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Enantioselective synthesis of allenecarboxylates from phenyl acetates through C–C bond forming reactions

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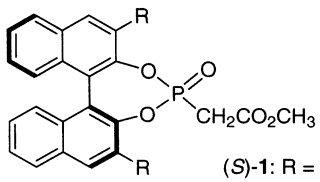
Abstract—A variety of optically active 4,4-disubstituted allenecarboxylic acid methyl esters were prepared from simple α,α-disubstituted phenyl acetate through base treatment of the esters to generate ketenes, followed by successive Horner–Wadsworth–Emmons reaction. The transformation was further developed as a one-pot procedure with satisfactory yields and high enantioselectivity. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Allenecarboxylates bearing different substituents at the 4-position possess axial chirality; hence, together with their versatile reactivity,[1] these derivatives are interesting building blocks for many asymmetric transformations. By appropriate synthetic manipulation transcription to central chirality is possible.

Most of the preceding preparative methods for optically active allenic compounds are based on the isomerisation of propargylic derivatives bearing a stereogenic centre.[2] Thus, except for two examples,[3] producing allenecarboxylates with e.e.s of up to 23%, little was known about direct transformation through C–C bond forming reactions of ketenes[4] before a new one-flask procedure was described by us.[5] In our method 2,6-di-*tert*-butyl-4-methylphenyl (BHT) esters[6] were used as precursors for labile ketene species. This procedure, however, involved difficulties such as low yields in the preparation of the starting materials probably due to the bulkiness of the BHT group and the limited availability of bases for both the subsequent generation of ketenes and appropriate anions for the Horner–Wadsworth–Emmons (HWE) reactions. Thus, *n*-BuLi was found to be the sole effective base for in situ generation of ketenes whilst KHMDS was found to be essential for the generation of reactive HWE reagents.

In this study, re-examination of ester candidates which allow in situ generation of the ketene species for the successive HWE reactions to allenic compounds, was carried out. We report herein an improved one-pot procedure for highly enantioselective preparation of optically active allenecarboxylates from phenyl esters.



(*S*)-**1**: R = H, (*S*)-**2**: R = CH_3, (*S*)-**3**: R = TMS

2. Results and discussion

After a systematic examination of several aromatic esters, (phenyl, 4-nitrophenyl, pentafluorophenyl, 2,6-dimethylphenyl, α- and β-naphthyl esters—the alkoxides of which were expected to have good leaving ability under the reaction conditions), phenyl esters were found to give satisfactory results in the presence of a $ZnCl_2$ additive (Scheme 1).

To confirm the effectiveness of phenyl esters, such as **4**, as precursors of ketenes, a competitive experiment was carried out between the corresponding methyl ester **5** with Still's reagent using lithium 2,2,6,6-tetramethylpiperidide (LiTMP) as a base (Scheme 2). Clear chemoselectivity was observed in this reaction, where together with formation of the allenic product, the methyl ester **5** was recovered unreacted nearly quantitatively.

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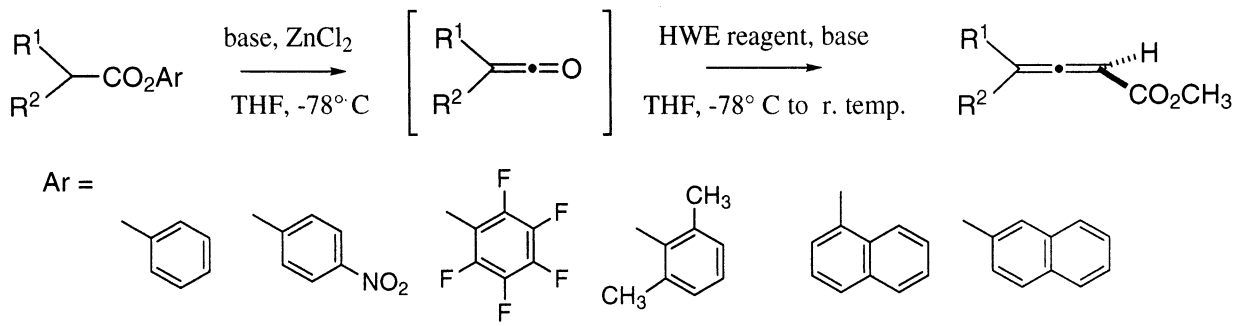
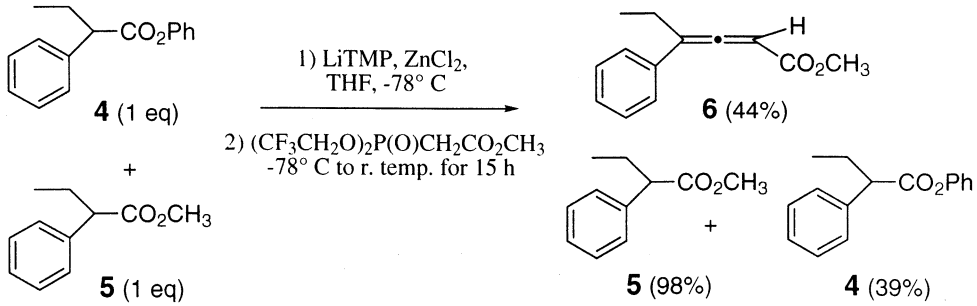
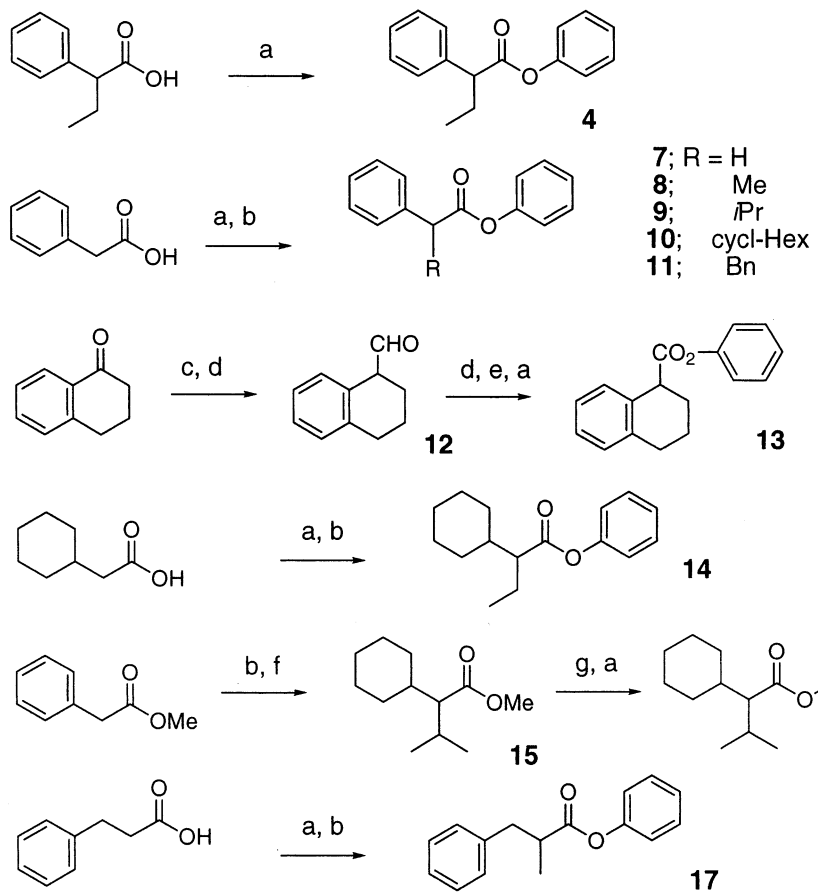


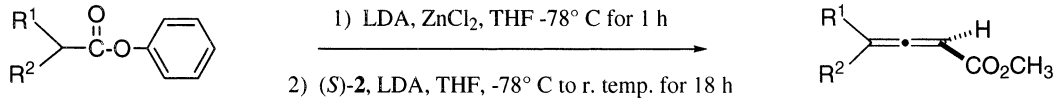
Scheme 1.



Scheme 2.



Scheme 3. (a) Phenol, DCC, DMAP, CH_2Cl_2, rt; (b) LDA, RX (R = Me, Et, *i*Pr, cycl-Hex, Bn), HMPA THF, −78°C; (c) $Ph_3PCH_2OCH_3Cl$, PhLi, Et_2O, −78°C to rt; (d) 98% HCO_2H, H_2O, rt; (e) Jones reagent, acetone, 0°C; (f) H_2, 5% Rh/Al_2O_3, *t*-BuOH, rt; (g) BBr_3, CH_2Cl_2, rt.



Scheme 4.

Table 1. Formation of optically active methyl allenecarboxylates from phenyl acetates

Entry	Phenyl esters			HWE reagent	Allenecarboxylates		
	Compound	R^1	R^2		Compound	% E.e.[a] (config.)	Chemical yield (%)[b]
1	**7**	H	Ph	(*S*)-**2**	–	–	–
2	**8**	CH_3	Ph	(*S*)-**2**	**18**	77 (a*R*)	31
3	**4**	C_2H_5	Ph	(*S*)-**1**	**6**	23 (a*R*)	48
4	**4**	C_2H_5	Ph	(*S*)-**2**	**6**	88 (a*R*)	57
5	**4**	C_2H_5	Ph	(*S*)-**3**	**6**	55 (a*R*)	57
6[c]	**4**	C_2H_5	Ph	(*S*)-**2**	**6**	87 (a*R*)	61
7	**9**	Ph	*i*-Pr	(*S*)-**2**	**19**	88 (a*S*)	69
8	**10**	Ph	Cycl-Hex	(*S*)-**2**	**20**	83 (a*S*)	71
9	**13**			(*S*)-**2**	**21**	89 (a*R*)	39
10	**11**	$PhCH_2$	Ph	(*S*)-**2**	**22**	89 (a*R*)	55
11	**14**	C_2H_5	Cycl-Hex	(*S*)-**2**	**23**	78 (a*R*)	43
12	**17**	CH_3	$PhCH_2$	(*S*)-**2**	**24**	32 (a*R*)	21
13	**16**	*i*-Pr	Cycl-Hex	(*S*)-**2**	–	–	–

[a] Determined by HPLC analysis on chiral column CHIRALPAK AS or AD.
[b] Isolated yield based on the consumed starting material.
[c] The reaction was carried out at −78 to −45°C for 2 h.

Using the phenyl ester as a substrate and an achiral trimethylphosphonoacetate as a HWE reagent, several bases adaptable to allene formation, such as amides and *n*-BuLi, were next examined. From this, LDA was also found to be a satisfactory base for this transformation. Among the homochiral HWE reagents[7] used, (*S*)-**2** gave the best result in accord with the BHT esters previously reported. Several derivatives of phenyl acetates were prepared (Scheme 3).

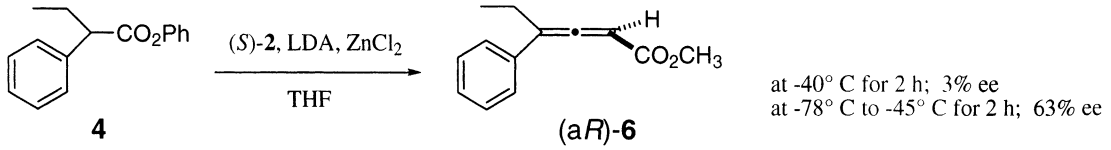
Both the rate and enantioselectivity of the reactions were then examined using the optimised (*S*)-**2**/LDA system (Scheme 4).

Thus, starting from a variety of the α,α-disubstituted phenyl acetates, the corresponding methyl allenecarboxylates were obtained in moderate to good yields, and these results are tabulated (Table 1). Generally, the same yields and levels of enantioselectivity as the previous BHT procedure were obtained, and in some cases improved selectivity was observed. The best e.e. of 89% was observed in the reaction of the benzyl and phenyl substituted derivative (entry 10).

For comparison, Table 1 also includes results of the reactions with (*S*)-**1** and (*S*)-**3** (entries 3 and 5). Moderately good e.e.s were achieved even where the difference in size between R^1 and R^2 was small (entries 7 and 8). The reaction time could be shortened to 2 h at −78 to −45°C without any significant effect on either the yield or the enantioselectivity of the reaction (entry 6).

E.e.s were determined by HPLC analysis on a chiral stationary phase and the absolute configuration of the products was assigned by comparison with specific rotation data in the literature and measurement of the CD spectra. The stereostructures of the products were in good agreement with the mechanistic consideration previously described with the same HWE reagents.[5c] Contrary to the α,α-disubstituted phenyl acetate, the α-monosubstituted phenyl ester is not a suitable starting material for this transformation (entry 1), probably due to instability of the intermediate ketene species.

Since LDA could be used for the generation of both anions, a one-pot procedure, in which all the substrates, reagents and additives were simultaneously added, was attempted. Using this protocol, allenecarboxylates were obtained in comparable yields with the procedure described above. The induction of enantioselectivity significantly in the one-pot reaction was found to be heavily dependent on the reaction temperature. Thus, a reaction carried out at −40°C for 2 hours afforded near racemic mixtures (with up to 3% e.e.), but a much higher e.e. was observed at −78 to −45°C over 2 hours (Scheme 5).



4 (aR)-6

Scheme 5.

3. Conclusion

In conclusion, we have developed a convenient and efficient one-flask procedure for the preparation of optically active allenecarboxylate from simple and readily available phenyl esters. This protocol is not only practical but also complementary to the previously reported BHT method, and therefore might lead to more extensive usage of allenecarboxylates as chiral synthons.

4. Experimental

4.1. General

Melting points are uncorrected. Nuclear magnetic resonance (NMR) spectra were taken at 200 or 270 MHz in $CDCl_3$ with chemical shifts being reported as δ ppm from tetramethylsilane as an internal standard and couplings are expressed in hertz. Infrared (IR) spectra were measured in $CHCl_3$ solution. Analytical and preparative HPLC was carried out using Shimadzu LC-10AT (Daicel chiral columns) and JAI LC-908 (direct connection of 1H and 2H columns) with hexane–*iso*-propanol and chloroform solvent systems, respectively. THF was distilled from sodium benzophenone ketyl and dichloromethane was distilled from calcium hydride. Unless otherwise noted, all reactions were run under an argon atmosphere. All extractive organic solutions were dried over anhydrous $MgSO_4$. Column chromatography was carried out with silica gel 60 (spherical, 150–325 mesh), and silica gel 60 F_{254} plates (Merck) were used for preparative TLC (pTLC).

4.2. Preparation of derivatives of phenyl acetate

4.2.1. α-Ethyl-benzeneacetic acid phenyl ester 4. To a stirred solution of 2-phenylbutanoic acid (5.00 g, 30.5 mmol), DCC (6.92 g, 33.6 mmol), DMAP (745 mg, 6.1 mmol) in CH_2Cl_2 (40 mL) was added a solution of phenol (36.6 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for a further 18 h at room temperature. The mixture was concentrated under reduced pressure, dissolved in AcOEt and filtered through a Celite pad. The filtrate was evaporated and subjected to column chromatography on silica gel (AcOEt:hexane = 1:9) to give α-ethyl-benzeneacetic acid phenyl ester (6.81 g, 93%). α-Ethyl-benzeneacetic acid phenyl ester **4**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3H, J = 7.3 Hz), 1.86–2.29 (m, 1H), 2.15–2.29 (m, 1H), 3.70 (t, 1H, J = 7.6 Hz), 6.96–7.43 (m, 10H).

4.2.2. Benzeneacetic acid phenyl ester 7. In the same way as above, benzeneacetic acid phenyl ester (4.7 g, 100%) was obtained from phenyl acetic acid (3.0 g, 22.0 mmol) and phenol (2.5 g, 26.6 mmol). Benzeneacetic acid phenyl ester **7**: pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 2H), 7.04–7.39 (m, 10H).

4.2.3. General procedure for the synthesis of alkylated esters: α-methyl-benzeneacetic acid phenyl ester 8. To a stirred solution of LDA (60 mL, 0.3 M in THF) was added dropwise a solution of benzeneacetic acid phenyl ester (1.9 g, 9.0 mmol) in THF (20 mL) at −78°C and the mixture was stirred for a further 30 min at the same temperature. Methyl iodide (5.6 mL, 90.0 mmol) and HMPA (15.6 mL, 90.0 mmol) were added and the mixture stirred for 18 h at the same temperature. The mixture was quenched by addition of 2N HCl and extracted with AcOEt. The extract was washed with brine, water and then dried. Concentration of the extract gave a residue, which was subjected to column chromatography on silica gel with AcOEt:hexane (1:20) as solvent system, to afford α-methyl-benzeneacetic acid phenyl ester **8** as a pale yellow oil (1.9 g, 93%); ^{1}H NMR ($CDCl_3$) δ 1.62 (d, 3H, J = 7.3 Hz), 3.97 (q, 1H, J = 7.3 Hz), 6.97–7.42 (m, 10H).

4.2.4. α-*iso*-Propyl-benzeneacetic acid phenyl ester 9. Using the same procedure for the preparation of **8**, α-*iso*-propyl-benzeneacetic acid phenyl ester **9** (514 mg, 22%) was obtained from benzeneacetic acid phenyl ester (1.9 g, 9.0 mmol) and *iso*-propyl iodide (7.8 mL, 45.0 mmol). α-Isopropyl-benzeneacetic acid phenyl ester **9**: pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.79 (d, 3H, J = 6.6 Hz), 1.19 (d, 3H, J = 6.6 Hz), 2.42–2.51 (m, 1H), 3.39 (d, 1H, J = 10.6 Hz), 6.97–7.43 (m, 10H); IR ($CHCl_3$) 3030, 2964, 2874, 1751, 1595, 1493, 1211, 1196, 1161, 1142 and 1111 cm^{-1}; MS (m/z) 255 (M^++H); HRMS (m/z) calcd for $C_{17}H_{19}O_2$ (M^++H) 255.1385, found: 255.1383.

4.2.5. α-Phenyl-cyclohexaneacetic acid phenyl ester 10. Using the same procedure for the preparation of **8**, α-phenyl-cyclohexaneacetic acid phenyl ester (1.2 g, 45%) was obtained from alkylation with cyclohexyl iodide (11.6 mL, 90.0 mmol). α-Phenyl-cyclohexaneacetic acid phenyl ester **10**: pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.81–2.16 (m, 11H), 3.46 (d, 1H, J = 10.6 Hz), 6.97–7.43 (m, 10H); IR ($CHCl_3$) 3032, 2932, 2854, 1750, 1595, 1493, 1211, 1196, 1161, 1142 and 1117 cm^{-1}; MS (m/z) 295 (M^++H); HRMS (m/z) calcd for $C_{20}H_{23}O_2$ (M^++H) 295.1698, found: 295.1700.

4.2.6. 2,3-Diphenylpropanoic acid phenyl ester 11. Using the same procedure for the preparation of **8**, ester **11** (1.9 g, 70%) was formed from benzeneacetic acid phenyl ester (1.9 g, 9.0 mmol) and benzyl bromide (10.7 mL, 90.0 mmol). 2,3-Diphenylpropanoic acid phenyl ester **11**: white crystals; mp 67–70°C; ^{1}H NMR ($CDCl_3$) δ 3.15 (dd, 1H, $J=6.3$, 13.9 Hz), 3.51 (dd, 1H, $J=9.3$, 13.9 Hz), 4.11 (dd, 1H, $J=6.3$, 9.3 Hz), 6.81–6.84 and 7.14–7.44 (m, 15H); IR ($CHCl_3$) 3032, 1753, 1595, 1493, 1194, 1163 and 1134 cm^{-1}. Anal. calcd for $C_{21}H_{18}O_2$: C, 83.44; H, 5.96. Found: C, 83.42; H, 5.97.

4.2.7. 1,2,3,4-Tetrahydro-1-naphthalenecarboxylic acid phenyl ester 13. To a stirred suspension of $Ph_3PCH_2OCH_3Cl$ in dry ether (40 mL) was added *n*-BuLi (6.0 mL, 1.66 M in hexane) and PhLi (27.0 mL, 0.88 M in ether) at −78°C and the reaction temperature was allowed to rise to 0°C for 1 h. After re-cooling to −78°C, α-tetralone (2.92 g, 20.0 mmol) in ether (15 mL) was added and the reaction mixture was stirred for 2 h at 0°C. The mixture was poured into ice-cold satd NH_4Cl solution and extracted with AcOEt. The extract was washed with water, brine, dried and then evaporated to give the residue. Chromatographic separation on silica gel (AcOEt:hexane = 1:45) afforded the crude enol-methyl ether (3.4 g, 97%). Enol-methyl ether: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.73–1.83 (m, 2H), 2.51 (t, 2H, $J=6.6$ Hz), 2.73 (t, 2H, $J=6.3$ Hz), 3.73 (s, 3H), 6.62 (s, 1H), 7.05–7.37 (m, 4H).

A mixture of the enol ether (3.4 g) and 98% HCO_2H (20 mL) was stirred for 10 h at room temperature. The reaction mixture was brought to pH 8.2 by addition of satd aq. $NaHCO_3$ solution and extracted with AcOEt. The extract was washed with water, brine and then dried. Concentration of the extract gave the residue, which was purified by column chromatography on silica gel with AcOEt:hexane (1:45) to give crude aldehyde (2.29 g). Further purification by preparative HPLC with chloroform yielded pure 1,2,3,4-tetrahydro-1-naphthalenecarboxaldehyde **12** (1.47 g, 47%). 1,2,3,4-Tetrahydro-1-naphthalenecarboxaldehyde **12**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.75–2.28 (m, 4H), 2.79 (t, 2H, $J=6.3$ Hz), 3.58–3.61 (m, 1H), 7.17–7.26 (m, 4H), 9.68 (d, 1H, $J=2.0$ Hz).

To a stirred solution of **12** (300 mg, 1.88 mmol) in acetone (3 mL) was added dropwise Jones reagent at 0°C until the orange colour of the mixture disappeared (within 5 min). The mixture was poured into ice-water and extracted with CH_2Cl_2. The organic layer was re-extracted with 5% NaOH solution and the aqueous phase was washed with AcOEt. The aqueous layer was acidified by addition of cold HCl solution and then extracted with CH_2Cl_2. The organic extract was washed with brine, dried and then concentrated under reduced pressure to leave the residue, which was purified by preparative HPLC to give 1,2,3,4-tetrahydro-1-naphthalenecarboxylic acid (288 mg, 85%). 1,2,3,4-Tetrahydro-1-naphthalenecarboxylic acid: white crystal; ^{1}H NMR ($CDCl_3$) δ 1.75–2.24 (m, 4H), 2.72–2.90 (m, 2H), 3.85 (t, 1H, $J=5.6$ Hz), 7.13–7.26 (m, 4H).

Compound **13** (1.36 g, 95%) was obtained from 1,2,3,4-tetrahydro-1-naphthalenecarboxylic acid (999 mg, 5.7 mmol) and phenol (643 mg, 6.84 mmol) in the same way as described above. 1,2,3,4-Tetrahydro-1-naphthalenecarboxylic acid phenyl ester **13**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.80–2.37 (m, 4H), 2.75–2.96 (m, 2H), 4.07 (t, 1H, $J=5.9$ Hz), 7.05–7.39 (m, 9H).

4.2.8. α-Ethyl-cyclohexaneacetic acid phenyl ester 14. Cyclohexaneacetic acid phenyl ester (4.0 g, 100%) was obtained from cyclohexaneacetic acid (2.6 mL, 18.1 mmol) and phenol (643 mg, 6.84 mmol) in a similar way to above. Cyclohexaneacetic acid phenyl ester: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.02–1.99 (m, 11H), 2.43 (d, 2H, $J=7.0$ Hz), 7.05–7.40 (m, 5H); IR ($CHCl_3$) 3029, 2928, 2855, 1749, 1595, 1493, 1217, 1213, 1196, 1161 and 1111 cm^{-1}; MS (m/z) 219 (M^++H); HRMS (m/z) calcd for $C_{14}H_{19}O_2$ (M^++H) 219.1385, found: 219.1379.

Using the same procedure for the preparation of **8**, **14** (407 mg, 30%) was obtained from cyclohexaneacetic acid phenyl ester (1.2 g, 5.5 mmol) and ethyl iodide (4.4 mL, 55.0 mmol). α-Ethyl-cyclohexaneacetic acid phenyl ester **14**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.03 (t, 3H, $J=7.3$ Hz), 1.05–1.91 (m, 13H), 2.32 (q, 1H, $J=7.9$ Hz), 7.05–7.41 (m, 5H); IR ($CHCl_3$) 2932, 2855, 1748, 1593, 1493, 1209, 1196, 1159 and 1127 cm^{-1}; MS (m/z) 247 (M^++H); HRMS (m/z) calcd for $C_{16}H_{23}O_2$ (M^++H) 247.1698, found: 247.1698.

4.2.9. α-*iso*-Propyl-cyclohexaneacetic acid phenyl ester 16. α-*iso*-Propyl-benzeneacetic acid methyl ester (2.2 g, 100%) was obtained from α-phenylacetic acid methyl ester (1.5 g, 10.0 mmol) and isopropyl iodide (10.0 mL, 100.0 mmol). α-*iso*-Propyl-benzeneacetic acid methyl ester: colourless oil; ^{1}H NMR ($CDCl_3$) δ 0.70 (d, 3H, $J=6.6$ Hz), 1.03 (d, 3H, $J=6.6$ Hz), 2.27–2.38 (m, 1H), 3.15 (d, 1H, $J=10.5$ Hz), 3.65 (s, 3H), 7.26–7.32 (m, 5H).

Catalytic hydrogenation of α-*iso*-propyl-benzeneacetic acid methyl ester (960 mg, 5.0 mmol) with 5% Rh/Al_2O_3 (455 mg) in *t*-BuOH (30 mL) was carried out under atmospheric pressure of hydrogen at room temperature for 50 h. The crude residue was purified by preparative HPLC to give α-*iso*-propyl-cyclohexaneacetic acid methyl ester **15** (988 mg, 100%). α-*iso*-Propyl-cyclohexaneacetic acid methyl ester **15**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 0.89 (d, 3H, $J=3.0$ Hz), 0.92 (d, 3H, $J=3.0$ Hz), 1.02–1.75 (m, 11H), 1.97–2.04 (m, 2H), 3.65 (s, 3H); IR ($CHCl_3$) 3029, 2932, 2855, 1746, 1595, 1493, 1219, 1211, 1192, 1157 and 1109 cm^{-1}.

A mixture of **15** (1.3 g, 6.6 mmol), CH_2Cl_2 (40 mL), BBr_3 (20.0 mL, 1.0 M in CH_2Cl_2) was stirred for 2 h at room temperature. The mixture was poured into ice-cold water and extracted with CH_2Cl_2. The organic layer was treated with 5% aq. NaOH solution and the aqueous solution was washed with AcOEt and then acidified with HCl solution. The aqueous layer was extracted with CH_2Cl_2 and washed with water, brine

and then dried. Concentration of the extract left α-*iso*-propyl-cyclohexaneacetic acid (560 mg, 46%). α-*iso*-Propyl-cyclohexaneacetic acid: colourless oil; ^{1}H NMR ($CDCl_3$) δ 0.95 (d, 3H, $J=3.3$ Hz), 0.97 (d, 3H, $J=3.3$ Hz), 1.03–1.76 (m, 11H), 2.00–2.07 (m, 2H). Esterification of the acid α-*iso*-propyl-cyclohexaneacetic acid (834 mg, 4.5 mmol) with phenol (508 mg, 5.4 mmol) was carried out to give **16** (1.00 g, 86%). α-*iso*-Propyl-cyclohexaneacetic acid phenyl ester **16**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 1.03 (d, 3H, $J=3.0$ Hz), 1.06 (d, 3H, $J=3.0$ Hz), 1.11–1.94 (m, 11H), 2.11–2.19 (m, 1H), 2.28 (t, 1H, $J=7.6$ Hz), 7.05–7.41 (m, 5H); IR ($CHCl_3$) 3029, 2932, 2855, 1746, 1595, 1493, 1219, 1211, 1192, 1157 and 1109 cm^{-1}; MS (*m*/*z*) 261 (M^++H); HRMS (*m*/*z*) calcd for $C_{17}H_{25}O_2$ (M^++H) 261.1854, found: 261.1852.

4.2.10. 2-Methyl-3-phenylpropanoic acid phenyl ester 17. Esterification of 3-phenylpropanoic acid (1.5 g, 10.0 mmol) with phenol (1.1 g, 12.0 mmol) was completed as above and afforded benzenepropanoic acid phenyl ester (2.3 g, 100%).

Benzenepropanoic acid phenyl ester: colourless oil; ^{1}H NMR ($CDCl_3$) δ 2.89 (t, 2H, $J=6.9$ Hz), 3.08 (t, 2H, $J=6.9$ Hz), 6.99–7.39 (m, 5H). Using the same procedure for the preparation of **8**, benzenepropanoic acid phenyl ester (1.36 g, 6.0 mmol) and methyl iodide (3.7 mL, 60.0 mmol) afforded **17** (1.22 g, 84%). 2-Methyl-3-phenylpropanoic acid phenyl ester **17**: pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.33 (d, 3H, $J=6.6$ Hz), 2.83 (q, 1H, $J=6.9$ Hz), 2.94–3.07 (m, 1H), 3.14 (q, 1H, $J=7.6$ Hz), 6.91–7.37 (m, 5H); IR ($CHCl_3$) 3030, 2936, 1752, 1595, 1493, 1219, 1213, 1194, 1163 and 1144 cm^{-1}; MS (*m*/*z*) 241 (M^++H); HRMS (*m*/*z*) calcd for $C_{16}H_{17}O_2$ (M^++H) 241.1228, found: 241.1234.

4.3. Competitive experiment between methyl and phenyl esters

A solution of LiTMP (1.0 mL in THF, 1.06 M) was added dropwise to the stirred solution of methyl- (**5**, 60 mg, 0.25 mmol) and phenyl-2-phenylbutanoate **4** (44.5 mg, 0.25 mmol) in THF (2 mL) at −78°C under Ar and the mixture was stirred for 0.5 h at the same temperature. To this stirred mixture was added a solution of bis(2,2,2 - trifluoroethyl)(methoxycarbonylmethyl)phosphonate (160 mg, 0.50 mmol) in THF (1.0 mL) and the resulting mixture was stirred for 20 min at the same temperature. After addition of a solution of $ZnCl_2$ (1.45 mL, 0.73 M in ether) and stirring for 10 min at the same temperature, the cooling bath was removed and the reaction temperature was allowed to rise from −78°C to room temperature for 4 h with stirring. The reaction mixture was poured into cold dil. HCl and extracted with AcOEt. The organic phase was washed with brine, dried and then evaporated to give the residual mixture. Separation by pTLC with hexane:AcOEt (15:1) gave allenic product **6** (22.3 mg, 44%) together with the recovered methyl ester **5** (43.5 mg, 98%) and phenyl ester **4** (23.5 mg, 39%).

4.4. General procedure for the preparation of optically active methyl allenecarboxylates

The phenyl ester (0.7 mmol) in THF (2 mL) was treated with LDA (0.7 mmol) in THF at −78°C for 1 h under Ar. This was treated with a solution of freshly prepared $ZnCl_2$ (0.7 M in THF, 1.0 mmol) and the mixture was stirred for 5 min at the same temperature. The anion of the HWE reagent (0.7 mmol in 2 mL of THF) was prepared by treatment of LDA (0.7 mmol) in THF at −78°C for 1 h under Ar in a separate vessel, and then transferred to the above solution of ketene. The reaction mixture was stirred initially at −78°C and then allowed to warm to room temperature over 18 h under Ar with stirring. The usual work-up and purification of the residue by pTLC or preparative HPLC afforded pure allenecarboxylate in the yields shown in Table 1.

4.4.1. (a*R*)-(−)-4-Phenyl-2,3-hexadienoic acid methyl ester 6[3]. Yellow oil; $[\alpha]_D^{24}$ −173 (*c* 1.9, CCl_4) (Ref. 3 $[\alpha]_D^{25}$ −225 (*c* 5.0, CCl_4)); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 88%; ^{1}H NMR ($CDCl_3$) δ 1.18 (t, 3H, $J=7.3$ Hz), 2.54–2.60 (m, 2H), 3.76 (s, 3H), 5.98 (t, 1H, $J=3.3$ Hz), 7.26–7.40 (m, 5H).

4.4.2. (a*R*)-(−)-4-Phenyl-2,3-pentadienoic acid methyl ester 18[3]. Yellow oil; $[\alpha]_D^{24}$ −200 (*c* 1.1, CCl_4); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 77%; ^{1}H NMR ($CDCl_3$) δ 2.21 (d, 3H, $J=3.0$ Hz), 3.75 (s, 3H), 5.91 (q, 1H, $J=3.0$ Hz), 6.97–7.41 (m, 5H).

4.4.3. (a*S*)-(+)-5-Methyl-4-phenyl-2,3-hexadienoic acid methyl ester 19. Yellow oil; $[\alpha]_D^{23}$ +161 (*c* 2.3, $CHCl_3$); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 88%; ^{1}H NMR ($CDCl_3$) δ 1.15–1.19 (dd, 6H, $J=2.3$, 6.6 Hz), 2.89–2.95 (m, 1H), 3.75 (s, 3H), 5.93–5.94 (d, 1H, $J=2.6$ Hz), 7.26–7.37 (m, 5H). IR ($CHCl_3$) 2965, 1945, 1721, 1449, 1255, and 1148 cm^{-1}; MS (*m*/*z*) 216 (M^+), 201; HRMS (*m*/*z*) calcd for $C_{14}H_{16}O_2$ (M^+) 216.1149, found: 216.1137. Anal. calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.45. Found: C, 77.68; H, 7.38%.

4.4.4. (a*S*)-(+)-4-Cyclohexyl-4-phenyl-2,3-butadienoic acid methyl ester 20. White powder; $[\alpha]_D^{31}$ +102 (*c* 2.8, $CHCl_3$); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 83%; ^{1}H NMR ($CDCl_3$) δ 1.19–2.04 (m, 10H), 2.51–2.58 (m, 1H), 3.75 (s, 3H), 5.92 (d, 1H, $J=2.3$ Hz), 7.26–7.36 (m, 5H). IR ($CHCl_3$) 2927, 1944, 1723, 1449, 1150, 1034, 831, 767 and 695 cm^{-1}; MS (*m*/*z*) 256 (M^+), 197; HRMS (*m*/*z*) calcd for $C_{17}H_{20}O_2$ (M^+) 256.1462, found: 256.1450. Anal. calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.59; H, 7.95%.

4.4.5. (a*R*)-(−)-3-(3,4-Dihydro-1(2*H*)-naphthalenylidene)-2-propenoic acid methyl ester 21[3]. Yellow oil; $[\alpha]_D^{31}$ −110 (*c* 1.9, CCl_4); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 89%; ^{1}H NMR ($CDCl_3$) δ 1.88–2.86 (m, 6H), 3.75 (s, 3H), 5.94 (t, 1H, $J=3.0$ Hz), 7.06–7.39 (m, 4H).

4.4.6. (a*R*)-(−)-4,5-Diphenyl-2,3-pentadienoic acid methyl ester 22. Yellow oil; $[\alpha]_D^{24}$ −155 (*c* 3.0, $CHCl_3$); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 89%; ^1H NMR ($CDCl_3$) δ 3.76 (s, 3H), 3.88 (s, 2H), 5.87 (t, 1H, J = 2.6 Hz), 7.20–7.41 (m, 10H); IR ($CHCl_3$) 3029, 2953, 1948, 1717, 1221, 1211 and 1163 cm^{-1}; MS (*m*/*z*) 264 (M^+); HRMS (*m*/*z*) calcd for $C_{18}H_{16}O_2$ (M^+) 264.1150, found: 264.1155.

4.4.7. (a*R*)-(−)-4-Ethyl-4-cyclohexyl-2,3-butadienoic acid methyl ester 23. Yellow oil; $[\alpha]_D^{24}$ −53 (*c* 1.0, CCl_4); HPLC (Chiralpak AD. 0.5% *iso*-propanol/hexane), e.e. = 78%; ^1H NMR ($CDCl_3$) δ 1.02 (t, 3H, J = 7.3 Hz), 1.09–1.86 (m, 11H), 2.06–2.14 (m, 2H), 3.72 (s, 3H), 5.63 (q, 1H, J = 3.3 Hz); IR ($CHCl_3$) 2932, 2857, 1954, 1709, 1267, 1219 and 1161 cm^{-1}; MS (*m*/*z*) 208 (M^+); HRMS (*m*/*z*) calcd for $C_{13}H_{20}O_2$ (M^+) 208.1463, found: 208.1456.

4.4.8. (a*R*)-(−)-4-Methyl-5-phenyl-2,3-pentadienoic acid methyl ester 24. Yellow oil; $[\alpha]_D^{24}$ −19 (*c* 0.15, $CHCl_3$); HPLC (Chiralpak AS. 0.5% *iso*-propanol/hexane), e.e. = 32%; ^1H NMR ($CDCl_3$) δ 1.74 (d, 3H, J = 2.6 Hz), 3.40 (d, 2H, J = 2.0 Hz), 3.74 (s, 3H), 5.52 (q, 1H, J = 2.6 Hz), 7.20–7.34 (m, 5H); IR ($CHCl_3$) 3029, 2926, 1966, 1709, 1269, 1211 and 1163 cm^{-1}; MS (*m*/*z*) 202 (M^+); HRMS (*m*/*z*) calcd for $C_{13}H_{14}O_2$ (M^+) 202.0994, found: 202.0995.

4.5. General procedure for one-pot preparation of methyl allenecarboxylates

To a stirred solution of the phenyl ester (0.7 mmol), the HWE reagent (0.7 mmol), and $ZnCl_2$ (0.7 M solution in THF, 1.0 mmol) in THF (4 mL) was added LDA in THF (1.4 mmol) at −78°C under Ar. The reaction mixture was stirred for 2 h. During this period of time, the reaction temperature was allowed to rise from −78 to −45°C. The reaction mixture was quenched by the addition of satd NH_4Cl solution, and then worked-up in the usual manner to give the residue, which was purified by pTLC or preparative HPLC.

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