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$Sc(OTf)_3$-Catalyzed Tandem [3+2] Cycloaddition/Nucleophilic Ring-Opening Reaction of Cyclopropane 1,1-Diesters with Azomethine Ylides

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A new $Sc(OTf)_3$-catalyzed tandem reaction combined with a dimerized self-[3+2] cycloaddition of azomethine ylide and a nucleophilic ring-opening of cyclopropane 1,1-diester has been developed. A series of polyfunctionalized imidazolidine derivatives were synthesized by this reaction (Yield 44-77 %). In some cases, this tandem reaction was also accompanied by a cross-[3+2] cycloaddition of cyclopropane 1,1-diester with imine.

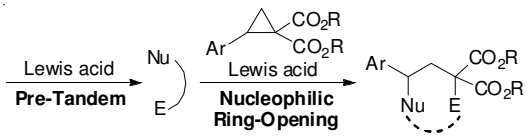
Key Words: Lewis acid, Cyclopropane 1,1-diesters, Tandem, Imidazolidine.

INTRODUCTION

Efficient construction of complex heterocyclic skeletons from simple and easily available starting material continues an attractive theme in organic synthesis. Cyclopropane 1,1-diester, an easily available synthon, has got great attentions due to its good reactivity[1]. Lewis acid-catalyzed nucleophilic ring-opening of cyclopropane 1,1-diester provides a useful synthetic method[1,2]. Tandem reactions have been widely accepted by chemists because of their high efficiency in construction of complex molecular skeletons[3]. One of our research interests is to develop new methodology by combination of a pre-tandem reaction (for generation of a new nucleophile) and a nucleophilic ring-opening of cyclopropane 1,1-diester (**Scheme-I**).

On the other hand, imidazolidine is an important building block and intermediate in organic synthesis and construction of a variety of biologically active compounds. 1,3-Dipolar cycloaddition between azomethine ylides and imines is an efficient method for this heterocyclic skeleton[4].

Recently we found a new $Sc(OTf)_3$-catalyzed tandem nucleophilic ring-opening reaction of cyclopropane 1,1-diester (**Scheme-II**). In this tandem process, the precursor of azomethine ylide played as a dienophile (C=N) to take a cross-[3+2] cycloaddition with cyclopropane as well as played as a 1,3-dipole to take a self-[3+2] cycloaddtion with another molecule of azomethine ylide and the cyclopropane ring was subsequently opened by the corresponding self-[3+2] cycloadduct imidazolidinene. Herein we hope to report our recent results.

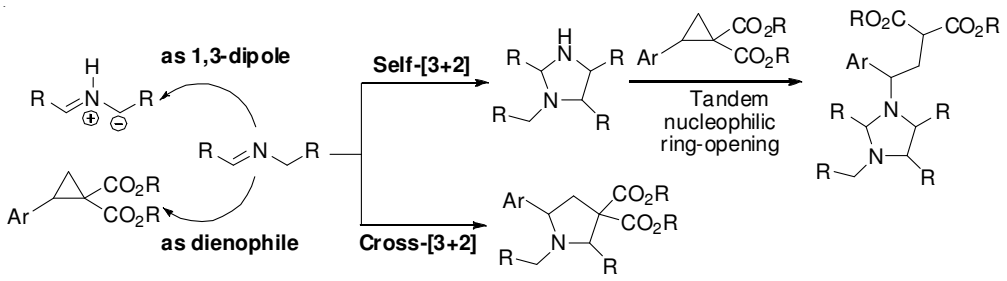


Scheme-I

EXPERIMENTAL

General methods: All reactions were carried out under nitrogen atmosphere in dry flask and were monitored by analytical thin-layer chromatography (TLC), which was visualized by ultraviolet light (254 nm). All solvents were obtained from commercial sources and were purified according to standard procedures. A series of cyclopropane 1,1-diesters (**1**)[5] and precursors of azomethine ylides (**2**)[6] were easily prepared according to literature methods. Purification of products was accomplished by flash column chromatography using silica gel (200-300 mesh). MS 4 Å was powdered and vacuum activated at 250 °C before use.

All NMR spectra were recorded with a Varian spectrometer at 300 MHz or 400 MHz (^{1}H NMR) and 75 MHz or 100 MHz (^{13}C NMR) in $CDCl_3$: chemical shifts (δ) are given in ppm, coupling constants (*J*) in Hz, the solvent signals were used as references ($CDCl_3$: δ = 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δ = 7.26 ppm). High-resolution mass spectra were recorded on a FTMS spectrometer. IR spectra were recorded on a MAGNA-560 spectrometer made by Nicolet Company. Melting points were obtained on a Yanaco-241 apparatus and were uncorrected.



Scheme-II

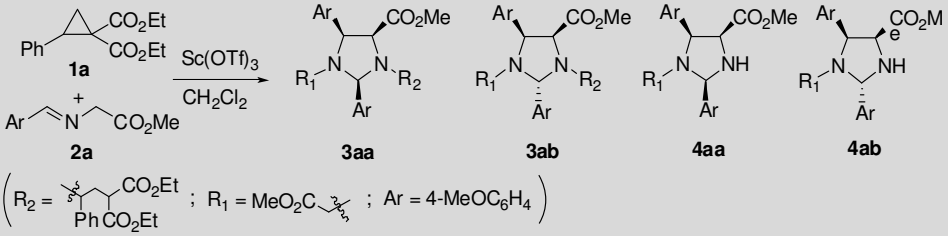
General procedure for the tandem reaction of cyclopropanes (1) and azomethine ylides (2): $Sc(OTf)_3$ (9.8 mg, 0.02 mmol, 10 mol %) and cyclopropane (0.20 mmol in 1.0 mL of CH_2Cl_2) were dissolved in dry CH_2Cl_2 (3.0 mL) and stirred over activated 4 Å molecular sieves (200 mg) under a balloon of argon for 0.5 h azomethine ylides (0.44 mmol in 1.0 mL of CH_2Cl_2) were added and the mixture were refluxed for the time indicated in Table-1. The progress of the reaction was monitored by TLC. Upon disappearance of the cyclopropane 1,1-diester, the reaction mixture was filtered and purified by column chromatography (elution with EtOAc/petroleum ether mixtures). Samples could be recrystallized from EtOAc/petroleum ether if desired.

Typical produce for the preparation of diethyl 2-phenylcyclopropane 1,1-dicarboxylate (1a): In a 100 mL of three-necked round-bottomed flask was added benzaldehyde (2.54 g, 24.0 mmol), diethyl malonate (3.84g, 26.2 mmol), piperidine (0.24 mL), acetic acid (0.12 mL) and toluene (12 mL). The mixture was stirred and heated to reflux for 12 h. After being cooled to room temperature, the mixture was washed with 5 % of $NaHCO_3$ (5 mL × 3) and the organic phase was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford the title compound diethyl 2-benzylidenemalonate as colourless oil (5.35 g, 90 %).

In an oven-dried 100 mL three-necked flask, NaH (50 % in mineral oil, 0.41 g, 8.5 mmol), trimethylsulfoxonium iodide (1.86 g, 8.5 mmol) and DMSO (12.5 mL) were added under an atmosphere of nitrogen. After being stirred for 0.5 h at room temperature, a solution of diethyl 2-benzylidene-malonate (1.91 g, 7.7 mmol) in THF (12.5 mL) was added dropwise to the above-prepared dimethylsulfoxonium methylide over 0.5 h. After being stirred for 1 h at room temperature and 3 h at 50 ºC, the reaction mixture was cooled to room temperature and poured into ice-cold water (25 mL). The solution was extracted with ether (15 mL × 3). The combined organic phases were washed with brine (10 mL × 3), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to afford **1a** 1.63 g (80 %) of **1a** as colourless oil.

General procedure for the preparation of azomethine ylides (2): To a suspension of the corresponding amino acid ester hydrochloride (23.9 mmol) and $MgSO_4$ (25.0 mmol) in CH_2Cl_2 (25 mL) was added Et_3N (3.4 mL, 23.9 mmol). The mixture was stirred at room temperature for 1 h and then the corresponding aldehyde (20.0 mmol) was added. The reaction

TABLE-1
OPTIMIZATION OF THE CONDITIONS FOR THE TANDEM REACTION

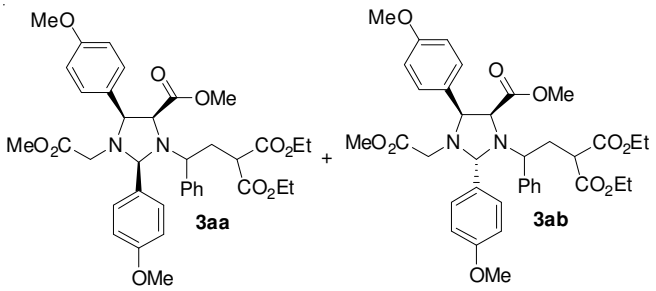


Entry	Lewis acid (equiv)	Temperature (ºC)	Time (h)	3X yield (%)[b,c] (**3aa**:**3ab**)[d]	4X yield (%)[b,c] (**4aa**:**4ab**)[d]
1	$Sc(OTf)_3$ (0.1)	40	14.0	63 (1:1.7)	Trace
2	$Yb(OTf)_3$ (0.1)	40	34.5	34 (1:1.9)	Trace
3	$MgI_2{\cdot}Et_2O$ (0.3)	40	30.0	36 (1:3.6)	13 (1:0)
4	$Mg(ClO_4)_2{\cdot}6H_2O$ (0.1)	40	15.0	38 (1:2.3)	10 (1:0)
5[e]	$SnCl_4$ (0.1)	-78	2.0	0	Trace
6	$BF_3{\cdot}Et_2O$ (0.2)	40	16.0	0	21 (1:0.6)
7	$ZnCl_2$ (0.1)	Room temperature	Over night	0	26 (1:0.8)
8	$Cu(OTf)_2$ (0.1)	40	22.5	0	16 (1:0.7)
9	CuOTf (0.1)	40	36.0	0	16 (1:0.8)
10	$Sn(OTf)_2$ (0.1)	40	36.0	0	13 (1:1.0)
11	$Zn(OTf)_2$ (0.1)	40	18.0	0	27 (1:0.7)
12[f]	-	40	7.0	0	0

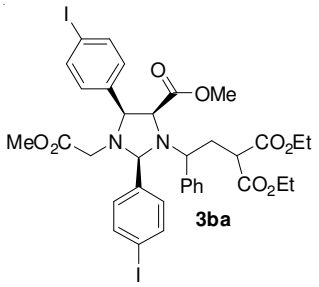
[a]Conditions: Molar ratio of **1a** to **2a** = 1:2.2, 4 Å MS, N_2. [b]Isolated yields by silica gel chromatography. [c]The total yield is given for a mixture of two diastereomers. [d]Determined by ^1H NMR. [e]Imine were decomposed in this condition. [f]None of any Lewis acid was added.

was stirred at room temperature overnight and the resulting precipitate was removed by filtration. The filtrate was washed with water (15 mL), the aqueous phase was extracted with CH_2Cl_2 (10 mL × 3) and the combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated. The resulting imino esters were obtained pure and used in cycloadditions without further purification.

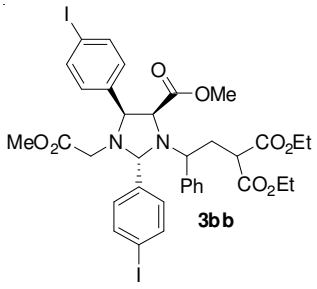
Characterization data of compounds 3, 4 and 5



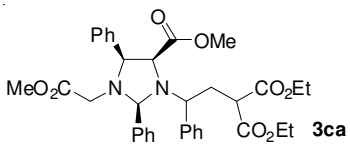
Compounds 3aa/3ab: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenyl-propyl)-1-((methoxycarbonyl)methyl)-2,5-*bis*(4-methoxyphenyl)imidazolidine-4-carboxylate: Colourless viscous oil; isomers (**3aa**:**3ab** = 1.0:1.7); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.51 (d, *J* = 8.4 Hz, 1.26H), 7.42-7.33 (m, 2H), 7.27-7.12 (m, 5H), 7.07 (d, *J* = 8.0 Hz, 0.86H), 6.94 (d, *J* = 8.8 Hz, 1.38H), 6.84 (d, *J* = 8.4 Hz, 0.86H), 6.80 (d, *J* = 7.6 Hz, 2.2H), 4.6-4.59 (m, 2H), 4.17-4.03 (m, 4H), 3.83-3.67 (m, 9H), 3.43 (s, 1.15H), 3.36 (s, 1.88H), 3.22(s, 1.90H), 3.05 (s, 1.20H), 2.98 (m, 2H), 2.36-2.04 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 3.91H),1.06 (t, *J* = 7.2 Hz, 2.10H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 172.7, 170.8, 170.2, 169.7, 169.5, 169.4, 160.2, 159.7, 159.6, 138.9, 138.6, 138.4, 138.2, 133.5, 132.3,131.3, 129.9, 129.8, 129.7, 129.0, 128.8, 128.6, 128.0, 127.7, 113.8, 113.7, 113.6, 82.0, 81.1, 67.1, 66.6, 66.0, 63.5, 61.6, 61.4, 61.3, 61.0, 55.4, 51.6, 51.3, 51.2, 49.0, 48.6, 47.6, 46.9, 46.5, 32.7, 29.3, 14.2, 14.0; IR (thin film, cm^{-1}): 3341, 3062, 2959, 2926, 2848, 2055, 1731, 1612, 1512, 1384, 1260, 1094, 804, 768, 704; HRMS (ESI) calcd. for $C_{37}H_{44}N_2O_{10}Na^+$: 699.2888, found: 699.2884.



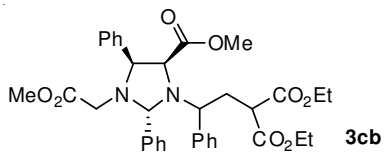
Compound 3ba: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-*bis*(4-iodophenyl)imidazolidine-4-carboxylate: White solid, m.p. 141-142 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.76 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 4H), 7.40 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 6.8 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 2H), 4.73 (s, 1H), 4.21 (d, *J* = 7.2 Hz, 1H), 4.16-4.05 (m, 2H), 4.09 (d, *J* = 9.2 Hz, 1H), 3.78-3.70 (m, 2H), 3.69-3.60 (m, 1H), 3.39 (s, 3H), 3.20 (s, 3H), 2.96 (dd, *J* = 17.2, 4.8 Hz, 2H), 2.21-2.09 (m, 1H), 2.09-2.00 (m, 1H), 1.92 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.8, 170.4, 170.0, 169.5, 140.3, 137.9, 137.8, 137.7, 135.9, 132.2, 130.7, 128.9, 128.3, 95.1, 94.2, 82.0, 66.7, 63.7, 61.6, 61.4, 59.0, 51.8, 51.4, 48.6, 47.4, 32.8, 14.3; IR (thin film, cm^{-1}): 3059, 3027, 2980, 2950, 1731, 1589, 1482, 1452, 1435, 1368, 1325, 1290, 1262, 1198, 1174, 1095, 1055, 1027, 1006, 823, 800, 769, 704; HRMS (ESI) calcd. for $C_{35}H_{38}I_2N_2O_8H^+$: 869.0790 found: 869.0798.



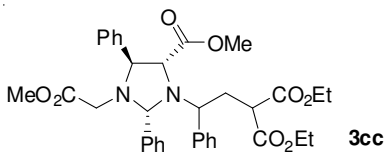
Compound 3bb: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-*bis*(4-iodophenyl)-imidazolidine-4-carboxylate: White solid, m.p. 135-136 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61 (d, *J* = 8.0 Hz, 4H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.20-7.14 (m, 3H), 7.10-7.00 (m, 4H), 4.70 (s, 1H), 4.67 (d, *J* = 9.2 Hz, 1H), 4.20 (d, *J* = 9.2 Hz, 1H), 4.16-4.04 (m, 4H), 3.77 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.46 (s, 3H), 3.23 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.06 (s, 3H), 2.95 (dd, *J* = 44.0, 17.6 Hz, 2H), 2.37-2.20 (m, 2H), 1.21 (t, *J* = 7.6 Hz, 3H), 1.19 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.0, 170.3, 169.3, 169.1, 141.2, 137.8, 137.4, 137.2, 136.1, 131.5, 130.4, 128.9, 128.1, 127.8, 94.2, 93.8, 81.3, 67.1, 65.9, 62.0, 61.4, 51.1, 48.7, 46.4, 29.9, 14.1, 14.0; IR (thin film, cm^{-1}) 3022, 2985, 2952, 2923, 2851, 1748, 1738, 1723, 1585, 1481, 1455, 1435, 1406, 1371, 1337, 1325, 1293, 1261, 1241, 1196, 1178, 1148, 1096, 1005, 810, 707; HRMS (ESI) calcd. for $C_{35}H_{38}I_2N_2O_8H^+$: 869.0790 found: 869.0793.



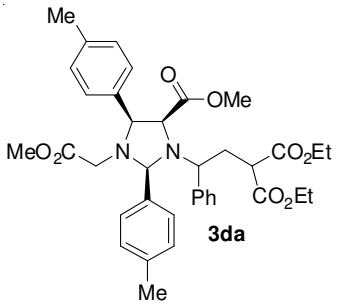
Compound 3ca: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-diphenylimidazolidine-4-carboxylate: White solid, m.p. 98-99 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.86 (d, *J* = 7.2 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 4H), 7.37 (t, *J* = 7.2 Hz, 3H), 7.28 (t, *J* = 7.6 Hz, 6H), 4.78 (s, 1H), 4.28 (d, *J* = 9.2 Hz, 1H), 4.12 (d, *J* = 9.2 Hz, 1H), 4.09-4.02 (m, 2H), 3.96-3.84 (m, 1H), 3.79-3.73 (m, 1H), 3.72-3.64 (m, 2H), 3.37 (s, 3H), 3.15 (s, 3H), 3.02 (dd, *J* = 25.6, 8.8 Hz, 2H), 2.23-2.13 (m, 1H), 2.10-2.00 (m, 1H), 1.19 (t, *J* = 6.8 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): d 173.0, 170.7, 170.1, 169.4, 140.5, 138.2, 136.3, 130.2, 129.0, 128.9, 128.7, 128.5, 128.4, 128.0, 82.6, 67.2, 64.0, 61.4, 61.0, 59.0, 51.5, 51.1, 48.7, 47.6, 32.8, 14.2, 14.1; IR (thin film, cm^{-1}) 3031, 3001, 2980, 2950, 2937, 2869, 1745, 1719, 1493, 1457, 1440, 1375, 1268, 1197, 1174, 1148, 1136, 1100, 1082, 1026, 809, 769, 755, 703; HRMS (ESI) calcd. for $C_{35}H_{40}N_2O_8H^+$: 617.2857 found: 617.2861.



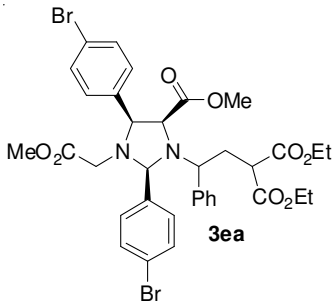
Compound 3cb: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-diphenylimidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.65 (d, *J* = 6.0 Hz, 2H), 7.39-7.03 (m, 13H), 4.76 (s, 1H), 4.70 (d, *J* = 9.2 Hz, 1H), 4.23 (d, *J* = 9.2 Hz, 1H), 4.13-4.02 (m, 4H), 3.79 (dd, *J* = 15.2, 6.3 Hz, 1H), 3.44 (s, 3H), 3.20 (dd, *J* = 14.4, 5.7 Hz, 1H), 3.01 (s, 3H), 3.00 (dd, *J* = 31.6, 11.1 Hz, 2H), 2.37-2.23 (m, 2H), 1.18 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.2, 170.7, 169.4, 169.2, 141.4, 138.1, 136.6, 134.4, 129.7, 129.6, 129.0, 128.9, 128.5, 128.4, 128.3, 128.1, 128.0, 128.0, 127.6, 81.5, 67.4, 66.4, 61.6, 61.3, 61.2, 50.9, 48.8, 46.7, 29.6, 14.0, 14.0; HRMS (ESI) calcd. for $C_{35}H_{40}N_2O_8Na^+$: 639.2677 found: 639.2686.



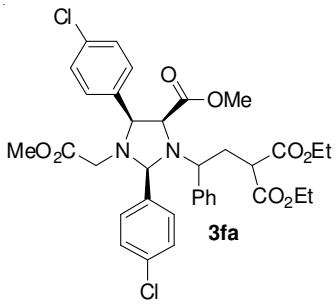
Compound 3cc: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl) methyl)-2,5-diphenylimidazolidine-4-carboxylate: White solid, m.p. 85-86 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.20 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.37-7.26 (m, 7H), 7.20-7.12 (m, 4H), 6.93 (d, *J* = 6.8 Hz, 2H),5.29 (s, 1H), 4.38 (d, *J* = 6.8 Hz, 1H), 4.16 (dd, *J* = 14.0, 6.8 Hz, 2H), 3.93-3.84 (m, 2H), 3.78-3.70 (m, 1H), 3.67 (d, *J* = 6.8Hz, 1H), 3.51 (s, 3H), 3.48 (s, 3H), 3.42 (t, *J* = 6.0 Hz, 2H), 2.93 (d, *J* = 17.6 Hz, 1H), 2.54 (d, *J* = 17.6 Hz, 1H), 2.43-2.31 (m, 1H), 2.12-2.02 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.04 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.4, 171.3, 169.8, 169.4, 140.4, 138.1, 138.0, 129.6, 128.7, 128.6, 128.4, 128.2, 83.1, 69.5, 69.1, 63.4, 61.6. 61.3, 52.3, 51.7, 49.2, 48.5, 33.4, 14.3, 14.1; HRMS (ESI) calcd. for $C_{35}H_{40}N_2O_8H^+$: 617.2857 found: 617.2858.



Compound 3da: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl) methyl)-2,5-diptolylimidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73 (d, *J* = 7.8 Hz, 2H), 7.48-7.13 (m, 9H), 7.07 (d, *J* = 7.8 Hz, 2H), 4.72 (s, 1H), 4.22 (d, *J* = 6.0 Hz, 1H), 4.15-4.03 (m, 2H), 4.08 (d, *J* = 7.5 Hz, 1H), 3.98-3.84 (m, 1H), 3.78 (dd, *J* = 9.9, 6.9 Hz, 1H), 3.75-3.62 (m, 2H), 3.36 (s, 3H), 3.20 (s, 3H), 3.00 (dd, *J* = 21.9, 16.8 Hz, 2H), 2.22-2.00 (m, 2H), 1.86 (t, *J* = 7.2 Hz, 3H), 1.06 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.0, 170.6, 169.9, 169.2, 138.2, 137.7, 137.2, 133.1, 129.9, 128.9, 128.8, 128.7, 128.5, 128.4, 127.7, 82.1, 66.8, 63.6, 61.1, 60.7, 58.6, 51.2, 50.8, 48.5, 47.4, 32.6, 21.3, 21.1, 14.0, 13.8; IR (thin film, cm^{-1}): 3060, 3028, 2991, 2951, 1749, 1732, 1515, 1494, 1452, 1435, 1368, 1309, 1291, 1247, 1219, 1188, 1172, 1132, 1091, 1021, 832, 804, 723, 711. HRMS (ESI) calcd. for $C_{37}H_{44}N_2O_8H^+$: 645.3170 found: 645.3164.

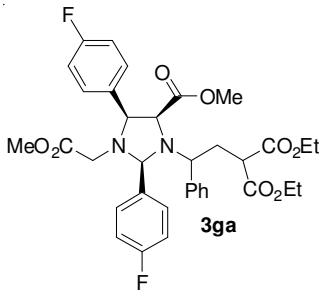


Compound 3ea: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-*bis*(4-bromophenyl)imidazolidine-4-carboxylate: Yellow solid, m.p. 120-121 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.47-7.33 (m, 5H), 7.25 (d, *J* = 5.7 Hz, 2H), 7.17 (d, *J* = 5.4 Hz, 2H), 4.77 (s, 1H), 4.24 (d, *J* = 9.0 Hz, 1H), 4.16-4.05 (m, 1H), 4.10 (d, *J* = 9.0 Hz, 1H), 4.02-3.92 (m, 1H), 3.79-3.72 (m, 1H), 3.71-3.61 (m, 2H), 3.40 (s, 3H), 3.21 (s, 3H), 2.97 (dd, *J* = 21.0, 17.1 Hz, 2H), 2.22-2.02 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.5, 170.1, 169.7, 169.2, 139.4, 137.8, 135.0, 131.7, 131.5, 131.4, 130.2, 128.6, 128.5, 128.0, 122.9, 122.2, 81.7, 66.4, 63.5, 61.3, 61.0, 58.8, 51.4, 51.1, 48.4, 47.2, 32.5, 14.0, 13.9; IR (thin film, cm^{-1}): 3026, 2982, 2953, 2935, 1743, 1592, 1487, 1440, 1374, 1290, 1260, 1237, 1197, 1197, 1175, 1140, 1090, 1012, 840, 822, 810, 700: HRMS (ESI) calcd. for $C_{35}H_{38}Br_2N_2O_8H^+$: 773.1068 found: 773.1063.



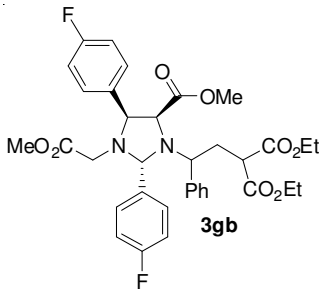
Compound 3fa: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-*bis*(4-chlorophenyl)imidazolidine-4-carboxylate: Yellow solid, m.p. 102-103 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.47-7.18 (m, 11H), 4.77 (s, 1H), 4.24 (d, *J* = 9.2 Hz, 1H), 4.15-4.03 (m, 2H), 4.09 (d, *J* = 9.6 Hz, 1H), 3.99-3.92 (m, 1H), 3.74-3.60 (m, 3H), 3.39 (s, 3H), 3.20 (s, 3H),

2.96 (dd, *J* = 21.6, 17.2 Hz, 2H), 2.24-2.11 (m, 1H), 2.10-2.00 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.6, 170.1, 169.7, 169.1, 138.8, 137.7, 134.5, 134.4, 134.0, 131.3, 129.8, 129.4, 128.5, 128.4, 128.0, 81.6, 66.3, 63.5, 61.2, 61.0, 58.8, 51.4, 51.1, 48.3, 47.2, 32.5, 14.0, 13.8; IR (thin film, cm^{-1}): 3028, 2982, 2954, 2926, 2870, 2853, 1744, 1598, 1491, 1439, 1414, 1371, 1321, 1290, 1261, 1237, 1197, 1174, 1089, 1051, 1015, 823, 769, 703; HRMS (ESI) calcd. for $C_{35}H_{38}Cl_2N_2O_8H^+$: 685.2078 found: 685.2083.



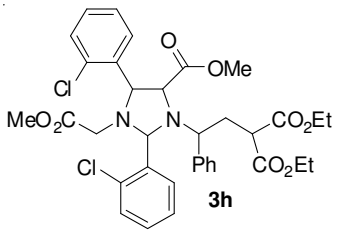
3ga

Compound 3ga: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl)methyl)-2,5-*bis*(4-fluorophenyl)imidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85 (dd, *J* = 8.4, 5.7 Hz, 2H), 7.48-7.21 (m, 7H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H), 4.76 (s, 1H), 4.24 (d, *J* = 9.0 Hz, 1H), 4.15-4.05 (m, 3H), 4.01-3.90 (m, 1H), 3.80-3.72 (m, 1H), 3.71-3.61 (m, 2H), 3.40 (s, 3H), 3.20 (s, 3H), 3.98 (dd, *J* = 18.9, 16.8 Hz, 2H), 2.23-1.99 (m, 2H), 1.94 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.7, 170.2, 169.7, 169.2, 137.9, 136.0, 131.7, 131.6, 130.2, 130.1, 128.5, 127.9, 115.3, 115.0, 81.7, 66.3, 63.6, 61.2, 60.9, 58.8, 51.3, 51.0, 48.4, 47.3, 32.5, 14.0, 13.8; IR (thin film, cm^{-1}): 3030, 2987, 2954, 2850, 1749, 1732, 1605, 1510, 1438, 1371, 1293, 1249, 1225, 1194, 1175, 1154, 1095, 1021, 841, 707; HRMS (ESI) calcd. for $C_{35}H_{38}F_2N_2O_8H^+$: 653.2669 found: 653.2666.



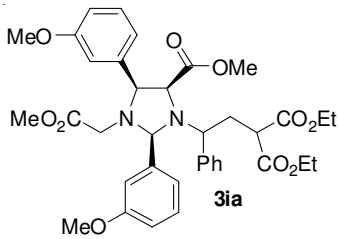
3gb

Compound 3gb: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl) methyl)-2,5-*bis*(4-fluorophenyl)imidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.60 (dd, *J* = 8.4, 6.0 Hz, 2H), 7.37-7.27 (m, 2H), 7.21-7.13 (m, 3H), 7.08-7.02 (m, 2H), 6.98 (t, *J* = 8.4 Hz, 4H), 4.74 (s, 1H), 4.69 (d, *J* = 9.0 Hz, 1H), 4.20 (d, *J* = 9.3 Hz, 1H), 4.17-4.03 (m, 4H), 3.78 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.46 (s, 3H), 3.24 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.06 (s, 3H), 2.97 (dd, *J* = 34.2, 17.1 Hz, 2H), 2.42-2.19 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.2, 170.4, 169.3, 169.1, 138.0, 137.1, 137.1, 131.3, 131.2, 130.1, 130.0, 128.8, 128.1, 127.7, 115.3, 115.0, 114.7, 81.1, 67.1, 65.7, 61.8, 61.4, 61.3, 51.0, 48.7, 46.6, 29.7, 14.0, 13.9; IR (thin film, cm^{-1}): 2959, 2924, 2871, 2850, 1732, 1605, 1455, 1435, 1373, 1330, 1261, 1223, 1180, 1152, 1095, 1018, 841, 799, 703; HRMS (ESI) calcd. for $C_{35}H_{38}F_2N_2O_8H^+$: 653.2669 found: 653.2666.



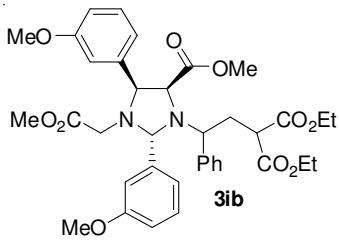
3h

Compound 3h: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl) methyl) -2,5-*bis*(2-chlorophenyl)imidazolidine-4-carboxylate: Colourless viscous oil; the four isomers can not be separated, the ^{1}H NMR and ^{13}CNMR ($CDCl_3$, 100 MHz) can be found at S30; IR (thin film, cm^{-1}): 3063, 3028, 2982, 2950, 2905, 1747, 1593, 1472, 1264, 1198, 1049, 760, 707; HRMS (ESI) calcd. for $C_{35}H_{38}Cl_2N_2O_8Na^+$: 707.1897 found: 707.1899.



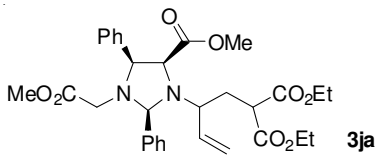
3ia

Compound 3ia: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl) methyl)-2,5-*bis*(3-methoxyphenyl)imidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.70 (s, 1H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.36 (d, *J* = 6.9 Hz, 1H), 7.33-7.27 (m, 3H), 7.18 (d, *J* = 7.8 Hz, 2H), 9.96-6.84 (m, 3H), 6.82-6.74 (m, 1H), 4.78 (s, 1H), 4.25 (d, *J* = 9.0 Hz, 1H), 4.16-4.06 (m, 2H), 4.12 (d, *J* = 9.6 Hz, 1H), 3.96 (s, 3H), 3.88-3.79 (m, 2H), 3.77 (s, 3H), 3.75-3.66 (m, 2H), 3.40 (s, 3H), 3.22 (s, 3H), 3.04 (dd, *J* = 21.9, 17.1 Hz, 2H), 2.25-2.02 (m, 2H), 1.19 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 2H); ^{13}CNMR ($CDCl_3$, 75 MHz): δ 172.9, 170.5, 169.9, 169.2, 142.1, 138.1, 137.8, 129.1, 128.8, 128.6, 128.5, 127.8, 122.3, 120.9, 115.8, 114.0, 113.8, 113.7, 82.1, 67.0, 63.5, 61.1, 60.8, 58.5, 55.2, 51.3, 50.9, 48.5, 47.3, 32.5, 14.0, 13.7; IR (thin film, cm^{-1}): 3062, 3028, 2952, 2839, 1738, 1731, 1601, 1488, 1455, 1435, 1372, 1322, 1260, 1197, 1178, 1095, 1075, 1040, 877, 788, 749, 701; HRMS (ESI) calcd. for $C_{37}H_{44}N_2O_{10}H^+$: 677.3069 found: 677.3065.



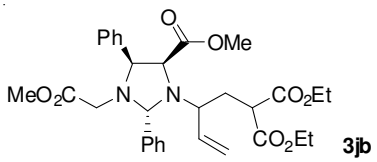
3ib

Compound 3ib: Methyl 3-(3,3-di(ethoxycarbonyl)-1-phenylpropyl)-1-((methoxycarbonyl) methyl)-2,5-*bis*(3-methoxyphenyl)imidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42 (s, 1H), 7.24-7.26 (m, 7H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.86-6.74 (m, 3H), 4.76 (s, 3H), 4.68 (d, *J* = 9.0 Hz, 1H), 4.23 (d, *J* = 9.3 Hz, 1H), 4.16-4.02 (m, 4H), 3.87 (s, 3H), 3.86-3.80 (m, 1H), 3.77 (s, 3H), 3.46 (s, 3H), 3.38 (t, *J* = 6.0 Hz, 1H), 3.08 (s, 3H), 3.04 (dd, *J* = 35.7, 17.1 Hz, 2H), 2.40-2.21 (m, 2H), 1.19 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.3, 170.7, 169.5, 169.2, 143.2, 138.3, 129.1, 128.9, 128.7, 128.0, 127.6, 121.9, 120.9, 115.0, 114.1, 114.0, 113.6, 81.3, 67.4, 66.4, 61.5, 61.3, 61.2, 55.2, 51.0, 50.9, 48.9, 46.6, 29.6, 14.0; IR (thin film, cm^{-1}): 3062, 2954, 2922, 2870, 2849, 1731, 1600, 1487, 1456, 1437, 1376, 1321, 1259, 1197, 1180, 1095, 1075, 1043, 878, 785, 700; HRMS (ESI) calcd. for $C_{37}H_{44}N_2O_{10}H^+$: 677.3069 found: 677.3075.



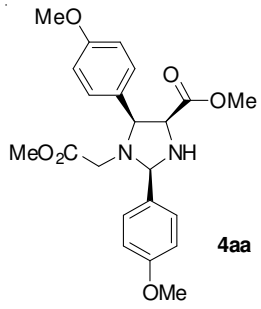
3ja

Compound 3ja: Methyl 3-(1,1-di(ethoxycarbonyl)-pent-4-en-3-yl)-1-((methoxycarbonyl)methyl)-2,5-diphenylimidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.74 (d, *J* = 6.3 Hz, 2H), 7.74-7.27 (m, 8H), 6.11-5.97 (m, 1H), 5.41 (d, *J* = 10.5 Hz, 1H), 5.23 (d, *J* = 17.1 Hz, H), 4.87 (s, 1H), 4.79 (d, *J* = 9.0 Hz, 1H), 4.11 (d, *J* = 9.0 Hz, 1H), 4.09-4.00 (m, 2H), 3.95-3.85 (m, 1H), 3.84-3.78 (m, 1H), 3.69-3.58 (m, 1H), 3.49 (s, 3H), 3.11 (dd, *J* = 34.8, 17.1 Hz, 2H), 3.16 (s, 3H), 3.15-3.06 (m, 1H), 2.07-1.94 (m, 1H), 1.71-1.63 (m, 1H), 1.15 (t, *J* = 7.2 Hz, 1H), 1.04 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.8, 170.7, 170.1, 169.3, 140.2, 136.2, 134.5, 129.8, 128.6, 128.5, 128.2, 128.2, 128.1, 118.7, 82.3, 67.2, 63.3, 61.1, 60.7, 56.7, 51.2, 50.9, 47.7, 46.7, 32.0, 13.9, 13.8; IR (thin film, cm^{-1}): 3064, 3028, 2980, 2951, 2926, 2872, 2850, 1932, 1457, 1435, 1370, 1334, 1262, 1197, 1176, 1098, 1074, 1029, 927, 827, 754, 703; HRMS (ESI) calcd. for $C_{31}H_{38}N_2O_8H^+$: 567.2701 found: 567.2704.



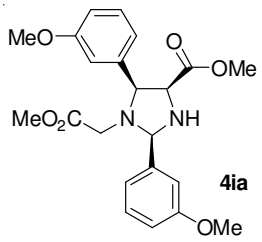
3jb

Compound 3jb: Methyl 3-(1,1-di(ethoxycarbonyl)pent-4-en-3-yl)-1-((methoxycarbonyl)methyl)-2,5-diphenylimidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.77 (d, *J* = 6.6 Hz, 2H), 7.42-7.24 (m, 8H), 5.88-5.74 (m, 1H), 5.21 (d, *J* = 10.5 Hz, 1H), 5.13 (d, *J* = 17.1 Hz, 1H), 5.01 (s, 1H), 4.81 (d, *J* = 9.3 Hz, 1H), 4.16-3.99 (m, 4H), 4.08 (d, *J* = 8.7 Hz, 1H), 3.60-3.47 (m, H), 3.54 (s, 3H), 3.28-3.18 (m, 1H), 3.14 (s, 3H), 3.07 (dd, *J* = 39.9, 17.4 Hz, 2H), 1.87-1.75 (m, 2H), 1.20 (t, *J* = 5.1 Hz, 3H), 1.18 (t, *J* = 5.1 Hz, 3H); ^{13}CNMR ($CDCl_3$, 75 MHz): δ 172.3, 170.9, 169.6, 169.3, 141.5, 137.0, 136.1, 129.6, 128.5, 128.2, 128.2, 128.1, 118.0, 80.2, 68.5, 66.2, 61.5, 61.1, 61.0, 51.0, 48.3, 46.2, 30.6, 29.7, 14.0; IR (thin film, cm^{-1}): 3064, 3029, 2981, 2952, 2873, 1732, 1603, 1493, 1457, 1435, 1389, 1370, 1271, 1197, 1175, 1097, 1074, 1029, 930, 827, 754, 703; HRMS (ESI) calcd. for $C_{31}H_{38}N_2O_8H^+$: 567.2701 found: 567.2694.



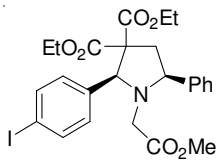
4aa

Compound 4aa: Methyl 1-((methoxycarbonyl)methyl)-2,5-*bis*(4-methoxyphenyl)imidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 4H), 5.05 (s, 1H), 4.37(d, *J* = 6.8 Hz, 1H), 3.86 (d, *J* = 6.8 Hz, 1H), 3.81 (s, 6H), 3.75 (s, 3H), 3.50 (s, 3H), 3.17 (dd, *J* = 28.0, 16.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.7, 171.1, 160.2, 159.6, 132.4, 132.2, 129.4, 129.0, 114.2, 79.5, 68.3, 67.0, 55.5, 52.5, 51.4, 47.9; IR (thin film, cm^{-1}): 3325, 3193, 2990, 2953, 2838, 1740, 1679, 1601, 1513, 1456, 1440, 1391, 1303, 1249, 1214, 1179, 1031, 833; HRMS (ESI) calcd. for $C_{22}H_{26}N_2O_6H^+$: 415.1864. found: 415.1868.



4ia

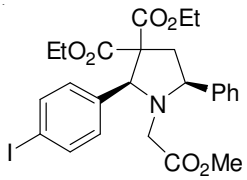
Compound 4ia: Methyl-1-((methoxycarbonyl)methyl)-2,5-*bis*(3-methoxyphenyl)imidazolidine-4-carboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.24-7.19 (m, 2H), 7.11-7.02 (m, 4H), 6.82-6.76 (m, 2H), 5.07 (s, 1H), 4.41 (d, *J* = 6.0 Hz, 1H), 3.81 (d, *J* = 6.0 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.70 (s, 3H), 3.46 (s, 3H), 3.25-3.10 (m, 2H), 2.75 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 170.9, 159.8, 142.4, 141.6, 129.7, 120.1, 119.8, 144.4, 113.2, 113.4, 79.5, 68.2, 66.9, 55.3, 55.2, 52.4, 51.2,47.5; IR (thin film, cm^{-1}): 3337, 3001, 2951, 2836, 2593, 2077, 1738, 1600, 1488, 1260, 1045, 784, 698; HRMS (ESI) calcd. for $C_{22}H_{26}N_2O_6Na^+$: 437.1683. found: 437.1676.



cis-5b

Compound *cis*-5b: Diethyl1-((methoxycarbonyl)-methyl)-2-(4-iodophenyl)-5-phenylpyrrolidine-3,3-dicarboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H),

7.37 (t, *J* = 7.2 Hz, 2H), 7.33-7.21 (m, 2H), 5.16 (s, 1H), 4.36-4.27 (m, 1H), 4.27-4.17 (m, 2H), 3.78-3.67 (m, 1H), 3.49 (s, 3H), 3.46-3.38 (m, 1H), 3.12 (s, 2H), 2.88 (dd, *J* =10.8, 2.4 Hz, 1H), 2.54 (dd, *J* =6.4,7.2 Hz, 1H), 1.25 (t, *J* = 6.8 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.4, 170.9, 169.4, 140.9, 139.0, 138.9, 137.3, 131.3, 128.9, 128.3, 93.8, 69.4, 64.5, 62.1, 61.7, 51.4, 48.9, 46.5, 42.3; IR (thin film, cm^{-1}): 3062, 3029, 2962, 2904, 2873, 1729, 1482, 1367, 1261, 1231, 1181, 1096, 1061, 1022, 801, 762, 702; HRMS (ESI) calcd. for $C_{25}H_{28}INO_2H^+$: 566.1034 found: 566.1033.



cis-5b

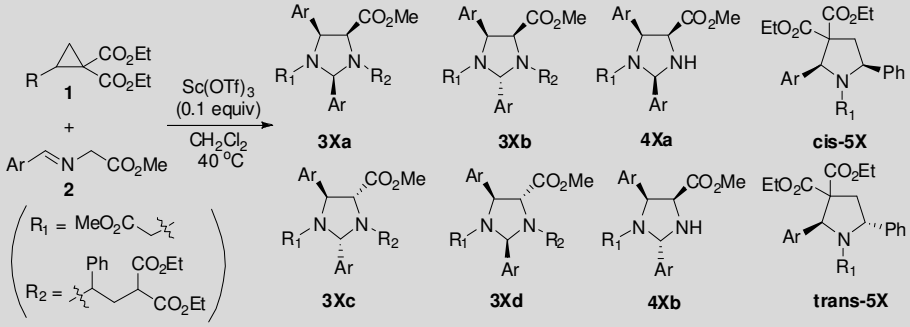
Comound *cis*-5h: Diethyl-1-((methoxycarbonyl)-methyl)-2-(2-chlorophenyl)-5-phenylpyrrolidine-3,3-dicarboxylate: Colourless viscous oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.78 (d, *J* = 6.0 Hz, 1H), 7.51 (d, *J* = 6.9 Hz, 2H), 7.43-7.23 (m, 5H), 7.17 (t, *J* = 7.5 Hz, 1H), 5.82 (s, 1H), 4.43-4.33 (m, 1H), 4.32-4.22 (m, 2H), 3.78-3.65 (m, 1H), 3.52 (s, 3H), 3.43-3.30 (m, 1H), 3.11 (dd, *J* = 22.2, 16.2 Hz, 2H), 2.93 (dd, *J* = 13.2, 12.0 Hz, 1H), 2.46 (dd, *J* = 13.2, 5.1 Hz, 1H), 1.28 (t, *J* = 7.2 Hz, 3H), 0. 85 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.8, 170.6, 168.7, 140.2, 137.7, 135.6, 130.5, 129.0, 128.7, 128.6, 128.0, 127.8, 126.5, 65.1, 64.3, 61.8, 61.2, 51.1, 49.7, 43.0, 29.7, 14.0, 13.3; IR (thin film, cm^{-1}): 3064, 3030, 2956, 2925, 2854, 1732, 1463, 1377, 1367, 1260, 1179, 1096, 1050, 1022, 800, 756, 701; HRMS (ESI) calcd. for $C_{25}H_{28}ClNO_6H^+$: 474.1678 found: 474.1670.

RESULTS AND DISCUSSION

In an initial attempt, the reaction of cyclopropane 1,1-diester **1a** and the precursor of azomethine ylide **2a** was examined under various reaction conditions. It was found that the tandem reaction proceeded smoothly by using Sc(OTf)$_3$ (10 mol %) in CH_2Cl_2 at 40 °C under nitrogen to produce two tandem ring-opening products as a mixture of chromatographically inseparable isomers (**3aa**:**3ab** = 1:1.7) in a total 63 % yield, together with a trace amount of dimerized self-[3+2] cycloaddcuts (**4aa** and **4ab**)[5] of **2a** (entry 1 in Table-2).

With the optimized reaction conditions in hand, the scope of this reaction was explored, with some typical results summarized in Table-2. As shown in Table-2, reactions of **1a** with both electron-rich and electron-deficient aryl-substituted **2a-i** proceeded smoothly with moderate yields (entries 1-9). In most cases, the tandem self-[3+2] cycloaddition/nucelophilic ring-opening products were obtained exclusively. The products were obtained either as two or three or all the four diastereoisomers. As in the case of **2a**, reaction of **2i** with **1a** gave only two chromatographically inseparable diastereoisomers (entry 9). The reactions of **1a** with **2b-f** gave three or all the four diastereoisomers which could be separated by column chromatography into two fractions (entries 2-6). In cases of **2c**, **2d** and **2f**, one of the two fractions contained only one single diastereoisomer (entries 3, 4 and 6). In cases of **2b** and **2e**, each fraction consisted of two chromatographically inseparable isomers (entries 2 and 5). The reaction of **1a** with **2g** or **2h**

TABLE-2
THE TANDEM REACTION OF CYCLOPROPANE 1,1-DIESTERS **1** WITH AZOMETHINE YLIDES **2**[a]



Entry	R	Ar	Time (h)	Yield (%)[b] of **3X** (ratio[c])		Yield (%)[b] of **4X** (ratio[c])	Yield (%)[b] of **5X** (ratio[c])
1	Ph (**1a**)	4-MeOC$_6$H$_4$ (**2a**)	14	63 (**3aa**:**3ab** = 1:1.7)	–	Trace	–
2	Ph (**1a**)	4-IC$_6$H$_4$ (**2b**)[d]	16	29 (**3ba**:**3bd** = 1:0.9)	33 (**3bb**:**3bc** = 3:1)	Trace	16 (1:0.2)[e]
3	Ph (**1a**)	C$_6$H$_5$ (**2c**)	15	65 (**3ca**:**3cb** = 1:0.4)	12 (**3cc**:**3cd** = 1:0)	–	–
4	Ph (**1a**)	4-MeC$_6$H$_4$ (**2d**)	15	31 (**3da**:**3dc** = 1:0)	28 (**3db**:**3dd** = 1:0.3)	–	–
5	Ph (**1a**)	4-BrC$_6$H$_4$ (**2e**)	17	32 (**3ea**:**3ed** = 1:0.4)	30 (**3eb**:**3ec** = 1:0.6)	–	–
6	Ph (**1a**)	4-ClC$_6$H$_4$ (**2f**)	19	25 (**3fa**:**3fd** = 1:0)	34 (**3fb**:**3fc** = 1:0.4)	Trace	–
7	Ph (**1a**)	4-FC$_6$H$_4$ (**2g**)	23	56 (**3ga**:**3gb**:**3gc**:**3gd** = 1:0.9:0.2:0.3)		Trace	–
8	Ph (**1a**)	2-ClC$_6$H$_4$ (**2h**)	24	51 (**3ha**:**3hb**:**3hc**:**3hd** = 1:0.7:0.5:0.9)		–	17 (1:0)[e]
9	Ph (**1a**)	3-MeOC$_6$H$_4$ (**2i**)	48	46 (**3ia**:**3ib** = 1:0.8)	–	16 (**4ia**:**4ib** = 1:0.7)	–
10	Vinyl (**1b**)	C$_6$H$_5$ (**2c**)	28	44 (**3ca**:**3cb** = 1:1.2)	–	–	–
11	^{i}Bu (**1c**)	C$_6$H$_5$ (**2c**)	11	–	–	10 (**4ca**:**4cb** = 1:1)	–
12	H (**1d**)	C$_6$H$_5$ (**2c**)	27	–	–	–	–

[a]Conditions: Molar ratio of **1** to **2** = 1:2.2, 4 Å MS, N_2; [b]Isolated yields by silica gel chromatography; [c]Determined by ^{1}H NMR; [d]Et$_3$N (0.1 equivalent) was added; [e]*cis*:*trans*

gave all the four diastereoisomers which could not be separated by column chromatography (entries 7 and 8). Like the reaction of **1a** with **2a** or **2i**, reaction of vinyl-substituted cyclopropane 1,1-diester **1b** with **2c** also gave two chromatographically inseparable diastereoisomers (entry 10) but with a lower yield (44 %). Reaction of iso-butyl-substituted cyclopropane 1,1-diester **1c** with **2c** only gave a small amount of two inseparable self-[3+2] cycloadducts (**4ca** and **4cb**) of **2c** (entry 11). Due to the predictable poor reactivity, reaction of non-substituted cyclopropane 1,1-diester **1d** with **2c** did not proceed (entry 12). It should be noted that in the reaction of **1a** with **2b** or **2h** besides the tandem ring-opening products **3**, cross-[3+2] cycloaddcuts **5** of cyclopropane 1,1-diester **1a** with C=N were also isolated[7].

Structures of all the four possible diastereoisomers of products **3** were confirmed by $^{1}H/^{13}C$ NMR, MS, X-ray single-crystal and 2D NOESY experiments. **3ca** and **3cc** were purified by recrystallization and the structures of which were confirmed by X-ray single-crystal analysis[8], respectively (Fig. 1). *Ha* and *Hb* in **3cb** (*cis*-HaHb) has strong NOE correlation, however the NOE correlation of *Ha* and *Hb* (*trans*-HaHb) in **3cc** was not observed obviously.

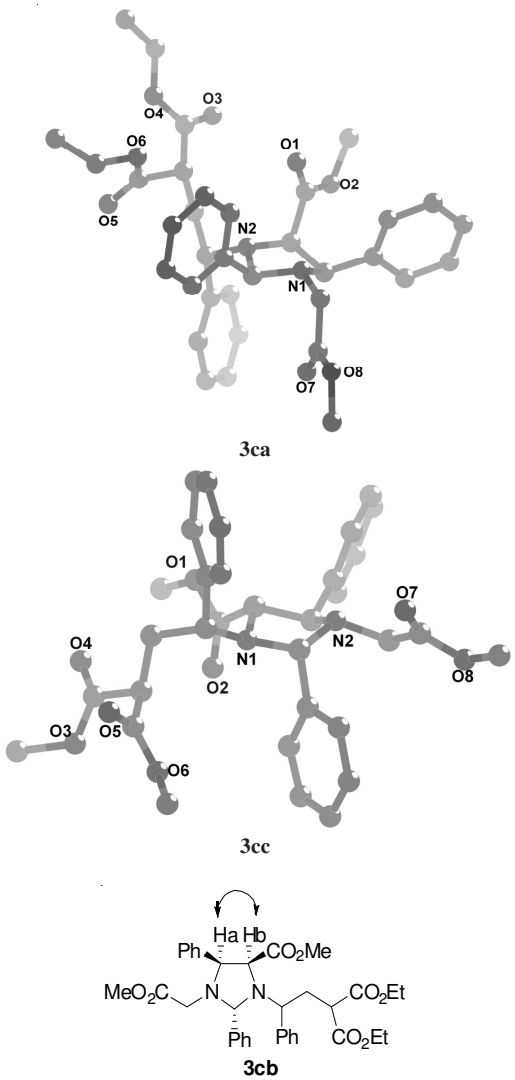
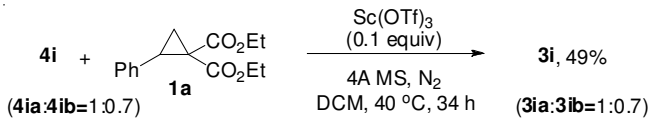


Fig. 1. X-ray crystallographic structure of **3ca** and **3cc** and 2D NOESY correlation for **3cb**

In order to better understand the mechanism of the tandem process, reaction of cyclopropane 1,1-diester **1a** with imidazolidines **4i** (1.2 equivalent) was carried out and the desired product **3i** was obtained in 49 % yield (**Scheme-III**). Thus a possible tandem dimerized self-[3+2] cycloaddition/ nucelophilic ring-opening mechanism could well demonstrate the formation of **3**.



Scheme-III: Reacion of cyclopropane 1,1-diester **1a** with imidazolidine **4i** in the presence of $Sc(OTf)_3$

Conclusion

In summary, a new tandem reaction combined with a dimerized self-[3+2] cycloaddition of azomethine ylide and a nucleophilic ring-opening of cyclopropane 1,1-diester is developed. A series of polyfunctionalized imidazolidine derivatives were synthesiszed by this reaction. In some cases, this tandem reaction was also accompanied by a cross-[3+2] cycloaddition of cyclopropane 1,1-diester with imine.

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REFERENCES

1. (a) S. Danishefsky, *Acc. Chem. Res.*, **12**, 66 (1979); (b) H.N.C. Wong, M.-Y. Hon, C.-W. Tse and Y.-C. Yip, *Chem. Rev.*, **89**, 165 (1989); (c) H.-U. Reissig and R. Zimmer, *Chem. Rev.*, **103**, 1151 (2003); (d) M. Yu and B.L. Pagenkopf, *Tetrahedron*, **61**, 321 (2005); (e) E. Wenkert, *Acc. Chem. Res.*, **13**, 27 (1980); (f) O.G. Kulinkovich, *Chem. Rev.*, **103**, 2597 (2003); (g) L.A. Paquette, *Chem. Rev.*, **86**, 733 (1986); (h) C.A. Carson and M.A. Kerr, *Chem. Soc. Rev.*, **38**, 3051 (2009).
2. (a) M. Shi, Y.H. Yang and B. Xu, *Tetrahedron*, **61**, 1893 (2005); (b) C. Timmons, D. Chen, J.F. Cannon, A.D. Headley and G. Li, *Org. Lett.*, **4**, 2075 (2006); (c) F. Bertozzi, B.V. Gundersen, M. Gustafsson and R. Olsson, *Org. Lett.*, **5**, 1551 (2003); (d) Y.H. Yang and M. Shi, *J. Org. Chem.*, **70**, 10082 (2005); (e) Z. Han, S. Uehira, T. Tsuritani, H. Shinokubo and K. Oshima, *Tetrahedron*, **57**, 987 (2001); (f) O.A. Ivanova, E.M. Budynina, Y.K. Grishin, I.V. Trushkov and P.V. Verteletskii, *Eur. J. Org. Chem.*, 5329 (2008); (g) A.B. Leduc, T.P. Lebold and M.A. Kerr, *J. Org. Chem.*, **74**, 8414 (2009); (h) J. Magolan and M.A. Kerr, *Org. Lett.*, **8**, 4561 (2006); (i) T.P. Lebold, A.B. Leduc and M.A. Kerr, *Org. Lett.*, **11**, 3770 (2009); (j) Md. I. Uddin, A. Mimoto, K. Nakano, Y. Ichikawa and H. Kotsuki, *Tetrahedron Lett.*, **49**, 5867 (2008); (k) O. Lifchits and A.B. Charette, *Org. Lett.*, **10**, 2809 (2008).
3. (a) L.F. Tietze and U. Beifuss, *Angew. Chem., Int. Ed. Engl.*, **32**, 131 (1993); (b) L.F. Tieze, *Chem. Rev.*, **96**, 115 (1996); (c) P.J. Parsons, C.S. Penkett and A.J. Shell, *Chem. Rev.*, **96**, 195 (1996); (d) R.A. Bunce, *Tetrahedron*, **51**, 13103 (1995); (e) K.C. Nicolaou, D.J. Edmonds and P.G. Bulger, *Angew. Chem., Int. Ed.*, **45**, 7134 (2006); (f) H. Pellissier, *Tetrahedron*, **62**, 1619 (2006); (g) H. Pellissier, *Tetrahedron*, **62**, 2143 (2006).
4. (a) W.-J. Liu, X.-H. Chen and L.-Z. Gong, *Org. Lett.*, **10**, 5357 (2008); (b) M.-J. Jin, V.B. Takale, M.S. Sarkar and Y.-M. Kim, *Chem. Commun.*, 663 (2006); (c) A. Viso, R.F. de la Pradilla, A. Garcia, C. Guerrero-Strachan, M. Alonso, M. Tortosa, A. Flores, M. Martinez-Ripoll, I. Fonseca, I. Andre and A. Rodriguez, *Chem. Eur. J.*, **9**, 2867 (2003); (d)

A. Szollosy, T. Tischer, I. Kadas, L. Toke and G. Toth, *Tetrahedron*, **55**, 7279 (1999); (e) D. Alker, L.M. Harwood and C.E. Williams, *Tetrahedron Lett.*, **39**, 475 (1998); (f) A. Viso, R.F. de la Pradilla, C. Guerrero-Strachan, M. Alonso, M. Martinez-Ripll and I. Andre, *J. Org. Chem.*, **62**, 2316 (1997); (g) Y. Nagao, K. Kim, Y. Komaki, S. Sano, M. Kihara and M. Shiro, *Heterocycles*, **38**, 587 (1994); (h) A. Padwa, D.C. Dean, M.H. Osterhout, L. Precedo and M.A. Somones, *J. Org. Chem.*, **59**, 5347 (1994); (i) J.M. Lerestif, J.P. Bzaureau and J. Hamelin, *Tetrahedron Lett.*, **29**, 4639 (1993); (j) K. Amornraksa, D. Barr, G. Donegan, R. Grigg, P. Ratananukul and V. Sridharan, *Tetrahedron*, **45**, 4649 (1989); (k) R. Grigg, G. Donegan, H.Q.N. Gunaratne, D.A. Kennedy, J.F. Malone, V. Sridharan and S. Thianpatanagul, *Tetrahedron*, **45**, 1723 (1989); (l) J. Chastanet and G. Roussi, *J. Org. Chem.*, **53**, 3808 (1988); (m) R. Beugelmans, J. Chastanet and G. Roussi, *Heterocycles*, **26**, 3197 (1987); (n) Z. Bende, I. Bitter, L. Toke, L. Weber, G. Toth and F. Janke, *Liebigs. Ann. Chem.*, 2146 (1982); (o) R. Grigg and J. Kemp, *J. Chem., J. Chem. Soc., Chem. Commun.*, 109 (1978); (p) G. Dallas, J.W. Lown and J.P. Moser, *J. Chem. Soc., Chem. Commun.*, 2383 (1970).

5. (a) C. Mapelli, G. Turocy, F.L. Switzer and C.H. Stammer, *J. Org. Chem.*, **54**, 145 (1989); (b) W. Fraser, C.J. Suckling and H.C.S. Wood, *J. Chem. Soc. Perkin Trans. I*, 3137 (1990); (c) E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
6. (a) S. Cabrera, R.-G. Arrayas, M.-M. Belen, F.-P. Cossio and J.-C. Carretero, *Tetrahedron*, **63**, 6587 (2007); (b) M. Ayerbe, A. Arrieta and F.P. Cossío, *J. Org. Chem.*, **63**, 1795 (1998).
7. (a) Y.-B. Kang, Y. Tang and X.-L. Sun, *Org. Biomol. Chem.*, **4**, 299 (2006); (b) C.A. Carson and M.A. Kerr, *J. Org. Chem.*, **70**, 8242 (2005); (c) S.K. Jackson, A. Karadeolian, A.B. Driega and M.A. Kerr, *J. Am. Chem. Soc.*, **130**, 4196 (2008); (d) S.D.R.R. Christie, J. Davoile and R.C.F. Jones, *Org. Biomol. Chem.*, **4**, 2683 (2006); (e) T.P. Lebold and M.A. Kerr, *Org. Lett.*, **11**, 4354 (2009).
8. The crystal data of **3ca** and **3cc** have been deposited in CCDC with Nos. 761028 and 761029, respectively.