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A convenient route to chiral γ-lactones via asymmetric hydrogenation of γ-ketoesters using the $RuCl_3$–BINAP–HCl catalytic system

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ABSTRACT

A convenient one-step synthesis of chiral γ-lactones has been performed. The method is based on enantioselective hydrogenation of γ-ketoesters using the $RuCl_3$–BINAP–HCl catalytic system. Chiral γ-lactones (91–99% ee) have been isolated in 57–88% yield.

1. Introduction

γ-Lactones are well-known natural flavour compounds,[1] pheromone components[2] and useful building blocks[3–6] for pharmaceutical purposes. The most common approach to the synthesis of γ-lactones is founded on asymmetric hydrogenation of γ-ketoesters. A few methods can be applied to perform this reaction: stoichiometric reduction with chiral reagents,[7] microbiological reduction,[8] transition metal-catalyzed hydrogenation,[5,9] hydroboration[3,6,10] and hydrosilylation.[4,11] Over recent years, ruthenium-catalyzed asymmetric hydrogenation has attracted more attention.[5,9] The advantage of this method is the use of H_2, the simplest reducing agent, and its universality in relation to high enantioselectivity. This also allows a reuse of the catalyst immobilized on a polymeric carrier.[12] However, in view of the much lower reactivity of γ-ketoesters in a hydrogenation reaction compared to that of α- and β-ketoester, a longer period (up to several days) is required in this case to achieve a satisfactory conversion.[9a]

It had been earlier shown[9f] on the asymmetric catalytic hydrogenation of levulinic acid ester **3g** that adding 5–10 equiv of a strong acid such as HCl to the catalyst {[(*R*)-BINAP]$RuCl_2$}, formed in situ from the precursor (COD)Ru(2-methylallyl)$_2$ [BINAP—2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] causes considerable acceleration of the reaction to give ethyl (*R*)-γ-hydroxylevulinate **4g** readily convertible under the hydrogenation conditions into (*R*)-γ-valerolactone **5a** (98–99% ee). In this research, an available precatalyst $RuCl_3$ was used instead of a relatively expensive bis-methylallyl ruthenium complex to prepare chiral γ-lactones **5a–f** by asymmetric hydrogenation of γ-ketoesters **3a–f** (Scheme 1).

Scarce literature data is available regarding the use of $RuCl_3$-containing homogeneous catalytic systems in organic reactions,[13] including hydrogenation. As concerns the latter, asymmetric hydrogenation of α-ketoesters,[13c] β-ketoesters[13c] and β-hydroxyketones[13i] using $RuCl_3$ as a precatalyst was studied by Genêt's research group. To our knowledge, no data has been reported until now regarding the use of the catalytic system $RuCl_3$–chiral ligand–acid promoter in asymmetric catalysis.

2. Results and discussion

To prepare starting γ-ketoesters **3b–d**, free radical addition of aldehydes **1b–d** to dimethyl maleate initiated by air oxygen in the presence of a Co(II) acetate catalyst was performed.[14] The subsequent acidic decomposition[15] of adducts **2b–d** gave target γ-ketoesters (Scheme 1). Other γ-ketoesters were prepared by etherification of commercial γ-ketoacids under standard conditions.

2.1. Influence of the reaction conditions on hydrogenation efficiency

In order to study the influence of reaction conditions on the conversion of **3**, the **4**/**5** ratio and hydrogenation enantioselectivity, γ-ketoester **3a** was used as a model substrate.

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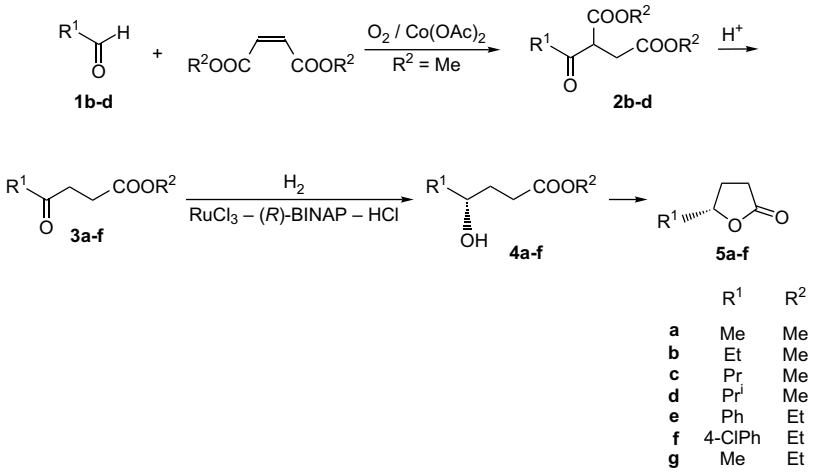


Scheme 1. Preparation of starting ketoesters **3b–d** and chiral γ-lactones **5a–f**.

2.1.1. Influence of HCl

As shown in Table 1, only a moderate conversion of ketoester **3a** into hydrogenation products **4a** and **5a** was observed where no acid promoter was added to the $RuCl_3$–BINAP catalytic system (entry 1), whereas a complete conversion of **3a** was achieved in the presence of 4–10 equiv of HCl with respect to the ruthenium catalyst under the same reaction conditions (entries 3 and 4). Notably, a similar effect of HCl addition had been earlier revealed[9f] for the asymmetric hydrogenation of **3a** using the Ru(II)–BINAP catalytic system.

2.1.2. $RuCl_3 \cdot nH_2O$ versus anhydrous $RuCl_3$

As follows from the results summarized in Table 2, the catalytic systems involving aqueous Ru(III) chloride as well as the anhydrous salt show similar activity and provide high enantioselectivity of **3a** hydrogenation. Thus, 6 h are needed in both cases for the reaction to complete at [**3a**]/[Ru]=200, 60 atm (H_2) and 65 °C (entries 1 and 2). At the same time, the product's composition strongly depends on the availability of water in $RuCl_3$: the use of the anhydrous precatalyst gives selectively (96%) lactone **5a** (entry 1), whereas in the presence of $RuCl_3 \cdot nH_2O$ the reaction yields **4a** and **5a** in the 1:(2–5) ratio (entries 2–5).

2.1.3. The temperature and H_2 pressure influence

Catalytic activity of the $RuCl_3 \cdot nH_2O$–BINAP–HCl system is only slightly affected by H_2 pressure, **3a** conversion decreasing by 10% at a starting pressure drop from 60 to 15 atm (Table 2, entries 2 and 3). The H_2 pressure drop and reaction temperature rise from 60 to 100 °C cause some decline in the ee values for the hydrogenation products (entries 3–5). It should be also noted that no enhancement of **3a** conversion takes place at the elevated temperatures: it does not exceed 90% at 80–100 °C (entries 4 and 5) probably as a result of the catalyst deactivation.

2.1.4. The solvent nature influence

Lower alcohols such as MeOH or EtOH proved to be the best solvents for the reaction. In contrast, hydrogenation practically does not occur in aprotic solvents (C_6H_6, CH_2Cl_2 and THF). This may be explained by the fact that polar protic solvents facilitate the heterolysis of molecular hydrogen coordinated with ruthenium to give catalytically active metal hydride intermediates.[16] The hydrogenation of γ-ketoester in the presence of the Ru(III)-containing catalytic system is most probably to run with the participation of Ru(II) species[13a,c,g] formed from $RuCl_3$ in the course of aforesaid reaction.

2.2. Synthesis of chiral γ-lactones

The results of asymmetric hydrogenation of γ-ketoesters **3a–f** with anhydrous $RuCl_3$ as a precatalyst are provided in Table 3. Using the $RuCl_3$–BINAP–HCl catalytic system, chiral γ-lactones **5a–f** were synthesized in good yields as practically the single isolated products. The enantiomeric purity of alkyl-substituted lactones **5a–d** and aryl-substituted **5e**,**f** was 98–99 and 91–92% ee, respectively. For comparison, only a 30% conversion was achieved in hydrogenation of ketoester **3e** for 11 days using the known catalytic system based on $Ru(OAc)_2$(BINAP).[9a] For hydrogenation of γ-aryl-γ-ketoesters **3e**,**f** in MeOH, some amounts (up to 20%) of γ-methoxyesters were found to form, most probably, as a result of the

Table 1
Asymmetric hydrogenation of ketoester **3a** in the presence of the catalytic system $RuCl_3 \cdot nH_2O$–(*R*)-BINAP–HCl at different [HCl]/[Ru] ratios[a]

Entry	[HCl]/[Ru]	Conversion of **3a** [%]	Reaction products [mol %]		(*R*) [% ee]
			4a	**5a**	
1	—	58	20	80	99
2	2	96	32	68	98.5
3	4	100	25	75	99
4	10	100	19	81	99.5

[a] [**3a**]/[Ru]=200, [**3a**]=1.5 M, abs MeOH, 15 atm (H_2), 65 °C, 6 h.

Table 2
The influence of the hydrogenation conditions on the ketoester **3a** conversion, products composition and reaction enantioselectivity using the $RuCl_3 \cdot nH_2O$–(*R*)-BINAP–HCl catalytic system[a]

Entry	Hydrogenation conditions		Conversion of **3a** [%]	Hydrogenation products [mol %]		(*R*) [% ee]
	$p(H_2)$ [atm]	*T* [°C]		**4a**	**5a**	
1[b]	60	65	100	4	96	99
2	60	65	100	30	70	99
3	15	65	90	20	80	98
4	15	80	80	25	75	97
5	15	100	90	17	83	96

[a] [HCl]/[Ru]=10, [**3a**]/[Ru]=200, [**3a**]=1.5 M, abs MeOH, 6 h.
[b] Anhydrous $RuCl_3$ was applied.

Table 3
The synthesis of chiral γ-lactones **5a–f** using asymmetric hydrogenation of ketoesters **3a–f** catalyzed by the $RuCl_3$–(*R*)-BINAP–HCl system[a]

Substrate	Time [h]	Product	Conversion of **3** [%]	Yield[b] [%]	[% ee][c]
3a	10	**5a**	100	88	99 (*R*)
3b	10	**5b**	87	57	99 (*R*)
3c	10	**5c**	75	66	98 (*R*)
3d	20	**5d**	70	63	99 (*S*)
3e	65[d]	**5e**	75	65	91 (*S*)
3f	65[d]	**5f**	73	62	92 (*S*)

[a] Anhydrous $RuCl_3$ was used. [HCl]/[Ru]=10, [**3**]/[Ru]=500, [**3**]=2.5 M, abs MeOH, 60 atm (H_2), 60 °C.
[b] For isolated and purified lactone **5** with respect to starting γ-ketoester **3**.
[c] Differences in the **5a–c** and **5d–f** configuration are formal as a consequence of a change in substituent's ranking at the chiral carbon center.
[d] Solvent: abs EtOH.

acid-catalyzed substitution reaction involving the solvolysis of the intermediate benzyl cation (Scheme 2).

However, when hydrogenation of **3e**,**f** was carried out in less polar alcohol (EtOH), we observed no corresponding ethoxy derivatives among the reaction products. Noteworthily, hydrogenation of **3e**,**f** in both MeOH and EtOH is characterized by the same enantioselectivity (91–92 ee). In this connection, it is difficult to explain the lesser ee values for aryl-substituted lactones **5e**,**f** than for alkyl-substituted products **5a–d** (Table 3) by partial racemization of hydroxyesters **4e**,**f** via the intermediate benzyl cation. This fact is most probably related to different steric effects of alkyl and aryl substituents in molecules of the starting ketoesters.

In summary, asymmetric hydrogenation of γ-ketoesters in the presence of the catalytic system $RuCl_3$–BINAP–HCl is a convenient method for the synthesis of chiral γ-lactones in preparative yield and with a high enantiomeric purity.

3. Experimental section

3.1. General

$RuCl_3$, $RuCl_3 \cdot nH_2O$, $Co(OAc)_2$, (*R*)-BINAP, levulinic acid, 3-benzoyl- and 3-(4-chlorobenzoyl)propionic acids, propanal, butanal and *iso*-butanal are commercial reagents (Aldrich) and were used without additional purification. Prior to the use, all solvents were dehydrated and distilled under a flow of argon. Argon was purified by passing through columns containing a nickel/chromium catalyst, copper supported on Kieselguhr (80 °C) and molecular sieves (4 Å). Hydrogen was purified by passing through columns with a nickel/chromium catalyst and molecular sieves.

Flash chromatography was performed using a 12×240 mm column filled with silica 60 (Fluka) and petroleum ether/2-propanol (3–25%) as an eluent. ^1H NMR spectra were registered by Bruker AM-300. An enantiomeric analysis of lactones **5a–f** was performed by GLC on a Biochrom-21 chromatograph with a quartz capillary column (30 m×0.2 mm×0.25 μm) with 2,6-dipentyl-3-(fluoroacethyl)-β-cyclodextrin stationary phase. The absolute configuration of chiral lactones was determined through comparing their optical rotation sign with that known from the literature.

γ-Ketoesters prepared by etherification of corresponding γ-ketocarbonic3 acids. Compound **3a**, colourless oil, bp 80 °C (10 mm) [lit.[17] 94–95.5 °C (20 mm)]; δ_H (300 MHz, $CDCl_3$) 3.65 (3H, s, O*Me*), 2.75 (2H, t, *J* 6.5 Hz, CH_2COMe), 2.55 (2H, t, *J* 6.5 Hz, CH_2COOMe), 2.15 (3H, s, CO*Me*). Compound **3e**, colourless oil, bp 159–160 °C (5 mm) [lit.[18] 143–145 °C (6 mm)]; δ_H (300 MHz, $CDCl_3$) 7.94 (2H, d, *J* 7.5 Hz, Ph), 7.60–7.40, (3H, m, Ph), 4.15 (2H, q, *J* 7.1 Hz, OCH_2CH$_3$), 3.25 (2H, t, *J* 6.6 Hz, CH_2COPh), 2.75 (2H, t, *J* 6.6 Hz, CH_2COOEt), 1.20 (3H, t, *J* 7.1 Hz, *Me*). Compound **3f**, colourless oil, bp 182–185 °C (5 mm) [lit.[19] 132–134 °C (0.1 mm)]; δ_H (300 MHz, $CDCl_3$) 7.95 (2H, d, *J* 8.5 Hz, Ar), 7.45 (2H, d, *J* 8.5 Hz, Ar), 4.15 (2H, q, *J* 7.1 Hz, OCH_2Me), 3.25 (2H, t, *J* 6.6 Hz, CH_2COAr), 2.75 (2H, t, *J* 6.6 Hz, CH_2COOEt), 1.25 (3H, t, *J* 7.1 Hz, *Me*).

3.2. Preparation of γ-ketoesters 3b–d

*3.2.1. Addition of aldehydes **1b–d** to dimethyl maleate*

Freshly distilled aldehyde (1 mol) and $Co(OAc)_2$ (17.7 mg, 0.1 mmol) dissolved in glacial AcOH (3 mL) were placed into a flask equipped with an efficient backflow condenser, and dry air was bubbled through the solution at temperature close to the reflux one, dimethyl maleate (12.5 mL, 0.1 mol) being added to the mixture in modest portions for 6 h, and then air passing was continued for another 24 h. The reaction mixture was magnetically stirred during the overall period. The air rate should be not high though sufficient to keep the solution green. After removing excess aldehyde and corresponding acid (the main byproduct), adducts **2b–d** were isolated by distillation under reduced pressure.

*3.2.1.1. Dimethyl propionylsuccinate (**2b**).* Yield 15.8 g (79%) as a white solid, mp 58–59 °C [lit.[20] 56 °C], bp 128–130 °C (5 mm); δ_H (300 MHz, $CDCl_3$) 3.98 (1H, dd, *J* 8.1, 6.5 Hz, COC*H*COO), 3.73 (3H, s, CHCOO*Me*), 3.65 (3H, s, CH_2COO*Me*), 2.98 (1H, dd, *J* 17.5, 8.2 Hz, CH_aH$_b$COO), 2.82 (1H, dd, *J* 17.5, 6.3 Hz, CH$_a$*H*$_b$COO), 2.77–2.55 (2H, m, MeCH_2CO), 1.07 (3H, t, *J* 7.2, *Me*CH$_2$).

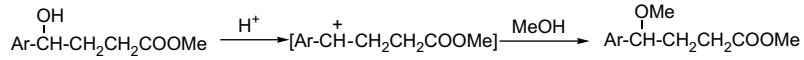
*3.2.1.2. Dimethyl butyroylsuccinate (**2c**).* Yield 17.7 g (82%) as a white solid, mp 30–31 °C, bp 142–145 °C (5 mm);[14] δ_H (300 MHz, $CDCl_3$) 3.97 (1H, br t, *J* 7.5, COC*H*COO), 3.73 (3H, s, CHCOO*Me*), 3.65 (3H, s, CH_2COO*Me*), 2.97 (1H, dd, *J* 17.5, 8.1 Hz, CH_aH$_b$COO), 2.82 (1H, dd, *J* 17.5, 6.3 Hz, CH$_a$*H*$_b$COO), 2.75–2.50 (2H, m, MeCH$_2$CH_2CO), 1.70–1.55 (2H, m, MeCH_2CH$_2$CO), 0.90 (3H, t, *J* 7.4 Hz, *Me*CH$_2$).

*3.2.1.3. Dimethyl iso-butyroylsuccinate (**2d**).* Yield 17.3 g (80%) as a colourless oil, mp 21–22 °C, bp 137–140 °C (5 mm); δ_H (300 MHz, $CDCl_3$) 4.13 (1H, br t, *J* 7.2 Hz, COC*H*COO), 3.70 (3H, s, CHCOO*Me*), 3.63 (3H, s, CH_2COO*Me*), 3.00–2.70 (3H, m, Me$_2$C*H*, CH_2COOMe), 1.12 (3H, d, *J* 7.0 Hz, *Me*$_a$CH), 1.07 (3H, d, *J* 6.7 Hz, *Me*$_b$CH).

3.2.2. Hydrolysis of dimethyl acylsuccinates

A mixture of acylsuccinate (55 mmol) and H_3BO_3 (3.4 g, 55 mmol) was heated at stirring on the oil bath (150 °C) for 1 h, with CO_2 being evolved and MeOH distilled off. Then, the bath temperature was raised up to 170 °C and the hydrolysis continued till no condensate is formed. The rest was poured into ice water (25 mL), and the product was extracted with toluene (3×25 mL). The combined extracts were dried ($MgSO_4$) and evaporated. The remaining crude product was purified by distillation under reduced pressure.

*3.2.2.1. Methyl 4-ketohexanoate (**3b**).* Yield 2.8 g (35%) as a colourless oil, bp 85 °C (5 mm) [lit.[21] 90–92 °C (9 mm)]; R_f (3% 2-propanol/petroleum ether) 0.30; δ_H (300 MHz, $CDCl_3$) 3.62 (3H, s,



Scheme 2.

O*Me*), 2.67 (2H, t, *J* 6.4 Hz, CH_2COEt), 2.53 (2H, t, *J* 6.4 Hz, CH_2COO), 2.43 (2H, q, *J* 7.3 Hz, MeCH_2CO), 1.02 (3H, t, *J* 7.3 Hz, *Me*CH_2).

*3.2.2.2. Methyl 4-ketoheptanoate (**3c**).* Yield 3.5 g (40%) as a colourless oil, bp 110 °C (10 mm) [lit.[22] 100–103 °C (10 mm)]; R_f (3% 2-propanol/petroleum ether) 0.40; δ_H (300 MHz, $CDCl_3$) 3.60 (3H, s, *OMe*), 2.67 (2H, t, *J* 6.4 Hz, CH_2COPr), 2.53 (2H, t, *J* 6.4 Hz, CH_2COO), 2.38 (2H, t, *J* 7.3 Hz, EtCH_2CO), 1.65–1.50 (2H, m, CH_2Me), 0.82 (3H, t, *J* 7.4 Hz, CH$_2$*Me*).

*3.2.2.3. Methyl 4-keto-5-methylhexanoate (**3d**).* Yield 2.9 g (33%) as a colourless oil, bp 89–90 °C (7 mm) [lit.[23] 73–75 °C (2 mm); R_f (3% 2-propanol/petroleum ether) 0.45; δ_H (300 MHz, $CDCl_3$) 3.60 (3H, s, O*Me*), 2.72 (2H, t, *J* 6.5 Hz, CH_2CO^{i}Pr), 2.65–2.48 (3H, m, C*H*CO, CH_2COO), 1.06 (6H, d, *J* 7.0 Hz, *Me*$_2$CH).

3.3. General asymmetric hydrogenation procedure

(*R*)-BINAP (12 mg, 0.019 mmol) and anhydrous $RuCl_3$ (3.9 mg, 0.019 mmol) were placed for hydrogenation into a pre-evacuated and argon-filled glass tube. Ketoester **3** (9.5 mmol) was dissolved in a mixture of MeOH (4 mL) and 2 M solution of HCl in MeOH (95 μL, 0.19 mmol). The solution was then degassed through a three times repeated cycle: freezing–evacuation–thawing–argon filling. After that, the degassed solution was poured into the tube for hydrogenation, and the tube was placed in a rotary stainless-steel autoclave (50 mL) pre-filled with argon. Then, the autoclave was purged with purified hydrogen and pressurized with H_2 up to 60 atm. The reaction mixture was agitated at 60 °C for the time indicated in Table 3. The reaction solution was passed through a 1 cm thick silica bed to remove the catalyst (eluent: CH_2Cl_2), and the solvent was evaporated. Where the conversion of ketoester **3** was incomplete (in experiments with **3b**–**f**), it was separated by flash chromatography. Evaporation of the combined fractions containing the main product followed by distillation of the residue under reduced pressure gave pure lactone **5**.

*3.3.1. (R)-5-Methyl-dihydro-2(3H)-furanone (**5a**)*

Yield 836 mg (88%) as a colourless oil, bp 82–85 °C (10 mm);[24] 99% ee according to GLC [retention time (t_R), min, He, 125 °C]: CH_4 (non-sorbable component) 1.1, (*R*)-**5a** (major) 2.9, (*S*)-**5a** (minor) 3.4; $[\alpha]_D^{20}$ +33.7 (*c* 1.75, CH_2Cl_2) [lit.[9a] +31.6 (*c* 0.86, CH_2Cl_2)]; δ_H (300 MHz, $CDCl_3$) 4.60–4.45 (1H, m, C*H*O), 2.47–2.38 (2H, m, CH_2COO), 2.33–2.20 (1H, m, CH_aCH$_2$COO), 1.80–1.65 (1H, m, CH_bCH$_2$COO), 1.30 (3H, d, *J* 6.3 Hz, *Me*CH).

*3.3.2. (R)-5-Ethyl-dihydro-2(3H)-furanone (**5b**)*

Yield 617 mg (57%) as a colourless oil, bp 95–97 °C (10 mm);[25] 99% ee according to GLC (t_R, min, He, 125 °C): CH_4, 1.1; (*R*)-**5b** (major), 3.8; (*S*)-**5b** (minor), 4.1; $[\alpha]_D^{20}$ +52.0 (*c* 1.00, MeOH) [lit.[26] +53.0 (*c* 1.00, MeOH)]; R_f (3% 2-propanol/petroleum ether) 0.17; δ_H (300 MHz, $CDCl_3$) 4.43–4.30 (1H, m, C*H*O), 2.50–2.40 (2H, m, CH_2COO), 2.32–2.17 (1H, m, CH_aCOO), 1.87–1.48 (3H, m, CH_bCOO, CH_2Me), 0.92 (3H, t, *J* 7.4 Hz, *Me*CH$_2$).

*3.3.3. (R)-5-(1-Propyl)-dihydro-2(3H)-furanone (**5c**)*

Yield 802 mg (66%) as a colourless oil, bp 108–110 °C (10 mm); [27] 98% ee according to GLC (t_R, min, He, 125 °C): CH_4, 1.1; (*R*)-**5c** (major), 5.3; (*S*)-**5c** (minor), 5.6; $[\alpha]_D^{20}$ +38.1 (*c* 0.65, MeOH) [lit.[28] +35.7 (*c* 0.50, MeOH)]; R_f (3% 2-propanol/petroleum ether) 0.25; δ_H (300 MHz, $CDCl_3$) 4.55–4.40 (1H, m, C*H*O), 2.55–2.43 (2H, m, CH_2COO), 2.35–2.20 (1H, m, CH_aCH$_2$COO), 1.90–1.30 (5H, m, CH_bCH$_2$COO, CH_2CH_2Me), 0.90 (3H, t, *J* 7.3 Hz, *Me*).

*3.3.4. (S)-5-(2-Propyl)-dihydro-2(3H)-furanone (**5d**)*

Yield 766 mg (63%) as a colourless oil, bp 100–103 °C (10 mmHg);[29] 99% ee according to GLC (t_R, min, He, 125 °C): CH_4, 1.1; (*S*)-**5d** (major), 7.6; (*R*)-**5d** (minor), 7.9; $[\alpha]_D^{20}$ +34.9 (*c* 1.1, CH_2Cl_2) [lit. [30] +24.2 (*c* 1.0, CH_2Cl_2)]; R_f (3% 2-propanol/petroleum ether) 0.29; δ_H (300 MHz, $CDCl_3$) 4.20–4.10 (1H, m, C*H*O), 2.53–2.42 (2H, m, CH_2COO), 2.28–2.14 (1H, m, CH_aCH$_2$COO), 1.95–1.72 (2H, m, CH_bCH$_2$COO, C*H*Me$_2$), 0.97 (3H, d, *J* 6.6 Hz, *Me*$_a$), 0.90 (3H, d, *J* 6.8 Hz, *Me*$_b$).

*3.3.5. (S)-5-Phenyl-dihydro-2(3H)-furanone (**5e**)*

Yield 1005 mg (65%) as a white solid, mp 35–36 °C,[31] bp 147 °C (5 mm);[32] 91% ee according to GLC (t_R, min, He, 125 °C): CH_4, 1.1; (*R*)-**5e** (minor), 8.9; (*S*)-**5e** (major), 9.3; $[\alpha]_D^{20}$ −26.6 (*c* 2.4, $CHCl_3$) [lit.[24] −35.5 (*c* 2.5, $CHCl_3$)]; R_f (3% 2-propanol/petroleum ether) 0.51; δ_H (300 MHz, $CDCl_3$) 7.40–7.23 (5H, m, *Ph*), 5.48 (1H, t, *J* 7.0 Hz, C*H*O), 2.70–2.55 (3H, m, CH_aCH_2COO), 2.25–2.05 (1H, m, CH_bCH$_2$COO).

*3.3.6. (S)-5-(4-Chlorophenyl)-dihydro-2(3H)-furanone (**5f**)*

Yield 1250 mg (67%) as a white solid, mp 48–49 °C,[33] bp 163 °C (5 mm);[34] 92% ee according to GLC (t_R, min, He, 125 °C): CH_4, 1.1; (*R*)-**5f** (minor), 18.4; (*S*)-**5f** (major), 18.9; $[\alpha]_D^{20}$ −14.6 (*c* 0.9, CH_2Cl_2) [lit.[35] −14.8 (*c* 0.46, CH_2Cl_2, 76% ee)]; R_f (25% 2-propanol/petroleum ether) 0.54; δ_H (300 MHz, $CDCl_3$) 7.45–7.23 (4H, m, *Ar*), 5.55–5.45 (1H, m, C*H*O), 2.76–2.60 (3H, m, CH_aCH_2COO), 2.27–2.07 (1H, m, CH_bCH$_2$COO).

References and notes

1. Brenna, E.; Fuganti, C.; Serra, S. *Tetrahedron: Asymmetry* **2003**, *14*, 1.
2. Brown, H. C.; Kulkarni, S. V.; Racherla, U. S. *J. Org. Chem.* **1994**, *59*, 365.
3. Ghosh, A. K.; Swanson, L. *J. Org. Chem.* **2003**, *68*, 9823.
4. Lipshutz, B. H.; Lower, A.; Kucejko, R. J.; Noson, K. *Org. Lett.* **2006**, *8*, 2969.
5. Stangeland, E. L.; Sammakia, T. *J. Org. Chem.* **2004**, *69*, 2381.
6. Hilborn, J. W.; Lu, Z.-H.; Jurgens, A. R.; Fang, O. K.; Byers, H.; Wald, S. A.; Senanayake, C. H. *Tetrahedron Lett.* **2001**, *42*, 8919.
7. Ramachandran, P. V.; Pitre, S.; Brown, H. C. *J. Org. Chem.* **2002**, *67*, 5315.
8. Ema, T.; Yagasaki, H.; Okita, N.; Takeda, M.; Sakai, T. *Tetrahedron* **2006**, *62*, 6143.
9. (a) Ohkuma, T.; Kitamura, M.; Noyori, R. *Tetrahedron Lett.* **1990**, *31*, 5509; (b) King, S. A. *J. Org. Chem.* **1994**, *59*, 2253; (c) Saito, T.; Yokozava, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264; (d) Juszkiewicz, G.; Asztemborska, M.; Jurczak, J. *Pol. J. Chem.* **2002**, *76*, 1707; (e) Benincori, T.; Rizzo, S.; Pilati, T.; Pjnti, A.; Sada, M.; Pagliarini, E.; Ratti, S.; Giuseppe, C.; Ferra, L.; Sannicolo, F. *Tetrahedron: Asymmetry* **2004**, *15*, 2289; (f) Starodubtseva, E. V.; Turova, O. V.; Vinogradov, M. G.; Gorshkova, L. S.; Ferapontov, V. A. *Izv. Akad. Nauk, Ser. Khim.* **2005**, 2301; [*Russ. Chem. Bull., Int. Ed.* **2005**, *54*, 2374].
10. Yang, G.-S.; Hu, J.-B.; Zhao, G.; Ding, Y.; Tang, M.-H. *Tetrahedron: Asymmetry* **1999**, *10*, 4307.
11. (a) Kuwano, R.; Sawamura, M.; Shirai, J.; Takahashi, M.; Ito, Y. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 485; (b) Lipshutz, B. H.; Frieman, B. A.; Tomaso, A. E., Jr. *Angew. Chem., Int. Ed.* **2006**, *45*, 1259; (c) Matsumura, Y.; Ogura, K.; Kouchi, Y.; Iwasaki, F.; Onomura, O. *Org. Lett.* **2006**, *8*, 3789.
12. Starodubtseva, E. V.; Turova, O. V.; Vinogradov, M. G.; Ferapontov, V. A.; Razmanov, I. V.; Zlotin, S. G.; Rucherenko, A. S. *Mendeleev Commun.* **2007**, *17*, 20.
13. (a) Manimaran, T.; Wu, T.-C.; Klobucar, W. D.; Kolich, C. H.; Stahly, G. P. *Organometallics* **1993**, *12*, 1467; (b) Nubel, P. O.; Hunt, C. L. *J. Mol. Catal. A: Chem.* **1999**, *145*, 323; (c) Madec, J.; Pfister, X.; Phansavath, P.; Ratovelomanana-Vidal, V.; Genêt, J.-P. *Tetrahedron* **2001**, *57*, 2563; (d) Schalkwyk, C.; Vosloo, H. C. M.; Botha, J. M. *J. Mol. Catal. A: Chem.* **2002**, *190*, 185; (e) Katho, A.; Opre, Z.; Laurenczy, G.; Joo, F. *J. Mol. Catal. A: Chem.* **2003**, *204–205*, 143; (f) Rohr, M.; Grunwaldt, J.-D.; Baiker, A. *J. Mol. Catal. A: Chem.* **2005**, *226*, 253; (g) Araujo, M. H.; Valle, E. M. A.; Ellena, J.; Castellano, E. E.; Santos, E. N.; Batista, A. A. *Polyhedron* **2004**, *23*, 3163; (h) Junge, H.; Beller, M. *Tetrahedron Lett.* **2005**, *46*, 1031; (i) Labeeuw, O.; Roche, C.; Phansavath, P.; Genêt, J.-P. *Org. Lett.* **2007**, *9*, 105.
14. Vinogradov, M. G.; Kereselidze, R. V.; Gachechiladze, G. G.; Nikishin, G. I. *Izv. Akad. Nauk, Ser. Khim.* **1969**, 322; [*Russ. Chem. Bull., Int. Ed.* **1969**, *18*, 276].
15. *Org. Synth.* **1978**, *58*, 79–82.
16. Starodubtseva, E. V.; Turova, O. V.; Vinogradov, M. G.; Gorshkova, L. S.; Ferapontov, V. A. *Izv. Akad. Nauk, Ser. Khim.* **2007**, 531; [*Russ. Chem. Bull., Int. Ed.* **2007**, *56*, 552].
17. Terasawa, T.; Okada, T. *Tetrahedron* **1977**, *33*, 595.
18. Mortenson, C. W.; Spielman, M. A. *J. Am. Chem. Soc.* **1940**, *62*, 1609.
19. Stetter, H.; Schreckenberg, M.; Wiemann, K. *Chem. Ber.* **1976**, *109*, 541.
20. Kawenoki, I.; Maurel, D.; Kossanyi, J. *Bull. Soc. Chim. Fr.* **1982**, *2*, 385.
21. Reinheckel, H.; Gensike, R. *J. Prakt. Chem. (Leipzig)* **1968**, *37*, 214.

22. Vereshyagin, L. I.; Gavrilov, L. D.; Bolshedvorskaya, R. L. *Zh. Org. Khim.* **1975**, *11*, 2311; [*J. Org. Chem. USSR* **1975**, *11*, 2352 (Engl. Transl.)].
23. Royals, E. E.; Hoppe, J. C.; Jordan, A. D., Jr.; Robinson, A. G. *J. Am. Chem. Soc.* **1951**, *73*, 5857.
24. Najera, C.; Yus, M.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 289.
25. Mandal, A. K.; Mahajan, S. W. *Synthesis* **1991**, *4*, 311.
26. Mori, K. *Tetrahedron* **1975**, *31*, 3011.
27. Watanabe, S. *Agric. Biol. Chem.* **1969**, *33*, 242.
28. Utaka, M.; Watabu, H.; Takeda, A. *J. Org. Chem.* **1987**, *52*, 4363.
29. Anand, R. C.; Selvapalam, N. *J. Chem. Res., Miniprint* **1998**, *1*, 126.
30. Takahashi, H.; Morimoto, T.; Achiwa, K. *Chem. Lett.* **1987**, 855.
31. Barton, P.; Page, M. *J. Chem. Soc.* **1993**, *12*, 2317.
32. Manzocchi, A.; Casati, R.; Fiecchi, A.; Santaniello, E. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2753.
33. Sakurai, K.; Matsumoto, H.; Adachi, J. *Yakugaku Zasshi* **1968**, *88*, 919; *Chem. Abstr.* **1968**, *69*, 94792.
34. Scraup, S. *Justus Liebigs Ann. Chem.* **1928**, *462*, 147.
35. Kamal, A.; Sandbhor, M.; Shaik, A. A. *Tetrahedron: Asymmetry* **2003**, *14*, 1575.