

Asymmetric Synthesis of 4*H*-1,3-Oxazines: Enantioselective Reductive Cyclization of *N*-Acylated β -Amino Enones with Trichlorosilane Catalyzed by Chiral Lewis Bases

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Supplementary Information

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General Methods

Melting points (mp) are uncorrected. ¹H and ¹³C NMR spectra were measured in CDCl₃ with JEOL JNM-ECX400 spectrometer. Tetramethylsilane (TMS) ($\delta = 0$ ppm) and CDCl₃ ($\delta = 77.0$ ppm) served as internal standards for ¹H and ¹³C NMR, respectively. Infrared spectra were recorded on JEOL JIR-6500W. Mass spectra were measured with JEOL JMS-DX303HF mass spectrometer. Optical rotations were recorded on JASCO P-1010 polarimeter. High-pressure liquid chromatography (HPLC) was performed on JASCO P-980 and UV-1575.

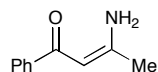
Thin-layer chromatography (TLC) analysis was carried out using Merck silica gel plates. Visualization was accomplished with UV light, phosphomolybdic acid and/or anisaldehyde. Column chromatography was performed using Kanto Chemical Silica Gel 60N (spherical, neutral, 63-210 μ m).

Dry dichloromethane (dehydrated) was purchased from Kanto Chemical and stored over 4Å MS prior to use. All other solvents were purified based on standard procedures.

Trichlorosilane was purchased from Tokyo Kasei Kogyo (TCI) and used without further purification. A dichloromethane solution (ca. 3 M) of this reagent was prepared and stocked in a screw-top test tube with a Teflon packing. (*S*)-BINAP dioxide (BINAPO) and other chiral phosphine oxides were prepared by oxidation of the corresponding phosphines with hydrogen peroxide in acetone.¹ (*R*)-BQNO was prepared according to the literature.² All other chemicals were purified based on standard procedures.

All reactions using trichlorosilane were performed under argon atmosphere using oven- and heating gun-dried glassware equipped with a rubber septum and a magnetic stirring bar. All glassware and syringes used for trichlorosilane were rinsed with ethanol and soaked in aqueous NaOH (ca. 1 M) for several hours and washed as usual.

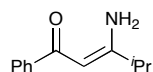
Synthesis of β -Amino Enones



(*Z*)-3-Amino-1-phenylbut-2-en-1-one

The title compound was prepared according to the literature procedure with a slight modification.³ A solution of 1-phenylbutane-1,3-dione (3.00 g, 18.5 mmol) and ammonium acetate (7.14 g, 92.4 mmol) in dry methanol (30 mL) was refluxed for 2.5 h. After cooling to room temperature, water (15 mL) was added and the mixture was stirred well. Precipitated colorless crystals were collected by filtration and dried at 50 °C under vacuum to give (*Z*)-3-amino-1-phenylbut-2-en-1-one (2.76 g, 93%). Spectroscopic data were consistent with the literature data.³

¹H-NMR (400 MHz, CDCl₃) δ 2.07 (s, 3H), 5.17 (brs, 1H), 5.75 (s, 1H), 7.39-7.48 (m, 3H), 7.86-7.90 (m, 2H), 10.21 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.9, 92.3, 127.1, 128.2, 130.8, 140.2, 162.8, 189.5.



(*Z*)-3-Amino-4-methyl-1-phenylpent-2-en-1-one

A solution of 4-methyl-1-phenylpentane-1,3-dione⁴ (2.27 g, 12.0 mmol) and ammonium acetate (4.62 g, 60 mmol) in dry methanol (23 mL) was refluxed for 3 h. After cooling to room temperature, water (15 mL) was added and the mixture was extracted with diethyl ether (3×). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, and

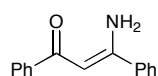
concentrated under vacuum. The residue was purified by silica gel column chromatography (hexane/AcOEt = 4/1) to give the title compound (0.948 g, 42%) and a 79:21 mixture of the title compound and (Z)-1-amino-4-methyl-1-phenylpent-1-en-3-one (0.809 g, 36%).

(Z)-3-Amino-4-methyl-1-phenylpent-2-en-1-one

¹H-NMR (400 MHz, CDCl₃) δ 1.25 (d, *J* = 6.9 Hz, 6H), 2.47 (sept, *J* = 6.9 Hz, 1H), 5.24 (brs, 1H), 5.78 (s, 1H) 7.40-7.46 (m, 3H), 7.87-7.89 (m, 2H), 10.40 (brs, 1H).

(Z)-1-Amino-4-methyl-1-phenylpent-1-en-3-one

¹H-NMR (400 MHz, CDCl₃) δ 1.16 (d, *J* = 6.9 Hz, 6H), 2.61 (sept, *J* = 6.9 Hz, 1H), 5.24 (brs, 1H), 5.47 (s, 1H) 7.40-7.46 (m, 3H), 7.52-7.62 (m, 2H), 9.98 (brs, 1H).

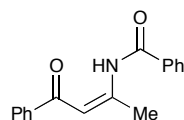


(Z)-3-Amino-1,3-diphenylprop-2-en-1-one

A solution of 1,3-diphenylpropane-1,3-dione (2.00 g, 9.0 mmol) and ammonium formate (2.80 g, 45 mmol) in dry ethanol (20 mL) was refluxed for 21.5 h. After cooling to room temperature, the mixture was concentrated under vacuum. Water was added to the residue and the mixture was extracted with AcOEt (3×). The combined organic layers were washed with saturated aqueous NaHCO₃ (2×) and brine (1×), dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuum to give crude (Z)-3-amino-1,3-diphenylprop-2-en-1-one (2.017 g) which was used without further purification. Spectroscopic data were consistent with the literature data.⁵

¹H-NMR (400 MHz, CDCl₃) δ 5.45 (brs, 1H), 6.16 (s, 1H), 7.42-7.55 (m, 6H), 7.60-7.70 (m, 2H), 7.90-8.03 (m, 2H), 10.43 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 91.4, 126.2, 126.9, 128.1, 128.7, 130.4, 130.8, 137.1, 140.1, 163.0, 189.7.

Synthesis of N-Acylated β-Amino Enones

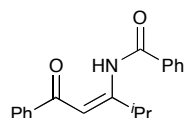


N-((Z)-4-Oxo-4-phenylbut-2-en-2-yl)benzamide (1a)

Typical Procedure A: Pyridine (0.44 mL, 2 equiv.) and benzoyl chloride (0.62 mL, 2 equiv.) were added successively to a solution of (Z)-3-amino-1-phenylbut-2-en-1-one (436.7 mg, 2.71 mmol) in dichloromethane (5.4 mL) at room temperature. After being stirred for 1 h, water was added and the mixture was extracted with AcOEt (3×). The combined organic layers were dried over anhydrous MgSO₄, filtered, and concentrated under vacuum to give crude

crystals which was purified by recrystallization from ethanol/water (4/1) to afford **1a** as yellowish needles (the 1st crop: 554.4 mg, the 2nd crop: 81.5 mg; total 88%).

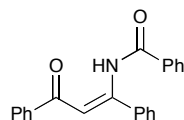
mp 108-110 °C; IR (KBr, cm⁻¹) 3059, 1691, 1622, 1616, 1589, 1583, 1269, 1063, 702; ¹H-NMR (400 MHz, CDCl₃) δ 2.69 (s, 3H), 6.19 (s, 1H), 7.48-7.61 (m, 6H), 7.93-7.98 (m, 2H), 8.09-8.13 (m, 2H), 13.82 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.8, 102.5, 127.7, 128.0, 128.6, 128.9, 132.4, 132.7, 133.7, 138.7, 158.2, 166.2, 191.9; Anal. Calcd. for C₁₇H₁₅NO₂: C, 76.96; H, 5.70; N, 5.28; Found: C, 76.72; H, 5.83; N, 5.33.



***N*-((*Z*)-4-Methyl-1-oxo-1-phenylpent-2-en-3-yl)benzamide (**1b**)**

According to Typical Procedure A, the reaction of (*Z*)-3-amino-4-methyl-1-phenylpent-2-en-1-one (473 mg, 2.5 mmol), pyridine (0.40 mL, 2 equiv.), and benzoyl chloride (0.56 mL, 2 equiv.) in dichloromethane (5 mL) at rt for 2.5 h gave the crude product. The crude product was diluted with dry dichloromethane (5 mL) and treated with diethylamine (0.45 mL) at rt for 9 h to remove excess benzoyl chloride. The mixture was concentrated under vacuum and the residue was purified by silica gel chromatography (hexane/AcOEt = 15/1) to afford **1b** as yellowish crystals (578 mg, 78%).

mp 80-81 °C; IR (KBr, cm⁻¹) 2964, 1693, 1618, 1591, 1257, 1236, 712, 687; ¹H-NMR (400 MHz, CDCl₃) δ 1.32 (d, *J* = 6.4 Hz, 6H), 4.24 (sept, *J* = 6.4 Hz, 1H), 6.36 (s, 1H) 7.48-7.67 (m, 6H), 7.93-8.02 (m, 2H), 8.12-8.20 (m, 2H), 13.87 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.6, 30.0, 97.7, 127.7, 128.0, 128.5, 128.8, 132.36, 132.41, 134.1, 139.1, 165.5, 168.4, 192.4; Anal. Calcd. for C₁₉H₁₉NO₂: C, 77.79; H, 6.53; N, 4.77; Found: C, 77.87; H, 6.45; N, 4.81.

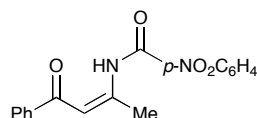


***N*-((*Z*)-3-Oxo-1,3-diphenylprop-1-en-1-yl)benzamide (**1c**)**

According to Typical Procedure A, the reaction of (*Z*)-3-amino-1,3-diphenylprop-2-en-1-one (970 mg, 4.0 mmol), pyridine (0.65 mL, 2 equiv.), and benzoyl chloride (0.92 mL, 2 equiv.) in dichloromethane (8 mL) at rt for 18.5 h gave the crude product. The crude product was diluted with dry dichloromethane (10 mL) and treated with diethylamine (0.83 mL) at rt for 1.5 h to remove excess benzoyl chloride. The mixture was concentrated under vacuum and

the residue was purified by silica gel chromatography (hexane/AcOEt = 15/1) to afford **1c** as yellowish oil which gradually crystallized on standing (1.133 g, 91%).

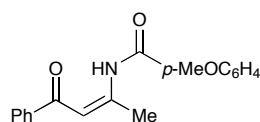
mp 118-119 °C; IR (KBr, cm^{-1}) 3057, 1687, 1624, 1583, 1564, 1464, 1290, 1225, 1045, 719; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 6.46 (s, 1H), 7.42-7.64 (m, 11H), 7.97-8.04 (m, 2H), 8.08-8.13 (m, 2H), 13.36 (brs, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 105.2, 127.3, 127.8, 128.0 (2C), 128.6, 128.8, 129.7, 132.66, 132.69, 133.2, 136.3, 138.4, 157.0, 165.1, 191.9; Anal. Calcd. for $\text{C}_{22}\text{H}_{17}\text{NO}_2$: C, 80.71; H, 5.23; N, 4.28; Found: C, 80.39; H, 5.35; N, 4.26.



4-Nitro-N-((Z)-4-oxo-4-phenylbut-2-en-2-yl)benzamide (**1d**)

According to Typical Procedure A, the reaction of (Z)-3-amino-1-phenylbut-2-en-1-one (322 mg, 2.0 mmol), pyridine (0.32 mL, 2 equiv.), and *p*-nitrobenzoyl chloride (742 mg, 2 equiv.) in dichloromethane (10 mL) at rt for 1 h gave the crude product which was purified by recrystallization from AcOEt to afford **1d** as orange needles (the 1st crop: 346 mg, 56%).

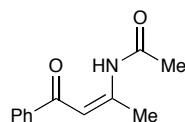
mp 196-197 °C; IR (KBr, cm^{-1}) 3113, 1697, 1626, 1593, 1475, 1346, 1277, 710; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.67 (s, 3H), 6.27 (s, 1H), 7.48-7.61 (m, 3H), 7.93-7.99 (m, 2H), 8.24-8.30 (m, 2H), 8.35-8.42 (m, 2H), 14.05 (brs, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 22.5, 103.4, 124.1, 127.8, 128.7, 129.2, 132.9, 138.3, 139.2, 150.1, 157.4, 164.0, 192.2; Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_4$: C, 65.80; H, 4.55; N, 9.03; Found: C, 65.57; H, 4.57; N, 9.01.



4-Methoxy-N-((Z)-4-oxo-4-phenylbut-2-en-2-yl)benzamide (**1e**)

According to Typical Procedure A, the reaction of (Z)-3-amino-1-phenylbut-2-en-1-one (1.612 g, 10.0 mmol), pyridine (1.62 mL, 2 equiv.), and *p*-methoxybenzoyl chloride (2.71 mL, 2 equiv.) in dichloromethane (20 mL) at rt for 4 h gave the crude product which was purified by recrystallization from ethanol to afford **1e** as orange needles (the 1st crop: 2.1267 g, 72%).

mp 127-128 °C; IR (KBr, cm^{-1}) 3001, 2970, 2943, 2841, 1687, 1606, 1498, 1477, 1273, 1246, 1178, 1061, 1032, 847, 758; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 2.67 (s, 3H), 3.89 (s, 3H), 6.15 (s, 1H), 6.99-7.05 (m, 2H), 7.45-7.60 (m, 3H), 7.92-7.98 (m, 2H), 8.06-8.12 (m, 2H), 13.82 (brs, 1H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 22.7, 55.4, 102.1, 114.1, 126.0, 127.6, 128.6, 130.1, 132.3, 138.8, 158.6, 163.2, 165.7, 191.8; Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_3$: C, 73.20; H, 5.80; N, 4.74; Found: C, 72.94; H, 5.82; N, 4.65.



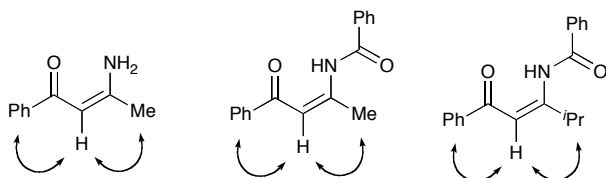
***N*-((*Z*)-4-Oxo-4-phenylbut-2-en-2-yl)acetamide (**1f**)**

According to Typical Procedure A, the reaction of (*Z*)-3-amino-1-phenylbut-2-en-1-one (806 mg, 5 mmol), pyridine (0.81 mL, 2 equiv.) and acetyl chloride (0.71 mL, 2 equiv.) in dichloromethane (10 mL) at rt for 20 h gave the crude product which was purified by recrystallization from ethanol/water (4/1) to afford **1f** as yellowish prisms (the 1st crop: 512 mg, the 2nd crop: 171 mg; total 67%).

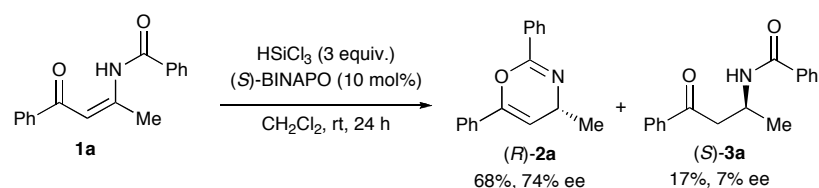
mp 98-99 °C; IR (KBr, cm⁻¹) 3072, 1711, 1616, 1585, 1560, 1502, 1473, 1439, 1308, 1261, 1200, 1086, 1065, 1003, 858, 777, 681; ¹H-NMR (400 MHz, CDCl₃) δ 2.22 (s, 3H), 2.52 (s, 3H), 6.04 (s, 1H), 7.41-7.58 (m, 3H), 7.88-7.93 (m, 2H), 12.81 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.5, 25.4, 101.5, 127.6, 128.5, 132.4, 138.6, 157.5, 169.8, 191.4; Anal. Calcd. for C₁₂H₁₃NO₂: C, 70.92; H, 6.45; N, 6.89; Found: C, 70.66; H, 6.50; N, 6.83.

NOESY Correlations of Selected Compounds

The geometry of selected β-amino enones was determined to be *Z* by observation of the NOESY correlations as shown below. That of other enones was determined by analogy.



The Reaction of *N*-Acylated β -Amino Enone with HSiCl_3



Typical Procedure B: To a solution of (S) -BINAPO (16.4 mg, 10 mol%) and **1a** (66.2 mg, 0.25 mmol) in dry dichloromethane (1 mL) was added dropwise trichlorosilane (ca. 3 M CH_2Cl_2 solution, 3 equiv.) at 0 °C. The reaction was stirred at rt for 24 h and quenched with water (3 mL) and dichloromethane (5 mL). The mixture was stirred for 1 h, filtered through a Celite pad with dichloromethane and extracted with dichloromethane (3 \times). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, evaporated, and purified by silica gel column chromatography (hexane/AcOEt = 20/1 ~ 2/1) to give 4*H*-1,3-oxazine **2a** [42.3 mg, 68%, 74% ee (*R*)] and keto amide **3a** [11.5 mg, 17%, 7% ee (*S*)].

The sense of the enantioselectivity of **2a** was found to be opposite to that of **3a** by transforming **2a** to **3a** with hydrobromic acid in ethanol. Their absolute configurations were tentatively assigned by analogy.

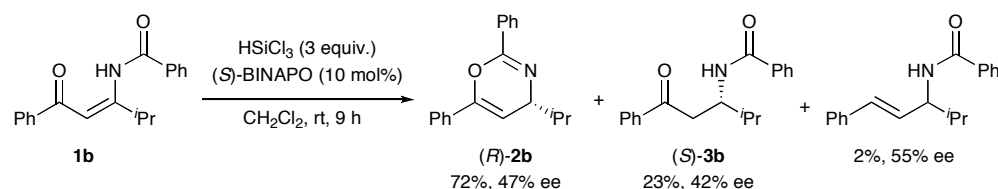
(*R*)-4-Methyl-2,6-diphenyl-4*H*-1,3-oxazine (**2a**)

Viscous oil; TLC: R_f 0.68 (hexane/AcOEt = 3/1); $[\alpha]_D^{28} +8.8$ (c 0.600, CHCl_3) for 72% ee (*R*); IR (neat, cm^{-1}) 3061, 2966, 1686, 1647, 1350, 1238, 1146, 1063, 760, 690; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.45 (d, $J = 6.9$ Hz, 3H), 4.38 (dq, $J = 6.9, 3.2$ Hz, 1H), 5.52 (d, $J = 3.2$ Hz, 1H), 7.33-7.51 (m, 6H), 7.64-7.70 (m, 2H), 8.05-8.12 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 25.0, 48.1, 102.3, 124.1, 127.3, 128.2, 128.5, 128.7, 130.8, 132.5, 133.0, 146.7, 152.0; HRMS (FAB) calcd. for $\text{C}_{17}\text{H}_{16}\text{NO}$ ($\text{M}+\text{H}^+$) 250.1232, found 250.1250; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 4.6$ min (*R*, major), 6.8 min (*S*, minor).

(*S*)-*N*-(4-Oxo-4-phenylbutan-2-yl)benzamide (**3a**)

Spectroscopic data were consistent with the literature data.⁶

Yellowish solid; TLC: R_f 0.09 (hexane/AcOEt = 3/1); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.42 (d, $J = 6.9$ Hz, 3H), 3.21 (dd, $J = 17.0, 5.9$ Hz, 1H), 3.48 (dd, $J = 17.0, 4.1$ Hz, 1H), 4.70 (dddq, $J = 7.8, 5.9, 4.1, 6.9$ Hz, 1H), 7.06 (brd, $J = 7.8$ Hz, 1H), 7.41-7.55 (m, 5H), 7.60 (apparent t, $J = 7.8$ Hz, 1H), 7.78 (apparent d, $J = 7.8$ Hz, 2H), 7.99 (apparent d, $J = 7.8$ Hz, 2H); HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 15.8$ min (*S*, major), 17.2 min (*R*, minor).



According to Typical Procedure B, the reaction of **1b** (73.6 mg, 0.25 mmol) and trichlorosilane (ca. 3 M CH_2Cl_2 solution, 2 equiv.) with (S) -BINAPO (16.6 mg, 10 mol%) in dry dichloromethane (1 mL) at rt for 9 h gave $4H$ -1,3-oxazine **2b** [49.8 mg, 72%, 47% ee (R)], keto amide **3b** [17.1 mg, 23%, 42% ee (S)] and an allylic amide (1.3 mg, 2%, 55% ee).

The sense of the enantioselectivity of **2b** was found to be same as that of **3b** by transforming **2b** to **3b** with hydrobromic acid in ethanol. Their absolute configurations were tentatively assigned by analogy.

(R)-4-Isopropyl-2,6-diphenyl-4H-1,3-oxazine (2b)

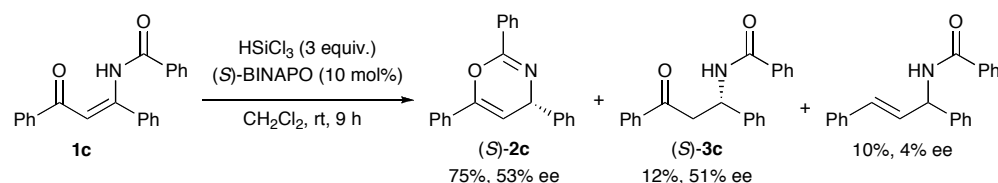
Viscous oil, TLC: R_f 0.71 (hexane/AcOEt = 3/1); $[\alpha]_D^{21} -1.2$ (c 1.115, CHCl_3) for 47% ee (R); IR (neat, cm^{-1}) 2962, 1691, 1495, 1448, 1261, 762, 692; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.03 (d, $J = 6.8$ Hz, 3H), 1.04 (d, $J = 6.8$ Hz, 3H), 2.00 (d sept, $J = 4.1, 6.8$ Hz, 1H), 4.20 (dd, $J = 4.1, 3.7$ Hz, 1H), 5.47 (d, $J = 3.7$ Hz, 1H), 7.36-7.50 (m, 6H), 7.65-7.72 (m, 2H), 8.06-8.11 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 17.97, 18.05, 35.2, 57.9, 99.0, 124.1, 127.3, 128.2, 128.5, 128.7, 130.8, 132.6, 133.1, 147.8, 152.1; HRMS (FAB) calcd. for $\text{C}_{19}\text{H}_{20}\text{NO}$ ($\text{M}+\text{H}^+$) 278.1545, found 278.1581; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 49/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 5.0$ min (R , major), 7.0 min (S , minor).

(S)-N-(4-Methyl-1-oxo-1-phenylpentan-3-yl)benzamide (3b)

Yellowish solid; mp 129-131 $^\circ\text{C}$; R_f 0.25 (hexane/AcOEt = 3/1); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 0.97 (d, $J = 6.9$ Hz, 3H), 1.04 (d, $J = 6.9$ Hz, 3H), 2.20 (d sept, $J = 8.2, 6.9$ Hz, 1H), 3.22 (dd, $J = 17.0, 5.0$ Hz, 1H), 3.49 (dd, $J = 17.0, 5.0$ Hz, 1H), 4.33 (dddd, $J = 9.2, 8.2, 5.0, 5.0$ Hz, 1H), 7.18 (brd, $J = 9.2$ Hz, 1H), 7.40-7.53 (m, 6H), 7.59 (apparent t, $J = 7.3$ Hz, 1H), 7.76-7.80 (m, 2H), 7.95-7.99 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 19.52, 19.86, 31.0, 39.3, 52.7, 126.9, 128.06, 128.51, 128.74, 131.3, 133.5, 134.7, 136.8, 166.9, 200.0; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 26.0$ min (R , minor), 34.0 min (S , major).

(E)-N-(4-Methyl-1-phenylpent-1-en-3-yl)benzamide

Colorless solid; R_f 0.38 (hexane/AcOEt = 3/1); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.03 (d, $J = 6.9$ Hz, 6H), 2.02 (d sept, $J = 6.9, 6.9$ Hz, 1H), 4.72 (ddd, $J = 8.7, 6.9, 6.9$ Hz, 1H), 6.14 (brd, $J = 8.7$ Hz, 1H), 6.21 (dd, $J = 15.8, 6.9$ Hz, 1H), 6.60 (d, $J = 15.8$ Hz, 1H), 7.20-7.58 (m, 8H), 7.79-7.83 (m, 2H); HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 12/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 16.8$ min (minor), 21.6 min (major).



According to Typical Procedure B, the reaction of **1c** (81.6 mg, 0.25 mmol) and trichlorosilane (ca. 3 M CH_2Cl_2 solution, 2 equiv.) with (S) -BINAPO (16.4 mg, 10 mol%) in dry dichloromethane (1 mL) at rt for 9 h gave $4H$ -1,3-oxazine **2c** [58.5 mg, 75%, 53% ee (S)], keto amide **3c** [9.7 mg, 12%, 51% ee (S)] and an allylic amide (7.7 mg, 10%, 4% ee).

The sense of the enantioselectivity of **2c** was found to be same as that of **3c** by transforming **2c** to **3c** with hydrobromic acid in ethanol. The absolute configuration of **3c** was unequivocally determined on comparison with the literature data.⁷ Thus, that of **2c** was also determined.

(S)-2,4,6-Triphenyl-4H-1,3-oxazine (2c)

Colorless solid; mp 96-97 °C; TLC: R_f 0.63 (hexane/AcOEt = 3/1); $[\alpha]_D^{19}$ -33.5 (c 1.075, CHCl_3) for 53% ee (S); IR (KBr, cm^{-1}) 3088, 3061, 3028, 2862, 1687, 1647, 1495, 1450, 1319, 1240, 1119, 1070, 1024, 758, 696; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 5.44 (d, $J = 3.7$ Hz, 1H), 5.65 (d, $J = 3.7$ Hz, 1H), 7.23-7.32 (m, 1H), 7.34-7.55 (m, 10H), 7.68-7.73 (m, 2H), 8.10-8.17 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 56.6, 100.8, 124.2, 127.28, 127.36, 127.48, 128.23, 128.51, 128.70, 128.95, 131.1, 132.4, 132.8, 144.4, 146.3, 152.2; HRMS (FAB) calcd. for $\text{C}_{22}\text{H}_{18}\text{NO}$ ($\text{M}+\text{H}^+$) 312.1388, found 312.1383; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 29/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 10.5$ min (S , major), 14.6 min (R , minor).

(S)-N-(3-Oxo-1,3-diphenylpropyl)benzamide (3c)

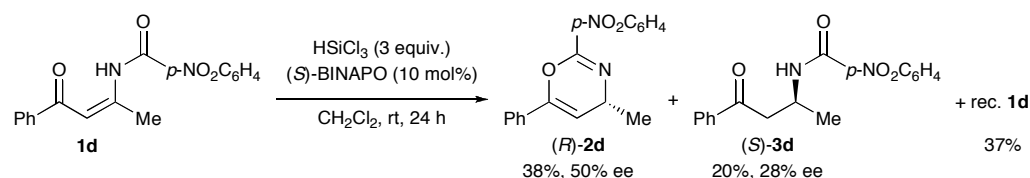
Spectroscopic data were consistent with the literature data.⁷

Colorless solid; TLC: R_f 0.15 (hexane/AcOEt = 3/1); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 3.56 (dd, $J = 17.0, 6.0$ Hz, 1H), 3.86 (dd, $J = 17.0, 4.6$ Hz, 1H), 5.77 (ddd, $J = 7.8, 6.0, 4.6$ Hz, 1H), 7.20-7.60 (m, 11H), 7.60 (brd, $J = 7.8$ Hz, 1H), 7.83-7.87 (m, 2H), 7.91-7.95 (m, 2H); HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 4/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 21.5$ min (R , minor), 28.7 min (S , major).

N-(1,3-Diphenylallyl)benzamide

Spectroscopic data were consistent with the literature data.⁸

Colorless solid; TLC: R_f 0.39 (hexane/AcOEt = 3/1); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 6.04 (apparent t, $J = 6.7$ Hz, 1H), 6.46 (dd, $J = 16.0, 6.5$ Hz, 1H), 6.53 (brd, $J = 7.8$ Hz, 1H), 6.62 (d, $J = 16.0$ Hz, 1H), 7.21-7.54 (m, 13H), 7.81-7.86 (m, 2H); HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 6/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 18.2$ min (minor), 20.2 min (major).



According to Typical Procedure B, the reaction of **1d** (78.1 mg, 0.25 mmol) and trichlorosilane (ca. 3 M CH_2Cl_2 solution, 2 equiv.) with (S) -BINAPO (16.6 mg, 10 mol%) in dry dichloromethane (2 mL; **1d** was partially dissolved at the beginning) at rt for 24 h gave $4H$ -1,3-oxazine **2d** [27.8 mg, 38%, 50% ee (R)] and keto amide **3d** [15.7 mg, 20%, 28% ee (S)]. **1d** was recovered in 37% (29.0 mg).

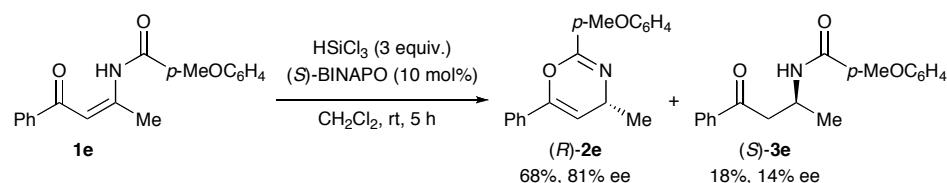
The sense of the enantioselectivity of **2d** was found to be opposite to that of **3d** by transforming **2d** to **3d** with hydrobromic acid in ethanol. Their absolute configurations were tentatively assigned by analogy.

(R)-4-Methyl-2-(4-nitrophenyl)-6-phenyl-4H-1,3-oxazine (2d)

Yellowish solid; mp 143-144 °C; TLC: R_f 0.61 (hexane/AcOEt = 3/1); $[\alpha]_D^{29} +5.8$ (c 1.170, CHCl_3) for 61% ee (R); IR (KBr, cm^{-1}) 2974, 2929, 2848, 1689, 1649, 1601, 1522, 1340, 1244, 1146, 1093, 862, 760, 702; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.47 (d, $J = 6.9$ Hz, 3H), 4.44 (dq, $J = 6.9, 2.8$ Hz, 1H), 5.52 (d, $J = 2.8$ Hz, 1H), 7.36-7.50 (m, 3H), 7.62-7.68 (m, 2H), 8.20-8.32 (m, 4H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 25.0, 48.5, 102.2, 123.4, 124.1, 128.3, 128.6, 129.1, 132.5, 138.4, 146.7, 149.3, 150.3; HRMS (FAB) calcd. for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_3$ ($\text{M}+\text{H}^+$) 295.1083, found 295.1073; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 29/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 8.7$ min (R , major), 11.1 min (S , minor).

(S)-4-Nitro-N-(4-oxo-4-phenylbutan-2-yl)benzamide (3d)

Viscous oil; TLC: R_f 0.11 (hexane/AcOEt = 3/1); IR (neat, cm^{-1}) 3307, 3070, 2976, 1684, 1645, 1601, 1525, 1346, 1213, 1003, 870, 841, 754, 721, 690; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.44 (d, $J = 6.9$ Hz, 3H), 3.25 (dd, $J = 17.0, 5.5$ Hz, 1H), 3.48 (dd, $J = 17.0, 4.1$ Hz, 1H), 4.71 (dddq, $J = 7.8, 5.5, 4.1, 6.9$ Hz, 1H), 7.37 (brd, $J = 7.8$ Hz, 1H), 7.50 (apparent t, $J = 7.8$ Hz, 2H), 7.62 (apparent t, $J = 7.3$ Hz, 1H), 7.95 (apparent d, $J = 8.7$ Hz, 2H), 7.98 (apparent d, $J = 8.0$ Hz, 2H), 8.28 (apparent d, $J = 8.7$ Hz, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 20.0, 42.5, 43.2, 123.7, 128.09, 128.13, 128.81, 133.8, 136.7, 140.1, 149.5, 164.5, 199.8; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 28.1$ min (R , minor), 33.3 min (S , major).



According to Typical Procedure B, the reaction of **1e** (73.8 mg, 0.25 mmol) and trichlorosilane (ca. 3 M CH_2Cl_2 solution, 2 equiv.) with (S) -BINAPO (16.4 mg, 10 mol%) in dry dichloromethane (1 mL) at rt for 5 h gave $4H$ -1,3-oxazine **2e** [47.2 mg, 68%, 81% ee (R)] and keto amide **3e** [13.7 mg, 18%, 14% ee (S)].

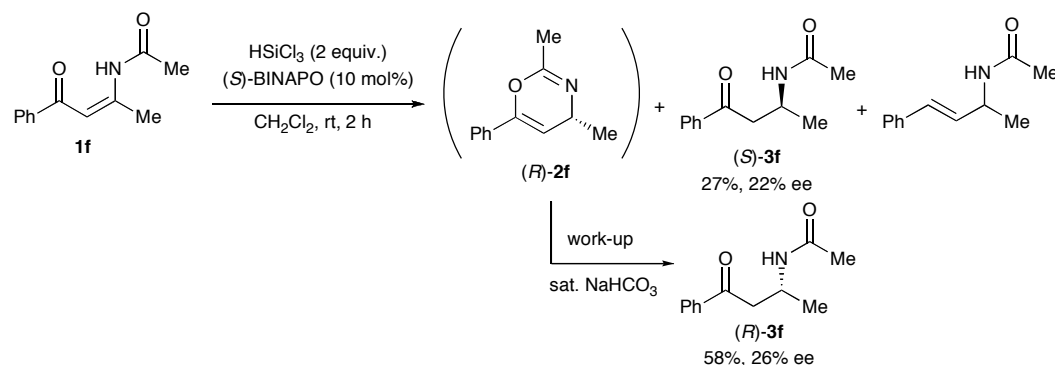
The sense of the enantioselectivity of **2e** was found to be opposite to that of **3e** by transforming **2e** to **3e** with hydrobromic acid in ethanol. The absolute configuration of **2e** was unequivocally determined as described later.

(R)-2-(4-Methoxyphenyl)-4-methyl-6-phenyl-4H-1,3-oxazine (2e)

Viscous oil; TLC: R_f 0.40 (hexane/AcOEt = 3/1); $[\alpha]_D^{30} +5.3$ (c 1.295, CHCl_3) for 78% ee (R); IR (neat, cm^{-1}) 2966, 2926, 2837, 1689, 1608, 1512, 1250, 1169, 1146, 1068, 1030, 839, 760, 690; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.43 (d, $J = 6.9$ Hz, 3H), 3.86 (s, 3H), 4.35 (dq, $J = 6.9$, 3.2 Hz, 1H), 5.51 (d, $J = 3.2$ Hz, 1H), 6.94-6.96 (m, 2H), 7.36-7.42 (m, 3H), 7.66-7.68 (m, 2H), 8.01-8.03 (m, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 25.1, 48.0, 55.3, 102.4, 113.5, 124.1, 125.1, 128.45, 128.67, 128.93, 133.1, 146.7, 151.8, 161.7; HRMS (FAB) calcd. for $\text{C}_{18}\text{H}_{18}\text{NO}_2$ ($\text{M}+\text{H}^+$) 280.1338, found 280.1331; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 8.7$ min (R , major), 19.8 min (S , minor).

(S)-4-Methoxy-N-(4-oxo-4-phenylbutan-2-yl)benzamide (3e)

Yellowish solid; mp 119-121 $^\circ\text{C}$; TLC: R_f 0.06 (hexane/AcOEt = 3/1); IR (KBr, cm^{-1}) 3321, 3062, 2958, 1687, 1666, 1637, 1549, 1529, 756, 692; $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.40 (d, $J = 6.9$ Hz, 3H), 3.20 (dd, $J = 16.8$, 6.1 Hz, 1H), 3.47 (dd, $J = 16.8$, 4.0 Hz, 1H), 3.85 (s, 3H), 4.68 (dddq, $J = 7.3$, 6.1, 4.0, 6.9 Hz, 1H), 6.91 (apparent d, $J = 8.9$ Hz, 2H), 6.96 (brd, $J = 7.3$ Hz, 1H), 7.48 (apparent t, $J = 7.3$ Hz, 2H), 7.58 (apparent t, $J = 7.3$ Hz, 1H), 7.75 (apparent d, $J = 8.9$ Hz, 2H), 7.99 (apparent d, $J = 7.4$ Hz, 2H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 20.1, 42.8, 43.3, 55.4, 113.7, 126.8, 128.1, 128.7 (2C), 133.5, 136.9, 162.1, 166.2, 199.7; HRMS (FAB) calcd. for $\text{C}_{18}\text{H}_{20}\text{NO}_3$ ($\text{M}+\text{H}^+$) 298.1443, found 298.1470; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 77.8$ min (S , major), 82.8 min (R , minor).



To a solution of (S) -BINAPO (16.3 mg, 10 mol%) and **1f** (50.9 mg, 0.25 mmol) in dry dichloromethane (2 mL) was added dropwise trichlorosilane (ca. 3 M CH_2Cl_2 solution, 2 equiv.) at 0 °C. The reaction was stirred at rt for 2 h and quenched with water (3 mL) and dichloromethane (5 mL). The mixture was stirred for 1 h, filtered through a Celite pad with dichloromethane and extracted with dichloromethane (3 \times). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, evaporated, and purified by silica gel column chromatography (hexane/AcOEt = 1/1, AcOEt only, then $\text{CH}_2\text{Cl}_2/\text{EtOH}$ = 10/1) to give keto amide **3f** [13.9 mg, 27%, 22% ee (S)]. On the other hand, the acidic aqueous layer (pH ca. 3) was basified with saturated aq. NaHCO_3 (pH ca. 9) and extracted with dichloromethane (3 \times). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and evaporated to give pure keto amide **3f** [29.8 mg, 58%, 26% ee (R)].

The sense of the enantioselectivity of **3f** extracted from the acidic aqueous layer was opposite to that of **3f** extracted from the basic aqueous layer. The absolute configuration was assigned by analogy.

(R)-N-(4-Oxo-4-phenylbutan-2-yl)acetamide (3f)

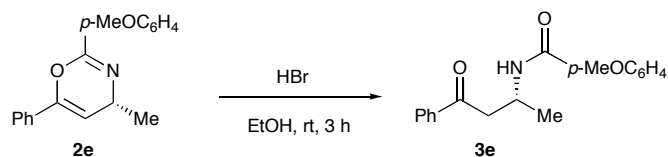
Yellowish solid; mp 74-76 °C; TLC: R_f 0.20 (hexane/AcOEt = 1/2); $[\alpha]_D^{20} +15.5$ (c 0.995, CHCl_3) for 26% ee (R); $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.29 (d, J = 6.4 Hz, 3H), 1.96 (s, 3H), 3.09 (dd, J = 16.5, 6.4 Hz, 1H), 3.34 (brd, J = 16.5, 4.1 Hz, 1H), 4.47 (dddq, J = 7.1, 6.9, 6.4, 4.1 Hz, 1H), 6.32 (brd, J = 7.1 Hz, 1H), 7.47 (apparent t, J = 7.8 Hz, 2H), 7.58 (apparent t, J = 7.3 Hz, 1H), 7.96 (apparent d, J = 8.3 Hz, 2H), 7.25-7.97 (m, 5H); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 19.9, 23.4, 42.4, 43.4, 128.04, 128.65, 133.4, 136.7, 169.4, 199.2; HPLC (CHIRALPAK AS-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 29/1, flow rate 1.0 mL/min, UV detection at 254 nm): t_R = 13.6 min (S , minor), 19.2 min (R , major).

The formation of oxazine **2f** was confirmed by quenching the reaction mixture (another batch of the reaction) with deuterium oxide. After removal of the precipitates by filtration, the acidic deuterium oxide layer was washed with dichloromethane (3 \times) and checked directly by ^1H and ^{13}C NMR analyses (for the spectra, see page S-21).

(*R*)-2-Methyl-4-methyl-6-phenyl-4*H*-1,3-oxazine (**2f**)

¹H-NMR (400 MHz, D₂O) δ 1.44 (d, *J* = 6.8 Hz, 3H), 2.40 (s, 3H), 4.34 (dq, *J* = 9.6, 6.8 Hz, 1H), 5.99 (d, *J* = 9.6 Hz, 1H), 7.21-7.28 (m, 3H), 7.31-7.37 (m, 2H); ¹³C-NMR (100 MHz, D₂O, MeOH was used as an internal standard) δ 19.0, 20.7, 44.5, 114.8, 125.6, 129.6, 130.6, 133.2, 149.9, 173.0.

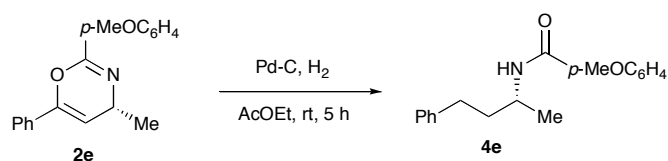
Transformations of 4*H*-1,3-Oxazine **2e**



Hydrolysis: To a solution of **2e** [28.1 mg, 0.10 mmol, 81% ee (*R*)] in dry ethanol (1.0 mL) was added dropwise 47 % HBr (0.1 mL) at rt. The reaction was stirred at rt for 3 h and quenched with saturated aqueous NaHCO₃. The mixture was extracted with dichloromethane (3×). The combined organic layers were dried over anhydrous Na₂SO₄, filtered, evaporated, and purified by silica gel column chromatography (hexane/AcOEt = 2/1) to give keto amide **3e** [23.3 mg, 78%, 81% ee (*R*)].

(*R*)-4-Methoxy-*N*-(4-oxo-4-phenylbutan-2-yl)benzamide (**3e**)

For physical data, see page S-11. [α]³⁰_D -12.8 (c 0.795, CHCl₃) for 81% ee (*R*); HPLC (CHIRALPAK AD-H, 0.46 cm ϕ × 25cmL, hexane/2-propanol = 19/1, flow rate 1.0 mL/min, UV detection at 254 nm): *t*_R = 71.5 min (*S*, minor), 75.0 min (*R*, major).



Reduction: A suspension of **2e** [26.8 mg, 0.096 mmol, 81% ee (*R*)] and 10% Pd/C (5.4 mg) in AcOEt (1.9 mL) was stirred at rt for 5 h under hydrogen atmosphere. The mixture was filtered through a Celite pad with AcOEt, evaporated, and purified by silica gel column chromatography (hexane/AcOEt = 3/1 ~ 2/1) to give amide **4e** [24.5 mg, 90%, 81% ee (*R*)].

(*R*)-4-Methoxy-*N*-(4-phenylbutan-2-yl)benzamide (**4e**)

Colorless solid; mp 119-121 °C; TLC: *R*_f 0.32 (hexane/AcOEt = 2/1); [α]²¹_D -8.3 (c 0.915, CHCl₃) for 81% ee (*R*); IR (KBr, cm⁻¹) 3313, 2964, 2926, 2860, 1630, 1608, 1537, 1508, 1300, 1254, 1182, 1028, 843, 702, 700; ¹H-NMR (400 MHz, CDCl₃) δ 1.27 (d, *J* = 6.4 Hz, 3H), 1.89 (dt, *J* = 6.4, 7.8 Hz, 2H), 2.72 (t, *J* = 7.8 Hz, 2H), 3.84 (s, 3H), 4.27 (dtq, *J* = 7.8, 6.4, 6.4 Hz, 1H), 5.85 (brd, *J* = 7.8 Hz, 1H), 6.89 (apparent d, *J* = 8.7 Hz, 2H), 7.14-7.30 (m,

5H), 7.65 (apparent d, $J = 8.7$ Hz, 2H); ^{13}C -NMR (100 MHz, CDCl_3) δ 21.1, 32.5, 38.6, 45.6, 55.4, 113.6, 125.9, 127.1, 128.32, 128.46, 128.54, 141.8, 162.0, 166.3; HRMS (FAB) calcd. for $\text{C}_{18}\text{H}_{22}\text{NO}_2$ ($\text{M}+\text{H}^+$) 284.1651, found 284.1628; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 9/1, flow rate 1.0 mL/min, UV detection at 254 nm): $t_R = 19.5$ min (R , major), 23.1 min (S , minor).



Oxidation: To a solution of **2e** [31.7 mg, 0.11 mmol, 81% ee (R)] in dry dichloromethane (1.1 mL) was added dropwise bromine (0.76 M solution in dichloromethane, 0.3 mL) at rt. The reaction was stirred for 30 min and quenched with water. After being stirred for 5 min, the mixture was transferred to a separation funnel, basified with saturated aqueous NaHCO_3 , and extracted with dichloromethane (3 \times). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and evaporated. The residue was then diluted with dichloromethane (2 mL) and ethanol (0.4 mL). Silica gel (ca. 300 mg) was added to the solution. The mixture was stirred for 3 h, evaporated, and charged directly on a silica gel column for chromatography (hexane/AcOEt = 3/1 \sim 1/1 then $\text{CH}_2\text{Cl}_2/\text{EtOH} = 20/1$; **5e** was partially crystallized in the silica gel column. Therefore, elution with $\text{CH}_2\text{Cl}_2/\text{EtOH}$ was needed) to give *trans*-**5e** (4.7 mg, 14%, 81% ee) and *cis*-**5e** (24.1 mg, 72%, 81% ee).

The relative configurations were assigned based on the coupling constants between H4 and H5 protons (*trans*-**5e**: 6.4 Hz, *cis*-**5e**: 10.5 Hz).

(4*R*,5*S*)-5-Benzoyl-2-(4-methoxyphenyl)-4-methyl-4,5-dihydrooxazole (*trans*-5e**)**

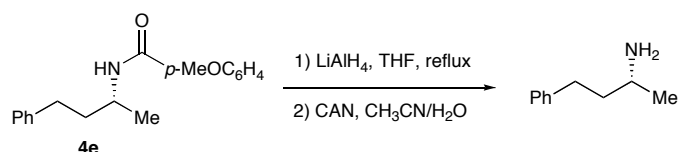
Viscous oil; TLC: R_f 0.31 (hexane/AcOEt = 2/1); IR (neat, cm^{-1}) 2970, 2933, 2839, 1695, 1653, 1608, 1514, 1257, 1173, 1028, 841, 692; ^1H -NMR (400 MHz, CDCl_3) δ 1.55 (d, $J = 6.9$ Hz, 3H), 3.86 (s, 3H), 4.50 (dq, $J = 6.9, 6.4$ Hz, 1H), 5.38 (d, $J = 6.4$ Hz, 1H), 6.93 (apparent d, $J = 8.7$ Hz, 2H), 7.53 (apparent t, $J = 7.8$ Hz, 2H), 7.65 (apparent t, $J = 7.3$ Hz, 1H), 7.93-8.02 (m, 4H); HRMS (FAB) calcd. for $\text{C}_{18}\text{H}_{18}\text{NO}_3$ ($\text{M}+\text{H}^+$) 296.1287, found 296.1292; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 4/1, flow rate 0.4 mL/min, UV detection at 254 nm): $t_R = 46.0$ min (4*S*,5*R*, minor), 49.1 min (4*R*,5*S*, major).

(4*R*,5*R*)-5-Benzoyl-2-(4-methoxyphenyl)-4-methyl-4,5-dihydrooxazole (*cis*-5e**)**

Colorless solid; mp 127-129 $^\circ\text{C}$; TLC: R_f 0.19 (hexane/AcOEt = 2/1); $[\alpha]_D^{22} +210.2$ (c 0.245, CHCl_3) for 81% ee (4*R*,5*R*); IR (KBr, cm^{-1}) 2968, 1697, 1649, 1606, 1514, 1377, 1259, 1221, 1167, 1099, 1026, 960, 847, 694; ^1H -NMR (400 MHz, CDCl_3) δ 1.08 (d, $J = 6.9$ Hz, 3H), 3.87 (s, 3H), 4.85 (dq, $J = 10.4, 6.9$ Hz, 1H), 5.96 (d, $J = 10.4$ Hz, 1H), 6.93 (apparent d, $J =$

8.6 Hz, 2H), 7.53 (apparent t, $J = 8.0$ Hz, 2H), 7.64 (apparent t, $J = 7.4$ Hz, 1H), 7.93-8.02 (m, 4H); ^{13}C -NMR (100 MHz, CDCl_3) δ 17.5, 55.4, 65.1, 83.2, 113.7, 119.4, 128.0, 129.0, 130.3, 133.9, 135.4, 162.4, 163.1, 194.5; HRMS (FAB) calcd. for $\text{C}_{18}\text{H}_{18}\text{NO}_3$ ($\text{M}+\text{H}^+$) 296.1287, found 296.1298; HPLC (CHIRALPAK AD-H, 0.46 cm ϕ \times 25cmL, hexane/2-propanol = 1/1, flow rate 0.6 mL/min, UV detection at 254 nm): $t_R = 12.9$ min (4*S*,5*S*; minor), 48.2 min (4*R*,5*R*; major).

Determination of the Absolute Configuration of 2e



To a solution of **4e** (17.9 mg, 0.063 mmol, 81% ee) in dry THF (2.0 mL) was added LiAlH₄ (24.0 mg, 0.63 mmol) at rt. The reaction was refluxed for 16 h and, after cooling to rt, carefully quenched with water and 4M aq. NaOH. The mixture was extracted with dichloromethane (3 \times). The filtrate was dried over anhydrous Na₂CO₃, filtered, and evaporated to give crude (*R*)-*N*-(4-methoxybenzyl)-4-phenylbutan-2-amine. This crude amine was diluted with acetonitrile/water (2/1, 2 mL) and treated with CAN (173.1 mg, 0.32 mmol). The reaction was stirred at rt for 6 h and quenched with 1.0 M hydrochloric acid (5 mL). The mixture was filtered through a Celite pad with dichloromethane. The filtrate was washed with dichloromethane (4 \times) and basified with 4 M aqueous NaOH. The aqueous layer was extracted with dichloromethane (3 \times). The combined organic layers were dried over anhydrous Na₂CO₃, filtered, and evaporated to afford (*R*)-4-phenylbutan-2-amine (4.3 mg, 46% over 2 steps).

(*R*)-*N*-(4-Methoxybenzyl)-4-phenylbutan-2-amine

^1H -NMR (400 MHz, CDCl_3) δ 1.14 (d, $J = 6.1$ Hz, 3H), 1.48 (brd, 1H), 1.62-1.70 (m, 1H), 1.76-1.85 (m, 1H), 2.59-2.69 (m, 2H), 2.69-2.76 (m, 1H), 3.67 (d, $J = 12.8$ Hz, 1H), 3.76 (d, $J = 12.8$ Hz, 1H), 3.80 (s, 3H), 6.85 (apparent d, $J = 8.6$ Hz, 2H), 7.16-7.29 (m, 7H); ^{13}C -NMR (100 MHz, CDCl_3) δ 20.3, 32.3, 38.7, 50.7, 51.9, 55.2, 113.7, 125.7, 128.31, 128.32, 129.3, 132.9, 142.4, 158.5.

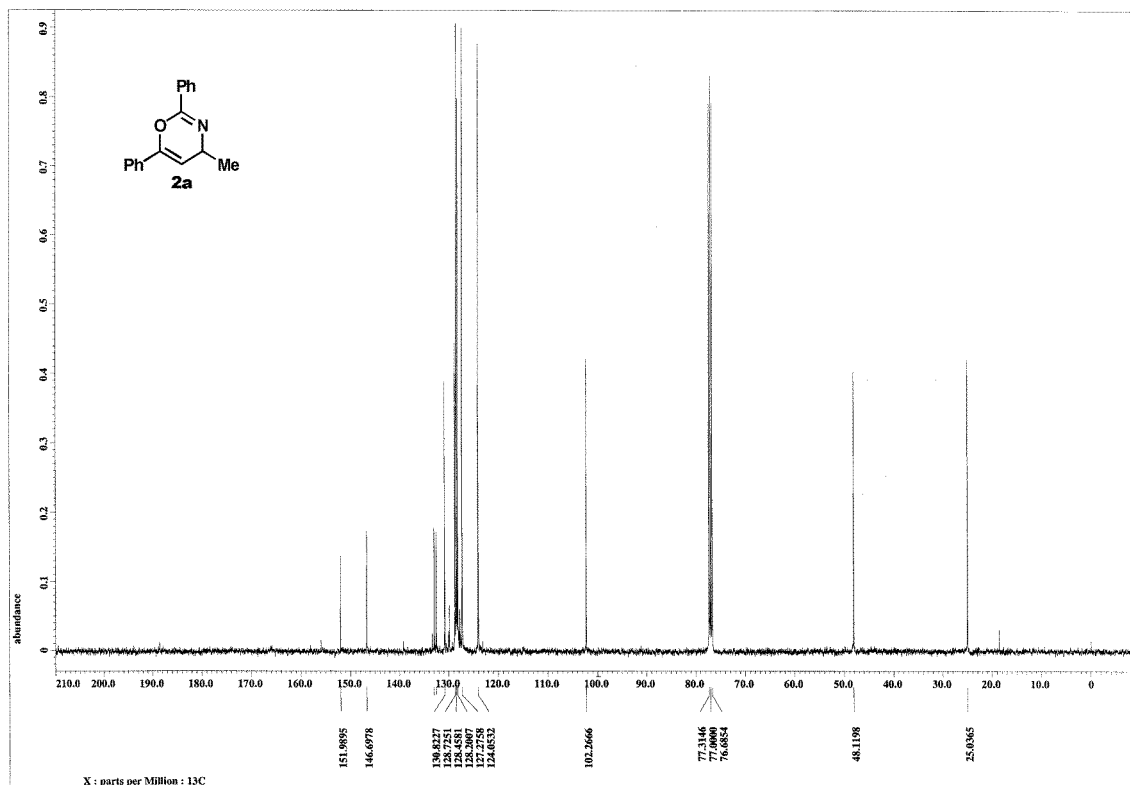
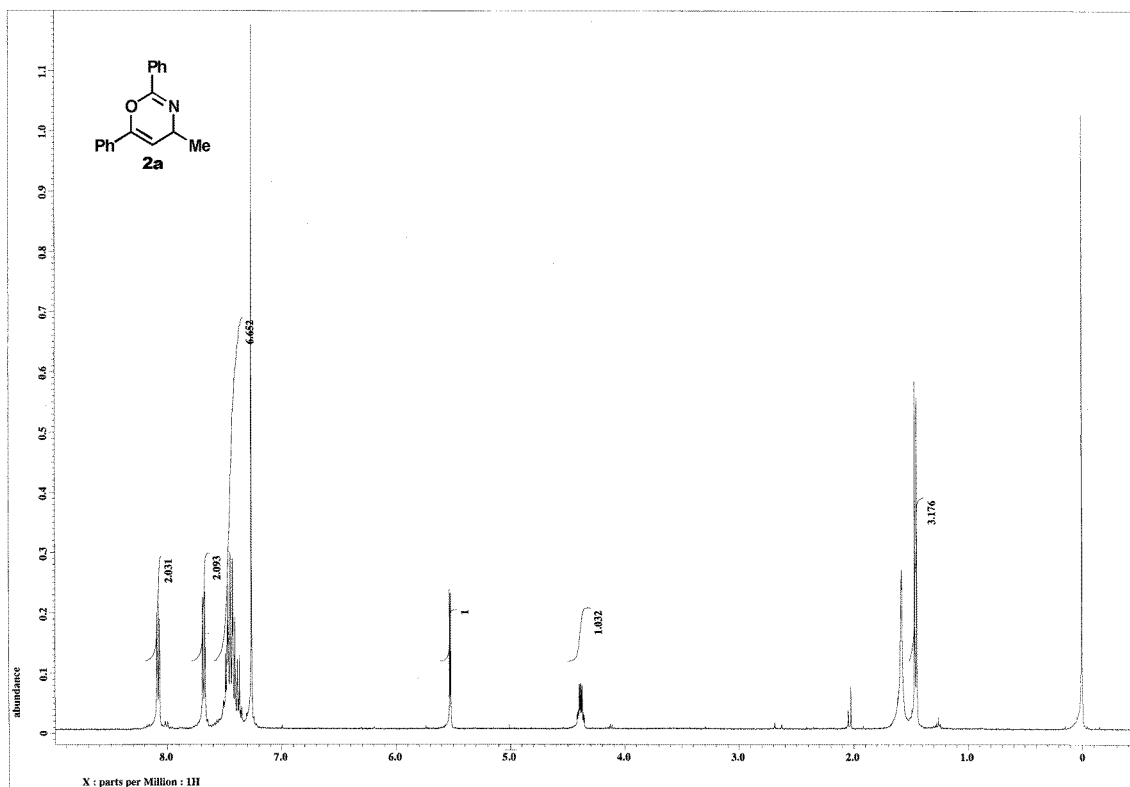
(*R*)-4-Phenylbutan-2-amine

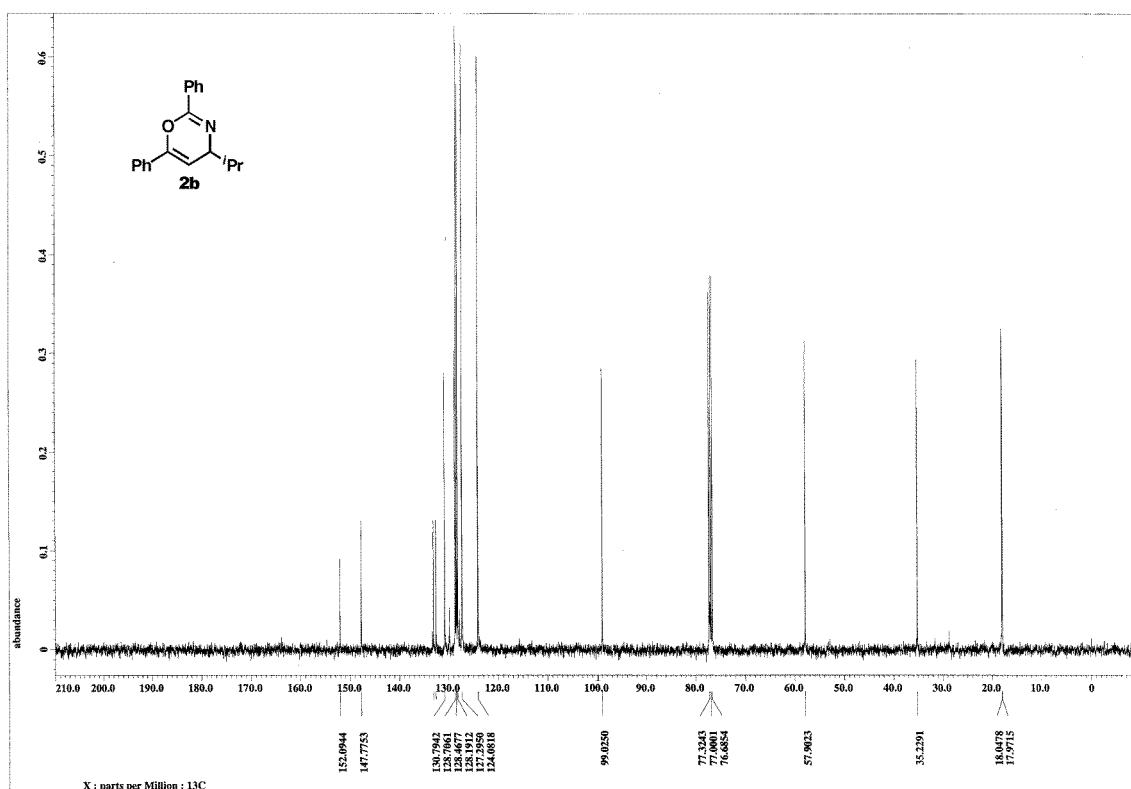
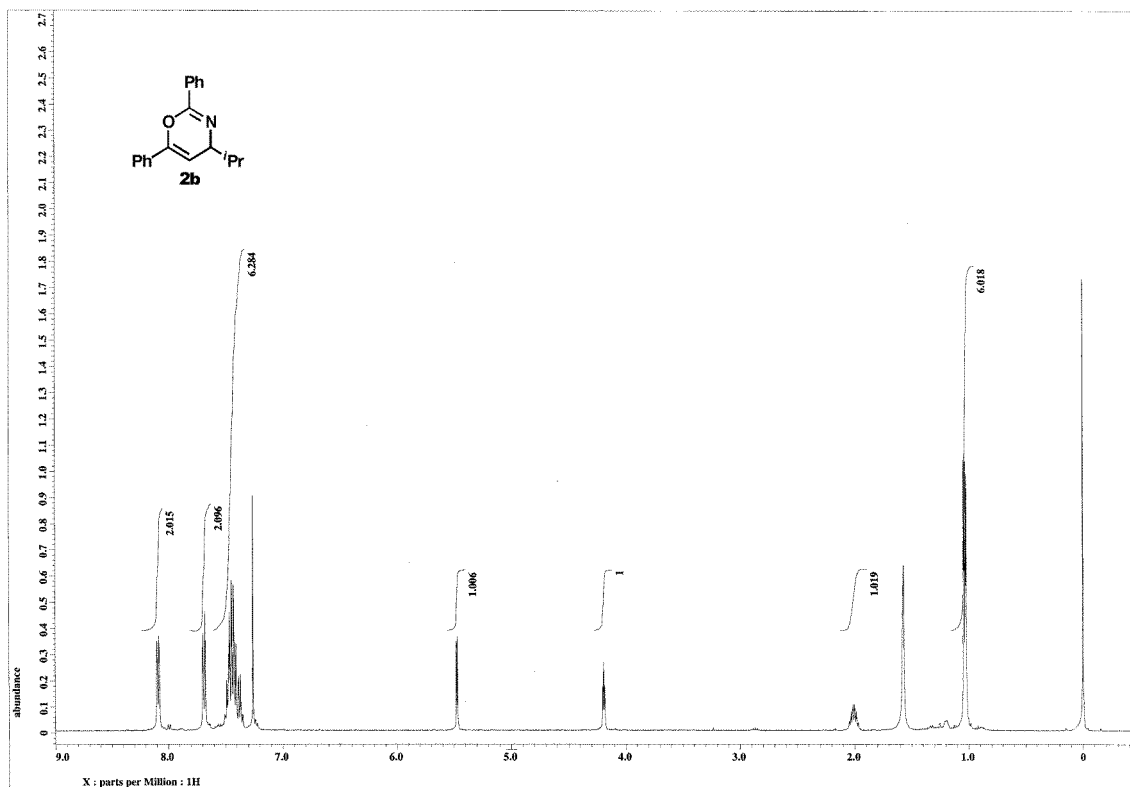
Spectroscopic data are consistent with the literature data.⁹

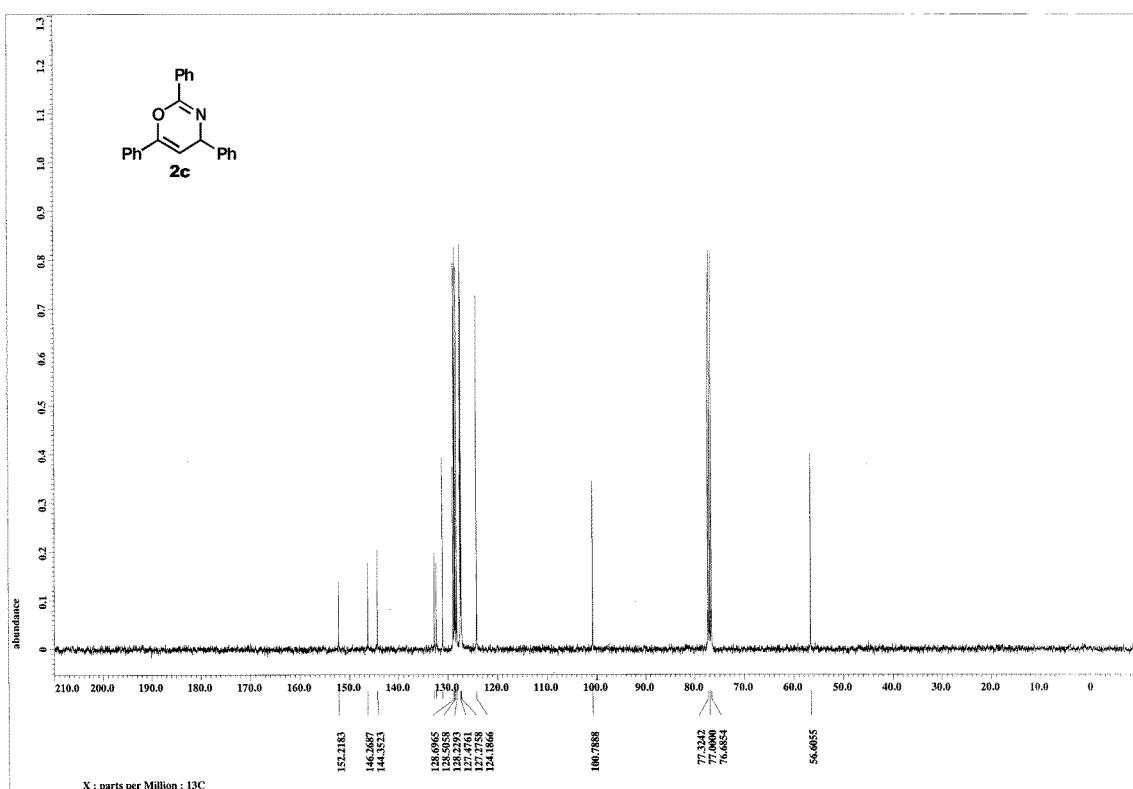
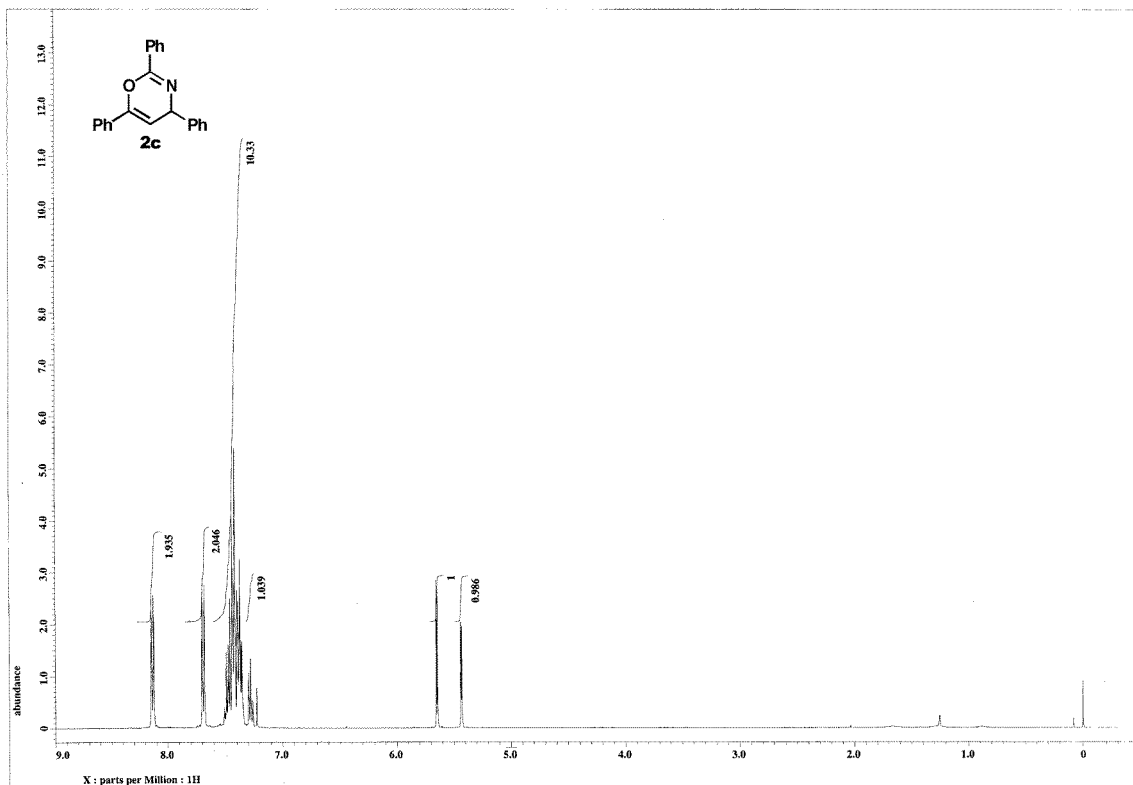
$[\alpha]_D^{20} -8.7$ (c 0.215, CHCl_3) for 81% ee (*R*) [*lit.*⁹ $[\alpha]_D^{20} +6.4$ (c 0.47, CHCl_3) for 98% ee (*S*)];

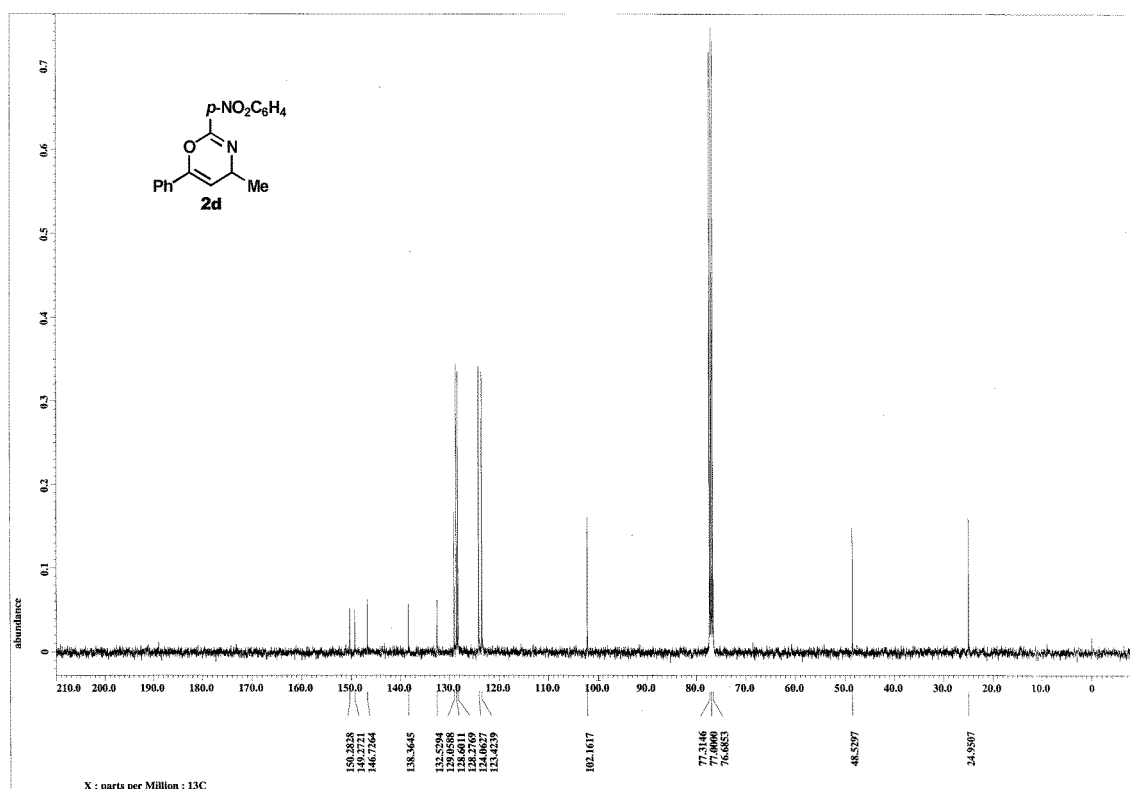
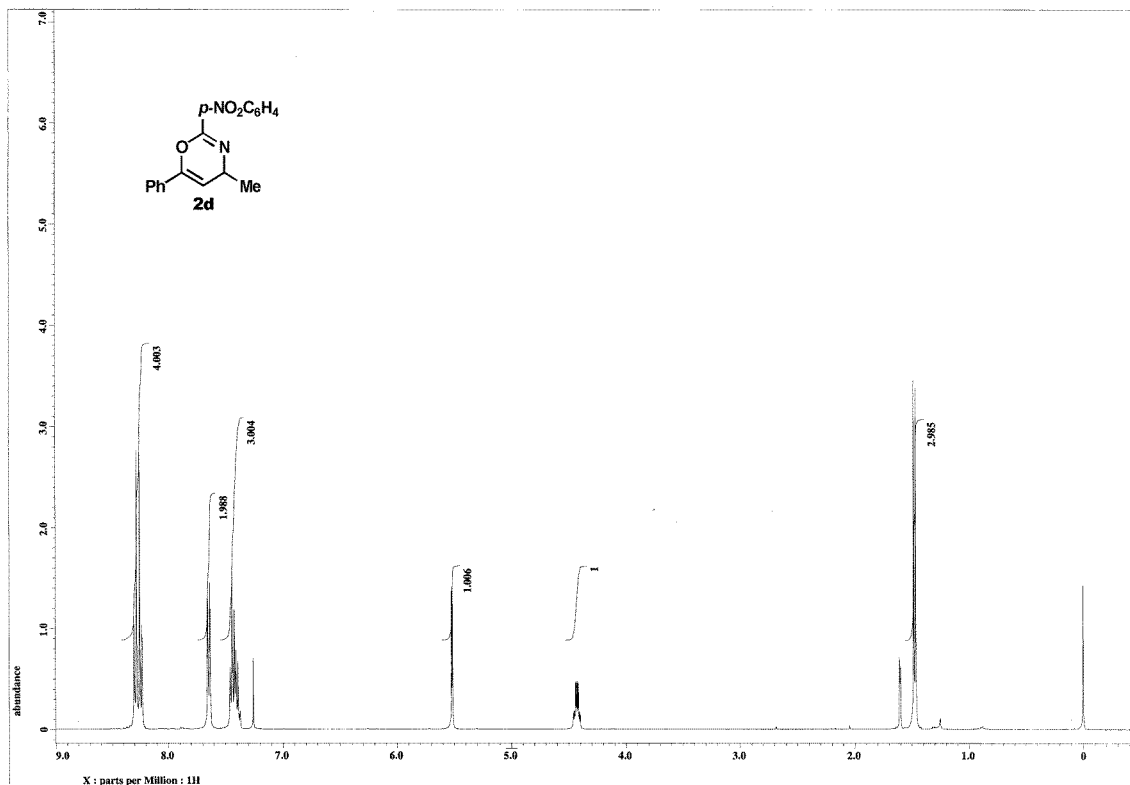
^1H -NMR (400 MHz, CDCl_3) δ 1.11 (d, $J = 6.1$ Hz, 3H), 1.62 (brs, 2H, NH₂), 1.60-1.72 (m, 2H), 2.59-2.73 (m, 2H), 2.92 (sext, $J = 6.1$ Hz, 1H), 7.16-7.31 (m, 5H).

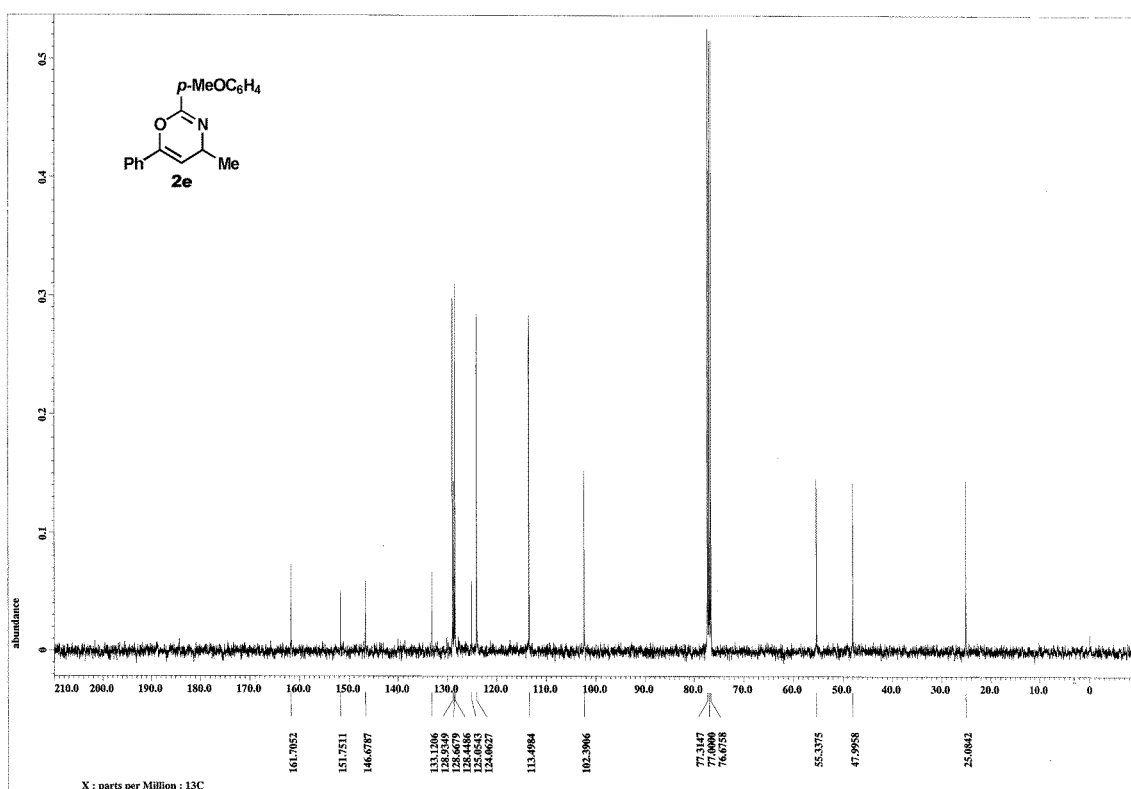
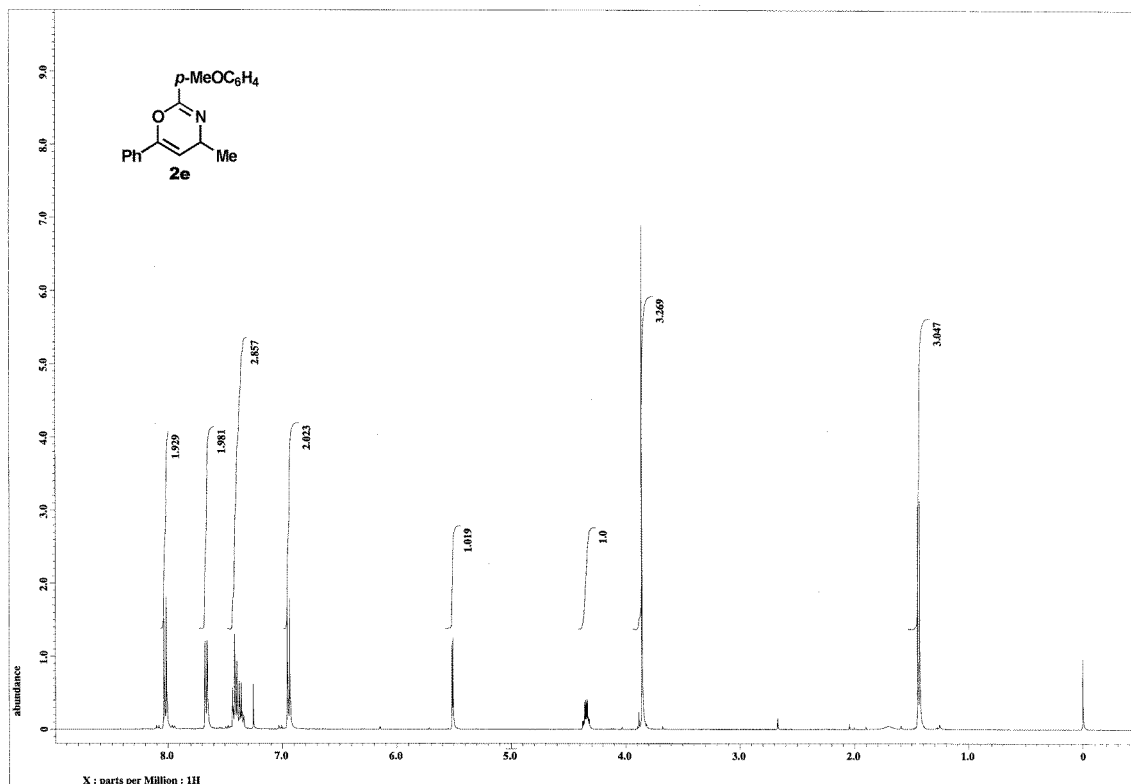
¹H and ¹³C NMR Spectra of 4H-1,3-Oxazines

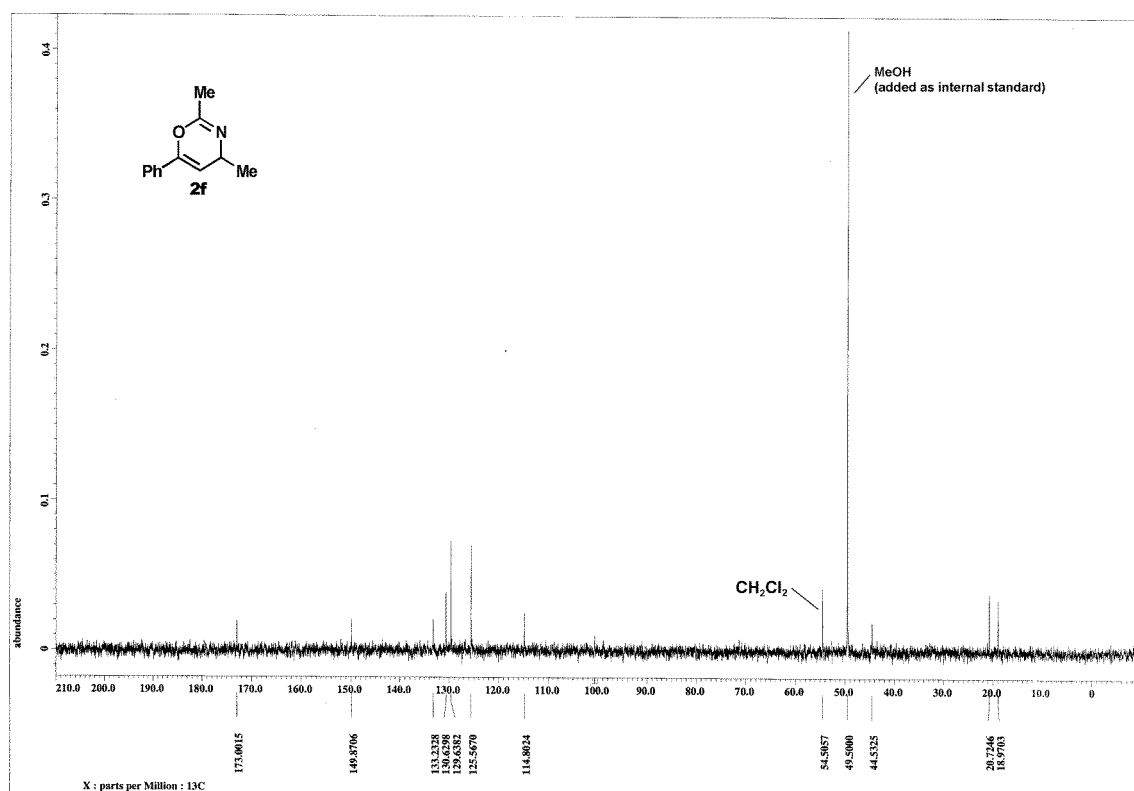
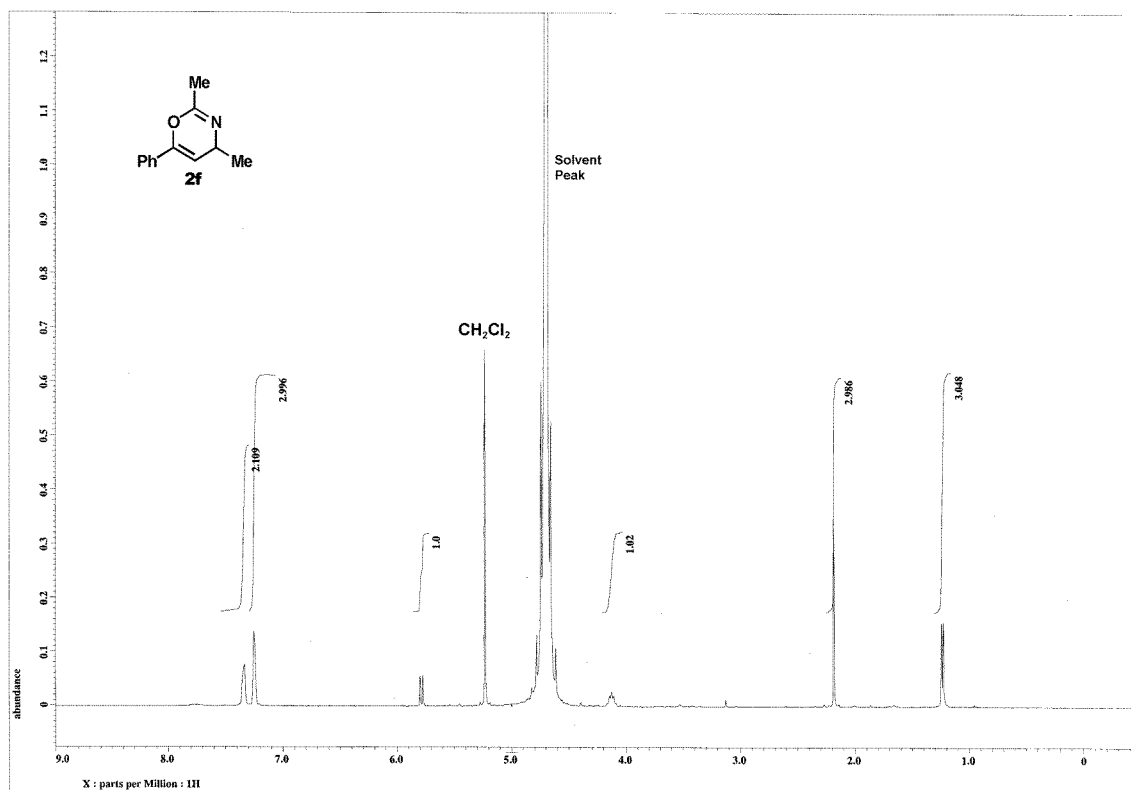




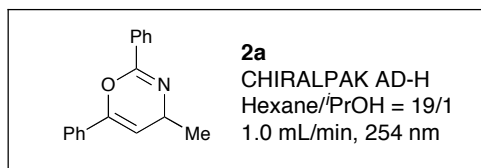






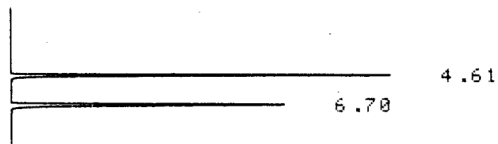


HPLC Traces of Optically Active Compounds



1. Racemic

CH. 1 C.S 2.50 ATT 8 OFFS 0 00/00/00 04:11



D-2500

00/00/00 04:11

METHOD: TAG: 4 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	4.61	614007	49.998	BB
2	6.70	614060	50.002	BB

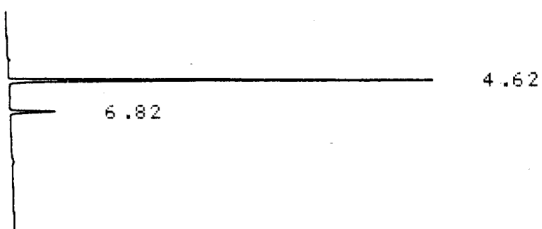
TOTAL

1228067 100.000

PEAK REJ : 0

2. Optically active (74% ee)

CH. 1 C.S 2.50 ATT 6 OFFS 0 00/00/00 00:20



D-2500

00/00/00 00:20

METHOD: TAG: 2 CH: 1

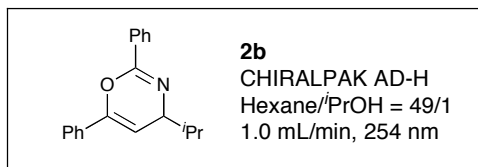
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	4.62	174135	87.054	BB
2	6.82	25895	12.946	BB

TOTAL

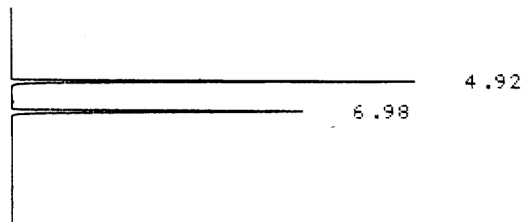
200030 100.000

PEAK REJ : 0



1. Racemic

CH. 1 C.S 2.50 ATT 8 OFFS 0 00/00/00 00:45



D-2500 00/00/00 00:45

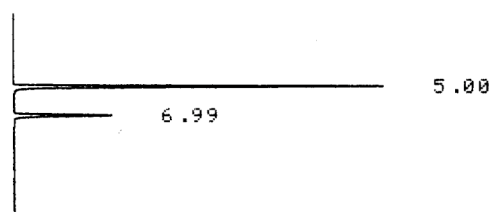
METHOD: TAG: 2 CH: 1
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	4.92	694697	50.312	BB
2	6.98	686082	49.688	BB
TOTAL		1380779	100.000	

PEAK REJ : 0

2. Optically active (47% ee)

CH. 1 C.S 2.50 ATT 8 OFFS 0 00/00/00 01:14

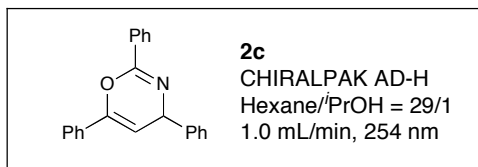


D-2500 00/00/00 01:14

METHOD: TAG: 2 CH: 1
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

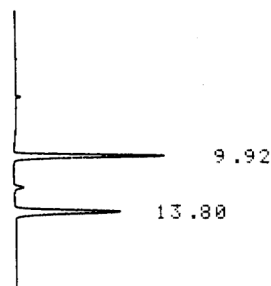
NO.	RT	AREA	CONC	BC
1	5.00	646183	73.547	BB
2	6.99	232415	26.453	BB
TOTAL		878598	100.000	

PEAK REJ : 0



1. Racemic

CH. 1 C.S 2.50 ATT 6 OFFS 0 00/00/00 02:05



D-2500 00/00/00 02:05

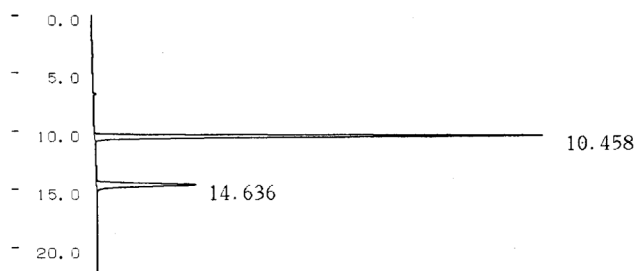
METHOD: TAG: 3 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	9.92	129911	49.917	BB
2	13.80	130344	50.083	BB
TOTAL		260255	100.000	
PEAK REJ :		0		

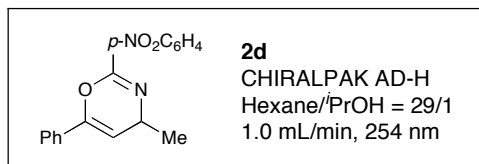
2. Optically active [53% ee (S)]

C-RSA CHROMATOPAC CH=1 Report No.=3 DATA=1:@CHRM1.C00 09/02/20 12:48:14



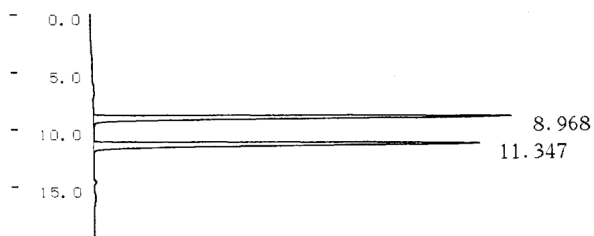
** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	2	10.458	494122	35604			76.4374	
	3	14.636	152318	7917			23.5626	
TOTAL			646440	43521			100	



1. Racemic

C-R8A CHROMATOPAC CH=1 Report No.=8 DATA=1:@CHRM1.C00 09/02/09 18:31:18

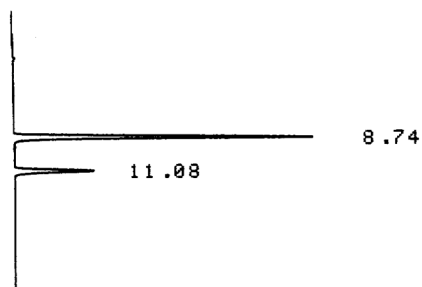


** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	4	8.968	1227585	66346			50.0402	
	5	11.347	1225614	61370			49.9598	
TOTAL			2453198	127715			100	

2. Optically active (50% ee)

CH. 1 C.S 2.50 ATT 6 OFFS 0 00/00/00 01:04



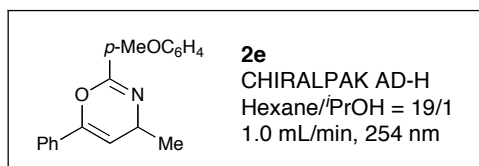
D-2500

00/00/00 01:04

METHOD: TAG: 2 CH: 1

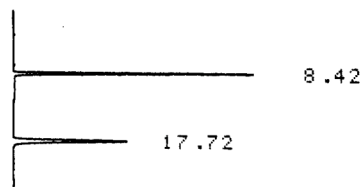
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	8.74	219736	74.971	BB
2	11.08	73360	25.029	BB
TOTAL		293096	100.000	
PEAK REJ :		0		



1. Racemic

CH. 1 C.S 1.25 ATT 7 OFFS 0 00/00/00 03:13



D-2500 00/00/00 03:13

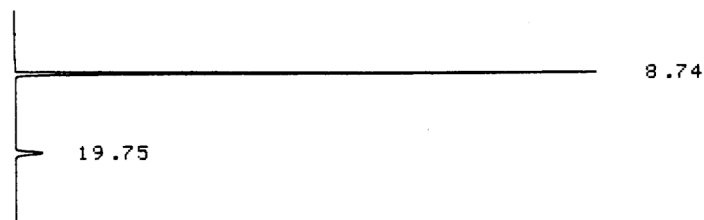
METHOD: TAG: 3 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	8.42	344879	50.077	BB
2	17.72	343816	49.923	BB
TOTAL		688695	100.000	
PEAK REJ :		0		

2. Optically active [81% ee (*R*)]

CH. 1 C.S 1.25 ATT 8 OFFS 0 00/00/00 00:44

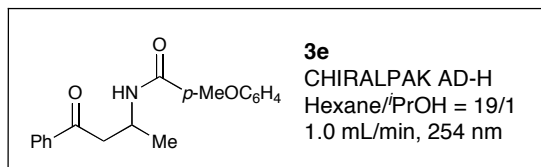


D-2500 00/00/00 00:44

METHOD: TAG: 2 CH: 1

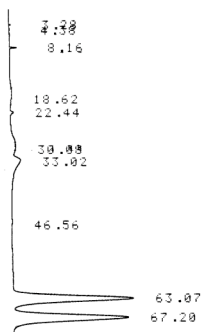
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	8.74	1775558	90.353	BB
2	19.75	189584	9.647	BB
TOTAL		1965142	100.000	
PEAK REJ :		0		



1. Racemic

CH. 1 C.S 1.25 ATT 8 OFFS 0 00/00/00 08:54



D-2500

00/00/00 08:54

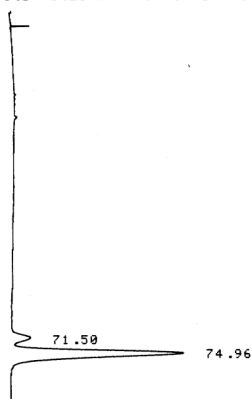
METHOD: TAG: 10 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	3.28	4667	0.045	BB
2	4.38	1106	0.011	BB
3	8.16	32105	0.310	BB
4	18.62	96053	0.929	BB
5	22.44	36463	0.353	BB
6	30.08	243532	2.354	BU
7	33.02	547857	5.297	UB
8	46.56	16521	0.160	BB
9	63.07	4611172	44.579	BU
10	67.20	4754272	45.963	UB
TOTAL		10343748	100.000	
PEAK REJ :		0		

2. Optically active [81% ee (R)]

CH. 1 C.S 1.25 ATT 5 OFFS 0 00/00/00 00:35



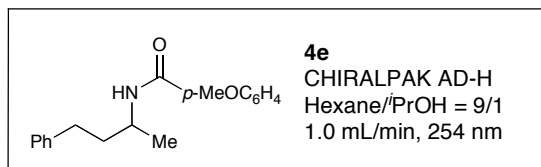
D-2500

00/00/00 00:35

METHOD: TAG: 2 CH: 1

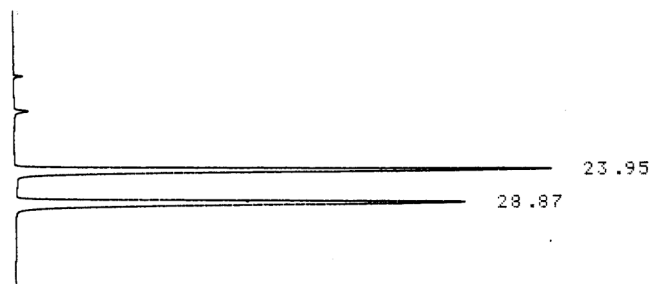
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	71.50	101233	9.322	BU
2	74.96	984713	90.678	UB
TOTAL		1085946	100.000	
PEAK REJ :		0		



1. Racemic

CH. 1 C.S 1.25 ATT 8 OFFS 0 00/00/00 01:47



D-2500 00/00/00 01:47

METHOD: TAG: 3 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	23.95	6179755	49.991	BB
2	28.87	6182022	50.009	BB

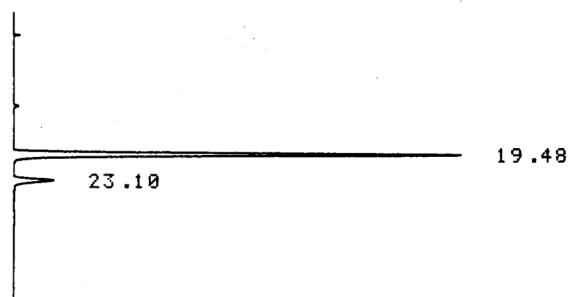
TOTAL

12361777 100.000

PEAK REJ : 0

2. Optically active [81% ee (*R*)]

CH. 1 C.S 1.25 ATT 7 OFFS 0 00/00/00 02:33



D-2500 00/00/00 02:33

METHOD: TAG: 3 CH: 1

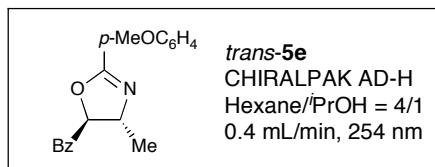
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	19.48	1731279	90.561	BB
2	23.10	180442	9.439	BB

TOTAL

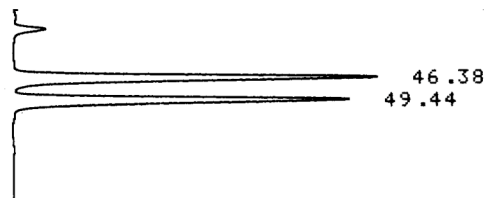
1911721 100.000

PEAK REJ : 0



1. Racemic

CH. 1 C.S 1.25 ATT 7 OFFS 0 00/00/00 03:53



D-2500

00/00/00 03:53

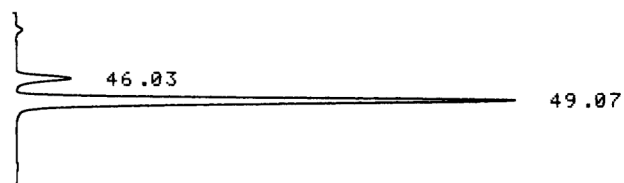
METHOD: TAG: 4 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	46.38	2727637	51.050	BV
2	49.44	2615401	48.950	VB
TOTAL		5343038	100.000	
PEAK REJ :		0		

2. Optically active [81% ee (4R, 5S)]

CH. 1 C.S 1.25 ATT 7 OFFS 0 00/00/00 02:43



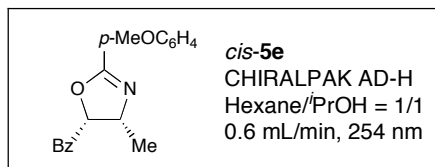
D-2500

00/00/00 02:43

METHOD: TAG: 3 CH: 1

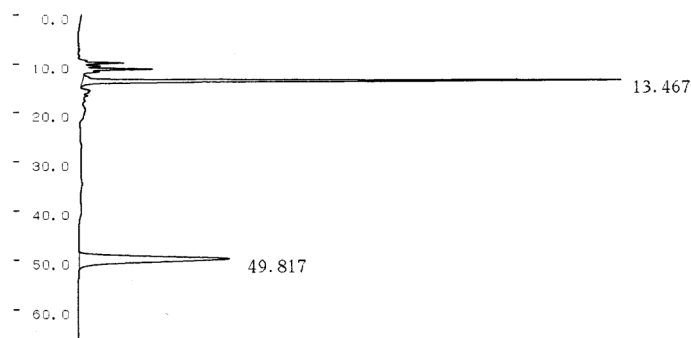
FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	46.03	404548	9.505	BV
2	49.07	3851608	90.495	VB
TOTAL		4256156	100.000	
PEAK REJ :		0		



1. Racemic

C-R8A CHROMATOPAC CH=1 Report No.=7 DATA=1:@CHRM1.C00 09/02/18 14:47:26

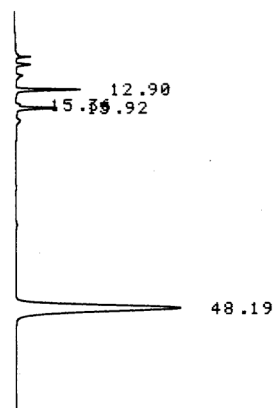


** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC	NAME
1	7	13.467	1275274	50096			54.8455	
	10	49.817	1049936	14057			45.1545	
TOTAL			2325209	64153			100	

2. Optically active [81% ee (4R, 5R)]

CH. 1 C.S 1.25 ATT 8 OFFS 0 00/00/00 04:10



D-2500

00/00/00 04:10

METHOD: TAG: 4 CH: 1

FILE: 1 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	12.90	400352	8.707	BB ←
2	15.36	29384	0.639	BU ←
3	15.92	321861	7.000	VB ←
4	48.19	3846702	83.655	BB ←
TOTAL		4598299	100.000	
PEAK REJ :		0		

References

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