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The effect of vinyl esters on the enantioselectivity of the lipase-catalysed transesterification of alcohols

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Abstract—The enantioselectivity of the lipase from *Pseudomonas cepacia* (PCL) in the transesterification of 2-phenyl-1-propanol **1** was studied using a series of vinyl 3-arylpropanoates as acyl donors. The most enantioselective transesterification reaction of the alcohol was attained by using vinyl 3-(*p*-iodophenyl)- or 3-(*p*-trifluoromethylphenyl)propanoates, with enantiomer ratios, *E*, of 116 and 138, respectively. Vinyl 3-phenylpropanoate was also effective for the resolution of **1** mediated by lipases from *P. fluorescens* and porcine pancreas and for the PCL-catalysed transesterification of several 2-phenyl-1-alkanols. The enantiomeric resolution of **1** was practically carried out by the first enantioselective transesterification using PCL and vinyl 3-(*p*-iodophenyl)propanoate to afford (*R*)-**1** and then the enantioselective hydrolysis of the resultant ester to afford (*S*)-**1**.

1. Introduction

Among the various methods for synthesising optically active alcohols, the resolution of alcohol racemates by lipase-catalysed transesterification in organic solvents is widely used today because of its convenience.[1] Although lipases can accept a wide range of alcohols as their substrates, the enantioselectivity of the transesterification of a racemic alcohol is not always high. Therefore, much effort has been devoted to increasing the enantioselectivity. As such, various solvents have been used in the reaction[2] and the effect of additives,[3] temperature[4] and microwave irradiation[5] on the reaction have also been examined.

During the transesterification reaction, the lipase is initially acylated by an acyl donor, such as a vinyl ester, and the acylated lipase then reacts enantioselectively with an alcohol.[6] As the lipase-catalysed transesterification proceeds through a ping–pong mechanism, we wished to ascertain which acylated lipase exerts the highest enantioselectivity;[6] thus, we became interested in the effect of structural changes in the acyl moiety of the vinyl ester on the observed enantioselectivity.

Several studies have previously showed that moderately enantioselective transesterification reactions of racemic alcohols with vinyl acetate were improved by using other vinyl esters which have a longer chain length in the acyl moiety, such as vinyl propanoate and vinyl butanoate.[5,7–10] However, few examples report improvement of very low selectivity[11] ($E<10$) reactions by changing only the chain length of the vinyl ester.[8,12] Although some examples of special acyl donors having a phenyl group in the acyl moiety have been reported, the effects of the acyl donor structure have not previously been systematically investigated.[6,13–15]

Recently, we reported a preliminary result for the enantioselective transesterification of 2-phenyl-1-propanol **1**, which had never been efficiently resolved by lipase-catalysed reactions with the lipase from *Pseudomonas cepacia* (PCL) and vinyl ω-phenylalkanoates.[16] Although the *E* value with vinyl acetate was 5, the value was improved to 31 with vinyl 3-phenylpropanoate. This is the first example that shows the utility of vinyl esters having a bulky substituent for the lipase-catalysed transesterification. In this paper, we report the results obtained by using vinyl 3-(aryl)propanoates bearing a variety of substituents on the phenyl group, to increase the enantioselectivity toward **1**, the validity of these compounds for different lipases, and their use in the resolution of other alcohols.

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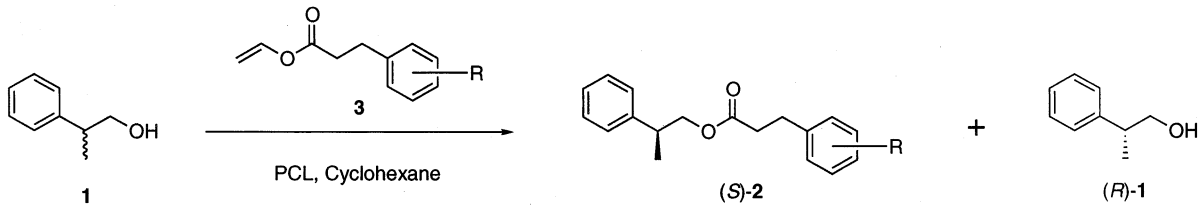


Scheme 1. PCL-catalysed transesterification of **1** with vinyl 3-(substituted phenyl)propanoates.

2. Results and discussion

2.1. PCL-catalysed transesterification of 1 with a variety of vinyl 3-(*para*-substituted phenyl)propanoates

While the PCL-catalysed transesterification with vinyl 3-phenylpropanoate had an E value of 32, the reaction took place with higher enantioselectivity in the presence of vinyl 3-(4-methylphenyl)propanoate ($E=62$).[16] Therefore, we focused on the PCL-catalysed transesterification between **1** and a variety of vinyl 3-(*para*-substituted phenyl)propanoates in cyclohexane (Scheme 1). Fourteen *p*-substituted vinyl 3-arylpropanoates were compared with **3a** as shown in Table 1.

The enantiomer preferentially esterified by PCL had the (*S*)-configuration in all reactions, which was established by comparing the HPLC retention time of the unreacted alcohol in the reaction mixture with that of an authentic sample.

The vinyl 3-phenylpropanoates **3a–o** are more effective acylating agents for the enantioselective transesterification of **1** compared to vinyl acetate (VA). Furthermore, all the *para*-substituted phenyl derivatives except **3f** are more efficient for the resolution compared to **3a**, the non-substituted phenyl derivatives. The rates of the reactions[†] performed using the vinyl 3-arylpropanoates except for **3j** and **3o** are lower than that with VA.

The enantioselectivity of the lipase-catalysed transesterification of alcohols with carboxylic acids (or their vinyl esters) irregularly varies with the chain lengths of the acids.[5–10,12] In our case, the variation of the chain length of their substituents have little influence on the E value although **3b–d** are more effective acyl donors than **3a**. The reaction rates reduced with lengthening alkyl chain. The *tert*-butyl derivative **3e** is an effective acylating reagent among the vinyl 3-(*p*-alkylphenyl)-propanoates. The E values with the *p*-alkoxyphenyl **3f–h** and biphenyl derivatives **3i** are approximately

[†] The reaction rates were calculated from the conversion and reaction time values. Therefore, the rates are average reaction rates, which mean 'approximate reaction rates'. All the reaction rates in this paper are the 'approximate reaction rates'.

Table 1. PCL-catalysed transesterification of **1** with vinyl 3-(*para*-substituted phenyl)propanoates (p-$RC_6H_4CH_2CH_2CO_2CH{=}CH_2$) in cyclohexane[a]

Acyl donor	R	Time (h)	Conv. (%)[b]	%[b] e.e.$_P$ ((*S*)-**2**)	%[b] e.e.$_S$ ((*R*)-**1**)	E[b]
VA[c]		2.5	25	60	20	5
3a	H	5	32	91	43	32
3b	CH_3	4	20	96	24	62
3c[d]	C_2H_5	4	30	94	41	48
3d[e]	n-C_3H_7	4.5	24	95	30	52
3e[e]	t-C_4H_9	24	22	97	27	85
3f[d]	CH_3O	3	37	88	52	26
3g	n-$C_6H_{13}O$	19	41	92	64	46
3h[e]	n-$C_8H_{17}O$	5	34	92	47	38
3i[d]	C_6H_5	25	32	92	43	37
3j	F	1.5	25	95	32	53
3k	Cl	3	23	96	29	65
3l	Br	5	38	95	57	69
3m	I	9	37	97	56	116
3n[e]	CF_3	3	26	98	34	138
3o	CN	3	43	95	73	86

[a] Conditions: PCL (5 mg /mL), **1** (30 mM), acyl donor (30 mM), 10°C.

[b] Transesterification with an acyl donor was repeated three times and the median E value calculated in each reaction is shown in Table 1. For the reactions with E under 80, the differences between the median E values and the maxima or minima were within ±5. On the other hand, for the reactions with E over 80, the differences between the median E values and the maxima or minima were within ±10. Values of an e.e.$_P$ and an e.e.$_S$ were measured three times, respectively, and the averages were used to calculate an E.

[c] VA, vinyl acetate.

[d] PCL (15 mg/mL).

[e] PCL (25 mg/mL).

equal to the *E* observed for **3a**. Thus, the alkoxy and phenyl substituents have little influence on the enantioselectivity of the reaction.

In the case of the 3-(*p*-halogenated phenyl)propanoates, although *p*-fluoro, *p*-chloro and *p*-bromo esters **3j–l** are more effective acyl donors than **3a**, variation of their substituents had little influence on the observed *E* values. *p*-Iodo derivative **3m** is an exceptionally efficient acylating agent. The other vinyl esters having electron-withdrawing groups such as **3n** and **3o** with trifluoromethyl and cyano groups also markedly increased the enantioselectivity. It appears that acyl donors containing electron-withdrawing groups are more efficient for the enantioselective transesterification of **1** than those containing electron-donating groups. Among these seven vinyl esters, the *p*-iodo- and *p*-trifluoromethyl derivatives exhibited more than a 100 *E* value of 116 and 138, respectively. The *E* value with **3n** is about 30 times larger than that of VA. Although there are reports that poorly selective ($E<10$) lipase-catalysed transesterifications were improved when acyl donors other than vinyl acetate were used,[8,12] our results should be recorded as one of the most successful studies.

2.2. PCL-catalysed transesterification of 1 with vinyl 3-(*ortho*-substituted phenyl)propanoates or vinyl 3-(*meta*-substituted phenyl)propanoates

We next tried 3-(*ortho*-substituted phenyl)- and 3-(*meta*-substituted phenyl)propanoates for the transesterification of **1**. As shown in Table 2, all the vinyl esters are more effective acylating agents for the enantioselective transesterification of **1** compared to VA. The fluoro-substituted derivatives **3j**, **3p**, and **3q** exhibited moderate results. The *E* values for the *o*-iodo and *m*-iodo derivatives **3r** and **3s** were much lower than the *p*-iodo derivative **3m**. In contrast, the *E* with **3r** is the smallest among the vinyl 3-arylpropanoates examined in this study. Furthermore, the rate of the reaction performed with **3r** is much smaller than those of **3m** and **3s**. It is thought that the acyl–enzyme intermediate from PCL and **3r**, which has a bulky group (iodine atom) on the *o*-position, is too difficult to form. Even if the formation of the intermediate occurs, it may be hard to react with **1**.

2.3. Application of vinyl 3-(substituted phenyl)propanoates in the transesterification of 1 by other lipases

We examined the vinyl 3-arylpropanoates as acyl donors for lipases from *Pseudomonas fluorecens* (PFL), *Candida antarctica* (CAL), *C. Rugosa* (CRL), and porcine pancreas (PPL). The vinyl 3-phenylpropanoate **3a** and vinyl 3-(4-chlorophenyl)propanoate **3k** were used as the acyl donors. As shown in Table 3, both the enantioselectivity of the PFL-catalysed transesterifications and that of PPL were increased using the 3-arylpropanoates. Notably, the *E* with **3k** by PFL is about 24 times larger than that with VA. CAL and CRL were influenced minimally by changing the acylating agents, which shows that the acylating agent does not always affect the enantioselectivity of the lipase-catalysed transesterification.[13]

Table 2. PCL-catalysed transesterification of **1** with vinyl 3-(*ortho*-substituted phenyl)propanoates or vinyl 3-(*meta*-substituted phenyl)propanoates (*o*- or *m*-$RC_6H_4CH_2CH_2CO_2CH{=}CH_2$)[a]

Acyl donor	R	Time (h)	Conv. (%)	% e.e.$_P$ ((*S*)-**2**)	% e.e.$_S$ ((*R*)-**1**)	*E*
3p	*o*-F	1.5	35	94	50	53
3q[b]	*m*-F	5	30	92	39	35
3r	*o*-I	195	30	86	36	19
3s	*m*-I	2	31	92	42	36

[a] Conditions: PCL (25 mg/mL), **1** (30 mM), acyl donor (30 mM), 10°C.
[b] PCL (15 mg/mL).

Table 3. Transesterification of **1** with vinyl 3-arylpropanoates using various lipases in cyclohexane[a]

Lipase	Acyl donor	Time (h)	Conv. (%)	% e.e.$_P$ ((*S*)-**2**)	% e.e.$_S$ ((*R*)-**1**)	*E*
PFL	VA	1.5	38	40	25	3
	3a	1.5	53	77	88	22
	3k	2	47	93	84	73
CAL	VA	1	49	25	24	2
	3a	1.5	47	52	47	5
	3k	2	41	63	44	7
CRL[b]	VA	40	38	5	3	1.1
	3a	96	13	14	2	1.4
	3k	96	17	5	1	1.1
PPL[c]	VA[d]	8	12	78	11	9
	3a[d]	38.5	30	93	39	40
	3k[d]	40	46	93	80	68

[a] Conditions: lipase (5 mg/mL), **1** (30 mM), acyl donor (60 mM), 10°C.
[b] Lipase (50 mg/mL).
[c] Lipase (25 mg/mL).
[d] Acyl donor (30 mM).

2.4. Application of vinyl 3-(substituted phenyl)-propanoates for transesterification of other alcohols

We then investigated whether a combination of PCL and vinyl 3-(substituted phenyl)propanoates effectively resolved alcohols **4**–**8**. We first examined the primary alcohols 2-phenyl-1-alkanols **4**–**6**, 3-chloro-2-phenyl-1-propanol **7** and 2-methyl-1-hexanol **8**. These results are summarised in Table 4.

All enantiomers preferentially esterified by PCL had (*S*)-configuration, as established by HPLC, comparing the retention time of the unreacted alcohol in the reaction with those of the authentic samples prepared by us (see Section 3). We observed that the change in the acyl donor from VA to **3a** induced an improvement in the enantioselectivity for the transesterification of **4**–**7**. Thus, it was concluded that **3a** is an efficient reagent for the PCL-catalysed transesterification of 2-phenyl-1-alkanols. Replacing the phenyl group of **1** with an *n*-butyl group was unsuccessful, and **3a** was ineffective for the resolution of **8**.

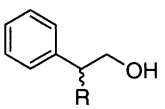
During the transesterification of 3-phenyl-1-butanol **9** with VA, PCL showed an extremely low enantioselectivity ($E=2$) with preference for the (*S*)-enantiomer. Therefore, the vinyl 3-arylpropanoates **3a** and **3k** and three vinyl ω-phenylalkanoates ($C_6H_5(CH_2)_{n-1}CO_2CH{=}CH_2$, $n=4$–6) were examined as acyl donors, however, the *E* values were hardly changed by variation of the acyl donors. There have been few reports on the lipase-catalysed resolution of racemic alcohols in which the stereogenic centre and the hydroxy function (the site of enzymatic reaction) are separated by more than two carbons.[17–25] In the transesterification reaction of octan-2-ol **10**, PCL favoured the (*R*)-enantiomer. An *E* of 5 was obtained for the reaction with VA, while the reaction with **3a** had an *E* of 10. The reaction of **10** was only slightly influenced by the acyl donor. These results suggest that the optimal structure of the acyl donor required for maximal enantioselectivity varies with the alcohol.

2.5. Preparative kinetic resolution of 1

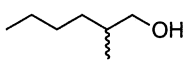
As a conclusion to the study we conducted the resolution of **1** on a preparative scale (Scheme 2). We first carried out the PCL-catalysed asymmetric transesterification of (±)-**1** with **3m** to obtain optically pure (*R*)-**1** with >99% e.e. The product, ester (*S*)-**11**, was then hydrolysed using PPL to obtain the optically active (*S*)-**1**. Because we have succeeded in the highly enantioselective hydrolysis ($E=107$) of 2-phenyl-1-propyl 3-phenylpropanoate,[26] an analogue of **11**, using PPL, we employed the PPL-catalysed hydrolysis. Thus, (±)-**1** (1.00 g) was first subjected to the PCL-catalysed transesterification with **3m** in cyclohexane at 30°C to give (*R*)-**1** (0.28 g, 28% with e.e. of >99%) and (*S*)-**11** (1.34 g, 43% with e.e. of >84%). (*S*)-**11** was then subjected to PPL-catalysed hydrolysis in phosphate buffer (pH 7.0) at 30°C to give (*S*)-**1** (0.21 g, 21% with 97% e.e.).

Each enantiomer of a racemic alcohol may interact with an acylated lipase to give different transition states. The size of this activation energy difference dictates the enantioselectivity of a given lipase.[6] Therefore, the acylated lipases, even if they are of the same origin, will exert their inherent interaction with alcohols.[6] It can also be postulated that the acyl group of

Table 4. PCL-catalysed transesterification of primary alcohols with vinyl 3-arylpropanoates[a]



4: R = C_2H_5
5: R = *n*-C_3H_7
6: R = *n*-C_4H_9
7: R = CH_2Cl



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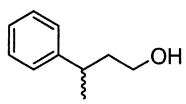

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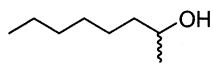

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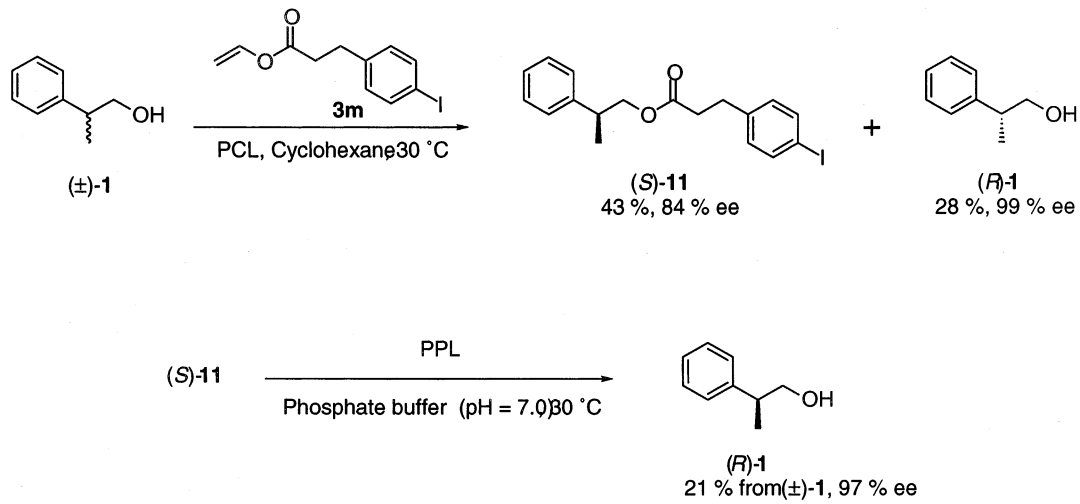
Alcohol	Acyl donor	Time (h)	Conv. (%)	% e.e.$_P$	% e.e.$_S$	*E*
4	VA	3.5	27	82	30	14
	3a	4	27	98	37	142
5[b]	VA	3	27	90	33	26
	3a	2	23	97	29	87
6[b]	VA	2	25	92	31	32
	3a	2	48	97	91	210
7[b]	VA[c]	1.5	21	33	9	2
	3a	1.5	48	72	65	12
8[d]	VA	0.5	23	40	12	3
	3a	2	27	19	7	2

[a] Conditions: PCL (25 mg/mL), alcohol (30 mM), acyl donor (60 mM), 10°C.
[b] Temperature: 30°C.
[c] Lipase (5 mg/mL).
[d] Lipase (5 mg/mL), acyl donor (30 mM).



Scheme 2. Preparative kinetic resolution of **1**.

an acylated lipase is located in its alcohol-binding site, where the steric and/or electronic interactions between the acyl moiety and the alcohol can occur,[6] thus causing variations in the active site environment.[9] On the basis of these assumptions, we considered two effects (direct and indirect effects) of the acyl moieties of VA and **3a** on the enantioselectivity of PCL.[16]

When a series of vinyl 3-(substituted phenyl)propanoates were employed in the PCL-catalysed transesterification of **1**, the enantioselectivities were increased, with several exceptions, compared to the enantioselectivity with **3a**. The complicated factor(s) composed of steric and/or electronic effects induced by the substituents of the benzene ring may contribute to the variation in the active site environment to increase the enantioselectivity of the lipase. We are now trying to clarify the mechanism of the enantioselectivity enhancement induced by the acyl donors using the X-ray crystal structures of covalent complexes of PCL[27] with transition-state analogues for the transesterification of **1** with **3a**.

In conclusion, we have synthesised a variety of vinyl 3-arylpropanoates and demonstrated their validity for the lipase-catalysed transesterification of 2-phenyl-1-alkanols. Vinyl 3-arylpropanoates appear to be useful in the optical resolution of 2-phenyl-1-alkanols. We are currently investigating the development of other acyl donors for effective enantiomeric resolution of other alcohols.

3. Experimental

3.1. General

PCL, PFL and CRL were supplied by Amano Pharmaceutical. CAL and PPL were supplied by Novo Nordisk and Sigma, respectively. All commercially available reagent chemicals were obtained from Acros Organics, Aldrich, Lancaster, Nacalai Tesque, Tokyo Kasei and Wako Chemicals and generally used without further purification. ^{1}H NMR spectra were recorded on a Jeol JNM-LA 400 spectrometer for solutions in $CDCl_3$ with TMS as an internal standard and J values are given in hertz (Hz). IR spectra were obtained using a Jasco FT/IR-410 spectrometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. Gas chromatograms were recorded on a Shimadzu GC-14B with OV 101 bonded capillary column (Gaschro Industry), 17 m×0.25 mm or CP-Cyclodextrin-B-236-M-19 capillary column (Chrompack), 25 m×0.25 mm. HPLC analyses were carried out on a Hitachi L-6250 intelligent pump with a Hitachi L-4000 UV detector using CHIRALCEL OB-H (Daicel), 250×4.6 mm or CHIRALCEL OD-H (Daicel), 250×4.6 mm or CHIRALCEL OJ (Daicel), 250×4.6 mm chiral columns.

3.2. Lipase-catalysed transesterification of alcohols

In a typical run as in the transesterification of **1**, **4**–**7**, **9** and **10**, PCL (10 mg) was placed in a vial to which was added a cyclohexane solution (2 mL) containing the alcohol (60 μmol) and the acyl donor (60 μmol). The resulting suspension was then magnetically stirred at 10°C. The reaction was quenched by filtration and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column using hexane–ethyl acetate as the eluent. An aliquot of the combined fractions containing the unreacted alcohol was analysed by HPLC or GC to determine the e.e. of the alcohol. The produced ester was hydrolysed (1 M NaOH, MeOH) to the corresponding alcohol, the e.e. of which was determined as mentioned above. The E value and the conversion of the reaction were calculated from the e.e.s of the unreacted alcohol and the produced ester.[11]

Conditions for the determination of the e.e.s of the alcohols are as follows. **1**: HPLC (Chiralcel OB-H), hexane:2-propanol = 30:1 (v/v); **4**: GC (CP-Cyclodextrin-B-236-M-19), 99°C; **5**: HPLC (Chiralcel OJ), hex-

ane:2-propanol = 15:1 (v/v); **6**: HPLC (Chiralcel OJ), hexane:2-propanol = 50:1 (v/v); **7**: GC (CP-Cyclodextrin-B-236-M-19), 117°C; **9**: HPLC (Chiralcel OD-H), hexane:2-propanol = 15:1 (v/v); **10**: the e.e.s were determined after conversion to the corresponding acetate ester with acetyl chloride and pyridine in benzene. GC (CP-Cyclodextrin-B-236-M-19), 105°C.

In the transesterification of **8**, decane or heptadecane was also added to the reaction mixture as an internal standard for gas chromatography to measure the conversion of the reaction. The e.e. of the unreacted alcohol was determined by GC (CP-Cyclodextrin-B-236-M-19, 115°C) after oxidation (Jones reagent, acetone) of the alcohol to the corresponding carboxylic acid. The *E* value and the e.e. of the produced ester were calculated from the conversion and the e.e. of the unreacted alcohol.[11]

3.3. Vinyl 3-phenylpropanoate 3a

Vinyl ester **3a** was prepared from 3-phenylpropanoic acid (1.50 g, 10.0 mmol) and freshly distilled vinyl acetate (90 mL, 970 mmol) in the presence of $Pd(OAc)_2$ (0.32 g, 1.4 mmol) according to the procedure to vinylate hydroxycarboxylic acids.[28] Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product provided **3a** as a colourless oil (1.00 g, 57%); ^{1}H NMR: δ 7.32–7.20 (6H, m, ArH and C$\underline{H}$=C$\underline{H}_2$), 4.88 (1H, dd, J=1.7, J=13.9, CH=C$\underline{H}_2$ (*cis*)), 4.57 (1H, dd, J=1.7, J=6.3, CH=C$\underline{H}_2$ (*trans*)), 2.99 (2H, t, J=7.8, ArC$\underline{H}_2$CH$_2$), 2.72 (2H, t, J=7.7, ArCH$_2$C$\underline{H}_2$); IR (neat): 1754 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$) cm^{-1}. Found: C, 74.49; H, 6.87. Calcd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86%.

3.4. Vinyl 3-(4-methylphenyl)propanoate 3b

THF (210 mL) and sodium hydride (60%, 5.33 g, 133.3 mmol) were stirred under an inert gas atmosphere. Diethyl malonate (16.00 g, 99.9 mmol) was added slowly via a syringe. To the solution was added gradually 4-methylbenzyl chloride (16.86 g, 119.9 mmol) via a syringe. The reaction mixture was stirred for 1 h at room temperature under N_2. The mixture was acidified with HCl (2 M) and extracted three times with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The residue was chromatographed (silica gel, hexane–ethyl acetate 7:1 (v/v)) to give diethyl 4-methylbenzylmalonate as a colourless oil (15.20 g, 58%); ^{1}H NMR: δ 7.09 (4H, s, ArH), 4.16 (4H, q, J=7.0, CO$_2$C$\underline{H}_2$CH$_3$), 3.63 (1H, t, J=7.7, ArCH$_2$C$\underline{H}$), 3.21 (2H, d, J=7.9, ArC$\underline{H}_2$CH), 2.13 (3H, s, ArC$\underline{H}_3$), 1.23 (6H, t, J=7.2, CO$_2$CH$_2$C$\underline{H}_3$).

To a solution of diethyl 4-methylbenzylmalonate (15.20 g, 57.5 mmol) in EtOH (150 mL) was added NaOH (2.5 M, 150 mL, 380 mmol). After stirring under reflux for 7 h, ethanol was evaporated under reduced pressure. The residue was washed three times with ether. The aqueous layer was acidified with HCl (2 M) and extracted three times with ethyl acetate. Crude 4-methylbenzylmalonic acid, isolated after drying over anhydrous magnesium sulfate and removal of the solvent, was used without further purification in the next step (white solid, 8.90 g, 75%); ^{1}H NMR: δ 7.11 (4H, s, ArH), 3.74 (1H, t, J=7.2, ArCH$_2$C$\underline{H}$), 3.25 (2H, d, J=7.3, ArC$\underline{H}_2$CH), 2.32 (3H, s, ArC$\underline{H}_3$).

A solution of crude 4-methylbenzylmalonic acid (6.90 g, 33.1 mmol) in xylene (50 mL) was stirred under reflux for 5 h and cooled. After standing overnight in a refrigerator, a white solid was collected on a Büchner funnel and washed with hexane to give 3-(4-methylphenyl)propanoic acid (3.52 g, 65%); ^{1}H NMR: δ 7.11 (4H, s, ArH), 2.93 (2H, t, J=7.8, ArC$\underline{H}_2$CH$_2$), 2.66 (2H, t, J=7.8, ArCH$_2$C$\underline{H}_2$), 2.32 (3H, s, ArC$\underline{H}_3$).

Vinylation of 3-(4-methylphenyl)propanoic acid was carried out according to the procedure for the preparation of **3a**. Chromatography (silica gel, hexane–ethyl acetate 36:1 (v/v)) of the crude product provided **3b** as a colourless oil (65%); ^{1}H NMR: δ 7.28 (1H, dd, J=6.4, J=13.9, C$\underline{H}$=CH$_2$), 7.10 (4H, s, ArH), 4.88 (1H, dd, J=1.7, J=13.9, CH=C$\underline{H}_2$ (*cis*)), 4.57 (1H, dd, J=1.7, J=6.3, CH=C$\underline{H}_2$ (*trans*)), 2.95 (2H, t, J=7.7, ArC$\underline{H}_2$CH$_2$), 2.69 (2H, t, J=7.7, ArCH$_2$C$\underline{H}_2$), 2.32 (3H, s, ArCH$_3$); IR (neat): 1755 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$) cm^{-1}. Found: C, 75.62; H, 7.42. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

3.5. Vinyl 3-(4-ethylphenyl)propanoate 3c

In a three-necked flask, sodium (0.47 g, 20.4 mmol) was added gradually to absolute ethanol (15 mL). The solution was stirred at about 40°C, after which diethyl malonate (3.36 g, 21.0 mmol) was added slowly via a syringe. To the solution was added gradually 4-ethylbenzyl bromide (4.04 g, 20.3 mmol) through a dropping funnel. The reaction mixture was refluxed for 5 h and cooled to room temperature. As much ethanol as possible was evaporated in vacuo. The residue was treated with water at 0°C and then extracted with ether. The organic layer was washed with brine, and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was distilled under reduced pressure (120–210°C/1.0 mmHg) to give diethyl 4-ethylbenzylmalonate (2.03 g, 36%) as a colourless oil; ^{1}H NMR: δ 7.11 (4H, s, ArH), 4.16 (1H, q, J=7.3, CO$_2$C$\underline{H}_2$CH$_3$), 3.62 (1H, t, J=8.0, ArCH$_2$C$\underline{H}$), 3.18 (2H, d, J=7.8, ArC$\underline{H}_2$CH), 2.60 (2H, q, J=5.7, ArC$\underline{H}_2$CH$_3$), 1.22 (3H, t, J=11.0, ArCH$_2$C$\underline{H}_3$), 1.22 (3H, t, J=11.0, CO$_2$CH$_2$C$\underline{H}_3$).

Diethyl 4-ethylbenzylmalonate was converted to vinyl 3-(4-ethylphenyl)propanoate **3c** through three steps described for the preparation of vinyl 3-(4-methylphenyl)propanoate **3b**; 4-ethylbenzylmalonic acid as a white solid (crude, 84%); ^{1}H NMR: δ 7.14 (4H, s, ArH), 3.75 (1H, t, J=7.2, ArCH$_2$C$\underline{H}$), 3.25 (2H, d, J=7.6, ArC$\underline{H}_2$CH), 2.62 (2H, q, J=7.6, ArC$\underline{H}_2$CH$_3$), 1.22 (3H, t, J=7.6, ArCH$_2$C$\underline{H}_3$); 3-(4-ethylphenyl)propanoic acid (54%) as a white solid; ^{1}H NMR: δ 7.14 (4H, s, ArH), 2.94 (2H, t, J=7.8, ArC$\underline{H}_2$CH$_2$CO$_2$), 2.68 (2H, t, J=7.7, ArCH$_2$C$\underline{H}_2$CO$_2$),

2.62 (2H, q, $J=7.6$, $ArC\underline{H}_2CH_3$)), 1.22 (3H, t, $J=7.6$, $ArCH_2C\underline{H}_3$); vinyl 3-(4-ethylphenyl)propanoate **3c** (94%) as a colourless oil; ^{1}H NMR: δ 7.28 (1H, dd, $J=6.4$, $J=13.9$, $C\underline{H}{=}CH_2$), 7.13 (4H, s, ArH), 4.88 (1H, dd, $J=1.6$, $J=14.0$, $CH{=}C\underline{H}_2$ (*cis*)), 4.57 (1H, dd, $J=1.7$, $J=6.4$, $CH{=}C\underline{H}_2$ (*trans*)), 2.95 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2CO_2$), 2.70 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2CO_2$), 2.62 (2H, q, $J=7.6$, $ArC\underline{H}_2CH_3$), 1.22 (3H, t, $J=7.7$, $ArCH_2C\underline{H}_3$); IR (neat): 1756 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$) cm^{-1}. Found: C, 76.14; H, 7.99. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90%.

3.6. Vinyl 3-(4-propylphenyl)propanoate 3d

A mixture of 4-propylbenzaldehyde diethyl acetal (4.45 g, 20.0 mmol), acetic acid (20 mL), and water (10 mL) was stirred under reflux for 17 h. The mixture was cooled to 0°C and cold NaOH (6 M, 50 mL) was added. The mixture was extracted with ether. The organic layer was washed with brine, then dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was distilled (150–195°C/20 mmHg) to give 4-propylbenzaldehyde (2.68 g, 91%) as a colourless oil; ^{1}H NMR: δ 9.97 (1H, s, CHO), 7.80 (2H, d, $J=8.0$, ArH (2, 6)), 7.34 (2H, d, $J=8.3$, ArH (3, 5)), 2.67 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2CH_3$), 1.68 (2H, m, $ArCH_2C\underline{H}_2CH_3$), 0.96 (3H, t, $J=7.3$, $ArCH_2CH_2C\underline{H}_3$).

3-(4-Propylphenyl)propanoic acid was prepared from the 4-propylbenzaldehyde (2.68 g, 18.1 mmol) and 2,2-dimethyl-1,3-dioxane-4,6-dione (2.56 g, 17.8 mmol) in triethylammonium formate (TEAF) with the composition of $(Et_3N)_2{\cdot}(HCO_2H)_5$ (20 mL) according to the method for the preparation of 3-arylpropanoic acids.[29] Recrystallisation (2,2,4-trimethylpentane) of the crude product provided 3-(4-propylphenyl)propanoic acid (2.15 g, 63%) as a white powder; ^{1}H NMR: δ 7.11 (4H, s, ArH), 2.94 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2CO_2$), 2.67 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2CO_2$), 2.55 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2CH_3$), 1.60 (2H, m, $ArCH_2C\underline{H}_2CH_3$), 0.93 (3H, t, $J=7.3$, $ArCH_2CH_2C\underline{H}_3$).

Vinylation of the 3-(4-propylphenyl)propanoic acid was carried out according to the procedure for the preparation of **3a**. Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product provided **3d** (80%) as a colourless oil; ^{1}H NMR: δ 7.28 (1H, dd, $J=6.2$, $J=13.9$, $C\underline{H}{=}CH_2$), 7.11 (4H, s, ArH), 4.88 (1H, dd, $J=1.3$, $J=14.0$, $CH{=}C\underline{H}_2$ (*cis*)), 4.57 (1H, dd, $J=1.5$, $J=6.1$, $CH{=}C\underline{H}_2$ (*trans*)), 2.95 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2CO_2$), 2.70 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2CO_2$), 2.55 (2H, t, $J=7.6$, $ArC\underline{H}_2CH_2CH_3$), 1.62 (2H, m, $ArCH_2C\underline{H}_2CH_3$), 0.93 (3H, t, $J=7.3$, $ArCH_2CH_2C\underline{H}_3$); IR (neat): 1756 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$) cm^{-1}. Found: C, 77.44; H, 8.47. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31%.

3.7. Vinyl 3-(4-*t*-butylphenyl)propanoate 3e

Compound **3e** was prepared from 4-*tert*-butylbenzaldehyde as the starting material according to the procedure for the preparation of vinyl 3-(4-propylphenyl)propanoate **3d**; 3-(4-*t*-butylphenyl)propanoic acid (83%) as a white powder; ^{1}H NMR: δ 7.32 (2H, d, $J=8.3$, ArH (2, 6)), 7.15 (2H, d, $J=8.1$, ArH (3, 5)), 2.94 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2$), 2.68 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2$), 1.31 (9H, s, $C(CH_3)_3$); vinyl 3-(4-*t*-butylphenyl)propanoate **3e** (63%) as a colourless oil; ^{1}H NMR: δ 7.31 (1H, dd, $J=7.8$, $J=14.2$, $C\underline{H}{=}CH_2$), 7.29 (2H, d, $J=20.3$, ArH (2, 6)), 7.15 (2H, d, $J=8.3$, ArH (3, 5)), 4.88 (1H, dd, $J=1.6$, $J=14.0$, $CH{=}C\underline{H}_2$ (*cis*)), 4.58 (1H, dd, $J=1.6$, $J=6.2$, $CH{=}C\underline{H}_2$ (*trans*)), 2.96 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2$), 2.71 (2H, t, $J=7.9$, $ArCH_2C\underline{H}_2$), 1.31 (9H, s, $C(CH_3)_3$); IR (neat): 1757 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$) cm^{-1}. Found: C, 77.34; H, 8.82. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

3.8. Vinyl 3-(4-methoxyphenyl)propanoate 3f

A mixture of 3-(4-hydroxyphenyl)propanoic acid (1.67 g, 10.0 mmol), aqueous NaOH (6 M, 4 mL 24 mmol), iodomethane (1.56 g, 11.0 mmol) and methanol (40 mL) was stirred at 50°C for 10 h. After evaporation, aqueous NaOH (1 M) was added to the residue, and the aqueous layer washed with ether. The aqueous layer was acidified with aqueous HCl (1 M) at 0°C. The white solid produced was filtered and recrystallised from hexane to give 3-(4-methoxyphenyl)-propanoic acid as a white powder (1.25 g, 70%); ^{1}H NMR: δ 7.13 (2H, d, $J=8.3$, ArH (2, 6)), 6.84 (2H, d, $J=8.5$, ArH (3, 5)), 3.79 (3H, s, OCH_3), 2.91 (2H, t, $J=7.7$, $ArCH_2CH_2$), 2.65 (2H, t, $J=7.7$, $ArCH_2CH_2$).

Vinylation of the 3-(4-methoxyphenyl)propanoic acid was carried out according to the procedure for the preparation of **3a**. Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product afforded **3f** as a colourless oil (68%); ^{1}H NMR: δ 7.26 (1H, dd, $J=5.8$, $J=14.5$, $C\underline{H}{=}CH_2$), 7.13 (2H, d, $J=8.8$, ArH (2, 6)), 6.84 (2H, d, $J=8.0$, ArH (3, 5)), 4.88 (1H, dd, $J=1.4$, $J=14.3$, $CH{=}C\underline{H}_2$ (*cis*)), 4.57 (1H, dd, $J=1.6$, $J=6.2$, $CH{=}C\underline{H}_2$ (*trans*)), 3.79 (3H, s, OCH_3), 2.93 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2$), 2.68 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); IR (neat): 1753 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$), 1248 ($\nu_{as\ C-O-C}$), 1036 ($\nu_{s\ C-O-C}$) cm^{-1}. Found: C, 70.16; H, 7.09. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84%.

3.9. Vinyl 3-(4-*n*-hexyloxyphenyl)propanoate 3g

Compound **3g** was prepared from 1-bromohexane and 3-(4-hydroxyphenyl)propanoic acid as the starting materials according to the procedure for the preparation of vinyl 3-(4-methoxyphenyl)propanoate **3f**; 3-(4-*n*-hexyloxyphenyl)propanoic acid as a white solid (71%); ^{1}H NMR: δ 7.12 (2H, d, $J=8.6$, ArH (2, 6)), 6.83 (2H, d, $J=8.8$, ArH (3, 5)), 3.93 (2H, t, $J=6.6$, $ArOC\underline{H}_2(CH_2)_4CH_3$), 2.90 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2CO_2$), 2.65 (2H, t, $J=7.6$, $ArCH_2C\underline{H}_2CO_2$), 1.78–1.71 (2H, m, $ArOCH_2C\underline{H}_2(CH_2)_3CH_3$), 1.46–1.41 (2H, m, $ArO(CH_2)_2C\underline{H}_2(CH_2)_2CH_3$), 1.35–1.33 (4H, m,

$ArO(CH_2)_3C\underline{H}_2C\underline{H}_2CH_3$), 0.90 (3H, t, $J=7.0$, $ArO(CH_2)_5C\underline{H}_3$); vinyl 3-(4-*n*-hexyloxyphenyl)propanoate **3g** as a colourless oil (70%); ^{1}H NMR: δ 7.27 (1H, dd, $J=6.4$, $J=13.9$, $C\underline{H}=CH_2$), 7.11 (2H, d, $J=8.8$, ArH (2, 6)), 6.82 (2H, d, $J=8.8$, ArH (3, 5)), 4.87 (1H, dd, $J=1.6$, $J=14.0$, $CH=C\underline{H}_2$ (*cis*)), 4.56 (1H, dd, $J=1.5$, $J=6.3$, $CH=C\underline{H}_2$ (*trans*)), 3.92 (2H, t, $J=6.6$, $ArOC\underline{H}_2(CH_2)_4CH_3$), 2.92 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2CO_2$), 2.67 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2CO_2$), 1.80–1.72 (2H, m, $ArOCH_2C\underline{H}_2(CH_2)_3CH_3$), 1.48–1.41 (2H, m, $ArO(CH_2)_2C\underline{H}_2(CH_2)_2CH_3$), 1.36–1.31 (4H, m, $ArO(CH_2)_3C\underline{H}_2C\underline{H}_2CH_3$), 0.90 (3H, t, $J=7.1$, $ArO(CH_2)_5C\underline{H}_3$); IR (neat): 1756 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$), 1245 ($\nu_{as\ C-O-C}$), 1032 ($\nu_{s\ C-O-C}$) cm^{-1}. Found: C, 73.58; H, 8.73. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75%.

3.10. Vinyl 3-(4-*n*-octyloxyphenyl)propanoate 3h

Compound **3h** was prepared from 1-bromooctane and 3-(4-hydroxyphenyl)propanoic acid according to the procedure for the preparation of vinyl 3-(4-methoxyphenyl)propanoate **3f**; 3-(4-*n*-octyloxyphenyl)-propanoic acid (65%) as a white powder; ^{1}H NMR: δ 7.11 (2H, d, $J=8.3$, ArH (2, 6)), 6.83 (2H, d, $J=8.5$, ArH (3, 5)), 3.92 (2H, t, $J=6.6$, $ArOC\underline{H}_2(CH_2)_6CH_3$), 2.90 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2CO_2$), 2.65 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2CO_2$), 1.80–1.73 (2H, m, $ArOCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.58–1.28 (10H, m, $ArO(CH_2)_2(C\underline{H}_2)_5CH_3$), 0.88 (3H, t, $J=7.0$, $ArO(CH_2)_7C\underline{H}_3$); vinyl 3-(4-*n*-octyloxyphenyl)propanoate **3h** as a colourless oil (78%); ^{1}H NMR: δ 7.27 (1H, dd, $J=6.3$, $J=12.0$, $C\underline{H}=CH_2$), 7.11 (2H, d, $J=8.5$, ArH (2, 6)), 6.82 (2H, d, $J=7.6$, ArH (3, 5)), 4.88 (1H, dd, $J=1.6$, $J=14.0$, $CH=C\underline{H}_2$ (*cis*)), 4.57 (1H, dd, $J=1.7$, $J=6.3$, $CH=C\underline{H}_2$ (*trans*)), 3.92 (2H, t, $J=6.1$, $ArOC\underline{H}_2(CH_2)_6CH_3$), 2.92 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2CO_2$), 2.68 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2CO_2$), 1.80–1.73 (2H, m, $ArOCH_2C\underline{H}_2(CH_2)_5CH_3$), 1.48–1.41 (2H, m, $ArO(CH_2)_2C\underline{H}_2(CH_2)_4CH_3$), 1.32–1.28 (8H, m, $ArO(CH_2)_3(C\underline{H}_2)_4CH_3$), 0.88 (3H, t, $J=6.3$, $ArO(CH_2)_7C\underline{H}_3$); IR (neat): 1758 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$), 1246 ($\nu_{as\ C-O-C}$), 1032 ($\nu_{s\ C-O-C}$) cm^{-1}. Found: C, 74.67; H, 9.43. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%.

3.11. Vinyl 3-(4-biphenyl)propanoate 3i

To a solution of 4-biphenylacetic acid (3.20 g, 15.1 mmol) in dry THF (35 mL) at 0°C was slowly added $LiAlH_4$ (0.46 g, 12 mmol). After stirring at room temperature for 5 h, the mixture was quenched at 0°C with HCl (3 M, 30 mL). The resulting mixture was extracted with ether. The organic phase was washed with 1 M sodium hydroxide solution, saturated sodium chloride solution and dried over sodium sulfate, followed by recrystallisation from benzene–hexane to give 2-(4-biphenyl)ethanol as a white solid (2.10 g, 71%); ^{1}H NMR: δ 7.59–7.31 (9H, m, ArH), 3.92 (2H, m, $ArCH_2C\underline{H}_2$), 2.93 (2H, t, $J=6.5$, $ArC\underline{H}_2CH_2$).

Bromination of the 2-(4-biphenyl)ethanol (2.08 g, 10.5 mmol) with CBr_4 (3.92 g, 11.8 mmol) and Ph_3P (3.03 g, 11.6 mmol) in CH_2Cl_2 (30 mL) was carried out according to the literature procedure.[30] Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product followed by distillation (162–210°C/0.35 mmHg) provided 1-bromo-2-(4-biphenyl)ethane as a white solid (2.10 g, 77%); ^{1}H NMR: δ 7.59–7.28 (9H, m, ArH), 3.61 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$), 3.21 (2H, t, $J=7.6$, $ArC\underline{H}_2CH_2$).

In a three-necked flask was placed magnesium shavings (0.25 g, 10.3 mmol). The shavings were covered with about 1 mL of a solution of 1-bromo-2-(4-biphenyl)ethane (2.08 g, 8.0 mmol) in anhydrous THF (10 mL) under Ar. When the reaction started, the remainder of the halide solution in THF was added. The reaction mixture was warmed with mantle heater for 1 h. After cooling to room temperature, the mixture was poured on crushed dry ice. 6 M HCl was added to the mixture at 0°C after the dry ice was evaporated. The mixture was extracted with ether and the organic extract washed twice with 1 M NaOH. The aqueous layer was acidified with 6 M HCl and left to crystallise at 0°C. After filtration, the solid collected was recrystallised from benzene–hexane to give 3-(4-biphenyl)propanoic acid as a white solid (0.59 g, 33%); ^{1}H NMR: δ 7.59–7.28 (9H, m, ArH), 3.02 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2$), 2.73 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2$).

Vinylation of the 3-(4-biphenyl)propanoic acid was carried out according to the procedure for the preparation of **3a**. Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product provided **3i** as a colourless oil (70%); ^{1}H NMR: δ 7.59–7.28 (10H, m, ArH and $C\underline{H}=CH_2$), 4.89 (1H, dd, $J=1.6$, $J=14.0$, $CH=C\underline{H}_2$ (*cis*)), 4.57 (1H, dd, $J=1.6$, $J=6.2$, $CH=C\underline{H}_2$ (*trans*)), 3.02 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.75 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); IR (neat): 1753 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$) cm^{-1}. Found: C, 80.96; H, 6.44. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39%.

3.12. Vinyl 3-(4-fluorophenyl)propanoate 3j

Prepared from 4-fluorophenylacetic acid according to the procedure for the preparation of vinyl 3-(4-biphenyl)propanoate **3i**; 2-(4-fluorophenyl)ethanol was isolated as a colourless oil (86%); ^{1}H NMR: δ 7.21–7.17 (2H, m, ArH (3, 5)), 7.00 (2H, t, $J=8.5$, ArH (2, 5), 3.84 (2H, m, $ArCH_2C\underline{H}_2$), 2.84 (2H, t, $J=6.6$, $ArC\underline{H}_2CH_2$); 1-bromo-2-(4-fluorophenyl)ethane (96%) was isolated as a colourless oil; ^{1}H NMR: δ 7.19–7.16 (2H, m, ArH (3, 5)), 7.01 (2H, t, $J=8.7$, ArH (2, 6)), 3.54 (2H, t, $J=7.4$, $ArCH_2C\underline{H}_2$), 3.14 (2H, t, $J=7.1$, $ArC\underline{H}_2CH_2$); 3-(4-fluorophenyl)propanoic acid (crude, 28%) was obtained as a white solid; ^{1}H NMR: δ 7.19–7.15 (2H, m, ArH (3, 5)), 6.98 (2H, t, $J=8.7$, ArH (2, 6)), 2.93 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.66 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); vinyl 3-(4-fluorophenyl)-propanoate **3j** (82%) was isolated as a colourless oil; ^{1}H NMR: δ 7.27 (1H, dd, $J=6.3$, $J=14.2$, $C\underline{H}=CH_2$), 7.18–7.15 (2H, m, ArH (3, 5)), 6.98 (2H, t, $J=8.8$, ArH (2, 6)), 4.88 (1H, dd, $J=1.6$, $J=14.0$, $CH=C\underline{H}_2$ (*cis*)), 4.58 (1H, dd, $J=1.7$, $J=6.3$, $CH=C\underline{H}_2$ (*trans*)), 2.96 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.69 (2H, t, $J=7.7$,

$ArCH_2C\underline{H}_2$); IR (neat): 1754 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$), 1148 (ν_{C-F}) cm^{-1}. Found: C, 67.97; H, 5.94. Calcd for $C_{11}H_{11}FO_2$: C, 68.03; H, 5.71%.

3.13. Vinyl 3-(4-chlorophenyl)propanoate 3k

Prepared from 4-chlorobenzyl bromide according to the procedure for the preparation of vinyl 3-(4-ethylphenyl)propanoate **3c**; diethyl 4-chlorobenzylmalonate (35%) was obtained as a colourless oil; ^1H NMR: δ 7.25 (2H, d, $J=9.6$, ArH (3, 5)), 7.14 (2H, d, $J=8.3$, ArH (2, 6)), 4.20–4.12 (4H, m, $CO_2C\underline{H}_2CH_3$), 3.60 (1H, t, $J=7.8$, $ArCH_2C\underline{H}$), 3.18 (2H, d, $J=7.8$, $ArC\underline{H}_2CH$), 1.22 (6H, t, $J=7.2$, $CO_2CH_2C\underline{H}_3$); 4-chlorobenzylmalonic acid (crude, 96%) was obtained as a white solid; ^1H NMR: δ 7.27 (2H, d, $J=6.1$, ArH (3, 5)), 7.17 (2H, d, $J=8.6$, ArH (2, 6)), 3.71 (1H, t, $J=7.3$, $ArCH_2C\underline{H}$), 3.26 (2H, d, $J=7.3$, $ArC\underline{H}_2CH$); 3-(4-chlorophenyl)propanoic acid as a white solid (62%); ^1H NMR: δ 7.27 (2H, d, $J=5.4$, ArH (3, 5)), 7.15 (2H, t, $J=8.1$, ArH (2, 6)), 2.93 (2H, t, $J=7.6$, $ArC\underline{H}_2CH_2$), 2.67 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); vinyl 3-(4-chlorophenyl)propanoate **3k** (66%) as a colourless oil; ^1H NMR: δ 7.29–7.24 (3H, m, ArH (3, 5) and $C\underline{H}$=CH_2), 7.14 (2H, d, $J=8.3$, ArH (2, 6)), 4.88 (1H, dd, $J=1.6$, $J=14.0$, CH=C$\underline{H}_2$ (*cis*)), 4.58 (1H, dd, $J=1.7$, $J=6.4$, CH=C$\underline{H}_2$ (*trans*)), 2.95 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.69 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); IR (neat): 1754 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$), 1092 (ν_{C-Cl}) cm^{-1}. Found: C, 62.98; H, 5.16. Calcd for $C_{11}H_{11}ClO_2$: C, 62.72; H, 5.26%.

3.14. Vinyl 3-(4-bromophenyl)propanoate 3l

Compound **3l** was prepared from 4-bromobenzyl bromide according to the procedure for the preparation of vinyl 3-(4-ethylphenyl)propanoate **3c**; diethyl 4-bromobenzylmalonate (44%) was isolated as a colourless oil; ^1H NMR: δ 7.40 (2H, d, $J=7.8$, ArH (3, 5)), 7.09 (2H, d, $J=8.3$, ArH (2, 6)), 4.24–4.09 (4H, m, $CO_2C\underline{H}_2CH_3$), 3.60 (1H, t, $J=7.8$, $ArCH_2C\underline{H}$), 3.16 (2H, d, $J=7.8$, $ArC\underline{H}_2CH$), 1.22 (6H, t, $J=7.2$, $CO_2CH_2C\underline{H}_3$); 4-bromobenzylmalonic acid (93%) was isolated as a white solid; ^1H NMR: δ 7.45 (2H, d, $J=6.6$, ArH (3, 5)), 7.17 (2H, d, $J=8.3$, ArH (2, 6)), 3.63 (1H, t, $J=7.8$, $ArCH_2C\underline{H}$), 3.09 (2H, d, $J=7.8$, $ArC\underline{H}_2CH$); 3-(4-bromophenyl)propanoic acid (67%) was isolated as a white solid; ^1H NMR: δ 7.42 (2H, d, $J=7.8$, ArH (3, 5)), 7.09 (2H, d, $J=8.3$, ArH (2, 6)), 2.92 (2H, t, $J=7.6$, $ArC\underline{H}_2CH_2$), 2.67 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); vinyl 3-(4-bromophenyl)propanoate (50%) was isolated as a colourless oil; ^1H NMR: δ 7.41 (2H, d, $J=8.3$, ArH (3, 5)), 7.25 (1H, dd, $J=6.0$, $J=19.9$, $C\underline{H}$=CH_2), 7.08 (2H, d, $J=8.1$, ArH (2, 6)), 4.87 (1H, dd, $J=1.6$, $J=14.0$, CH=C$\underline{H}_2$ (*cis*)), 4.57 (1H, dd, $J=1.7$, $J=6.3$, CH=C$\underline{H}_2$ (*trans*)), 2.93 (2H, t, $J=7.6$, $ArC\underline{H}_2CH_2$), 2.69 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); IR (neat): 1754 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$) cm^{-1}. Found: C, 51.91; H, 4.34. Calcd for $C_{11}H_{11}BrO_2$: C, 51.79; H, 4.35%.

3.15. Vinyl 3-(4-iodophenyl)propanoate 3m

3-(4-Iodophenyl)propanoic acid was prepared from 3-phenylpropanoic acid (3.00 g, 20.0 mmol), periodic acid dihydrate (0.98 g, 4.3 mmol), and iodine (2.03 g, 8.0 mmol) according to the method for the iodination of aromatic compounds.[31] Recrystallisation (heptane) of the crude product provided 3-(4-iodophenyl)propanoic acid (2.41 g, 44%) as a white powder; ^1H NMR: δ 7.62 (2H, d, $J=8.3$, ArH (3, 5)), 6.97 (2H, d, $J=8.1$, ArH (2, 6)), 2.91 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.66 (2H, t, $J=7.6$, $ArCH_2C\underline{H}_2$).

Vinylation of the 3-(4-iodophenyl)propanoic acid was carried out according to the procedure for the preparation of **3a**. Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product provided **3m** (53%) as a colourless oil; ^1H NMR: δ 7.61 (2H, d, $J=8.3$, ArH (3, 5)), 7.26 (1H, dd, $J=6.3$, $J=13.9$, $C\underline{H}$=CH_2), 6.96 (2H, d, $J=8.0$, ArH (2, 6)), 4.88 (1H, dd, $J=1.7$, $J=13.9$, CH=C$\underline{H}_2$ (*cis*)), 4.58 (1H, dd, $J=1.7$, $J=6.4$, CH=C$\underline{H}_2$ (*trans*)), 2.92 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.68 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); IR (neat): 1753 ($\nu_{C=O}$), 1645 ($\nu_{C=C}$) cm^{-1}. Found: C, 43.69; H, 3.68. Calcd for $C_{11}H_{11}IO_2$: C, 43.73%; H, 3.67%.

3.16. Vinyl 3-(4-trifluoromethylphenyl)propanoate (3n)

Vinylation of 3-(4-trifluoromethylphenyl)propanoic acid was carried out according to the procedure for the preparation of **3a**. Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product provided **3n** as a colourless oil (82%); ^1H NMR: δ 7.56 (2H, d, $J=8.1$, ArH (3, 5)), 7.33 (2H, d, $J=8.1$, ArH (2, 6)), 7.27 (1H, dd, $J=6.3$, $J=13.9$, $C\underline{H}$=CH_2), 4.89 (1H, dd, $J=1.7$, $J=14.2$, CH=C$\underline{H}_2$ (*cis*)), 4.59 (1H, dd, $J=1.7$, $J=6.4$, CH=C$\underline{H}_2$ (*trans*)), 3.05 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.74 (2H, t, $J=7.6$, $ArCH_2C\underline{H}_2$); IR (neat): 1756 ($\nu_{C=O}$), 1648 ($\nu_{C=C}$), 1326 (ν_{C-F}) cm^{-1}. Found: C, 59.24; H, 4.73. Calcd for $C_{12}H_{11}F_3O_2$: C, 59.02; H, 4.54%.

3.17. Vinyl 3-(4-cyanophenyl)propanoate 3o

Compound **3o** was prepared from 4-cyanobenzaldehyde as the starting material according to the procedure for the preparation of vinyl 3-(4-propylphenyl)propanoate **3d**; the product 3-(4-cyanophenyl)propanoic acid was obtained as a white powder (53%); ^1H NMR: δ 7.60 (2H, d, $J=7.3$, ArH (3, 5)), 7.33 (2H, d, $J=7.3$, ArH (2, 6)), 3.02 (2H, t, $J=7.4$, $ArC\underline{H}_2CH_2$), 2.71 (2H, t, $J=7.1$, $ArCH_2C\underline{H}_2$); Vinyl 3-(4-cyanophenyl)propanoate **3o** (83%) as a colourless oil; ^1H NMR: δ 7.60 (2H, d, $J=8.0$, ArH (3, 5)), 7.33 (2H, d, $J=8.0$, ArH (2, 6)), 7.25 (1H, dd, $J=6.4$, $J=13.9$, $C\underline{H}$=CH_2), 4.89 (1H, dd, $J=1.7$, $J=13.9$, CH=C$\underline{H}_2$ (*cis*)), 4.60 (1H, dd, $J=1.7$, $J=6.4$, CH=C$\underline{H}_2$ (*trans*)), 3.05 (2H, t, $J=7.4$, $ArC\underline{H}_2CH_2$), 2.74 (2H, t, $J=7.4$, $ArCH_2C\underline{H}_2$); IR (neat): 2228 ($\nu_{C\equiv N}$), 1753 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$) cm^{-1}. Found: C, 71.77; H, 5.54; N, 6.91. Calcd for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96%.

3.18. Vinyl 3-(2-fluorophenyl)propanoate 3p

Compound **3p** was prepared from 2-fluorophenylacetic acid as the starting material according to the procedure for the preparation of vinyl 3-(4-biphenyl)propanoate

3i; 2-(2-fluorophenyl)ethanol (88%) was isolated as a colourless oil; ^{1}H NMR: δ 7.29–7.10 (2H, m, ArH (3, 5)), 7.10–7.01 (2H, m, ArH (4, 6)), 3.87 (2H, t, $J=6.6$, $ArCH_2C\underline{H}_2$), 2.93 (2H, t, $J=6.7$, $ArC\underline{H}_2CH_2$); 1-bromo-2-(2-fluorophenyl)ethane (58%) was isolated as a colourless oil; ^{1}H NMR: δ 7.29–7.21 (2H, m, ArH (3, 5)), 7.12–7.02 (2H, m, ArH (4, 6)), 3.58 (2H, t, $J=7.6$, $ArCH_2C\underline{H}_2$), 3.21 (2H, t, $J=7.4$, $ArC\underline{H}_2CH_2$); 3-(2-fluorophenyl)propanoic acid (50%) was isolated as a colourless oil; ^{1}H NMR: δ 7.30–7.18 (2H, m, ArH (3, 5)), 7.09–7.00 (2H, m, ArH (4, 6)), 3.00 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.70 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); vinyl 3-(2-fluorophenyl)propanoate **3p** (83%) as a colourless oil; ^{1}H NMR: δ 7.30–7.18 (3H, m, ArH (3, 5) and $C\underline{H}$=CH_2), 7.08–7.00 (2H, m, ArH (4, 6)), 4.88 (1H, dd, $J=1.7$, $J=13.9$, CH=C$\underline{H}_2$ (*cis*)), 4.58 (1H, dd, $J=1.7$, $J=6.3$, CH=C$\underline{H}_2$ (*trans*)), 3.01 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.73 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2$); IR (neat): 1755 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$), 1149 (ν_{C-F}) cm^{-1}. Found: C, 68.18; H, 5.74. Calcd for $C_{11}H_{11}FO_2$: C, 68.03; H, 5.71.

3.19. Vinyl 3-(3-fluorophenyl)propanoate 3q

This compound was prepared from 3-fluorophenylacetic acid according to the procedure for the preparation of vinyl 3-(4-biphenyl)propanoate **3i**; 2-(3-fluorophenyl)ethanol was isolated as a colourless oil (84%); ^{1}H NMR: δ 7.30–7.25 (1H, m, ArH (4)), 7.02–6.91 (3H, m, ArH (2, 5, 6)), 3.87 (2H, t, $J=6.3$, $ArCH_2C\underline{H}_2$), 2.87 (2H, t, $J=6.6$, $ArC\underline{H}_2CH_2$); 1-bromo-2-(3-fluorophenyl)ethane was isolated as a colourless oil (66%); ^{1}H NMR: δ 7.31–7.28 (1H, m, ArH (4)), 7.00–6.92 (3H, m, ArH (2, 5, 6)), 3.57 (2H, t, $J=7.4$, $ArCH_2C\underline{H}_2$), 3.17 (2H, t, $J=7.4$, $ArC\underline{H}_2CH_2$); 3-(3-fluorophenyl)propanoic acid was obtained as a colourless oil (55%); ^{1}H NMR: δ 7.30–7.23 (1H, m, ArH (4)), 7.00–6.89 (3H, m, ArH (2, 5, 6)), 2.96 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.69 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); vinyl 3-(3-fluorophenyl)propanoate (**3q**) was isolated as a colourless oil (71%); ^{1}H NMR: δ 7.30–7.23 (2H, m, ArH (4) and $C\underline{H}$=CH_2), 7.00–6.89 (3H, m, ArH (2, 5, 6)), 4.89 (1H, dd, $J=1.7$, $J=13.9$, CH=C$\underline{H}_2$ (*cis*)), 4.58 (1H, dd, $J=1.7$, $J=6.4$, CH=C$\underline{H}_2$ (*trans*)), 2.98 (2H, t, $J=7.6$, $ArC\underline{H}_2CH_2$), 2.71 (2H, t, $J=7.7$, $ArCH_2C\underline{H}_2$); IR (neat): 1755 ($\nu_{C=O}$), 1647 ($\nu_{C=C}$), 1150 (ν_{C-F}) cm^{-1}. Found: C, 67.91; H, 5.77. Calcd for $C_{11}H_{11}FO_2$: C, 68.03; H, 5.71%.

3.20. Vinyl 3-(2-iodophenyl)propanoate 3r

2-Iodobenzaldehyde was prepared from 2-iodobenzyl alcohol (4.62 g, 19.7 mmol) and PCC (6.49 g, 30.1 mmol) according to the method for the oxidation of alcohols to aldehydes.[32] Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product provided 2-iodobenzaldehyde (4.11 g, 90%) as a pale brown solid; ^{1}H NMR: δ 10.08 (1H, s, CHO), 7.96 (1H, d, $J=7.8$, ArH (6)), 7.89 (1H, d, $J=7.8$, ArH (3)), 7.47 (1H, t, $J=7.6$, ArH (4)), 7.29 (1H, t, $J=7.8$, ArH (5)).

2-Iodobenzaldehyde was converted to vinyl 3-(2-iodophenyl)propanoate **3r** through two steps described for the preparation of vinyl 3-(4-propylphenyl)-propanoate **3d**; 3-(2-iodophenyl)propanoic acid (60%) was isolated as a white powder; ^{1}H NMR: δ 7.83 (1H, d, $J=8.3$, ArH (3)), 7.31–7.25 (2H, m, ArH (4, 5)), 6.94–6.90 (1H, m, ArH (6)), 3.06 (2H, t, $J=7.9$, $ArC\underline{H}_2CH_2$), 2.69 (2H, t, $J=7.9$, $ArCH_2C\underline{H}_2$); vinyl 3-(2-iodophenyl)propanoate **3r** was isolated as a colourless oil (82%); ^{1}H NMR: δ 7.83 (1H, d, $J=7.8$, ArH(3)), 7.32–7.24 (3H, m, ArH (4, 5) and $C\underline{H}$=CH_2), 6.94–6.90 (1H, m, ArH (6)), 4.90 (1H, dd, $J=1.6$, $J=13.8$, CH=C$\underline{H}_2$ (*cis*)), 4.59 (1H, dd, $J=1.7$, $J=6.3$, CH=C$\underline{H}_2$ (*trans*)), 3.09 (2H, t, $J=7.8$, $ArC\underline{H}_2CH_2$), 2.72 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2$); IR (neat): 1753 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$) cm^{-1}. Found: C, 43.97; H, 3.63. Calcd for $C_{11}H_{11}IO_2$: C, 43.73; H, 3.67.

3.21. Vinyl 3-(3-iodophenyl)propanoate 3s

This compound was prepared from 3-iodobenzyl alcohol according to the procedure for the preparation of vinyl 3-(2-iodophenyl)propanoate **3r**; 3-iodobenzaldehyde (91%) was isolated as a colourless oil; ^{1}H NMR: δ 9.93 (1H, s, CHO), 8.21 (1H, s, ArH (2)), 7.96 (1H, d, $J=7.8$, ArH (6)), 7.85 (1H, d, $J=7.8$, ArH (4)), 7.29 (1H, t, $J=7.8$, ArH (5)); 3-(3-iodophenyl)propanoic acid (65%) was isolated as a white solid; ^{1}H NMR: δ 7.58–7.55 (2H, m, ArH (2, 4)), 7.18 (1H, d, $J=7.6$, ArH (6)), 7.03 (1H, t, $J=7.7$, ArH (5)), 2.91 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.67 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2$); vinyl 3-(3-iodophenyl)propanoate **3s** was isolated as a colourless oil (77%); ^{1}H NMR: δ 7.58–7.55 (2H, m, ArH (2, 4)), 7.27 (1H, dd, $J=6.3$, $J=13.9$, $C\underline{H}$=CH_2), 7.18 (1H, d, $J=7.6$, ArH (6)), 7.03 (1H, t, $J=7.8$, ArH (5)), 4.89 (1H, dd, $J=1.7$, $J=13.9$, CH=C$\underline{H}_2$ (*cis*)), 4.59 (1H, dd, $J=1.7$, $J=6.3$, CH=C$\underline{H}_2$ (*trans*)), 2.93 (2H, t, $J=7.7$, $ArC\underline{H}_2CH_2$), 2.70 (2H, t, $J=7.8$, $ArCH_2C\underline{H}_2$); IR (neat): 1754 ($\nu_{C=O}$), 1646 ($\nu_{C=C}$) cm^{-1}. Found: C, 43.90; H, 3.66. Calcd for $C_{11}H_{11}IO_2$: C, 43.73; H, 3.67%.

3.22. 3-Chloro-2-phenyl-1-propanol 7

Monochlorination of 2-phenyl-1,3-propanediol (3.49 g, 22.9 mmol) with CCl_4 (20 mL) and Ph_3P (3.05 g, 11.6 mmol) in CH_2Cl_2 (60 mmol) was carried out as described for the preparation of 1-bromo-2-(4-biphenyl)ethane. Chromatography (silica gel, hexane–ethyl acetate 5:1 (v/v)) of the crude product followed by distillation (122–164°C/0.7 mmHg) gave **7** as a colourless oil (0.79 g, 40%); ^{1}H NMR: δ 7.39–7.25 (5H, m, ArH), 3.98 (1H, t, $J=5.5$, $ArCHC\underline{H}_2OH$), 3.91–3.78 (2H, m, $ArCHC\underline{H}_2Cl$), 3.25–3.16 (1H, m, ArCH); IR (neat): 3353 (ν_{O-H}), 700 (ν_{C-Cl}) cm^{-1}. Found: C, 63.05; H, 6.49. Calcd for $C_9H_{11}ClO$: C, 63.35; H, 6.50%.

3.23. Preparation of optically active alcohols as authentic samples

We prepared the optically active isomers of **4**–**9** for the authentic samples used to determine the absolute configurations of the enantiomers preferentially

esterified in their transesterification mediated by the lipases studied in the present study. Since optically active (*S*)-**1** and (*S*)-**10** are commercially available, we used these as the authentic samples.

Racemic **4**–**6**, **8**, and **9** (0.1–0.2 g) were esterified with vinyl acetate (2–4 equiv.) by PCL in cyclohexane according to the procedure described in Section 3.2. In the reaction of **7** (0.2 g), vinyl 3-phenylpropanoate **3a** (1.5 equiv.) was employed.

In the reaction of **5**–**8**, the unreacted alcohols were recovered and their e.e. and optical rotations were measured, which are as follows. (*R*)-**5**: e.e. = 78%, $[\alpha]_D^{23}$ −7.8 (*c* 1.16, $CHCl_3$) (lit.[33] $[\alpha]_D^{25}$ −9.0 (*c* 2.33, $CHCl_3$), 56% e.e. (*R*)); (*R*)-**6**: e.e. = 80%, $[\alpha]_D^{22}$ −26.0 (*c* 0.93, MeOH) (lit.[34] $[\alpha]_D^{23}$ −16.3 (*c* 1.21, MeOH), 63% e.e. (*R*)); (*R*)-**7**: e.e. = 61%, treatment of (*R*)-**7** with Jones reagent in acetone gave the corresponding carboxylic acid of (*R*)-configuration, $[\alpha]_D^{19}$ −45.1 (*c* 1.13, EtOH) (lit.[35] $[\alpha]_D^{20}$ −115 (*c* 0.3, EtOH), (*R*)); (*R*)-**8**: e.e. = 96% (measured after oxidation to the corresponding carboxylic acid), $[\alpha]_D^{21}$ +12.8 (*c* 1.51, $CHCl_3$) (lit.[36] $[\alpha]_D^{25}$ +11 (*c* 2.5, $CHCl_3$), e.e. >98% (*R*)).

In the reaction of **4** and **9**, the produced acetate esters were recovered and their optical rotations were measured. After the measurement, the esters were hydrolysed (NaOH, MeOH) to the corresponding alcohols and their e.e. determined, these are as follows. Acetate ester of (*S*)-**4**: e.e. = 62%, $[\alpha]_D^{21}$ +10.4 (*c* 2.17, $CHCl_3$) (lit.[34] $[\alpha]_D^{24}$ +10.3 (*c* 1.08, $CHCl_3$), e.e. = 62% (*S*)). Acetic acid ester of (*S*)-**9**: e.e. = 29%, $[\alpha]_D^{22}$ +15.9 (*c* 2.13, benzene) (lit.[37] $[\alpha]_D^{20}$ −35.2 (*c* 3.36, benzene), e.e. = 64% (*R*)).

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References

1. For a review, see: Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1–21.
2. For a review, see: Wescott, C. R.; Klibanov, A. M. *Biochim. Biophys. Acta* **1994**, *1206*, 1–9.
3. For a review, see: Theil, F. *Tetrahedron* **2000**, *56*, 2905–2919.
4. Sakai, T.; Kishimoto, T.; Tanaka, Y.; Ema, T.; Utaka, M. *Tetrahedron Lett.* **1998**, *39*, 7881–7884.
5. Lin, G.; Lin, W.-Y. *Tetrahedron Lett.* **1998**, *39*, 4333–4336.
6. Chen, C.-S.; Sih, C. J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 695–707.
7. Nakamura, K.; Takenaka, K.; Ohno, A. *Tetrahedron: Asymmetry* **1998**, *9*, 4429–4439.
8. Péter, M.; Van der Eycken, J.; Bernáth, G.; Fülöp, F. *Tetrahedron: Asymmetry* **1998**, *9*, 2339–2347.
9. Ema, T.; Maeno, S.; Takaya, Y.; Sakai, T.; Utaka, M. *J. Org. Chem.* **1996**, *61*, 8610–8616 and references cited therein.
10. Ema, T.; Maeno, S.; Takaya, Y.; Sakai, T.; Utaka, M. *Tetrahedron: Asymmetry* **1996**, *7*, 625–628.
11. Chen, C.-S.; Fujimoto, Y.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294–7299.
12. For carboxylic acids as acyl donors in a lipase-catalysed esterification, see: Guo, Z.-W.; Wu, S.-H.; Chen, C.-S.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1990**, *112*, 4942–4945.
13. Hirose, K.; Naka, H.; Yano, M.; Ohashi, S.; Naemura, K.; Tobe, Y. *Tetrahedron: Asymmetry* **2000**, *11*, 1199–1210.
14. Pozo, M.; Gotor, V. *Tetrahedron: Asymmetry* **1995**, *6*, 2797–2802.
15. Koshiro, S.; Sonomoto, K.; Tanaka, A.; Fukui, S. *J. Biotechnol.* **1985**, *2*, 47–57.
16. Kawasaki, M.; Goto, M.; Kawabata, S.; Kodama, T.; Kometani, T. *Tetrahedron Lett.* **1999**, *40*, 5223–5226.
17. Kawasaki, M.; Nakamura, K.; Kawabata, S. *J. Mol. Catal. B: Enzym.* **1999**, *6*, 447–451.
18. Im, D. S.; Cheong, C. S.; Lee, S. H.; Park, H.; Youn, B. H. *Tetrahedron: Asymmetry* **1999**, *10*, 3759–3767.
19. Kitano, K.; Matsubara, J.; Ohtani, T.; Otsubo, K.; Kawano, Y.; Morita, S.; Uchida, M. *Tetrahedron Lett.* **1999**, *40*, 5235–5238.
20. Gamalevich, G. D.; Serebryakov, E. P. *Russ. Chem. Bull.* **1997**, *46*, 171–183.
21. Morita, S.; Matsubara, J.; Otsubo, K.; Kitano, K.; Ohtani, T.; Kawano, Y.; Uchida, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3707–3710.
22. Serebryakov, E. P.; Gamalevich, G. D. *Mendeleev Commun.* **1996**, 221–224.
23. Nagai, H.; Shiozawa, T.; Achiwa, K.; Terao, Y. *Chem. Pharm. Bull.* **1993**, *41*, 1933–1938.
24. Ikushima, Y.; Saito, N.; Yokoyama, T.; Hatakeda, K.; Ito, S.; Arai, M.; Blanch, H. W. *Chem. Lett.* **1993**, 109–112.
25. Nagai, H.; Shiozawa, T.; Achiwa, K.; Terao, Y. *Chem. Pharm. Bull.* **1992**, *40*, 2227–2229.
26. Goto, M.; Kawasaki, M.; Kometani, T. *J. Mol. Catal. B: Enzym.* **2000**, *9*, 245–250.
27. Cygler, M.; Grochulski, P.; Kazlauskas, R. J.; Schrag, J. D.; Bouthillier, F.; Rubin, B.; Serreqi, A. N.; Gupta, A. K. *J. Am. Chem. Soc.* **1994**, *116*, 3180–3186.
28. Lobell, M.; Schneider, M. P. *Synthesis* **1994**, 375–377.
29. Tóth, G.; Kövér, K. E. *Synth. Commun.* **1995**, *25*, 3067–3074.
30. Kocienski, P. J.; Cernigliaro, G.; Feldstein, G. *J. Org. Chem.* **1977**, *42*, 353–355.
31. Suzuki, H. *Org. Synth.* **1988**, *6*, 700–704.
32. Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2650.
33. Naemura, K.; Fukuda, R.; Murata, M.; Konishi, M.; Hirose, K.; Tobe, Y. *Tetrahedron: Asymmetry* **1995**, *6*, 2385–2394.

34. Naemura, K.; Murata, M.; Tanaka, R.; Yano, M.; Hirose, K.; Tobe, Y. *Tetrahedron: Asymmetry* **1996**, *7*, 3285–3294.
35. Fodor, G.; Csepreghy, G. *J. Chem. Soc.* **1961**, 3222–3223.
36. Ferraboschi, P.; Casati, S.; Grandi, S. D.; Grisenti, P.; Santaniello, E. *Biocatalysis* **1994**, *10*, 279–288.
37. Ahlbrecht, H.; Bonnet, G.; Enders, D.; Zimmermann, G. *Tetrahedron Lett.* **1980**, *21*, 3175–3178.