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Ag(I)-Fesulphos Catalyzed Enantioselective Synthesis of 3-Silylproline Derivatives

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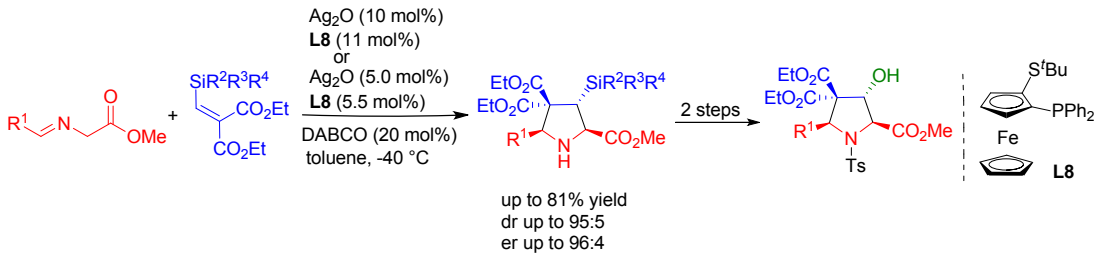
Abstract: An efficient catalytic asymmetric 1,3-dipolar cycloaddition of *N*-benzylidineiminoglycinate derived azomethine ylides to β-silylmethylene malonates catalysed by a Ag(I)-Fesulphos complex has been developed, affording fully substituted 3-silylproline derivatives with an all carbon quaternary center. The silylproline derivatives were obtained in moderate-to-good yields (up to 81%) in high diastereo- and enantioselectivities (dr up to 95:5; er up to 96:4). Tamao-Fleming oxidation of selected 3-silylproline derivatives provided efficient and shortest route to 3-hydroxyproline derivatives which are not accessible by direct 1,3-dipolar cycloadditions of azomethine ylide with frequently used arylidene/alkylidene malonates.



INTRODUCTION

Organosilicon compounds are known to have enormous applicability starting from protecting group to intermediates in natural product synthesis.[1,2] In recent time, silicon-containing amino acids (Figure 1) are getting considerable attention because they are well-suited to provide the protein structure and also can act as a structural probes for finding drug-protein binding

interaction.[3,4] In addition, many silicon-containing molecules and peptides are known for their inhibitory activity towards certain enzymes (Figure 1) and some of them are in the final stage of clinical trials.[3,4] Silicon is considered as a bioisostere of carbon since both belong to the same group in the periodic table. Incorporation of the silicon into the amino acid or peptide enhances the lipophilicity due to unique properties of the silyl group.[5] Enhancement of lipophilicity may ease membrane permeability and cellular uptake.[5] It has also been found that the integration of silicon-containing amino acids into peptide changes the properties of these biomolecules such as conformational freedom, enhanced stability, hydrophobicity, and increase in resistance to enzymatic degradation and bioavailability.[3] Despite their alluring medicinal and biological applications, only a handful of methods are available for synthesis of silicon-containing amino acids and their derivatives.[3,4] The use of stoichiometric reagents, auxiliaries and resolution of intermediates are still common protocols for their synthesis.[3,4]The catalytic methods for their preparation is rare in literature.[6] Therefore, development of new catalytic methods for synthesis of novel silicon-containing amino acid derivatives is a pre-requisite and at the same time challenging.

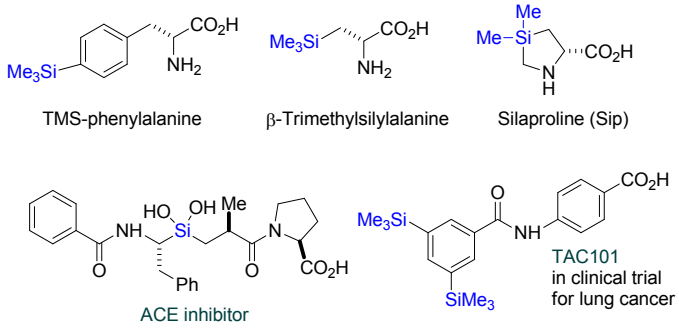


Figure 1. Representative examples of silicon-containing amino acids and medicinally important silicon-containing molecules.

To understand the mechanism of conformational stability of protein triple helix structures and development of novel peptide-based drug molecules, new 3-hydroxyproline

derivatives and 3-silylproline derivatives are likely to play significant roles. 3-hydroxyproline is known to induce *β*-turn in peptide and is also present in many bioactive peptides including important structural protein collagen.[7] Furthermore, 3-hydroxypyrrolidines are privileged substructures widespread in numerous biologically active natural products (Figure 2) and also crucial intermediates for variety of natural products and drug molecules.[8]

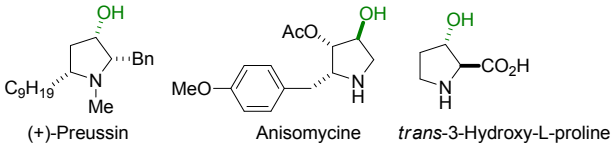
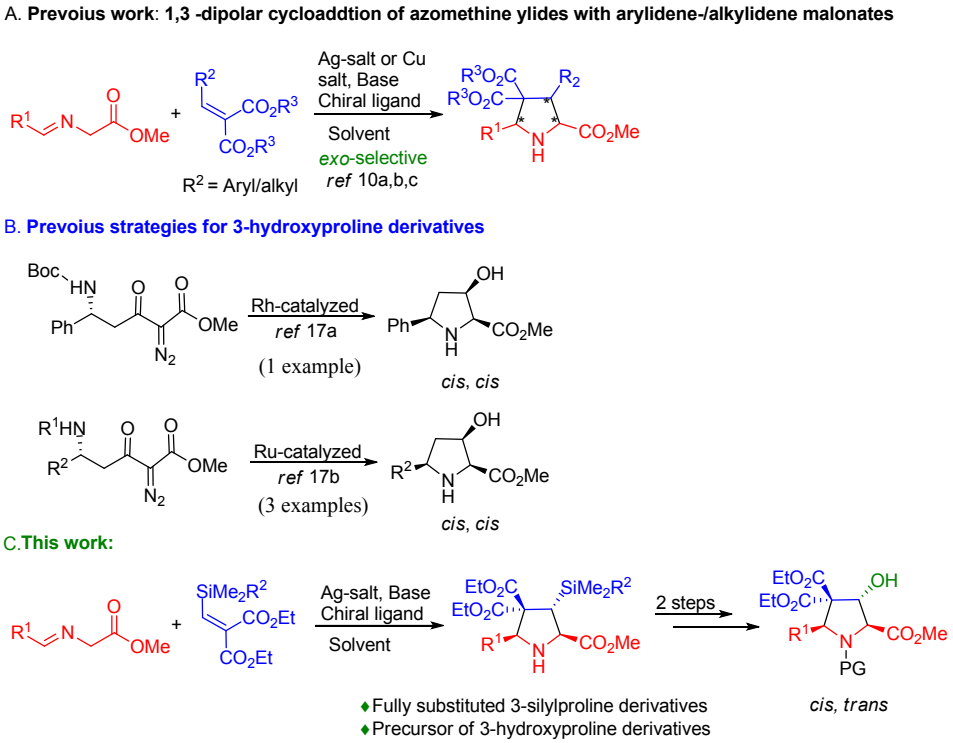


Figure 2. 3-Hydroxypyrrolidine based natural products and amino acid.

The catalytic asymmetric1,3-dipolar cycloadditions of azomethine ylides to variety of electron-deficient alkenes as dipolarophiles is the most explored route for the construction of enantioenriched densely substituted pyrrolidines because of its efficacy, straightforwardness and atom economy.[9,10] Research groups of Zhang[11] and Jørgensen[12] independently reported first examples of metal catalyzed asymmetric1,3-dipolar cycloaddition of azomethine ylides derived from iminoesters with activated alkenes. Since then, diverse electron deficient alkenes including aryl- and alkylidene malonates (Scheme 1 A) and different variety of azomethine ylides have been enrolled in catalytic asymmetric1,3-dipolar cycloadditions affording pyrrolidines with diverse substitution patterns.[9,10]However, presumably β-silylmethylene malonate **2** has not so far been employed as a dipolarophile in 1,3-dipolar cycloaddition with azomethine ylide.[13] Considering the importance of 3-silylproline derivatives and 3-hydroxypyrrolidine derivatives, we envisaged that 1,3-dipolar cycloaddition reaction of *N*-benzylideneiminoglycinates derived azomethine ylides with β-silylmethylene malonates[14] would lead to 3-silylproline derivatives. Subsequent conversion of dimethyl(phenyl)silyl group to a hydroxy group following the Tamao–Fleming oxidation[15] would lead to 3-hydroxyproline derivatives. Several methods[16] have been reported for the preparation of enantiopure 3-

hydroxyproline whereas the synthetic routes for the substituted 3-hydroxyproline derivatives are in dearth. To best of our knowledge, there are only two reports for the enantioselective synthesis of substituted 3-hydroxyproline derivatives wherein Rh or Ru catalyzed intramolecular carbenoid N-H insertion reaction of appropriately designed chiral *δ*-amino β-ketoester based diazo compounds followed by stereoselective reduction have been used (Scheme 1 B).[17] Herein, we report a straightforward synthetic route for the asymmetric synthesis of fully substituted 3-silylproline derivatives and 3-hydroxyproline derivatives starting from simple and easily accessible achiral starting materials (Scheme 1C).

Scheme 1. Asymmetric 1,3-dipolar cycloadditions of azomethine ylides with arylidene-/ alkylidene-/ β-silylmethylene malonates and synthesis of 3-hydroxyproline derivatives.

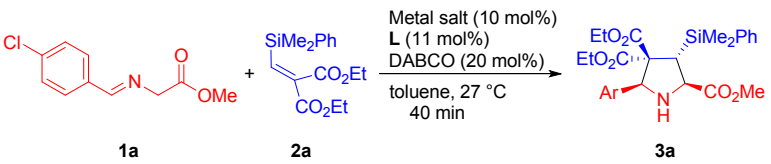


RESULTS AND DISCUSSION

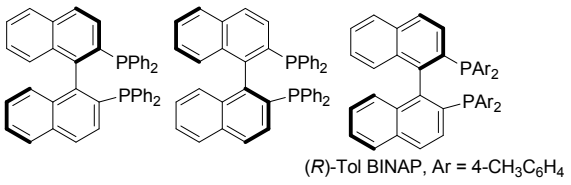
Our investigation began with the optimization studies of the 1,3-dipolar cycloaddition reaction of azomethine ylide, derived *in-situ* from *N*-(4-chlorobenzylidene)glycine methyl ester **1a** and

β-silylmethylene malonate **2a**. When the reaction between **1a** and **2a** was performed in toluene without addition of silver salt, ligand and base at 27 °C, the conversion to desired pyrrolidine derivative **3a** was very slow as judged by ^{1}H NMR spectroscopy.[18] Then, we investigated the catalytic version of the reaction using the *cinchona* alkaloid derived tertiary amino-(thio)urea derivatives and *trans*-1,2-diaminocyclohexane based-(thio)urea derivatives. We found that these (thio)urea derivatives were not promising for this 1,3-dipolar cycloaddition reaction (see Supporting Information). Subsequently, we switched to commercially available axially chiral bisphosphine ligands. When the reaction between model substrates**1a** and **2a** was carried out in the presence of (*R*)-BINAP ligand **L1** in combination with Ag_2O as the catalyst system and DABCO as the base in toluene at 27 °C, the reaction proceeded smoothly and to our delight, the *exo*-**3a** was formed with moderate yield and enantioselectivity (Table 1, entry 1). Encouraged by this preliminary result, an array of bisphosphine ligands **L2**-**L7** were screened (Table 1, entries 2-7). In all the cases, the desired *exo*-**3a** was obtained without any improvement of enantioselectivity. The next series of attempts were performed with ligands **L8** and **L9** having ferrocene backbone. (*R*)-Fesulphos ligand **L8**/Ag_2O catalyst system was found to be more promising, furnishing the *exo*-product **3a** in 74% yield, with high diastereoselectivity (96:4 dr) and moderate enantioselectivity (86:14 er) (Table 1, entry 8). Therefore, Fesulphos **L8** was selected as the ligand for further studies. Exploration of the reaction with silver carbonate (Table 1, entry 10), silver acetate (Table 1, entry 11), and cupric acetate (Table 1, entry 12) did not give superior result compared to Ag_2O.

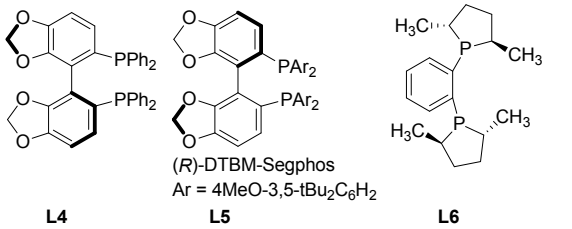
Table 1. **Screening of the ligand and metal salt** [a]



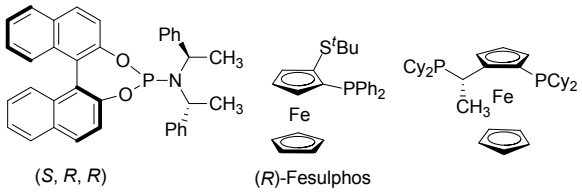
1a **2a** **3a**



L1 **L2** **L3**



L4 **L5** **L6**



L7 **L8** **L9**

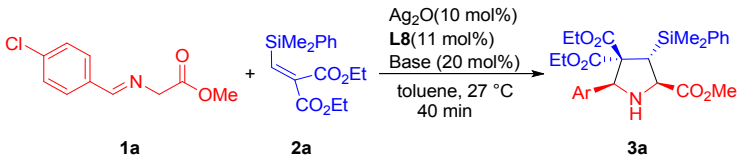
entry	metal salt	ligand	% conv.[b]	dr[c]	yield[d] (%)	er[e]
1	Ag_2O	**L1**	>98	ND	62	19:81
2	Ag_2O	**L2**	>98	90:10	65	77:23
3	Ag_2O	**L3**	ND[f]	ND[f]	67	28:72
4	Ag_2O	**L4**	>98	90:10	65	76:24
5	Ag_2O	**L5**	>98	88:12	66	45:55
6	Ag_2O	**L6**	>99	88:12	73	25:75
7	Ag_2O	**L7**	>97	95:5	61	66:34
8	Ag_2O	**L8**	>99	95:5	74	86:14
9	Ag_2O	**L9**	>98	85:15	ND[f]	52:48
10[g]	Ag_2CO_3	**L8**	>96	94:6	74	85:15
11	AgOAc	**L8**	>99	94:6	75	82:18

12[g]	$Cu(OAc)_2$	**L8**	>42	ND	ND	ND

[a]Unless otherwise stated, reactions were carried out with 0.2 mmol of **1a** and 0.1 mmol of **2a** in 1 mL of toluene at 27 °C. [b]Indicate percentage of conversion of the starting material **2a**, determined by ^{1}H NMR analysis of the crude reaction mixture. [c]The dr[19] was determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Yield of the major diastereomer. [e]The enantiomeric ratio (er) was determined by HPLC analysis using a chiral stationary phase. [f]Not determined. [g]Reaction time 2h.

Subsequently different organic bases were surveyed (Table 2, entries 1-3) in the reaction but found inferior than DABCO. A solvent screening (Table 2, entries 2 and 4-6) revealed that toluene remained the best choice of solvent in terms of yield, diastereo-and enantioselectivity. Dilution of the reaction did no effect on the enantioselectivity of **3a**. Lowering the temperature had a beneficial effect on enantioselectivity. When the reaction was carried out at 0 °C, the *exo*-adduct **3a** was obtained with excellent diastereoselectivity and improved enantioselectivity (Table 2, entry 8). Lowering of the temperature to -40 °C lead to improvement in enantioselectivity of **3a** while the yield and diastereoselectivity remained unchanged (Table 2, entry 10). Further enhancement of enantioselectivity of **3a** could not be achieved by performing the reaction at -60 °C (Table 2, entry 11). Lowering in the loading of catalyst system viz. Ag_2O (5 mol%), and ligand **L8** (5.5 mol%), resulted in slightly reduced yield without much change in selectivities (Table 2, entry 12). From the above studies, we chose two sets of optimized reaction conditions: *Conditions A*: **1a** (0.2 mmol), **2a** (0.1 mmol), Ag_2O (0.01mmol), **L8** (0.011mmol) and DABCO (0.02 mmol) in 1mL of toluene at -40 °C (Table 2, entry 10) and *Conditions B*: **1a** (0.4 mmol), **2a** (0.2 mmol), Ag_2O (0.01mmol), **L8** (0.011mmol) and DABCO (0.04 mmol) in 2 mL of toluene at -40 °C (Table 2, entry 12).

Table 2. Reaction optimizations[a]



1a 2a 3a

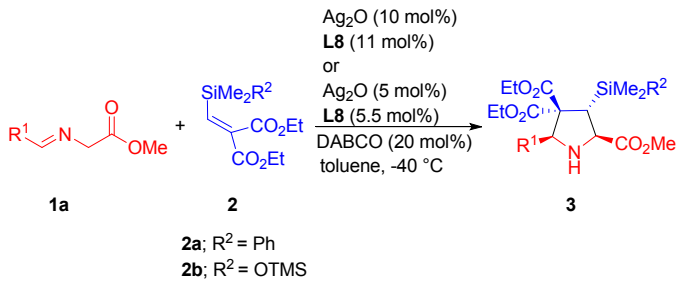
entry	base	solvent	% conv.[b]	dr[c]	yield[d] (%)	er (%)[e]
1	Et_3N	$C_6H_5CF_3$	90	90:10	58	81:19
2	$^iPr_2NEt_2$	$C_6H_5CF_3$	86	90:10	54	85:15
3	DBU	toluene	>40	70:30	ND[f]	ND[f]
4[g]	DABCO	Et_2O	>90	82:18	57	85:15
5	DABCO	THF	>99	75:25	55	85:15
6	DABCO	MTBE	90	ND[f]	58	85:15
7[h]	DABCO	toluene	ND[f]	95:5	62	85:15
8[i]	DABCO	toluene	>99	96:4	76	89.5:10.5
9[j]	DABCO	toluene	>99	95:5	75	90.5:9.5
10[k]	DABCO	toluene	>99	95:5	77	94.5:5.5
11[l]	DABCO	toluene	>98	95:5	70	94:6
12[m]	DABCO	toluene	>98	95:5	74	94.5:5.5

[a] Reactions were carried out with 0.2 mmol of **1a** and 0.1 mmol of **2a**, Ag_2O (0.01 mmol), **L8** (0.011 mmol) and DABCO (0.02 mmol) in 1 mL of solvent at 27°C. [b] Determined by ^1H NMR analysis of the crude reaction mixture. [c]The dr[19] was determined by ^1H NMR analysis of the crude reaction mixture. [d] Yield of the major diastereoisomer. [e]The enantiomeric ratio (er) was determined by HPLC analysis using a chiral stationary phase. [f] Not determined. [g]Reaction time was 2 h. [h]2 mL of toluene was used. [i]The reaction was carried out at 0°C, reaction time 5 h,

10 mol% of **L8** was used. [j]The reaction was performed at -20°C and reaction time 10 h, 10 mol% **L8** was used. [k] The reaction was performed at -40 °C and reaction time was 10 h. [l]The reaction was performed at -60°C and reaction time 12 h. [m]Reactions was carried out with 0.4 mmol of **1a** and 0.2 mmol of **2a**, Ag_2O (0.01mmol), **L8** (0.011 mmol) and DABCO (0.04 mmol) in 2 mL of toluene at -40 °C, reaction time was 12 h.

With the established optimization reaction conditions in hand, we explored the reaction of β-silylmethylene malonate **2a** with various imino esters **1**. The results are summarised in Table 3. Imino esters **1** with the aryl group substituted at *para* position with electron withdrawing or donating groups were well tolerated and afforded desired *exo*-products **3a**, **3c-3f** in moderate to high yield and high diastereo - and enantioselectivity. The imino esters with substituent at *meta* and *ortho* position on the aromatic ring was also equally effective and provided the *exo*-cycloadducts **3g-3k** in high yield, diastereo- and enantioselectivity. It is noteworthy that the reaction worked well with heteroaromatic-substituted imino ester and the product **3l** was formed in high yield and enantioselectivity. The scope of this methodology was further extended to exploring the reaction of azomethine ylide derived from *N*-(4-chlorobenzylidene)glycine methyl ester **1a** with alkyl substituted β-silylmethylene malonate **2b**. The desired product **3m** was obtained in high yield and excellent stereoselectivity.

Table 3. Scope of substrates[a,b]



1a **2** **3**

2a; R^2 = Ph
2b; R^2 = OTMS

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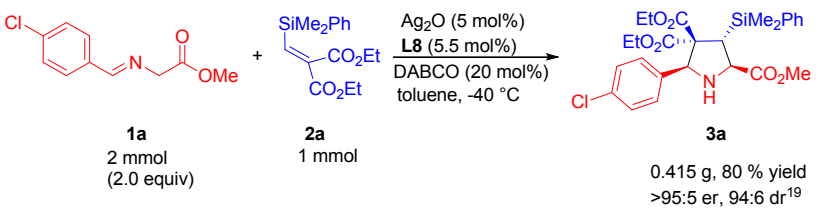
entry	R^1/R^2	**3**	dr[c]	yield[d] (%)	er (%)[e]
1[a]	4-ClC_6H_4/Ph	**3a**	95:5	77	94.5:5.5
2[b]	Ph/Ph	**3b**	94:6	73	93:7
3[b]	4-BrC_6H_4/Ph	**3c**	94:6	77	95:5
4[b]	4-FC_6H_4/Ph	**3d**	95:5	74	94.5:5.5
5[a]	4-$CF_3C_6H_4$/Ph	**3e**	94:6	74	95:5
6[a,f]	4-EtC_6H_4/Ph	**3f**	90:10	66	91.5:8.5
7	3-BrC_6H_4/Ph	**3g**	94:6	76	92:8
8[a]	3-ClC_6H_4/Ph	**3h**	92:8	75	93:7
9[a]	3-FC_6H_4/Ph	**3i**	95:5	78	92:8
10[a]	2-ClC_6H_4/Ph	**3j**	92:8	71	95:5
11[a]	2-FC_6H_4/Ph	**3k**	91:9	71	95:5
12[a]	2-thienyl/Ph	**3l**	95:5	81[g]	93.5:6.5
13[a]	4-ClC_6H_4/OTMS	**3m**	94:6	72	96:4

[a]Reaction *conditions A*: **1** (0.2 mmol), **2a** (0.1 mmol), Ag_2O (0.01 mmol), **L8** (0.011 mmol), DABCO (0.02 mmol) in 1.0 mL toluene at -40 °C for 10-16 h. [b]Reaction *conditions B*: **1** (0.4 mmol), **2a** (0.2 mmol), Ag_2O (0.01 mmol), **L8** (0.011 mmol) and DABCO (0.04 mmol) in 2.0 mL of toluene at -40 °C for 10-14 h. [c]The dr[18] was determined by ^1H NMR of the crude reaction mixture. [d]Isolated yield of the major diastereomer. [e]Enantiomeric ratio (er) was determined by HPLC analysis using a chiral stationary phase. [f]The reaction was performed at 0 °C, 2.3 equiv of imino ester was used. [g]Combined yield of two diastereomers.

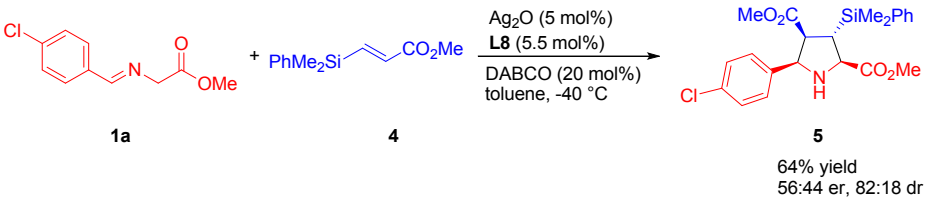
To demonstrate the practicality of the above developed method, the asymmetric 1,3-dipolar cycloaddition between **1a** and **2a** was conducted on a 1 mmol scale under the optimized conditions, affording **3a** with 80% yield and with >95:5 er (Scheme 2).

Scheme 2. Scale-up synthesis of **3a**



Next, we turned our attention to extend the scope for other dipolarophiles. Thus the reaction between *N*-(4-chlorobenzylidene)glycine methyl ester **1a** and β-dimethylphenylsilyl-acrylate **4** was performed under optimized reaction conditions (*Conditions B*), which provided the *exo*-product **5** in good yield but with poor enantioselectivity (Scheme 3). The configuration of **5** was confirmed by comparison with literature data.[13]

Scheme 3. **1,3-Dipolar cycloaddition reaction of β-dimethylphenylsilyl acrylate**



The asymmetric 1,3-dipolar cycloaddition reaction of azomethine ylide derived from *N*-(4-chlorobenzylidene)glycine methyl ester **1a** to benzylidene-malonate **6** was examined under the optimized reaction conditions (*Conditions A*), the cycloadduct ***exo*-7** was obtained in good yield and excellent diastereoselectivity but in moderate enantioselectivity (Scheme 5). The relative stereochemistry of **7** was confirmed from literature report.[10c]

Scheme 4. **1,3-Dipolar cycloaddition reaction of benzylidene malonate 6**

The relative and absolute configuration of **3j** was established by single crystal X-ray crystallography as shown in Figure 4 which confirmed the cycloaddition took place in *exo* fashion. The configurations of the other products were assigned in analogy as *exo* products.

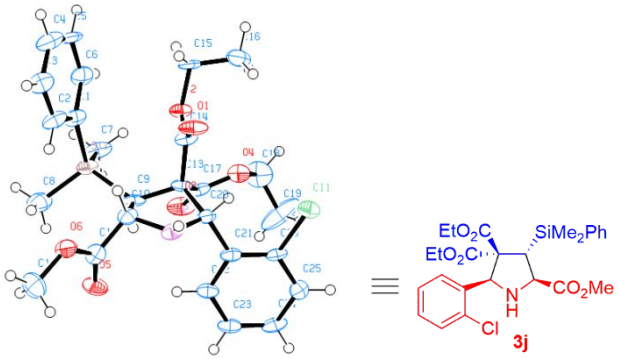


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Figure 4. ORTEP diagram of **3j,** ellipsoids show 50% probability levels.

The observed high stereoselectivity in the above developed 1,3-dipolar cycloaddition reaction could be explained by the proposed transition state (Figure 5).[10g] The azomethine ylide coordinates with Ag(I)–Fesulphos preferably in the orientation where the carbonyl oxygen atom of azomethine ylide and sulphur atom of Fesulphos ligand are *trans* to each other.[10c] The "bottom" face of the azomethine ylide is shielded by the bulky ^{t}Bu group of the Fesulphos ligand. Therefore, the dipolarophile **2** would preferably approach from the less hindered "top" face. Between the two faces of the dipolarophile **2**, a *Si*-face attack would lead to less stable transition state **I** due to steric repulsion between bulky silicon group of dipolarophile and PPh_2 group of the Fesulphos ligand while *Re*-face attack would lead to favourable transition state **II**.

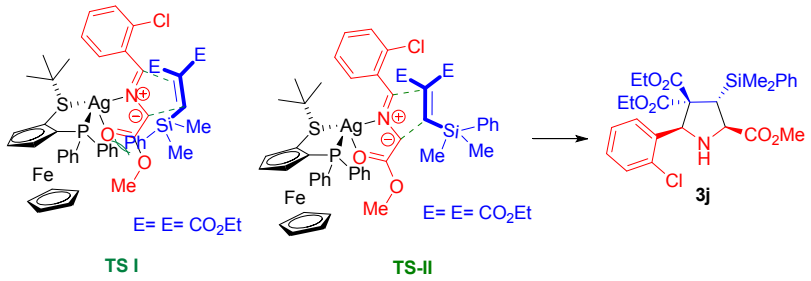
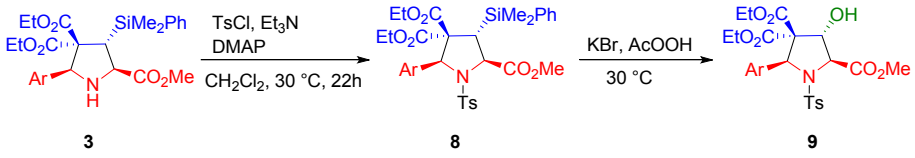


Figure 5. Proposed transition states

After successfully demonstrating the synthesis of fully substituted 3-silylproline derivative with an all carbon quaternary centre, we focussed our efforts to the synthesis of 3-hydroxyproline derivatives. Treatment of **3** with *p*-toluene sulfonyl chloride in presence of Et_3N in dichloromethane furnished the products **8**. Subsequently, the dimethyl(phenyl)silyl group in **8** was converted to hydroxy group (Table 4) with retention of configuration following the Tamao–Fleming oxidation.[15]

Table 4. Synthesis of 3-hydroxyproline derivatives[a,b]



3 **8** **9**

entry	**3**, Ar	**8**, yield[c] (%)	**9**, yield[d] (%)
1	**3a**, 4-ClC_6H_4	**8a**, 90	**9a**, 72
2	**3b**, C_6H_5	**8b**, 88	**9b**,70
3	**3c**, 4-BrC_6H_4	**8c**, 92	**9c**, 71
4	**3i**, 3-FC_6H_4	**8i**, 84	**9i**, 65

[a] Step1: Reactions were carried out with 0.15 mmol of **3**, 0.45 mmol of TsCl, 0.6 mmol of Et_3N and 20 mol% of DMAP in 3 mL of CH_2Cl_2. [b] Step 2: Reactions were carried out with 0.12 mmol of **8**, 0.16 mmol of potassium bromide, 0.1 mL of H_2O_2, 3 mL of peroxyacetic acid (35% solution in acetic acid). [c] Isolated yield of **8**. [d] Isolated yield of **9**.

Conclusion

In summary, we have developed an efficient Ag(I)-Fesulphos catalytic system for asymmetric 1,3-dipolar cycloaddition reaction of azomethine ylides with β-silylmethylene malonates, affording 3-silylproline derivatives in good yield and excellent stereoselectivities. Notably, β-silylmethylene malonates has been introduced for the first time as dipolarophiles in the 1,3-dipolar cycloaddition reactions of azomethine ylides. The usefulness of the developed reaction has been demonstrated by converting four cyclo-adducts into 3-hydoxyproline derivatives in two steps.

EXPERIMENTAL SECTION

General information. Solvent removal was performed with a rotary evaporator that was connected to a dry ice condenser. TLC (0.5 mm) was carried out using homemade silica gel plates with fluorescence indicator. Column chromatography was performed on silica gel (230-400 mesh). The ^{1}H and ^{13}C NMR spectroscopic data were recorded with 500 MHz (^{1}H NMR: 500 MHz, ^{13}C NMR: 125 MHz) Varian spectrometer and 200 MHz (^{1}H NMR: 200 MHz, ^{13}C NMR: 50 MHz) Bruker spectrometer. The ^{1}H and ^{13}C chemical shifts are given in ppm (δ scale) and are measured relative to $CHCl_3$ (7.27 ppm) and $CDCl_3$ (77.0 ppm), respectively, as internal standards. High resolution mass spectra were recorded at 60-70 eV with a Waters Micromass Q-TOF spectrometer (ESI, Ar). Enantiomeric ratio (*er*) values were determined by HPLC analysis with a JASCO (JASCOPU-2080) instrument fitted with a Daicel Chiralpak AD-H column, Daicel Chiralcel OD-H column and Daicel Chiralpak AS-H with UV-2075 detector (λ fixed at 254 nm). Melting points (mp) were measured in a Büchi B-540 apparatus. *N*-Benzylideneiminoglycinates **1** were prepared according to previously reported procedure.[20] β-Silylmethylene malonate **2a** and **2c** was prepared according to reported procedure.[9,21] Ag (I)-

salts, DABCO and chiral ligands were purchased from the commercial source and used as received without further purification. Et_3N, iPr_2EtN, DBU and TMG were dried over CaH_2 and stored over it. All the solvents were dried according to standard procedures.

General Procedure A for the preparation of *rac*-3-silyl proline derivatives 3a-3m

In an oven and vacuum-dried round-bottom flask, Ag_2O (2.3 mg, 0.01 mmol) and DABCO (2.3 mg, 0.02 mmol) were taken with 0.5 mL of freshly distilled toluene under argon. The reaction mixture was stirred at 30 ºC for 30 min. A solution of *N*-benzylideneiminoglycinates **1** (0.2 mmol, 2.0 equiv) in toluene (0.25 mL) was added slowly to the reaction mixture followed by the addition of a solution of β-silylmethylene malonate **2** (0.1 mmol, 1 equiv) in toluene (0.25 mL) and the reaction mixture was stirred at 30 ºC for 40 min-24 h. Once starting material was consumed (monitored by TLC), the reaction mixture was passed through a small pad of Celite and flushing with 100 mL of 50% EtOAc/hexane. The solvent was removed under reduced pressure and the residue was directly subjected to column chromatography on silica gel to afford the corresponding products ***rac* 3a-3m**.

General Procedure B for the preparation of chiral 3-silylproline derivatives 3a, 3e-3m

Condition A. Under Argon atmosphere, Ag_2O (2.3 mg, 0.01 mmol), DABCO (2.3 mg, 0.02 mmol) and ligand **L8** (5.0 mg, 0.011 mmol) were dissolved in 0.5 mL of freshly distilled toluene and stirred at room temperature for about 50 min. Then, the reaction mixture was cooled to -40 °C and a solution of *N*-benzylideneiminoglycinates **1** (0.2 mmol, 2.0 equiv) in toluene (0.25 mL) was added slowly to the reaction mixture followed by the addition of a solution of β-silylmethylene malonate **2** (0.1 mmol, 1 equiv) in toluene (0.25 mL). The reaction mixture was stirred at this temperature and once the β-silylmethylene malonate **2** was consumed (monitored by TLC), the reaction mixture was passed through a small pad of silica and flushing with 100 mL of 50% EtOAc/hexane. The solvent was removed under reduced

pressure and the residue was directly subjected to column chromatography on silica gel to afford the corresponding products **3a**, **3e-3m**.

General Procedure C for the preparation of chiral 3-silylproline derivatives 3a-3d

Condition B. Under Argon atmosphere, Ag_2O (2.3 mg, 0.01 mmol), DABCO (~4.5 mg, 0.04 mmol) and ligand **L8** (5.0 mg, 0.011 mmol) were dissolved in 1.0 mL of freshly distilled toluene and stirred at room temperature for about 50 min. Then, the reaction mixture was cooled to -40 °C and a solution of *N*-benzylideneiminoglycinates **1** (0.4 mmol, 2.0 equiv) in toluene (0.5 mL) was added slowly to the reaction mixture followed by the addition of a solution of β-silylmethylene malonate **2** (0.2 mmol, 1 equiv) in toluene (0.5 mL). The reaction mixture was stirred at this temperature and once the β-silylmethylene malonate **2** was consumed the reaction mixture (monitored by TLC), was passed through a small pad of silica and flushing with 150 mL of 50% EtOAc/hexane. The solvent was removed under reduced pressure and the residue was directly subjected to column chromatography on silica gel to afford the corresponding products **3a-3d.**

(2R,3S,5S)-4,4-diethyl 2-methyl 5-(4-chlorophenyl)-3-(dimethylphenylsilyl)pyrrolidine-2,4,4-tricarboxylate (**3a**). The title compound was prepared according to the general procedure C (*Condition B*). Yield : 77 mg (74 %); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54-7.52 (m, 2 H), 7.47 (d, J = 8.5 Hz, 2 H), 7.37-7.35 (m, 3H), 7.27-7.26 (m, 2 H), 5.05 (s, 1 H), 4.21 (dq, J = 10.8, 7.2 Hz, 1 H), 3.88 (d, J = 10.5 Hz, 1 H), 3.87-3.82 (m, 1 H), 3.80-3.76 (m, 1 H), 3.56 (dq, J = 10.8, 7.2 Hz, 1 H), 3.30 (s, 3 H), 2.86 (d, J = 10.5 Hz, 1 H), 1.21 (t, J = 7.5 Hz, 3 H), 0.94 (t, J = 7.5 Hz, 3 H), 0.40 (s, 3 H), 0.33 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 174.2, 170.4, 168.6, 139.6, 137.7, 134.0 (3 C), 133.5, 129.5 (2 C), 129.1, 128.0 (2 C), 127.6, 69.0, 67.7, 62.1, 61.7, 61.3, 51.8, 36.4, 13.7, 13.5, -1.6, -4.8; The er was determined by HPLC using a Daicel Chiralpak AD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 9.54 min, τ_{minor} = 13.37 min, $[\alpha]_D^{27}$ = +3.22 (*c* 4.16, $CHCl_3$, ee>89%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}ClNO_6Si$ 518.1760; Found 518.1761.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5 phenylpyrrolidine-2,4,4-tricarboxylate (**3b**). The title compound was prepared according to the general procedure C (*Condition B*). Yield: 71 mg (73 %); colorless liquid; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.57-7.46 (m, 4 H), 7.38-7.33 (m, 3 H), 7.29-7.25 (m, 3 H), 5.08 (s, 1 H), 4.21 (dq, J = 11.0, 7.0, Hz, 1 H), 3.90 (d, J = 10.5 Hz, 1 H), 3.92-3.79 (m, 1 H), 3.76-3.63 (m, 1 H), 3.48 (dq, J = 10.5, 6.5, Hz, 1 H), 3.28 (s, 3 H), 2.88 (d, J = 10.5 Hz, 1 H), 2.45(bs, 1 H), 1.20 (t, J = 7.5 Hz, 3 H), 0.87 (t, J = 7.0 Hz, 3 H), 0.41 (s, 3 H), 0.33 (s, 3H); 13C{1H} NMR (50 MHz, $CDCl_3$): δ 174.1, 170.6, 168.8, 140.7, 137.9, 134.0 (2 C), 129.0, 128.0 (2 C), 127.9 (2 C), 127.7, 127.6 (2 C), 69.1, 68.5, 62.1, 61.6, 61.1, 51.8, 36.8, 13.7, 13.4, -1.5, -4.9; The er was determined by HPLC using a Daicel Chiralpak AD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 9.07 min, τ_{minor} = 11.60 min, $[\alpha]_D^{26}$ = +3.0 (*c* 1.1, $CHCl_3$, ee >84%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{34}NO_6Si$ 484.2150; Found 484.2143.

(2R,3S,5S)-4,4-diethyl 2-methyl 5-(4-bromophenyl)-3-(dimethylphenylsilyl)pyrrolidine-2,4,4-tricarboxylate (**3c**). The title compound was prepared according to the general procedure C (*Condition B*). Yield: 87 mg (77 %); colorless liquid; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.55-7.51 (m, 2 H), 7.41(s, 4 H), 7.38-7.33 (m, 3 H), 5.04 (s, 1 H), 4.21 (dq, J = 10.9, 7.2 Hz, 1 H), 3.89 (d, J = 11.0 Hz, 1 H), 3.87-3.71 (m, 2 H), 3.61-3.47 (m, 1 H), 3.29 (s, 3 H), 2.86 (d, J = 10.5 Hz, 1 H), 2.63 (bs, 1 H), 1.21 (t, J = 7.0 Hz, 3 H), 0.94 (t, J = 7.5 Hz, 3 H), 0.40 (s, 3 H), 0.33 (s, 3H); 13C{1H} NMR (50 MHz, $CDCl_3$): δ 174.2, 170.3, 168.5, 140.0, 137.6, 134.0 (2 C), 131.0 (2 C), 129.8 (2 C), 129.1, 127.6 (2 C), 121.6, 68.8, 67.6, 61.9, 61.7, 61.3, 51.9, 36.2, 13.7, 13.5, -1.6, -4.8; The er was determined by HPLC using a Daicel Chiralpak AD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 9.67 min, τ_{minor} = 13.32 min, $[\alpha]_D^{26}$ = +5.6 (*c* 4.9, $CHCl_3$, ee = 90%); HRMS (ESI) calcd for $C_{26}H_{33}BrNO_6Si$ $[M + H]^+$: 562.1255, found 562.1258.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-(4-fluorophenyl)-pyrrolidine-2,4,4-tricarboxylate (**3d**). The title compound was prepared according to the general procedure C (*Condition B*). Yield: 74 mg (74 %); colorless liquid; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.56-7.46 (m, 4 H), 7.38-7.34 (m, 3 H), 7.02-6.94 (m, 2 H), 5.07 (s, 1 H), 4.21 (dq, J = 11.0, 7.2 Hz, 1 H), 3.89 (d, J = 10.6 Hz, 1 H), 3.89-3.70 (m, 2 H), 3.59-3.49 (m, 1 H), 3.29 (s, 3 H), 2.87 (d, J = 10.5 Hz, 1 H), 2.68 (bs, 1 H), 1.21 (t, J = 7.2 Hz, 3 H), 0.94 (t, J = 7.2 Hz, 3 H), 0.41 (s, 3 H), 0.34 (s, 3H); 13C{1H} NMR (50 MHz, $CDCl_3$): δ 174.2, 170.5, 168.7, 162.4 (d, $J_{C\text{-}F}$ = 244.6 Hz), 137.7, 136.7 (d, $J_{C\text{-}F}$ = 3.2 Hz), 134.0 (3 C), 129.7 (d, $J_{C\text{-}F}$ = 8.0 Hz), 129.1, 127.7 (3 C), 114.7 (d, $J_{C\text{-}F}$ = 21.0 Hz), 68.9, 67.6, 62.1, 61.7, 61.3, 51.9, 36.3, 13.8, 13.5, -1.5, -4.9; The er was determined by HPLC using a Daicel Chiralpak AD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 8.96 min, τ_{minor} = 14.58 min, $[\alpha]_D^{26}$ = +8.2 (*c* 2.2, $CHCl_3$, ee >89%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}FNO_6Si$ 502.2079; Found 502.2072.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-(4-(trifluoromethyl)phenyl)-pyrrolidine-2,4,4-tricarboxylate (**3e**). The title compound was prepared according to the general procedure B (*Condition A*). Yield: 41 mg (74 %); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68-7.66 (m, 2 H), 7.56-7.52 (m, 4 H), 7.38-7.35 (m, 3 H), 5.15 (s, 1 H), 4.22 (dq, J = 11.0, 7.0 Hz, 1 H), 3.92 (d, J = 10.5 Hz, 1 H), 3.83 (dq, J = 11.0, 7.0 Hz, 1 H), 3.74 (dq, J = 10.5, 7.0 Hz, 1 H), 3.53 (dq, J = 11.0, 7.0, Hz 1 H), 3.32 (s, 3 H), 2.89 (d, J = 10.0 Hz, 1 H), 1.21 (t, J = 7.0 Hz, 3 H), 0.88 (t, J = 7.0 Hz, 3 H), 0.42 (s, 3 H), 0.35 (s, 3H); ^{1}13C{1H} NMR (125 MHz, $CDCl_3$): δ 174.2, 170.3, 168.4, 145.2, 137.5, 134.0 (3 C), 129.8 (q, $Jc\text{-}_F$ = 32.0 Hz), 129.1, 128.5 (2 C), 127.6 (2 C), 124.7 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.1 (q, $J_{C\text{-}F}$ = 270.5 Hz), 68.8, 67.6, 62.0, 61.8, 61.3, 51.9, 36.1, 13.7, 13.3, -1.7, -4.9; The er was determined by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 4.99 min, τ_{minor} = 6.79 min, $[\alpha]_D^{26}$ = +2.3 (*c* 2.1, $CHCl_3$, ee = 90%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{27}H_{33}F_3NO_6Si$ 552.2052; Found 552.2046.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-(4-ethylphenyl)-pyrrolidine-2,4,4-tricarboxylate (**3f**). The title compound was prepared according to the general procedure B (*Condition A*). Yield: 34 mg (66 %); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.54 (m, 2 H), 7.38-7.34 (m, 5 H), 7.12 (d, J = 8.0 Hz, 2 H), 5.06 (s, 1 H), 4.21 (dq, J = 7.0, 10.5 Hz, 1 H), 3.88 (d, J = 10.5 Hz, 1 H), 3.87-3.81 (m, 1 H), 3.72 (dq, J = 10.5, 7.0 Hz, 1 H), 3.50 (dq, J = 10.5, 7.0 Hz, 1 H), 3.28 (s, 3 H), 2.87 (d, J = 10.5 Hz, 1 H), 2.61 (q, J = 7.5 Hz, 2 H), 1.20 (m, 6 H), 0.87 (t, J = 7.0 Hz, 3 H), 0.41 (s, 3 H), 0.33 (s, 3H); 13C{1H} NMR (125 MHz, $CDCl_3$) δ 174.1, 170.6, 168.9, 143.8, 138.0, 137.8, 134.0 (2 C), 128.9, 127.9 (2 C), 127.6 (2 C), 127.4 (2 C), 69.1, 68.4, 62.2, 61.5, 61.1, 51.8, 36.9, 28.5, 15.6, 13.7, 13.4, -1.5, -4.9; The er was determined by HPLC using a Daicel Chiralpak AD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 11.65 min, τ_{minor} = 13.93 min, $[\alpha]_D^{26}$ = +4.4 (*c* 1.27, $CHCl_3$, ee >83%, mixture of **3f** and ~ 4% of minor isomer); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{28}H_{38}NO_6Si$ 512.2463; Found 512.2463.

(2R,3S,5S)-4,4-diethyl 2-methyl 5-(3-bromophenyl)-3-(dimethylphenylsilyl)-pyrrolidine-2,4,4-tricarboxylate (**3g**). The title compound was prepared according to the general procedure B (*Condition A*).Yield: 43 mg (76 %); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (brs, 1 H), 7.55-7.53 (m, 3 H), 7.38-7.35 (m, 4 H), 7.19 (t, J = 7.0 Hz, 1 H), 5.04 (s, 1 H), 4.22 (dq, J = 10.5, 7.0 Hz, 1 H), 3.89 (d, J = 10.5 Hz, 1 H), 3.88-3.78 (m, 2 H), 3.61 (dq, J = 11.0, 7.0 Hz, 1 H), 3.30 (s, 3 H), 2.86 (d, J = 10.5 Hz, 1 H), 1.22 (t, J = 7.0 Hz, 3 H), 0.98 (t, J = 7.5 Hz, 3 H), 0.40 (s, 3 H), 0.33 (s, 3H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 174.0, 170.3, 168.4, 143.5, 137.6, 134.0 (2 C), 131.3, 130.6, 129.6, 129.1, 127.6 (2 C), 126.6, 121.8, 68.8, 67.5, 62.0, 61.7, 61.4, 51.8, 36.0, 13.7, 13.5, -1.6, -4.9; The er was determined by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 5.53 min, τ_{minor} = 7.05 min, $[\alpha]_D^{26}$ = +6.51 (*c* 1.2, $CHCl_3$, ee ~84 %); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}BrNO_6Si$ 562.1255; Found 562.1257.

(2R,3S,5S)-4,4-diethyl 2-methyl 5-(3-chlorophenyl)-3-(dimethylphenylsilyl)-pyrrolidine-2,4,4-tricarboxylate (**3h**). The title compound was prepared according to the general procedure B (*Condition A*). Yield: 39 mg (75%); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55-7.53 (m, 2 H), 7.47 (bs 2 H), 7.37-7.35 (m, 3 H), 7.25-7.22 (m, 2 H), 5.06 (s, 1 H), 4.21 (dq, J = 11.0, 7.0 Hz, 1 H), 3.91 (d, J = 10.5 Hz, 1 H), 3.88-3.78 (m, 2 H), 3.60 (dq, J = 10.5, 7.0 Hz, 1 H), 3.32 (s, 3 H), 2.87 (d, J = 10.5 Hz, 1 H), 1.21 (t, J = 7.0 Hz, 3 H), 0.97 (t, J = 7.0 Hz, 3 H), 0.41 (s, 3 H), 0.34 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 173.9, 170.2, 168.5, 142.9, 137.7, 134.1 (2 C), 133.8, 129.3, 129.1, 128.5, 127.8, 127.6 (2 C), 126.1, 69.0, 67.7, 62.1, 61.8, 61.4, 51.9, 36.3, 13.7, 13.5, -1.6, -4.7; The er was determined by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 5.75 min, τ_{minor} = 7.93 min, $[\alpha]_D^{22}$ = +4.1 (*c* 1.8, CH_2Cl_2, ee = 86%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}ClNO_6Si$ 518.1760; Found 518.1779.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-(3-fluorophenyl)-pyrrolidine-2,4,4-tricarboxylate (**3i**). The title compound was prepared according to the general procedure B (*Condition A*). Yield: 39 mg (78 %); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55-7.53 (m, 2 H), 7.38-7.35 (m, 3 H), 7.30-7.23 (m, 3 H), 6.96-6.92 (m, 1 H), 5.08 (s, 1 H), 4.22 (dq, J = 11.5, 7.5 Hz, 1 H), 3.89 (d, J = 10.0 Hz, 1 H), 3.87-3.76 (m, 2 H), 3.59 (dq, J = 10.5, 7.0 Hz, 1 H), 3.30 (s, 3 H), 2.87 (d, J = 11.0 Hz, 1 H), 1.21 (t, J = 7.0 Hz, 3 H), 0.94 (t, J = 7.0 Hz, 3 H), 0.41 (s, 3 H), 0.34 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 174.0, 170.4, 168.5, 162.5 (d, $J_{C\text{-}F}$ = 244.0 Hz), 143.8 (d, $J_{C\text{-}F}$ = 6.8 Hz), 137.8, 134.1 (2 C), 129.3 (d, $J_{C\text{-}F}$ = 8.0 Hz), 129.1, 127.6 (2 C), 123.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 115.3 (d, $J_{C\text{-}F}$ = 21.8 Hz), 114.5 (d, $J_{C\text{-}F}$ = 21.8 Hz), 69.1, 67.8 (d, $J_{C\text{-}F}$ = 1.74 Hz), 62.2, 61.7, 61.3, 51.8, 36.4, 13.7, 13.5, -1.5, -4.7; The er was determined by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 5.35 min, τ_{minor} = 6.94 min; $[\alpha]_D^{22}$ = -3.1 (*c* 3.42, $CHCl_3$, ee = 84%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}FNO_6Si$ 502.2079; Found 502.2074.

*(2R,3S,5R)-4,4-diethyl 2-methyl 5-(2-chlorophenyl)-3-(dimethylphenylsilyl)-pyrrolidine-2,4,4-tricarboxylate (**3j**).* The title compound was prepared according to the general procedure B (*Condition A*). Yield: 37 mg (71 %); white solid; mp: 92-94 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.93 (dd, J = 1.5, 7.8 Hz, 1 H), 7.57-7.52 (m, 2 H), 7.37-7.26 (m, 5 H), 7.23-7.13 (m, 1 H), 5.79 (s, 1 H), 4.29 (dq, J = 10.8, 7.1 Hz, 1 H), 4.09 (dq, J = 10.8, 7.1, Hz, 1 H), 3.94 (d, J = 12.3 Hz, 1 H), 3.78 (dq, J = 10.8, 7.2 Hz, 1 H), 3.53 (dq, J = 10.7, 7.1, Hz, 1 H), 3.20 (s, 3 H), 2.91 (d, J = 12.4 Hz, 1 H), 2.80 (bs, 1 H), 1.29 (t, J = 7.0 Hz, 3 H), 0.98 (t, J = 7.2 Hz, 3 H), 0.42 (s, 3 H), 0.30 (s, 3 H); 13C{1H}NMR (50 MHz, $CDCl_3$): δ 173.8, 170.6, 168.3, 139.2, 137.9, 134.0 (2 C), 133.7, 130.1, 129.0, 128.8, 128.7, 127.6 (2 C), 127.0, 69.0, 63.4, 62.2, 61.9, 61.4, 51.8, 37.2, 13.8, 13.4, -1.1, -5.4; The er was determined by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 5.85 min, τ_{minor} = 12.55 min; $[\alpha]_D^{29}$ = +29.4 (*c* 2.8, $CHCl_3$, ee >90%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}ClNO_6Si$ 518.1760; Found 518.1764. After recrystallization from petroleum ether at - 20 ºC, a suitable crystal for X-ray diffraction was obtained.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-(2-fluorophenyl)-pyrrolidine-2,4,4-tricarboxylate (**3k**). The title compound was prepared according to the general procedure B (*Condition A*). Yield: 36 mg (71 %); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88-7.85 (m, 1 H), 7.55-7.54 (m, 2 H), 7.38-7.35 (m, 3 H), 7.24-7.20 (m, 1 H), 7.18-7.15 (m, 1 H), 6.94 (t, J = 9.0 Hz, 1 H), 5.49 (s, 1 H), 4.23 (dq, J = 10.5, 7.0 Hz, 1 H), 3.96 (dq, J = 10.5, 7.0 Hz, 1 H), 3.92 (d, J = 11.5 Hz, 1 H), 3.82 (dq, J = 10.5, 7.0 Hz, 1 H), 3.58 (dq, J = 10.5, 7.0 Hz, 1 H), 3.24 (s, 3 H), 2.90 (d, J = 12.0 Hz, 1 H), 1.25 (t, J = 7.0 Hz, 3 H), 0.98 (t, J = 7.0 Hz, 3 H), 0.41 (s, 3 H), 0.32 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 173.8, 170.4, 168.5, 160.2 (d, $J_{C\text{-}F}$ = 245.8Hz), 137.7, 134.0 (2 C), 130.2 (d, $J_{C\text{-}F}$ = 3.4 Hz), 129.3 (d, $J_{C\text{-}F}$ = 8.4 Hz), 129.0, 128.1 (d, $J_{C\text{-}F}$ = 11.2 Hz), 127.6 (2 C), 124.3 (d, $J_{C\text{-}F}$ = 3.5 Hz), 114.6 (d, $J_{C\text{-}F}$ = 22.5 Hz), 68.7, 62.1, 61.8, 61.4, 60.8 (d, $J_{C\text{-}F}$ = 4.0 Hz), 51.9, 36.7, 13.8, 13.4, -1.3, -5.1; The er was determined

by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 5.30 min, τ_{minor} = 9.41 min; $[\alpha]_D^{26}$ = +6.83 (*c* 3.14, $CHCl_3$, ee >90%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{26}H_{33}FNO_6Si$ 502.2079; Found 502.2072.

(2R,3S,5R)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-(thiophen-2-yl)-pyrrolidine-2,4,4-tricarboxylate (**3l**). The title compound was prepared according to the general procedure B (*Condition A*). Yield: 40 mg (81%); colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.54 (m, 2 H), 7.37-7.34 (m, 3 H), 7.21-7.20 (m, 1 H), 7.10 (d, *J* = 3.5 Hz, 1 H), 6.94 (dd, *J* = 3.5, 5.5 Hz 1 H), 5.30 (s, 1 H), 4.25 (dq, *J* = 10.5, 7.0 Hz, 1 H), 3.94-3.86 (m, 2 H), 3.85 (d, *J* = 11.0 Hz, 1 H), 3.72 (dq, *J* = 10.5, 7.0 Hz, 1 H), 3.26 (s, 3 H), 2.94 (d, *J* = 10.5 Hz, 1 H), 1.23 (t, *J* = 7.0 Hz, 3 H), 1.02 (t, *J* = 7.0 Hz, 3 H), 0.42 (s, 3 H), 0.34 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 173.7, 170.3, 168.4, 144.8, 138.1, 134.0 (2 C), 128.9, 127.6 (2 C), 126.4, 125.6, 124.9, 69.2, 64.1, 62.0, 61.7, 61.4, 51.7, 35.8, 13.7, 13.5, -1.4, -4.7;The er was determined by HPLC using a Daicel Chiralcel AD-H [hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; τ_{major} = 9.44 min, τ_{minor} = 15.20 min; $[\alpha]_D^{28}$ = -7.2 (*c* 2.4, $CHCl_3$, ee = 87%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{24}H_{32}NO_6SSi$ 490.1740; Found 490.1738.

(2R,3S,5S)-4,4-diethyl2-methyl5-(4-chlorophenyl)-3-(1,1,3,3-pentamethyldisiloxanyl)pyrrolidine-2,4,4-tricarboxylate (**3m**). The title compound was prepared according to the general procedure B (*Condition A*).Yield: 38 mg (72 %); colorless liquid;^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.4 Hz, 2 H), 7.26-7.25 (m, 2 H), 5.03 (s, 1 H), 4.38 (dq, *J* = 11.0, 7.4 Hz, 1 H), 4.06 (dq, *J* = 10.8, 7.2 Hz, 1 H), 3.91 (d, *J* = 11.0 Hz, 1 H), 3.82-3.76 (m, 1 H), 3.80 (s, 3 H), 3.56 (dq, *J* = 10.8, 7.2 Hz, 1 H), 2.53 (d, *J* = 11.0 Hz, 1 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 0.95 (t, *J* = 7.2 Hz, 3 H), 0.16 (s, 3 H), 0.12 (s, 3 H), 0.87 (s, 9 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 174.6, 170.5, 168.3, 139.7, 133.4, 129.5 (2 C), 127.9 (2 C), 68.5, 67.3, 61.6, 61.4, 61.2, 52.2, 37.7, 13.8, 13.5, 1.90 (3 C), 1.41, 0.60; The er was determined by HPLC using a Daicel Chiralcel OD-H [hexane/*i*-PrOH (90:10)]; flow rate 0.5

mL/min; τ_{major} = 8.25 min, τ_{minor} = 9.30 min; $[\alpha]_D^{28}$ = -39.02 (*c* 1.68, CH_2Cl_2, ee = 92%); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{23}H_{37}ClNO_7Si_2$ 530.1792; Found 530.1793.

(2R,3S,4S,5R)-dimethyl5-(*4-chlorophenyl)-3-(dimethylphenylsilyl)pyrrolidine-2,4-dicarboxylate* **5**: Under Argon atmosphere, Ag_2O (2.3 mg, 0.01 mmol), DABCO (~4.5 mg, 0.04 mmol) and ligand **L8** (5.0 mg, 0.011 mmol) were dissolved in 1.0 mL of freshly distilled toluene and stirred at room temperature for about 50 min. Then, the reaction mixture was cooled to -40 °C and a solution of (4-chlorobenzylidene)glycine methyl ester **1a** (~85 mg, 0.4 mmol) in toluene (0.5 mL) was added slowly to the reaction mixture followed by the addition of a solution of β-dimethylphenylsilyl-acrylate **4** (44 mg, 0.2 mmol) in toluene (0.5 mL). The reaction mixture was stirred at this temperature overnight and then reaction mixture was passed through a small pad of silica and flushing with 100 mL EtOAc. The solvent was removed under reduced pressure and the residue was directly subjected to column chromatography on silica gel to afford the product **5**[13]as a colourless liquid in 64% yield (55 mg, combined yield of two diastereomers); Data of Major isomer ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54-7.52 (m, 2 H), 7.39-7.38 (m, 3 H), 7.25 (d, *J* = 8.3 Hz, 2 H), 7.19 (d, *J* = 8.5 Hz, 2 H), 4.14 (d, *J* = 8.2 Hz, 1 H), 3.79 (d, *J* = 9.7 Hz, 1 H), 3.65 (s, 3 H), 3.18-3.15 (m, 4 H), 2.21 (dd, *J* = 9.5, 7.9 Hz, 1 H), 0.40 (s, 3 H), 0.39 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 173.4, 173.1, 137.3, 135.9, 134.0 (2 C), 133.2, 129.6, 128.2 (2 C), 128.15 (2 C), 127.9 (2 C), 65.2, 62.5, 53.0, 52.1, 51.4, 34.6, -4.1, -4.3; The er was determined by HPLC using a Daicel Chiralpak AD-H [hexane/*i*-PrOH (90:10)]; flow rate 0.8 mL/min, λ = 220 nm; τ_{major} = 14.18 min, τ_{minor} = 29.25 min.

(2S,3S,5S)-4,4-diethyl 2-methyl5-(4-chlorophenyl)-3phenylpyrrolidine-2,4,4-tricarboxylate **7**: Under Argon atmosphere, Ag_2O (2.3 mg, 0.01 mmol), DABCO (2.3 mg, 0.02 mmol) and ligand **L8** (5.0 mg, 0.011 mmol) were dissolved in 0.5 mL of freshly distilled toluene and stirred at room temperature for about 50 min. Then, the reaction mixture was cooled to -40 °C and a solution of (4-chlorobenzylidene)glycine methyl ester **1a** (42 mg, 0.2 mmol) in toluene (0.25

mL) was added slowly to the reaction mixture followed by the addition of a solution of benzylidene malonate **6** (0.1 mmol, 1 equiv) in toluene (0.25 mL). The reaction mixture was stirred at this temperature overnight and then the reaction mixture was passed through a small pad of silica and flushing with 100 mL EtOAc. The solvent was removed under reduced pressure and the residue was directly subjected to column chromatography on silica gel to afford the product **7**[10c] as a white solid in 72% yield (33 mg). mp 106-108 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.46 (d, J = 8.4 Hz, 2 H), 7.33-7.26 (m, 7 H), 5.33 (s, 1 H), 4.41 (d, J = 6.6 Hz, 1 H), 4.21 (d, J = 6.6 Hz, 1 H), 3.88-3.79 (m, 2 H), 3.77 (s, 3 H), 3.48-3.40 (m, 2 H), 0.82-0.77 (m, 6 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 173.0, 169.3, 168.6, 138.7, 136.9, 133.8, 129.0 (2 C), 128.9 (2 C), 128.4 (2 C), 128.2 (2 C), 127.6, 70.6, 67.2, 66.2, 61.4, 61.1, 55.8, 52.5, 13.3, 13.2; $[\alpha]_D^{26}$ = -39.5 (*c* 1.88, $CHCl_3$); The er was determined by HPLC using a Daicel Chiralpak AS-H [hexane/*i*-PrOH (80:20)]; flow rate 1.0 mL/min; τ_{major} = 4.84 min, τ_{minor} = 6.07 min.

*Scale up procedure for the catalytic asymmetric 1,3-dipolar cycloaddition of azomethine ylide**1a** with β-silylmethylene malonate **2a***

Under an Argon atmosphere, Ag_2O (11.5 mg, 0.05 mmol), ligand **L8** (25 mg, 0.055 mmol, mmol), and DABCO (22.5 mg, 0.2 mmol) were dissolved in toluene (5.0 mL) and stirred at room temperature for approximately 1h. Then, the reaction mixture was cooled to -40 °C and a solution of imino ester **1a** (423 mg, 2.0 mmol) in toluene (2.5 mL) was added slowly over a period of 5 min and the resulting mixture was stirred for 5 min followed by addition of a solution of β-silylmethylene malonate **2** (306 mg, 1.0 mmol) in toluene (2.5 mL) over a period of 5 min. Once the starting material was consumed (monitored by TLC), then the mixture was filtered through a small pad of silica flushing with 150 mL of CH_2Cl_2 and 250 mL of 50% EtOAc/hexane. The filtrates were concentrated and purified by column chromatography to give **3a** as a colorless liquid in 80% yield (415 mg).

General Procedure D for the preparation of *N*-tosyl-3-silylyproline derivatives 8

Under nitrogen atmosphere, compound **3** (0.15 mmol, 1.0 equiv) was dissolved in 3 mL of dry CH_2Cl_2. TsCl (0.45 mmol, 3.0 equiv), Et_3N (0.6 mmol, 4.0 equiv) and DMAP (0.03 mmol, 20 mol%) were added sequentially and the reaction mixture was stirred for 22 h at 27 ºC. The solvent was evaporated and the residue was purified by column chromatography to give the corresponding product **8a**-**8c** and **8i**.

(2R,3S,5S)-4,4-diethyl 2-methyl 5-(4-chlorophenyl) 3-(dimethylphenylsilyl) -1-tosylpyrrolidine-2,4,4-tricarboxylate **8a**. The title compound was prepared according to the general procedure D. Yield: 91mg (90 %); colorless liquid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.49 (m, 3 H), 7.45-7.43 (m, 4 H), 7.34-7.33 (m, 3 H), 7.16 (d, J = 8.5 Hz, 1 H), 7.08 (d, J = 8.5 Hz, 2 H), 5.65 (s, 1 H), 4.29 (d, J = 12.4 Hz, 1 H), 4.15-4.04 (m, 2 H), 3.76-3.70 (m, 1 H), 3.63-3.56 (m, 1 H), 3.14 (s, 3 H), 2.93 (d, J = 12.4 Hz, 1 H), 2.33 (s, 3 H), 1.27 (t, J = 7.0 Hz, 3 H), 0.99 (t, J = 7.2 Hz, 3 H), 0.46 (s, 3 H), 0.24 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 171.7, 168.9, 166.4, 143.6, 137.4, 136.5, 135.4, 133.9 (2 C), 133.88, 129.7 (2 C), 129.2, 128.9 (2 C), 128.0 (2 C), 127.9 (2 C), 127.7 (2 C), 67.9, 67.3, 63.1, 62.5, 61.9, 52.1, 35.0, 21.4, 13.8, 13.5, -0.84, -5.4; $[\alpha]_D^{24}$ = +11.4 (*c* 3.37, $CHCl_3$); HRMS (ESI) m/z: $[M+Na]^+$Calcd for $C_{33}H_{38}ClNNaO_8SSi$ 694.1668; Found 694.1662.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl)-5-phenyl-1-tosylpyrrolidine-2,4,4-tricarboxylate **8b**.The title compound was prepared according to the general procedure D. Yield: 84 mg (88 %); colorless liquid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52-7.48 (m, 4 H), 7.44 (d, J = 8.2 Hz, 2 H), 7.34-7.32 (m, 3 H), 7.19-7.18 (m, 3 H), 7.05 (d, J = 8.0 Hz, 2 H), 5.70 (s, 1 H), 4.30 (d, J = 12.0 Hz, 1 H), 4.13-4.06 (m, 2 H), 3.68-3.63 (m, 1 H), 3.59-3.53 (m,1 H), 3.13 (s, 3 H), 3.00 (d, J = 12.4 Hz, 1 H), 2.30 (s, 3 H), 1.29 (t, J = 7.0 Hz, 3 H), 0.95 (t, J = 7.2 Hz, 3 H), 0.47 (s, 3 H), 0.24 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 171.6, 169.2,

166.5, 143.3, 137.8, 137.6, 135.7, 134.0 (2 C), 129.1, 128.8 (2 C), 128.3 (2 C), 128.0, 127.9 (3 C), 127.8, 127.6 (2 C), 68.1, 68.0, 63.2, 62.4, 61.8, 52.0, 35.0, 21.4, 13.8, 13.5, -0.7, -5.4; $[\alpha]_D^{24}$ = +10.3 (*c* 2.5, $CHCl_3$); HRMS (ESI) m/z: $[M+Na]^+$Calcd for $C_{33}H_{39}NNaO_8SSi$ 660.2058; Found 660.2056.

(2R,3S,5S)-4,4-diethyl 2-methyl 5-(4-bromophenyl) 3-(dimethylphenylsilyl) -1-tosylpyrrolidine-2,4,4-tricarboxylate **8c** The title compound was prepared according to the general procedure D. Yield: 99 mg (92 %); colorless liquid;^{1}H NMR (200 MHz, $CDCl_3$): δ 7.52-7.40 (m, 5 H), 7.35-7.28 (m, 7 H), 7.08 (d, J = 8.0 Hz, 2 H), 4.29 (d, J = 12.3 Hz, 1 H), 4.15-4.01 (m, 2 H), 3.78-3.51 (m, 2 H), 3.15 (s, 3 H), 2.91(d, J = 12.3 Hz, 1 H), 2.33 (s, 3 H), 1.27 (t, J = 7.0 Hz, 3 H), 0.98 (t, J = 7.0 Hz, 3 H), 0.46 (s, 3 H), 0.24 (s, 3 H); 13C{1H} NMR (50 MHz, $CDCl_3$): δ 171.6, 168.8, 166.3, 143.6, 137.3, 137.0, 135.4, 133.9 (2 C), 130.9 (2 C), 130.0 (2 C), 129.1, 128.9 (2 C), 127.8 (2 C), 127.6 (2 C), 122.1, 67.9, 67.4, 63.1, 62.5, 61.9, 52.0, 35.0, 21.4, 13.7, 13.4, -0.91, -5.4; $[\alpha]_D^{25}$ = +11.3 (*c* 2.0, $CHCl_3$); HRMS (ESI) m/z: $[M+Na]^+$Calcd for $C_{33}H_{38}BrNNaO_8SSi$ 738.1163; Found 738.1161.

(2R,3S,5S)-4,4-diethyl 2-methyl 3-(dimethylphenylsilyl) 5-(3-fluorophenyl) -1-tosylpyrrolidine-2,4,4-tricarboxylate **8i**. The title compound was prepared according to the general procedure D. Yield: 83 mg (84 %); colorless liquid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50-7.46 (m, 4 H), 7.34-7.33 (m, 3 H), 7.26 (bs, 2 H), 7.16 (q, J = 7.8 Hz, 1 H), 7.09 (d, J = 8.1 Hz, 2 H), 6.91-6.87 (m, 1 H), 5.67 (s, 1 H), 4.28 (d, J = 12.4 Hz, 1 H), 4.14-4.03 (m, 2 H), 3.76-3.69 (m, 1 H), 3.66-3.60 (m, 1 H), 3.15 (s, 3 H), 2.93 (d, J = 12.4 Hz, 1 H), 2.32 (s, 3 H), 1.27 (t, J = 7.2 Hz, 3 H), 0.99(t, J = 7.2 Hz, 3 H), 0.46 (s, 3 H), 0.24 (s, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 171.5, 168.8, 166.3, 162.3 (d, $J_{C\text{-}F}$ = 244.5 Hz), 143.6, 140.6 (d, $J_{C\text{-}F}$ = 7.0 Hz), 137.4, 135.4, 133.9 (2 C), 129.3 (d, $J_{C\text{-}F}$ = 8.0 Hz), 129.2, 128.9 (2 C), 127.9 (2 C), 127.6 (2 C), 123.8 (d, $J_{C\text{-}F}$ = 2.8 Hz), 115.3 (d, $J_{C\text{-}F}$ = 22.7 Hz), 114.7 (d, $J_{C\text{-}F}$ = 21.0 Hz), 68.0, 67.4 (d, $J_{C\text{-}F}$ = 1.8 Hz), 63.2, 62.5, 61.9, 52.1, 35.0, 21.4, 13.8, 13.4, -0.86, -5.3; $[\alpha]_D^{25}$ = +5.3

(c 1.71, $CHCl_3$); HRMS (ESI) m/z: $[M+Na]^+$Calcd for $C_{33}H_{38}FNNaO_8SSi$ 678.1964; Found 678.1964.

General Procedure E for the preparation of 3-hydroxyproline derivatives

Potassium bromide (0.16 mmol, 1.2 equiv) was added to a stirred solution of **8** (0.12 mmol, 1.0 equiv) and peracetic acid (35% solution in acetic acid, 3 mL) at 0 °C followed by H_2O_2 (30%, 0.1 mL). The reaction mixture was warmed slowly to room temperature and stir for 2d. Sodium thiosulphate was added to the reaction mixture and stirred until (approx. 10 min) the clear solution became turbid. Solvent was removed under reduced pressure and the residue was dissolved in dichloromethane and passed through Na_2SO_4. The organic solvent was evaporated under reduced pressure. The residue was purified by column chromatography to give **9a-9c** and **9i**.

(2S,3S,5S)-4,4-diethyl2-methyl5-(4-chlorophenyl)3-hydroxy-1-tosylpyrrolidine-2,4,4-tricarboxylate **9a**. The title compound was prepared according to the general procedure E. Yield: 48 mg (72 %); white amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (d, J = 8.1 Hz, 2 H), 7.33 (d, J = 8.4 Hz, 2 H), 7.12 (d, J = 8.0 Hz, 2 H), 7.09 (d, J = 8.0 Hz, 2 H), 5.57 (s, 1 H), 5.10 (s, 1 H), 4.59 (d, J = 4.8 Hz, 1 H), 4.26-4.21 (m, 1 H), 4.17-4.13 (m, 1 H), 3.88 (s, 3 H), 3.82-3.76 (m, 1 H), 3.49 (dq, J = 10.7, 7.2 Hz, 1 H), 3.01 (d, J = 5.0 Hz, 1 H), 2.37 (s, 3 H), 1.23 (t, J = 7.1 Hz, 3 H), 0.81 (t, J = 7.2 Hz, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 170.5, 166.72, 166.70, 143.9, 135.4, 135.0, 133.8, 129.8 (2 C), 129.0 (2 C), 128.2 (2 C), 127.9 (2 C), 76.4, 69.5, 67.0, 65.7, 62.5, 62.0, 52.9, 21.5, 13.9, 13.2; $[\alpha]_D^{26}$ = -23.0 (c 0.7, $CHCl_3$); $[M+H]^+$Calcd for $C_{25}H_{29}ClNO_9S$ 554.1246; Found 554.1241.

(2S,3S,5S)-4,4-diethyl 2-methyl 3-hydroxy-5-phenyl-1-tosylpyrrolidine-2,4,4-tricarboxylate **9b**. The title compound was prepared according to the general procedure E. Yield = 44 mg (70 %); white amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (d, J = 8.0 Hz, 2 H), 7.38-

7.37 (m, 2 H), 7.14-7.13 (m, 3 H), 7.09 (d, J = 8.0 Hz, 2 H), 5.60 (s, 1 H), 5.17 (d, J = 5.5 Hz, 1 H), 4.53 (d, J = 5.8 Hz, 1 H), 4.28-4.14 (m, 2 H), 3.88 (s, 3 H), 3.75 (dq, J = 10.6, 7.1 Hz, 1 H), 3.45 (dq, J = 10.5, 7.2 Hz, 1 H), 2.98 (bs, 1 H), 2.34 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 0.78 (t, J = 7.2 Hz, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 170.6, 167.1, 166.8, 143.6, 136.8, 135.2, 128.9 (3 C), 128.4, 128.2 (2 C), 127.9, 127.8 (2 C), 76.4, 69.1, 66.4 (2 C), 62.5, 61.8, 52.9, 21.5, 13.9, 13.2; $[\alpha]_D^{26}$ = -23.2 (*c* 1.4, $CHCl_3$); $[M+H]^+$Calcd for $C_{25}H_{30}NO_9S$ 520.1636; Found 520.1631.

(2S,3S,5S)-4,4-diethyl 2-methyl 5-(4-bromophenyl-3-hydroxy-1-tosylpyrrolidine-2,4,4-tricarboxylate **9c**. The title compound was prepared according to the general procedure E. Yield: 51 mg (71 %); colorless liquid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, J = 8.5 Hz, 2 H), 7.25-7.20 (m, 4 H), 7.12 (d, J = 8.0 Hz, 2 H), 5.55 (s, 1 H), 5.09 (d, J = 4.3 Hz, 1 H), 4.61 (d, J = 4.3 Hz, 1 H), 4.26-4.18 (m, 1 H), 4.17-4.09 (m,1 H), 3.88 (s, 3 H), 3.79 (dq, J = 10.8, 7.2 Hz, 1 H), 3.48 (dq, J = 10.7, 7.2 Hz, 1 H), 3.17 (bs, 1 H), 2.32 (s, 3 H), 1.22 (t, J = 7.1 Hz, 3 H), 0.80 (t, J = 7.2 Hz, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 170.5, 166.73, 166.66, 144.0, 135.8, 135.0, 130.8, 130.2, 129.0 (3 C), 128.2 (3 C), 122.0, 76.4, 69.6, 67.2, 65.8, 62.4, 62.0, 52.9, 21.5, 13.9, 13.2; $[\alpha]_D^{25}$ = -20.1 (*c* 3.0, $CHCl_3$); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{29}BrNO_9$ 598.0741; Found 598.0742.

(2S,3S,5S)-4,4-diethyl 2-methyl 5-(3-fluorophenyl-3-hydroxy-1-tosylpyrrolidine-2,4,4-tricarboxylate **9i**. The title compound was prepared according to the general procedure E. Yield: 42 mg (65 %); colorless liquid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, J = 8.2 Hz, 2 H), 7.21 (d, J = 7.5 Hz, 1 H), 7.13-7.10 (m, 4 H), 6.84 (dd, J = 2.0, 8.0 Hz, 1 H), 5.59 (s, 1 H), 5.10 (d, J = 4.9 Hz, 1 H), 4.59 (d, J = 4.9 Hz, 1 H), 4.26-4.19 (m, 1 H), 4.18-4.12 (m, 1 H), 3.88 (s, 3 H), 3.78 (dq, J = 10.7, 7.1 Hz, 1 H), 3.51 (dq, J = 10.8, 7.2 Hz, 1 H), 3.11 (bs, 1 H), 2.35 (s, 3 H), 1.23 (t, J = 7.1 Hz, 3 H), 0.81 (t, J = 7.2 Hz, 3 H); 13C{1H} NMR (125 MHz, $CDCl_3$): δ 170.4, 166.7, 166.66, 162.2 (d, $J_{C\text{-}F}$ = 244.5 Hz), 143.9, 139.4 (d, $J_{C\text{-}F}$ = 7.2 Hz),

134.9, 129.3 (d, J_{C-F} = 8.0 Hz), 129.0 (2 C), 128.2 (2 C), 124.1 (d, J_{C-F} = 2.8 Hz), 115.4 (d, J_{C-F} = 22.8 Hz), 114.7 (d, J_{C-F} = 21.0 Hz), 76.4, 69.5, 67.0, 65.8 (d, J_{C-F} = 1.84 Hz), 62.5, 61.9, 52.9, 21.5, 13.9, 13.2; $[\alpha]_D^{25}$ = -21.6 (*c* 2.35, $CHCl_3$); HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{25}H_{29}BrNO_9S$ 538.1542; Found 538.1540.

"Supporting Information:"

The Supporting Information is available free of charge on the

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X-ray crystallographic information of **3j** (PDF)

X-ray crystallographic data for **3j** (CIF)

^1H and ^{13}C spectra for **3a-3m**, **5, 7, 8a-8c, 8i, 9a-9c** and **9i** (PDF)

HPLC trace of **3a-3m, 5 and 7**(PDF)

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