electronic supplementary information

Design of bifunctional chiral phenanthroline ligand with Lewis basic site for palladium-catalyzed asymmetric allylic substitution

Yuki Naganawa,*[a,b] Hiroki Abe[a] and Hisao Nishiyama*[a]

[a]Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa, Nagoya 464-8603, Japan
[b]Interdisciplinary Research Center for Catalytic Chemistry, National Insutitute of Advanced Industrial Science and Technology, Tsukuba 305-8565, Japan

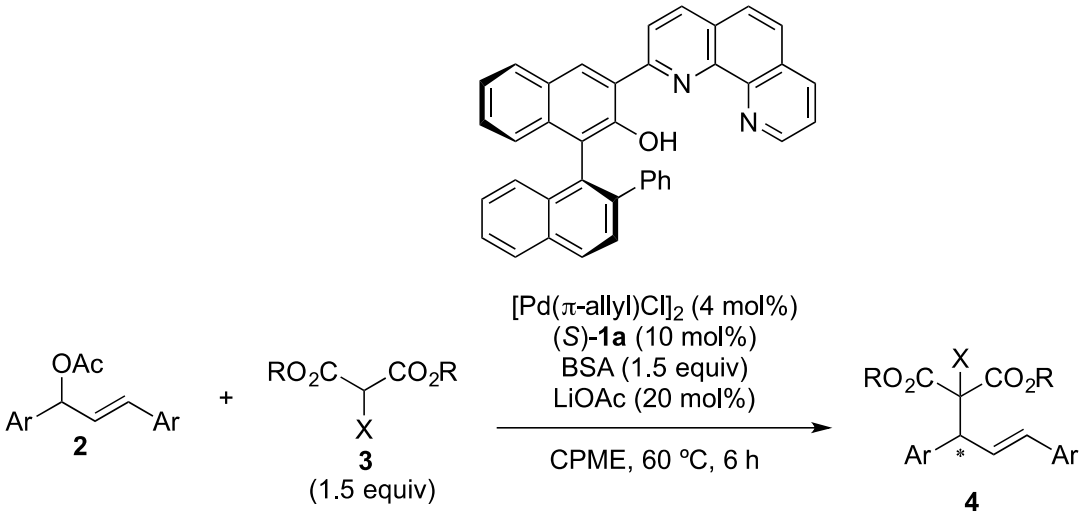
General Information.

Infrared (IR) spectra were recorded on a JASCO FT/IR-230 spectrometer. ^{1}H NMR spectra were measured at 25 ˚C on a Varian Mercury 300 (300 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, ddd = double-double-doublet, dt =double-triplet, m = multiplet, br = broad, and app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured at 25 ˚C on a Varian Mercury 300 (75 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed carried out on a JASCO GULLIVER 1500 series using 4.6 mm x 25 cm Daicel Chiral Columns. High-resolution mass spectra (HRMS) were performed on a double-focusing magnetic sector mass spectrometer JEOL JMS-700. For thin layer chromatography (TLC) analysis throughout this work, TLC Silica gel 60 F_{254} were used. The products were purified by flash column chromatography on silica gel 60 N (Kanto, 60-210 μm).

In experiments requiring dry solvent, CH_2Cl_2 and DMF were purchased from Wako Pure Chemical Industry as “Dehydrated”. CPME was purchased from Sigma-Aldrich as “Dehydrated”. Toluene and THF were purchased from Kanto Chemical as “Dehydrated” and further purified by passing through neutral alumina under nitrogen atmosphere. (*S*)-**1** were prepared according to our previous reports.[S1] Allyl acetates **2** were synthesized according to the literature.[S2] Other commercially available chemicals were purchased and used as received.

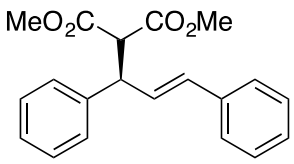
(S1) a) Y. Naganawa, T. Namba, T. Aoyama, K. Shoji, H. Nishiyama, H. *Chem. Commun*. **2014**, *50*, 13224; b) Y. Naganawa, H. Abe, H. Nishiyama *Synlett* **2016**, *27*, 1973.
(S2) I. D. G. Watson, S. A. Styler, A. K. Yudin, *J. Am. Chem. Soc.* **2004**, *126*, 5086.

·General procedure for asymmetric allylic substitution of 2 and 3.



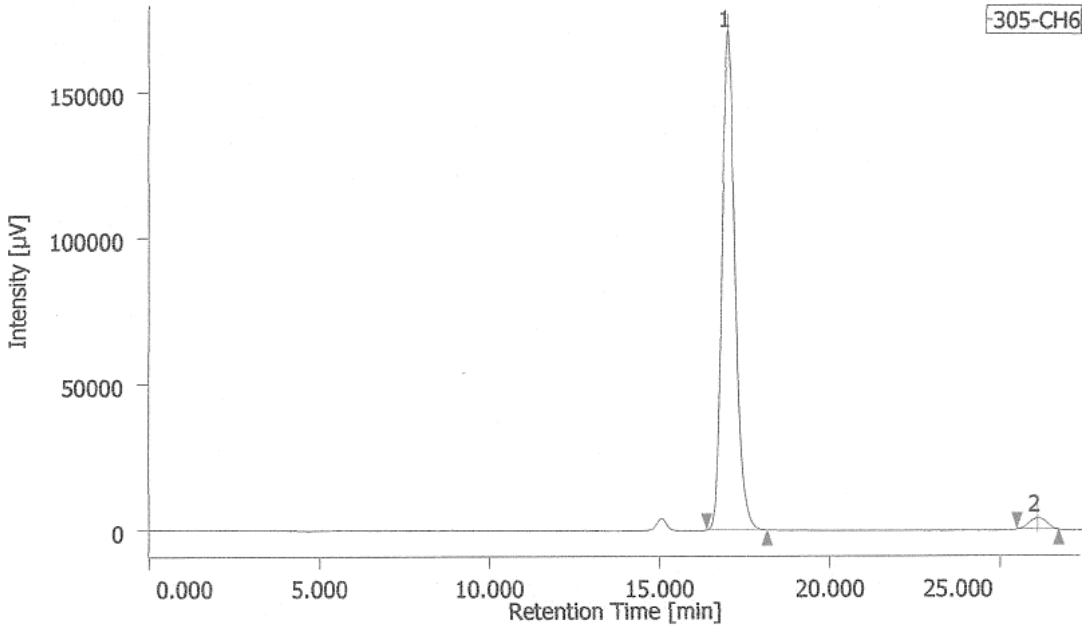
A solution of (*S*)-**1a** (5.25 mg, 0.01 mmol), [Pd(π-allyl)Cl]$_2$ (2.48 mg, 0.004 mmol), allyl acetate **2** (0.1 mmol), dialkyl malonate **3** (0.15 mmol) and LiOAc (1.44 mg, 0.02 mmol) in CPME (1.0 mL) was stirred at 60 °C for 1 h. Then, BSA (50 μL, 0.15 mmol) was added to this solution. After stirring for the additional 6 h, the reaction mixture was evaporated and the residue was purified by silica gel column chromatography with hexane and EtOAc (10:1) to give **4**.

Dimethyl (*R*,*E*)-2-(1,3-diphenylallyl)malonate (4a).



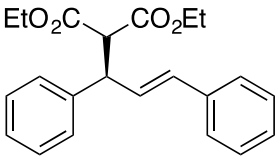
Colorless oil: 22.7 mg, 70% yield
The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* **2015**, *71*, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 17.0 min (*R*) and 26.1 min (*S*)). [e.r. = 96.9/3.1][e.e. = 94%]



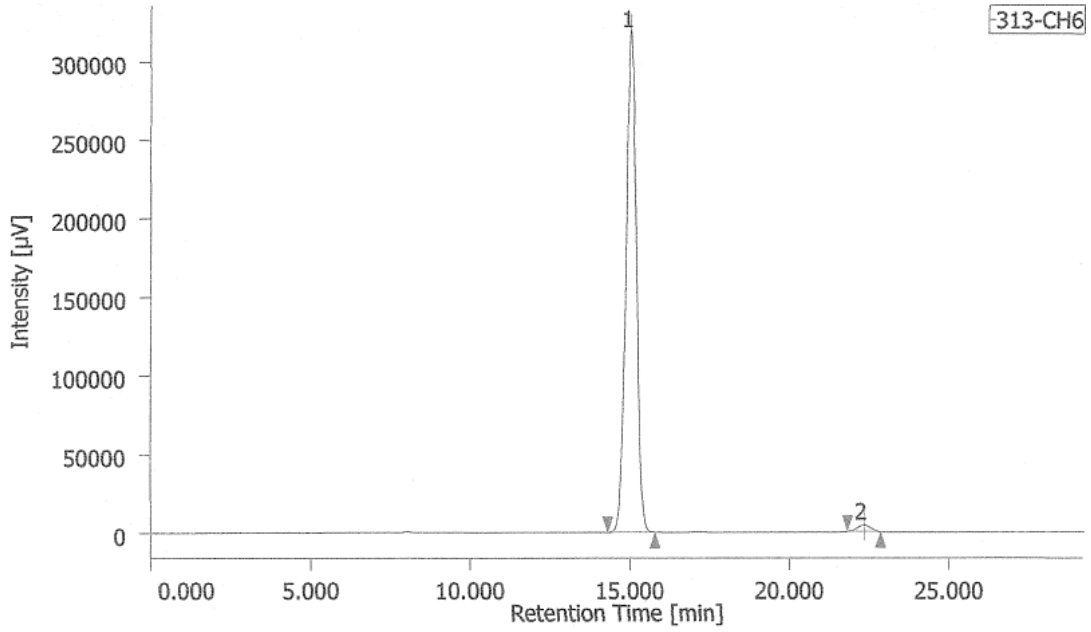
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	16.957	4570726	171650	96.904	97.714
2	26.070	146029	4016	3.096	2.286

Diethyl (*R*,*E*)-2-(1,3-diphenylallyl)malonate (4b).



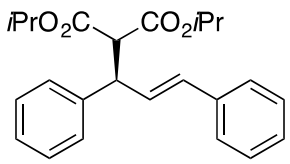
Colorless oil: 20.1 mg, 57% yield
The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* **2015**, *71*, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 15.0 min (*R*) and 22.3 min (*S*)). [e.r. = 98.2/1.8][e.e. = 96%]



#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	15.000	7346849	319560	98.154	98.638
2	22.307	138170	4414	1.846	1.362

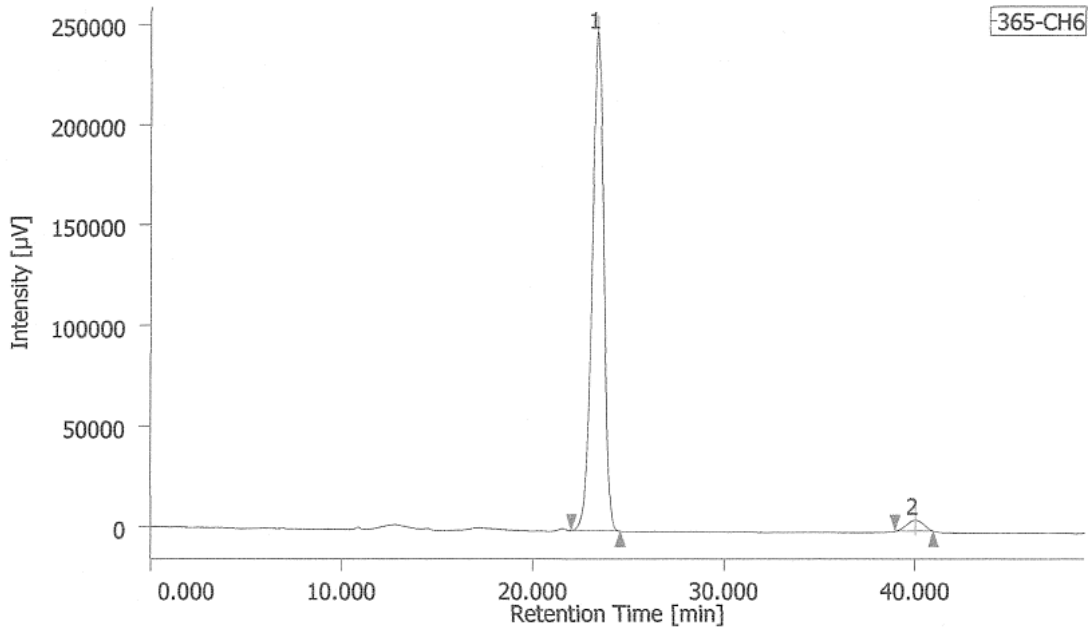
Diisopropyl (*R*,*E*)-2-(1,3-diphenylallyl)malonate (4c).



Colorless oil: 24.0 mg, 63% yield

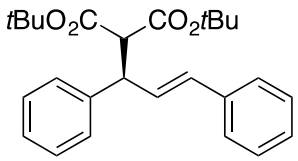
The detailed spectral data has been reported in the following literature: H.-G. Cheng, B. Feng, L.-Y. Chen, W. Guo, X.-Y. Yu, L.-Q. Lu, J.-R. Chen, W.-J. Xiao, *Chem. Commun.* **2014**, *50*, 2873.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 23.4 min (*R*) and 40.0 min (*S*)). [e.r. = 96.8/3.2][e.e. = 94%]



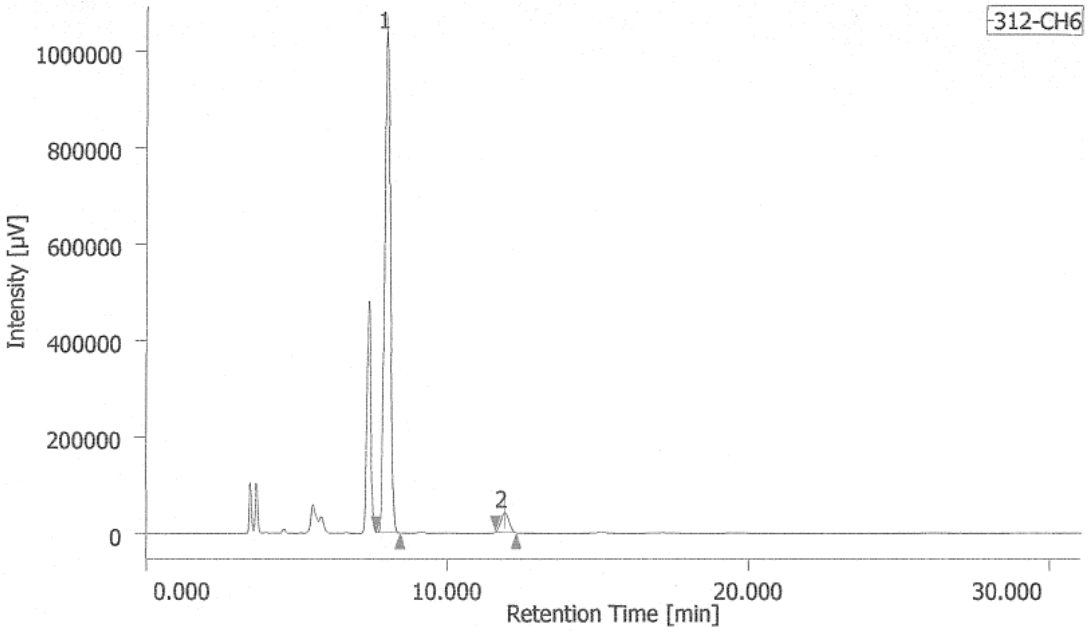
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	23.363	10436801	248307	96.833	97.850
2	39.988	341311	5457	3.167	2.150

Di-*tert*-butyl (*R*,*E*)-2-(1,3-diphenylallyl)malonate (4d).



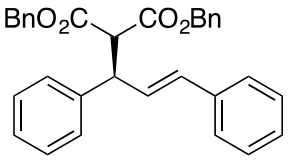
Colorless oil: 21.2 mg, 52% yield
The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* **2015**, *71*, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 8.0 min (*R*) and 11.9 min (*S*)). [e.r. = 94.7/5.3][e.e. = 89%]



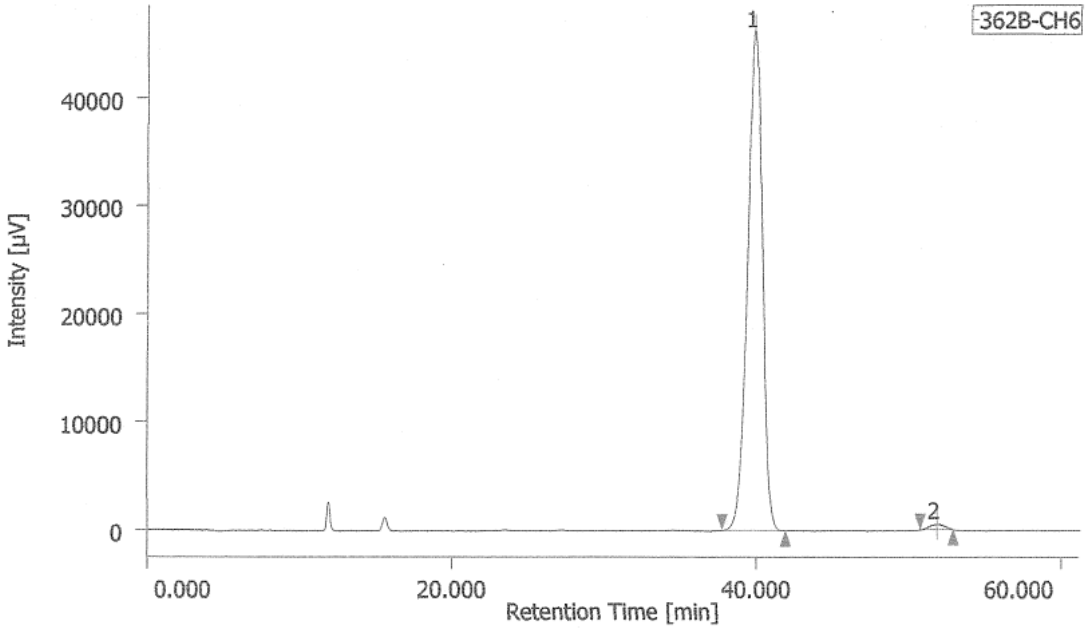
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	7.995	13672886	1039919	94.726	96.259
2	11.890	761185	40416	5.274	3.741

Dibenzyl (*R*,*E*)-2-(1,3-diphenylallyl)malonate (4e).



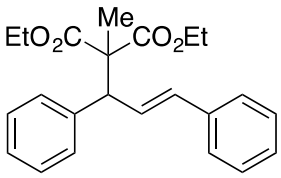
Colorless oil: 29.5 mg, 62% yield
The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* **2015**, *71*, 5985.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 0.5 mL/min, retention time; 39.8 min (*R*) and 51.8 min (*S*)). [e.r. = 98.9/1.1][e.e. = 98%]



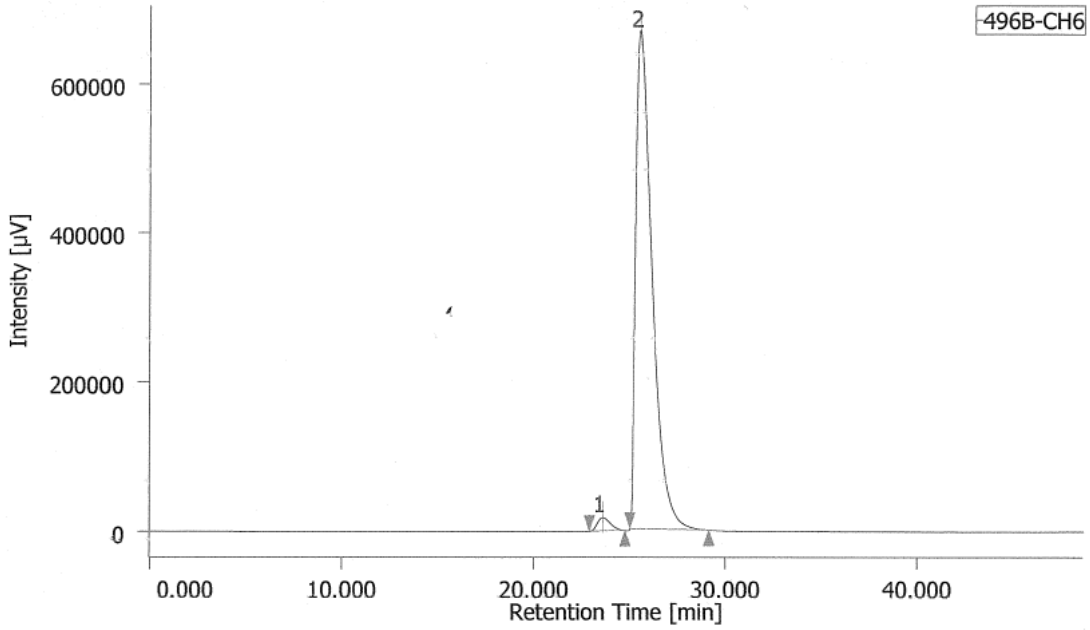
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	39.820	3152200	46363	98.905	98.927
2	51.815	34909	503	1.095	1.073

Diethyl (*E*)-2-(1,3-diphenylallyl)-2-methylmalonate (4f).



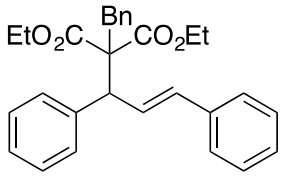
Colorless oil: 23.8 mg, 65% yield
The detailed spectral data has been reported in the following literature: T. Mino, M. Asakawa, Y. Shima, H. Yamada, F. Yagishita, M. Sakamoto, *Tetrahedron* **2015**, *71*, 5985.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 99/1, flow rate = 0.5 mL/min, retention time; 23.6 min (*minor*) and 25.5 min (*major*)). [e.r. = 2.2/97.8][e.e. = 96%]



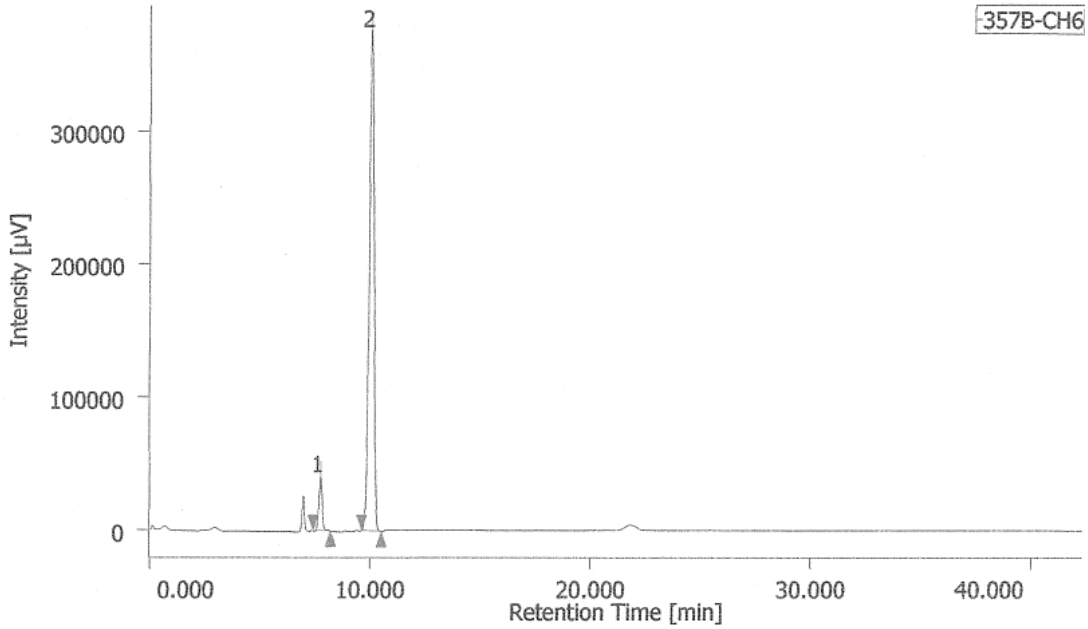
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	23.562	879889	18305	2.160	2.668
2	25.508	39847230	667817	97.840	97.332

Diethyl (*E*)-2-benzyl-2-(1,3-diphenylallyl)malonate (4g).



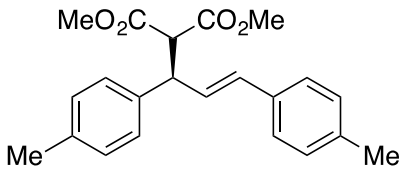
Colorless oil: 26.1 mg, 59% yield
The detailed spectral data has been reported in the following literature: Z. Liu, H. Du, *Org. Lett.* **2010**, *12*, 3054.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 95/5, flow rate = 1.0 mL/min, retention time; 7.8 min (*minor*) and 10.0 min (*major*)). [e.r. = 7.8/92.9][e.e. = 86%]



#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	7.765	431348	40244	7.088	9.647
2	10.035	5654649	376930	92.912	90.353

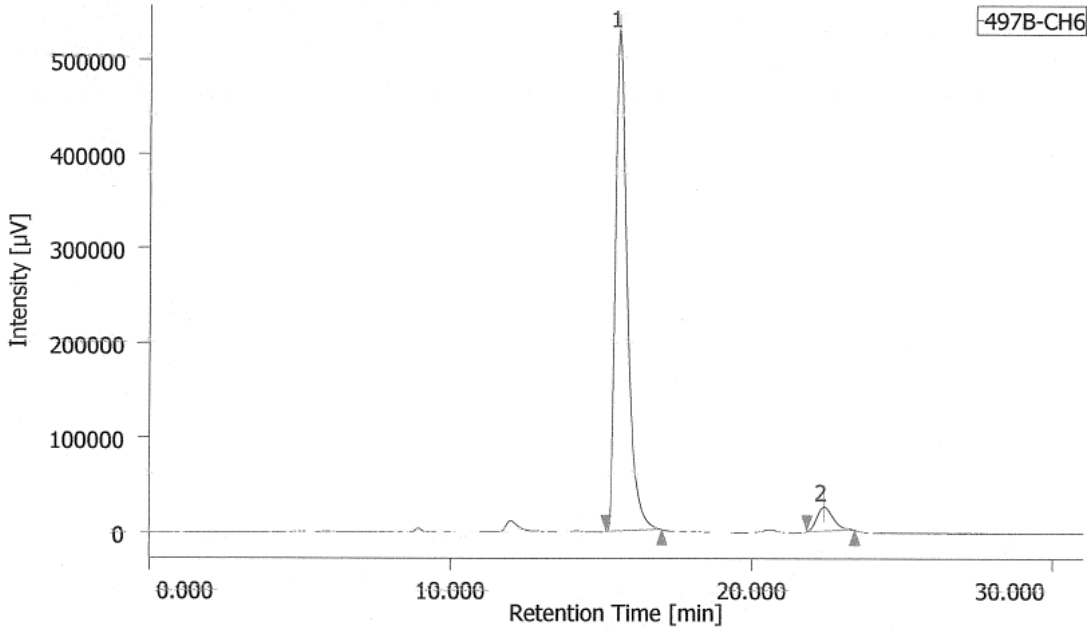
Dimethyl (*R*,*E*)-2-(1,3-di-*p*-tolylallyl)malonate (4h).



Colorless oil: 19.4 mg, 55% yield

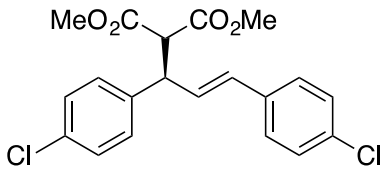
The detailed spectral data has been reported in the following literature: H.-G. Cheng, B. Feng, L.-Y. Chen, W. Guo, X.-Y. Yu, L.-Q. Lu, J.-R. Chen, W.-J. Xiao, *Chem. Commun.* **2014**, *50*, 2873.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 15.6 min (*R*) and 22.4 min (*S*)). [e.r. = 93.6/6.4][e.e. = 87%]



#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	15.558	14551569	529692	93.646	95.364
2	22.378	987351	25748	6.354	4.636

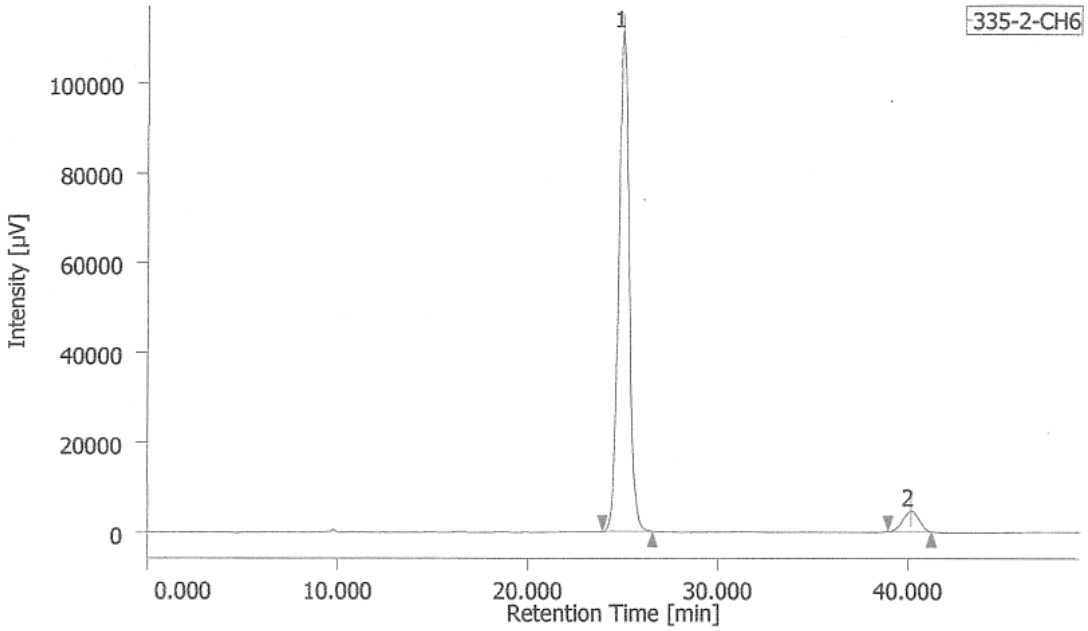
Dimethyl (*R*,*E*)-2-(1,3-bis(4-chlorophenyl)allyl)malonate (4i).



Colorless oil: 24.8 mg, 63% yield

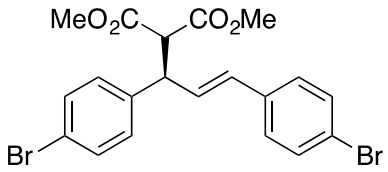
The detailed spectral data has been reported in the following literature: H.-G. Cheng, B. Feng, L.-Y. Chen, W. Guo, X.-Y. Yu, L.-Q. Lu, J.-R. Chen, W.-J. Xiao, *Chem. Commun.* **2014**, *50*, 2873.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 24.9 min (*R*) and 40.1 min (*S*)). [e.r. = 94.0/6.0][e.e. = 88%]



#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	24.937	4325962	111354	94.013	96.108
2	40.132	275491	4510	5.987	3.892

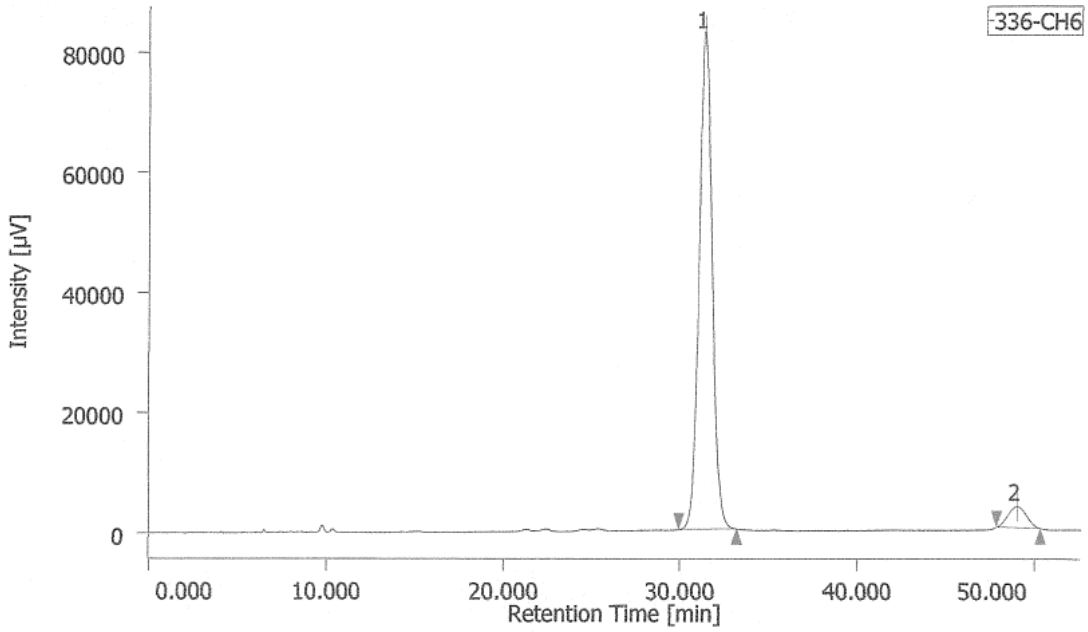
Dimethyl (*R*,*E*)-2-(1,3-bis(4-bromophenyl)allyl)malonate (4j).



Colorless oil: 32.3 mg, 67% yield

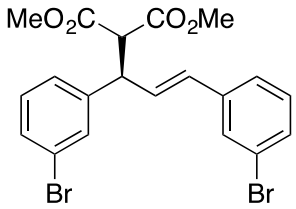
The detailed spectral data has been reported in the following literature: H.-G. Cheng, B. Feng, L.-Y. Chen, W. Guo, X.-Y. Yu, L.-Q. Lu, J.-R. Chen, W.-J. Xiao, *Chem. Commun.* **2014**, *50*, 2873.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPACK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 31.3 min (*R*) and 49.0 min (*S*)). [e.r. = 94.2/5.8][e.e. = 88%]



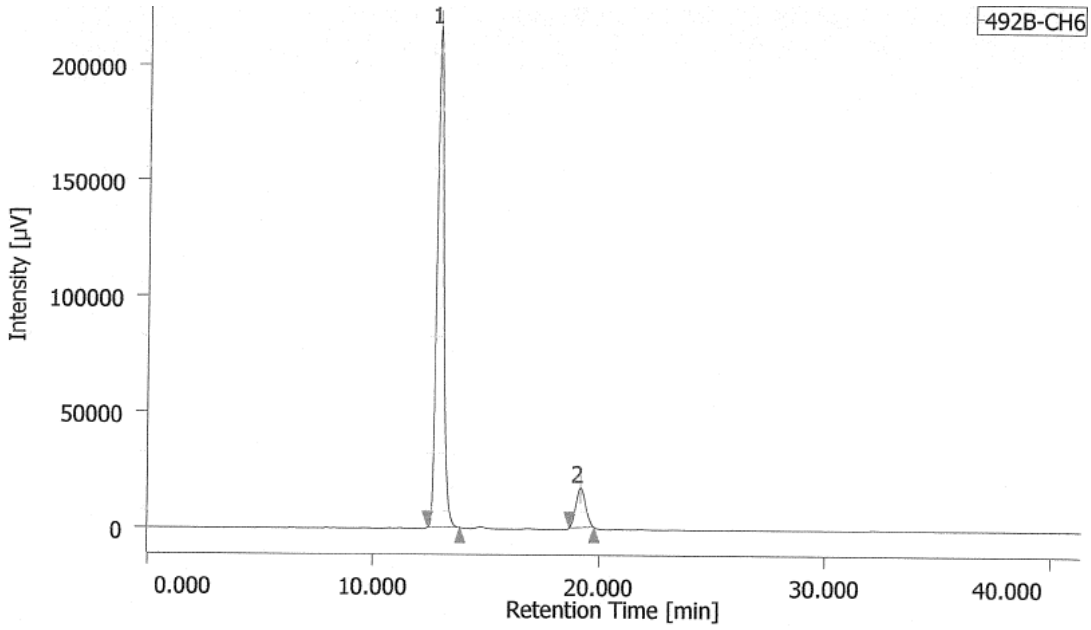
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	31.338	4164831	82821	94.223	95.838
2	48.997	255365	3597	5.777	4.162

Dimethyl (*R*,*E*)-2-(1,3-bis(3-bromophenyl)allyl)malonate (4k).



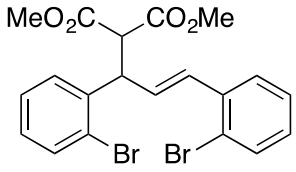
Colorless oil: 13.0 mg, 27% yield
The detailed spectral data has been reported in the following literature: K. Balaraman, R. Vasanthan, V. Kesavan, *Tetrahedron* **2013**, *69*, 6162.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPACK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 12.9 min (*major*) and 19.2 min (*minor*)). [e.r. = 90.0/10.0][e.e. = 80%]



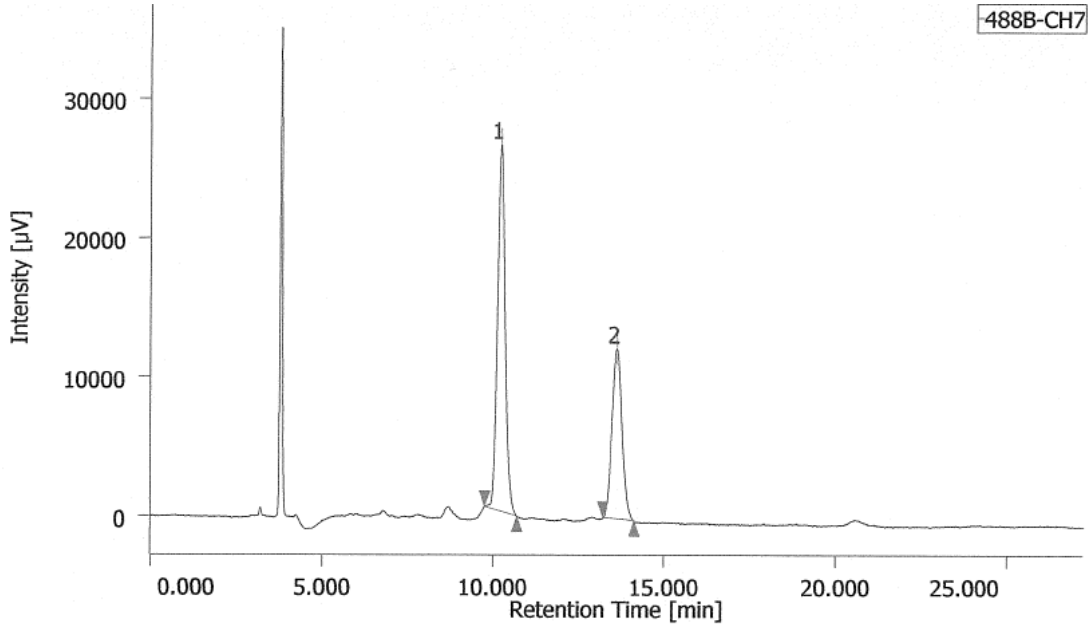
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	12.865	4589286	216268	90.022	92.685
2	19.165	508669	17067	9.978	7.315

Dimethyl (*E*)-2-(1,3-bis(2-bromophenyl)allyl)malonate (4l).



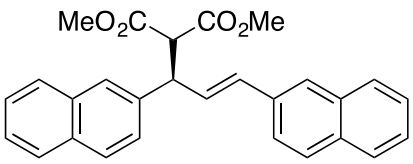
Colorless oil: 3.9 mg, 8% yield
The detailed spectral data has been reported in the following literature: A.-P. Xing, Z.-B. Pang, H.-F. Li, L.-L. Wang, *Tetrahedron* **2014**, *70*, 8822.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 10.2 min (*major*) and 13.6 min (*minor*)). [e.r. = 62.7/37.4][e.e. = 25%]



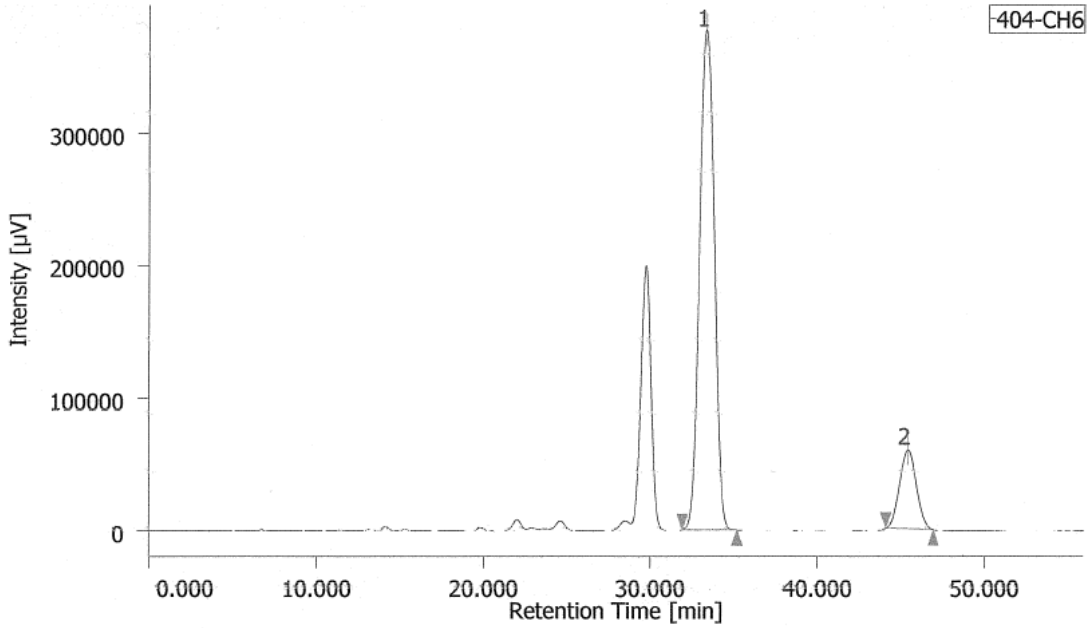
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	10.212	417744	26382	62.662	68.293
2	13.608	248919	12249	37.338	31.707

Dimethyl (*R*,*E*)-2-(1,3-di(naphthalen-2-yl)allyl)malonate (4m).



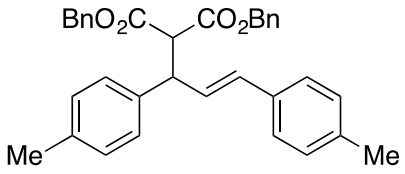
Colorless oil: 16.1 mg, 38% yield
The detailed spectral data has been reported in the following literature: K. Balaraman, R. Vasanthan, V. Kesavan, *Tetrahedron* **2013**, *69*, 6162.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 33.3 min (*S*) and 45.4 min (*R*)). [e.r. = 85.0/15.0][e.e. = 70%]



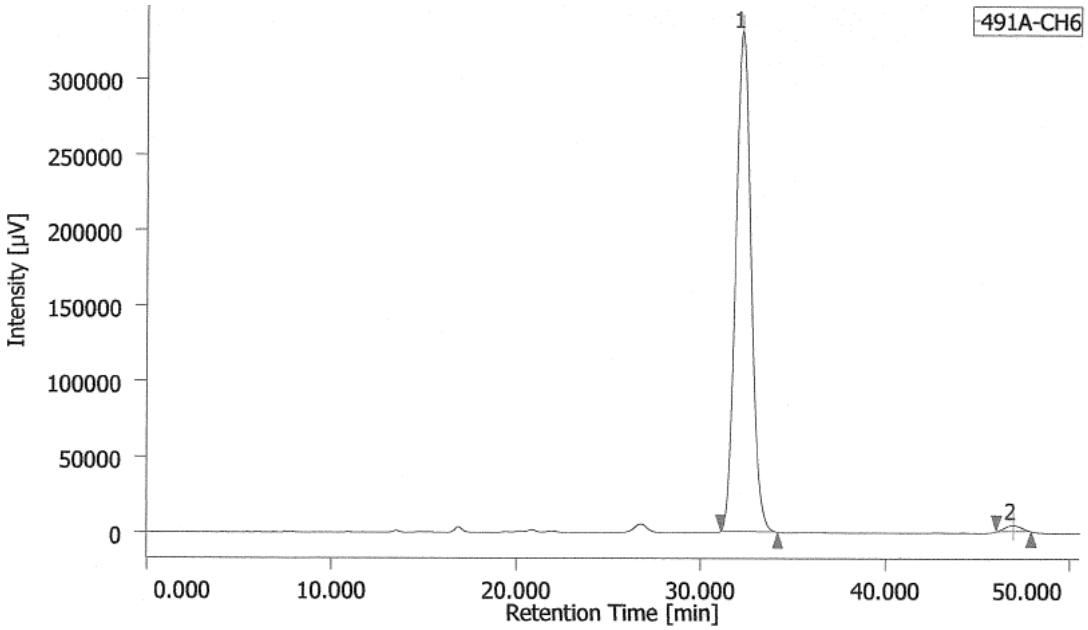
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	33.322	23313446	377953	84.967	86.360
2	45.385	4124728	59694	15.033	13.640

Dibenzyl (*E*)-2-(1,3-di-*p*-tolylallyl)malonate (4n).



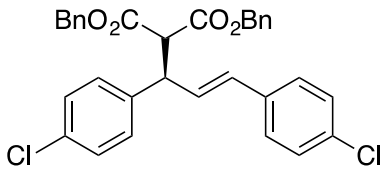
Colorless oil: 30.2 mg, 60% yield
The detailed spectral data has been reported in the following literature: A.-P. Xing, Z.-B. Pang, H.-F. Li, L.-L. Wang, *Tetrahedron* **2014**, *70*, 8822.

The isolation condition was determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min, retention time; 32.2 min (*major*) and 46.9 min (*minor*)). [e.r. = 98.6/1.4][e.e. = 97%]



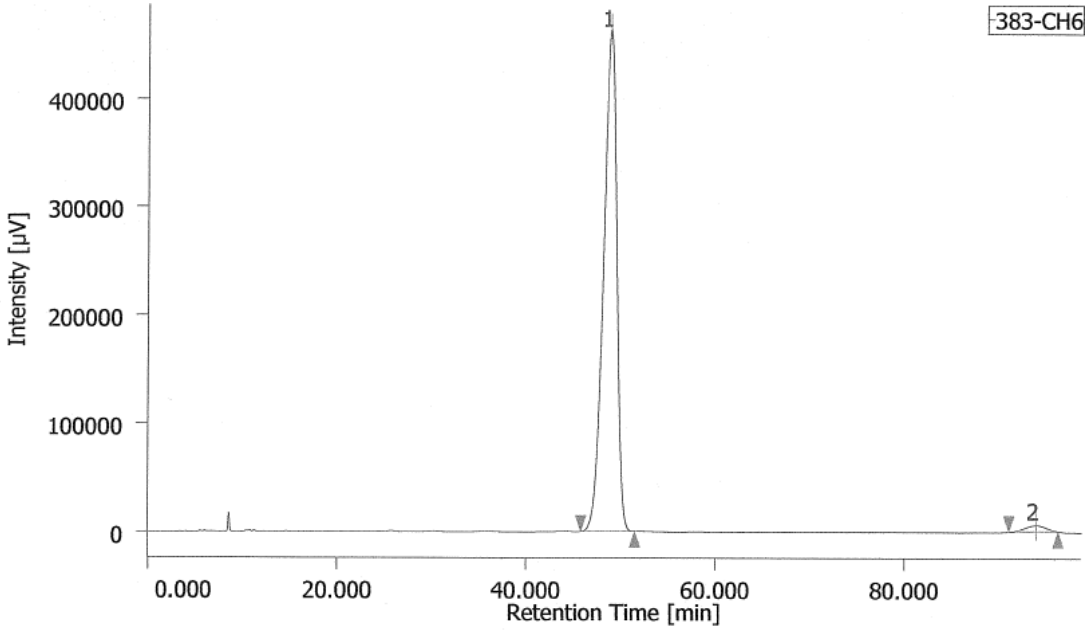
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	32.197	19057870	331384	98.589	98.728
2	46.903	272668	4270	1.411	1.272

Dibenzyl (*R*,*E*)-2-(1,3-bis(4-chlorophenyl)allyl)malonate (4o).



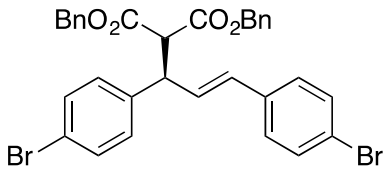
Colorless oil: 31.6 mg, 58% yield
The detailed spectral data has been reported in the following literature: Y. Jin, D.-M. Du, *Tetrahedron* **2012**, *68*, 3633.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK IA, hexane/*i*PrOH = 8/2, flow rate = 1.0 mL/min, retention time; 48.8 min (*R*) and 93.9 min (*S*)). [e.r. = 97.8/2.2][e.e. = 96%]



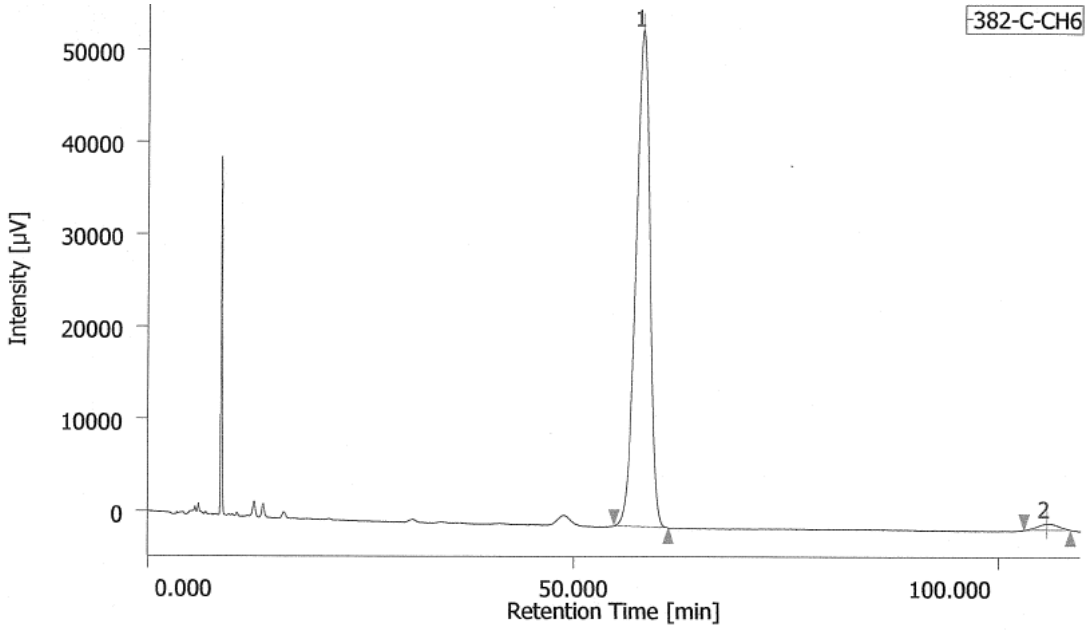
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	48.782	44920315	463648	97.828	98.681
2	93.852	997260	6199	2.172	1.319

Dibenzyl (*R*,*E*)-2-(1,3-bis(4-bromophenyl)allyl)malonate (4p).



Colorless oil: 40.0 mg, 63% yield
The detailed spectral data has been reported in the following literature: Y. Jin, D.-M. Du, *Tetrahedron* **2012**, *68*, 3633.

The absolute configuration and isolation condition were determined in reference to the same literature. The enantiomeric purity of the product was determined by HPLC analysis (Daicel CHIRALPAK AD-H, hexane/*i*PrOH = 8/2, flow rate = 1.0 mL/min, retention time; 58.1 min (*R*) and 105.6 min (*S*)). [e.r. = 98.0/2.0][e.e. = 96%]



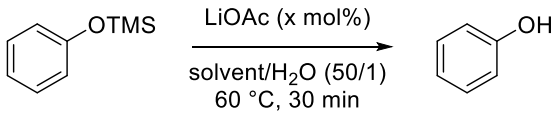
#	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%
1	58.053	6193051	53847	97.983	98.625
2	105.612	127503	751	2.017	1.375

·Supporting information about mechanistic studies.

1) Investigation of desilylation of aryl silyl ether by LiOAc in CPME

We carried out reproductive experiments of LiOAc-catalyzed desilylation of aryl silyl ether reported by Wang (Ref. 17 in the main manuscript). Several reactions of PhOTMS in various moisture solvents were tested at 60 °C and the result was summarized in the following Table S1. We obtained the same result as Wang's report, namely LiOAc worked well only in a combination of DMF and H_2O (entry 2). No reaction proceeded in moisture THF and CPME even for the smallest trimethylsilyl ether (entries 3 and 4).

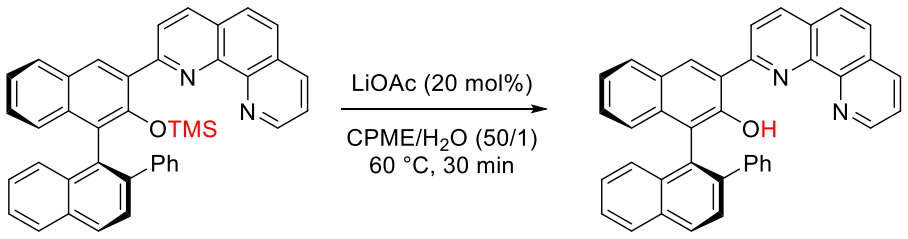
Table S1.



entry	LiOAc (x mol%)	solvent	% yield
1	0	DMF	no reaction
2	20	DMF	>95
3	20	THF	no reaction
4	20	CPME	no reaction

In contrast to the aforementioned model reaction of PhOTMS, the desilylation of TMS-(*S*)-**1a** in moisture CPME proceeded at 60 °C for 30 min (Scheme S1). The conversion ratio of TMS-(*S*)-**1a** was ca. 50%.

Scheme S1

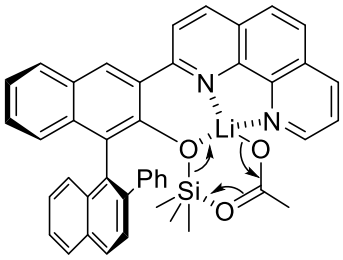


TMS-(*S*)-**1a**

1a/TMS-**1a** = ca. 1/1

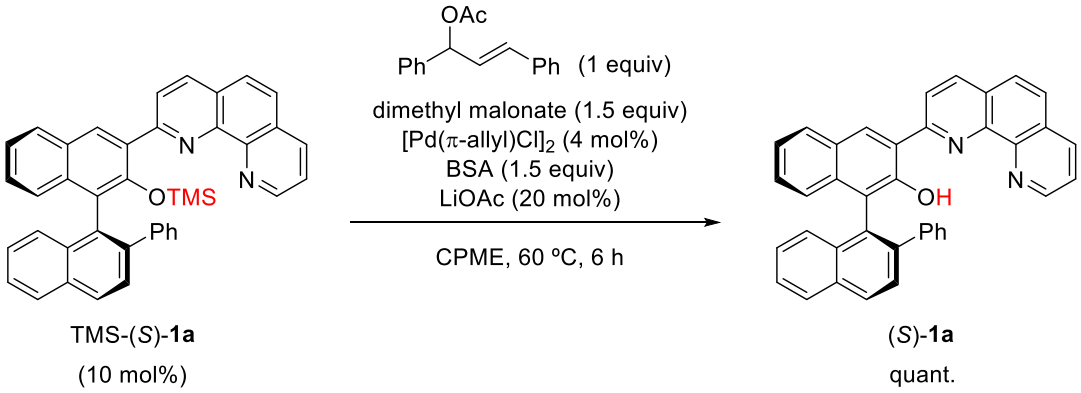
Compared to the model reaction, the presence of phenanthroline moiety in (*S*)-**1a** seems to contribute to the higher reactivity toward LiOAc-catalyzed desilylation. One possible explanation is that a lithium cation coordinated with phenanthroline moiety enables a Lewis acidic activation of oxygen atom of siloxy group and thus the desilylation by acetoxy anion undergoes more smoothly through the six-membered cyclic transition state as proposed in

Wang's report.



More directly, we observed the complete conversion of TMS-(*S*)-**1a** to (*S*)-**1a** with ^{1}H NMR analysis of crude reaction mixture (Scheme S2). Therefore, the desilylation step of the corresponding palladium complex of TMS-(*S*)-**1a** should be involved in the catalytic cycle.

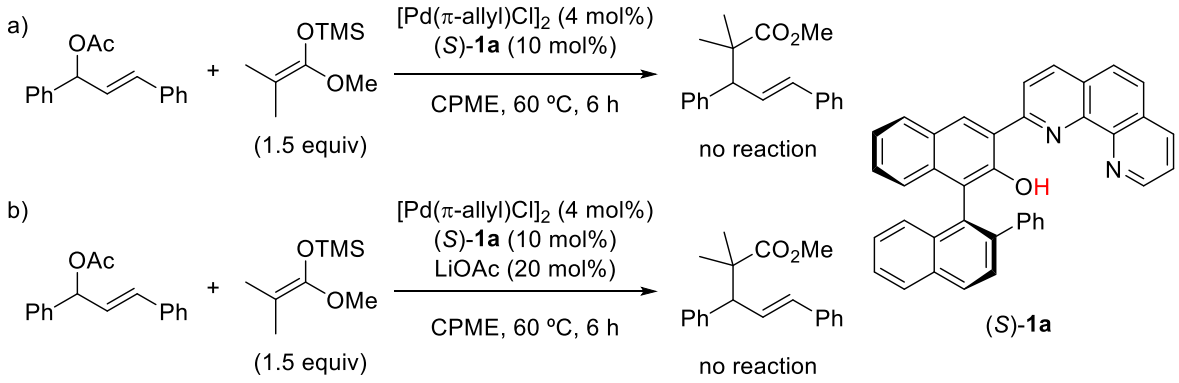
Scheme S2



2) Effect of hydrogen bonding provided from hydroxy group in ligand

To check the possibility of hydrogen bonding activation, we carried out the reaction with commercially available isolated ketene trimethylsilyl acetal in the absence of acetate salt, but no reaction proceeded (Scheme S3a). This result supports that the possibility of hydrogen bond activation can be omitted. Furthermore, the same reaction with LiOAc was also unsuccessful, and thus weaker Lewis basic LiOAc itself was found to be not the effective catalyst for the activation of silyl enolate in this system (Scheme S3b).

Scheme S3



3) Other control experiments

To check the deprotection of TMS-(*S*)-**1a** with LiOAc promoted in CPME at 60 °C quickly, we tried other control reactions i) using (*S*)-**1a**, BSA and LiOAc in moisture CPME and ii) using TMS-(*S*)-**1a** and NaH in dry CPME. Unfortunately, the former reaction with ligand **1a**, BSA and LiOAc in CPME/H_2O (20/1) resulted in no reaction probably due to the complete decomposition of BSA by H_2O (Scheme S4a). Also, the later reaction with TMS-(*S*)-**1a** and NaH in dry CPME led to the formation of complex mixture (Scheme S4b).

Scheme S4