Final Report
For the Marshall Plan Scholarship

Asymmetric synthesis of α-quaternary phenylacetic acids via Ireland-Claisen rearrangement

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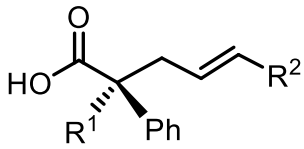
Short Description of Research Agenda

The synthetic work described in this research proposal was conducted in Professor Stoltz's group at the California Institute of Technology. The focus was laid on synthetic methodology for the construction of α-quaternary acids from allyl esters. This plan included the utility of the Ireland-Claisen rearrangement. This reliable reaction was used to attempt the assembly of two contiguous quaternary stereogenic centers. Key to realize this challenging task is control of *E/Z* enol formation in the allyl ester staring material. Recent findings in the Stoltz laboratories show that enolization can be performed with excellent geometrical selectivity. With this tool in hand, a simple protocol could be developed to furnish acyclic vicinal stereocenters in high diastereoselectivity, with the goal in mind of forming exceedingly hindered vicinal quaternary stereocenters. Notably, the allyl ester substrates were derived from widely available phenylacetic acids and allylic alcohols, allowing for complex acyclic stereodyads to be rapidly formed from simple and inexpensive starting materials by taking advantage of a new stereoselective enolization protocol.

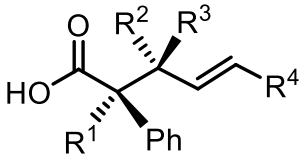
General Goals

From the outset, it was planned to develop a methodology for the construction of α-quaternary phenylacetic acids from allyl esters by means of Ireland-Claisen reaction (Fig 1). Findings from the Stoltz laboratories demonstrate selective *E/Z*- enolization, which is key for efficient chirality transfer in [3,3] sigmatropic rearrangements.[2] Through judicious choice of temperature, reagents/additives it should be feasible to synthesize carboxylic acids with high diastereomeric ratios (*dr*) and reliably predictable stereochemical outcome. Extension of this concept ultimately allowed the formation of exceedingly hindered vicinal quaternary stereocenters (Fig 2). Despite the sterically congestion, further functionalization of these highly complex scaffolds is still viable, by means of functional group manipulation of either the carboxylic acid or/and the olefin moiety



$R^1 \neq Ph$, $R^2 \neq H$

Fig 1



$R^1 \neq Ph$, $R^2 \neq R^3$, $R^4 \neq H$

Fig 2

Introduction

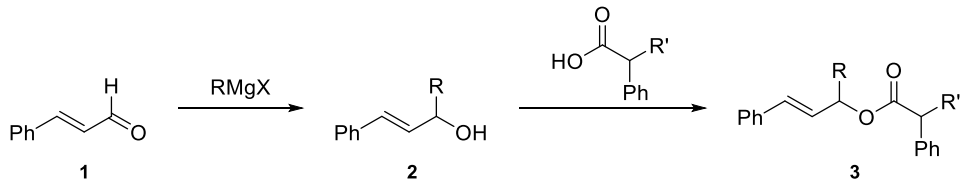
Quaternary carbon stereocenters α-positioned to a carboxylic acid or its derivatives are a structural motif often met in natural products, semisynthetic and synthetic pharmaceutical.[3] Most of these biologically active compounds incorporate a nonracemic quaternary center, mostly derived from the chiral pool.

The need for a synthetically feasible method to construct this structural motif in an asymmetric fashion was met by several groups in the past two decades. Our findings will be presented in results and discussion.

Results and discussion

Precursor synthesis for α-Quaternary, β-Tertiary carboxylic acids

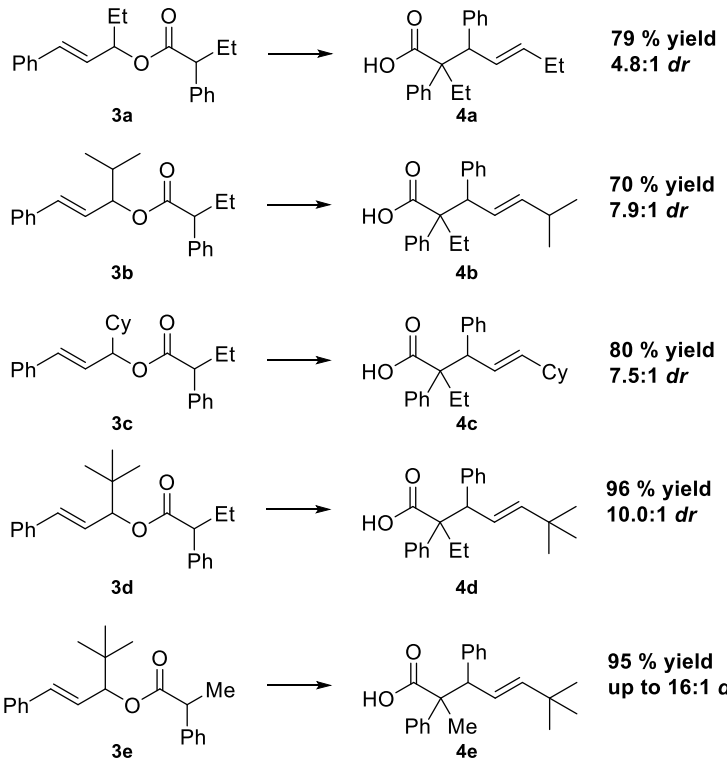
Cinnamaldehyde-derived



R= Et, iPr, cyHex or t-Bu; R'= Me or Et; X= Cl or Br

Scheme 1

One set of substrates was derived from cinnamaldehyde **1**. Treatment with Grignard reagent formed allylic alcohols **2**. Esterification with 2-phenylpropanoic acid (R'=Me) or 2-phenylbutanoic acid (R'=Et) furnished Ireland-Claisen precursors **3** (Scheme 1).

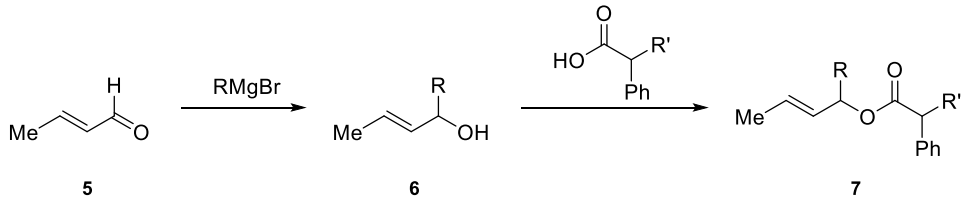


Scheme 2

Transformation of ester **3a** to acid **4a** under *standard conditions*[4,5] (2.0 equiv LiHMDS, 2.0 equiv DMEA, 2.0 equiv TMSCl in toluene 0.1M, -78°C to 0°C or 19°C – see experimental part) gave 79 % and 4.8:1 *dr*. Incorporation of the bulkier iPr= R group in **3b** then allowed the formation of acid **4b** in 70 % yield and 7.9:1 *dr*. Changing R to Cy (cyclohexyl) in ester **3c** gave comparable results with respect to yield and *dr* of acid **4c**. Installation of sterically very demanding *t*-butyl in ester **3d** resulted in increased yield of 96 % and 10.0:1 *dr* of product **4d**. Reducing the steric demand in α-position by switching from Et to Me in **3e** lead to formation

of acid **4e** in similar yield and increased *dr* of up tp 16:1. Although, it is noteworthy to mention that the high diastereomer ratio is difficult to reproduce due to formation of minor side products (Scheme 2). With these encouraging results in hand, the further scope of this reaction was investigated.

Crotonaldehyde-derived and its TMS-analogues

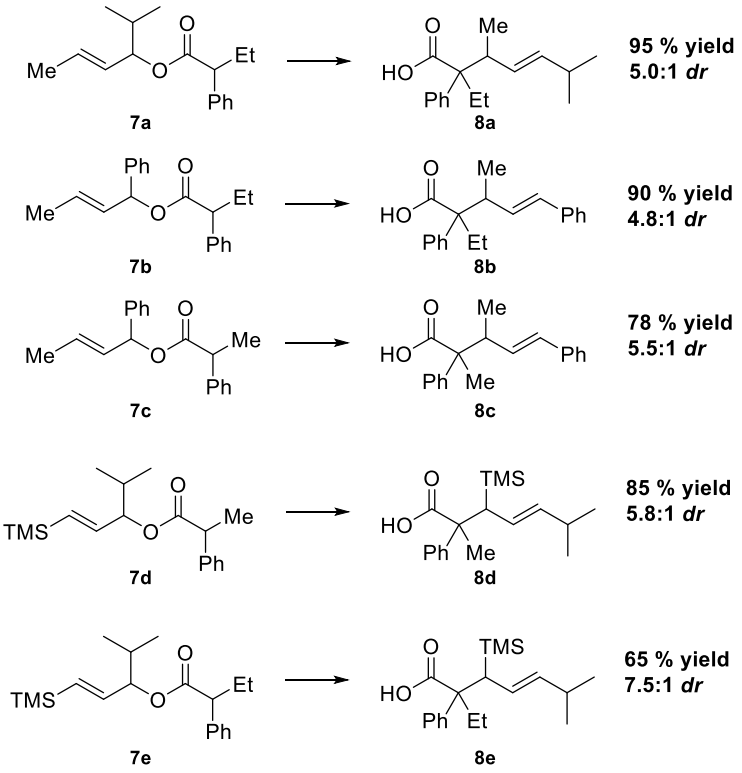


5 **6** **7**

R= iPr or Ph; R'= Me or Et

Scheme 3

Crotonaldehyde **5** was treated with Grignard reagent to give allylic alcohols **6**, which were directly subjected to esterification leading to compounds **7** (Scheme 3).
Following Ireland-Claisen rearrangement of ester **7a** allowed formation of **8a** in 95 % yield and 5.0:1 *dr*. Similar results with respect to yield and *dr* were achieved when compound **7b** was converted to acid **8b**. Decreasing the bulk in α-position (Et to Me) of **7c** did not have a beneficial impact with respect to yield (78 %) of **8c**, although the *dr* could be slightly increased.



Scheme 4

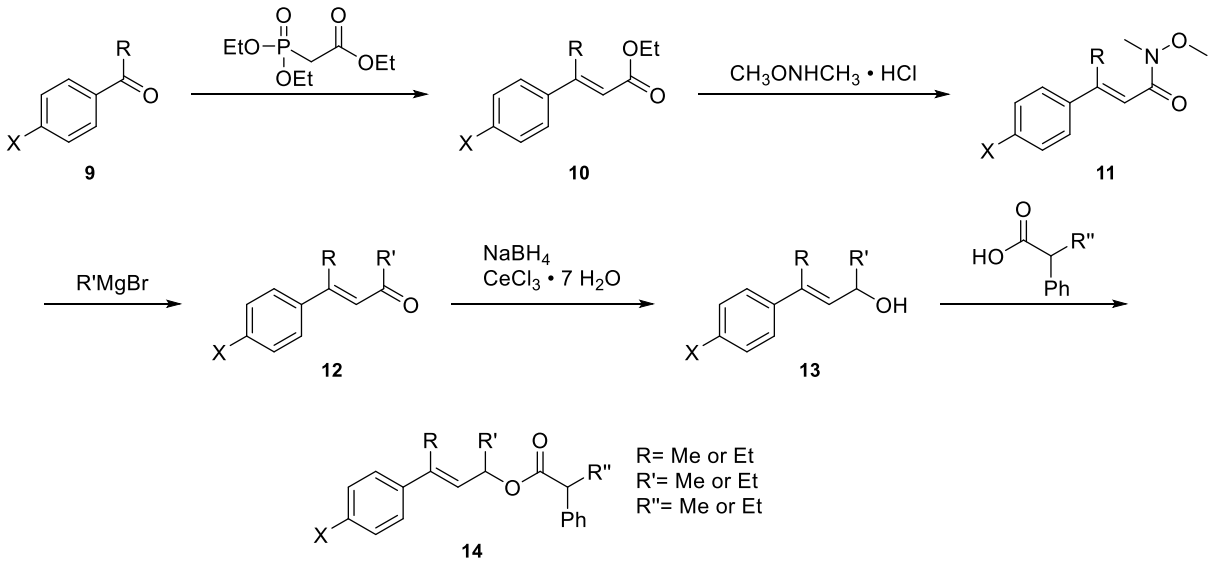
Conversion of TMS analogue **7d** to acid **8e** could be achieved in 85 % yield and 5.8:1 *dr*.

Interestingly, formation of acid **8e** from **7e** (bulkier Et> Me in α-position) increased the *dr* to 7.5:1 although accompanied with diminished yield of 65 % (Scheme 4).
With these preliminary findings in mind, the attention was *dr*awn towards the formation of carboxylic acids bearing vicinal quaternary centers.

Precursor synthesis for α-Quaternary, β-Quaternary carboxylic acids

Ketone-derived

A generalized overview of precursor preparation is given in Scheme 5.
Ketones **9** were subjected to Horner-Wadsworth-Emmons conditions forming ethyl esters **10**. Following treatment with *N,O*-Dimethyl hydroxylamine furnished Weinreb amides **11**. Treatment with Grignard reagent (Me or Et) allowed preparation of 10 different allylic ketones **12**. Subsequent Luche reductions gave rise to the corresponding allylic alcohols **13**. Esterification with 2-phenylpropanoic acid (R''=Me) or 2-phenylbutanoic acid (R''=Et) finalized the preparation of the desired Ireland-Claisen precursors **14**.



Scheme 5

This mode of operation allowed the preparation of 20 substrates from 5 different starting materials (Fig 1).

Acetophenone-derived **14a-d**

Propiophenone-derived **14e-h**

4-Methoxyacetophenone-derived **14i-l**

4-Methoxypropiophenone-derived **14m-p**

4-Bromoacetophenone-derived **14q-t**

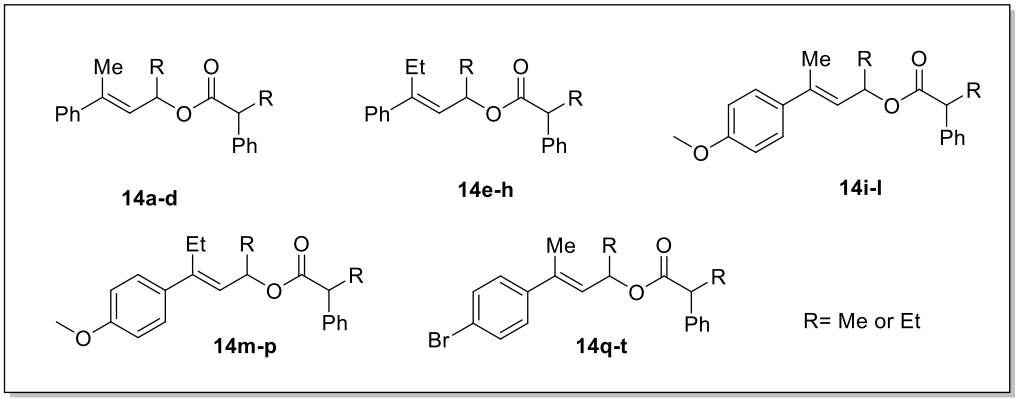
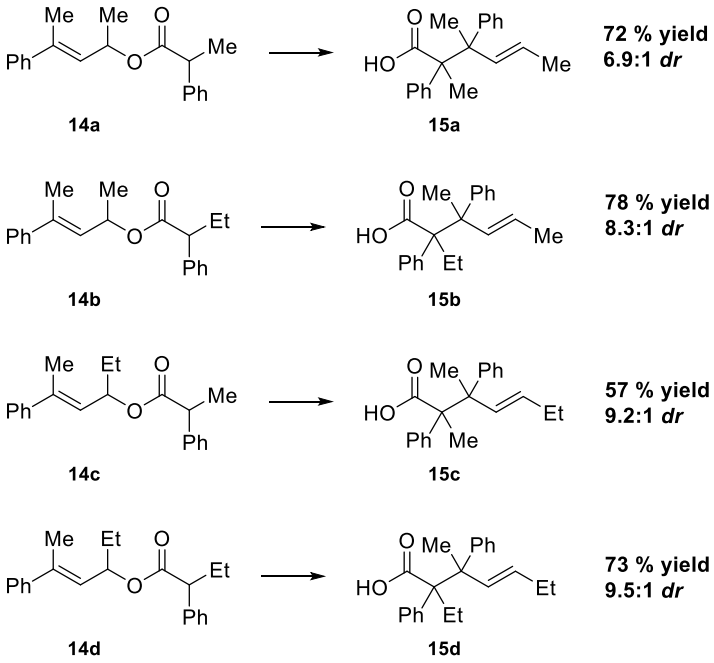


Fig 3

All 20 esters **14** were subjected to ICR *standard conditions*.

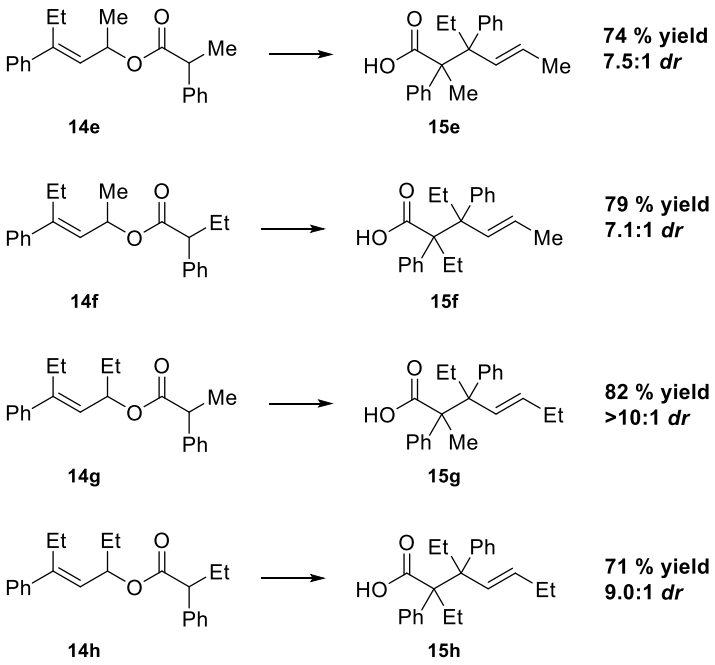
Acetophenone-derived



Scheme 6

Conversion of ester **14a** to acid **15a** could be achieved with 72 % and 6.9:1 *dr.*
Transformation of compound 14a to 15b was accomplished in 78 % yield and 8.3:1 *dr.*
Rearrangement of esters **14c** and **14d** gave rise to acids **15c** in moderate 57 % yield and 9.2:1 *dr* and **15d** in 73 % yield and satisfying 9.5:1 *dr* respectively (Scheme 6).

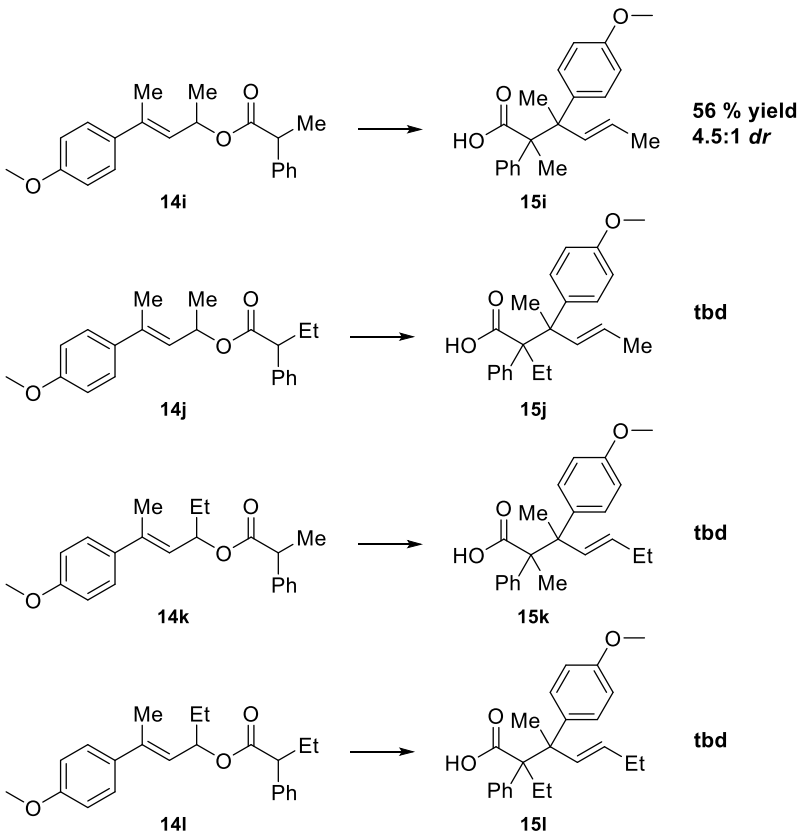
Propiophenone-derived



Scheme 7

All 4 acids **15e** to **15h** gave comparable results with respect to yield (71-82 %) but differed in *dr*. Acids **15e** could be obtained in 7.5:1 *dr* from ester **14e**. Conversion of compound **14f** to acid **15f** was achieved in 7.1:1 *dr*. An increase in *dr* was observed for the conversion of **14g** to **15g**. It must be stated at this point, that the obtained compound seems to contain minor impurities. Therefore, it is difficult to distinguish which "minor" signal belongs to the corresponding diastereomer. The ">10:1 *dr*" is to be interpreted as the minimum *dr*, as the *dr* is higher IF the other minor signal is the diastereomer. Finally, acid **15h** could be produced in 71 % yield and satisfying *dr* of 9.0:1 from precursor **14h** (Scheme 7).

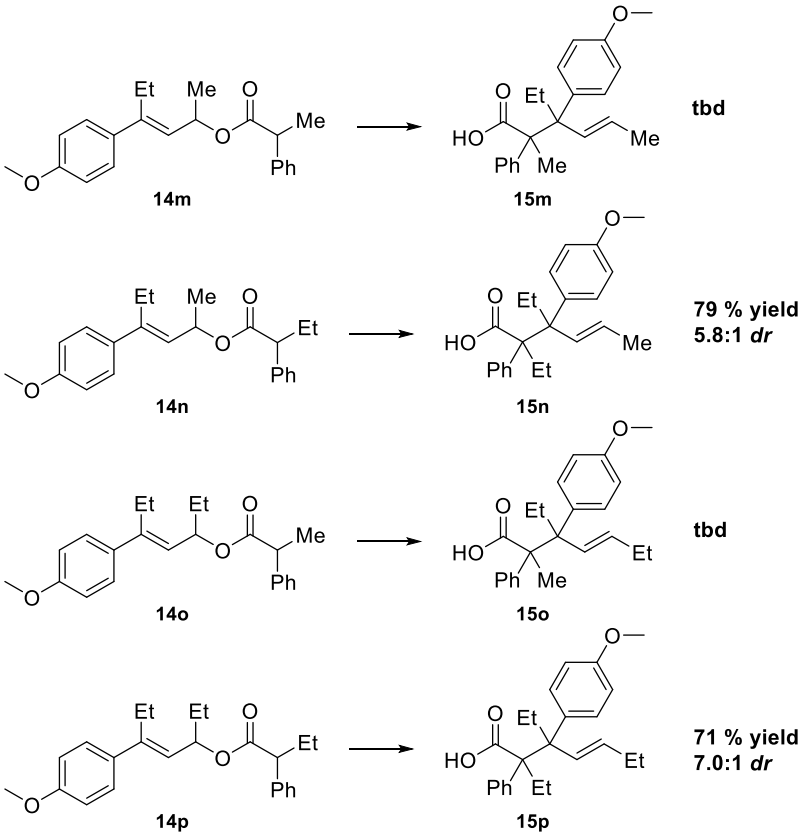
4-Methoxyacetophenone-derived



Scheme 8

Conversion of **14i** to **15i** was achieved with only moderate yield of 56 % as well as moderate 4.5:1 *dr*. For the rest of the series **14j-l** to **15j-l** no yields and no *dr* could be secured as the obtained products did not show sufficient purity. For further information see experimental part and/or NMRs (and digital notebook). Due to a lack of time these reactions could not be repeated. Also, no further derivatization (eg. methyl ester formation) could be conducted which could help determine *dr* and yield over 2 steps (Scheme 8).

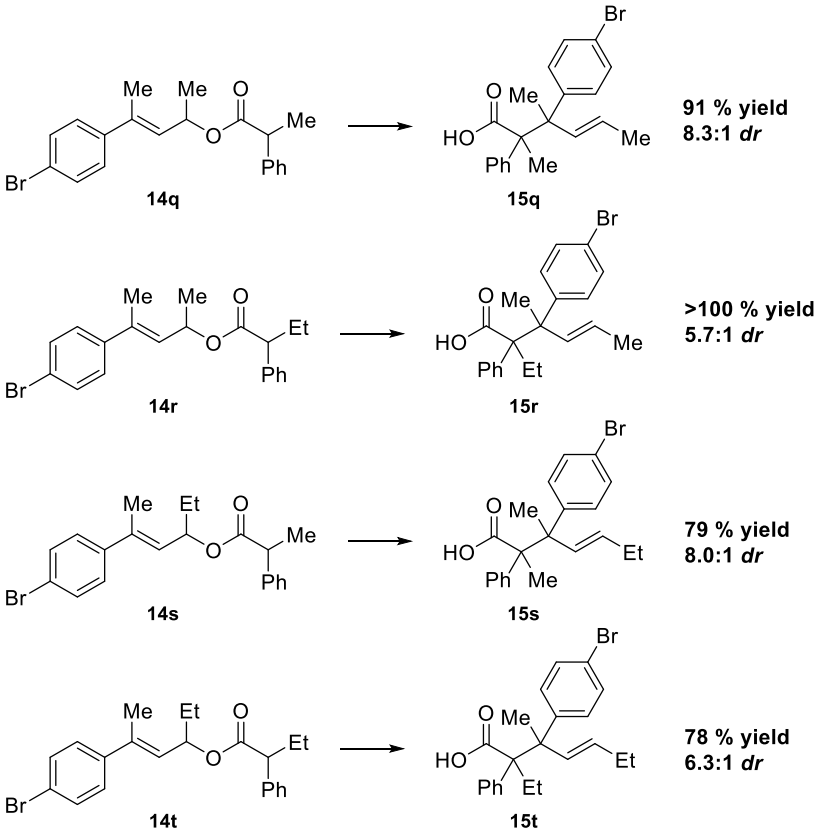
4-Methoxypropiophenone-derived



Scheme 9

This series of substrates proof to be a similar challenge as the 4-Methoxyacetophenone-derived ones. In the first case, conversion of ester **14m** to acid **15m**, the collected product showed many minor impurities in the ^{1}H-NMR spectra. Therefore, no yield can be given. Same is true for the dr, although – if assumed that the doublets at 6.22 and 6.04 belong to minor and major diastereomer – it can be judged to be in the region of approx. 8:1. As suggested above, methyl ester formation could help determine yield and *dr*. **15n** on the other hand could be obtained from precursor **14n** in sufficient purity to at determine a *dr* of 5.8:1 and yield. Although, it must be stated that the NMR spectra contain minor impurities. Transformation of compound **14o** to **15o** proofed to be as messy as **14m** to **15m**. 1H NMR again shows many minor impurities and therefore no meaningful yield can be given. The same is true for *dr*, although, it can be assumed in a similar way as for **15m**. If the 2 doublets, 6.20 (minor) and 6.01 (major) are compared, the *dr* is approx. 14:1. To determine if this is a great result or just wishful thinking derivatization would be necessary. For the final rearrangement of this series, **14p** to **15p**, desired product could be obtained in 71 % yield and 7.0:1 *dr* (Scheme 9).

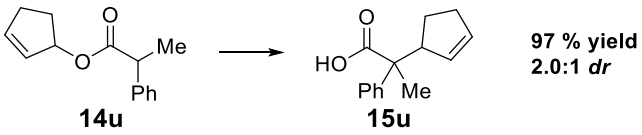
4-Bromoacetophenone-derived



Scheme 10

Formation of **15q** from **14q** was achieved in very good yield of 91 % and satisfying 8.3:1 *dr*. Acid **15r** was obtained in >100% yield (directly subjected to methyl ester formation) from ester **14r** and moderate 5.7:1 *dr*. Again, satisfying *dr* of 8.0:1 and 79% yield could be achieved for the conversion of **14s** to **15s**. Similar yield but slightly lower *dr* of 6.3:1 was observed in the formation of **15t** from **14t** (Scheme 10).

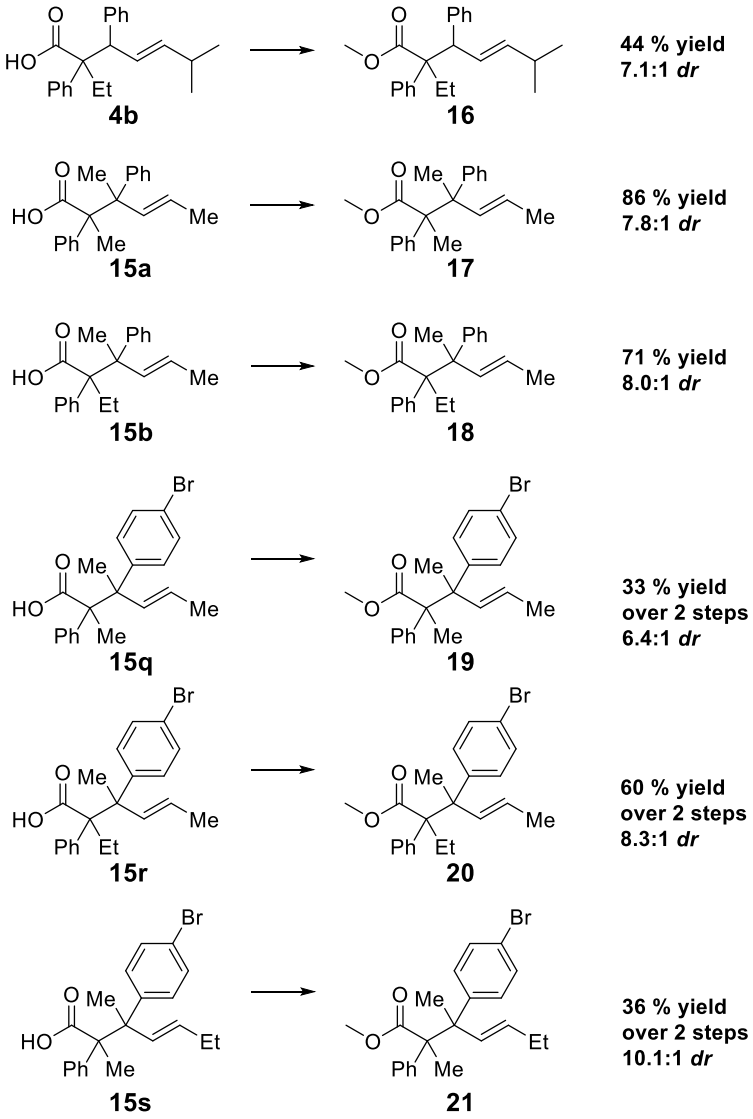
Cyclopentenol-derived



Scheme 11

It could also be demonstrated that cyclic substrates, such as ester **14u** could also be converted to its corresponding carboxylic acid derivative **15u** (Scheme 11). The desired product could be collected in excellent yield of 97 % but only 2.0:1 *dr*.

Some selected carboxylic acids were subjected to methyl ester formation. This allowed confirmation of *dr* assignments of the (crude) Ireland-Claisen rearrangement products.



Scheme 12

Carboxylic acids **4b**, **15a**, **15b**, **15q**, **15r** and **15s** were converted to their corresponding methyl esters (Scheme 12). Comparison of the ^{1}H spectra of methyl ester vs. the crude acid gave the following results:

Ester **16** –7.1:1 *dr* vs crude **4b** –7.9:1 *dr*

Ester **17** –7.8:1 *dr* vs crude **15a** –6.9:1 *dr*

Ester **18** –8.0:1 *dr* vs crude **15b** –8.3:1 *dr*

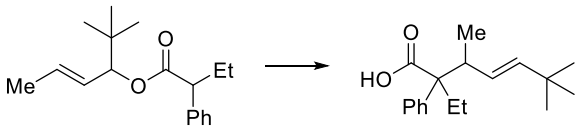
Ester **19** –6.4:1 *dr* vs crude **15q** –8.3:1 *dr*

Ester **20** –8.3:1 *dr* vs crude **15r** –5.7:1 *dr*

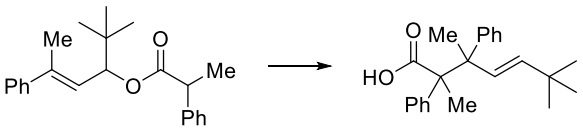
Ester **21** –10.1:1 *dr* vs crude **15s** –8.0:1 *dr*

For ester **16**, **18** and **19** the *dr* slightly decreased compared to the crude carboxylic acid. Ester **17**, **20** and **21** on the other hand see a slight increase in *dr*. The nature of the observed changes in *dr* cannot be explained with certainty. One possibility is incorrect assignment of diastereomer ratios in the crude acid products due to impurities. Another explanation could be, that one diastereomer decomposes (faster) on silica gel in the purification step (see acid **4e**).

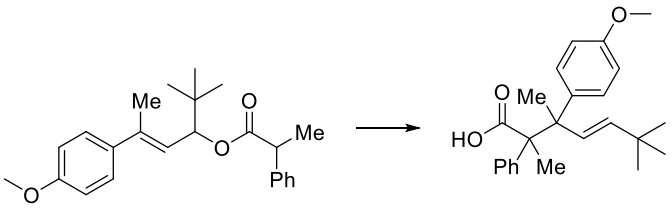
Poor substrates for Ireland-Claisen rearrangement:



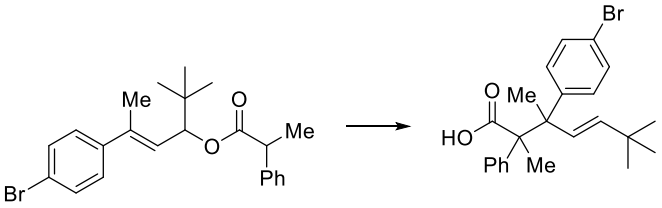
~3:1 dr



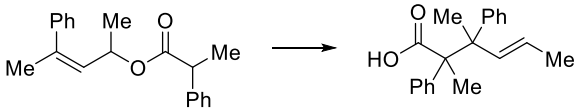
98 % yield
1.1:1 *dr*



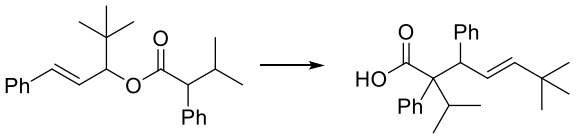
4.1:1 *dr*



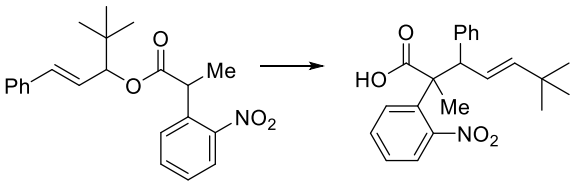
94 % yield
3.0:1 *dr*



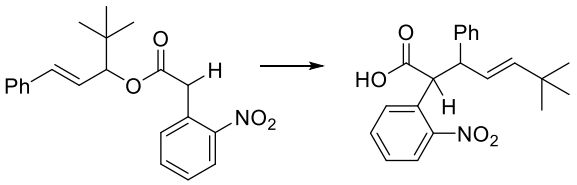
no clean spec
1:3.2 *dr*
Opposite to 15a



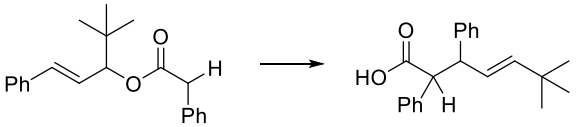
No Conversion



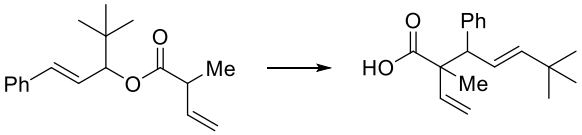
Decomposition



No clean product obtained



No clean product obtained



No Conversion

Experimental part

α-Quaternary, β-Tertiary carboxylic acids

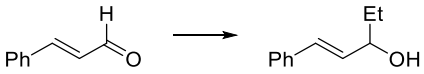
Cinnamaldehyde-derived

Grignard addition

General procedure

A 100 mL flame-dried round bottom flask was equipped with cinnamaldehyde **1** (1.0 equiv.) in dry THF (c= 0.23M). The pale-yellow solution was cooled via ice bath and Grignard reagent (1.60 equiv.) was added dropwise over 6 minutes. After TLC (hexanes: ethyl acetate 3:1) indicated full conversion the reaction was quenched by addition of saturated NH_4Cl solution and little H_2O. Layers were separated and the aqueous layer was extracted with ethyl acetate 3 times. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo.

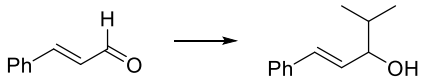
(*E*)-1-phenylpent-1-en-3-ol **2a**



Grignard reagent: 1.0M EtMgBr

The crude material was subjected to flash chromatography (hexanes: ethyl acetate 4:1) and the product could be collected as clear colorless oil in 65 % yield (555 mg, 3.42 mmol). The material was used in the next step without further purification.

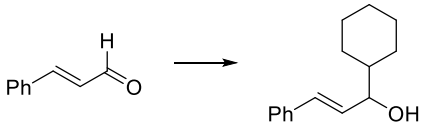
(*E*)-4-methyl-1-phenylpent-1-en-3-ol **2b**



Grignard reagent: 1.0M iPrMgBr

The crude material was subjected to column chromatography (silica gel, hexanes: ethyl acetate 10:1 to 5:1) and the product could be collected as yellow oil in 44 % yield (415 mg, 2.35 mmol).

(*E*)-1-cyclohexyl-3-phenylprop-2-en-1-ol **2c**



Grignard reagent: 1.0M CyMgBr

The crude material was subjected to column chromatography (silica gel, hexanes: ethyl acetate 20:1 to 10:1) and product could be collected as yellow oil in 59 % yield (675 mg, 3.12 mmol).

(*E*)-4,4-dimethyl-1-phenylpent-1-en-3-ol **2d**

Grignard reagent: 2.0M *tert*-ButylMgCl

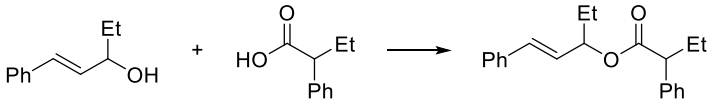
The crude material was subjected to column chromatography (silica gel, hexanes: ethyl acetate 25:1 to 10:1) and product could be collected as yellow oil in 88 % yield (1.90 g, 9.98 mmol).

Esterification

General procedure:

A 25 mL round bottom flask was equipped with 2-phenylbutanoic acid *or* 2-phenylpropanoic acid (1.20 equiv.), EDCI (1.20 equiv.) and DMAP (0.20 equiv.). Alcohol **2** (1.0 equiv.) dissolved in dry DCM (c= 0.3M) was added and the mixture was stirred until TLC (hexanes: ethylacetate 6:1) indicated full consumption of starting material. The reaction was quenched by addition of H_2O and layers were separated. The aqueous layer was extracted with DCM three times and the combined organic layer was washed with H_2O. It was dried over Na_2SO_4 and concentrated in vacuo.

(*E*)-1-phenylpent-1-en-3-yl 2-phenylbutanoate **3a**



Starting material: Compound **2a**

The crude material was purified by column chromatography (hexanes: ethyl acetate 25:1) and the desired ester could be collected as colorless oil in 76 % yield (360 mg, 1.17 mmol) and 6.6:1 *dr.*

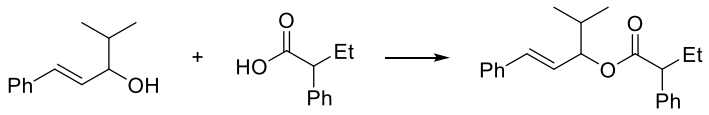
Major:

^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.35 – 7.16 (m, 10H), 6.30 (dd, *J*= 16.0, 1.2 Hz, 1H), 6.01 (ddd, *J*= 16.0, 6.4, 0.9 Hz, 1H), 5.36 (qd, *J*= 6.5, 1.2 Hz, 1H), 3.55 – 3.45 (m, 1H), 2.20 – 2.07 (m, 1H), 1.92 – 1.53 (m, 3H), 1.00 – 0.84 (m, 6H).

Minor:

^{1}H NMR (300 MHz, $CDCl_3$) δ= 7.35 – 7.16 (m, 10H), 6.53 (dd, *J*= 16.0, 1.1 Hz, 1H), 6.11 (ddd, *J*= 15.9, 6.9, 0.9 Hz, 1H), 5.36 (qd, *J*= 6.5, 1.2 Hz, 1H), 3.55 – 3.45 (m, 1H), 2.20 – 2.07 (m, 1H), 1.92 – 1.53 (m, 3H), 1.00 – 0.84 (m, 3H), 0.77 (td, *J*= 7.4, 0.8 Hz, 3H).

(*E*)-4-methyl-1-phenylpent-1-en-3-yl 2-phenylbutanoate 3b



Starting material: Compound **2b**

The crude material was purified by column chromatography (hexanes: ethyl acetate 20:1) and the desired ester could be collected as colorless oil in 80 % yield (390 mg, 1.21 mmol) and 4.6:1 *dr.*

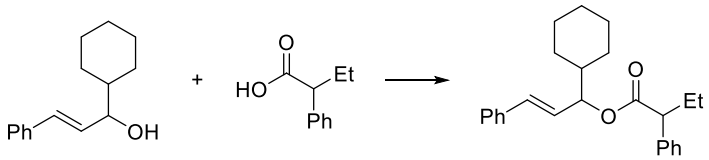
Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 – 7.19 (m, 10H), 6.26 (dd, *J*= 16.1, 1.3 Hz, 1H), 6.00 (dd, *J*= 15.9, 6.6 Hz, 1H), 5.23 (ddd, *J*= 6.9, 6.1, 1.2 Hz, 1H), 3.54 – 3.50 (m, 1H), 2.20 – 2.11 (m, 1H), 1.98 – 1.78 (m, 2H), 0.95 – 0.91 (m, 9H).

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 – 7.19 (m, 10H), 6.49 (dd, *J*= 16.0, 1.3 Hz, 1H), 6.10 (dd, *J*= 15.9, 7.3 Hz, 1H), 5.20 (ddd, *J*= 7.3, 6.1, 1.2 Hz, 1H), 3.54 – 3.50 (m, 1H), 2.20 – 2.11 (m, 1H), 1.98 – 1.78 (m, 2H), 0.95 – 0.91 (m, 3H)., 0.81 (d, *J*= 1.9 Hz, 3H), 0.80 (d, *J*= 1.8 Hz, 3H).

(*E*)-1-cyclohexyl-3-phenylallyl 2-phenylbutanoate **3c**



Starting material: Compound **2c**

The crude material was purified by column chromatography (hexanes: ethyl acetate 10:1) and the desired ester could be collected as pale yellow oil in 93 % yield (528 mg, 1.41 mmol) and 6.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.17 (m, 10H), 6.25 (d, *J*= 15.9 Hz, 1H), 6.00 (dd, *J*= 16.0, 6.8 Hz, 1H), 5.25 – 5.17 (m, 1H), 3.54 – 3.46 (m, 1H), 2.19 – 2.09 (m, 1H), 1.89 – 1.78 (m, 1H), 1.78 – 1.52 (m, 6H), 1.25 – 0.96 (m, 5H), 0.95 – 0.89 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.2, 139.3, 136.6, 132.2, 128.6, 128.5, 128.1, 127.6, 127.1, 126.5, 126.3, 78.4, 53.9, 42.1, 28.9, 28.5, 26.5, 26.4, 26.0, 26.0, 12.3.

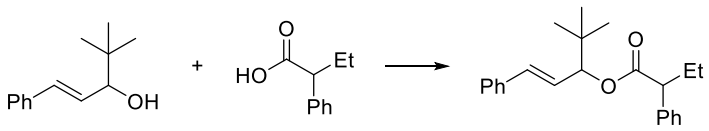
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.17 (m, 10H), 6.47 (d, *J*= 15.8 Hz, 1H), 6.10 (dd, *J*= 15.9, 7.3 Hz, 1H), 5.25 – 5.17 (m, 1H), 3.54 – 3.46 (m, 1H), 2.19 – 2.09 (m, 1H), 1.89 – 1.78 (m, 1H), 1.78 – 1.52 (m, 6H), 1.25 – 0.96 (m, 5H), 0.95 – 0.89 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.3, 139.4, 136.6, 132.8, 128.5, 128.5, 128.1, 127.8, 127.1, 126.6, 126.5, 78.7, 54.0, 42.1, 28.7, 28.2, 26.3, 26.3, 26.0, 25.9, 12.2.

IR (Neat Film, NaCl) 3442, 3083, 3060, 3028, 2963, 2929, 2853, 2664, 1947, 1875, 1801, 1733, 1600, 1584, 1495, 1450, 1380, 1355, 1298, 1264, 1222, 1199, 1164, 1119, 1072, 1030, 968, 912, 890, 846, 749, 697 cm^{-1}

(*E*)-4,4-dimethyl-1-phenylpent-1-en-3-yl 2-phenylbutanoate **3d**



Starting material: Compound **2d**

The crude material was purified by column chromatography (hexanes: ethyl acetate 10:1) and the desired ester could be collected as colorless oil in 82 % yield (383 mg, 1.14 mmol) and 3.1:1 *dr.* Solidification was observed after storing the sample in the freezer over night.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.14 (m, 10H), 6.23 (d, *J*= 15.9 Hz, 1H), 6.04 (dd, *J*= 15.9, 6.8 Hz, 1H), 5.15 (dd, *J*= 6.8, 1.2 Hz, 1H), 3.55 – 3.48 (m, 1H), 2.21 – 2.11 (m, 1H), 1.90 – 1.79 (m, 1H), 0.95 – 0.88 (m, 12H),

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.1, 139.2, 136.6, 132.8, 128.6, 128.5, 128.1, 127.6, 127.2, 126.5, 124.8, 81.3, 54.0, 34.9, 26.2, 26.0, 12.3.

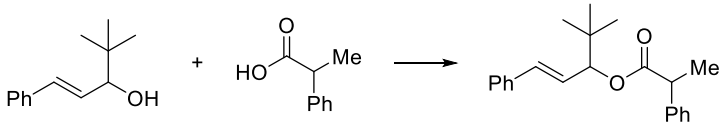
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.14 (m, 10H), 6.48 – 6.42 (m, 1H), 6.13 (dd, *J*= 15.9, 7.3 Hz, 1H), 5.11 (dd, *J*= 7.3, 1.1 Hz, 1H), 3.55 – 3.48 (m, 1H), 2.21 – 2.11 (m, 1H), 1.90 – 1.79 (m, 1H), 0.95 – 0.88 (m, 3H), 0.83 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.1, 139.3, 136.6, 133.5, 128.6, 128.5, 128.1, 127.8, 127.2, 126.6, 125.1, 81.6, 54.0, 35.0, 26.1, 26.0, 25.8, 12.2.

IR (Neat Film, NaCl) 3060, 3028, 2965, 2873, 1733, 1601, 1494, 1478, 1454, 1395, 1365, 1298, 1265, 1226, 1198, 1162, 1120, 1072, 1033, 968, 934, 847, 767, 742, 698 cm^{-1}

(*E*)-4,4-dimethyl-1-phenylpent-1-en-3-yl 2-phenylpropanoate **3e**



Starting material: Compound **2e**

The crude material was purified by column chromatography (hexanes: ethyl acetate 25:1) and the desired ester could be collected as colorless oil in 65 % yield (110 mg, 341 µmol). was observed after storing the sample in the freezer over night.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.17 (m, 10H), 6.23 (d, *J*= 15.9 Hz, 1H), 6.03 (dd, *J*= 15.9, 6.8 Hz, 1H), 5.13 (dd, *J*= 6.8, 1.2 Hz, 1H), 3.83 – 3.72 (m, 1H), 1.56 – 1.53 (m, 3H), 0.92 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 140.6, 136.6, 133.7, 132.9, 128.6, 128.6, 128.5, 127.7, 127.1, 126.5, 124.8, 81.4, 45.9, 34.9, 25.9, 18.2.

Minor:

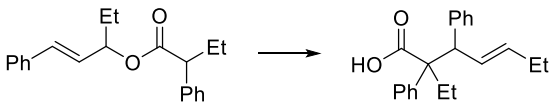
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.17 (m, 10H), 6.48 (d, *J*= 15.9 Hz, 1H), 6.13 (dd, *J*= 15.9, 7.6 Hz, 1H), 5.11 (dd, *J*= 7.6, 1.1 Hz, 1H), 3.83 – 3.72 (m, 1H), 1.56 – 1.53 (m, 3H), 0.80 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 140.7, 136.6, 133.7, 128.6, 128.6, 128.5, 127.7, 127.7, 127.1, 126.6, 125.0, 81.7, 46.0, 35.0, 25.8, 18.0.

IR (Neat Film, NaCl) 3060, 3028, 2967, 2870, 1944, 1734, 1601, 1495, 1478, 1452, 1395, 1365, 1328, 1241, 1201, 1164, 1119, 1096, 1069, 1030, 966, 935, 846, 781, 761, 742, 697, 650 cm^{-1}.

Ireland-Claisen rearrangement

(*E*)-2-ethyl-2,3-diphenylhept-4-enoic acid **4a**



A flame-dried 25 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 2.03 mL, 648 µmol, 2.0 equiv.), followed by *N,N*-dimethyl ethylamine (70 µL, 648 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **3a** (100 mg, 227 µmol, 1.0 equiv.) dissolved in 1.1 mL dry toluene was added dropwise over 3 minutes. The reaction was kept at -78° C and after 2 hours TMSCl (86 µL, 648 µmol, 2.0 equiv.) was added dropwise. After 20 minutes, the reaction flask was transferred into a -12° C acetone/ice bath and then allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 10:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl, then dried over Na_2SO_4. The solvent was removed in vacuo, the residue was filtered through a plug of silica (DCM). NMR after evaporation still shows TMS-ester signals. The residue was taken up in 2 mL THF and stirred with 100 µL 2M HCl for 45 minutes. Then, the mixture was diluted with H_2O and the aqueous layer was extracted with DCM three times. The combined

organic layer was dried over Na_2SO_4 and concentrated in vacuo. The product could be collected as pale yellow oil in 79 % yield (79 mg, 256 µmol) and 4.8:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.43 – 7.16 (m, 10H), 6.43 (d, *J*= 15.8 Hz, 1H), 5.73 (ddd, *J*= 15.8, 9.5, 1.4 Hz, 1H), 3.22 – 3.12 (m, 1H), 2.29 – 2.14 (m, 2H), 1.09 (dd, *J*= 6.8, 1.5 Hz, 3H), 0.97 (t, 3H).

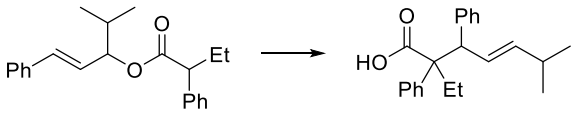
^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.4, 137.9, 137.6, 131.7, 131.0, 129.2, 128.6, 127.6, 127.3, 127.0, 126.3, 59.3, 42.7, 29.8, 18.0, 9.3.

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.43 – 7.16 (m, 10H), 6.48 – 6.43 (m, 1H), 6.11 (ddd, *J*= 15.9, 8.8, 1.6 Hz, 1H), 3.22 – 3.12 (m, 1H), 2.29 – 2.14 (m, 2H), 1.04 (d, *J*= 6.6 Hz, 3H), 0.91 – 0.86 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.0, 138.4, 137.8, 132.4, 131.0, 129.0, 128.9, 127.7, 127.3, 126.9, 126.3, 59.9, 43.2, 30.5, 16.1, 9.5.

(*E*)-2-ethyl-6-methyl-2,3-diphenylhept-4-enoic acid **4b**



A flame-dried 10 mL round bottom flask was equipped LiHMDS (388 mg, 124 µmol, 2.0 equiv.) and 400 µL dry toluene was added, followed by *N,N*-dimethyl ethylamine (13 µL, 124 µmol, 2.0 equiv.). The colorless mix was cooled to -78°C and after 5 minutes ester **3b** (20 mg, 62 µmol, 1.0 equiv.) dissolved in 300 µL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 1 hour 45 minutes TMSCl (16 µL, 124 µmol, 2.0 equiv.) was added. After 15 minutes the flask was removed from cooling and allowed to warm to 18-19° C. TLC (hexanes: ethyl acetate 10:1) after 1 hour 20 minutes showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and Et_2O, layers were separated and organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. Crude product still showed TMS-signals and was therefore subjected to column chromatography (1g silica gel, hexanes: ethyl acetate 10:1 to pure ethyl acetate). The desired product was obtained as colorless oil solid in 70 % yield (14 mg, 43 µmol) and 7.9:1 *dr.*

Note: Most signals overlap in $CDCl_3$ therefore C_6D_6

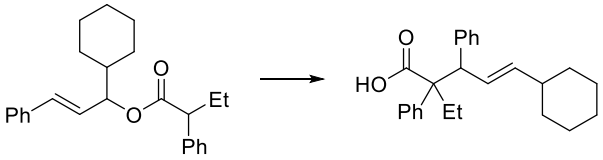
Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.18 – 7.03 (m, 10H), 5.85 – 5.79 (m, 1H), 5.38 (dd, *J*= 15.1, 6.7 Hz, 1H), 4.21 (d, *J*= 9.6 Hz, 1H), 2.29 – 2.20 (m, 1H), 2.16 – 2.06 (m, 2H), 0.93 (t, *J*= 7.3 Hz, 3H), 0.86 (d, *J*= 6.7 Hz, 3H), 0.82 (d, *J*= 6.7 Hz, 3H).

Minor:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.18 – 7.03 (m, 10H), 5.88 – 5.82 (m, 1H), 5.74 (dd, *J*= 15.3, 6.6 Hz, 1H), 4.28 (d, *J*= 9.1 Hz, 1H), 2.29 – 2.20 (m, 1H), 2.16 – 2.06 (m, 2H), 0.99 (d, *J*= 6.7 Hz, 3H), 0.95 – 0.90 (m, 6H).

(*E*)-5-cyclohexyl-2-ethyl-2,3-diphenylpent-4-enoic acid **4c**



A flame-dried 10 mL round bottom flask was equipped LiHMDS (19 mg, 110 µmol, 2.0 equiv.) and 340 µL dry toluene was added, followed by *N,N*-dimethylethylamine (12 µL, 110 µmol, 2.0 equiv.). The colorless mix was cooled to -78°C and after 5 minutes ester **3c** (20 mg, 55 µmol, 1.0 equiv.) dissolved in 200 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours 40 minutes TMSCl (14 µL, 110 µmol, 2.0 equiv.) was added. Warm acetone was added to the cooling bath to slowly raise the temperature. After 30 minutes (+13° C) the flask was removed from cooing and stirred at 18°-19° C over night. TLC (hexanes: ethyl acetate 10:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and Et_2O, layers were separated and the organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was obtained as colorless oil solid in 80 % yield (16 mg, 44 µmol) and 7.5:1 *dr.*

Note: Most signals overlap in $CDCl_3$ therefore C_6D_6

Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.22 – 7.00 (m, 10H), 5.90 – 5.83 (m, 1H), 5.44 (dd, *J*= 15.3, 6.8 Hz, 1H), 4.26 (d, *J*= 9.5 Hz, 1H), 2.35 – 2.24 (m, 1H), 2.16 (dq, *J*= 14.5, 7.4 Hz, 1H), 1.88 – 1.77 (m, 1H), 1.71 – 1.03 (m, 10H), 0.97 (t, *J*= 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.2, 141.5, 139.7, 137.7, 130.1, 129.9, 127.6, 127.2, 126.9, 126.5, 126.1, 60.7, 55.2, 40.8, 33.1, 30.5, 30.1, 26.3, 26.1, 9.5.

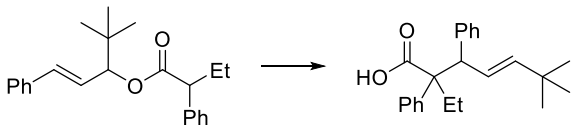
Minor:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.22 – 7.00 (m, 10H), 5.93 – 5.88 (m, 1H), 5.79 (dd, *J*= 15.3, 6.7 Hz, 1H), 4.32 (d, *J*= 9.1 Hz, 1H), 2.35 – 2.24 (m, 1H), 2.16 (dq, *J*= 14.5, 7.4 Hz, 1H), 1.88 – 1.77 (m, 1H), 1.71 – 1.03 (m, 10H), 0.97 (t, *J*= 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.7, 141.5, 139.5, 137.7, 130.7, 130.0, 127.4, 127.1, 127.0, 126.7, 125.7, 61.3, 56.4, 40.9, 33.0, 29.9, 29.4, 26.2, 26.1, 9.5.

IR (Neat Film, NaCl) 3027, 2924, 2851, 1701, 1600, 1497, 1448, 14011251, 1034, 974, 910, 785, 756, 737, 701 cm^{-1}

(*E*)-2-ethyl-6,6-dimethyl-2,3-diphenylhept-4-enoic acid **4d**



A flame-dried 10 mL round bottom flask was equipped LiHMDS (23 mg, 137 µmol, 2.0 equiv.) and 400 µL dry toluene was added, followed by *N,N*-dimethylethylamine (15 µL, 137 µmol, 2.0 equiv.). The colorless mix was cooled to -78°C and after 10 minutes ester **3d** (23 mg, 68 µmol, 1.0 equiv.) dissolved in 300 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (17 µL, 137 µmol, 2.0 equiv.) was added. After 5 minutes the flask was removed from cooling and allowed to warm to 18-19° C. TLC (hexanes: ethyl acetate 6:1) after 6 hours showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 2 hours, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was obtained as colorless to pale yellow oil in 96 % yield (22 mg, 65 µmol) and 10.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.18 – 6.98 (m, 10H), 5.81 (dd, *J*= 15.5, 9.8 Hz, 1H), 5.48 (d, *J*= 15.5 Hz, 1H), 4.20 (d, *J*= 9.8 Hz, 1H), 2.31 – 2.22 (m, 1H), 2.12 (dq, *J*= 14.2, 7.2 Hz, 1H), 0.94 (t, *J*= 7.3 Hz, 3H), 0.90 (s, 9H).

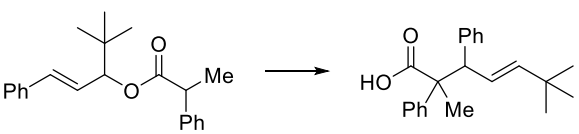
^{13}C NMR (101 MHz, $CDCl_3$) δ=

Minor:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.18 – 6.98 (m, 10H), 5.81 (dd, *J*= 15.5, 9.8 Hz, 1H), 5.48 (d, *J*= 15.5 Hz, 1H), 4.29 (d, *J*= 8.6 Hz, 1H), 2.31 – 2.22 (m, 1H), 2.12 (dq, *J*= 14.2, 7.2 Hz, 1H), 1.02 (s, 9H), 0.94 (t, *J*= 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ=

(*E*)-2,6,6-trimethyl-2,3-diphenylhept-4-enoic acid **4e**



A flame-dried 10 mL round bottom flask was equipped LiHMDS (26 mg, 155 µmol, 2.0 equiv.) and 480 µL dry toluene was added, followed by *N,N*-dimethylethylamine (17 µL, 155 µmol, 2.0 equiv.). The colorless mix was cooled to -78°C and after 5 minutes ester **3e** (25 mg, 78 µmol, 1.0 equiv.) dissolved in 260 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 1 hour 30 minutes TMSCl (20 µL, 155 µmol, 2.0 equiv.) was added. It was allowed to slowly (flask left in cooling bath) warm to 18°-19° C over night. TLC (hexanes: ethyl acetate 6:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour 15 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was obtained as colorless oil in 95 % yield (24 mg, 74 µmol) and 16:1 *dr.*

Note: The high *dr* is difficult to reproduce and tends to vary between 7:1 to 16:1.

The yield always refers to a crude mixture of diastereomers and some minor impurities. The impurity formation is not avoidable and its intensity in the NMR also varies.

It was once attempted to purify the crude mixture by column chromatography which led to decomposition of the minor diastereomer. Impurities remained --> see MK-I-155 (crude) and MK-I-155-2-1

Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.38 – 6.89 (m, 10H), 6.00 (dd, *J*= 15.4, 9.3 Hz, 1H), 5.74 (dd, *J*= 15.5, 0.8 Hz, 1H), 4.34 (d, *J*= 9.2 Hz, 1H), 1.67 (s, 3H), 1.39 (s, 1H), 0.98 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= MK-II-69 ^{13}C not pure enough

Minor:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.38 – 6.89 (m, 10H), 5.53 (dd, *J*= 15.4, 9.5 Hz, 1H), 5.29 (d, *J*= 15.4 Hz, 1H), 4.48 (d, *J*= 9.4 Hz, 1H), 1.59 (s, 3H), 1.39 (s, 3H), 0.77 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= MK-II-69 13C not pure enough

IR sample: MK-II-69

IR (Neat Film, NaCl) 3027, 2959, 2869, 1708, 1598, 1458, 1362, 1225, 1029, 974, 920, 736, 699,680 cm^{-1}

Crotonaldehyde-derived

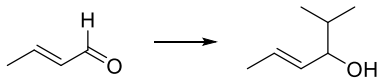
Grignard addition

General procedure:

A flame-dried 100 mL round bottom flask was equipped with crotonaldehyde **5** (1.0 equiv.) in dry THF (c= 0.29M). The colorless solution was cooled to -78°C and after 10 minutes Grignard reagent (1.20 equiv.) was added dropwise over 10 minutes. The reaction was allowed to warm

to 18-19° C over night and quenched by addition of saturated NH_4Cl solution and little H_2O the next day. The aqueous layer was extracted 3 times with Et_2O, the combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo.

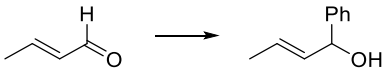
(*E*)-2-methylhex-4-en-3-ol **6a**



Grignard reagent: 1.0M iPrMgBr

The crude material was subjected to flash chromatography and product could be collected as colorless oil in 85 % yield (692 mg, 6.06 mmol). The material was used in the next step without further purification.

(*E*)-1-phenylbut-2-en-1-ol **6b**



Grignard reagent: 1.0M PhMgBr

The crude residue was subjected to flash chromatography and product could be collected as colorless oil in >100 % yield. The material was used in the next step without further purification.

(*E*)-2,2-dimethylhex-4-en-3-ol **6c**

Grignard reagent: 2.0M *tert*-ButylMgCl

The crude material was subjected to flash chromatography and product could be collected as colorless oil in >100 % yield. The material was used in the next step without further purification.

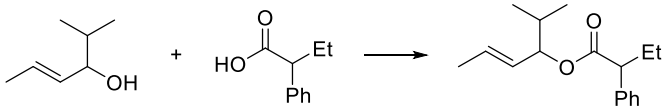
Esterification

General procedure:

A 25 mL round bottom flask was equipped with 2-phenylbutanoic acid *or* 2-phenylpropanoic acid (1.20 equiv.), EDCI (1.20 equiv.) and DMAP (0.20 equiv.). Alcohol **6** (1.0 equiv.) dissolved in dry DCM (c= 0.3M) was added and the mixture was stirred until TLC indicated full consumption of starting material. The reaction was quenched by addition of H_2O and layers

were separated. The aqueous layer was extracted with DCM three times and the combined organic layer was washed with H_2O. It was dried over Na_2SO_4 and concentrated in vacuo.

(*E*)-2-methylhex-4-en-3-yl 2-phenylbutanoate **7a**



The crude material was purified by column chromatography (hexanes: ethyl acetate 20:1) and the desired ester could be collected as colorless oil in 28 % yield (220 mg, 846 mmol) and 1:5:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 7.19 (m, 5H), 5.50 (dq, *J*= 15.5, 6.4 Hz, 1H), 5.27 (ddq, *J*= 15.2, 7.3, 1.7 Hz, 1H), 4.99 – 4.93 (m, 1H), 3.48 – 3.40 (m, 1H), 2.16 – 2.07 (m, 1H), 1.84 – 1.71 (m, 2H), 1.60 (dd, *J*= 6.4, 1.7 Hz, 3H), 0.96 – 0.81 (m, 6H), 0.72 (dd, *J*= 6.8, 2.4 Hz, 3H).

Note: HUUUGH ethyl acetate peak

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.4, 139.3, 129.6, 128.5, 128.2, 127.6, 127.1, 79.7, 54.1, 32.2, 26.7, 18.2, 18.2, 18.1, 12.3.

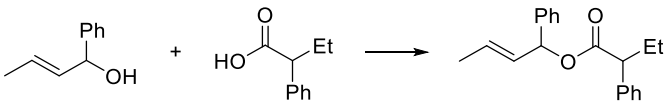
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 7.19 (m, 5H), 5.36 (ddq, *J*= 15.3, 7.6, 1.7 Hz, 1H), 4.96 (dt, *J*= 10.6, 6.9 Hz, 1H), 4.99 – 4.93 (m, 1H), 3.48 – 3.40 (m, 1H), 2.16 – 2.07 (m, 1H), 1.84 – 1.71 (m, 2H), 1.68 (dd, *J*= 6.7, 1.6 Hz, 3H), 0.96 – 0.81 (m, 6H), 0.72 (dd, *J*= 6.8, 2.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 139.6, 129.9, 128.5, 128.1, 127.9, 127.1, 79.8, 54.0, 32.2, 26.5, 18.0, 17.9, 17.8, 12.3.

IR (Neat Film, NaCl) 3063, 3030, 2964, 2936, 2876, 1732, 1674, 1602, 1496, 1454, 1380, 1368, 1299, 1264, 1225, 1199, 1166, 1118, 1076, 1033, 968, 916, 846, 768, 732, 698, 680 cm^{-1}

(*E*)-1-phenylbut-2-en-1-yl 2-phenylbutanoate **7b**



The crude material was purified by column chromatography (hexanes: ethyl acetate 25:1) and the desired ester could be collected as colorless oil in 91 % yield (990 mg, 3.07 mmol) over two steps and 1.6:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.35 – 7.07 (m, 10H), 6.22 – 6.16 (m, 1H), 5.77 – 5.49 (m, 2H), 3.55 – 3.49 (m, 1H), 2.18 – 2.05 (m, 1H), 1.87 – 1.77 (m, 1H), 1.72 – 1.69 (m, 3H), 0.91 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.0, 139.8, 139.0, 129.8, 129.7, 128.6, 128.4, 128.2, 127.7, 127.2, 126.5, 76.5, 53.8, 26.6, 17.9, 12.2.

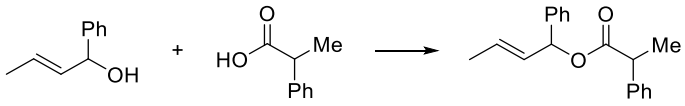
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.35 – 7.07 (m, 10H), 6.22 – 6.16 (m, 1H), 5.77 – 5.49 (m, 2H), 3.55 – 3.49 (m, 1H), 2.18 – 2.05 (m, 1H), 1.87 – 1.77 (m, 1H), 1.65 – 1.77 (m, 3H), 0.87 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.1, 139.9, 139.1, 129.4, 129.3, 128.5, 128.4, 128.2, 127.9, 127.2, 126.9, 76.4, 53.8, 26.8, 17.8, 12.2.

IR (Neat Film, NaCl) 3450, 3086, 3063, 3031, 2966, 2934, 2876, 2736, 2314, 2174, 1949, 1876, 1806, 1725, 1671, 1602, 1585, 1538, 1494, 1454, 1379, 1356, 1298, 1264, 1221, 1197, 1160, 1118, 1073, 1031, 1002, 964, 928, 847, 754, 702, 614 cm^{-1}

(*E*)-1-phenylbut-2-en-1-yl 2-phenylpropanoate **7c**



The crude material was filtered through a plug of silica (with pure DCM) and the desired ester could be collected as colorless oil in near quantitative yield (377 mg, 1.34 mmol) and 1.4:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 7.06 (m, 10H), 6.24 – 6.18 (m, 1H), 5.79 – 5.49 (m, 2H), 3.83 – 3.74 (m, 1H), 1.74 – 1.69 (m, 3H), 1.57 – 1.48 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 140.5, 139.8, 129.7, 129.3, 128.6, 128.4, 127.8, 127.2, 126.9, 126.5, 76.7, 45.9, 18.4, 17.9.

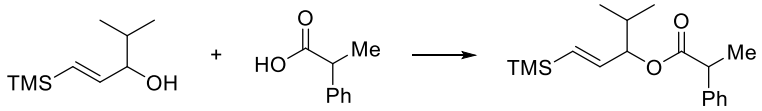
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 7.06 (m, 10H), 6.24 – 6.18 (m, 1H), 5.79 – 5.49 (m, 2H), 3.83 – 3.74 (m, 1H), 1.64 (d, *J*= 5.5 Hz, 3H), 1.57 – 1.48 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 140.6, 139.9, 129.9, 129.4, 128.6, 128.4, 127.7, 127.2, 126.9, 126.5, 76.5, 45.9, 18.6, 17.8.

IR (Neat Film, NaCl) 3063, 3030, 2978, 2937, 2876, 1949, 1735, 1602, 1495, 1453, 1377, 1317, 1237, 1200, 1165, 1075, 1030, 996, 965, 846, 815, 755, 698, 615 cm^{-1}

(*E*)-4-methyl-1-(trimethylsilyl)pent-1-en-3-yl 2-phenylpropanoate **7d**



A Scin vial was equipped with 2-phenylpropanoic acid (111 mg, 738 µmol, 1.20 equiv.), EDCI (141 mg, 738 µmol, 1.20 equiv.) and DMAP (15 mg, 123 µmol, 0.20 equiv.). Alcohol (106 mg, 615 µmol, 1.0 equiv. – generous donation of TF) dissolved in 3 mL dry DCM was added and the mixture was stirred over night. The next day, the reaction was quenched by addition of H_2O. The aqueous layer was extracted with DCM twice and the combined organic layer was dried over Na_2SO_4. The solvent was removed in vacuo and the crude residue was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in 76 % yield (142 mg, 466 µmol) and 1.7:1 *dr*. The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 7.22 (m, 5H), 5.79 – 5.74 (m, 1H), 5.47 (dd, *J*= 18.8, 1.4 Hz, 1H), 5.05 – 5.00 (m, 1H), 3.80 – 3.74 (m, 1H), 1.82 (dq, *J*= 13.3, 6.7 Hz, 1H), 1.55 – 1.50 (m, 3H), 0.86 (dd, *J*= 6.7, 1.5 Hz, 6H), -0.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.8, 141.8, 140.9, 132.0, 128.6, 127.7, 127.1, 80.3, 45.8, 31.9, 18.4, 18.2, 17.8, -1.3.

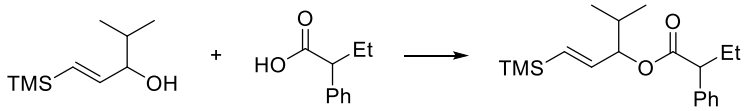
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 7.22 (m, 5H), 5.87 (dd, *J*= 18.8, 5.6 Hz, 1H), 5.74 – 5.70 (m, 1H), 5.05 – 5.00 (m, 1H), 3.80 – 3.74 (m, 1H), 1.79 – 1.72 (m, 1H), 1.55 – 1.50 (m, 3H), 0.72 (dd, *J*= 6.8, 4.3 Hz, 6H), 0.05 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.8, 142.1, 140.9, 132.5, 128.6, 127.7, 127.2, 80.6, 46.0, 32.0, 18.2, 18.2, 17.6, -1.2.

IR (Neat Film, NaCl) 3064, 3030, 2960, 2875, 1815, 1736, 1622, 1602, 1496, 1454, 1368, 1322, 1248, 1202, 1168, 1128, 1069, 1066, 1031, 990, 866, 840, 764, 731, 698, 680, 666 cm^{-1}

(*E*)-4-methyl-1-(trimethylsilyl)pent-1-en-3-yl 2-phenylbutanoate **7e**



A Scin vial was equipped with 2-phenylbutanoic acid (140 mg, 850 µmol, 1.20 equiv.), EDCI (163 mg, 850 µmol, 1.20 equiv.) and DMAP (17 mg, 142 µmol, 0.20 equiv.). Alcohol (122 mg, 708 µmol, 1.0 equiv. – generous donation of TF) dissolved in 3 mL dry DCM was added and the mixture was stirred over night. The next day, the reaction was quenched by addition of H_2O. The aqueous layer was extracted with DCM twice and the combined organic layer was dried over Na_2SO_4. The solvent was removed in vacuo and the crude residue was filtered through a

plug of silica (with DCM). The desired ester could be collected as colorless oil in 92 % yield (207 mg, 650 µmol) and 1.5:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.09 (m, 5H), 5.80 – 5.74 (m, 1H), 5.49 (dd, *J*= 18.9, 1.5 Hz, 1H), 5.07 – 5.00 (m, 1H), 3.50 (dd, *J*= 7.7 Hz, 1H), 2.21 – 2.00 (m, 1H), 1.89 – 1.71 (m, 2H), 0.95 – 0.89 (m, 3H), 0.86 (d, *J*= 6.7 Hz, 3H), 0.75 (t, *J*= 6.4 Hz, 3H), -0.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.2, 141.8, 139.4, 132.0, 128.5, 128.1, 127.1, 80.2, 53.9, 31.9, 26.4, 18.4, 17.8, 12.3, -1.4.

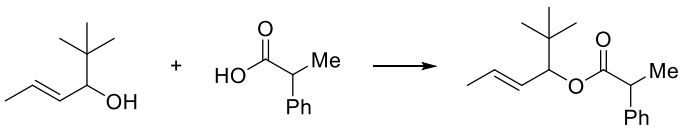
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.09 (m, 5H), 5.88 (dd, *J*= 18.8, 5.6 Hz, 1H), 5.74 – 5.70 (m, 1H), 5.07 – 5.00 (m, 1H), 3.50 (dd, *J*= 7.7 Hz, 1H), 2.21 – 2.00 (m, 1H), 1.89 – 1.71 (m, 2H), 0.95 – 0.89 (m, 3H), 0.86 (d, *J*= 6.7 Hz, 3H), 0.75 (t, *J*= 6.4 Hz, 3H), 0.04 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.3, 142.1, 139.4, 132.4, 128.5, 128.1, 127.2, 80.5, 54.0, 31.9, 26.3, 18.2, 17.6, 12.3, -1.3.

IR (Neat Film, NaCl) 3064, 3030, 2963, 2876, 1814, 1735, 1622, 1603, 1496, 1455, 1386, 1365, 1261, 1248, 1222, 1199, 1165, 1121, 1073, 1033, 989, 866, 838, 769, 730, 698 cm^{-1}

(*E*)-2,2-dimethylhex-4-en-3-yl 2-phenylpropanoate (Substrate not mentioned above)



The crude material was purified by column chromatography (hexanes: ethyl acetate 25:1) and the desired ester could be collected as colorless oil in 45 % yield (182 mg, 699 µmol) over two steps and 1.6:1 *dr.*

Major:

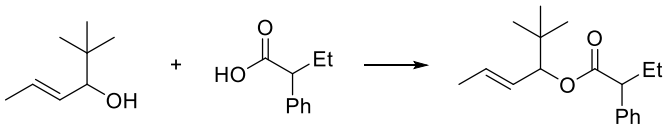
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.21 (m, 5H), 5.69 – 5.61 (m, 1H), 5.42 – 5.36 (m, 1H), 4.89 (t, *J*= 7.2 Hz, 1H), 3.78 – 3.68 (m, 1H), 1.69 (dd, *J*= 6.5, 1.7 Hz, 3H), 1.55 – 1.49 (m, 3H), 0.72 (s, 9H).

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.21 (m, 5H), 5.52 – 5.44 (m, 1H), 5.33 – 5.20 (m, 1H), 4.89 (t, *J*= 7.2 Hz, 1H), 3.78 – 3.68 (m, 3H), 1.61 (dd, *J*= 6.5, 1.7 Hz, 3H), 1.55 – 1.49 (m, 3H), 0.84 (s, 9H).

IR (Neat Film, NaCl) 3030, 2967, 2870, 1733, 1670, 1602, 1478, 1454, 1394, 1365, 1330, 1241, 1201, 1167, 1076, 1031, 996, 968, 934, 731, 698 cm^{-1}

(*E*)-2,2-dimethylhex-4-en-3-yl 2-phenylbutanoate (Substrate not mentioned above)



The crude material was filtered through a plug of silica (with pure DCM) and the desired ester could be collected as colorless oil in 45 % yield (290 mg, 1.06 mmol) over two steps. The material was used in the next step without further purification.

Major:

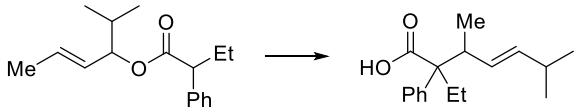
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 – 7.20 (m, 5H), 5.63 (dq, *J*= 15.5, 6.5 Hz, 1H), 5.39 (ddq, *J*= 15.4, 7.9, 1.7 Hz, 1H), 4.88 (d, *J*= 7.8 Hz, 1H), 3.49 – 3.40, (m, 1H), 2.18 – 2.09 (m, 1H), 1.87 – 1.78 (m, 1H), 1.67 (dd, *J*= 6.6, 1.6 Hz, 3H), 0.94 – 0.86 (m, 3H), 0.74 (s, 9H).

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 – 7.20 (m, 5H), 5.48 (dq, *J*= 15.3, 6.5 Hz, 1H), 5.29 (ddq, *J*= 15.3, 7.5, 1.8 Hz, 1H), 4.91 (d, *J*= 7.5 Hz, 1H), 3.49 – 3.40, (m, 1H), 2.18 – 2.09 (m, 1H), 1.87 – 1.78 (m, 1H), 1.59 (dd, *J*= 6.6, 1.6 Hz, 3H), 0.95 – 0.87 (m, 3H), 0.84 (s, 9H).

Ireland Claisen rearrangement

(*E*)-2-ethyl-3,6-dimethyl-2-phenylhept-4-enoic acid **8a**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (26 mg, 154 µmol, 2.0 equiv.) and 480 µL dry toluene was added, followed by *N,N*-dimethylethylamine (17 µL, 154 µmol, 2.0 equiv.). The colorless mix was cooled to -78°C and after 19 min, ester **7a** (20 mg, 256 µmol, 1.0 equiv.) dissolved in 260 µL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 2 hours TMSCl (20 µL, 164 µmol, 2.0 equiv.) was added dropwise. After 5 minutes acetone was added to warm the cooling bath to +4° C over 1 hour 30 minutes. Then the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and Et_2O, layers were separated and the organic layer was washed with H_2O once. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was obtained as pale yellow oil in 95 % yield (19 mg, 73 µmol) and 5.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.33 – 7.01 (m, 5H), 5.31 (dd, *J*= 15.4, 6.8 Hz, 1H), 5.07 (dd, *J*= 15.4, 9.2 Hz, 1H), 3.08 – 2.99 (m, 1H), 2.24 – 2.02 (m, 3H), 1.11 (d, *J*= 6.7 Hz, 3H), 1.01 – 0.94 (m, 3H), 0.91 – 0.85 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.9, 139.2, 138.2, 129.3, 128.1, 127.4, 126.7, 59.2, 42.0, 31.2, 29.5, 22.8, 22.7, 18.1, 9.2.

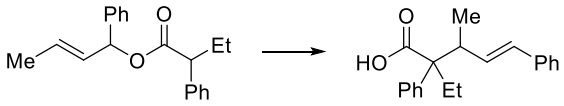
Minor:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.33 – 7.01 (m, 5H), 5.55 – 5.41 (m, 2H), 2.97 – 2.89 (m, 1H), 2.24 – 2.02 (m, 3H), 1.11 (d, *J*= 6.7 Hz, 3H), 1.01 – 0.94 (m, 3H), 0.91 – 0.85 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.5, 139.2, 138.6, 129.0, 128.6, 127.5, 126.6, 59.9, 43.0, 31.3, 29.7, 22.8, 22.6, 18.1, 9.5.

MK-II-81
IR (Neat Film, NaCl) 2962, 1699, 1602, 1498, 1458, 1383, 1252, 1034, 977, 794, 762, 733, 701, 680, 658 cm^{-1}

(*E*)-2-ethyl-3-methyl-2,5-diphenylpent-4-enoic acid **8b**



A flame-dried 10 mL round bottom flask was equipped LiHMDS (46 mg, 272 µmol, 2.0 equiv.) and 850 µL dry toluene was added, followed by *N,N*-dimethylethylamine (29 µL, 272 µmol, 2.0 equiv.). The colorless mix was cooled to -78°C and after 5 minutes ester **7b** (40 mg, 135 µmol, 1.0 equiv.) dissolved in 450 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 1 hour 40 minutes TMSBr (36 µL, 272 µmol, 2.0 equiv.) was added and the reaction was allowed to warm to 18°-19° C over night. TLC (hexanes: ethyl acetate 6:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After hours, the mix was diluted with H_2O and Et_2O, layers were separated and organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was obtained as pale yellow oil in 90 % yield (66 mg, 122 µmol) and 4.8:1 *dr.*

Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.43 – 7.16 (m, 10H), 6.43 (d, *J*= 15.8 Hz, 1H), 5.73 (ddd, *J*= 15.8, 9.5, 1.4 Hz, 1H), 3.22 – 3.12 (m, 1H), 2.29 – 2.14 (m, 2H), 1.09 (dd, *J*= 6.8, 1.5 Hz, 3H), 0.99 – 0.94 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.4, 137.9, 137.6, 131.7, 131.0, 129.2, 128.6, 127.6, 127.3, 127.0, 126.3, 59.3, 42.7, 29.8, 18.0, 9.3.

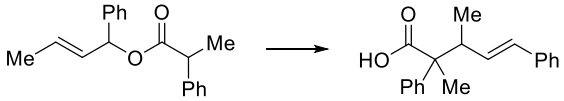
Minor:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.43 – 7.16 (m, 10H), 6.48 – 6.43 (m, 1H), 6.11 (ddd, *J*= 15.9, 8.8, 1.6 Hz, 1H), 3.22 – 3.12 (m, 1H), 2.29 – 2.14 (m, 2H), 1.04 (d, *J*= 6.6 Hz, 3H), 0.91 – 0.86 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.0, 138.4, 137.8, 132.4, 131.0, 129.0, 128.9, 127.7, 127.3, 126.9, 126.3, 59.9, 43.2, 30.5, 16.1, 9.5.

IR (Neat Film, NaCl) 3026, 2972, 1698, 1599, 1495, 1447, 1402, 1252, 1120, 1033, 972, 847, 788, 749, 694, 658 cm^{-1}

(*E*)-2,3-dimethyl-2,5-diphenylpent-4-enoic acid **8c**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.29 mL, 413 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (45 µL, 413 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **7c** (58 mg, 207 µmol, 1.0 equiv.) dissolved in 700 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (53 µL, 413 µmol, 2.0 equiv.) was added dropwise. After 45 minutes the flask was removed from cooling and allowed to warm to 18-19° C. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered over a plug of silica (DCM) and desired product was obtained as white solids in 78 % yield (45 mg, 161 µmol) and 5.5:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.51 – 7.12 (m, 10H), 6.49 (d, *J*= 15.9 Hz, 1H), 6.18 (dd, *J*= 15.9, 7.5 Hz, 1H), 3.42 – 3.32 (m, 1H), 1.58 (d, *J*= 11.6 Hz, 3H), 0.88 (d, *J*= 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.0, 141.0, 137.7, 131.9, 131.5, 128.6, 128.4, 127.2, 127.1, 126.3, 54.0, 43.5, 17.0, 15.0.

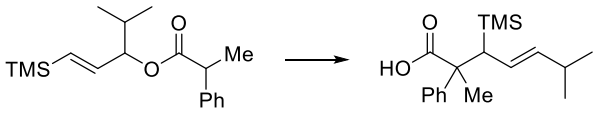
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.51 – 7.12 (m, 10H), 6.23 – 6.19 (m, 1H) 5.83 (dd, *J*= 15.9, 7.2 Hz, 1H), 3.42 – 3.32 (m, 1H), 1.58 (d, *J*= 11.6 Hz, 3H), 1.21 (d, *J*= 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.0, 141.5, 137.7, 131.1, 131.0, 128.6, 128.5, 127.3, 126.9, 126.1, 53.8, 43.7, 16.8, 16.3.

IR (Neat Film, NaCl) 3059, 3026, 2974, 2637, 2249, 1949, 1807, 1698, 1581, 1599, 1495, 1446, 1403, 1384, 1275, 1120, 1070, 1031, 1005, 971, 910, 751, 724, 695, 660, 606 cm^{-1}

(*E*)-2,6-dimethyl-2-phenyl-3-(trimethylsilyl)hept-4-enoic acid **8d**



A flame-dried 25 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.23 mL, 394 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (43 µL, 394 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **7d** (60 mg, 197 µmol, 1.0 equiv.) dissolved in 660 µL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 2 hours TMSCl (50 µL, 394 µmol, 2.0 equiv.) was added and the reaction was allowed to warm to 18°-19° C over night. TLC (hexanes: ethyl acetate 4:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo and the residue was filtered through a plug of silica (with DCM). The desired product was obtained as colorless oil in 85 % yield (51 mg, 167 µmol) and 5.8:1 *dr*.

Note: *dr* hard to tell. 5.8:1 *dr* at 0.91 vs 0.67 ppm. Maybe after methylation + purification

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.53 – 7.16 (m, 5H), 5.44 – 5.27 (m, 2H), 2.57 (d, *J*= 10.1 Hz, 1H), 2.24 – 2.14 (m, 1H), 1.63 (s, 3H), 0.91 (d, *J*= 6.7 Hz, 3H), 0.87 (d, *J*= 6.6 Hz, 3H), -0.27 (s, 9H).

1H not super pure

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.9, 142.3, 140.8, 128.1, 127.6, 127.1, 123.8, 52.6, 42.9, 31.5, 22.8, 22.8, 20.1, -0.7.

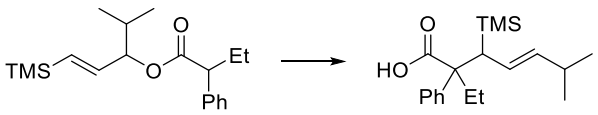
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.53 – 7.16 (m, 5H), 5.44 – 5.27 (m, 2H), 2.66 – 2.62 (m, 1H), 2.33 – 2.24 (m, 1H), 1.65 (s, 3H), 1.00 – 0.95 (m, 6H), 0.17 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.8, 143.1, 139.8, 128.0, 127.9, 126.8, 123.6, 51.8, 42.1, 31.5, 22.8, 22.6, 20.9, -0.9.

IR (Neat Film, NaCl) 2956, 2635, 1698, 1599, 1498, 1464, 1446, 1404, 1382, 1249, 1120, 1075, 973, 839, 756, 722, 696, 658, 616 cm^{-1}

(*E*)-2-ethyl-6-methyl-2-phenyl-3-(trimethylsilyl)hept-4-enoic acid **8e**



A flame-dried 25 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.14 mL, 365 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (40 µL, 365 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **7e** (58 mg, 183 µmol, 1.0 equiv.) dissolved in 600 µL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 2

hours TMSCl (46 µL, 365 µmol, 2.0 equiv.) was added and the reaction was allowed to warm to 18°-19° C over night. TLC (hexanes: ethyl acetate 4:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo and the residue was filtered through a plug of silica (with DCM). The desired product was obtained as colorless oil in 65 % yield (37 mg, 119µmol).

Note: *dr* hard to tell. Maybe after methylation + purification

NMR MK-II-49-1-1 in C_6D_6 7.5:1 *dr* with respect to double bond Hs

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 7.16 (m, 5H), 5.29 (dd, *J*= 15.1, 7.0 Hz, 1H), 5.08 (dd, *J*= 15.2, 11.3 Hz, 1H), 2.38 (dd, *J*= 9.0, 5.3 Hz, 1H), 2.28 – 1.97 (m, 3H), 0.93 (d, *J*= 6.8 Hz, 6H), 0.80 (t, *J*= 7.3 Hz, 3H), -0.17 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.4, 140.6, 139.9, 128.9, 127.7, 126.6, 124.0, 57.1, 40.9, 31.7, 23.0, 22.9, 9.2, -0.7.

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= Hard to tell, NMR not too pure

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.7, 141.4, 139.0, 127.9, 127.9, 126.6, 124.8, 57.6, 42.2, 32.5, 23.0, 22.9, 8.9, -0.6.

IR (Neat Film, NaCl) 2959, 1698, 1498, 1464, 1403, 1247, 980, 924, 865, 835, 763, 701, 658 cm^{-1}

α-Quaternary, β-Quaternary carboxylic acids

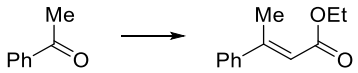
Ketone-derived

Horner-Wadsworth-Emmons

General procedure:

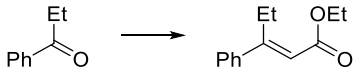
A flame-dried 250 mL round bottom flask was equipped with NaH (60 % in mineral oil, 1.50 equiv.) in dry THF (c= 1M) and the suspension was cooled via ice bath. Triethyl phosphonoacetate (2.0 equiv.) in dry THF (c= 2.5M) was added dropwise over 45 minutes. After all gas formation had ceased ketone **9** (1.0 equiv.) in dry THF (c= 5M) was added dropwise over 10 minutes. The reaction was stirred at given temperature until TLC (hexanes: ethyl acetate 10:1) indicated full consumption of starting material. The reaction was quenched by addition of saturated NH_4Cl solution and the layers were separated. The aqueous layer was extracted with ethyl acetate 3 times, the combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude mixture was purified by column chromatography (silica gel, hexanes: ethyl acetate 45:1 to 10:1).

Ethyl (*E*)-3-phenylbut-2-enoate **10a**



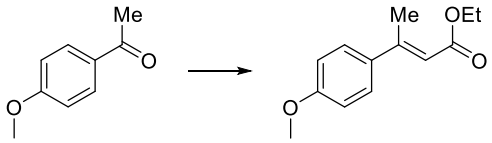
The reaction was conducted at 19°C. Pure *E*-isomer could be collected as colorless oil in 26 % yield (1.24 g, 6.52 mmol) accompanied by 2.92 g of mix fraction.

Ethyl (*E*)-3-phenylpent-2-enoate **10b**



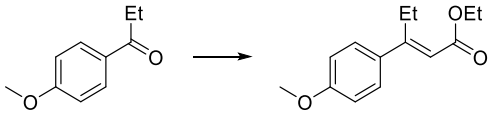
The reaction was conducted at 50°C. Pure *E*-isomer could be collected as colorless oil in 77 % yield (2.33 g, 11.41 mmol). Pure *Z*-isomer could be collected as colorless oil in 21 % yield (646 mg, 3.16 mmol).

Ethyl (*E*)-3-(4-methoxyphenyl)but-2-enoate **10c**



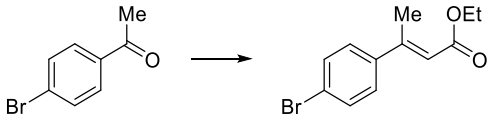
The reaction was conducted at 50°C. Pure *E*-isomer could be collected as colorless oil in 75 % yield (2.20 g, 9.99 mmol). Solidification was observed after storing the sample in the freezer over night. Pure *Z*-isomer could be collected as colorless oil in 14 % yield (415 mg, 1.88 mmol).

Ethyl (*E*)-3-(4-methoxyphenyl)pent-2-enoate **10d**



The reaction was conducted at 50°C. Pure *E*-isomer could be collected as colorless oil in 47 % yield (1.33 g, 5.68 mmol). Solidification was observed after storing the sample in the freezer over night. Pure *Z*-isomer could be collected as colorless oil in 13 % yield (383 mg, 1.63 mmol).

Ethyl (*E*)-3-(4-bromophenyl)but-2-enoate **10e**



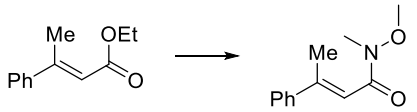
The reaction was conducted at 19°C.Pure *E*-isomer could be collected as colorless oil in 41 % yield (2.24 g, 8.32 mmol), accompanied by 2.28 g of mix fraction.

Weinreb amide formation

General procedure:

A flame-dried 100 mL round bottom flask was equipped with ester (1.0 equiv.) in dry THF (c= 0.3M) and *N,O*-dimethylhydroxylamine hydrochloride (2.0 equiv.) was added. The colorless mixture was cooled to -78° C and isopropylmagnesium chloride (2.0 M, 4.0 equiv.) was added dropwise over 10 minutes. The reaction was allowed to warm to 18-19° C over night. After TLC (hexanes: ethyl acetate 10:1) indicated full consumption of starting material the reaction was quenched by addition of saturated NH_4Cl solution. Layers were separated and the aqueous layer was extracted with ethyl acetate 3 times. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo.

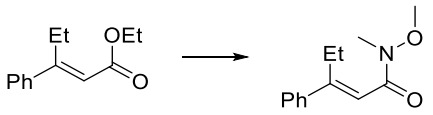
(*E*)-N-methoxy-N-methyl-3-phenylbut-2-enamide **11a**



This substrate did not go to full completion and was purified by column chromatography (silica gel, hexanes: ethyl acetate 10:1 to 3:1). Product could be collected as yellow oil in 66 % yield (882 mg, 4.30 mmol) accompanied by 17 % (213 mg, 1.12 mmol) of recovered starting material.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.51 – 7.44 (m, 2H), 7.42 – 7.31 (m, 3H), 6.57 (s, 1H), 3.72 (s, 3H), 3.28 (s, 3H), 2.54 (d, *J*= 1.5 Hz, 3H).

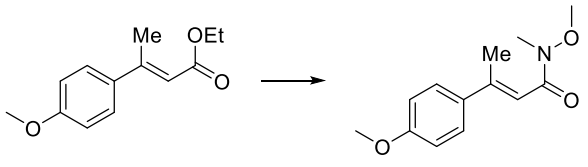
(*E*)-N-methoxy-N-methyl-3-phenylpent-2-enamide **11b**



The product could be collected as yellow oil in 77 % yield (1.92 g, 8.75 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.42 (m, 2H), 7.41 – 7.31 (m, 3H), 6.44 (s, 1H), 3.70 (s, 3H), 3.27 (s, 3H), 3.05 (q, *J*= 7.5 Hz, 2H), 1.07 (t, *J*= 7.5 Hz, 3H).

(*E*)-N-methoxy-3-(4-methoxyphenyl)-N-methylbut-2-enamide **11c**

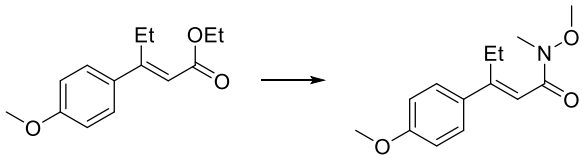


The product could be collected as yellow-white amorphous solid in 91 % yield (2.13 g, 9.07 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.48 – 7.41 (m, 2H), 6.93 – 6.85 (m, 2H), 6.54 (s, 1H), 3.83 (s, 3H), 3.71 (s, 3H), 3.26 (s, 3H), 2.52 (d, *J*= 1.3 Hz, 3H).

Note: NMR shows 7 % starting material

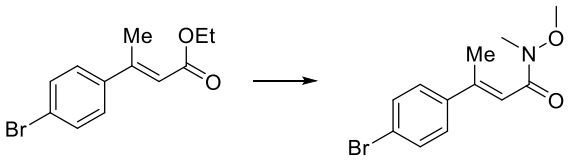
(*E*)-N-methoxy-3-(4-methoxyphenyl)-N-methylpent-2-enamide **11d**



The product could be collected as yellow oil in 91 % yield (1.32 g, 5.29 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.45 – 7.38 (m, 2H), 6.94 – 6.87 (m, 2H), 6.42 (s, 1H), 3.84 (s, 3H), 3.70 (s, 3H), 3.26 (s, 3H), 3.04 (q, *J*= 7.5 Hz, 2H), 1.08 (t, *J*= 7.4 Hz, 3H).

(*E*)-3-(4-bromophenyl)-N-methoxy-N-methylbut-2-enamide **11e**



The product could be collected as orange oil in 86 % yield (993 mg, 3.49 mmol). Solidification was observed after storing the sample in the freezer over night. The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.52 – 7.47 (m, 2H), 7.37 – 7.32 (m, 2H), 6.55 (s, 1H), 3.71 (s, 3H), 3.27 (s, 3H), 2.52 – 2.48 (m, 3H).

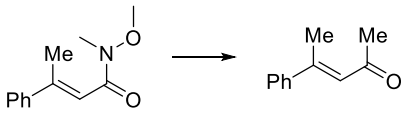
Literature unknown compound

Grignard Addition to Weinreb amide

General procedure:

A flame-dried 50 mL round bottom flask was equipped with Weinreb amide **11** (1.0 equiv.) in dry THF (c= 0.28). It was cooled to -78°C and after 5 minutes Grignard reagent (2.0 equiv.) was added dropwise. The reaction was allowed to warm to 18-19° C. After TLC (hexanes: ethyl acetate 2:1) confirmed full conversion the reaction was quenched by addition of saturated NH_4Cl solution and little H_2O. Layers were separated and the aqueous layer was extracted with Et_2O 3 times. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo.

(*E*)-4-phenylpent-3-en-2-one **12a**

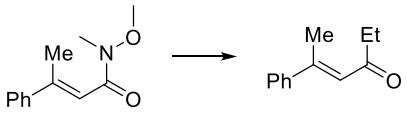


Grignard reagent: 3.0M MeMgBr

The product could be collected as yellow oil in near quantitative yield (156 mg, 974 µmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.51 – 7.35 (m, 5H), 6.52 (t, *J*= 1.4 Hz, 1H), 2.55 (d, *J*= 1.4 Hz, 3H), 2.30 (s, 3H).

(*E*)-5-phenylhex-4-en-3-one **12b**

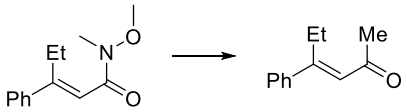


Grignard reagent: 1.0M EtMgBr

The product could be collected as orange oil in >100 % yield and was directly used in the next step without purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.50 – 7.35 (m, 5H), 6.50 (q, *J*= 1.4 Hz, 1H), 2.61 – 2.55 (m, 5H), 1.14 (t, *J*= 7.3 Hz, 3H).

(*E*)-4-phenylhex-3-en-2-one **12c**

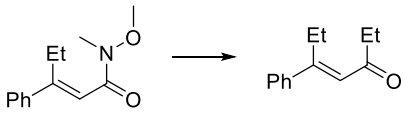


Grignard reagent: 3.0M MeMgBr

The product could be collected as orange oil in 86 %yield (369 mg, 2.12 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.49 – 7.34 (m, 5H), 6.39 (s, 1H), 3.05 (q, *J*= 7.5 Hz, 2H), 2.29 (s, 3H), 1.07 (t, *J*= 7.4 Hz, 3H).

(*E*)-5-phenylhept-4-en-3-one **12d**

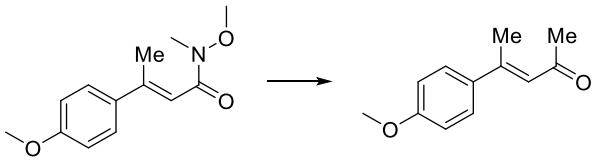


Grignard reagent: 1.0M EtMgBr

The product could be collected as dark orange oil in 93 % yield (447 mg, 2.37 mmol). The material was used in the next step without further purification. NMR shows product with ~10 % *Z*-isomer.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.32 (m, 5H), 6.38 (s, 1H), 3.06 (q, *J*= 7.5 Hz, 2H), 2.57 (q, *J*= 7.3 Hz, 2H), 1.13 (t, *J*= 7.3 Hz, 3H), 1.07 (t, *J*= 7.4 Hz, 3H).

(*E*)-4-(4-methoxyphenyl)pent-3-en-2-one **12e**

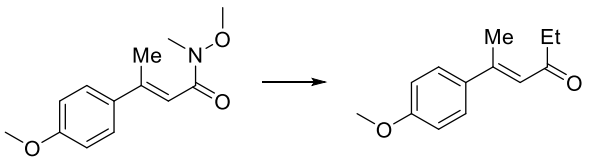


Grignard reagent: 3.0M MeMgBr

The product could be collected as orange oil in near quantitative yield (426 mg, 2.24 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.50 – 7.42 (m, 2H), 6.94 – 6.86 (m, 2H), 6.50 (d, *J*= 1.5 Hz, 1H), 3.84 (s, 3H), 2.53 (d, *J*= 1.2 Hz, 3H), 2.29 (s, 3H).

(*E*)-5-(4-methoxyphenyl)hex-4-en-3-one **12f**

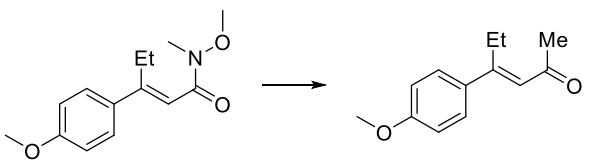


Grignard reagent: 1.0M EtMgBr

The product could be collected as yellow oil in near quantitative yield (443 mg, 2.17 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.50 – 7.43 (m, 2H), 6.93 – 6.88 (m, 2H), 6.49 (d, *J*= 1.5 Hz, 1H), 3.84 (s, 3H), 2.60 – 2.53 (m, 5H), 1.13 (t, *J*= 7.3 Hz, 3H).

(*E*)-4-(4-methoxyphenyl)hex-3-en-2-one **12g**

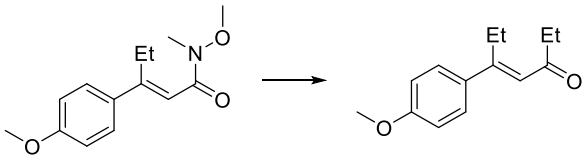


Grignard reagent: 3.0M MeMgBr

The product could be collected as yellow-orange oil in 96 % yield (335 mg, 1.64 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.41 (m, 2H), 6.94 – 6.87 (m, 2H), 6.39 (s, 1H), 3.84 (s, 3H), 3.04 (q, *J*= 7.5 Hz, 2H), 2.28 (s, 3H), 1.07 (t, *J*= 7.4 Hz, 3H).

(*E*)-5-(4-methoxyphenyl)hept-4-en-3-one **12h**



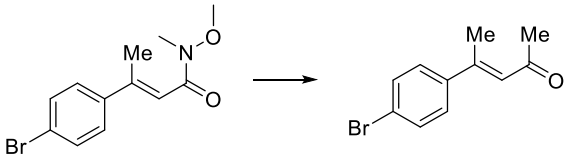
Grignard reagent: 1.0M EtMgBr

The product could be collected as dark orange oil in 94 % (342 mg, 1.57 mmol). The material was used in the next step without further purification.

NMR shows product with 10 % *Z*-isomer.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.41 (m, 2H), 6.93 – 6.88 (m, 2H), 6.38 (s, 1H), 3.84 (s, 3H), 3.05 (q, *J*= 7.5 Hz, 2H), 2.56 (q, *J*= 7.3 Hz, 2H), 1.12 (t, *J*= 7.3 Hz, 3H), 1.08 (t, *J*= 7.5 Hz, 3H).

(*E*)-4-(4-bromophenyl)pent-3-en-2-one **12i**

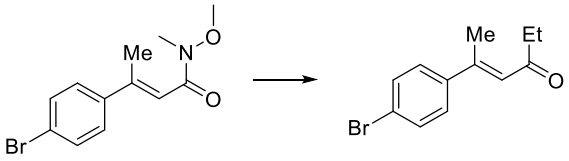


Grignard reagent: 3.0M MeMgBr

The product could be collected as orange oil in 91 % yield (376 mg, 1.57 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.53 – 7.47 (m, 2H), 7.37 – 7.32 (m, 2H), 6.48 (d, *J*= 1.5 Hz, 1H), 2.51 (d, *J*= 1.4 Hz, 3H), 2.30 (s, 3H).

(*E*)-5-(4-bromophenyl)hex-4-en-3-one **12j**



Grignard reagent: 1.0M EtMgBr

The product could be collected as dark orange oil in 94 % yield (411 mg, 1.62 mmol). The material was used in the next step without further purification.

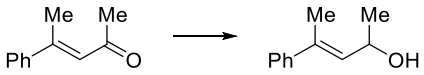
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.52 – 7.48 (m, 2H), 7.36 – 7.32 (m, 2H), 6.47 (d, *J*= 1.6 Hz, 1H), 2.57 (q, *J*= 7.0 Hz, 2H), 2.52 (d, *J*= 1.3 Hz, 3H), 1.13 (t, *J*= 7.3 Hz, 3H).

Luche reduction

General procedure:

A 50 mL round bottom flask was equipped with ketone **12** (1.0 equiv.) in MeOH (c= 0.1M) and $CeCl_3 \bullet 7H_2O$ (0.20 equiv.) was added. The mix was cooled via ice bath and after 20 minutes $NaBH_4$ (1.20 equiv.) was added. After TLC (hexanes: ethyl acetate 2:1) indicated full conversion reaction was quenched by addition of solid NH_4Cl. The solvent was removed in vacuo and the residue was taken up in ethyl acetate and little water. Layers were separated and the aqueous layer was extracted with ethyl acetate 3 times. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo.

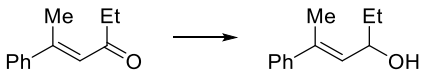
(*E*)-4-phenylpent-3-en-2-ol **13a**



The desired product could be collected as yellow oil in 92 % yield (146 mg, 900 µmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 (dd, *J*= 8.2, 1.4 Hz, 2H), 7.32 (dd, *J*= 8.4, 6.7 Hz, 2H), 7.29 – 7.25 (m, 1H), 5.81 (dp, *J*= 8.4, 1.4 Hz, 1H), 4.76 (dq, *J*= 8.3, 6.3 Hz, 1H), 2.10 (d, *J*= 1.4 Hz, 3H), 1.36 (d, *J*= 6.2 Hz, 3H).

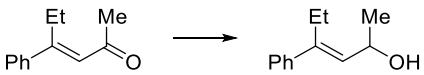
(*E*)-5-phenylhex-4-en-3-ol **13b**



The desired product could be collected as yellow oil in 96 % yield (266 mg, 1.51 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.44 – 7.24 (m, 5H), 5.76 (dd, *J*= 8.6, 1.5 Hz, 1H), 4.49 (dt, *J*= 8.8, 6.6 Hz, 1H), 2.12 (d, *J*= 1.4 Hz, 3H), 1.77 – 1.69 (m, 1H), 1.65 – 1.57, (m, 1H), 0.97 (t, *J*= 7.5 Hz, 3H).

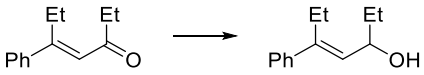
(*E*)-4-phenylhex-3-en-2-ol **13c**



The desired product could be collected as pale yellow oil in 94 % yield (337 mg, 1.91 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 7.25 (m, 5H), 5.66 (d, *J*= 8.7 Hz, 1H), 4.77 (dq, *J*= 8.6, 6.3 Hz, 1H), 2.65 – 2.50 (m, *J*= 7.1 Hz, 2H), 1.36 (d, *J*= 6.3 Hz, 3H), 1.01 (t, *J*= 7.5 Hz, 3H).

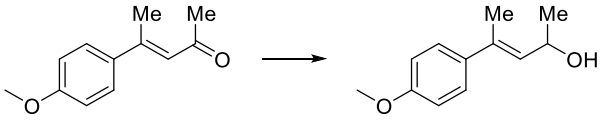
(*E*)-5-phenylhept-4-en-3-ol **13d**



The desired product could be collected as yellow oil in 69 % yield (301 mg, 1.58 mmol). The material was used in the next step without further purification. NMR shows ~ 7 % *Z*-isomer

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 7.25 (m, 6H), 5.60 (d, *J*= 8.9 Hz, 1H), 4.47 (dt, *J*= 8.8, 6.5 Hz, 1H), 2.59 (qd, *J*= 7.5, 2.0 Hz, 2H), 1.77 – 1.68 (m, 1H), 1.63 – 1.57 (m, 1H), 0.99 (m, 6H).

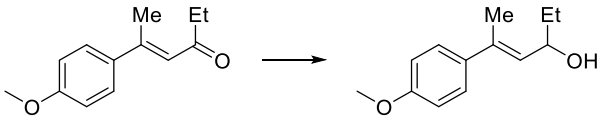
(*E*)-4-(4-methoxyphenyl)pent-3-en-2-ol **13e**



The desired product could be collected as colorless needles in 95 % yield (386 mg, 2.01 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 7.31 (m, 2H), 6.91 – 6.82 (m, 2H), 5.74 (dd, *J*= 8.3, 1.5 Hz, 1H), 4.75 (dq, *J*= 8.5, 6.3 Hz, 1H), 3.82 (s, 3H), 2.08 (d, *J*= 1.4 Hz, 3H), 1.35 (d, *J*= 6.2 Hz, 3H).

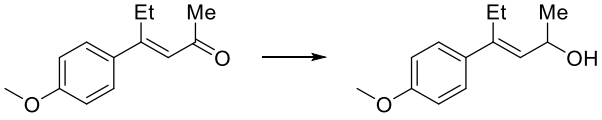
(*E*)-5-(4-methoxyphenyl)hex-4-en-3-ol **13f**



The desired product could be collected as yellow orange oil in 96 % yield (415 mg, 2.01 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 7.33 (m, 2H), 6.92 – 6.82 (m, 2H), 5.69 (dq, *J*= 8.6, 1.5 Hz, 1H), 4.47 (dt, *J*= 8.8, 6.6 Hz, 1H), 3.82 (s, 3H), 2.09 (d, *J*= 1.5 Hz, 3H), 1.76 – 1.67 (m, 1H), 1.64 – 1.53 (m, 1H), 0.96 (t, *J*= 7.4 Hz, 3H).

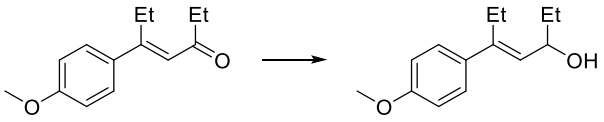
(*E*)-4-(4-methoxyphenyl)hex-3-en-2-ol **13g**



The desired product could be collected as yellow orange oil in 92 % yield (294 mg, 1.43 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 7.28 (m, 2H), 6.88 – 6.83 (m, 2H), 5.60 (d, *J*= 8.7 Hz, 1H), 4.75 (dq, *J*= 8.7, 6.2 Hz, 1H), 3.82 (s, 3H), 2.61 – 2.49 (m, 2H), 1.35 (d, *J*= 6.2 Hz, 3H), 1.00 (t, *J*= 7.5 Hz, 3H).

(*E*)-5-(4-methoxyphenyl)hept-4-en-3-ol **13h**

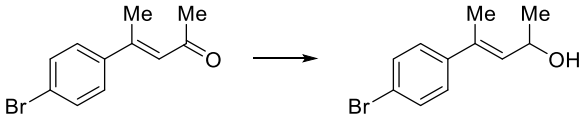


The desired product could be collected as yellow orange oil in 95 % yield (318 mg, 1.44 mmol). The material was used in the next step without further purification.

NMR shows ~10% *Z*-isomer.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 7.28 (m, 2H), 6.88 – 6.84 (m, 2H), 5.54 (d, *J*= 8.9 Hz, 1H), 4.45 (dt, *J*= 8.8, 6.5 Hz, 1H), 3.82 (s, 3H), 2.60 – 2.50 (m, 2H), 1.76 – 1.66 (m, 1H), 1.62 – 1.54 (m, 1H), 1.02 – 0.95 (m, 6H).

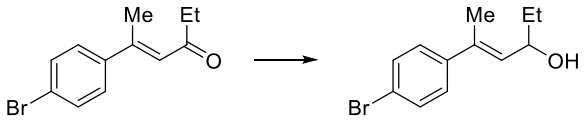
(*E*)-4-(4-bromophenyl)pent-3-en-2-ol **13i**



The crude material was subjected to flash chromatography (pure DCM) and product could be collected as orange oil in 94 % yield (336 mg, 1.39 mmol). The material was used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.45 – 7.41 (m, 2H), 7.28 – 7.23 (m, 2H), 5.82 – 5.76 (m, 1H), 4.74 (dq, *J*= 8.3, 6.3 Hz, 1H), 2.07 (d, *J*= 1.4 Hz, 3H), 1.34 (d, *J*= 6.3 Hz, 3H).

(*E*)-5-(4-bromophenyl)hex-4-en-3-ol **13j**



The crude material was subjected to flash chromatography (pure DCM) and product could be collected as yellow orange oil in 84 % yield (326 mg, 1.28 mmol). The material was used in the next step without further purification.

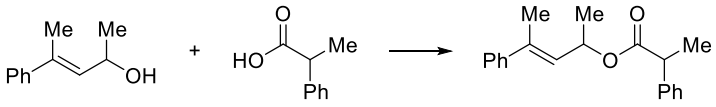
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.45 – 7.41 (m, 2H), 7.28 – 7.25 (m, 2H), 5.74 (dq, *J*= 8.5, 1.4 Hz, 1H), 4.46 (dt, *J*= 8.6, 6.5 Hz, 1H), 2.08 (d, *J*= 1.5 Hz, 3H), 1.71 (m, 1H), 1.59 (m, 1H), 0.96 (t, *J*= 7.4 Hz, 3H).

Esterification

General procedure:

A 25 mL round bottom flask was equipped with 2-phenylbutanoic acid *or* 2-phenylpropanoic acid (1.20 equiv.), EDCI (1.20 equiv.) and DMAP (0.20 equiv.). Alcohol **13** (1.0 equiv.) dissolved in dry DCM (c= 0.3M) was added and the mixture was stirred until TLC indicated full consumption of starting material. The reaction was quenched by addition of H_2O and layers were separated. The aqueous layer was extracted with DCM three times and the combined organic layer was washed with H_2O. It was dried over Na_2SO_4 and concentrated in vacuo.

(*E*)-4-phenylpent-3-en-2-yl 2-phenylpropanoate **14a**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as pale yellow oil in 70 % yield (139 mg, 472 µmol) and 2.2:1 *dr.* The material was used in the next step without further purification.

Major

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 7.22 (m, 10H), 5.80 – 5.70 (m, 1H), 5.57 (dd, *J*= 8.5, 1.6 Hz, 1H), 3.76 – 3.67 (m, 1H) 2.03 (d, *J*= 1.4 Hz, 3H), 1.53 – 1.50 (m, 3H), 1.37 (d, *J*= 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ= 174.0, 142.7, 140.8, 138.4, 128.6, 128.3, 127.6, 127.4, 127.3, 127.1, 125.9, 68.6, 45.8, 20.7, 18.6, 16.3.

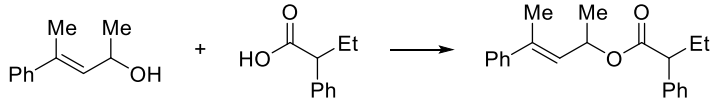
Minor

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 7.22 (m, 10H), 5.80 – 5.70 (m, 2H), 3.76 – 3.67 (m, 1H), 2.11 (d, *J*= 1.3 Hz, 3H), 1.45 (dd, *J*= 7.1, 4.8 Hz, 3H), 1.28 (d, *J*= 6.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ= 174.0, 142.7, 140.8, 138.4, 128.6, 128.3, 127.5, 127.4, 127.3, 127.1, 125.9, 68.7, 45.8, 20.6, 18.6, 16.4.

IR (Neat Film, NaCl) 3028, 2978, 2932, 1813, 1729, 1600, 1494, 1453, 1376, 1243, 1202, 1166, 1039, 856, 785, 758, 697 cm^{-1}

(*E*)-4-phenylpent-3-en-2-yl 2-phenylbutanoate **14b**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as pale yellow oil in 75 % yield (156 mg, 506 µmol) and 2.3:1 *dr.* The material was used in the next step without further purification.

Major

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 7.24 (m, 10H), 5.84 – 5.74 (m, 1H) 5.63 (dt, *J*= 8.6, 1.7 Hz, 1H), 3.55 – 3.46 (m, 1H), 2.24 – 2.11 (m, 1H), 2.07 (d, *J*= 1.6 Hz, 3H), 1.93 – 1.79 (m, 1H), 1.42 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.00 – 0.93 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ= 173.5, 142.8, 139.4, 138.4, 128.6, 128.3, 128.0, 127.4, 127.3, 127.1, 126.0, 68.6, 53.8, 26.8, 20.8, 16.4, 12.3.

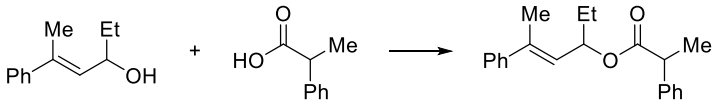
Minor

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 7.24 (m, 10H), 5.84 – 5.74 (m, 2H), 3.55 – 3.46 (m, 1H), 2.24 – 2.11 (m, 4H), 1.93 – 1.79 (m, 1H), 1.00 – 0.93 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ= 173.5, 142.8, 139.4, 138.3, 128.6, 128.3, 128.0, 127.5, 127.3, 127.2, 126.0, 68.6, 53.8, 26.9, 20.6, 16.4, 12.3.

IR (Neat Film, NaCl) 3060, 3029, 2968, 2931, 2875, 1948, 1809, 1729, 1630, 1600, 1494, 1454, 1379, 1266, 1226, 1199, 1165, 1117, 1079, 1040, 1008, 976, 918, 867, 824, 758, 735, 698 cm^{-1}

(*E*)-5-phenylhex-4-en-3-yl 2-phenylpropanoate **14c**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in near quantitative yield (223 mg, 723 µmol) and 2.7:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.23 (m, 10H), 5.61 – 5.55 (m, 1H), 5.51 (dd, *J*= 8.9, 1.6 Hz, 1H), 3.80 – 3.70 (m, 1H), 2.08 (d, *J*= 1.4 Hz, 3H), 1.82 – 1.73 (m, 1H), 1.71 – 1.62 (m, 1H), 1.56 – 1.50 (m, 3H), 0.93 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.2, 143.0, 140.9, 140.0, 139.3, 128.6, 128.3, 127.6, 127.4, 127.1, 126.0, 73.4, 45.9, 27.9, 18.7, 16.6, 9.6.

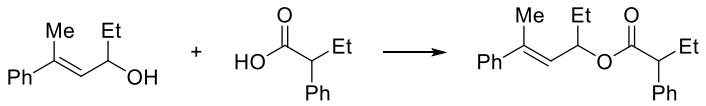
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.36 – 7.23 (m, 10H), 5.67 (dd, *J*= 8.9, 1.6 Hz, 1H), 5.61 – 5.55 (m, 1H), 3.80 – 3.70 (m, 1H), 2.14 (d, *J*= 1.5 Hz, 3H), 1.82 – 1.73 (m, 1H), 1.71 – 1.62 (m, 1H), 1.56 – 1.50 (m, 3H), 0.79 (t, *J*= 7.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 179.9, 143.0, 141.0, 140.0, 139.1, 128.8, 128.4, 127.7, 127.4, 127.1, 126.1, 73.4, 45.9, 27.9, 18.5, 16.7, 9.4.

IR (Neat Film, NaCl) 3059, 3028, 2972, 2935, 2876, 1730, 1706, 1601, 1495, 1455, 1379, 1330, 1241, 1202, 1168, 1067, 1029, 934, 899, 784, 757, 697 cm^{-1}

(*E*)-5-phenylhex-4-en-3-yl 2-phenylbutanoate **14d**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in 94 % yield (221 mg, 685 µmol) and 3.0:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 7.21 (m, 10H), 5.61 – 5.55 (m, 1H), 5.52 (dd, *J*= 8.8, 1.5 Hz, 1H), 3.52 – 3.41 (m, 1H), 2.17 – 2.08 (m, 1H), 2.06 (d, *J*= 1.4 Hz, 3H), 1.87 – 1.54 (m, 3H), 0.96 – 0.90 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 143.0, 139.4, 139.3, 128.6, 128.3, 128.1, 127.4, 127.1, 126.2, 126.0, 73.3, 53.9, 28.0, 26.8, 16.7, 12.4, 9.7.

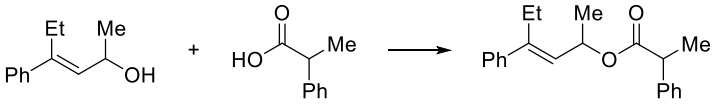
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 7.21 (m, 10H), 5.66 (dt, *J*= 9.0, 1.5 Hz, 1H), 5.61 – 5.55 (m, 1H), 3.52 – 3.41 (m, 1H), 2.17 – 2.09 (m, 4H), 1.87 – 1.54 (m, 3H), 0.85 (td, *J*= 7.4, 2.0 Hz, 3H), 0.79 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.7, 143.0, 139.5, 139.2, 128.6, 128.4, 128.1, 127.5, 127.2, 126.2, 126.0, 73.2, 53.9, 27.9, 26.7, 16.7, 12.3, 9.4.

IR (Neat Film, NaCl) 3060, 3028, 2967, 2934, 2876, 1813, 1729, 1494, 1455, 1381, 1266, 1224, 1199, 1166, 1073, 1028, 962, 928, 783, 757, 731, 697 cm^{-1}

(*E*)-4-phenylhex-3-en-2-yl 2-phenylpropanoate **14e**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in 98 % yield (275 mg, 892 µmol) and 2.6:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 7.22 (m, 10H), 5.81 – 5.73 (m, 1H), 5.43 (d, *J*= 8.8 Hz, 1H), 3.75 – 3.68 (m, 1H), 2.60 – 2.45 (m, 2H), 1.53 – 1.50 (m, 3H), 1.38 (d, *J*= 6.3 Hz, 3H), 0.92 (t, *J*= 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.0, 145.2, 141.9, 140.8, 128.7, 128.3, 127.6, 127.4, 127.1, 127.0, 126.7, 68.3, 45.9, 23.6, 21.2, 18.7, 13.8.

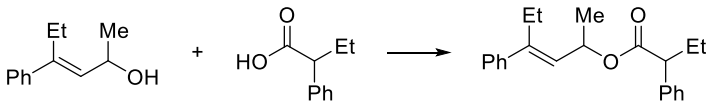
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 7.22 (m, 10H), 5.81 – 5.73 (m, 1H), 5.58 (d, *J*= 8.9 Hz, 1H), 3.75 – 3.68 (m, 1H), 2.70 – 2.43 (m, 2H), 1.53 – 1.50 (m, 3H), 1.29 (d, *J*= 6.3 Hz, 3H), 0.98 (t, *J*= 7.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.0, 145.1, 141.8, 140.9, 128.7, 128.4, 127.6, 127.5, 127.1, 127.0, 126.7, 68.4, 45.9,23.6, 21.1, 18.3, 13.9.

IR (Neat Film, NaCl) 3059, 3029, 2974, 2933, 2873, 1947, 1876, 1730, 1653, 1601, 1493, 1453, 1376, 1348, 1328, 1242, 1203, 1166, 1113, 1094, 1066, 1041, 1013, 941, 910, 886, 866, 806, 763, 698 cm^{-1}

(*E*)-4-phenylhex-3-en-2-yl 2-phenylbutanoate **14f**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in near quantitative yield (291 mg, 902 µmol) and 3.1:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 7.22 (m, 10H), 5.84 – 5.73 (m, 1H), 5.45 (d, *J*= 8.8 Hz, 1H), 3.50 – 3.43 (m, 1H), 2.69 – 2.45 (m, 2H), 2.18 – 2.09 (m, 1H), 1.89 – 1.77 (m, 1H), 1.39 (d, *J*= 6.4 Hz, 3H), 1.01 – 0.86 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 145.2, 141.9, 139.4, 128.8, 128.6, 128.3, 128.1, 127.4, 127.1, 127.0, 126.7, 68.3, 53.9, 26.9, 23.6, 21.3, 13.8, 12.3.

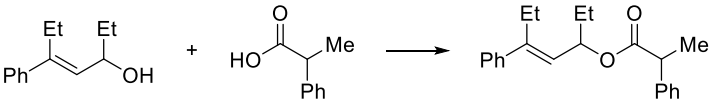
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 7.22 (m, 10H), 5.84 – 5.73 (m, 1H), 5.59 (d, *J*= 9.0 Hz, 1H), 3.50 – 3.43 (m, 1H), 2.69 – 2.45 (m, 2H), 2.18 – 2.09 (m, 1H), 1.89 – 1.77 (m, 1H), 1.30 (d, *J*= 6.4 Hz, 1H), 1.01 – 0.86 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 145.2, 141.9, 139.4, 128.8, 128.6, 128.4, 128.2, 128.1, 127.6, 127.2, 126.7, 68.3, 53.8, 26.9, 23.6, 21.1, 13.9, 12.2.

IR (Neat Film, NaCl) 3060, 3029, 2968, 2932, 2875, 1729, 1707, 1648, 1602, 1493, 1454, 1377, 1266, 1226, 1199, 1166, 1116, 1075, 1042, 955, 906, 869, 785, 762, 730 678, 658, cm^{-1}

(*E*)-5-phenylhept-4-en-3-yl 2-phenylpropanoate **14g**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in 98 % yield (231 mg, 716 µmol) and 2.2:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 7.22 (m, 10H), 5.63 – 5.55 (m, 1H), 5.37 (d, *J*= 9.3 Hz, 1H), 3.79 – 3.70 (m, 1H), 2.74 – 2.49 (m, 2H), 1.82 – 1.72 (m, 1H), 1.70 – 1.62 (m, 1H), 1.56 – 1.51 (m, 3H), 0.96 – 0.91 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 146.2, 142.0, 140.8, 139.9, 128.6, 128.3, 127.6, 127.4, 127.1, 126.7, 125.7, 73.0, 45.9, 28.2, 23.6, 18.7, 13.8, 9.8.

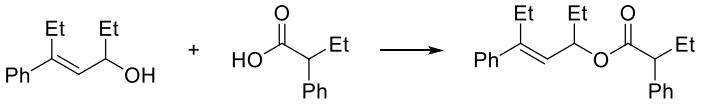
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 7.22 (m, 10H), 5.63 – 5.55 (m, 1H), 5.52 (d, *J*= 9.1 Hz, 1H), 3.79 – 3.70 (m, 1H), 2.74 – 2.49 (m, 2H), 1.82 – 1.72 (m, 1H), 1.70 – 1.62 (m, 1H), 1.56 – 1.51 (m, 3H), 0.98 (t, *J*= 7.6 Hz, 3H), 0.79 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 179.9, 146.1, 142.0, 141.0, 139.9, 128.7, 128.4, 127.7, 127.4, 127.1, 126.7, 125.9, 73.0, 45.9, 28.2, 23.7, 18.5, 13.8, 9.5.

IR (Neat Film, NaCl) 3060, 3028, 2971, 2934, 2876, 1730, 1706, 1646, 1601, 1495, 1454, 1417, 1377, 1323, 1240, 1202, 1170, 1066, 1030, 996, 937, 897, 806, 762, 730, 698 cm^{-1}

(*E*)-5-phenylhept-4-en-3-yl 2-phenylbutanoate **14h**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as colorless oil in 98 % yield (240 mg, 713 µmol) and 2.5:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 7.20 (m, 10H), 5.64 – 5.57 (m, 1H), 5.37 (d, *J*= 9.1 Hz, 1H), 3.51 – 3.44 (m, 1H), 2.70 – 2.48 (m, 2H), 2.18 – 2.08 (m, 1H), 1.88 – 1.73 (m, 2H), 1.70 – 1.53 (m, 1H), 1.00 – 0.88 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 146.2, 142.0, 139.4, 138.6, 128.6, 128.3, 128.1, 127.4, 127.1, 126.7, 125.8, 72.9, 54.0, 28.2, 26.8, 23.6, 13.7, 12.4, 9.8.

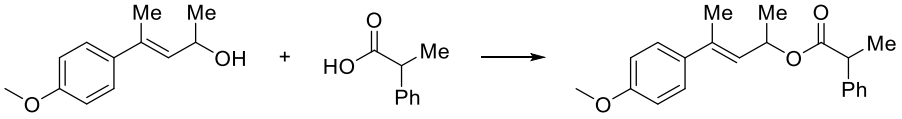
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 7.20 (m, 10H), 5.64 – 5.57 (m, 1H), 5.52 (d, *J*= 9.1 Hz, 1H), 3.51 – 3.44 (m, 1H), 2.70 – 2.48 (m, 2H), 2.18 – 2.08 (m, 1H), 1.88 – 1.73 (m, 2H), 1.70 – 1.53 (m, 1H), 1.00 – 0.88 (m, 6H), 0.80 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.7, 146.1, 142.0, 139.5, 138.6, 128.8, 128.6, 128.4, 128.2, 127.4, 127.2, 126.0, 72.8, 53.9, 28.2, 26.7, 23.7, 13.8, 12.3, 9.6.

IR (Neat Film, NaCl) 3060, 3028, 2967, 2934, 2876, 1730, 1707, 1601, 1494, 1455, 1380, 1265, 1224, 1199, 1166, 1072, 1031, 961, 921, 784, 762, 730, 698, 670 cm^{-1}

(*E*)-4-(4-methoxyphenyl)pent-3-en-2-yl 2-phenylpropanoate **14i**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as pale yellow oil in 98 % yield (336 mg, 1.04 mmol) and 2.5:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.78 (m, 9H), 5.80 – 5.70 (m, 1H), 5.56 – 5.50 (m, 1H), 3.82 (s, 3H), 3.80 – 3.66 (m, 1H), 2.01 (d, *J*= 1.3 Hz, 3H), 1.56 – 1.48 (m, 3H), 1.37 (d, *J*= 6.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 159.2, 140.9, 137.8, 135.2, 128.6, 127.6, 127.1, 125.8, 113.6, 68.8, 55.4, 45.9, 20.8, 18.7, 16.4.

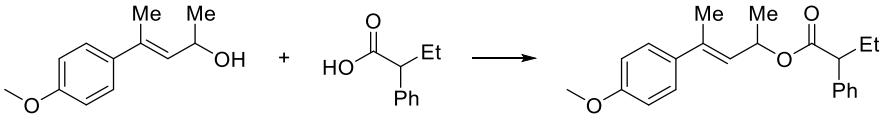
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.78 (m, 9H), 5.80 – 5.70 (m, 1H), 5.68 – 5.64 (m, 1H), 3.82 (s, 3H), 3.80 – 3.66 (m, 1H), 2.09 (d, *J*= 1.3 Hz, 3H), 1.56 – 1.48 (m, 3H), 1.28 (d, *J*= 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 179.8, 159.2, 140.0, 137.6, 135.2, 128.7, 127.6, 127.1, 125.9, 113.7, 68.9, 55.4, 45.4, 20.7, 18.7, 16.4.

IR (Neat Film, NaCl) 3030, 2977, 2934, 2836, 1728, 1646, 1606, 1576, 1512, 1496, 1454, 1418, 1376, 1289, 1246, 1203, 1179, 1114, 1094, 1065, 1034, 913, 827, 807, 771, 720, 699, 680 cm^{-1}

(*E*)-4-(4-methoxyphenyl)pent-3-en-2-yl 2-phenylbutanoate **14j**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as pale yellow oil in 82% yield (291 mg, 860 µmol) and 2.9:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.80 (m, 9H), 5.80 – 5.71 (m, 1H), 5.54 (dt, *J*= 8.6, 1.5 Hz, 1H), 3.82 (s, 3H), 3.50 – 3.43 (m, 1H), 2.17 – 2.09 (m, 1H), 2.00 (d, *J*= 1.4 Hz, 3H), 1.87 – 1.75 (m, 1H), 1.37 (dd, *J*= 6.3, 1.4 Hz, 3H), 0.96 – 0.88 (m, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 139.5, 137.8, 135.3, 128.8, 128.6, 128.2, 128.1, 127.1, 125.8, 113.6, 68.7, 55.4, 53.9, 26.9, 20.9, 16.4, 12.3.

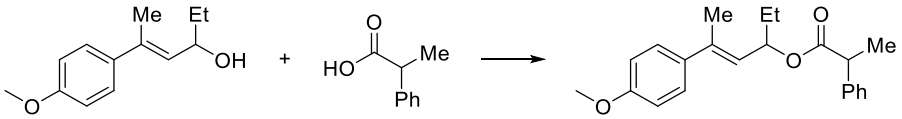
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.80 (m, 9H), 5.80 – 5.71 (m, 1H), 5.67 (dt, *J*= 8.5, 1.5 Hz, 1H), 3.82 (s, 3H), 3.50 – 3.43 (m, 1H), 2.17 – 2.09 (m, 1H), 2.08 (d, *J*= 1.4 Hz, 3H), 1.87 – 1.75 (m, 1H), 1.30 – 1.26 (m, 3H), 0.93 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 138.6, 137.7, 135.3, 128.6, 128.2, 128.1, 127.5, 127.1, 126.0, 113.7, 68.7, 53.8, 53.3, 26.9, 20.7, 16.5, 12.2.

IR (Neat Film, NaCl) 3030, 2966, 2933, 2875, 2836, 1728, 1707, 1654, 1606, 1576, 1512, 1455, 1418, 1380, 1246, 1287, 1200, 1179, 1116, 1072, 1034, 975, 827, 806, 772, 731, 699, 668 cm^{-1}

(*E*)-5-(4-methoxyphenyl)hex-4-en-3-yl 2-phenylpropanoate **14k**



The crude material was purified by column chromatography (hexanes: ethyl acetate 20:1). The desired product was collected as colorless oil in 63 % yield (201 mg, 594 µmol) and 2.7:1 *dr.*

Note:

Crude yield was 355 mg - 111 %.

Only 180 mg were subjected to CC and 102 mg (63 % yield) were obtained. The above mentioned 201 mg were calculated to be the full amount if the CC would have been done on the 343 mg.

Therefore, the 201 mg are a theoretical value and were never isolated in full amount.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 6.79 (m, 9H), 5.62 – 5.52 (m, 1H), 5.44 (dq, *J*= 9.0, 1.4 Hz, 1H), 3.81 (s, 3H), 3.76 – 3.70 (m, 1H), 2.04 (d, *J*= 1.4 Hz, 3H), 1.75 – 1.48 (m, 5H), 0.91 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 159.1, 140.9, 138.7, 135.4, 128.6, 127.6, 127.1, 124.6, 113.6, 73.5, 55.4, 45.9, 28.0, 18.7, 16.6, 9.7.

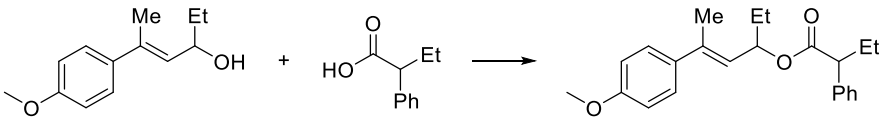
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.35 – 6.79 (m, 9H), 5.62 – 5.52 (m, 2H), 3.82 (s, 3H), 3.76 – 3.70 (m, 1H), 2.35 – 2.12 (m, 1H), 2.10 (d, *J*= 1.4 Hz, 3H), 1.75 – 1.48 (m, 5H), 0.77 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 159.2, 141.0, 138.5, 135.4, 128.6, 127.6, 127.0, 124.7, 113.7, 73.4, 55.4, 45.9, 28.0, 18.5, 16.6, 9.4.

IR (Neat Film, NaCl) 3029, 2970, 2935, 2876, 2836, 1728, 1652, 1607, 1575, 1513, 1455, 1418, 1378, 1291, 1249, 1202, 1178, 1168, 1115, 1066, 1033, 952, 932, 896, 826, 808, 768, 699 cm^{-1}

(*E*)-5-(4-methoxyphenyl)hex-4-en-3-yl 2-phenylbutanoate **14l**



The crude material was purified by column chromatography (hexanes: ethyl acetate 20:1). The desired product was collected as colorless oil in 64 % yield (214 mg, 607 µmol).

Note:

Crude yield was 343 mg - 103 %.

Only 255 mg were subjected to CC and 159 mg (64 % yield) were obtained. The above mentioned 214 mg were calculated to be the full amount if the CC would have been done on 343 mg.

Therefore, the 214 mg are a theoretical value and were never isolated in full amount.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.42 – 6.86 (m, 9H), 5.68 – 5.58 (m, 1H), 5.51 (dq, *J*= 9.1, 1.4 Hz, 1H), 3.87 (s, 3H), 3.56 – 3.48 (m, 1H), 2.08 (d, *J*= 1.4 Hz, 3H), 1.94 – 1.58 (m, 4H), 1.01 – 0.93 (m, 6H),

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 159.1, 139.4, 138.7, 135.4, 128.5, 128.1, 127.1, 127.1, 124.6, 113.6, 73.3, 55.3, 53.9, 28.0, 26.8, 16.6, 12.3, 9.7.

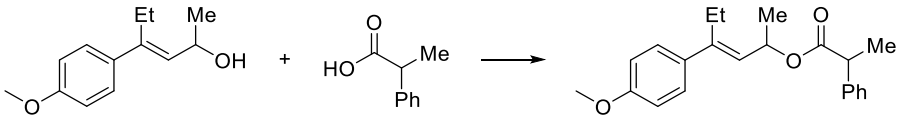
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.42 – 6.86 (m, 9H), 5.68 – 5.58 (m, 2H), 3.88 (s, 3H), 3.56 – 3.48 (m, 1H), 2.22 – 2.13 (m, 4H), 1.94 – 1.58 (m, 3H), 1.01 – 0.93 (m, 6H),

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.7, 159.2, 139.5, 138.6, 135.4, 128.6, 128.1, 127.1, 124.8, 113.7, 73.3, 55.3, 53.8, 28.0, 26.7, 16.6, 12.3, 9.4.

IR (Neat Film, NaCl) 3028, 2966, 2935, 2876, 2836, 1728, 1606, 1575, 1512, 1455, 1380, 1290, 1249, 1199, 1167, 1119, 1074, 1034, 960, 926, 826, 807, 732, 699, 680 cm^{-1}

(*E*)-4-(4-methoxyphenyl)hex-3-en-2-yl 2-phenylpropanoate **14m**



The crude material was purified by column chromatography (hexanes: ethyl acetate 20:1). The desired product was collected as colorless oil in 76 % yield (165 mg, 488 µmol) and 2.2:1 *dr.*

Note:

Crude yield was 291 mg - 133 %.

Only 206 mg were subjected to CC and 117 mg (76 % yield) were obtained. The above mentioned 165 mg were calculated to be the full amount if the CC would have been done on the 291 mg.

Therefore, the 165 mg are a theoretical value and were never isolated in full amount.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 6.82 (m, 9H), 5.81 – 5.72 (m, 1H), 5.39 (d, *J*= 8.9 Hz, 1H), 3.82 (s, 3H), 3.79 – 3.73 (m, 1H), 2.57 – 2.42 (m, 2H), 1.55 – 1.52 (m, 3H), 1.37 (d, *J*= 6.3 Hz, 3H), 0.91 (t, *J*= 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.0, 159.1, 144.5, 140.8, 134.1, 128.6, 127.7, 127.6, 127.0, 125.5, 113.7, 68.4, 55.3, 45.8, 23.5, 21.2, 18.7, 13.8.

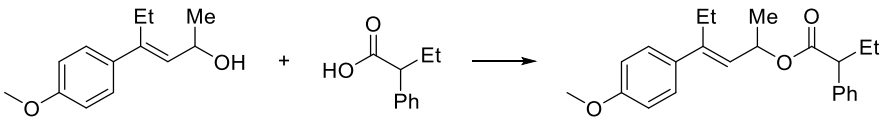
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 6.82 (m, 9H), 5.81 – 5.72 (m, 1H), 5.53 (d, *J*= 8.9 Hz, 1H), 3.83 (s, 3H), 3.79 – 3.67 (m, 1H), 2.66 – 2.49 (m, 2H), 1.52 –1.49 (m, 3H), 1.28 (d, *J*= 6.3 Hz, 3H), 0.98 (t, *J*= 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.0, 159.1, 144.5, 140.9, 134.1, 128.6, 127.7, 127.5, 127.1, 125.7, 113.7, 68.5, 55.3, 45.8, 23.5, 21.1, 18.6, 13.9.

IR (Neat Film, NaCl) 3030, 2972, 2935, 2836, 1814, 1727, 1647, 1607, 1576, 1511, 1455, 1376, 1287, 1249, 1203, 1178, 1156, 1115, 1037, 1066, 829, 806, 769, 730, 698, 666 cm^{-1}

(*E*)-4-(4-methoxyphenyl)hex-3-en-2-yl 2-phenylbutanoate **14n**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as pale yellow oil in 99 % yield (225 mg, 638 µmol) and 2.8:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 6.80 (m, 9H), 5.80 – 5.72 (m, 1H), 5.40 (d, *J*= 8.9 Hz, 1H), 3.81 (s, 3H), 3.45 (t, *J*= 7.7 Hz, 1H), 2.56 – 2.39 (m, 2H), 2.18 – 2.05 (m, 1H), 1.90 – 1.74 (m, 1H), 1.37 (d, *J*= 6.3 Hz, 3H), 0.96 – 0.88 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= = 173.5, 159.1, 144.6, 139.4, 134.2, 128.6, 128.1, 127.7, 127.1, 125.6, 113.7, 68.4, 55.4, 53.9, 26.9, 23.5, 21.3, 13.8, 12.3.

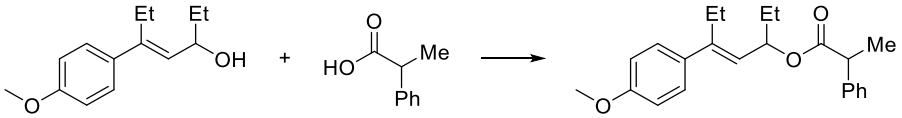
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.37 – 6.80 (m, 9H), 5.80 – 5.72 (m, 1H), 5.53 (d, *J*= 8.9 Hz, 1H), 3.82 (s, 3H), 3.45 (t, *J*= 7.7 Hz, 1H), 2.65 – 2.49 (m, 2H), 2.18 – 2.05 (m, 1H), 1.90 – 1.74 (m, 1H), 1.28 (d, *J*= 6.3 Hz, 3H), 0.96 – 0.88 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 159.2, 144.6, 139.5, 134.2, 128.6, 128.1, 127.7, 127.2, 125.8, 113.8, 68.3, 55.4, 53.8, 27.0, 23.6, 21.1, 13.9, 12.3.

IR (Neat Film, NaCl) 3029, 2967, 2933, 2875, 2836, 1727, 1646, 1575, 1511, 1455, 1417, 1376, 1284, 1249, 1200, 1167, 1115, 1068, 1038, 955, 894, 868, 830, 806, 771, 735, 699, 680 cm^{-1}

(*E*)-5-(4-methoxyphenyl)hept-4-en-3-yl 2-phenylpropanoate **14o**



The crude material was purified by column chromatography (hexanes: ethyl acetate 20:1). The desired product was collected as colorless oil in 61 % yield (147 mg, 417 µmol) and 2.0:1 *dr.*

Note:

Crude yield was 229 mg - 94 %.

Only 145 mg were subjected to CC and 93 mg (61 % yield) were obtained. The above mentioned 147 mg were calculated to be the full amount if the CC would have been done on the 229 mg.

Therefore, the 147 mg are a theoretical value and were never isolated in full amount.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 6.77 (m, 9H), 5.61 – 5.55 (m, 1H), 5.31 (d, *J*= 9.1 Hz, 1H), 3.82 (s, 3H), 3.78 – 3.69 (m, 1H), 2.69 – 2.44 (m, 2H), 1.78 – 1.70 (m, 1H), 1.69 – 1.56 (m, 1H), 1.57 – 1.49 (m, 3H), 0.94 – 0.89 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 159.1, 145.5, 140.9, 134.3, 128.6, 127.7, 127.6, 127.0, 124.4, 113.7, 73.1, 55.4, 45.9, 28.2, 23.5, 18.7, 13.8, 9.8.

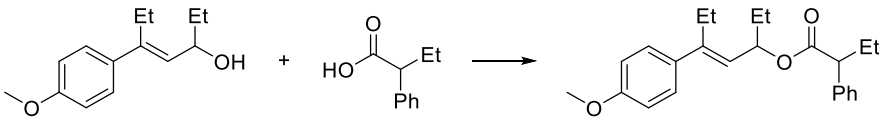
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 6.77 (m, 9H), 5.61 – 5.55 (m, 1H), 5.46 (d, *J*= 9.2 Hz, 1H), 3.82 (s, 3H), 3.78 – 3.69 (m, 1H), 2.69 – 2.44 (m, 2H), 1.78 – 1.70 (m, 1H), 1.69 – 1.56 (m, 1H), 1.57 – 1.49 (m, 3H), 0.97 (t, *J*= 7.6 Hz, 3H), 0.77 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 159.1, 145.4, 141.0, 134.2, 128.6, 127.7, 127.6, 127.1, 124.5, 113.7, 73.0, 55.4, 45.9, 28.3, 23.6, 18.5, 13.9, 9.5.

IR (Neat Film, NaCl) 3030, 2969, 2935, 2876, 2837, 1728, 1646, 1607, 1576, 1511, 1455, 1377, 1288, 1247, 1202, 1177, 1114, 1066, 1034, 936, 895, 830, 807, 771, 730, 699, 658 cm^{-1}

(*E*)-5-(4-methoxyphenyl)hept-4-en-3-yl 2-phenylbutanoate **14p**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as yellow oil in 94 % yield (236 mg, 644 µmol) and 2.0:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 6.79 (m, 9H), 5.61 – 5.55 (m, 1H), 5.32 (d, *J*= 9.2 Hz, 1H), 3.81 (s, 3H), 3.50 – 3.43 (m, 1H), 2.65 – 2.45 (m, 2H), 2.17 – 2.07 (m, 1H), 1.87 – 1.51 (m, 3H), 0.98 – 0.87 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 159.1, 145.6, 139.4, 134.3, 128.5, 128.1, 127.8, 127.1, 124.4, 113.7, 73.0, 55.4, 54.0, 28.3, 26.8, 23.6, 13.8, 12.4, 9.8.

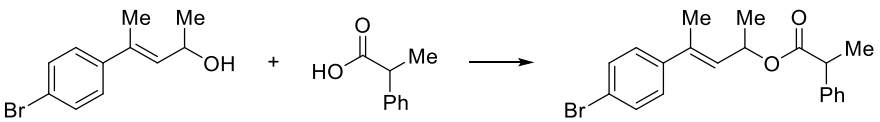
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.38 – 6.79 (m, 9H), 5.61 – 5.55 (m, 1H), 5.46 (d, *J*= 9.3 Hz, 1H), 3.82 (s, 3H), 3.50 – 3.43 (m, 1H), 2.65 – 2.45 (m, 2H), 2.17 – 2.07 (m, 1H), 1.87 – 1.51 (m, 3H), 0.98 – 0.87 (m, 6H), 0.78 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.7, 159.1, 145.5, 139.6, 134.3, 128.6, 128.1, 127.8, 127.1, 124.4, 113.7, 72.9, 55.4, 53.9, 28.2, 26.7, 23.6, 13.9, 12.3, 9.6.

IR (Neat Film, NaCl) 3030, 2967, 2935, 2875, 2836, 1728, 1648, 1606, 1576, 1511, 1457, 1380, 1286, 1248, 1199, 1178, 1117, 1074, 1035, 960, 919, 830, 807, 698, 731 cm^{-1}

(*E*)-4-(4-bromophenyl)pent-3-en-2-yl 2-phenylpropanoate **14q**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as yellow oil in 84 % yield (218 mg, 584 µmol) and 2.7:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.13 (m, 9H), 5.78 – 5.69 (m, 1H), 5.55 (dq, *J*= 8.6, 1.5 Hz, 1H), 3.77 – 3.70 (m, 1H), 2.02 (d, *J*= 1.4 Hz, 3H), 1.55 – 1.51 (m, 3H), 1.38 (d, *J*= 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.0, 141.6, 140.8, 137.3, 131.3, 128.7, 127.8, 127.6, 127.6, 127.1, 121.4, 68.5, 45.8, 20.6, 18.6, 16.2.

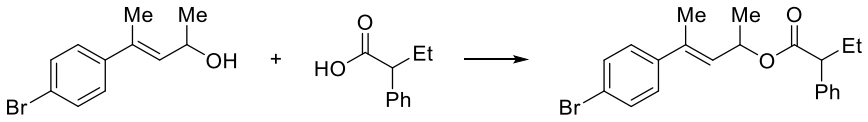
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.13 (m, 9H), 5.78 – 5.69 (m, 2H), 3.77 – 3.70 (m, 1H), 2.10 (d, *J*= 1.2 Hz, 3H), 1.55 – 1.51 (m, 3H), 1.29 (d, *J*= 6.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 179.9, 143.0, 141.0, 140.0, 139.1, 128.8, 128.4, 127.7, 127.4, 127.1, 126.1, 73.4, 45.9, 27.9, 18.5, 16.7, 9.4.

IR (Neat Film, NaCl) 3028, 2976, 2931, 1730, 1586, 1485, 1453, 1400, 1375, 1243, 1202, 1154, 1075, 1038, 1008, 817, 770, 732, 699 cm^{-1}

(*E*)-4-(4-bromophenyl)pent-3-en-2-yl 2-phenylbutanoate **14r**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as yellow oil in 76 % yield (204 mg, 527 µmol) and 2.7:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.48 – 7.10 (m, 9H), 5.78 – 5.69 (m, 1H), 5.56 (dd, *J*= 8.5, 1.5 Hz, 1H), 3.47 (t, *J*= 7.7 Hz, 1H), 2.19 – 2.10 (m, 1H), 2.01 (d, *J*= 1.4 Hz, 3H), 1.87 – 1.76 (m, 1H), 1.38 (d, *J*= 6.3 Hz, 3H), 0.97 – 0.91 (m, 3H).

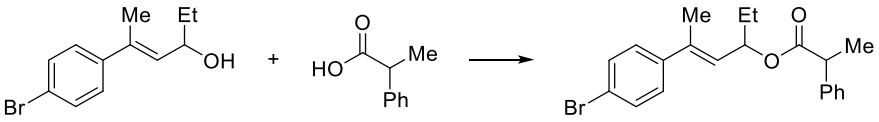
^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 141.6, 139.3, 137.3, 131.3, 128.6, 128.0, 127.9, 127.6, 127.2, 121.3, 68.4, 53.8, 26.8, 20.7, 16.3, 12.3.

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.48 – 7.10 (m, 9H), 5.78 – 5.69 (m, 2H), 3.47 (t, *J*= 7.7 Hz, 1H), 2.19 – 2.10 (m, 1H), 2.09 (d, *J*= 1.2 Hz, 3H), 1.87 – 1.76 (m, 1H), 1.30 (d, *J*= 5.9 Hz, 3H), 0.97 – 0.91 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 141.6, 139.3, 137.2, 131.4, 128.6, 128.0, 127.9, 127.6, 127.2, 121.3, 68.4, 53.8, 26.9, 20.5, 16.3, 12.3.

(*E*)-5-(4-bromophenyl)hex-4-en-3-yl 2-phenylpropanoate **14s**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as yellow oil in 72 % yield (173 mg, 447 µmol) and 2.5:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.10 (m, 9H), 5.59 – 5.52 (m, 1H), 5.48 (dq, *J*= 8.8, 1.4 Hz, 1H), 3.79 – 3.71 (m, 1H), 2.05 (d, *J*= 1.3 Hz, 3H), 1.81 – 1.73 (m, 1H), 1.70 – 1.59 (m, 1H), 1.54 – 1.51 (m, 3H), 0.93 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 141.8, 140.8, 138.2, 131.3, 128.7, 127.7, 127.6, 127.1, 126.7, 121.4, 73.2, 45.8, 27.8, 18.6, 16.5, 9.7.

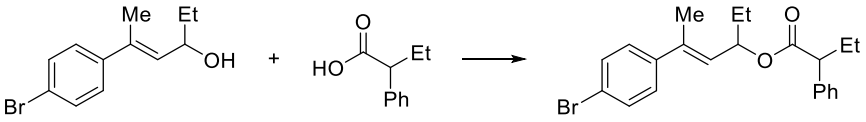
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.47 – 7.10 (m, 9H), 5.65 (dq, *J*= 8.9, 1.5 Hz, 1H), 5.59 – 5.52 (m, 1H), 3.79 – 3.71 (m, 1H), 2.12 (d, *J*= 1.4 Hz, 3H), 1.81 – 1.73 (m, 1H), 1.70 – 1.59 (m, 1H), 1.54 – 1.51 (m, 3H), 0.78 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.1, 141.8, 140.9, 138.0, 131.4, 128.7, 127.7, 127.6, 127.2, 126.9, 121.4, 73.2, 45.9, 27.9, 18.5, 16.6, 9.4.

IR (Neat Film, NaCl) 3029, 2970, 2933, 2876, 1730, 1486, 1455, 1400, 1377, 1243, 1201, 1168, 1076, 1030, 1008, 933, 897, 818, 767, 730, 699 cm^{-1}

(*E*)-5-(4-bromophenyl)hex-4-en-3-yl 2-phenylbutanoate **14t**



The crude material was filtered through a plug of silica (with DCM). The desired ester could be collected as yellow oil in 63 % yield (160 mg, 391 µmol) and 3.0:1 *dr.* The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.48 – 7.11 (m, 9H), 5.61 – 5.55 (m, 1H), 5.51 (dd, *J*= 8.8, 1.5 Hz, 1H), 3.53 – 3.47 (m, 1H), 2.21 – 2.14 (m, 1H), 2.06 (d, *J*= 1.4 Hz, 3H), 1.91 – 1.56 (m, 3H), 0.99 – 0.91 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.5, 141.8, 139.3, 138.2, 131.3, 128.6, 128.0, 127.6, 127.1, 126.7, 121.3, 73.1, 53.8, 27.8, 26.7, 16.5, 12.3, 9.6.

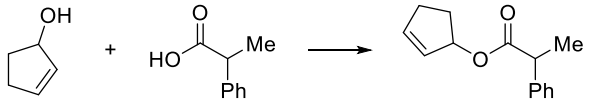
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.48 – 7.11 (m, 9H), 5.67 (dd, *J*= 9.0, 1.5 Hz, 1H), 5.61 – 5.55 (m, 1H), 3.53 – 3.47 (m, 1H), 2.21 – 2.11 (m, 4H), 1.91 – 1.56 (m, 3H), 0.99 – 0.91 (m, 3H), 0.82 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 173.6, 141.8, 139.4, 138.1, 131.4, 128.6, 128.0, 127.6, 127.2, 126.9, 121.4, 73.0, 53.8, 27.8, 26.6, 16.6, 12.3, 9.4.

IR (Neat Film, NaCl) 3027, 2966, 2929, 2875, 1730, 1489, 1456, 1380, 1266, 1225, 1198, 1166, 1075, 1008, 960, 928, 818, 732, 698 cm^{-1}

Cyclopent-2-en-1-yl 2-phenylpropanoate **14u**



A 50 mL round bottom flask was equipped with 2-phenylpropanoic acid (428 mg, 2.85 mmol, 1.20 equiv.), EDCI (547 mg, 2.85 mmol, 1.20 equiv.) and DMAP (58 mg, 475 µmol, 0.20 equiv.). Cyclopent-2-en-1-ol (200 mg, 2.38 mmol, 1.0 equiv.) dissolved in 8 mL dry DCM was added and the mixture was stirred. After 45 minutes TLC (hexanes: ethylacetate 10:1) confirmed full conversion and the reaction was quenched by addition of H_2O. The aqueous layer was extracted with DCM twice and the combined organic layer was dried over Na_2SO_4. The solvent was removed in vacuo and the crude residue was filtered through a plug of silica (with DCM). The desired ester could be collected as pale yellow oil in 84 % yield (430 mg, 1.99 mmol) and 1.2:1 *dr*. The material was used in the next step without further purification.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 – 7.22 (m, 5H), 6.10 – 6.07 (m, 1H), 5.84 – 5.80 (m, 1H), 5.72 – 5.67 (m, 1H), 3.72 – 3.65 (m, 1H), 2.54 – 2.40 (m, 1H), 2.34 – 2.17 (m, 2H), 1.83 – 1.61 (m, 1H), 1.51 – 1.48 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.6, 140.8, 137.7, 129.3, 128.7, 127.6, 127.1, 80.9, 45.7, 31.2, 29.7, 18.7.

Minor:

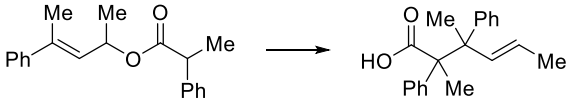
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.34 – 7.22 (m, 13H), 6.07 – 6.04 (m, 1H), 5.75 – 5.67 (m, 2H), 3.72 – 3.65 (m, 1H), 2.54 – 2.40 (m, 1H), 2.34 – 2.17 (m, 2H), 1.83 – 1.61 (m, 1H), 1.51 – 1.48 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.6, 140.8, 137.6, 129.3, 128.6, 127.6, 127.1, 81.0, 45.8, 31.2, 29.9, 18.8.

IR (Neat Film, NaCl) 3436, 3062, 3030, 2976, 2935, 2875, 2855, 1948, 1877, 1814, 1734, 1602, 1584, 1495, 1453, 1376, 1349, 1317, 1245, 1203, 1172, 1164, 1111, 1064, 1029, 948, 918, 891, 840, 815, 765, 732, 699, 680 cm^{-1}

Ireland-Claisen rearrangement

(*E*)-2,3-dimethyl-2,3-diphenylhex-4-enoic acid **15a**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 530 µL, 170 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (19 µL, 170 µmol, 2.0 equiv.) and the mix was cooled to -78° C. After 17 minutes ester **14a** (25 mg, 85 µmol, 1.0 equiv.) dissolved in 280 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 1 hour 50 minutes TMSCl (22 µL, 170 µmol, 2.0 equiv.) was added dropwise. After 50 minutes the flask was removed from cooling and allowed to warm to 18-19° C. TLC (hexanes: ethyl acetate 20:1) after 1 hour 20 minutes showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 25 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product was obtained as colorless oily solid in 72 % yield (18 mg, 61 µmol) and 6.9:1 *dr.* It was directly subjected to the next reaction without purification (decomposition issues on silica gel).

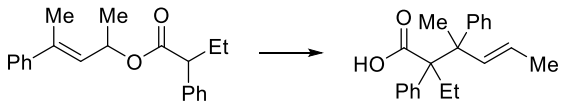
Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 7.02 (m, 10H), 6.40 (dd, *J*= 15.7, 1.9 Hz, 1H), 5.49 (dq, *J*= 15.6, 6.5 Hz, 1H), 1.80 (dd, *J*= 6.5, 1.6 Hz, 3H), 1.68 (s, 3H), 1.65 (s, 2H).

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 7.02 (m, 10H), 6.51 (dq, *J*= 15.5, 1.6 Hz, 1H), 5.38 (dq, *J*= 15.5, 6.4 Hz, 1H), 1.77 (dd, *J*= 6.4, 1.6 Hz, 2H), 1.71 (s, 3H), 1.66 (s, 3H).

(*E*)-2-ethyl-3-methyl-2,3-diphenylhex-4-enoic acid **15b**



A flame-dried 25 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.42 mL, 454 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (49 µL, 454 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14b** (70 mg, 227 µmol, 1.0 equiv.) dissolved in 0.76 mL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 1 hour 30 minutes TMSCl (58 µL, 454 µmol, 2.0 equiv.) was added dropwise. The reaction was allowed to warm to 18-19° C over night and TLC (hexanes: ethyl acetate 20:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and

Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (hexanes: ethyl acetate 4:1) and product was collected in 79 % yield (55 mg, 178 µmol) and 8.3:1 *dr.* The crude material was directly subjected to the next reaction without purification (decomposition issues on silica gel).

Major:

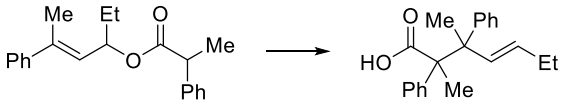
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.25 – 7.07 (m, 10H), 6.23 (d, *J*= 15.5 Hz, 1H), 5.48 (dq, *J*= 15.7, 6.3 Hz, 1H), 2.38 (dq, *J*= 14.3, 7.1 Hz, 1H), 2.20 (dq, *J*= 15.4, 8.1, 7.6 Hz, 1H), 1.77 – 1.74 (m, 3H), 1.65 (s, 3H), 0.87 (t, *J*= 7.2 Hz, 3H).

Note: Traces of THF in ^{1}H

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.25 – 7.07 (m, 10H), 6.72 (d, *J*= 15.5 Hz, 1H), 5.48 (dq, *J*= 15.7, 6.3 Hz, 1H), 2.47 (dq, *J*= 14.4, 7.2 Hz, 1H), 2.32 – 2.23 (m, 1H), 1.77 – 1.74 (m, 3H), 1.65 (s, 3H), 0.87 (t, *J*= 7.2 Hz, 3H).

(*E*)-2,3-dimethyl-2,3-diphenylhept-4-enoic acid **15c**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.07 mL, 344 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (37 µL, 344 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14c** (53 mg, 572 µmol, 1.0 equiv.) dissolved in 0.60 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 1 hour 24 minutes TMSCl (44 µL, 344 µmol, 2.0 equiv.) was added dropwise. After 38 minutes, the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 20:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected in 57 % yield (30 mg, 97 µmol), and 9.2:1 *dr.*

Note: 57 % yield - also 57 % yield over 2 steps. So maybe ester formation MK-II-185) was not quantitative ($CHCl_3$ impurities from evaporation).

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.29 – 7.03 (m, 10H), 6.32 (d, *J*= 15.7 Hz, 1H), 5.45 (dt, *J*= 15.6, 6.4 Hz, 1H), 2.14 – 2.04 (m, 2H), 1.62 (s, 3H), 1.59 (s, 3H), 0.99 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.9, 145.4, 139.5, 134.3, 131.8, 129.3, 129.2, 127.1, 127.0, 126.8, 126.1, 57.8, 49.2, 26.3, 23.2, 21.3, 13.9.

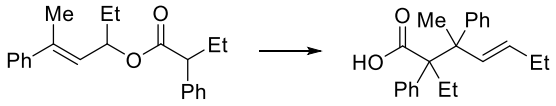
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.29 – 7.03 (m, 10H), 6.42 (d, *J*= 15.7 Hz, 1H), 5.34 (dt, *J*= 15.8, 6.5 Hz, 1H), 2.14 – 2.04 (m, 2H), 1.62 (s, 3H), 1.59 (s, 3H), 0.99 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.7, 144.7, 139.8, 134.9, 131.6, 129.6, 129.3, 127.1, 127.0, 126.6, 126.1, 57.9, 49.4, 26.2, 23.4, 21.3, 13.8.

IR (Neat Film, NaCl) 3056, 2961, 2628, 1697, 1599, 1496, 1458, 1444, 1373, 1266, 1113, 1072, 1030, 982, 907, 760, 730, 700, 680, 664, 651 cm^{-1}

(*E*)-2-ethyl-3-methyl-2,3-diphenylhept-4-enoic acid **15d**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.61 mL, 515 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (38 µL, 515 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14d** (83 mg, 257 µmol, 1.0 equiv.) dissolved in 0.83 mL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 2 hours 30 minutes TMSCl (56 µL, 514 µmol, 2.0 equiv.) was added dropwise. After 30 minutes, the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour 5 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected in 73 % yield (61 mg, 189 µmol), and 9.5:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.42 – 6.92 (m, 10H), 6.18 (d, *J*= 15.7 Hz, 1H), 5.49 (dt, *J*= 15.6, 6.3 Hz, 1H), 2.39 –2.31 (m, 1H), 2.27 – 2.04 (m, 3H), 1.62 (s, 3H), 0.98 (t, *J*= 7.5 Hz, 3H), 0.84 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.6, 145.4, 136.6, 134.0, 131.9, 131.1, 129.2, 127.0, 126.6, 126.5, 126.3, 63.9, 50.1, 26.3, 26.1, 23.3, 13.9, 10.6.

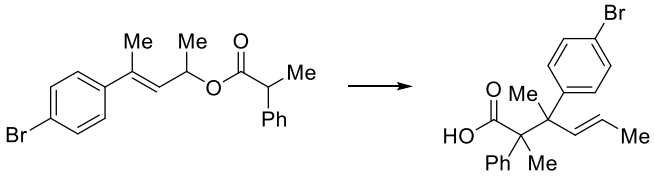
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.42 – 6.92 (m, 9H), 6.63 (d, *J*= 15.7 Hz, 1H), 5.42 (ddd, *J*= 15.7, 9.1, 6.4 Hz, 1H), 2.39 –2.31 (m, 1H), 2.27 – 2.04 (m, 3H), 1.45 (s, 3H), 0.98 (t, *J*= 7.5 Hz, 3H), 0.53 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.5, 145.1, 136.8, 134.7, 131.5, 131.0, 129.8, 128.9, 127.0, 126.4, 126.2, 64.4, 50.0, 26.5, 25.8, 22.4, 14.0, 9.8.

IR (Neat Film, NaCl) 2965, 1694, 1496, 1457, 1444, 1378, 1252, 1073, 1030, 904, 796, 700 cm^{-1}

(*E*)-3-(4-bromophenyl)-2,3-dimethyl-2-phenylhex-4-enoic acid **15q**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 670 µL, 214 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (23 µL, 214 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14q** (40 mg, 107 µmol, 1.0 equiv.) dissolved in 360 µL dry toluene was added dropwise over 3 minutes. The reaction was kept at -78° C and after 1 hour 56 minutes TMSCl (27 µL, 214 µmol, 2.0 equiv.) was added dropwise. The reaction was allowed to warm to 18-19° C over night and TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 40 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with DCM three times. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was directly used in the next reaction without purification.

Note: Crude yield: 91 % (38 mg, 102 µmol), *dr* = 8.3:1.

Traces of THF and DCM in NMR - no superpure spec

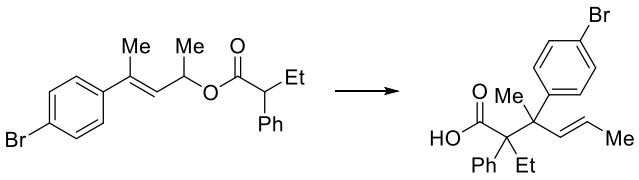
Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.49 – 7.07 (m, 7H), 6.89 (d, *J*= 8.3 Hz, 2H), 6.24 (d, *J*= 15.5 Hz, 1H), 5.42 (dq, *J*= 15.6, 6.4 Hz, 1H), 1.73 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.63 (s, 3H), 1.58 (s, 3H).

Minor:

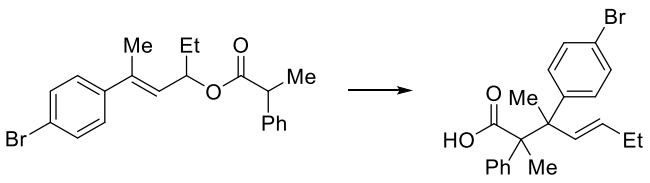
^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.49 – 7.07 (m, 7H), 6.83 (d, *J*= 8.4 Hz, 2H), 6.42 (dd, *J*= 15.6, 1.9 Hz, 1H), 5.35 – 5.27 (m, 1H), 1.73 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.65 (s, 3H), 1.55 (s, 3H).

(*E*)-3-(4-bromophenyl)-2-ethyl-3-methyl-2-phenylhex-4-enoic acid **15r**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 0.65 mL, 207 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (22 µL, 206 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14r** (40 mg, 103 µmol, 1.0 equiv.) dissolved in 0.34 mL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 1 hour 50 minutes TMSCl (26 µL, 207 µmol, 2.0 equiv.) was added dropwise. The reaction was allowed to warm to 18-19° C over night and TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with DCM three times. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. Crude product was collected in >100 % yield and 5.7:1 *dr.* The material was directly subjected to the next reaction without purification (decomposition issues on silica gel).

(*E*)-3-(4-bromophenyl)-2,3-dimethyl-2-phenylhept-4-enoic acid **15s**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 807 µL, 258 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (28 µL, 258 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14s** (50 mg, 129 µmol, 1.0 equiv.) dissolved in 430 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (33 µL, 258 µmol, 2.0 equiv.) was added dropwise. After 50 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered over a plug of silica (DCM) and desired product was obtained as yellow oil in 79 % yield (40 mg, 103 µmol) and 8.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 6.80 (m, 9H), 6.22 (d, *J*= 15.7 Hz, 1H), 5.44 (dt, *J*= 15.6, 6.5 Hz, 1H), 2.13 – 2.04 (m, 2H), 1.62 (s, 3H), 1.57 (s, 3H), 0.97 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.8, 144.6, 139.3, 133.9, 132.3, 131.3, 129.8, 129.3, 127.5, 127.3, 120.3, 57.7, 48.9, 26.4, 23.2, 21.4, 13.9.

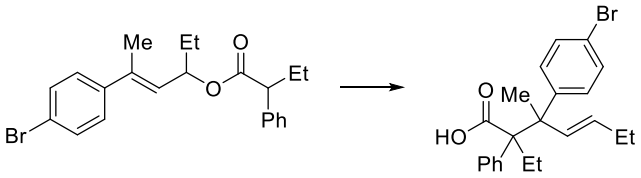
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 6.80 (m, 9H), 6.39 (d, *J*= 15.7 Hz, 1H), 5.37 – 5.28 (m, 1H), 2.13 – 2.04 (m, 2H), 1.62 (s, 3H), 1.57 (s, 3H), 0.97 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.7, 144.0, 139.6, 134.6, 132.2, 131.7, 129.6, 129.2, 127.5, 127.3, 120.3, 57.8, 49.3, 26.3, 23.7, 21.2, 13.9.

IR (Neat Film, NaCl) 2922, 1699, 1458, 1260, 1083, 1008, 818, 701 cm^{-1}

(*E*)-3-(4-bromophenyl)-2-ethyl-3-methyl-2-phenylhept-4-enoic acid **15t**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 810 µL, 259 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (28 µL, 259 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14t** (52 mg, 130 µmol, 1.0 equiv.) dissolved in 430 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours 10 minutes TMSCl (33 µL, 259 µmol, 2.0 equiv.) was added dropwise. After 40 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered over a plug of silica (DCM) and desired product was obtained as yellow oil in 78 % yield (40 mg, 101 µmol) and 6:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.42 – 6.87 (m, 9H), 6.14 (d, *J*= 15.6 Hz, 1H), 5.46 (dt, *J*= 15.6, 6.4 Hz, 1H), 2.35 – 2.27 (m, 1H), 2.21 – 2.04 (m, 3H), 1.58 (s, 3H), 0.98 (t, *J*= 7.4 Hz, 3H), 0.85 (td, *J*= 7.2, 2.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.0, 144.5, 136.4, 133.6, 132.4, 131.1, 131.0, 130.0, 126.9, 126.7, 120.5, 63.7, 49.9, 26.3, 26.1, 23.4, 13.9, 10.6.

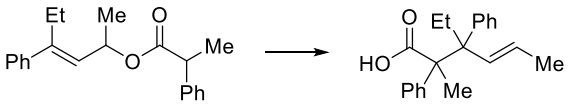
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.42 – 6.87 (m, 9H), 6.57 (d, *J*= 15.6 Hz, 1H), 5.43 (d, *J*= 2.9 Hz, 1H), 2.44 – 2.34 (m, 1H), 2.21 – 2.04 (m, 3H), 1.44 (s, 3H), 0.98 (t, *J*= 7.4 Hz, 3H), 0.85 (td, *J*= 7.2, 2.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 179.9, 144.4, 136.5, 134.3, 131.8, 131.4, 130.9, 130.1, 126.9, 126.7, 120.6, 64.2, 49.8, 26.4, 25.8, 22.6, 14.0, 10.6.

IR (Neat Film, NaCl) 2962, 1694, 1490, 1458, 1397, 1251, 1081, 1008, 819, 702, 680 cm^{-1}

(*E*)-3-ethyl-2-methyl-2,3-diphenylhex-4-enoic acid **15e**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.64 mL, 525 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (57 µL, 525 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14e** (81 mg, 262 µmol, 1.0 equiv.) dissolved in 0.88 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours 20 minutes TMSCl (67 µL, 525 µmol, 2.0 equiv.) was added dropwise. After 30 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 25 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected as white solids in 74 % yield (60 mg, 193 µmol) and 7.5:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 6.94 (m, 10H), 6.06 – 5.97 (m, 1H), 5.40 (dq, *J*= 15.9, 6.4 Hz, 1H), 2.34 – 2.14 (m, 2H), 1.79 (dd, *J*= 6.4, 1.6 Hz, 3H), 1.58 (s, 3H), 0.52 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.4, 140.6, 139.2, 131.4, 130.4, 129.8, 127.4, 127.2, 127.0, 127.0, 126.2, 59.1, 55.3, 24.9, 21.7, 18.9, 9.7.

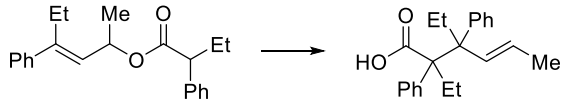
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.33 – 6.94 (m, 10H), 6.16 (d, *J*= 15.9 Hz, 1H), 5.19 – 5.09 (m, 1H), 2.34 – 2.14 (m, 2H), 1.74 (dd, *J*= 6.4, 1.6 Hz, 3H), 1.61 (s, 3H), 0.65 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.3, 139.8, 139.4, 131.9, 131.5, 129.4, 127.8, 127.2, 127.1, 126.5, 126.2, 58.5, 56.3, 25.1, 21.0, 18.6, 10.0.

IR (Neat Film, NaCl) 3057, 2964, 2933, 2879, 2626, 1694, 1599, 1496, 1444, 1398, 1377, 1266, 1216, 1166, 1097, 1081, 1033, 989, 907, 805, 757, 732, 702, 671 cm^{-1}

(*E*)-2,3-diethyl-2,3-diphenylhex-4-enoic acid **15f**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.63 mL, 521 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (55 µL, 521 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14f** (84 mg, 261 µmol, 1.0 equiv.) dissolved in 0.87 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours 30 minutes TMSCl (66 µL, 521 µmol, 2.0 equiv.) was added dropwise. After 25 minutes the flask was

removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected as white foam in 79 % yield (66 mg, 205 µmol) and 7.1:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.44 – 6.82 (m, 10H), 5.90 (d, *J*= 15.9 Hz, 1H), 5.37 (dq, *J*= 16.2, 6.5 Hz, 1H), 2.56 (dq, *J*= 14.3, 7.1 Hz, 1H), 2.39 (dq, *J*= 14.3, 7.3 Hz, 1H), 2.26 (dq, *J*= 14.4, 7.3 Hz, 1H), 2.03 (dq, *J*= 14.3, 7.1 Hz, 1H), 1.79 (dd, *J*= 6.4, 1.7 Hz, 3H), 0.87 (t, *J*= 7.2 Hz, 3H), 0.58 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.7, 140.7, 136.5, 131.6, 131.2, 130.2, 127.3, 127.0, 126.5, 126.3, 126.2, 64.9, 56.6, 25.9, 24.8, 18.8, 10.4, 10.1.

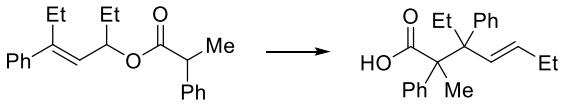
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.44 – 6.82 (m, 10H), 6.09 (dd, *J*= 15.8, 1.9 Hz, 1H), 5.39 – 5.27 (m, 1H), 2.56 (dq, *J*= 14.3, 7.1 Hz, 1H), 2.39 (dq, *J*= 14.3, 7.3 Hz, 1H), 2.26 (dq, *J*= 14.4, 7.3 Hz, 1H), 2.03 (dq, *J*= 14.3, 7.1 Hz, 1H), 1.83 – 1.79 (m, 3H), 0.83 (t, *J*= 7.4 Hz, 3H), 0.62 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.0, 139.8, 136.4, 131.6, 131.4, 130.6, 127.4, 127.0, 126.6, 126.3, 126.2, 65.5, 56.4, 24.9, 24.4, 18.8, 10.7, 10.0.

IR (Neat Film, NaCl) 3067, 2968, 2936, 2880, 1694, 1599, 1499, 1444, 1378, 1312, 1250, 1200, 1080, 1035, 1001, 909, 847, 797, 760, 732, 703, 670 cm^{-1}

(*E*)-3-ethyl-2-methyl-2,3-diphenylhept-4-enoic acid **15g**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.59 mL, 509 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (55 µL, 508 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14g** (82 mg, 254 µmol, 1.0 equiv.) dissolved in 0.85 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (65 µL, 509 µmol, 2.0 equiv.) was added dropwise. After 23 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic

layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected as white-yellow solids in 82 % yield (67 mg, 208 µmol), and 10:1 *dr* (or higher. Again, minor impurity in which cannot be distinguished from minor diastereomer).

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.45 – 6.89 (m, 10H), 6.00 (d, *J*= 16.0 Hz, 1H), 5.44 (dt, *J*= 15.9, 6.6 Hz, 1H), 2.40 – 2.26 (m, 1H), 2.26 – 2.06 (m, 3H), 1.58 (s, 3H), 1.02 (t, *J*= 7.4 Hz, 3H), 0.53 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.8, 140.7, 139.2, 134.5, 130.4, 129.8, 129.2, 127.2, 127.0, 127.0, 126.2, 59.1, 55.0, 26.7, 24.8, 21.7, 14.2, 9.7.

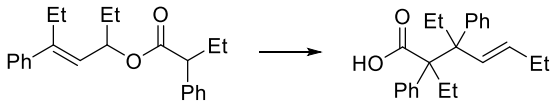
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.45 – 6.89 (m, 10H), 6.16 (d, *J*= 16.0 Hz, 1H), 5.17 (dt, *J*= 15.9, 6.5 Hz, 1H), 2.40 – 2.26 (m, 1H), 2.26 – 2.06 (m, 3H), 1.58 (s, 3H), 1.00 – 0.94 (m, 3H), 0.67 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.7, 140.7, 139.2, 134.9, 131.5, 130.7, 129.5, 127.2, 127.0, 127.0, 126.2, 58.5, 56.1, 26.5, 25.0, 21.7, 14.0, 10.0.

IR (Neat Film, NaCl) 2961, 2932, 2636, 1697, 1599, 1496, 1458, 1444, 1377, 1266, 1158, 1081, 1031, 989, 909, 846, 817, 728, 702, 675 cm^{-1}

(*E*)-2,3-diethyl-2,3-diphenylhept-4-enoic acid **15h**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.56 mL, 499 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (54 µL, 499 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14h** (84 mg, 250 µmol, 1.0 equiv.) dissolved in 0.83 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (63 µL, 499 µmol, 2.0 equiv.) was added dropwise. After 15 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and the aqueous layer was extracted with DCM three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected as pale yellow oil in 71 % yield (60 mg, 178 µmol) and 9.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 6.83 (m, 10H), 5.85 (d, *J*= 16.0 Hz, 1H), 5.39 (dt, *J*= 16.0, 6.4 Hz, 1H), 2.59 – 2.48 (m, 1H), 2.41 – 2.32 (m, 1H), 2.29 – 2.21 (m, 1H), 2.17 – 2.09 (m, 2H), 2.06 – 1.98 (m, 1H), 1.01 (t, *J*= 7.4 Hz, 3H), 0.85 (t, *J*= 7.2 Hz, 3H), 0.56 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.1, 140.8, 136.5, 134.3, 131.2, 130.2, 129.4, 127.0, 126.5, 126.3, 126.2, 64.9, 56.3, 26.6, 25.8, 24.7, 14.1, 10.4, 10.1.

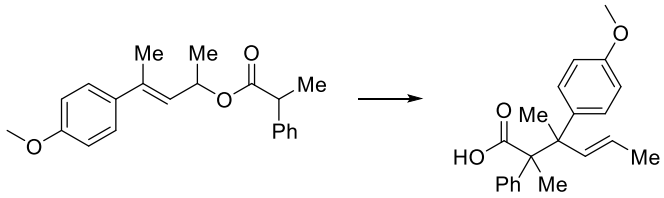
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 6.83 (m, 10H), 6.04 (d, *J*= 15.9 Hz, 1H), 5.36 – 5.28 (m, 1H), 2.59 – 2.48 (m, 1H), 2.41 – 2.32 (m, 1H), 2.29 – 2.21 (m, 1H), 2.17 – 2.09 (m, 2H), 2.06 – 1.98 (m, 1H), 0.95 (t, J= 7.3 Hz, 3H), 0.85 (t, *J*= 7.2 Hz, 3H), 0.62 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.5, 140.8, 136.4, 134.4, 131.3, 130.6, 128.8, 127.0, 126.5, 126.3, 126.2, 65.5, 56.2, 26.7, 26.0, 24.4, 14.1, 10.7, 10.0.

IR (Neat Film, NaCl) 2963, 2932, 1694, 1599, 1496, 1458, 1444, 1380, 1251 ,1199, 1081, 1034, 993, 907, 848, 802, 758, 730, 702, 680, 668 cm^{-1}

(*E*)-3-(4-methoxyphenyl)-2,3-dimethyl-2-phenylhex-4-enoic acid **15i**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.68 mL, 536 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (58 µL, 536 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14i** (87 mg, 268 µmol, 1.0 equiv.) dissolved in 900 µL dry toluene was added dropwise over 2 minutes. The reaction was kept at -78° C and after 2 hours 5 minutes TMSCl (68 µL, 536 µmol, 2.0 equiv.) was added dropwise. After 10 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered over a plug of silica (DCM) and desired product was obtained as yellow oil in 56 % yield (49 mg, 111 µmol) and 4.5:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.62 (m, 9H), 6.29 (d, *J*= 15.4 Hz, 1H), 5.42 (dq, *J*= 15.6, 6.4 Hz, 1H), 3.78 (s, 3H), 1.73 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.62 (s, 3H), 1.56 (d, *J*= 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.9, 157.8, 139.7, 137.5, 136.6, 130.5, 129.3, 127.1, 124.7, 112.1, 57.9, 55.2, 48.9, 23.4, 21.4, 18.7.

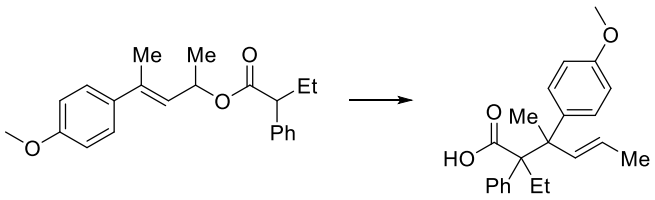
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.62 (m, 9H), 6.43 (dd, *J*= 15.7, 1.8 Hz, 1H), 5.36 – 5.27 (m, 1H), 3.78 (s, 3H), 1.71 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.64 (s, 3H), 1.56 (d, *J*= 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.9, 157.8, 140.0, 137.3, 136.9, 130.8, 129.3, 127.2, 124.4, 112.0, 58.0, 55.2, 49.1, 29.8, 23.6, 21.4, 18.7.

IR (Neat Film, NaCl) 2995, 2954, 1698, 1607, 1578, 1512, 1463, 1444, 1376, 1293, 1252, 1187, 1098, 1069, 1033, 966, 922, 836, 805, 759, 731, 701, 666 cm^{-1}

(*E*)-2-ethyl-3-(4-methoxyphenyl)-3-methyl-2-phenylhex-4-enoic acid **15j**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.55 mL, 496 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (54 µL, 496 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14j** (84 mg, 248 µmol, 1.0 equiv.) dissolved in 820 µL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (63 µL, 496 µmol, 2.0 equiv.) was added dropwise. After 10 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O twice. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was filtered over a plug of silica (DCM) and desired product was obtained as pale yellow oil in 88 % yield (74 mg, 219 µmol).

Note: *dr* hard to tell which signals belong to minor diastereomer. Depending on the signals chosen 3:1 to 12:1 (if olefin DB is integrated).

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 6.60 (m, 9H), 6.23 – 6.16 (m, 1H), 5.44 (dq, *J*= 15.9, 6.5 Hz, 1H), 3.78 (s, 3H), 2.37 – 2.27 (m, 1H), 2.19 – 2.09 (m, 1H), 1.72 (dd, *J*= 6.5, 1.7 Hz, 3H), 1.57 (s, 3H), 0.83 (t, *J*= 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.5, 157.9, 137.3, 136.8, 136.3, 131.0, 130.2, 126.6, 126.5, 124.7, 112.3, 63.9, 55.2, 49.8, 26.1, 23.4, 18.7, 10.6.

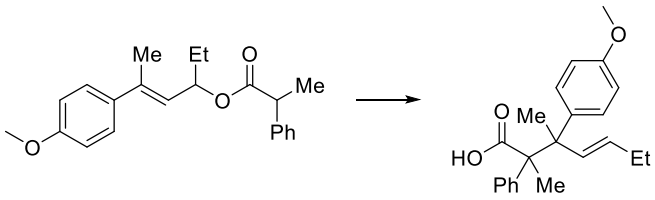
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.40 – 6.60 (m, 9H), 6.30 (d, *J*= 15.6 Hz, 1H), 5.44 (dq, *J*= 15.9, 6.5 Hz, 1H), 3.78 (s, 3H), 2.45 – 2.36 (m, 1H), 2.19 – 2.09 (m, 1H), 1.76 – 1.70 (m, 3H), 1.44 (s, 3H), 0.94 (t, *J*= 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.4, 158.0, 137.2, 137.1, 136.8, 130.4, 130.0, 127.6, 126.6, 123.9, 112.5, 64.5, 55.2, 49.6, 26.4, 22.5, 18.8, 12.2.

IR (Neat Film, NaCl) 2938, 1697, 1606, 1512, 1458, 1294, 1252, 1186, 1034, 975, 834, 701, 681 cm^{-1}

(*E*)-3-(4-methoxyphenyl)-2,3-dimethyl-2-phenylhept-4-enoic acid **15k**

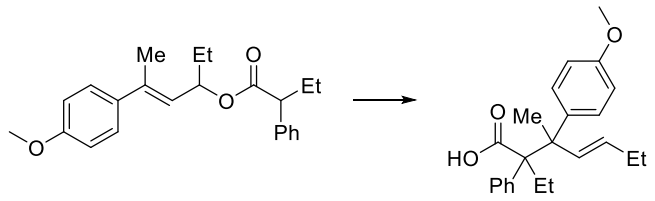


A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 0.74 mL, 236 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (26 µL, 236 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14k** (40 mg, 118 µmol, 1.0 equiv.) dissolved in 0.40 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (30 µL, 344 µmol, 2.0 equiv.) was added dropwise. After 2 hours the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM).

NMR not too clean. Maybe methylation + purification might help to determine yield + *dr.*

IR (Neat Film, NaCl) 2959, 1697, 1606, 1511, 1458, 1251, 1186, 1034, 833, 701 cm^{-1}

(*E*)-2-ethyl-3-(4-methoxyphenyl)-3-methyl-2-phenylhept-4-enoic acid **15l**



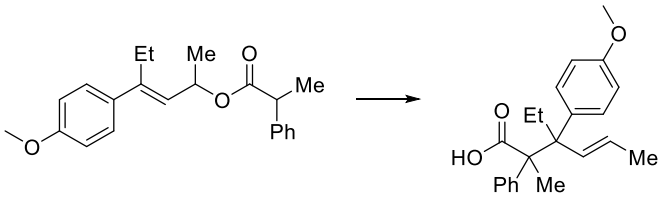
A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 0.73 mL, 233 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (25 µL, 233 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14l** (41 mg, 116 µmol, 1.0 equiv.) dissolved in 0.40 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (30 µL, 233 µmol, 2.0 equiv.) was added dropwise. After 2 hours the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined

organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM).

NMR not too clean. Maybe methylation + purification might help to determine yield and *dr.*

IR (Neat Film, NaCl) 2962, 1718, 1690, 1607, 1511, 1458, 1379, 1294, 1251, 1034, 975, 827, 701, 674 cm^{-1}

(*E*)-3-ethyl-3-(4-methoxyphenyl)-2-methyl-2-phenylhex-4-enoic acid **15m**

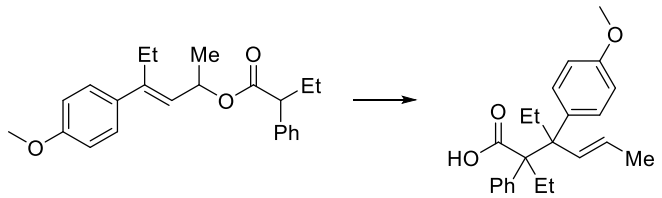


A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 0.79 mL, 254 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (28 µL, 254 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14m** (43 mg, 127 µmol, 1.0 equiv.) dissolved in 0.43 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (32 µL, 254 µmol, 2.0 equiv.) was added dropwise. After 2 hours the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and the aqueous layer was extracted with DCM three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM).

NMR shows some side product(s). Maybe methylation and purification allow determination of yield and (correct) *dr.*

IR (Neat Film, NaCl) 2967, 1698, 1608, 1578, 1512, 1464, 1378, 1251, 1186, 1159, 1081, 1035, 909, 828, 731, 701, 680 cm^{-1}

(*E*)-2,3-diethyl-3-(4-methoxyphenyl)-2-phenylhex-4-enoic acid **15n**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.49 mL, 477 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (52 µL, 477 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14n** (84 mg, 238 µmol, 1.0 equiv.) dissolved in 0.80 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours TMSCl (60

µL, 477 µmol, 2.0 equiv.) was added dropwise. After 10 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and the aqueous layer was extracted with DCM three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected as pale yellow oil in 79 % yield (66 mg, 187 µmol) and 5.8:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.65 (m, 9H), 5.87 (d, *J*= 15.8 Hz, 1H), 5.40 – 5.31 (m, 1H), 3.78 (s, 3H), 2.50 – 2.41 (m, 1H), 2.40 – 2.31 (m, 1H), 2.26 – 2.16 (m, 1H), 2.26 – 2.16 (m, 1H), 2.05 – 1.95 (m, 1H), 1.77 (dd, *J*= 6.3, 1.7 Hz, 3H), 0.86 (t, *J*= 7.2 Hz, 3H), 0.55 (t, *J*= 7.1 Hz, 3H).

Note: NMR not super clean

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.9, 157.8, 136.7, 132.5, 131.8, 131.3, 131.2, 127.0, 126.4, 126.3, 112.3, 65.0, 56.0, 55.2, 25.9, 24.8, 18.7, 10.4, 10.0.

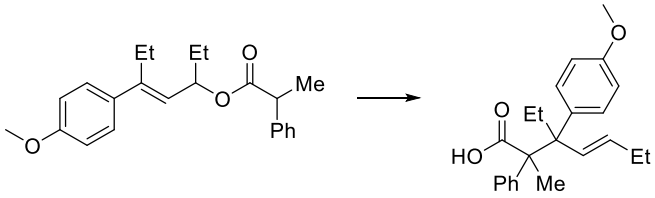
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.65 (m, 9H), 6.04 (d, *J*= 15.7 Hz, 1H), 5.27 (dt, *J*= 15.8, 6.4 Hz, 1H), 3.77 (d, *J*= 1.9 Hz, 9H), 2.50 – 2.41 (m, 1H), 2.40 – 2.31 (m, 1H), 2.26 – 2.16 (m, 1H), 2.26 – 2.16 (m, 1H), 2.05 – 1.95 (m, 1H), 1.77 (dd, *J*= 6.3, 1.7 Hz, 3H), 0.86 (t, *J*= 7.2 Hz, 3H), 0.55 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.3, 157.9, 136.5, 132.5, 131.9, 131.6, 131.4, 127.1, 126.5, 126.5, 112.2, 65.5, 55.9, 55.2, 25.7, 24.9, 18.8, 10.7, 9.9.

IR (Neat Film, NaCl) 2969, 2936, 1693, 1608, 1512, 1464, 1378, 1251, 1186, 1165, 1036, 826, 758, 732, 702, 680 cm^{-1}

(*E*)-3-ethyl-3-(4-methoxyphenyl)-2-methyl-2-phenylhept-4-enoic acid **15o**

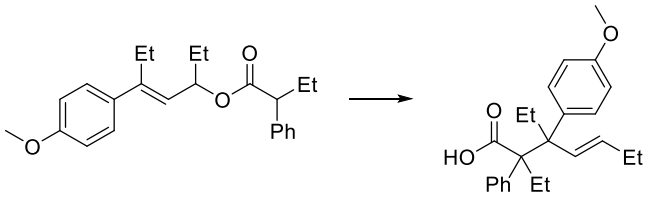


A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 0.71 mL, 227 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (25 µL, 227 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14o** (40 mg, 113 µmol, 1.0 equiv.) dissolved in 0.40 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 2 hours 10 minutes TMSCl (29 µL, 227 µmol, 2.0 equiv.) was added dropwise. After 2 hours the flask was removed

from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 45 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM). NMR shows some side product(s). Maybe methylation and purification allow determination of yield and (correct) *dr.*

IR (Neat Film, NaCl) 2961, 1694, 1608, 1578, 1512, 1463, 1444, 1377, 1252, 1186, 1159, 1069, 1036, 992, 911, 832, 733, 702, 680 cm^{-1}

(*E*)-2,3-diethyl-3-(4-methoxyphenyl)-2-phenylhept-4-enoic acid **15p**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 1.42 mL, 453 µmol, 2.0 equiv.), followed by *N,N*-dimethylethylamine (49 µL, 453 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14p** (84 mg, 226 µmol, 1.0 equiv.) dissolved in 0.80 mL dry toluene was added dropwise. The reaction was kept at -78° C and after 1 hour 40 minutes TMSCl (57 µL, 453 µmol, 2.0 equiv.) was added dropwise. After 10 minutes the flask was removed from cooling and allowed to warm to 18-19° C over night. TLC (hexanes: ethyl acetate 5:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 1 hour, the mix was diluted with H_2O and the aqueous layer was extracted with DCM three times. The combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude material was filtered through a plug of silica (DCM) and product was collected as colorless oil in 71 % yield (59 mg, 161 µmol) and 7.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.20 – 6.62 (m, 9H), 5.81 (d, *J*= 15.9 Hz, 1H), 5.38 (dt, *J*= 16.0, 6.4 Hz, 1H), 3.78 (s, 3H), 2.51 – 2.42 (m, 1H), 2.39 – 2.30 (m, 1H), 2.25 – 2.17 (m, 1H), 2.13 – 2.09 (m, 2H), 2.06 – 1.96 (m, 1H), 1.01 (t, *J*= 7.4 Hz, 3H), 0.86 (t, *J*= 7.2 Hz, 3H), 0.55 (t, *J*= 7.1 Hz, 3H).

Note: THF traces in

^{13}C NMR (101 MHz, $CDCl_3$) δ= 181.0, 157.8, 136.7, 134.1, 132.6, 131.3, 131.3, 129.6, 126.4, 126.3, 112.3, 65.0, 55.7, 55.2, 26.6, 25.8, 24.8, 14.1, 10.4, 10.0.

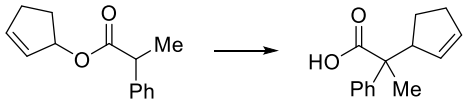
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.20 – 6.62 (m, 9H), 6.01 (d, *J*= 15.9 Hz, 1H), 5.31 (dt, *J*= 15.9, 6.6 Hz, 1H), 3.77 (s, 3H), 2.51 – 2.42 (m, 1H), 2.39 – 2.30 (m, 1H), 2.25 – 2.17 (m, 1H), 2.13 – 2.09 (m, 2H), 2.06 – 1.96 (m, 1H), 1.01 (t, *J*= 7.4 Hz, 3H), 0.81 (t, *J*= 7.1 Hz, 3H), 0.61 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 180.3, 157.9, 136.5, 134.2, 132.6, 131.8, 131.6, 129.7, 126.5, 126.4, 112.2, 65.5, 55.7, 55.2, 26.6, 25.7, 24.5, 14.1, 10.7, 9.9.

IR (Neat Film, NaCl) 2963, 1691, 1608, 1512, 1458, 1294, 1252, 1187, 1036, 996, 832, 802, 702 cm^{-1}

2-(cyclopent-2-en-1-yl)-2-phenylpropanoic acid **15u**



A flame-dried 10 mL round bottom flask was equipped with LiHMDS (0.32 M in toluene, 0.87 mL, 277 µmol, 2.0 equiv.), followed by N,N-dimethylethylamine (30 µL, 277 µmol, 2.0 equiv.) and the mix was cooled to -78° C. Ester **14u** (30 mg, 139 µmol, 1.0 equiv.) dissolved in 0.46 mL dry toluene was added dropwise over 4 minutes. The reaction was kept at -78° C and after 2 hours TMSCl (35 µL, 277 µmol, 2.0 equiv.) was added dropwise. The reaction was allowed to warm to 18-19° C over night and TLC (hexanes: ethyl acetate 20:1) the next day showed full consumption of starting material. The reaction was diluted with Et_2O and the organic layer was washed with 0.5 M HCl. The solvent was removed in vacuo, the residue was taken up in THF and stirred with 2M HCl. After 40 minutes, the mix was diluted with H_2O and Et_2O, layers were separated and the organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The desired product could be collected as colorless oil in 97 % yield (29 mg, 134 µmol) and 2.0:1 *dr*.

Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.54 – 7.02 (m, 5H), 5.69 – 5.66 (m, 1H), 5.39 – 5.33 (m, 1H), 3.91 (ddt, J = 6.3, 4.0, 2.2 Hz, 1H), 2.26 – 2.08 (m, 2H), 1.76 – 1.27 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.1, 142.2, 133.2, 132.2, 130.9, 128.4, 127.1, 126.8, 53.5, 52.8, 32.6, 26.3, 17.4.

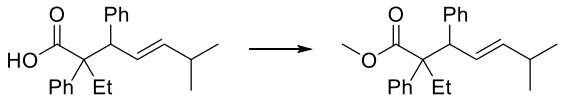
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.54 – 7.02 (m, 5H), 5.87 – 5.82 (m, 1H), 5.78 – 5.74 (m, 1H), 4.04 – 3.97 (m, 1H), 2.26 – 2.08 (m, 2H), 1.76 – 1.27 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 182.1, 142.3, 133.0, 132.2, 130.9, 128.5, 127.1, 126.8, 53.3, 52.8, 32.3, 25.1, 16.9.

Methylation

Methyl (*E*)-2-ethyl-6-methyl-2,3-diphenylhept-4-enoate **16**



A flame-dried 100 mL round bottom flask was equipped with acid **4b** (100 mg, 310 µmol, 1.0 equiv.), 1 mL dry DMF, K_2CO_3 (86 mg, 620 µmol, 2.0 equiv.). Then MeI (39 µL, 620 µmol, 2.0 equiv.) was added and the mix was stirred. After 20 minutes TLC (hexanes: ethyl acetate 6:1) confirmed full consumption of starting material. The reaction was quenched with solid NH_4Cl and diluted with toluene. The solvents were evaporated and the residue was taken up in Et_2O and little H_2O. The aqueous layer was extracted with Et_2O three times and the combined organic layer was washed with H_2O and Brine. It was dried over Na_2SO_4 and concentrated in vacuo. The crude (91 mg - NMR ok but not supernice) colorless mixture was subjected to column chromatography (~9 g silica, hexanes: ethyl acetate 100:1). Desired product could be obtained as colorless oil in 44 % yield (46 mg, 137 µmol) and 7.1:1 *dr.*

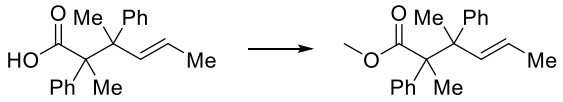
Major:

^{1}H NMR (500 MHz, C_6D_6) δ= 7.27 – 6.96 (m, 10H), 5.91 – 5.80 (m, 1H), 5.36 (dd, *J*= 15.2, 6.8 Hz, 1H), 4.21 (d, *J*= 9.7 Hz, 1H), 3.32 (s, 3H), 2.31 – 2.02 (m, 3H), 0.90 – 0.81 (m, 9H).

Minor:

^{1}H NMR (500 MHz, C_6D_6) d= 7.27 – 6.96 (m, 10H), 5.91 – 5.80 (m, 1H), 5.64 (dd, *J*= 15.3, 6.7 Hz, 1H), 4.31 (d, *J*= 9.1 Hz, 1H), 3.41 (s, 3H), 2.31 – 1.87 (m, 3H), 0.90 – 0.81 (m, 9H).

Methyl (*E*)-2,3-dimethyl-2,3-diphenylhex-4-enoate **17**



A Scin vial was equipped with acid **15a** (58 mg, 197 µmol, 1.0 equiv.) and K_2CO_3 (55 mg, 394 µmol, 2.0 equiv.) in 1 mL dry DMF. Then MeI (25 µL, 394 µmol, 2.0 equiv.) was added and the mix was stirred over night. The next day, the reaction was quenched with solid NH_4Cl and diluted with toluene. The solvents were evaporated and the residue was taken up in Et_2O and little H_2O. The organic layer was washed with saturated LiCl solution followed by H_2O and Brine. It was dried over Na_2SO_4 and concentrated in vacuo. The resulting residue was filtered through a plug of silica (DCM) and product was collected as yellow oil in 86 % yield (52 mg, 169 µmol) and 7.8:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 6.93 (m, 9H), 6.38 – 6.31 (m, 1H), 5.40 (dq, *J*= 15.6, 6.4 Hz, 1H), 3.61 (s, 3H), 1.75 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.58 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.2, 145.6, 140.4, 136.9, 129.4, 129.2, 127.1, 127.0, 126.8, 126.1, 124.4, 58.0, 51.8, 49.6, 23.2, 21.3, 18.7.

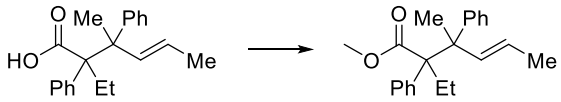
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.41 – 6.93 (m, 9H), 6.44 (dd, *J*= 15.6, 1.8 Hz, 1H), 5.37 – 5.29 (d, *J*= 6.4 Hz, 1H), 3.58 (s, 3H), 1.74 (d, *J*= 1.7 Hz, 3H), 1.58 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.2, 145.3, 140.7, 137.3, 129.7, 129.2, 127.1, 127.0, 126.8, 126.1, 124.3, 58.1, 51.8, 49.7, 23.4, 21.3, 18.7.

IR (Neat Film, NaCl) 2950, 2854, 1732, 1599, 1496, 1444, 1376, 1233, 1100, 1071, 1030, 974, 781, 762, 670 cm^{-1}

Methyl (*E*)-2-ethyl-3-methyl-2,3-diphenylhex-4-enoate **18**



A Scin vial was equipped with acid **15b** (55 mg, 178 µmol, 1.0 equiv.) and K_2CO_3 (49 mg, 357 µmol, 2.0 equiv.) in 1 mL dry DMF. Then MeI (22 µL, 357 µmol, 2.0 equiv.) was added and the mix was stirred over night. The next day, the reaction was quenched with solid NH_4Cl and diluted with toluene. The solvents were evaporated and the residue was taken up in Et_2O and little H_2O. The organic layer was washed with saturated LiCl solution followed by H_2O and Brine. It was dried over Na_2SO_4 and concentrated in vacuo. The resulting residue was filtered through a plug of silica (DCM) and product was collected as yellow oil in 71 % yield (42 mg, 127 µmol) and 8.0:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.32 – 7.02 (m, 10H), 6.27 – 6.19 (m, 1H), 5.39 (dq, *J*= 15.6, 6.4 Hz, 1H), 3.66 (s, 3H), 2.31 (dq, *J*= 13.8, 6.9 Hz, 1H), 2.09 (dq, *J*= 14.4, 7.2 Hz, 1H), 1.72 (dd, *J*= 6.4, 1.6 Hz, 3H), 1.54 (s, 3H), 0.73 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.4, 145.6, 137.6, 136.5, 130.9, 129.2, 126.9, 126.5, 126.5, 126.2, 124.3, 63.8, 51.3, 50.3, 26.2, 23.2, 18.7, 10.7.

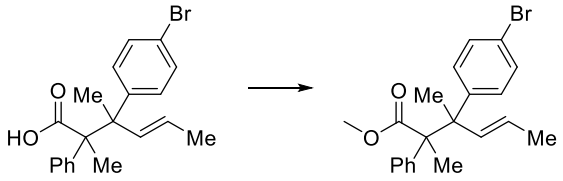
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.32 – 7.02 (m, 10H), 6.64 (d, *J*= 15.5 Hz, 1H), 5.39 (dq, *J*= 15.6, 6.4 Hz, 1H), 3.57 (s, 3H), 2.48 – 2.38 (m, 1H), 2.23 – 2.12 (m, 1H), 1.75 (dd, *J*= 6.5, 1.7 Hz, 3H), 1.56 (s, 3H), 0.73 (t, *J*= 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.3, 145.6, 137.8, 137.0, 130.7, 128.9, 126.9, 126.5, 126.5, 126.2, 124.0, 64.5, 51.3, 50.2, 26.1, 22.4, 18.8, 10.7.

IR (Neat Film, NaCl) 2945, 2854, 1732, 1599, 1496, 1444, 1378, 1228, 1112, 1028, 995, 816, 762, 738, 701, 680 cm^{-1}

Methyl (*E*)-3-(4-bromophenyl)-2,3-dimethyl-2-phenylhex-4-enoate **19**



A Scin vial was equipped with acid **15q** (38 mg, 102 µmol, 1.0 equiv.) and K_2CO_3 (28 mg, 204 µmol, 2.0 equiv.) in 1 mL dry DMF. Then MeI (14 µL, 204 µmol, 2.0 equiv.) was added and the mix was stirred. After TLC confirmed full conversion the reaction was quenched with NH_4Cl solution. The aqueous layer was extracted with DCM and the combined organic layer was dried over Na_2SO_4 filtered and concentrated in vacuo. The crude material was subjected to column chromatography (~1g silica, hexanes: ethyl acetate 50:1). Desired product could be obtained as yellow oil in 33 % yield (13 mg, 34 µmol) over 2 steps and 8.3:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.31 – 7.20 (m, 5H), 7.11 – 7.05 (m, 2H), 6.90 (d, *J*= 8.5 Hz, 2H), 6.28 – 6.21 (m, 1H), 5.40 (dq, *J*= 15.8, 6.5 Hz, 1H), 3.60 (s, 3H), 1.74 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.61 – 1.57 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.1, 144.7, 140.1, 136.5, 131.5, 129.7, 129.1, 127.2, 127.2, 124.9, 120.2, 57.8, 51.9, 49.2, 23.2, 21.3, 18.7.

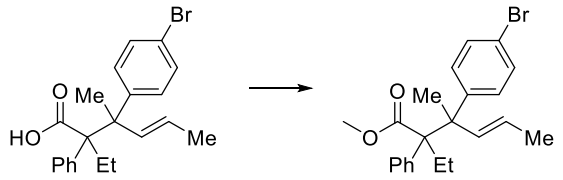
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.31 – 7.20 (m, 5H), 7.11 – 7.05 (m, 2H), 6.86 – 6.81 (m, 2H), 6.41 (dd, *J*= 15.6, 1.8 Hz, 1H), 5.39 – 5.29 (m, 2H), 3.59 (s, 3H), 1.74 (dd, *J*= 6.4, 1.7 Hz, 3H), 1.61 – 1.57 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.1, 144.7, 140.1, 136.9, 131.8, 129.5, 129.1, 127.2, 127.2, 124.9, 120.2, 58.0, 51.9, 49.2, 23.6, 21.2, 18.7.

IR (Neat Film, NaCl) 2948, 1732, 1491, 1445, 1396, 1232, 1083, 1008, 817, 716, 701 cm^{-1}

Methyl (*E*)-3-(4-bromophenyl)-2-ethyl-3-methyl-2-phenylhex-4-enoate **20**



A Scin vial was equipped with acid **15r** (crude from MK-II-123, only 40 mg in theory; 42 mg, 108 µmol, 1.0 equiv.) and K_2CO_3 (30 mg, 217 µmol, 2.0 equiv.) in 1 mL dry DMF. Then MeI (14 µL, 217 µmol, 2.0 equiv.) was added and the mix was stirred. After TLC confirmed full conversion the reaction was quenched with NH_4Cl solution. The aqueous layer was extracted with DCM and the combined organic layer was dried over Na_2SO_4 filtered and concentrated in

vacuo. The crude material was subjected to column chromatography (~1g silica, hexanes: ethyl acetate 50:1). Desired product could be obtained as colorless oil in 60 % yield (25 mg, 62 µmol) over 2 steps and 6.4:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.30 – 6.88 (m, 9H), 6.18 (dd, *J*= 15.6, 1.8 Hz, 1H), 5.38 (dq, *J*= 15.5, 6.3 Hz, 1H), 3.66 (s, 3H), 2.27 (dq, *J*= 14.2, 7.2 Hz, 1H), 2.08 (dq, *J*= 14.2, 7.2 Hz, 1H), 1.72 (dd, *J*= 6.5, 1.6 Hz, 3H), 1.50 (s, 3H), 0.77 – 0.73 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.3, 144.7, 137.3, 136.1, 131.2, 130.8, 129.9, 126.7, 126.7, 124.9, 120.4, 63.6, 51.4, 50.1, 26.2, 23.3, 18.7, 10.7.

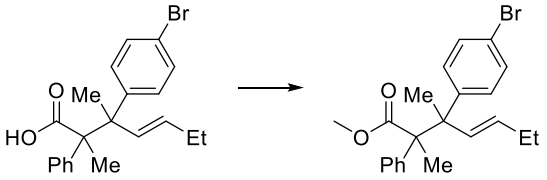
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.30 – 6.88 (m, 9H), 6.59 (dd, *J*= 15.5, 1.7 Hz, 1H), 5.38 (dq, *J*= 15.5, 6.3 Hz, 1H), 3.60 (s, 3H), 2.38 (dq, *J*= 14.3, 7.1 Hz, 1H), 2.21 – 2.13 (m, 1H), 1.75 (dd, *J*= 6.5, 1.7 Hz, 3H), 1.57 (s, 3H), 0.77 – 0.73 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 174.2, 144.8, 137.5, 136.7, 130.9, 130.7, 130.0, 126.7, 126.7, 124.5, 120.4, 64.2, 51.4, 50.0, 26.1, 22.7, 18.8, 10.7.

IR (Neat Film, NaCl) 2946, 1726, 1491, 1458, 1396, 1226, 1111, 1082, 1008, 840, 816, 702 cm^{-1}

Methyl (*E*)-3-(4-bromophenyl)-2,3-dimethyl-2-phenylhept-4-enoate **21**



A Scin vial was equipped with acid **15s** (35 mg, 90 µmol, 1.0 equiv.) and K_2CO_3 (25 mg, 181 µmol, 2.0 equiv.) in 1 mL dry DMF. Then MeI (12 µL, 180 µmol, 2.0 equiv.) was added and the mix was stirred. After TLC confirmed full conversion the reaction was quenched with NH_4Cl solution. The aqueous layer was extracted with DCM and the combined organic layer was dried over Na_2SO_4 filtered and concentrated in vacuo. The crude material was subjected to column chromatography (~1g silica, hexanes: ethyl acetate 50:1). Desired product could be obtained as orange oil in 36 % yield (13 mg, 33 µmol) over 2 steps and 10.1:1 *dr.*

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.31 – 7.05 (m, 7H), 6.91 (d, *J*= 8.3 Hz, 2H), 6.23 (d, *J*= 15.6 Hz, 1H), 5.41 (dt, *J*= 15.6, 6.4 Hz, 1H), 3.60 (s, 3H), 2.13 – 2.05 (m, 2H), 1.61 – 1.53 (m, 6H), 0.98 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.1, 144.8, 140.1, 134.4, 131.8, 131.4, 129.7, 129.2, 127.2, 127.2, 120.2, 57.8, 51.9, 49.0, 26.3, 23.1, 21.3, 14.0.

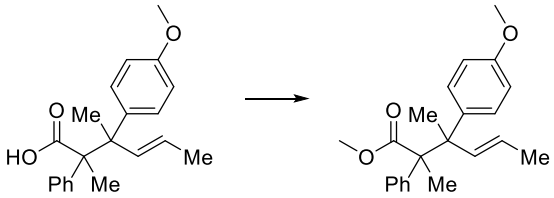
Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.31 – 7.05 (m, 7H), 6.84 (d, *J*= 8.5 Hz, 2H), 6.41 – 6.34 (m, 1H), 5.41 (dt, *J*= 15.6, 6.4 Hz, 1H), 3.59 (s, 3H), 2.13 – 2.05 (m, 2H), 1.61 – 1.53 (m, 6H), 0.98 (t, *J*= 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.1, 144.8, 140.1, 134.8, 131.8, 131.4, 129.5, 129.2, 127.2, 127.2, 120.2, 57.8, 49.3, 29.8, 23.6, 21.2, 14.0.

IR (Neat Film, NaCl) 2957, 1730, 1491, 1233, 1072, 1008, 818, 718, 701 cm^{-1}

Methyl (*E*)-3-(4-methoxyphenyl)-2,3-dimethyl-2-phenylhex-4-enoate



A Scin vial was equipped with acid **X** (97 mg, 299 µmol, 1.0 equiv.) and K_2CO_3 (83 mg, 598 µmol, 2.0 equiv.) in 1 mL dry DMF. Then MeI (37 µL, 598 µmol, 2.0 equiv.) was added and the mix was stirred over night. The next day, the reaction was quenched with solid NH_4Cl and diluted with toluene. The solvents were evaporated and the residue was taken up in Et_2O and little H_2O. The organic layer was washed with saturated LiCl solution followed by H_2O and Brine. It was dried over Na_2SO_4 and concentrated in vacuo. The resulting residue was filtered through a plug of silica (DCM) and product was collected as yellow oil in 99% yield (100 mg, 296 µmol).

Note: *dr* difficult to tell as NMR is not superpure – aka "semi crude" with DMF. Therefore, this compound wasn't mentioned in the discussion.

Major:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.63 (m, 9H), 6.25 – 6.17 (m, 1H), 5.40 – 5.31 (m, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 1.56 (s, 3H), 1.01 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ= 175.1, 157.6, 140.5, 139.9, 137.8, 130.6, 130.3, 129.2, 127.0, 126.9, 112.0, 58.2, 55.2, 51.7, 48.3, 33.3, 23.1, 21.3.

Minor:

^{1}H NMR (500 MHz, $CDCl_3$) δ= 7.39 – 6.63 (m, 9H), 6.31 (d, *J*= 16.1 Hz, 1H), 5.26 (d, *J*= 16.0 Hz, 1H), 3.77 (s, 3H), 3.59 (s, 3H), 1.57 – 1.51 (m, 3H), 0.99 (s, 6H).

IR (Neat Film, NaCl) 2953, 2835, 1731, 1608, 1578, 1512, 1463, 1444, 1362, 1293, 1252, 1188, 1111, 1077, 1034, 982, 832, 808, 737, 701, 680 cm^{-1}

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