Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry. This journal is © The Royal Society of Chemistry 2017

One-pot synthesis of α , β -epoxy ketones through domino reaction between alkenes and aldehydes catalyzed by proline based chiral organocatalysts

Veeramanoharan Ashokkumar, Ayyanar Siva*

Supramolecular and Organometallic Chemistry Lab, School of Chemistry, Madurai Kamaraj University, Madurai-625 021, Tamil Nadu, India.

E-mail: drasiva@gmail.com

Supporting Information

Table of Contents

S. No	Contents	Page no.		
1	1 Scheme S1 Synthesis of different symmetric proline based			
	organocatalysts			
2	Table S1 Catalyst optimization for the domino reaction (oxidative coupling) between benzaldehyde and styrene.	2		
3	NMR & Mass spectrum of intermediates, organocatalysts and α,β -	3-31		
	epoxy ketone derivatives			
4	HPLC chromatograms of α,β -epoxy ketone derivatives	32-73		
5	References	73		



Scheme S1 Synthesis of different symmetric proline based organocatalysts

Table S1 Catalyst optimization for the domino reaction (oxidative coupling) betweenbenzaldehyde and styrene.



Entry	organocatalysts	Symmetry of the	Time (h) ^a	Yield (%) ^b	ee (%) ^c
		organocatalysts			
1	12a	(C ₃ -symmetry)	10	90	95
2	12b	(C ₃ -symmetry)	10	95	99
3	12c	(C ₂ -symmetry)	24	70	82
4	12d	(<i>C</i> ₁ -symmetry)	36	57	73

^a The domino reaction was carried out between the benzaldehyde (1 mmol), styrene (1 mmol), TBHP (2 equiv.) and acetonitrile (2 mL) with different symmetric catalysts at room temperature with different time. ^b Isolated yield of purified material. ^c Enantiopurity was determined by HPLC analysis of epoxide product using a chiral column (Chiralcel OD-H) with hexane: IPA as an eluent. ^d Absolute configuration (2*R*,3*S*) was determined by comparison of the HPLC retention time using known literature data.¹⁻⁷







Figure S2: ¹³C NMR Spectrum of compound 6.



Figure S3: ¹H NMR Spectrum of scaffold 7.



Figure S4: ¹³C NMR Spectrum of scaffold 7.











Figure S8: ¹³C NMR Spectrum of scaffold 10.



Figure S10: ¹³C NMR Spectrum of organocatalyst 12a.



Figure S12: ¹³C NMR Spectrum of organocatalyst 12b.





Figure S13: ¹H NMR Spectrum of C₂-symmetric organocatalyst 12c.



Figure S14: ¹³C NMR Spectrum of C_2 -symmetric organocatalyst 12c.



Figure S15: ¹H NMR Spectrum of C_1 -symmetric organocatalyst 12d.



Figure S16: ¹³C NMR Spectrum of C_1 -symmetric organocatalyst **12d**.



Figure S17: HR Mass for organocatalyst 12a.



Figure S18: HR Mass for organocatalyst 12b.





Figure S20: ¹³C NMR Spectrum of α , β -epoxy ketone **3a**.





Figure S22: ¹³C NMR Spectrum of α , β -epoxy ketone 3b.



Figure S24: ¹³C NMR Spectrum of α , β -epoxy ketone 3c.





Figure S26: ¹³C NMR Spectrum of α , β -epoxy ketone 3d.



Figure S28: ¹³C NMR Spectrum of α , β -epoxy ketone 3e.



Figure S30: ¹³C NMR Spectrum of α , β -epoxy ketone 3f.

4.1815
 4.1055
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056
 4.1056



Figure S32: ¹³C NMR Spectrum of α , β -epoxy ketone 3g.





Figure S34: ¹³C NMR Spectrum of α , β -epoxy ketone 3h.



Figure S36: ¹³C NMR Spectrum of α , β -epoxy ketone 3i.





Figure S38: ¹³C NMR Spectrum of α , β -epoxy ketone **3j**.



Figure S40: ¹³C NMR Spectrum of α , β -epoxy ketone 4a.



Figure S42: ¹³C NMR Spectrum of α , β -epoxy ketone 4b.



Figure S44: ¹³C NMR Spectrum of α , β -epoxy ketone 4c.



Figure S46: ¹³C NMR Spectrum of α , β -epoxy ketone 4d.







Figure S48: ¹³C NMR Spectrum of α , β -epoxy ketone **4e**.



Figure S50: ¹³C NMR Spectrum of α , β -epoxy ketone 4f.





Figure S52: ¹³C NMR Spectrum of α , β -epoxy ketone 4g.





Figure S54: ¹³C NMR Spectrum of α , β -epoxy ketone 4h.





Figure S56: ¹³C NMR Spectrum of α , β -epoxy ketone 4i.



Figure S58: ¹³C NMR Spectrum of α , β -epoxy ketone 4j.



PDA Ch1 254nm 4nm								
Peak#	Ret. Time	Area	Height	Area %	Height %			
1	20.633	1973568	8839	50.216	51.640			
2	40.775	1877623	8633	49.784	48.360			
Total		3851191	17472	100.000	100.000			

Figure S59: HPLC chromatogram of (4a) Racemic mixture.



Figure S60: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12a) and TBHP/Ethanol in room temperature condition.



Figure S61: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/Ethanol in room temperature condition.



Figure S62: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12a) and TBHP/1-butanol in room temperature condition.



Figure S63: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/1-butanol in room temperature condition.



Figure S64: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12a) and TBHP/Acetonitrile in room temperature condition.



Figure S65: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/Acetonitrile in room temperature condition.



Figure S66: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12a) and TBHP/DMSO in room temperature condition.



Figure S67: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/DMSO in room temperature condition.



Figure S68: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12a) and TBHP/THF in room temperature condition.


Figure S69: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/THF in room temperature condition.



Figure S70: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and $H_2O_2/TEA/Acetonitrile$ in room temperature condition.



Figure S71: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and H_2O_2 /without base/Acetonitrile in room temperature condition.



Figure S72: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/TEA/Acetonitrile in room temperature condition.



Figure S73: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/Pyridine/Acetonitrile in room temperature condition.



Figure S74: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP/without base/Acetonitrile in room temperature condition.



Figure S75: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 65 °C temperature conditions.



Figure S76: HPLC chromatogram of (4a) in the presence 5 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 65 °C temperature conditions.



Figure S77: HPLC chromatogram of (4a) in the presence 15 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 65 °C temperature conditions.



Figure S78: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 30 °C temperature (RT) conditions.



Figure S79: HPLC chromatogram of (4a) in the presence 5 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 30 °C temperature (RT) conditions.



Figure S80: HPLC chromatogram of (4a) in the presence 15 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 30 °C temperature (RT) conditions.



Figure S81: HPLC chromatogram of (4a) in the presence 2 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 0 °C temperature conditions.



Figure S82: HPLC chromatogram of (4a) in the presence 5 mol % of organocatalyst (12b) and TBHP /Acetonitrile in 0 °C temperature conditions.



Figure S83: HPLC chromatogram of (4a) in the presence 2 mol % of C_2 -symmetric organocatalyst (12c) and TBHP/acetonitrile in room temperature condition.



Figure S84: HPLC chromatogram of (4a) in the presence 2 mol % of C_1 -symmetric organocatalyst (12d) and TBHP/acetonitrile in room temperature condition.



Figure S85: HPLC chromatogram of (3a) Racemic mixture.



Figure S86: HPLC chromatogram of (3a) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S87: HPLC chromatogram of (3a) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S88: HPLC chromatogram of (3b) Racemic mixture.



Figure S89: HPLC chromatogram of (3b) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S90: HPLC chromatogram of (3b) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S91: HPLC chromatogram of (3c) Racemic mixture.



Figure S92: HPLC chromatogram of (3c) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S93: HPLC chromatogram of (3c) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S94: HPLC chromatogram of (3d) Racemic mixture.



Figure S95: HPLC chromatogram of (3d) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S96: HPLC chromatogram of (3d) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Peak#	Ret Time	Area	Height	Area 0/	Height %
1 Cakm	Ret. Time	Aica	rieigin	Alca /0	fieight 70
1	17.862	143622513	1483220	50.741	51.794
2	40.964	142638897	1365126	49.259	48.206
Total		286261409	2848346	100.000	100.000

Figure S97: HPLC chromatogram of (3e) Racemic mixture.



Figure S98: HPLC chromatogram of (**3e**) in the presence 2 mol % of organocatalyst (**12a**) and TBHP/acetonitrile in room temperature condition.



Figure S99: HPLC chromatogram of (3e) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S100: HPLC chromatogram of (3f) Racemic mixture.



Figure S101: HPLC chromatogram of (3f) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S102: HPLC chromatogram of (3f) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



	PeakTable					
PDA Ch1 254nm 4nm						
Peak#	Ret. Time	Area	Height	Area %	Height %	
1	26.112	9236738	103209	50.607	51.001	
2	34.068	9187611	102591	49.393	48.999	
Total		18424349	205800	100.000	100.000	

Figure S103: HPLC chromatogram of (3g) Racemic mixture.



Figure S104: HPLC chromatogram of (3g) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



PDA Ch1 254nm 4nm							
Peak#	Ret. Time	Area	Height	Area %	Height %		
1	26.710	72949890	507459	99.113	98.604		
2	34.937	652804	7184	0.887	1.396		
Total		73602695	514642	100.000	100.000		

Figure S105: HPLC chromatogram of (3g) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S106: HPLC chromatogram of (3h) Racemic mixture.



Figure S107: HPLC chromatogram of (3h) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S108: HPLC chromatogram of (3h) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



PDA Ch1 244nm 4nm								
	Peak#	Ret. Time	Area	Height	Area %	Height %		
	1	15.328	4120354	196930	50.914	52.714		
	2	48.975	4011796	185535	49.086	47.286		
	Total		8132150	382465	100.000	100.000		

Figure S109: HPLC chromatogram of (3i) Racemic mixture.



Figure S110: HPLC chromatogram of (3i) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S111: HPLC chromatogram of (3i) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S112: HPLC chromatogram of (3j) Racemic mixture.



Figure S113: HPLC chromatogram of (3j) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S114: HPLC chromatogram of (3j) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S115: HPLC chromatogram of (4b) Racemic mixture.

382465

100.000

100.000

8132150

Tota



Figure S116: HPLC chromatogram of (4b) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S117: HPLC chromatogram of (4b) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S118: HPLC chromatogram of (4c) Racemic mixture.



Figure S119: HPLC chromatogram of (4c) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S120: HPLC chromatogram of (4c) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



PDA Ch1 254nm 4nm		T Cak Table				
Peak#	Ret. Time	Area	Height	Area %	Height %	
1	15.112	9151863	102571	50.394	51.420	
2	36.068	9065393	95256	49.606	48.580	
Total		18217256	197826	100.000	100.000	

Figure S121: HPLC chromatogram of (4d) Racemic mixture.



Figure S122: HPLC chromatogram of (4d) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S123: HPLC chromatogram of (4d) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S124: HPLC chromatogram of (4e) Racemic mixture.



Figure S125: HPLC chromatogram of (4e) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S126: HPLC chromatogram of (4e) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



	Peak Table					
PDA Ch1 25	4nm 4nm					
Peak#	Ret. Time	Area	Height	Area %	Height %	
1	22.829	1973568	8839	50.216	51.640	
2	42.549	1877623	8433	49.784	48.360	
Total		3851191	17272	100.000	100.000	

Figure S127: HPLC chromatogram of (4f) Racemic mixture.



Figure S128: HPLC chromatogram of (4f) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S129: HPLC chromatogram of (4f) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S130: HPLC chromatogram of (4g) Racemic mixture.



Figure S131: HPLC chromatogram of (4g) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S132: HPLC chromatogram of (4g) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S133: HPLC chromatogram of (4h) Racemic mixture.



Figure S134: HPLC chromatogram of (4h) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S135: HPLC chromatogram of (4h) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S136: HPLC chromatogram of (4i) Racemic mixture.



Figure S137: HPLC chromatogram of (4i) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.



Figure S138: HPLC chromatogram of (4i) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.



Figure S139: HPLC chromatogram of (4i) Racemic mixture.



Figure S140: HPLC chromatogram of (4j) in the presence 2 mol % of organocatalyst (12a) and TBHP/acetonitrile in room temperature condition.


Figure S141: HPLC chromatogram of (4j) in the presence 2 mol % of organocatalyst (12b) and TBHP/acetonitrile in room temperature condition.

References

- (a) Y. Chu, X. Liu, W. Li, X. Hu, L. Lin, X. Feng, *Chem. Sci.*, 2012, **3**, 1996; (b) V. Ashokkumar, R. Balasaravanan, V. Sadhasivam, S. M. Jenofar, A. Siva, *J. Mol. Catal. A.: Chem.*, 2015, **409**, 127; (c) J. Sivamani, V. Ashokkumar, V. Sadhasivam, K. Duraimurugan, A. Siva, *RSC Adv.*, 2014, **4**, 60293.
- (a) T. Hashimoto, K. Maruoka, *Chem. Rev.*, 2007, **107**, 5656. (b) G. D. Faveri, G. Ilyashenko, M. Watkinson, *Chem. Soc. Rev.*, 2011, **40**, 1722.
- 3. (a) X. Wang, L. Yin, T. Yang, Y. Wang, *Tetrahedron Asymmetry*, 2007, **18**, 108; (b) K. Hori, M. Tamura, K. Tani, N. Nishiwaki, M. Ariga, Y. Tohda, *Tetrahedron Lett.*, 2006, **47**, 3115.
- 4. (a) Y. Liu, B. A. Provencher, B. J. Bartelson, L. Deng, *Chem. Sci.*, 2011, 2, 1301; (b) O. Cusso, I. G. Bosch, X. Ribas, J. L. Fillol, M. Costas, *J. Am. Chem. Soc.*, 2013, 135, 14871.
- (a) J. Lv, X. Wang, J. Liu, L. Zhang, Y. Wang, *Tetrahedron Asymmetry*, 2006, **17**, 330; (b) B. Makoa, Z. Rapia, G. Keglevicha, A. Szollosy, L. Drahosc, L. Hegedusd, P. Bakoa, *Tetrahedron Asymmetry*, 2010, **21**, 919.
- (a).Wang, W. L. Shi, M. Li, K. Ding, Angew. Chem., Int. Ed., 2005, 44, 6362; (b) B. Wang, S. Wang, C. Xia, W. Sun, Chem. Eur. J., 2012, 18, 7332; (c) C. Zeng, D. Yuan, B. Zhao, Y. Yao, Org. Lett., 2015, 17, 2242.
- (a) X. Liu, Y. Li, G. Wang, Z. Chai, Y. Wua, G. Zhaoa, *Tetrahedron Asymmetry*, 2006, **17**, 750;
 (b) J. Lu, Y. H. Xu, F. Liu, T. P. Loh, *Tetrahedron Lett.*, 2008, **49**, 6007.