Ligand-enabled multiple absolute stereocontrol in metal-catalysed cycloaddition for construction of contiguous all-carbon quaternary stereocentres

Kohsuke Ohmatsu,†,‡ Naomichi Imagawa,§ and Takashi Ooi**,†

†Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Nagoya 464-8603, Japan.
§Institute of Transformative Bio-Molecules (WPI-ITbM), Nagoya University, Nagoya 464-8602, Japan.

tool@apchem.nagoya-u.ac.jp

General Information: Infrared spectra were recorded on a Shimadzu IRAffinity-1 spectrometer. 1H NMR spectra were recorded on a JEOL JNM-ECS400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from the tetramethylsilane (0.0 ppm) resonance as the internal standard (CDCl3). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet m = multiplet, br = broad) and coupling constants (Hz). 13C NMR spectra were recorded on a JEOL JNM-ECS400 (101 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance as the internal standard (CDCl3; 77.16 ppm). 31P NMR spectra were recorded on a JEOL JNM-ECS400 (162 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from H3PO4 (0.0 ppm) resonance as the external standard. 19F NMR spectra were recorded on a JEOL JNM-ECS400 (376 MHz) spectrometer. Chemical shifts are reported in ppm from benzotrifluoride (−64.0 ppm) resonance as the external standard. Optical rotations were measured on a HORIBA SEPA-500 polarimeter. The high resolution mass spectra were measured on a Thermo Fisher Scientific Exactive (ESI). Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm). Flash column chromatography was performed on PSQ60AB (spherical, 40-50 µm; FUJI SILYSIA CHEMICAL Co., Inc.). Enantiomeric excesses were determined by HPLC analysis using chiral columns (φ 4.6 mm x 250 mm, DAICEL CHIRALCEL OD-H (ODH) and CHIRALPAK AD-H (ADH), CHIRALPAK AD-3 (AD3), CHIRALCEL OZ-3 (OZ3), CHIRALPAK IA (IA), CHIRALPAK IC (IC)) with hexane (H), 2-propanol (IPA), and ethanol (EtOH) as eluent.

All air- and moisture-sensitive reactions were performed under an atmosphere of argon (Ar) in dried glassware. The manipulations for Pd-catalyzed reactions were carried out with standard Schlenk techniques under Ar. Toluene was supplied from Kanto Chemical Co., Inc. as “Dehydrated” and further purified by both A2 alumina and Q5 reactant using a GlassContour solvent dispensing system. Oxazolidinones were synthesized as described below.1 Alkenes were synthesized by following the literature procedure.2 Other simple chemicals were purchased and used as such. The data reported herein are basically the results of the single runs. The reactions of 8a and 8f with 6a, and the reaction of 8a with 12 were conducted several times, and the results obtained have proven highly reproducible.

Additional Experimental Data and Discussion:

(A) Kinetic Resolution

In order to elucidate the stereo-determining process in the construction of C-4 chiral carbon, we examined the possibility of the kinetic resolution in the reaction of racemic oxazolidinone 8a with trisubstituted alkene 6a because chiral Pd(0) complex might preferentially undergo oxidative addition to one enantiomer of 8a (Fig. S1). When the reaction was conducted with 2 equiv of 8a and 1 equiv of 6a under the optimized conditions, the pyrrolidine 11a was obtained in 99% yield (based on the amount of 6a) with near-complete stereoselectivities, and the starting material 8a was recovered in 95% (based on the amount of 6a) with 17% ee. This result indicated that the rigorous stereocontrol in the construction of C-4 chiral carbon stemmed not from the kinetic resolution of 8a but from the control of planar chirality of the π-allyl Pd(II) through the π-σ-π interconversion.

![Figure S1.](image)

(B) Additional Experimental Support for Individual Absolute Stereocontrol to Generate an All-Carbon Quaternary Stereocenter at C-3 Position of Pyrrolidine

While the stereochemical outcome of the reaction of 8a with 2-nitro-3-phenylacrylate (12) demonstrated the ability of chiral onium-phosphine ligand 2d-I to achieve the individual stereocontrol in the construction of C-3 chiral carbon (Fig. 3 in the manuscript), we also performed the reaction of oxazolidinone 3 with ethyl 2-cyanoacrylate S1 to gain a further insight (Fig. S2). Although the reaction gave a complex mixture due to the strong tendency of S1 toward polymerization, the corresponding pyrrolidine S2 was isolated in 25% yield with moderate enantioselectivity. The observed asymmetric induction could be accounted for by assuming the doubly ion-pairing intermediate, where conformation of the C-3 carbanion would be controlled by the ligand, particularly the chiral ammonium ion component.

![Figure S2.](image)

Therefore, one possible rationale for the multiple absolute stereocontrol in the annulation between oxazolidinone 8a and a geometrical mixture of ethyl 2-nitro-3-phenylacrylate (12; E/Z = 1:2, Fig. 3) would be as follows: the stereoselective intermolecular addition of zwitterionic allyl-Pd intermediate A either to the (E)- or (Z)-alkene, which constructs C-2 stereocenter, and the enantiofacial discrimination of the resulting nitronate ion would be managed by the chiral ammonium ion component of the ligand through the rotation around...
C2–C3 bond in concurrence with the control of planar chirality of the π-allyl Pd(II) moiety through π-σ-π interconversion, thereby establishing the C3 and C4 stereocenters in the ring-closing step (Figure S3). However, another yet initially hypothesized scenario based on the selective addition of the intermediate A to (E)-alkene with discrimination of its enantioface followed by the ring closure with retention of the stereochemical information of the trisubstituted alkene geometry could not be ruled out if rapid isomerization of the alkene occurs in the reaction system.

Figure S3.
(C) Control Experiments

We attempted a series of reactions of oxazolidinones with activated alkenes using PPh₃ as a ligand in the presence of chiral ammonium salt S₄ or using chiral monophosphine ligand S₃ in the presence of tetrabutylammonium bromide (TBAB). As summarized in Table S1, these reactions afforded the desired pyrrolidines in an almost racemic form or gave only a trace amount of the products, which clearly demonstrated that chiral onium-phosphine ligand 2d-I played a pivotal role in achieving the present Pd-catalyzed asymmetric [3+2] cycloaddition with high efficiency and absolute stereocontrols.

Table S1.

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<th>Entry</th>
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<th>Ligand</th>
<th>Ammonium salt</th>
<th>Temp.</th>
<th>Pyrrolidine</th>
<th>Yield (%)</th>
<th>e.e. (%)</th>
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<td>7</td>
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<td>-</td>
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Representative Procedure for Synthesis of Oxazolidinones, and Their Characterization:

Oxazolidinones 3 was synthesized from N-Boc glycine methyl ester as described below.

\[ \text{BocHN} \text{CO}_2\text{Me} \rightarrow 1) \text{CH}_2=\text{CHMgBr (3.5 equiv)} \hspace{1cm} \text{Et}_2\text{O}, 0 \, ^\circ \text{C to r.t.} \]
\[ \rightarrow 2) \text{KOt-Bu (1.3 equiv)} \hspace{1cm} \text{THF, 0 \, ^\circ \text{C to r.t.}} \]

To a solution of N-Boc glycine methyl ester (2.35 g, 12.4 mmol) in Et\(_2\)O (40 mL) was added vinylmagnesium bromide (1.0 M THF solution, 43.4 mL) at 0 \, ^\circ \text{C under Ar and this mixture was stirred at room temperature for 6 h. The reaction mixture was then poured into a saturated aqueous solution of NH\(_4\)Cl at 0 \, ^\circ \text{C and extracted with EtOAc three times. The combined organic phases were washed with brine, dried over Na\(_2\)SO\(_4\), and concentrated. This concentrate was passed through a short silica gel pad with H/EtOAc = 4:1 as eluent to remove the polar compounds. The crude material including N-Boc amino alcohol was used for the next step without further purification. To a solution of this crude material (1.42 g) in THF (11 mL) was added KOt-Bu (895 mg, 7.97 mmol) in THF (11 mL) at 0 \, ^\circ \text{C under Ar and this mixture was stirred at room temperature. After the stirring was kept for 10 h, the reaction was quenched by the slow addition of a saturated aqueous solution of NH\(_4\)Cl at 0 \, ^\circ \text{C and extractive work-up was conducted with EtOAc three times. The organic layer was washed with brine, dried over anhydrous Na\(_2\)SO\(_4\), and concentrated under reduced pressure to give crude product, which was purified by column chromatography on silica gel (H/EtOAc = 4:1 to 1:1 as eluent) to afford S5 (470 mg, 3.38 mmol, 27\% yield for 2 steps) as a brown oil. S5: \( ^1\text{H NMR (400 MHz, CDCl}_3\) \( \delta 5.97 \) (2H, dd, \( J = 17.6 \), 10.7 Hz), 5.85 (1H, brs), 5.44 (2H, d, \( J = 17.6 \) Hz), 5.32 (2H, d, \( J = 10.7 \) Hz), 3.56 (2H, s).\]

To a solution of S5 (470 mg, 3.38 mmol) in THF (9.70 mL) and DMF (24.1 mL) was slowly added NaH (60\%, 270 g, 6.76 mmol) at 0 \, ^\circ \text{C under Ar and the resulting mixture was stirred for 15 min. Then, 4-nitrobenzenesulfonyl chloride (973 mg, 4.39 mmol) was introduced into the flask, and the whole reaction mixture was warmed up to room temperature. After stirring for 4 h, a saturated aqueous solution of NH\(_4\)Cl was slowly added to the mixture at 0 \, ^\circ \text{C and the aqueous phase was extracted with EtOAc three times. The combined organic phases were washed with brine, dried over Na\(_2\)SO\(_4\), and concentrated. Purification of the residue by column chromatography on silica gel (H/Acetone = 9:1 to 6:1 as eluent) gave the oxazolidinone 3 (857 mg, 2.64 mmol, 78\% yield) as a white solid. 3: \( ^1\text{H NMR (400 MHz, CDCl}_3\) \( \delta 8.42 \) (2H, d, \( J = 9.2 \) Hz), 8.26 (2H, d, \( J = 9.2 \) Hz), 5.89 (2H, dd, \( J = 17.2 \), 11.0 Hz), 5.42 (2H, d, \( J = 17.2 \) Hz), 5.39 (2H, d, \( J = 11.0 \) Hz), 4.01 (2H, s); \( ^{13}\text{C NMR (101 MHz, CDCl}_3\) \( \delta 151.3, 150.7, 142.4, 134.7, 129.9, 124.6, 118.6, 82.3, 54.0; IR (film): 3107, 3071, 3030, 1778, 1531, 1348, 1175, 1155, 1090, 854, 735, 681, 611 \, \text{cm}^{-1}; HRMS (ESI) Calcd for C\(_{13}\)H\(_{12}\)N\(_2\)O\(_6\)Na\(^+\) ([M+Na\(^+\)]\(^+\)) 347.0308. Found 347.0308.\)
Oxazolidinones 8 were synthesized from N-Boc glycine N'-methoxy-N'-methylamide through the following representative procedure.

To a solution of N-Boc-glycine N'-methoxy-N'-methylamide (5.46 g, 25.0 mmol) in THF (83.0 mL) was added MeMgI (1.0 M Et₂O solution, 50.0 mL) at 0 °C under Ar. After stirring for 10 h, the reaction mixture was poured into a saturated aqueous solution of NH₄Cl at 0 °C and extracted with EtOAc three times. The combined organics were then washed with brine, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure to give crude product, which was purified by column chromatography on silica gel (H/EtOAc = 10:1 to 4:1 as eluent) to afford S6 (3.48 g, 20.1 mmol, 80% yield) as a colorless oil.

**S6**: ¹H NMR (400 MHz, CDCl₃)  δ 5.23 (1H, brs), 4.04 (2H, brd,  J = 4.6 Hz), 2.18 (3H, s), 1.45 (9H, s).

To a solution of S6 (3.48 g, 20.1 mmol) in Et₂O (60.0 mL) was added vinyl magnesium bromide (1.0 M THF solution, 50.3 mL) at 0 °C under Ar. The mixture was warmed up to room temperature and the stirring was maintained for 5 h. The reaction mixture was then poured into a saturated aqueous solution of NH₄Cl at 0 °C and extractive work-up was conducted with EtOAc three times. The organic phases were washed with brine, dried over Na₂SO₄, and concentrated. This concentrate was passed through a short silica gel pad with H/EtOAc = 4:1 as eluent to remove the polar compounds. This crude material including the corresponding N-Boc amino alcohol was used for the next step without further purification. To a solution of this crude material (2.52 g) in THF (33.0 mL) was added KOᵗ-Bu (1.83 g, 16.3 mmol) in THF (30.0 mL) at 0 °C under Ar and the resulting mixture was stirred at room temperature for 12 h. The reaction mixture was then quenched by the slow addition of a saturated aqueous solution of NH₄Cl at 0 °C, and the mixture was extracted with EtOAc three times, and washed with brine. The organic layer was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to give crude product, which was purified by column chromatography on silica gel (H/EtOAc = 4:1 to 1:1 as eluent) to afford S7 (959 mg, 7.55 mmol, 37% yield for 2 steps) as a brown oil.

**S7**: ¹H NMR (400 MHz, CDCl₃)  δ 5.95 (1H, dd,  J = 17.4, 11.0 Hz), 5.87 (1H, brs), 5.39 (1H, d,  J = 17.4 Hz), 5.22 (1H, d,  J = 11.0 Hz), 3.49 (1H, d,  J = 8.7 Hz), 3.40 (1H, d,  J = 8.7 Hz), 1.56 (3H, s).

To a solution of S7 (959 mg, 7.55 mmol) in THF (7.2 mL) and DMF (18.0 mL) was slowly added NaH (60%, 603 mg, 15.1 mmol) at 0 °C under Ar and the mixture was stirred for 15 min. Then, 4-nitrobenzenesulfonyl chloride (2.2 g, 9.8 mmol) was introduced into the flask, and the reaction mixture was warmed up to room temperature. After 5 h with stirring, a saturated aqueous solution of NH₄Cl was slowly added at 0 °C and extractive work-up was performed with EtOAc three times. The combined organic phases were washed with brine, dried over Na₂SO₄, and concentrated. Purification of the residue by column chromatography on silica gel (H/Acetone = 9:1 to 6:1 as eluent) gave the adduct 8a (1.49 g, 4.77 mmol, 63% yield) as a white solid.

**8a**: ¹H NMR (400 MHz, CDCl₃)  δ 8.42 (2H, d,  J = 9.2 Hz), 8.26 (2H, d,  J = 9.2 Hz), 5.87 (1H, dd,  J = 17.4, 11.0 Hz), 5.37 (1H, d,  J = 17.4 Hz), 5.29 (1H, d,  J = 11.0 Hz), 3.95 (1H, d,  J = 9.4 Hz).
Characterization of Oxazolidinones:

**8b**: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.42 (2H, $d$, $J = 9.2$ Hz), 8.25 (2H, $d$, $J = 8.7$ Hz), 5.79 (1H, dd, $J = 17.3$, $11.0$ Hz), 5.35 (1H, $d$, $J = 17.3$ Hz), 5.29 (1H, $d$, $J = 11.0$ Hz), 5.35 (1H, $d$, $J = 9.1$ Hz), 3.79 (1H, $d$, $J = 6.4$ Hz), 0.94 (3H, $d$, $J = 6.4$ Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 151.2, 150.7, 142.3, 138.4, 136.6, 129.8, 129.2, 124.8, 124.6, 117.8, 85.9, 55.6, one peak for aromatic carbon was not found probably due to overlapping; IR (film): 3109, 3073, 3032, 1775, 1531, 1373, 1350, 1217, 1177, 1134, 1090, 856, 756, 737, 683 cm$^{-1}$; HRMS (ESI) Calcd for C$_{16}$H$_{16}$O$_6$N$_2$NaS$^+$ ([M+Na]$^+$) 363.0621. Found 363.0620.

**8c**: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.37 (2H, $d$, $J = 8.9$ Hz), 8.20 (2H, $d$, $J = 8.9$ Hz), 7.35-7.42 (3H, m), 7.27-7.30 (2H, m), 6.08 (1H, dd, $J = 17.2$, $11.0$ Hz), 5.37 (1H, $d$, $J = 11.0$ Hz), 5.35 (1H, $d$, $J = 9.4$ Hz), 4.39 (1H, $d$, $J = 9.6$ Hz), 4.22 (1H, $d$, $J = 9.6$ Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 151.2, 150.7, 142.3, 138.4, 136.6, 129.8, 129.2, 124.8, 124.6, 117.8, 83.8, 55.6, one peak for aromatic carbon was not found probably due to overlapping; IR (film): 3107, 3069, 3032, 1782, 1531, 1379, 1364, 1348, 1217, 1177, 1157, 1094, 754, 735, 683 cm$^{-1}$; HRMS (ESI) Calcd for C$_{17}$H$_{14}$O$_6$N$_2$NaS$^+$ ([M+Na]$^+$) 397.0465. Found 397.0461.
Supplementary Information

8g: 1H NMR (400 MHz, CDCl3) δ 8.39 (2H, d, J = 8.9 Hz), 8.22 (2H, d, J = 8.9 Hz), 7.38 (2H, d, J = 8.9 Hz), 7.24 (2H, d, J = 17.4 Hz), 6.05 (1H, dd, J = 17.4, 10.7 Hz), 5.39 (1H, d, J = 10.7 Hz), 5.35 (1H, d, J = 17.4 Hz), 4.37 (1H, d, J = 9.4 Hz), 4.17 (1H, d, J = 9.4 Hz); 13C NMR (101 MHz, CDCl3) δ 151.3, 150.5, 142.2, 136.9, 136.3, 135.4, 129.9, 129.4, 126.4, 124.6, 118.2, 83.3, 55.4; IR (film): 3107, 3069, 3032, 1782, 1738, 1533, 1375, 1364, 1350, 1217, 1179, 1092, 754, 737, 683 cm⁻¹; HRMS (ESI) Calcd for C17H13O6N2ClNaS⁺ ([M+Na]+) 431.0075. Found 431.0072.

8h: 1H NMR (400 MHz, CDCl3) δ 8.37 (2H, d, J = 9.2 Hz), 8.20 (2H, d, J = 9.2 Hz), 7.21 (2H, d, J = 9.2 Hz), 6.89 (2H, d, J = 9.2 Hz), 6.06 (1H, dd, J = 17.4, 10.5 Hz), 5.36 (1H, d, J = 10.5 Hz), 5.32 (1H, d, J = 17.4 Hz), 4.33 (1H, d, J = 9.6 Hz), 4.22 (1H, d, J = 9.6 Hz), 3.81 (3H, s); 13C NMR (101 MHz, CDCl3) δ 160.2, 151.2, 150.8, 142.4, 136.8, 130.1, 129.8, 126.5, 124.6, 117.7, 114.4, 83.9, 55.6, 55.5; IR (film): 3107, 1775, 1736, 1533, 1364, 1350, 1217, 1177, 772, 756, 737, 683 cm⁻¹; HRMS (ESI) Calcd for C18H16O7N2NaS⁺ ([M+Na]+) 427.0570. Found 427.0571.

Representative Procedure for Synthesis of Chiral Onium-Phosphine Hybrid Ligands 2·X, and Their Characterization:

Chiral onium-phosphine hybrid ligand 2a·Br was synthesized from (R)-3,3’-diphenyl-2,2’-bis(bromomethyl)-1,1’-binaphthyl (S8) and N-methyl 2-diphenylphosphinobenzylamine as described below.

To a mixture of N-methyl 2-diphenylphosphinobenzylamine (264.8 mg, 0.60 mmol) and K₂CO₃ (248.8 mg, 1.8 mmol) in CH₃CN (3 mL) and CHCl₃ (3 mL) was added S8 (355.4 mg, 0.6 mmol) at room temperature under Ar. After stirring for 24 h, water was introduced into the reaction flask and extractive work-up was conducted with CHCl₃ three times. The combined organic phases were washed with brine, dried over Na₂SO₄, and concentrated. The resulting concentrate was purified by column chromatography on silica gel (CHCl₃ only to CHCl₃/MeOH = 20:1 as eluent) to afford 2a·Br (337.1 mg, 0.35 mmol, 59% yield) as a white solid.

2a·Br: 1H NMR (400 MHz, CDCl₃) δ 8.15 (1H, s), 8.12 (1H, d, J = 8.2 Hz), 8.00 (1H, d, J = 8.7 Hz), 7.95 (1H, s), 7.70 (1H, t, J = 7.8 Hz), 7.65 (1H, t, J = 7.6 Hz), 7.23-5.72 (20H, m), 7.19 (1H, t, J = 7.6 Hz), 7.00-7.06 (3H, m), 6.74 (2H, t, J = 7.3 Hz), 6.62 (2H, t, J = 8.0 Hz), 5.45 (1H, d, J = 13.3 Hz), 5.14 (1H, dd, J = 13.3, 7.3 Hz), 4.31 (1H, brd, J = 10.0 Hz), 3.93 (1H, dd, J = 13.3, 5.5 Hz), 3.83 (1H, dd, J = 13.3 Hz), 3.40 (1H, d, J = 13.3 Hz), 2.92 (3H, s); 13C NMR (101 MHz, CDCl₃) δ 141.0, 139.8, 138.9 (d, J = 7.7 Hz), 138.4, 138.1, 138.0, 138.6, 138.1, 137.0, (d, J = 7.7 Hz), 136.3, 134.7, 134.7, 134.0 (d, J = 7.7 Hz), 133.8, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 133.0, 132.6, 132.5, 27.8, 132.3, 131.4, 130.9 (d, J = 11.6 Hz), 130.5, 130.3, 130.1, 129.7, 129.7, 129.0, 128.9, 128.8, 128.8, 128.7, 128.7, 128.3, 128.1, 128.1, 127.7, 127.6, 127.2, 125.4, 123.7, 61.9 (d, J = 19.4 Hz), 61.8, 57.1 (d, J = 14.5 Hz), 48.0, two peaks for aromatic carbons were not found probably due to overlapping; 31P NMR (162 MHz, CDCl₃) δ −18.1; IR (film): 3377, 3053, 3011, 2907, 1466, 1449, 1435, 897, 866, 741, 698, 658 cm⁻¹; HRMS (ESI) Calcd for C₅₅H₄₃NP⁺ ([M+Br⁺]⁺) 736.3125. Found 736.3128.

References:


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SUPPLEMENTARY INFORMATION

Characterization Data for Chiral Onium-Phosphine Hybrid Ligands 2-X:

**2b-Br:** ¹H NMR (400 MHz, CDCl₃) δ 8.26 (1H, s), 8.16 (1H, d, J = 8.2 Hz), 8.07 (1H, s), 8.01-8.05 (3H, m), 7.90 (1H, dd, J = 6.4, 3.2 Hz), 7.77 (1H, dd, J = 6.0, 3.2 Hz), 7.72 (2H, t, J = 7.6 Hz), 7.67 (2H, t, J = 7.6 Hz), 7.61 (1H, d, J = 8.7 Hz), 7.44-7.78 (9H, m), 7.31-7.41 (5H, m), 7.21 (1H, t, J = 7.3 Hz), 7.03-7.07 (4H, m), 6.97 (1H, dd, J = 7.2, 3.4 Hz), 6.75-6.82 (3H, m), 6.64 (2H, t, J = 8.0 Hz), 5.60 (1H, d, J = 14.2 Hz), 5.24 (1H, d, J = 13.3, 7.5 Hz), 4.00 (1H, d, J = 14.2 Hz), 3.96 (1H, d, J = 13.3 Hz), 3.96 (1H, d, J = 12.4 Hz), 3.50 (1H, d, J = 12.4 Hz), 2.86 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 140.9, 139.7, 138.9 (d, Jₚ₋ₑ = 15.5 Hz), 138.3, 138.1, 136.8 (d, Jₚ₋ₑ = 7.7 Hz), 136.3, 136.1, 135.8, 134.1 (d, Jₚ₋ₑ = 22.3 Hz), 133.8 (d, Jₚ₋ₑ = 21.3 Hz), 133.0 (d, Jₚ₋ₑ = 8.1 Hz), 133.0, 132.9, 132.6 (d, Jₚ₋ₑ = 19.4 Hz), 132.4, 132.3, 132.1, 132.0, 131.0 (d, Jₚ₋ₑ = 13.5 Hz), 130.7, 130.5, 129.9, 129.7, 129.7, 129.5, 129.1, 129.0, 128.9, 128.9, 128.8, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.7, 127.4, 127.3, 127.1, 126.9, 126.9, 126.8, 125.6, 123.8, 62.4, 62.1, 57.2 (d, Jₚ₋ₑ = 10.6 Hz), 48.4, eight peaks for aromatic carbons were not found probably due to overlapping; ³¹P NMR (162 MHz, CDCl₃) δ −18.7; IR (film): 3377, 3053, 3011, 2176, 1464, 1435, 922, 907, 860, 824, 723, 698, 638 cm⁻¹; HRMS (ESI) Caled for C₆₂H₄₇NP⁺ [M-Br]⁺ 836.3441. Found 836.3434.; [α]₀²³ = −43.0 (c = 1.0, CHCl₃).

**2c-Br:** ¹H NMR (400 MHz, CDCl₃) δ 8.15 (1H, s), 8.13 (1H, d, J = 8.2 Hz), 8.02 (1H, d, J = 8.2 Hz), 7.99 (1H, s), 7.65-7.74 (3H, m), 7.58 (2H, d, J = 7.8 Hz), 7.42-7.53 (7H, m), 7.26-7.34 (11H, m), 6.92-6.95 (1H, m), 6.85 (2H, t, J = 7.8 Hz), 6.76 (2H, t, J = 7.8 Hz), 5.51 (1H, d, J = 13.8 Hz), 5.04 (1H, d, J = 13.3, 7.3 Hz), 4.67 (1H, d, J = 13.3 Hz), 3.81 (1H, d, J = 13.8 Hz), 3.81 (1H, J = 12.4, 7.3 Hz), 3.46 (1H, d, J = 12.4 Hz), 3.00 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 141.0, 140.7 (d, Jₚ₋ₑ = 10.6 Hz), 139.6, 138.4, 138.2, 138.1, 137.9, 137.4 (d, Jₚ₋ₑ = 10.6 Hz), 136.4 (d, Jₚ₋ₑ = 13.5 Hz), 136.1, 135.1, 135.1, 134.0 (d, Jₚ₋ₑ = 14.5 Hz), 133.9 (d, Jₚ₋ₑ = 21.3 Hz), 133.0 (d, Jₚ₋ₑ = 28.1 Hz), 132.7 (d, Jₚ₋ₑ = 19.4 Hz), 131.8 (q, Jₚ₋ₑ = 32.9 Hz), 131.4 (q, Jₚ₋ₑ = 32.9 Hz), 131.4, 131.1, 131.1, 130.8, 130.8, 130.5, 130.0, 129.8, 129.6, 128.9, 128.8, 128.5, 128.3, 128.2, 127.8, 127.5, 127.4, 125.8 (q, Jₚ₋ₑ = 3.9 Hz), 125.8 (q, Jₚ₋ₑ = 3.9 Hz), 125.2, 123.8 (q, Jₚ₋ₑ = 276.9 Hz), 123.4 (q, Jₚ₋ₑ = 275.8 Hz), 123.3, 61.8, 61.3 (d, Jₚ₋ₑ = 23.2 Hz), 57.3 (d, Jₚ₋ₑ = 19.9 Hz), 48.1, two peaks for aromatic carbons were not found probably due to overlapping; ³¹P NMR (162 MHz, CDCl₃) δ −17.3; ¹⁹F NMR (376 MHz, CDCl₃) δ −62.8, −63.0; IR (film): 3377, 3057, 3026, 2181, 1321, 1167, 1125, 1107, 1059, 1015, 920, 907, 831, 723, 700, 638 cm⁻¹; HRMS (ESI) Caled for C₉₆H₄₉NP⁺ ([M-Br]⁺) 872.2875. Found 872.2866.; [α]₀²³ = −34.8 (c = 1.0, CHCl₃).

**2d-Br:** ¹H NMR (400 MHz, CDCl₃) δ 8.27 (1H, s), 8.16 (1H, d, J = 8.2 Hz), 8.12 (1H, s), 8.07 (1H, d, J = 8.7 Hz), 8.01-8.05 (1H, m), 7.98 (1H, s), 7.89-7.92 (1H, m), 7.67-7.80 (5H, m), 7.56-7.59 (3H, m), 7.44-7.53 (9H, m), 7.27-7.33 (4H, m), 7.12-7.17 (2H, m), 6.90-6.91 (1H, m), 6.87 (3H, t, J = 7.8 Hz), 6.74 (2H, t, J = 8.0 Hz), 5.66 (1H, d, J = 13.9 Hz), 5.09 (1H, dd, J = 13.3, 7.3 Hz), 4.29 (1H, d, J = 13.3 Hz), 3.99 (1H, dd, J = 13.9 Hz), 3.82 (1H, brd), 3.62 (1H, d, J = 12.4 Hz), 2.91 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 141.0, 140.8 (d, Jₚ₋ₑ = 10.6 Hz), 139.6, 138.4, 137.9, 137.5 (d, Jₚ₋ₑ = 10.6 Hz), 136.4 (d, Jₚ₋ₑ = 13.5 Hz), 136.1, 135.9, 135.7, 134.3, 134.2 (d, Jₚ₋ₑ = 14.5 Hz), 133.8 (d, Jₚ₋ₑ = 21.3 Hz), 133.5, 133.0, 133.0 (d, Jₚ₋ₑ = 29.0 Hz), 132.7 (d, Jₚ₋ₑ = 19.4 Hz), 132.4, 132.0, 132.0, 131.8 (q, Jₚ₋ₑ = 13.5 Hz).
Ion-exchange of ammonium phosphine 2-X was conducted by following the established procedure.  

![Chemical structure](image)

**2d-Cl:** 1H NMR (400 MHz, CDCl3) δ 8.26 (1H, s), 8.16 (1H, d, J = 8.2 Hz), 8.12 (1H, s), 8.07 (1H, d, J = 8.2 Hz), 8.02 (1H, d, J = 7.8 Hz), 7.97 (1H, s), 7.89-7.91 (1H, m), 7.78-7.80 (1H, m), 7.74 (2H, t, J = 8.0 Hz), 7.70 (2H, t, J = 8.2 Hz), 7.45-7.60 (12H, m), 7.32 (1H, d, J = 8.7 Hz), 7.22-7.30 (4H, m), 7.08-7.13 (1H, m), 6.90-6.91 (1H, m), 6.87 (3H, t, J = 7.8 Hz), 6.75 (2H, t, J = 8.0 Hz), 5.65 (1H, d, J = 13.9 Hz), 5.11 (1H, dd, J = 13.3, 7.3 Hz), 4.32 (1H, d, J = 13.3 Hz), 3.98 (1H, d, J = 13.9 Hz), 3.82 (1H, brd), 3.58 (1H, d, J = 12.8 Hz), 2.91 (3H, s); 13C NMR (101 MHz, CDCl3) δ 141.0, 141.0 (d, J_{PC} = 14.5 Hz), 139.6, 138.4, 137.9, 137.6 (d, J_{PC} = 11.6 Hz), 136.3 (d, J_{PC} = 13.5 Hz), 136.0, 135.9, 135.7, 134.4, 134.4, 134.2 (d, J_{PC} = 14.5 Hz), 133.9 (d, J_{PC} = 21.3 Hz), 133.5, 133.5 (d, J_{PC} = 30.4 Hz), 133.0, 132.6 (d, J_{PC} = 19.4 Hz), 132.4, 132.0, 131.9, 131.8 (q, J_{PC} = 32.9 Hz), 131.4 (q, J_{PC} = 32.9 Hz), 131.0, 130.9, 130.8, 129.8, 129.6, 129.1, 128.9, 128.8, 128.6, 128.4, 128.1, 127.9, 127.8, 127.6, 127.6, 127.5, 127.3, 127.1, 127.1, 127.0, 125.8 (q, J_{PC} = 3.9 Hz), 125.8 (q, J_{PC} = 3.9 Hz), 125.6, 123.9 (q, J_{PC} = 276.7 Hz), 123.5 (q, J_{PC} = 276.7 Hz), 123.5, 62.3, 61.4 (d, J_{PC} = 25.2 Hz), 57.3 (d, J_{PC} = 8.7 Hz), 48.6, six peaks for aromatic carbons were not found probably due to overlapping; 31P NMR (162 MHz, CDCl3) δ −18.1; 19F NMR (376 MHz, CDCl3) δ −62.7, −62.9; IR (film): 3377, 3055, 3017, 1321, 1167, 1126, 1109, 1061, 1015, 831, 748, 729 cm⁻¹; HRMS (ESI) Calcd for C_{64}H_{45}NF_{6}P⁺ ([M-Cl]⁺) 972.3188. Found 972.3188.; [α]_{D}^{23} = −49.6 (c = 1.0, CHCl₃).

**2d-I:** 1H NMR (400 MHz, CDCl3) δ 8.28 (1H, s), 8.16 (1H, d, J = 8.2 Hz), 8.14 (1H, s), 8.06-8.08 (2H, m), 8.02 (1H, s), 7.91-7.93 (2H, m), 7.68-7.80 (5H, m), 7.62 (1H, d, J = 8.7 Hz), 7.57 (2H, d, J = 7.8 Hz), 7.45-7.54 (9H, m), 7.34 (1H, d, J = 8.7 Hz), 7.28 (2H, d, J = 8.2 Hz), 7.09-7.13 (1H, m), 6.80-6.89 (5H, m), 6.71 (2H, t, J = 7.8 Hz), 5.58 (1H, d, J = 13.8 Hz), 5.05 (1H, dd, J = 13.0, 6.9 Hz), 4.13 (1H, d, J = 13.0 Hz), 4.03 (1H, d, J = 13.8 Hz), 3.84 (1H, brd), 3.77 (1H, d, J = 12.4 Hz), 2.83 (3H, s); 13C NMR (101 MHz, CDCl3) δ 140.7, 140.5 (d, J_{PC} = 10.6 Hz), 139.5, 138.4, 137.9, 137.3 (d, J_{PC} = 10.6 Hz), 136.6 (d, J_{PC} = 13.5 Hz), 136.2, 135.9, 135.7, 134.2 (d, J_{PC} = 9.7 Hz), 133.8, 133.7 (d, J_{PC} = 21.3 Hz), 133.5, 133.2, 132.8 (d, J_{PC} = 23.2 Hz), 132.7 (d, J_{PC} = 19.4 Hz), 132.4, 131.9, 131.4 (q, J_{PC} = 32.9 Hz), 131.2, 131.0 (q, J_{PC} = 32.9 Hz), 131.0, 130.9, 130.2, 129.5, 129.1, 128.9, 128.8, 128.7, 128.7, 128.5, 128.5, 128.1, 128.1, 127.9, 127.8, 127.8, 127.6, 127.6, 127.5, 127.3, 127.2, 127.0, 125.8 (q, J_{PC} = 3.9 Hz), 125.8 (q, J_{PC} = 3.9 Hz), 125.1, 123.8 (q, J_{PC} = 276.7 Hz), 123.5 (q, J_{PC} = 275.8 Hz), 123.2, 62.3, 61.8 (d, J_{PC} = 25.2 Hz), 58.2, 48.8, six peaks for aromatic carbons were not found probably due to overlapping; 31P NMR (162 MHz, CDCl3) δ −18.0; 19F NMR (376 MHz, CDCl3) δ −62.8, −62.9; IR (film): 3055, 3019, 2187, 1321, 1167, 1126, 1107, 1015, 831, 748, 731 cm⁻¹; HRMS (ESI) Calcd for C_{64}H_{45}NF_{6}P⁺ ([M-Cl⁺]⁺) 972.3188. Found 972.3188.; [α]_{D}^{23} = −61.2 (c = 1.0, CHCl₃).

1059, 1015, 907, 826, 723, 700 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{64}\)H\(_{45}\)NF\(_6\)P\(^+\) ([M-I]\(^+\)) 972.3188. Found 972.3188.; [\(\alpha\)]\(_D\)\(=\) -33.7 (c = 1.0, CHCl\(_3\)).

Representative Procedure for Pd-Catalyzed Asymmetric Cycloaddition of 5-Vinyloxazolidinones with Activated Alkenes:

To a Schlenk flask was added Pd\(_2\)(dba)\(_3\)·CHCl\(_3\) (1.29 mg, 1.25 \(\mu\)mol), 2d·I (5.50 mg, 5 \(\mu\)mol), and ethyl 2-cyano 3-phenylacrylate 6a (60.4 mg, 0.3 mmol) and the flask was degassed by alternating vacuum evacuation/Ar backfill. Then, toluene (1 mL) was introduced, and the resulting catalyst mixture was evacuated and refilled with Ar three times. The mixture was cooled to 0 °C and 5-vinyloxazolidinone 8a (31.2 mg, 0.1 mmol) was successively added into the reaction flask. After stirring for 10 h, the reaction mixture was filtered through a pad of short silica gel and washed with acetone. The resulting filtrates were concentrated and purified by column chromatography on silica gel (H/Et\(_2\)O = 9:1 to 3:1 as eluent) to afford 11a (46.1 mg, 0.0981 mmol, 98% yield) as a white solid.

### Characterization Data for the Pyrrolidines:

The reaction was stirred for 10 h at 0 °C.

**11b:** \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.23 (2H, d, \(J = 8.9\) Hz), 7.31 (2H, d, \(J = 8.9\) Hz), 7.11 (2H, d, \(J = 8.2\) Hz), 5.75 (1H, dd, \(J = 17.4, 11.0\) Hz), 5.61 (1H, s), 5.42 (1H, d, \(J = 17.4\) Hz), 5.34 (1H, d, \(J = 11.0\) Hz), 4.27 (1H, dq, \(J = 11.0, 7.3\) Hz), 4.24 (1H, d, \(J = 11.4\) Hz), 4.16 (1H, dq, \(J = 11.0, 7.3\) Hz), 3.74 (1H, d, \(J = 11.4\) Hz), 1.56 (3H, s), 1.28 (3H, t, \(J = 7.3\) Hz); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.3, 150.1, 145.0, 134.9, 133.5, 131.5, 130.3, 128.5, 124.2, 123.7, 118.6, 114.9, 66.5, 64.7, 64.0, 58.3, 50.6, 19.4, 14.2; IR (film): 3103, 3071, 2986, 2970, 2920, 1744, 1531, 1350, 1240, 1165, 1090, 1042, 741, 698, 563 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{23}\)H\(_{22}\)N\(_3\)O\(_6\)BrSNa\(^+[\text{M+Na}]^+\) 570.0305. Found 570.0306.; HPLC AD3, H/IPA/EtOH = 18:1:1, flow rate = 1.0 mL/min, \(\lambda = 210\) nm, 22.5 min (minor), 26.5 min (major).

**11c:** \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.14 (2H, d, \(J = 9.1\) Hz), 7.60 (2H, d, \(J = 9.1\) Hz), 7.09 (2H, d, \(J = 8.7\) Hz), 6.63 (2H, d, \(J = 8.7\) Hz), 5.83 (1H, dd, \(J = 17.4, 10.8\) Hz), 5.70 (1H, d, \(J = 11.0\) Hz), 5.61 (1H, s), 5.42 (1H, d, \(J = 17.4\) Hz), 5.34 (1H, d, \(J = 11.0\) Hz), 4.27 (1H, dq, \(J = 11.0, 7.3\) Hz), 4.24 (1H, d, \(J = 11.4\) Hz), 4.16 (1H, dq, \(J = 11.0, 7.3\) Hz), 3.74 (1H, d, \(J = 11.4\) Hz), 1.56 (3H, s), 1.28 (3H, t, \(J = 7.3\) Hz); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 163.3, 150.1, 145.0, 134.9, 133.5, 131.5, 130.3, 128.5, 124.2, 123.7, 118.6, 114.9, 66.5, 64.7, 64.0, 58.3, 50.6, 19.4, 14.2; IR (film): 3103, 3071, 2986, 2970, 2920, 1744, 1531, 1350, 1240, 1167, 1042, 741, 698, 563 cm\(^{-1}\); HRMS (ESI) Calcd for C\(_{23}\)H\(_{22}\)N\(_3\)O\(_6\)BrSNa\(^+[\text{M+Na}]^+\) 570.0305. Found 570.0306.; HPLC AD3, H/IPA/EtOH = 18:1:1, flow rate = 1.0 mL/min, \(\lambda = 210\) nm, 22.5 min (minor), 26.5 min (major).
5.61 (1H, s), 5.44 (1H, d, J = 17.4 Hz), 5.36 (1H, d, J = 10.8 Hz), 4.30 (1H, d, J = 11.0 Hz), 4.27 (1H, dq, J = 11.0, 7.3 Hz), 4.15 (1H, dq, J = 11.0, 7.3 Hz), 3.75 (1H, d, J = 11.0 Hz), 3.73 (3H, s), 1.56 (3H, s), 1.27 (3H, t, J = 7.3 Hz); 13C NMR (101 MHz, CDCl3) δ 163.4, 160.3, 149.9, 145.5, 135.3, 130.2, 128.5, 125.7, 123.9, 118.3, 115.3, 113.5, 66.5, 65.0, 63.7, 58.1, 55.4, 50.4, 19.5, 14.2; IR (film): 3103, 3071, 2984, 2970, 2938, 1744, 1530, 1514, 1438, 1242, 1163, 1032, 752, 737 cm⁻¹; HRMS (ESI) Calcd for C24H25N3O7SNa⁺ ([M+Na]+) 522.1305. Found 522.1305.; HPLC IA, H/EtOH = 10:1, flow rate = 1.0 mL/min, λ = 254 nm, 24.8 min (minor), 33.0 min (major).

The reaction was stirred for 10 h at 0 °C.

11d: ¹H NMR (400 MHz, CDCl3) δ 7.92 (2H, d, J = 8.7 Hz), 7.76 (1H, d, J = 7.8 Hz), 7.59 (2H, d, J = 7.8 Hz), 7.51 (2H, d, J = 8.7 Hz), 7.41-7.55 (3H, m), 7.25-7.28 (1H, m), 5.91 (1H, dd, J = 17.4, 11.0 Hz), 5.83 (1H, s), 5.49 (1H, d, J = 17.4 Hz), 5.41 (1H, d, J = 11.0 Hz), 4.38 (1H, d, J = 11.4 Hz), 4.29 (1H, dq, J = 11.0, 7.3 Hz), 4.16 (1H, dq, J = 11.0, 7.3 Hz), 3.84 (1H, d, J = 11.4 Hz), 1.60 (3H, s), 1.27 (3H, t, J = 7.3 Hz); 13C NMR (101 MHz, CDCl3) δ 163.4, 149.7, 145.4, 135.3, 133.4, 132.5, 131.2, 128.8, 128.4, 128.0, 127.9, 127.8, 127.1, 126.6, 125.8, 123.8, 118.5, 115.2, 67.0, 64.9, 63.8, 58.2, 50.6, 19.4, 14.2; IR (film): 3107, 3061, 3017, 2988, 2926, 1742, 1530, 1348, 1238, 1163, 1040, 854, 741 cm⁻¹; HRMS (ESI) Calcd for C27H25N3O6SNa⁺ ([M+Na]+) 542.1356. Found 542.1356.; HPLC AD3, H/EtOH = 10:1, flow rate = 1.0 mL/min, λ = 210 nm, 20.0 min (minor), 33.8 min (major).

The reaction was stirred for 10 h at 0 °C.

11e: ¹H NMR (400 MHz, CDCl3) δ 8.25 (2H, d, J = 8.9 Hz), 7.72 (1H, d, J = 8.9 Hz), 7.14 (1H, d, J = 1.8 Hz), 6.41 (1H, d, J = 3.2 Hz), 6.28 (1H, dd, J = 3.2, 1.8 Hz), 5.81 (1H, dd, J = 17.6, 11.0 Hz), 5.63 (1H, s), 5.40 (1H, d, J = 17.6 Hz), 5.35 (1H, d, J = 11.0 Hz), 4.26 (1H, dq, J = 11.0, 7.3 Hz), 4.18 (1H, dq, J = 11.0, 7.3 Hz), 4.11 (1H, d, J = 11.0 Hz), 3.70 (1H, d, J = 11.4 Hz), 2.11 (1H, dq, J = 15.1, 7.3 Hz), 1.98 (1H, dq, J = 15.1, 7.3 Hz), 1.61 (3H, s), 1.29 (3H, t, J = 7.3 Hz); 13C NMR (101 MHz, CDCl3) δ 163.9, 150.0, 147.1, 144.8, 143.6, 135.4, 128.4, 124.1, 118.3, 114.6, 112.1, 110.9, 63.9, 62.3, 61.1, 57.3, 50.5, 20.4, 14.1; IR (film): 3107, 3061, 3017, 2988, 2926, 2970, 2928, 1744, 1531, 1350, 1238, 1215, 1167, 743, 613 cm⁻¹; HRMS (ESI) Calcd for C21H21N3O7SNa⁺ ([M+Na]+) 482.0992. Found 482.0991.; HPLC IA, H/EtOH = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 42.9 min (major), 49.1 min (minor).

The reaction was stirred for 10 h at 0 °C.

11f: ¹H NMR (400 MHz, CDCl3) δ 8.11 (2H, d, J = 8.9 Hz), 7.53 (2H, d, J = 8.9 Hz), 7.14 (1H, t, J = 7.3 Hz), 7.14 (2H, d, J = 7.3 Hz), 7.08 (2H, t, J = 7.3 Hz), 5.53 (1H, s), 5.49-5.63 (3H, m), 4.55 (1H, d, J = 11.4 Hz), 4.28 (1H, dq, J = 11.0, 7.3 Hz), 4.18 (1H, dq, J = 11.0, 7.3 Hz), 3.70 (1H, d, J = 11.4 Hz), 2.11 (1H, dq, J = 15.1, 7.3 Hz), 1.98 (1H, dq, J = 15.1, 7.3 Hz), 1.29 (3H, t, J = 7.3 Hz), 1.01 (3H, t, J = 7.3 Hz); 13C NMR (101 MHz, CDCl3) δ 163.2, 149.8, 145.9, 133.3, 133.2, 129.3, 128.4, 128.1, 123.9, 120.3, 115.3, 67.0, 65.2, 63.7, 54.6, 54.4, 27.2, 14.1, 9.4; one peak for aromatic carbon was not found probably due to overlapping; IR (film): 3105, 3067, 3034, 2938, 1744, 1530, 1348, 1231, 1163, 999, 741, 617, 610, 565 cm⁻¹; HRMS (ESI) Calcd for C24H25N3O6SNa⁺ ([M+Na]+) 506.1356. Found 506.1359.; HPLC AD3, H/EtOH = 10:1, flow rate = 0.5 mL/min, λ = 210 nm, 42.9 min (major), 49.1 min (minor).
The reaction was stirred for 10 h at 0 °C.

**11g:** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10 (2H, $d$, $J = 8.9$ Hz), 7.51 (2H, $d$, $J = 8.9$ Hz), 7.22 (1H, $t$, $J = 7.3$ Hz), 7.12 (2H, $d$, $J = 7.3$ Hz), 7.06 (2H, $t$, $J = 7.3$ Hz), 5.46 (1H, s), 5.51-5.70 (3H, m), 4.72 (1H, $d$, $J = 11.9$ Hz), 4.30 (1H, dq, $J = 11.0$, 7.3 Hz), 4.19 (1H, dq, $J = 11.0$, 7.3 Hz), 3.76 (1H, $d$, $J = 11.9$ Hz), 2.03 (1H, dd, $J = 14.4$, 4.4 Hz), 1.84 (1H, dd, $J = 14.4$, 6.4 Hz), 1.63-1.70 (1H, m), 1.29 (3H, $t$, $J = 7.3$ Hz), 0.96 (3H, $d$, $J = 6.9$ Hz), 0.95 (3H, $d$, $J = 6.4$ Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.1, 149.8, 146.1, 134.0, 133.0, 129.4, 129.3, 128.3, 128.1, 123.8, 119.7, 115.4, 66.1, 65.7, 63.7, 54.9, 54.1, 43.3, 25.2, 25.1, 23.5, 14.2; IR (film): 3105, 3069, 3054, 2959, 2938, 1744, 1531, 1350, 1234, 1163, 1094, 745, 619, 559 cm$^{-1}$; HRMS (ESI) Calcd for C$_{25}$H$_{25}$N$_3$O$_6$SNa$^+$ ([M+Na$^+$]) 534.1669. Found 534.1670.; HPLC AD3, H/IPA = 10:1, flow rate = 1.0 mL/min, $\lambda$ = 254 nm, 9.5 min (minor), 12.7 min (major).

The reaction was stirred for 24 h at 0 °C.

**11h:** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (2H, $d$, $J = 8.9$ Hz), 7.50 (2H, $d$, $J = 8.9$ Hz), 7.09-7.32 (10H, m), 5.65 (1H, dd, $J = 17.4$, 11.4 Hz), 5.50 (1H, $d$, $J = 11.4$ Hz), 5.47 (1H, s), 5.35 (1H, $d$, $J = 17.4$ Hz), 4.33 (1H, dq, $J = 10.5$, 7.3 Hz), 4.23 (1H, dq, $J = 10.5$, 7.3 Hz), 4.18 (1H, $d$, $J = 11.4$ Hz), 3.90 (1H, $d$, $J = 11.4$ Hz), 3.37 (1H, $d$, $J = 14.2$ Hz), 3.20 (1H, $d$, $J = 14.2$ Hz), 1.55 (3H, s), 1.33 (3H, $t$, $J = 7.3$ Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.3, 149.8, 145.6, 135.2, 133.2, 133.0, 130.3, 129.4, 128.5, 128.4, 128.1, 127.5, 123.8, 120.8, 115.4, 67.1, 64.8, 63.9, 54.5, 54.0, 41.0, 14.2; one peak for aromatic carbon was not found probably due to overlapping; IR (film): 3105, 3065, 3032, 2986, 2938, 1744, 1531, 1350, 1234, 1217, 1165, 1005, 741, 704 cm$^{-1}$; HRMS (ESI) Calcd for C$_{25}$H$_{25}$N$_3$O$_6$SNa$^+$ ([M+Na$^+$]) 568.1513. Found 568.1514.; HPLC AD3, H/IPA = 10:1, flow rate = 1.0 mL/min, $\lambda$ = 254 nm, 19.6 min (major), 23.9 min (minor).

The reaction was stirred for 96 h at room temperature.

**11i:** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.11 (2H, $d$, $J = 9.2$ Hz), 7.52 (2H, $d$, $J = 9.2$ Hz), 7.24 (1H, $t$, $J = 7.3$ Hz), 7.01-7.09 (4H, m), 5.93 (1H, $d$dd, $J = 17.4$, 11.4, 0.9 Hz), 5.69 (1H, $d$, $J = 17.4$ Hz), 5.66 (1H, $d$, $J = 11.4$ Hz), 5.37 (1H, s), 4.74 (1H, $d$, $J = 11.9$ Hz), 4.11-4.20 (2H, m), 3.67 (1H, dd, $J = 11.9$ Hz), 2.43 (1H, sept, $J = 6.8$ Hz), 1.17 (3H, $t$, $J = 7.3$ Hz), 0.95 (3H, $d$, $J = 6.9$ Hz), 0.87 (3H, $d$, $J = 6.9$ Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.9, 149.8, 146.2, 132.2, 129.8, 129.6, 128.8, 128.4, 128.2, 123.8, 120.3, 115.6, 69.9, 65.3, 63.7, 57.6, 55.5, 34.1, 19.0, 17.6, 13.8; IR (film): 3105, 3069, 3036, 2970, 2938, 1740, 1531, 1350, 1234, 1165, 1109, 1094, 1003, 743 cm$^{-1}$; HRMS (ESI) Calcd for C$_{25}$H$_{27}$N$_3$O$_6$SNa$^+$ ([M+Na$^+$]) 520.1513. Found 520.1515.; HPLC IA, H/IPA = 10:1, flow rate = 1.0 mL/min, $\lambda$ = 254 nm, 13.7 min (major), 18.4 min (minor).

The reaction was stirred for 40 h at room temperature.

**11j:** $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.15 (2H, $d$, $J = 8.9$ Hz), 7.63 (2H, $d$, $J = 8.9$ Hz), 7.33-7.41 (3H, m), 7.25-7.29 (3H, m), 7.11-7.15 (4H, m), 6.35 (1H, $d$, $J = 17.2$, 11.0 Hz), 5.75 (1H, $s$), 5.39 (1H, $d$, $J = 11.0$ Hz), 5.15 (1H, $d$, $J = 17.2$ Hz), 4.88 (1H, $d$, $J = 11.4$ Hz), 4.47 (1H, $d$, $J = 11.4$ Hz), 4.33 (1H, dq, $J = 11.0$, 7.3 Hz), 4.25 (1H, dq, $J = 11.0$, 7.3 Hz), 1.24 (3H, $t$, $J = 7.3$ Hz); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 164.1, 150.0, 145.7, 137.4, 136.1, 132.9, 129.7, 128.9, 128.6, 128.5, 128.4, 127.5, 124.0, 119.2, 115.3, 69.4, 65.6, 64.1, 59.0, 57.0, 14.0, one peak for aromatic carbon was not found.
probably due to overlapping; IR (film): 3105, 3065, 3038, 2986, 2926, 1740, 1531, 1350, 1236, 1167, 1009, 739, 698, 608 cm⁻¹; HRMS (ESI) Calcd for C_{28}H_{32}N_{10}O_{8}SNa⁺ ([M+Na⁺]⁺) 554.1356. Found 554.1357.; HPLC AD3, H/IPA = 10:1, flow rate = 1.0 mL/min, λ = 210 nm, 37.8 min (major), 55.2 min (minor).

The reaction was stirred for 40 h at room temperature.

11k: ¹H NMR (400 MHz, CDCl₃) δ 8.14 (2H, d, J = 9.2 Hz), 7.61 (2H, d, J = 9.2 Hz), 7.37 (2H, d, J = 8.7 Hz), 7.23-7.27 (3H, m), 7.09-7.15 (4H, m), 6.32 (1H, dd, J = 17.2, 11.0 Hz), 5.76 (1H, s), 5.42 (1H, d, J = 11.0 Hz), 5.14 (1H, d, J = 17.2 Hz), 4.84 (1H, d, J = 11.4 Hz), 4.42 (1H, d, J = 11.4 Hz), 4.33 (1H, dq, J = 10.5, 7.3 Hz), 4.26 (1H, dq, J = 10.5, 7.3 Hz), 1.24 (3H, t, J = 7.3 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 163.8, 150.0, 145.5, 135.8, 135.7, 134.7, 132.7, 129.7, 129.1, 129.0, 128.6, 128.5, 124.0, 119.7, 115.1, 69.2, 65.5, 64.2, 58.6, 57.0, 14.0; IR (film): 3105, 3069, 3028, 2974, 2924, 1740, 1531, 1350, 1236, 1167, 1098, 1011, 731, 608 cm⁻¹; HRMS (ESI) Calcd for C_{28}H_{32}N_{10}O_{8}CISNa⁺ ([M+Na⁺]⁺) 589.0697. Found 589.0697.; HPLC IA, H/EtOH = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, 31.4 min (minor), 55.4 min (major).

The reaction was stirred for 40 h at room temperature.

11I: ¹H NMR (400 MHz, CDCl₃) δ 8.15 (2H, d, J = 8.9 Hz), 7.63 (2H, d, J = 8.9 Hz), 7.24-7.27 (1H, m), 7.20 (2H, d, J = 8.9 Hz), 7.09-7.15 (4H, m), 6.90 (2H, d, J = 8.9 Hz), 6.32 (1H, dd, J = 16.9, 11.0 Hz), 5.74 (1H, s), 5.37 (1H, d, J = 11.0 Hz), 5.15 (1H, d, J = 16.9 Hz), 4.80 (1H, d, J = 11.4 Hz), 4.46 (1H, d, J = 11.4 Hz), 4.32 (1H, dq, J = 11.0, 7.3 Hz), 4.24 (1H, dq, J = 11.0, 7.3 Hz), 3.82 (3H, s), 1.24 (3H, t, J = 7.3 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 164.1, 159.4, 150.0, 145.6, 136.2, 133.0, 129.6, 129.1, 128.8, 128.6, 128.5, 124.0, 119.1, 115.3, 114.1, 69.3, 65.9, 64.0, 58.5, 57.2, 55.4, 14.0; IR (film): 3105, 3067, 3038, 2984, 2936, 1740, 1531, 1518, 1350, 1256, 1167, 739 cm⁻¹; HRMS (ESI) Calcd for C_{29}H_{27}N_{13}O_{7}SNa⁺ ([M+Na⁺]⁺) 584.1462. Found 584.1462.; HPLC ADH, H/EtOH = 10:1, flow rate = 1.0 mL/min, λ = 254 nm, 45.0 min (minor), 65.3 min (major).

5: [α]D⁻²⁵ = -41.8 (c = 1.0, CHCl₃) for 92% ee; ¹H NMR (400 MHz, CDCl₃) δ 8.16 (2H, d, J = 9.2 Hz), 7.57 (2H, d, J = 9.2 Hz), 7.36 (1H, t, J = 7.3 Hz), 7.20 (2H, t, J = 7.8 Hz), 7.13 (2H, d, J = 7.3 Hz), 6.14 (1H, ddd, J = 17.4, 11.0, 0.9 Hz), 6.08 (1H, ddd, J = 17.4, 11.0 Hz), 5.83 (1H, d, J = 17.4 Hz), 5.79 (1H, d, J = 11.0 Hz), 5.60 (1H, d, J = 11.0 Hz), 5.46 (1H, d, J = 17.4 Hz), 5.20 (1H, s), 4.67 (1H, d, J = 11.9 Hz), 3.93 (1H, dd, J = 11.9, 0.9 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 150.2, 145.2, 132.4, 131.4, 130.8, 130.6, 128.8, 128.6, 128.5, 124.1, 122.5, 122.3, 111.4, 110.9, 69.3, 56.2, 53.9, 53.4; IR (film) 3105, 3069, 3036, 2922, 1531, 1350, 1312, 1167, 1107, 991, 856, 756, 743, 613, 565 cm⁻¹; HRMS (ESI) Calcd for C_{29}H_{18}N_{6}O_{8}SNa⁺ ([M+Na⁺]⁺) 457.0941 Found 457.0942.; HPLC ODH, H/EtOH = 10:1, flow rate = 0.5 mL/min, λ = 254 nm, 28.0 min (minor), 30.6 min (major).

7: ¹H NMR (400 MHz, CDCl₃) δ 8.12 (2H, d, J = 8.7 Hz), 7.58 (2H, d, J = 8.7 Hz), 7.24 (1H, t, J = 7.3 Hz), 7.16 (2H, d, J = 7.3 Hz), 7.12 (2H, d, J = 7.3 Hz), 6.29 (1H, dd, J = 17.8, 11.0 Hz), 5.80 (1H, ddd, J = 17.4, 11.0 Hz), 5.66 (1H, s), 5.57 (1H, d, J = 17.4 Hz), 5.50 (1H, d, J = 11.0 Hz), 5.49 (1H, d, J = 11.0 Hz), 5.27 (1H, d, J = 17.8 Hz), 4.47 (1H, d, J = 11.5 Hz), 4.30 (1H, dq, J = 11.0, 7.1 Hz), 4.17 (1H, dq, J = 11.0, 7.1 Hz), 4.03 (1H, d, J = 11.5 Hz), 1.27 (3H, t, J = 7.1 Hz); ¹³C NMR (101 MHz, CDCl₃) δ 163.1, 149.9, 145.5, 134.4, 133.5, 132.8, 129.3, 128.9, 128.4, 128.2, 123.9, 120.4, 120.1,
115.0, 66.6, 64.5, 63.9, 56.2, 55.2, 14.1; IR (film) 3105, 3067, 3036, 2986, 2926, 1746, 1531, 1350, 1312, 1238, 1167, 1096, 1001, 743, 613, 565 cm⁻¹; HRMS (ESI) Calcd for C₂₃H₂₁N₃O₆SNa⁺ ([M+Na⁺]⁺) 504.1200. Found 504.1200.; HPLC IA, H/IPA = 10:1, flow rate = 0.5 mL/min, λ = 254 nm, 32.1 min (minor), 34.6 min (major).

10: [α]D₂₃ = -10.0 (c = 1.0, CHCl₃) for 94% ee; ¹H NMR (400 MHz, CDCl₃) δ 8.37 (2H, d, J = 8.9 Hz), 8.03 (2H, d, J = 8.9 Hz), 6.01 (1H, dd, J = 17.8, 11.0 Hz), 5.12 (1H, d, J = 11.0 Hz), 5.09 (1H, d, J = 17.8 Hz), 3.78 (1H, d, J = 11.9 Hz), 3.64 (1H, d, J = 8.9 Hz), 3.45 (1H, d, J = 8.9 Hz), 3.38 (1H, s), 3.34 (1H, s), 1.38 (9H, s), 1.34 (9H, s), 1.23 (3H, s), 1.22 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 167.4, 167.3, 150.2, 143.5, 139.1, 128.7, 124.3, 115.3, 83.1, 82.9, 65.2, 57.8, 52.6, 48.8, 27.9, 27.9, 20.8; IR (film) 3107, 2978, 2934, 1724, 1368, 1350, 1290, 1250, 1159, 1092, 1063, 737, 619 cm⁻¹; HRMS (ESI) Calcd for C₂₃H₃₂N₂O₈SNa⁺ ([M+Na⁺]⁺) 519.1772. Found 519.1774.; HPLC IC, H/IPA = 19:1, flow rate = 1.0 mL/min, λ = 254 nm, 63.8 min (major), 69.1 min (minor).

13: ¹H NMR (400 MHz, CDCl₃) δ 8.12 (2H, d, J = 8.7 Hz), 7.59 (2H, d, J = 8.7 Hz), 7.17-7.22 (1H, m), 7.05 -7.07 (4H, m), 6.08 (1H, s), 5.54 (1H, d, J = 17.4 Hz), 5.47 (1H, d, J = 11.2 Hz), 4.88 (1H, s), 4.22 (1H, d, J = 11.0 Hz), 3.85 (1H, d, J = 11.4 Hz), 3.67 (1H, d, J = 11.0 Hz), 3.66 (1H, d, J = 11.4 Hz), 1.82 (1H, brs), 1.53 (3H, s).

Derivatization of Cycloaddition Product 11a:

To a solution of 11a (46.5 mg, 0.10 mmol) in CH₂Cl₂ (1 mL) was dropwised diisobutylaluminium hydride (1.0 M toluene solution, 0.2 mL) at –78 °C under Ar, and the stirring was kept for 30 min. Then, the reaction mixture was warmed up to 0 °C. After stirring for 1 h at the same temperature, 1N HCl was carefully added to the reaction mixture and extractive work-up was performed with EtOAc three times. The combined organic phases were washed with brine, dried over Na₂SO₄, and concentrated. Purification of the residue by column chromatography on silica gel (H/Acetone = 8:1 to 4:1 as eluent) gave the corresponding alcohol 14 (26.1 mg, 0.0611 mmol, 62% yield) as a white solid. 14: ¹H NMR (400 MHz, CDCl₃) δ 8.12 (2H, d, J = 8.9 Hz), 7.55 (2H, d, J = 8.9 Hz), 7.25 (1H, t, J = 7.8 Hz), 7.14 (2H, t, J = 7.8 Hz), 7.08 (2H, d, J = 7.8 Hz), 6.02 (1H, dd, J = 17.4, 11.2 Hz), 5.54 (1H, d, J = 17.4 Hz), 5.47 (1H, d, J = 11.2 Hz), 4.88 (1H, s), 4.22 (1H, d, J = 11.0 Hz), 3.85 (1H, d, J = 11.4 Hz), 3.67 (1H, d, J = 11.0 Hz), 3.66 (1H, d, J = 11.4 Hz), 1.82 (1H, brs), 1.53 (3H, s).
To a mixture of 14 (26.1 mg, 0.0611 mmol) and Cs$_2$CO$_3$ (39.8 mg, 0.122 mmol) in CH$_3$CN (1 mL) was slowly added $n$-C$_{12}$H$_{25}$SH (29.2 μL, 0.122 mmol) at room temperature and the whole mixture was stirred for 4 h. After the completion of the reaction was confirmed by TLC analysis, the reaction mixture was directly subjected to the purification by column chromatography on silica gel (H/EtOAc = 8:1 to 2:1 as eluent) to afford pyrrolidine 15 in 64% yield (9.4 mg, 0.0388 mmol) as a white solid.

**S13:** $^1$H NMR (400 MHz, CDCl$_3$) δ 7.47 (2H, d, $J = 7.3$ Hz), 7.31-7.39 (3H, m), 6.08 (1H, dd, $J = 17.4, 11.4$ Hz), 5.32 (1H, d, $J = 17.4$ Hz), 5.32 (1H, d, $J = 11.4$ Hz), 4.33 (1H, s), 3.81 (1H, d, $J = 11.7$ Hz), 3.70 (1H, d, $J = 11.7$ Hz), 3.24 (2H, s), 2.01 (1H, brs), 1.51 (3H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 139.7, 138.9, 128.7, 128.6, 127.9, 119.6, 116.2, 67.2, 63.7, 59.4, 56.5, 50.5, 23.4; IR (film): 3019, 2930, 1215, 1088, 1078, 754, 700, 667 cm$^{-1}$; HRMS (ESI) Calcd for C$_{15}$H$_{19}$N$_2$O$^+$ ([M+H]$^+$) 243.1492. Found 243.1491.; HPLC OZ3, H/IPA = 10:1, flow rate = 1.0 mL/min, λ = 254 nm, 11.3 min (major), 15.3 min (minor).

To a solution of 11a (468 mg, 0.996 mmol) in CH$_2$Cl$_2$ (1 mL) was bubbled ozone at $-78$ °C for 10 min. Then, the mixture was purged by Ar gas to exclude ozone, and dimethyl sulfide (734 μL, 9.99 mmol) was added to the reaction solution at the same temperature. After warming up to room temperature, the stirring was maintained for 2 h. The reaction mixture was concentrated under reduced pressure to give crude product, which was purified by column chromatography on silica gel (H/EtOAc = 7:1 to 3:1 as eluent) to afford 16 in 97% yield (455 mg, 0.965 mmol) as a white solid. 16: $^1$H NMR (400 MHz, CDCl$_3$) δ 9.46 (1H, s), 8.18 (2H, d, $J = 8.7$ Hz), 7.64 (2H, d, $J = 8.7$ Hz), 7.20-7.33 (5H, m), 5.54 (1H, s), 4.50 (1H, d, $J = 12.4$ Hz), 4.30 (1H, dq, $J = 11.0, 7.3$ Hz), 4.25 (1H, dq, $J = 11.0, 7.3$ Hz), 3.70 (1H, d, $J = 12.4$ Hz), 1.63 (3H, s), 1.28 (3H, t, $J = 7.3$ Hz).

To a solution of 16 (455 mg, 0.965 mmol) in THF (10 mL) was dropwised diisobutylaluminium hydride (1.0 M toluene solution, 1.93 mL) at $-78$ °C under Ar, and the whole mixture was kept for 2 h with stirring. The reaction was then quenched by the slow addition of 1N HCl, and the mixture was extracted with EtOAc three times. The combined organics were washed with brine, dried over anhydrous Na$_2$SO$_4$, and concentrated under reduced pressure to give crude product. The crude material including the corresponding alcohol was used for the next step without further purification. 17: To a solution of this crude material in CH$_2$Cl$_2$...
(10.0 mL) was added trifluoroacetic acid (10.0 ml) at room temperature. After stirring for 7 h, a saturated aqueous solution of NaHCO₃ was carefully added to the reaction mixture at 0 °C and extractive work-up was performed with CHCl₃ three times. The combined organic phases were washed with brine, dried over Na₂SO₄, and concentrated. Purification of the residue by column chromatography on silica gel (H/EtOAc = 6:1 to 2:1 as eluent) gave the corresponding lactone 17 in 95% yield for 2 steps (392 mg, 0.917 mmol) as a white solid. 17: ¹H NMR (400 MHz, CDCl₃) δ 8.27 (2H, d, J = 8.7 Hz), 7.78 (2H, d, J = 8.7 Hz), 7.33-7.38 (3H, m), 7.24-7.26 (2H, m), 5.44 (1H, s), 4.34 (1H, d, J = 10.1 Hz), 4.19 (1H, d, J = 10.1 Hz), 3.88 (1H, d, J = 11.0 Hz), 3.77 (1H, d, J = 11.0 Hz), 1.52 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 168.7, 150.5, 142.8, 134.7, 129.9, 129.1, 128.8, 127.4, 124.5, 111.5, 75.0, 69.1, 59.7, 58.0, 51.3, 20.2; IR (film): 3107, 2251, 1784, 1531, 1350, 1169, 737, 613 cm⁻¹; HRMS (ESI) Calcd for C₂₀H₁₇N₃O₆NaS⁺ ([M+Na⁺]⁺) 450.0736. Found 450.0730.

To a solution of 17 (392 mg, 0.917 mmol) in CH₃CN (10 mL) was added 4-methoxybenzylamine (237 μL, 1.83 mmol) at room temperature. After 6 h of stirring, the reaction mixture was concentrated under reduced pressure to give crude product, which was purified by column chromatography on silica gel (H/ EtOAc = 6:1 to 3:1 as eluent) to afford 18 in 91% yield (471 mg, 0.835 mmol) as a white solid. 18: ¹H NMR (400 MHz, CDCl₃) δ 8.24 (2H, d, J = 8.7 Hz), 7.77 (2H, d, J = 8.7 Hz), 7.32 (1H, t, J = 7.1 Hz), 7.19-7.26 (4H, m), 7.07 (2H, d, J = 8.7 Hz), 6.83 (2H, d, J = 8.7 Hz), 6.52 (1H, brt), 5.80 (1H, s), 4.41 (1H, dd, J = 14.6, 6.0 Hz), 4.29 (1H, dd, J = 14.6, 5.5 Hz), 4.12 (1H, d, J = 11.9 Hz), 3.79 (3H, s), 3.58 (2H, d, J = 11.9 Hz), 3.53 (1H, dd, J = 12.4, 6.0 Hz), 3.44 (1H, dd, J = 12.4, 6.4 Hz), 2.33 (1H, brt), 1.34 (3H, s).

To a mixture of 18 (56.5 mg, 0.100 mmol) and triphenylphosphine (28.9 mg, 0.110 mmol) in THF (1 mL) was slowly added diethyl azodicarboxylate (40% toluene solution, 50.0 μL, 0.110 mmol) at room temperature, and the whole mixture was stirred for 10 h. The reaction mixture was diluted with water and extractive work-up was performed with EtOAc three times. The combined organics were washed with brine, dried over Na₂SO₄, and concentrated. Purification of the residue by column chromatography on silica gel (H/ EtOAc = 5:1 to 3:1 as eluent) afforded lactam 19 in 88% yield (47.9 mg, 0.0876 mmol) as a white solid. 19: ¹H NMR (400 MHz, CDCl₃) δ 8.27 (2H, d, J = 8.9 Hz), 7.79 (2H, d, J = 8.9 Hz), 7.27-7.34 (5H, m), 6.99 (2H, d, J = 8.9 Hz), 6.86 (2H, d, J = 8.9 Hz), 5.44 (1H, s), 4.37 (1H, d, J = 14.6 Hz), 4.23 (1H, d, J = 14.6 Hz), 3.82 (3H, s), 3.73 (1H, d, J = 10.5 Hz), 3.35 (1H, d, J = 10.5 Hz), 3.15 (1H, d, J = 11.0 Hz), 3.11 (1H, d, J = 11.0 Hz), 1.40 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 166.1, 159.8, 150.3, 143.0, 135.9, 129.7, 129.3, 129.0, 128.9, 127.5, 126.2, 124.3, 114.6, 113.5, 68.3, 61.7, 59.2, 55.5, 54.5, 47.2, 47.1, 21.7; IR (film): 2936, 2253, 1709, 1530, 1514, 1348, 1248, 1169, 737, 613 cm⁻¹; HRMS (ESI) Calcd for C₂₈H₂₆N₄O₆NaS⁺ ([M+Na⁺]⁺) 569.1471. Found 569.1465.; HPLC AD3, H/EtOH = 7:3, flow rate = 1.0 mL/min, λ = 254 nm, 43.2 min (minor), 51.4 min.
(major).

**Crystallographic Structure Determination:**

**Recrystallization of 11a (CCDC 954515), 11j (CCDC 954516), and 13 (CCDC 954517):** A single crystal of 11a, 11j, and 13 were obtained from CH2Cl2/acetone/CH3CN solvent system at room temperature. The single crystals thus obtained were mounted on CryoLoop. Data of X-ray diffraction were collected at 133 K on a Brucker SMART APEX CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). An absorption correction was made using SADABS. The structure was solved by direct methods and Fourier syntheses, and refined by full-matrix least squares on F2 by using SHELXTL. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms bonded to oxygen atoms were located from a difference synthesis and their coordinates and isotropic thermal parameters refined. The other hydrogen atoms were placed in calculated positions. The crystallographic data were summarized in Tables S2-S4 and ORTEP diagrams were shown in Figure S5. A checkcif file for compound 11a contains a ‘B’ level alert, which would be generated due to contamination of the anisotropic displacement parameters with disorder of the C(36–37) ethyl substituents.

**Table S2. Crystal data and structure refinement for 11a.**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C23 H23 N3 O6 S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>469.50</td>
</tr>
<tr>
<td>Temperature</td>
<td>153(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2(1)</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 11.0525(17) Å</td>
</tr>
<tr>
<td></td>
<td>α = 90°</td>
</tr>
<tr>
<td></td>
<td>b = 27.518(4) Å</td>
</tr>
<tr>
<td></td>
<td>β = 94.477(3°)</td>
</tr>
<tr>
<td></td>
<td>c = 11.4121(17) Å</td>
</tr>
<tr>
<td></td>
<td>γ = 90°</td>
</tr>
<tr>
<td>Volume</td>
<td>3460.3(9) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>6</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.352 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.185 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1476</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.60 x 0.50 x 0.30 mm³</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>1.94 to 28.37°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11≤h≤14, -35≤k≤36, -14≤l≤15</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>25674</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>16703 [R(int) = 0.0227]</td>
</tr>
<tr>
<td>Completeness to theta = 28.37°</td>
<td>99.5 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Empirical</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>16703 / 1 / 898</td>
</tr>
</tbody>
</table>

Table S3. Crystal data and structure refinement for 11j.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C28 H25 N3 O6 S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>531.57</td>
</tr>
<tr>
<td>Temperature</td>
<td>153(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P2(1)2(1)2(1)</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 7.704(2) Å</td>
</tr>
<tr>
<td></td>
<td>b = 12.588(3) Å</td>
</tr>
<tr>
<td></td>
<td>c = 26.614(7) Å</td>
</tr>
<tr>
<td></td>
<td>a= 90°.</td>
</tr>
<tr>
<td></td>
<td>β= 90°.</td>
</tr>
<tr>
<td></td>
<td>γ = 90°.</td>
</tr>
<tr>
<td>Volume</td>
<td>2580.9(12) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.368 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.174 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1112</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.50 x 0.50 x 0.30 mm³</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>1.53 to 28.42°.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-9&lt;=h&lt;=10, -11&lt;=k&lt;=16, -32&lt;=l&lt;=35</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>18546</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>6437 [R(int) = 0.0396]</td>
</tr>
<tr>
<td>Completeness to theta = 28.42°</td>
<td>99.4 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Empirical</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.9496 and 0.9180</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>6437 / 0 / 344</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.049</td>
</tr>
<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
<td>R1 = 0.0451, wR2 = 0.1223</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0463, wR2 = 0.1235</td>
</tr>
<tr>
<td>Absolute structure parameter</td>
<td>-0.03(6)</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.805 and -0.320 e.Å⁻³</td>
</tr>
</tbody>
</table>

Table S3. Crystal data and structure refinement for 13.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C22 H23 N3 O8 S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>489.49</td>
</tr>
<tr>
<td>Temperature</td>
<td>133(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
</tbody>
</table>
Crystal system: Orthorhombic

Space group: P2(1)2(1)2(1)

Unit cell dimensions:
- a = 10.901(2) Å, \( \alpha = 90^\circ \)
- b = 11.150(2) Å, \( \beta = 90^\circ \)
- c = 18.652(4) Å, \( \gamma = 90^\circ \)

Volume: 2267.1(8) Å³

Z: 4

Density (calculated): 1.434 Mg/m³

Absorption coefficient: 0.197 mm⁻¹

F(000): 1024

Crystal size: 0.60 x 0.50 x 0.20 mm³

Theta range for data collection: 2.13 to 28.25°.

Index ranges: -13 ≤ h ≤ 14, -14 ≤ k ≤ 14, -17 ≤ l ≤ 24

Reflections collected: 16924

Independent reflections: 5596 [R(int) = 0.0281]

Completeness to theta = 28.25°: 100.0 %

Absorption correction: Empirical

Max. and min. transmission: 0.9616 and 0.8908

Refinement method: Full-matrix least-squares on F²

Data / restraints / parameters: 5596 / 0 / 309

Goodness-of-fit on F²: 1.118

Final R indices [I>2sigma(I)]: R1 = 0.0344, wR2 = 0.0873

R indices (all data): R1 = 0.0357, wR2 = 0.0884

Absolute structure parameter: 0.11(5)

Largest diff. peak and hole: 0.357 and -0.210 e Å⁻³
Figure S5. Molecular structure of 11a, 11j, and 13. All calculated hydrogen atoms are omitted for clarity. Yellow and pink = sulfur, blue = nitrogen, red = oxygen, black = carbon.
Copies of $^1$H and $^{13}$C NMR Spectra
HPLC Chromatograms:
<table>
<thead>
<tr>
<th>Peak</th>
<th>Retention Time (min)</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.14</td>
<td>2343</td>
</tr>
<tr>
<td>2</td>
<td>11.34</td>
<td>2343</td>
</tr>
<tr>
<td>3</td>
<td>12.55</td>
<td>2343</td>
</tr>
<tr>
<td>4</td>
<td>13.76</td>
<td>2343</td>
</tr>
<tr>
<td>5</td>
<td>14.97</td>
<td>2343</td>
</tr>
<tr>
<td>6</td>
<td>16.18</td>
<td>2343</td>
</tr>
<tr>
<td>7</td>
<td>17.39</td>
<td>2343</td>
</tr>
<tr>
<td>8</td>
<td>18.60</td>
<td>2343</td>
</tr>
<tr>
<td>9</td>
<td>19.81</td>
<td>2343</td>
</tr>
</tbody>
</table>

**Figure 5:**
- Compound 5: Structure with two CN groups and two N=C=S groups.
- Compound 7: Structure with one CN group and one CO₂Et group.

**Figure 7:**
- Compound 10: Structure with two CO₂-Bu groups.
- Compound 13: Structure with one CO₂Et and one NO₂ group.