent).

(3S)-3,7-dimethyloct-6-en-1-yn-3-ol (19).[23c] ^1H NMR δ (300 MHz, $CDCl_3$) 5.17 (m, 1 H, $C\underline{H}=C(Me)_2$), 2.45 (s, 1 H, HC≡), 2.04-2.30 (m, 3 H, CH_2 + OH), 1.62-1.73 (m, 2 H, CH_2), 1.70 (d, 3 H, ^4J= 1.9 Hz, $CH=CMe_2$), 1.60 (s, 3 H, $CH=CMe_2$), 1.50 (s, 3 H, CMe(OH)). Anal. calcd. for $C_{10}H_{16}O$: C, 78.90 ; H, 10.59. Found : C, 78.25 ; H, 10.84. $[\alpha]_D$ = - 8.0 (c= 2.0, $CHCl_3$, 20 °C) ; ee = 65% (determined by ^1H NMR of the Mosher ester).

Synthesis of optically active propargylic alcohols via enzymatic hydrolysis.

(3S)-4,8-dimethylnon-7-en-1-yn-3-ol (20). Racemic 4,8-dimethylnon-7-en-1-yn-3-yl acetate (500 mg, 3.01 mmol) was added to a mixture of enzyme (P.P.L., 500 mg) and phosphate buffer (0.1 M, pH= 7.00, 10 ml). The mixture was vigorously stirred at room temperature for 32 h and the reaction was monitored by TLC. The reaction was stopped by filtration of the enzyme through a bed of *Celite*® when the conversion of the starting acetate had reached 50%. The aqueous layer was extracted with diethylether (2x20 ml). The organic layer was dried over $MgSO_4$ and evaporated. The alcohol was separated from the residual acetate by column chromatography over silica gel. IR ν/cm^{-1} 3395 (OH), 3303 (≡C-H), 2108 (C≡C) ; ^1H NMR δ (300 MHz, $CDCl_3$) 5.04-5.06 (m, 1 H, $C\underline{H}=CMe_2$), 4.18-4.23 (m, 1 H, $C\underline{H}OH$), 2.38 (t, 1 H, ^4J= 2.1 Hz, HC≡), 2.10 (s, 1 H, OH), 2.02 - 1.86 (m, 2 H, CH_2), 1.75- 1.64 (m, 2 H, CH_2), 1.62 (s, 3 H, $CH=C\underline{Me_2}$), 1.54 (s, 3 H, $CH=C\underline{Me_2}$), 1.26-1.13 (m, 1 H, $C\underline{H}Me$), 0.99 (d, 3/2 H, ^3J= 6.7 Hz, Me), 0.98 (d, 3/2 H, ^3J= 6.7 Hz, Me). HRMS calcd for $C_{11}H_{18}O$ (M^+) 166.136. Found 166.136. ee = 82% (determined by ^1H NMR with $Eu(hfc)_3$ as chiral shift reagent).

Synthesis of optically active β-oxopropyl esters

2-oxohex-3-yl benzoate (21). Obtained from **18** (4.08 mmol), benzoic acid (4.08 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.02 mmol) in anhydrous toluene (5 ml) after 17 h at 80 °C as a colourless oil (0.642 g, 73%) after bulb-to-bulb distillation (Kugelrohr) at 155 °C under 0.5 mm Hg ; IR ν/cm^{-1} 1721 (C=O), 1277 (C–O) ; ^1H NMR δ (300 MHz, $CDCl_3$) 8.17 - 7.43 (m, 5 H, Ph), 5.23 (t, 1 H, ^3J= 6.4 Hz, CH), 2.12 (s, 3 H, COMe), 1.91 - 1.83 (m, 2 H, CH_2), 1.58-1.44 (m, 2 H, CH_2), 0.98 (t, 3 H, ^3J= 7.4 Hz, Me). $[\alpha]_D$ = + 6.19 (c = 2.1, $CHCl_3$, 20 °C).

3,7-dimethyl-2-oxooct-6-en-3-yl benzoate (22). Obtained from **19** (3.00 mmol), benzoic acid (3.00 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.017 mmol) in anhydrous toluene (6 ml) after 35 h at 100 °C as a brown oil (681 mg, 83%) after bulb-to-bulb distillation (Kugelrohr) at 180 °C under 0.5 mm Hg ; IR ν/cm^{-1} 1720 (C=O), 1679 (C=C), 1603 (C=C), 1286 (C–O) ; ^1H NMR δ (300 MHz, $CDCl_3$) 8.08-7.36 (m, 5 H, Ph), 5.06-5.01 (m, 1 H, $C\underline{H}=CMe_2$), 2.10 (s, 3 H, COMe), 2.04-1.71 (m, 4 H, CH_2), 1.59 (s, 3 H), 1.56 (s, 3 H), 1.53 (s, 3 H). $[\alpha]_D$ = - 3.38 (c = 3.25, $CHCl_3$, 20 °C).

3,7-dimethyl-2-oxooct-6-en-3-yl acetate (23). Obtained from **19** (3.00 mmol), acetic acid (3.00 mmol) and $[Ru(\mu\text{-}O_2CH)(CO)_2(PPh_3)]_2$ (0.5 mol%, 0.017 mmol) in anhydrous toluene (6 ml) after 41 h at 100 °C as a yellow oil (468 mg, 74%) after bulb-to-bulb distillation (Kugelrohr) at 130 °C under 0.5 mm Hg ; IR ν/cm^{-1} 1737 (C=O), 1674 (C=C) ; ^{1}H NMR δ (300 MHz, CDCl$_3$) 5.03 (t hept, 1 H, ^{3}J= 6.7 Hz, ^{4}J= 1.4 Hz, CH=CMe$_2$), 2.12 (s, 3 H, COMe), 2.09 (s, 3 H, COMe) ; 1.82-2.08 (m, 4 H, CH$_2$), 1.68 (s, 3 H), 1.59 (s, 3 H), 1.50 (s, 3 H). [α]$_D$ = - 7.1 (c = 1.55, CHCl$_3$, 20 °C).

3,7-dimethyl-2-oxooct-6-en-3-yl formate (24). Obtained from **19** (3.00 mmol), formic acid (3.00 mmol) and [Ru(μ-O$_2$CH)(CO)$_2$(PPh$_3$)]$_2$ (0.5 mol%, 0.017 mmol) in anhydrous toluene (6 ml) after 14 h at 100 °C as a yellow oil (382 mg, 65%) after bulb-to-bulb distillation (Kugelrohr) at 150 °C under 0.5 mm Hg ; IR ν/cm^{-1} 1724 (C=O), 1721 (C=O), 1680 (C=C) ; ^{1}H NMR δ (300 MHz, CDCl$_3$) 8.01 (s, 1 H, HCO$_2$), 5.03 (m, 1 H, CH=CMe$_2$), 2.17 (s, 3 H, COMe), 1.72-1.10 (m, 4 H, CH$_2$), 1.68 (s, 3 H), 1.59 (s, 3 H), 1.57 (s, 3 H). [α]$_D$ = + 9.0 (c = 1.0, CHCl$_3$, 20 °C).

4,8-dimethyl-2-oxonon-7-en-3-yl benzoate (25). Obtained from **20** (2.41 mmol), benzoic acid (2.41 mmol) and [Ru(μ-O$_2$CH)(CO)$_2$(PPh$_3$)]$_2$ (0.5 mol%, 0.013 mmol) in anhydrous toluene (6 ml) after 26 h at 80 °C as a yellow oil (678 mg, 98%) after column chromatography over silica gel with hexane/ether mixtures as eluent ; IR ν/cm^{-1} 1720 (C=O), 1605 (C=C), 1283 (C–O) ; ^{1}H NMR δ (300 MHz, CDCl$_3$) 8.03-7.38 (m, 5 H, Ph), 5.20 (d, 1/2 H, ^{3}J= 3.1 Hz, MeCOC$\underline{H}$), 5.08 (d, 1/2 H, ^{3}J= 4.3 Hz, MeCOC$\underline{H}$), 5.03-4.98 (m, 1 H, CH=CMe$_2$), 2.14 (s, 3/2 H, MeCO), 2.13 (s, 3/2 H, MeCO), 1.81-2.06 (m, 2 H, CH$_2$), 1.61 (s, 3 H, CH=CMe$_2$), 1.53 (s, 3 H, CH=CMe$_2$), 1.49-1.11 (m, 3 H, CH$_2$ and C$\underline{H}$Me), 1.00 (d, 3/2 H, ^{3}J= 7.0 Hz, $\underline{Me}$CH), 0.96 (d, 3/2 H, ^{3}J= 6.8 Hz, $\underline{Me}$CH). Anal. calcd. for C$_{18}$H$_{24}$O$_3$: C, 74.97 ; H, 8.39. Found : C, 74.67 ; H, 8.68. HRMS calcd. for C$_{18}$H$_{24}$O$_3$ (M$^+$) 288.172. Found 288.170. [α]$_D$ = + 10.0 (c= 2.0, CHCl$_3$, 20 °C).

2-oxohex-3-yl-(R)-mandelate (26). Obtained from **18** (4.08 mmol), (R)-mandelic acid (4.08 mmol) and [Ru(μ-O$_2$CH)(CO)$_2$(PPh$_3$)]$_2$ (0.5 mol%, 0.02 mmol) in anhydrous toluene (5 ml) after 16 h at 80 °C as a yellow oil (521 mg, 54%) after bulb-to-bulb distillation (Kugelrohr) at 210 °C under 0.5 mm Hg ; IR ν/cm^{-1} 3463 (OH), 1727 (C=O) ; ^{1}H-NMR δ (300 MHz, CDCl$_3$)

1st diastereoisomer (85%) : 7.25-7.71 (m, 5 H, Ph), 5.32 (s, 1 H, C$\underline{H}$OH), 5.01 (d, 1/2 H, ^{3}J= 7.8 Hz, C$\underline{H}$CH$_2$), 4.99 (d, 1/2 H, ^{3}J= 7.2 Hz, C$\underline{H}$-CH$_2$), 2.15 (s, 3 H, COMe), 0.84-0.99 (m, 4 H, CH$_2$), 0.73 (t, 3 H, ^{3}J= 7.3 Hz, CH$_3$).

2nd diastereoisomer (15%) : 7.25-7.71 (m, 5 H, Ph), 5.27 (s, 1 H, C$\underline{H}$OH), 5.07 (d, 1/2 H, ^{3}J= 7.3 Hz, C$\underline{H}$COMe), 5.06 (d, 1/2 H, ^{3}J= 7.3 Hz, C$\underline{H}$COMe), 1.73 (s, 3 H, COMe), 1.25-1.71 (m, 4 H, CH$_2$), 0.92 (t, 3 H, ^{3}J= 7.3 Hz, CH$_3$).

[α]$_D$ = - 53 (c = 1.0, CHCl$_3$, 20 °C) ; de = 70%.

2-oxohex-3-yl-(S)-mandelate (27). Obtained from **18** (3.88 mmol), (S)-mandelic acid (3.88 mmol) and [Ru(μ-O$_2$CH)(CO)$_2$(PPh$_3$)]$_2$ (0.5 mol%, 0.02 mmol) in anhydrous toluene (5 ml) after 30 h at 80 °C as a yellow oil (662 mg, 68%) after a column chromatography over silica gel with hexane/ether mixtures as eluent ; IR ν/cm^{-1} 3450 (OH), 1742 (C=O), 1728 (C=O). Anal. calcd. for C$_{14}$H$_{18}$O$_4$: C, 67.18 ; H, 7.25. Found : C, 67.48 ; H, 7.58 ; [α]$_D$ = +58.0 (c= 1.5, CHCl$_3$, 20 °C) ; de = 75%.

^{1}H NMR δ (300 MHz, CDCl$_3$) :

1st diastereoisomer: (87.5%).: 7.25-7.71 (m, 5 H, Ph), 5.27 (s, 1 H, C$\underline{H}$OH), 5.07 (d, 1/2 H, ^{3}J= 7.3 Hz, C$\underline{H}$COMe), 5.06 (d, 1/2 H, ^{3}J= 7.3 Hz, C$\underline{H}$COMe), 1.73 (s, 3 H, COMe), 1.25-1.71 (m, 4 H, CH$_2$), 0.92 (t, 3 H, ^{3}J= 7.3 Hz, CH$_3$).

2nd diastereoisomer (12.5%) : 7.25-7.71 (m, 5 H, Ph), 5.32 (s, 1 H, C$\underline{H}$OH), 5.01 (d, 1/2 H, ^{3}J= 7.8 Hz, C$\underline{H}$CH$_2$), 4.99 (d, 1/2 H, ^{3}J= 7.2 Hz, C$\underline{H}$CH$_2$), 2.15 (s, 3 H, COMe), 0.84-0.99 (m, 4H, CH$_2$), 0.73 (t, 3 H, J= 7.3 Hz, CH$_3$).

4,8-dimethyl-2-oxonon-7-en-3-yl-(R)-mandelate (28). Obtained from **20** (2.41 mmol), (R)-mandelic acid (2.41 mmol) and [Ru(μ-O$_2$CH)(CO)$_2$(PPh$_3$)]$_2$ (0.5 mol%, 0.013 mmol) in anhydrous toluene (5 ml) after 20.5 h at 80 °C as a yellow oil (465 mg, 61%) after bulb-to-bulb distillation (Kugelrohr) at 180 °C under 0.5 mm Hg ; IR ν/cm^{-1} 3448 (OH), 1744 (C=O), 1724 (C=O), 1183 (C-O). Anal. calcd. for C$_{19}$H$_{26}$O$_4$: C, 71.67 ; H, 8.23. Found : C, 71.50 ; H, 8.14. [α]$_D$ = -36.25 (c= 1.6, CHCl$_3$, 20 °C). de = 76%.

^{1}H NMR δ (300 MHz, CDCl$_3$) :

1st couple of diastereoisomers(88%) : 7.54-7.27 (m, 5 H, Ph), 5.34 (s, 1/2 H, C$\underline{H}$OH), 5.33 (s, 1/2 H, C$\underline{H}$OH), 5.02 (d, 1/2 H, J= 2.9 Hz, CHOCO), 4.90 (d, 1/2 H, J= 4.1 Hz, CH-OCO), 4.80 (m, 1 H, CH=CMe$_2$), 3.48-3.39 (s, 1 H, OH), 2.15 (s, 3/2 H, COMe), 2.14 (s, 3/2 H, COMe), 1.80 - 2.10 (m, 2 H, CH_2), 1.64 (d, 3/2 H, J= 1.0 Hz, $CH{=}C\underline{Me}_2$), 1.62 (d, 3/2 H, J= 1.0 Hz, $CH{=}C\underline{Me}_2$), 1.54 (s, 3/2 H, $CH{=}C\underline{Me}_2$), 1.51 (s, 3/2 H, $CH{=}C\underline{Me}_2$), 1.45 - 1.15 (m, 2 H, CH_2), 1.12 - 1.00 (m, 1 H, $C\underline{H}Me$), 0.71 (d, 3/2 H, J= 6.9 Hz, $CH\underline{Me}$), 0.63 (d, 3/2 H, J= 6.8 Hz, $CH\underline{Me}$).

2nd couple of diastereoisomers (12%) : 7.54 - 7.27 (m, 5 H, Ph), 5.29 (s, 1 H, CHOH), 5.06 (d, 1/2 H, J= 3.2 Hz, CHOCO), 4.95 (d, 1/2 H, J= 4.4 Hz, CHOCO), 4.80 (m, 1 H, $C\underline{H}{=}CMe_2$), 3.39-3.48 (s, 1 H, OH), 2.15 (s, 3/2 H, COMe), 2.14 (s, 3/2 H, COMe), 2.10-1.80 (m, 2 H, CH_2), 1.69 (s, 3/2 H, $CH{=}C\underline{Me}_2$), 1.67 (s, 3/2 H, $CH{=}C\underline{Me}_2$), 1.59 (s, 3/2 H, $CH{=}C\underline{Me}_2$), 1.57 (s, 3/2 H, $CH{=}C\underline{Me}_2$), 1.45 - 1.15 (m, 2 H, CH_2), 1.00-1.12 (m, 1 H, $C\underline{H}Me$), 0.93 (d, 3/2 H, ^3J= 6.9 Hz, $CH\underline{Me}$), 0.80 (d, 3/2 H, ^3J= 6.9 Hz, $CH\underline{Me}$).

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