Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

for

Catalytic Asymmetric Synthesis of Pentacyclic Core of (–)-Nakadomarin A *via* Oxazolidine as an Iminium Cation Equivalent

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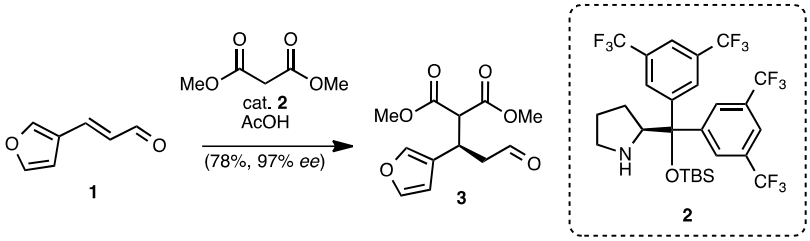
1. General informaiton

All non-aqueous reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise noted. Solvents and materials were obtained from commercial suppliers and used without further purification. Column chromatography was performed on Cica silica gel 60 (230−400 mesh) or Fuji Silysia silica gel (NH, 100−200 mesh), gel permeation chromatography was performed with LC-9201 and flash column chromatography was performed on Cica silica gel 60 (spherical/40−100 μm). Reactions and chromatography fractions were analyzed employing pre-coated silica gel plate (Merck Silica Gel 60 F_{254}). All melting points were measured on BÜCHI M-565 melting point apparatus and are uncorrected. IR spectra were measured on JASCO FT/IR-4100. Unless otherwise noted, NMR spectra were obtained in $CDCl_3$. ^1H NMR (500 MHz) spectra were recorded with JEOL ECP-500 spectrometers and chemical shifts are reported in δ (ppm) relative to TMS (in $CDCl_3$) as internal standard. Unless otherwise noted, ^{13}C NMR (126 MHz) spectra were also recorded using JEOL ECP-500 spectrometers and referenced to the residual $CHCl_3$ signals. ^1H NMR multiplicities are reported as follows: br = broad; m = multiplet; s = singlet; d = doublet; t = triplet; q = quartet; sep = septet. Low-resolution mass spectra were recorded on a JMS-HX/HX 110A or MS700 mass spectrometer. High-resolution mass spectra were obtained on a JMS-HX/MS700 (FAB) or a Shimazu LCMS-IT-TOF fitted with an ESI. Optical rotations were recorded on a JASCO P-2200 polarimater with a path length of 1 cm; concentrations are quoted in grams per 100 mL. $[\alpha]_D$ values are measured in 10^{-1} deg cm^2g^{-1}. Enantiomeric excess was determined by high performance liquid chromatography (HPLC) analyses. Unless otherwise noted, all materials and solvent were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used without purification. All non-commercially available substrates were prepared according to the literature procedure as indicated below.

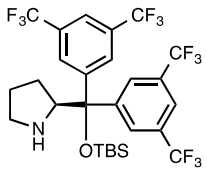
2. Preparation of substrates

Dimethyl (*R*)-2-(1-(furan-3-yl)-3-oxopropyl)malonate (3)



To a mixture of (*E*)-3-(furan-3-yl)acrylaldehyde **1** (8.8 g, 72 mmol), catalyst **2** (0.92 g, 2 mol %) and dimethylmalonate (24.8 mL, 3 equiv) was added H_2O (40 mL) and AcOH (0.9 mL, 5 mol %). After stirring at 45 ˚C for 24 h, the reaction mixture was cooled to room temperature and extracted with chloroform three times. The combined organic layer was dried over Na_2SO_4, and then evaporated *in vacuo*. Purification by column chromatography on SiO_2 (10–50% EtOAc in hexane) gave **3** as yellow oil (78 %, er = 98.5:1.5).

$[\alpha]^{24}_D$ (*c* 1.46, $CHCl_3$) –29.1; IR(ATR): 3134, 2955, 2841, 2733, 1752,1731, 1637, 1556, 1510, 1436, 1248, 1197, 1160, 1024, 874 cm^{-1}; ^1H NMR($CDCl_3$, 500MHz); δ= 9.64 (m, 1H), 7.34 (m, 1H), 7.31 (m, 1H), 6.30 (m, 1H), 3.99 (td, 1H, *J* = 8.8, 4.9 Hz), 3.74 (s, 3H), 3.69 (d, 1H, *J* = 8.3 Hz), 3.64 (s, 3H), 2.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$); δ= 200.1, 168.4, 168.1, 143.4, 140.2, 123.9, 109.6, 56.4, 52.8, 52.6, 46.6, 30.2; LRMS (CI^+) : *m/z* 255 [$M+H^+$] ; HRMS (CI^+) calcd for $C_{12}H_{15}O_6$ [$M+H^+$] 255.0869, found 255.0861.

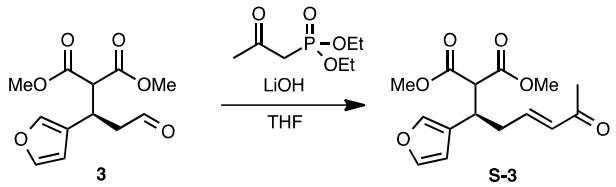


2

Catalyst **2** was prepared by the reported procedure[1] from (*L*)-proline.

Spectra were accorded to those of the enantiomer. $[\alpha]^{28}_D$ (*c* 1.15, $CHCl_3$) +1.82

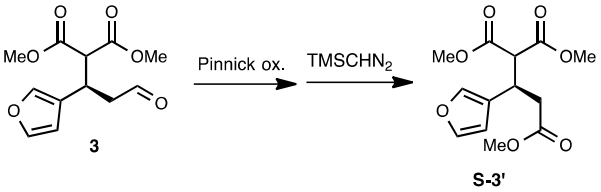
• For the determination of ee



3 **S-3**

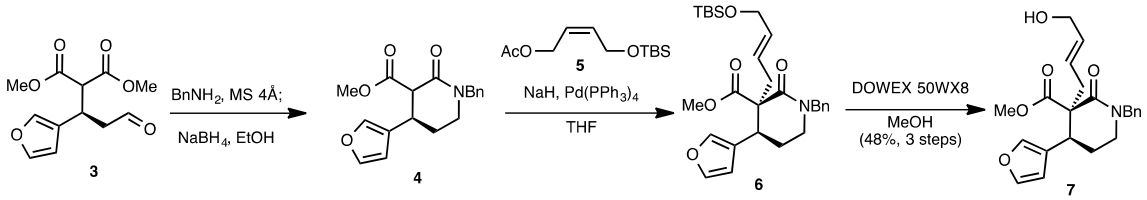
Ee of **3** was determined after conversion into unsaturated ketone **S-3**. HPLC separation condition for **S-3**: Chiralpak IC, *i*-PrOH/Hex = 15/85, 1.0 mL/min, λ = 254 nm, t_{major} = 27.1 min, t_{minor} = 23.9 min, 30 deg]

• For the determination of the absolute configuration



The absolute configuration of **3** was determined after conversion into unsaturated ester **S-3**'. In analogy to the related esters[2], the configuration was determined to be (*R*). HPLC separation condition for **S-3'**: [Chiralpak AD, *i*-PrOH/Hex = 5/95, 0.5 mL/min, λ = 220 nm, t_{major} = 23.5 min, t_{minor} = 21.8 min, 40 deg]

Methyl-(3*R*,4*S*)-1-benzyl-4-(furan-3-yl)-3-((*E*)-4-hydroxybut-2-en-1-yl)-2-oxopiperidine-3-carboxylate (7)



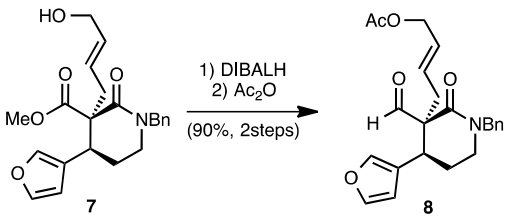
To the solution of aldehyde **3** (12.5 g, 49 mmol) in anhydrous dichloromethane (180 mL) was added $BnNH_2$ (5.9 mL, 1.1 equiv) and MS 4Å (11.5 g). After stirring for 24 h, MS was removed by filtration, and subsequently the reaction mixture was evaporated *in vacuo*. The resulting crude imine was dissolved in MeOH (150 mL), and $NaBH_4$ (2.2 g, 1.2 equiv) was added at 0 ºC. After stirring at room temperature overnight, the reaction mixture was concentrated *in vacuo.* The residue was extracted with chloroform three times, and the combined organic layer was evaporated *in vacuo*. The crude mixture was filtered through a pad of silica gel, and the resulting lactam was directly used for the next reaction without further purification.

To the solution of the crude lactam in THF was added NaH (≈ 60%, 2.45 g, 1.2 equiv) at 0 ºC. After stirring at room temperature for 5 min, acetate **5** (18.1 g, 1.5 equiv)[3] and $Pd(PPh_3)_4$ (2.77 g, 5 mol %) was added. After stirring at room temperature for three hours, water was added to the reaction mixture, which was extracted with chloroform. The organic layer was dried over sodium sulfate, and then evaporated *in vacuo*. The crude mixture was filtered through a pad of silica gel, and the obtained silylether was used for the next reaction without further purification.

To the solution of crude silylether in MeOH was added DOWEX 50WX8 (10.8 g). After gentle stirring at 25 °C overnight, the reaction mixture was filtered through Celite. Purification by column chromatography (50–100 % EtOAc in hexane) gave 9.1 g of alcohol **7** (48 % over four steps).

$[\alpha]^{28}_{D}$ (*c* 0.96, $CHCl_3$) +104.5; IR (ATR): 3426, 2932, 2860, 1743,1635, 1495, 1450, 1354, 1239, 1209, 1172, 1083, 1026, 984, 874, 811, 770, 700 cm^{-1}; ^1H NMR: 7.33–7.23 (m, 7H), 6.17 (s, 1H), 5.81(m, 1H), 5.48 (m, 1H), 4.65 (dd, 2H, *J* = 12.4, 11.6), 4.05 (m, 2H), 3.58 (s, 3H), 3.37–3.23 (m, 2H), 3.18 (dd, 1H, *J* = 2.9, 10.6 Hz), 3.14–3.03 (m, 1H), 2.59–2.49 (m, 1H), 2.49–2.42 (m, 1H), 1.7 (d, 1H, *J* = 13.3 Hz); ^{13}C NMR: 171.6, 168.3, 143.1, 139.8, 136.8, 134.9, 128.7, 128.1, 127.6, 126.5, 123.8, 109.6, 63.2, 58.8, 52.3, 51.1, 46.8, 36.2, 35.4, 25.4; FAB-LRMS: 384, 366, 327, 307, 289, 282, 154, 136, 91, 89, 57, 43; FAB-HRMS calcd for $C_{22}H_{26}NO_5$ $[M+H^+]$ 384.1805, found 384.1815.

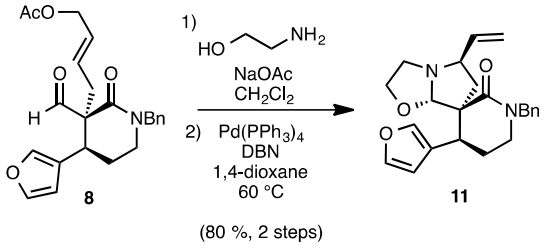
(*E*)-4-((3*S*,4*S*)-1-benzyl-3-formyl-4-(furan-3-yl)-2-oxopiperidin-3-yl)but-2-en-1-yl acetate (8)



To the solution of ester **6** (2.1 g, 5.49 mmol) in dichloromethane (60 mL) was added 3.0 M DIBAL-H in toluene (16.8 mL, 3 equiv) at –78 ˚C. After stirring at the same temperature for 4 h, MeOH was added at –78 ˚C. The reaction mixture was warmed to room temperature, and then aqueous rochelle salt solution was added. After stirring at room temperature for 3 hours, the reaction mixture was extracted with chloroform three times, and the combined organic layer was evaporated *in vacuo*. This residue was directly used for the next reaction without further purification. To the crude aldehyde in dichloromethane (60 mL) was added acetic anhydride (1.0 mL, 2.0 equiv), triethylamine (3 mL, 4.0 equiv) and DMAP (62 mg, 10 mol %). After stirring at room temperature for 18 h, the reaction was quenched with water, and extracted with chloroform for three times. The combined organic layer was concentrated *in vacuo*, and purification by column chromatography gave the title compound (1.87 g, 90 %, 2 steps) as yellowish oil.

$[\alpha]^{25}_{D}$ (*c* 0.82, $CHCl_3$) +29.8; IR ($CHCl_3$): 2937, 1730, 1633, 1495, 1453, 1362, 1236, 1163, 1075, 1027, 966, 874, 702 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ = 9.50 (s, 1H), 7.37–7.22 (m, 7H), 6.18 (m, 1H), 5.80–5.66 (m, 2H), 4.70–4.64 (m, 2H), 4.58–4.51 (m, 2H), 3.36–3.28 (m, 2H), 3.19–3.15 (m, 2H), 2.55–2.50 (m, 1H), 2.34–2.25 (m, 1H), 1.96–1.91 (m, 1H); ^{13}C NMR: δ = 201.1, 170.7, 167.4, 143.4, 140.2, 136.7, 129.5, 129.4, 128.8, 128.1, 127.7, 122.4, 110.4, 64.7, 60.7, 50.9, 46.1, 34.8, 34.5, 25.7, 21.0; HRMS (ESI): calcd. for $C_{23}H_{26}NO_5$ ([M+H]+): 396.1805, Found: 396.1800.

(3S,4S,5'R,7a'S)-1-benzyl-4-(furan-3-yl)-5'-vinyltetrahydro-7a'H-spiro[piperidine-3,7'-pyrrolo[2,1-b]oxazol]-2-one (11)



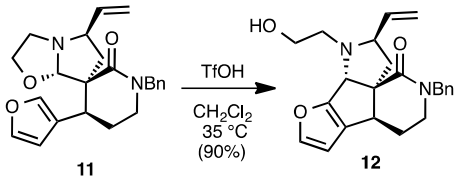
To the aldehyde **8** (412 mg, 1.04 mmol) in CH_2Cl_2 (16 mL) was added NaOAc (342 mg, 4.0 equiv) and 2-aminoethanol (0.13 mL, 2.0 equiv). After stirring at room temperature for 13 h, the reaction was quenched with water, and the product was extracted with chloroform three times. The combined organic layer was dried over sodium sulfate followed by concentration *in vacuo* to afford imine/hemiaminal mixture, which was used for the next reaction without further purification.

To the solution of crude imine mixture in 1,4-dioxane (30 mL) was added $Pd(PPh_3)_4$ (245 mg, 20 mol %) and DBN (0.26 mL, 2.1 equiv) at room temperature. After vigorous stirring at 60 °C for 20 h, the reaction mixture was evaporated *in vacuo*. Purification by column chromatography (40% acetone in hexane) gave title compound (317 mg, 80 % in two steps, single diastereoisomer) as a pale yellow solid.

Mp: 49–52 °C; $[\alpha]^{22}_{D}$ (*c* 1.07, $CHCl_3$) –13.7; IR (ATR): 2926, 1643, 1493, 1451, 1029, 748, 715, 673 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ = 7.33–7.24 (m, 6H), 7.15 (s, 1H), 6.20 (s, 1H), 5.93–5.85 (ddd, 1H, *J* = 17.1, 9.9, 8.3 Hz), 5.12–5.05 (m, 2H), 4.93 (s, 1H), 4.84 (d, 1H, *J* = 14.2 Hz), 4.29 (d, 1H, *J* = 14.2 Hz), 3.70–3.66 (m, 1H), 3.55 (td, 1H, *J* = 8.0, 3.2 Hz), 3.30 (t, 1H, *J* = 3.9 Hz), 3.30–3.00 (m, 5H), 2.24–2.10 (m, 3H), 1.87

(m, 1H); ^{13}C NMR: δ = 173.3, 142.6, 141.0, 139.7, 137.6, 129.0, 128.8, 127.8, 125.4, 116.4, 111.1, 100.9, 66.8, 62.1, 54.6, 50.8, 50.5, 45.7, 44.0, 36.6, 26.8; FAB-LRMS: *m/z* 379 [M+H$^+$]; FAB-HRMS calcd for $C_{23}H_{27}N_2O_3$[M+H$^+$] 379.2016, found 379.2018.

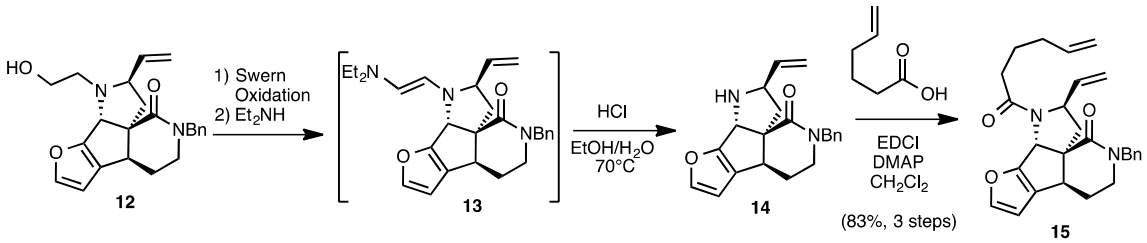
(2*R*,3a*S*,7a*S*,10b*R*)-5-benzyl-1-(2-hydroxyethyl)-2-vinyl-1,2,3,5,6,7,7a,10b-octahydro-4*H*-furo[3',2':3,4]pyrrolo[3',2':1,5]cyclopenta[1,2-*c*]pyridin-4-one (12)



To the solution of hemiaminalether **11** (184 mg, 0.487 mmol) in anhydrous CH_2Cl_2 (12 mL) was added TfOH (52 μL,1.2 equiv) at room temperature. After stirring at 35 °C for 24 h, the reaction mixture was cooled to room temperature, and quenched with saturated aqueous $NaHCO_3$ solution. The organic layer was separated, and aqueous layer was extracted with chloroform. The combined organic layer was dried over Na_2SO_4, and then evaporated *in vacuo.* Purification by silica gel chromatography (EtOAc) gave the title compound (186.2 mg, 90 %) as colorless oil.

$[\alpha]^{23}_D$ (*c* 0.79, $CHCl_3$) +26.5; IR($CHCl_3$): 3405, 2925, 1627, 1489, 1450,1059, 926, 753 cm^{-1}; ^{1}H NMR (500MHz, $CDCl_3$): δ = 7.42 (d, 1H, *J* = 1.9 Hz), 7.34–7.20 (m, 5H), 6.21 (d, 1H, *J* = 1.9 Hz), 5.74(dt, 1H, *J* = 18.2, 9.0 Hz), 5.17–5.13 (m, 2H), 4.76 (s, 1H), 4.71 (d, 1H, *J* = 14.7 Hz), 4.54 (d, 1H, *J* = 14.6 Hz), 3.89 (td, 1H, *J* = 10.5, 3.3 Hz), 3.67 (dt, 1H, *J* = 11.0, 4.1 Hz), 3.26–3.06 (m, 4H), 2.87 (ddd, 1H, *J* = 12.7, 9.9, 4.7 Hz), 2.71 (dt, 1H, *J* = 2.8, 3.3 Hz), 2.56 (t, 1H, *J* = 11.5 Hz), 2.13–2.06 (m, 1H), 1.98 (dd, 1H, *J* = 12.0, 5.0 Hz), 1.69–1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.1, 155.8, 148.3, 139.4, 137.1, 129.9, 128.7, 127.9, 127.4, 118.1, 106.3, 68.1, 66.3, 64.1, 59.3, 51.4, 49.6, 46.0, 44.0 (2C), 29.7; FAB-LRMS: *m/z* 379 [M+H$^+$]; FAB-HRMS: calcd for $C_{23}H_{27}N_2O_3$[M+H$^+$] 379.2016, found 379.2011

(2*R*,3a*S*,7a*S*,10b*R*)-5-benzyl-1-(hex-5-enoyl)-2-vinyl-1,2,3,5,6,7,7a,10b-octahydro-4*H*-furo[3',2':3,4]pyrrolo[3',2':1,5]cyclopenta[1,2-*c*]pyridin-4-one (15)



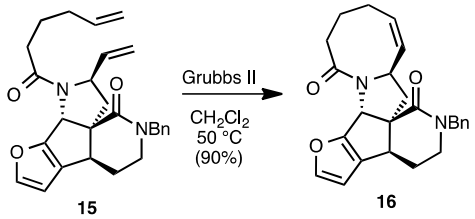
Oxalyl dichloride (0.24 mL, 2.5 equiv) was dissolved in dry dichloromethane (10 mL) under argon atmosphere, and the solution was cooled to –78 °C and kept for 15 min. To the solution was added DMSO (0.24 mL, 3.0 equiv) dropwise at –78 °C, and the reaction mixture was stirred at the same temperature for 10 min. After dropwise addition of alcohol **12** (418 mg, 1.1 mmol) in dry dichloromethane (10 mL) at –78 °C, the reaction mixture was stirred at –78 °C for 50 min, and treated with triethylamine (0.93 mL, 6 equiv) dropwise. The solution was stirred for 5 min at –78°C, then allowed to warm to room temperature, and stirred for 45 min before being poured into water. The organic layers were separated, and the aqueous layer was extracted with chloroform. The combined organic phase was dried over sodium sulfate and concentrated *in vacuo* to give unstable aldehyde (yellow oil), which was used for the next reaction without further purification.

To this crude aldehyde in ethanol (10 mL) was added Et_2NH (0.24 mL, 2.1 equiv) at room temperature. After 24 hours, 1N HCl aqueous solution (10 mL) was added and heated to 70 °C. The reaction mixture was stirred at 70 °C for 14 h before being quenched with sodium carbonate. The solution was evaporated *in vacuo*, and then the residue was dissolved to chloroform and water. The layers were separated, and the aqueous layer was extracted with chloroform. The combined organic phase was dried over sodium sulfate and concentrated *in vacuo*. Secondary amine was obtained as yellow oil, and the crude was used for the next reaction without further purification.

To the above obtained amine in dry dichloromethane (11 mL) was added 5-hexenoic acid (261 μL, 2.0 equiv), EDCI (276 mg, 1.3 equiv) and DMAP (7.1 mg, 5 mol %) at room temperature under argon atmosphere. The reaction mixture was stirred at room temperature for 4 h before being poured into water. The layers were separated, and the aqueous layer was extracted with chloroform. The combined organic phase was dried over sodium sulfate and concentrated *in vacuo*. Purification by silica gel chromatography (EtOAc-Hexane, 1:1) gave the title compound (408 mg, 83 %, three steps) as colorless oil.

$[\alpha]^{26}_{D}$ (*c* 0.43, $CHCl_3$) +45.8; IR (ATR): 2928, 1634, 1486, 1406, 1346, 1271, 1201, 1128, 994, 913, 729, 670 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$, mixture of amide rotamers): δ = 7.40 (d, 3/5H), 7.36 (d, 2/5H) 7.35–7.15 (m, 5H), 6.43–6.36 (m, 3/5H), 6.20–6.07 (m, 7/5H), 5.88–5.72 (m, 1H), 5.57 (s, 3/5H), 5.39 (s, 2/5 H) 5.16–4.90 (m, 4H), 4.73–4.39 (m, 3H), 3.23–3.08 (m, 3H), 2.74–2.67 (m, 1H), 2.61–2.54 (m, 3/5H), 2.49–2.45 (m, 3/5H), 2.42–2.33 (m, 4/5H), 2.27–1.96 (m, 3H), 1.84–1.62 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of amide rotamer): δ = 173.1, 172.8, 172.6, 172.1, 157.3, 155.8, 148.2, 148.1, 141.2, 139.8, 138.6, 137.0, 136.8, 128.8, 128.8, 128.1, 128.0, 128.0, 127.9, 127.7, 127.6, 127.4, 115.3, 115.0, 114.9, 113.9, 107.0, 106.6, 66.2, 65.7, 65.2, 62.5, 62.4, 62.2, 51.3, 51.1 (2C), 45.1, 44.5, 44.3, 44.1, 43.4, 42.6, 34.3, 33.4, 33.3, 29.8 (2C), 28.2, 24.2; HRMS (ESI): calcd. for $C_{27}H_{31}N_2O_3$ ([M+H]+): 431.2329, Found: 430.2320.

(4a*S*,7b*R*,14a*R*,15a*S*,*Z*)-2-benzyl-3,4,4a,7b,11,12,14a,15-octahydrofuro[2'',3'':3',4']pyrido[3'',4'':1',5']cyclopenta[1',2':4,5]pyrrolo[1,2-*a*]azocine-1,9(2*H*,10*H*)-dione (16)



15 16

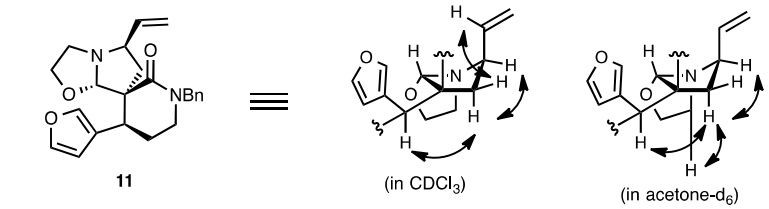
To the dinene **15** (85.1 mg, 0.198 mmol) in dry dichloromethane (200 mL, 1 mM) was added Grubbs 2nd generation catalyst (14.9 mg, 9 mol%). The reaction mixture was heated under reflux (oil bath temp. 50 °C) condition for 13 h. The mixture was evaporated *in vacuo*, and purification by silica gel chromatography (EtOAc) gave the title compound containing Ru residue. This mixture was dissolved in chloroform and QuadraSil AP was added in order to remove the Ru impurities. The suspension was stirred at room temperature for 24 h, and then filtration over Celite gave the pure **16** (74.4 mg, 90 %) as colorless powder.

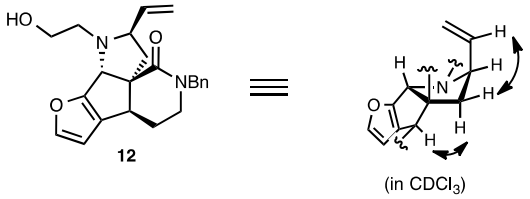
Mp: 178 °C (decomp.); $[\alpha]^{25}_{D}$ (*c* 0.63, $CHCl_3$) +106.3; IR (ATR): 2941, 2873, 2364, 2340, 1634, 1486, 1455, 1421, 1352, 1210, 1158, 1128, 771, 748, 701 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ = 7.40 (d, 1H, *J* = 1.9 Hz), 7.32–7.22 (m, 3H), 7.20–7.14 (m, 2 H), 6.17 (d, 1H, *J* = 1.9 Hz), 5.68–5.61(m, 2H), 5.54 (s, 1H), 4.62–4.58 (m, 2H), 4.54 (dd, 1H, *J* = 13.5, 6.1 Hz), 3.19 (dt, 1H, *J* = 1.2, 5.3 Hz), 3.14–3.11 (m, 2H), 2.77 (dd, 1H, *J* =

12.8, 7.8 Hz), 2.70 (ddd, 1H, *J* = 18.7, 12.6, 6.4 Hz), 2.56 (tt, 1H, *J* = 12.8, 6.2 Hz), 2.34–2.29 (m, 2H), 2.08–1.91 (m, 3H), 1.78–1.74 (m, 1H), 1.59–1.52 (m, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ = 172.8, 157.1, 148.2, 137.0, 131.4, 128.8, 128.2, 128.0, 127.6, 126.6, 106.3, 66.5, 61.9, 59.8, 51.2, 45.0, 44.0, 42.5, 32.8, 28.4, 23.9, 23.6; HRMS (ESI): calcd. for $C_{27}H_{27}N_2O_3$ ([M+H]$^+$): 403.2016, Found: 403.2009.

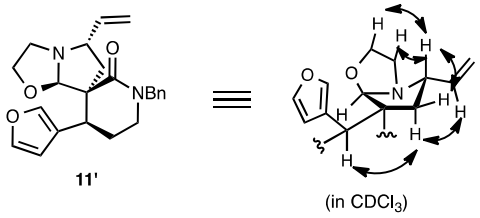
3. Determination of the relative configuration of <u>11</u>, <u>12</u> and <u>11'</u> by NOESY experiment

- Major isomer

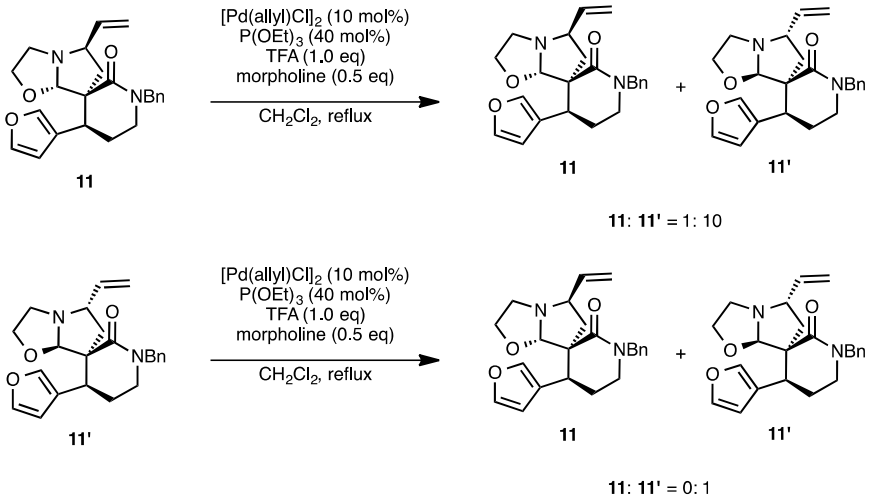




- Minor isomer

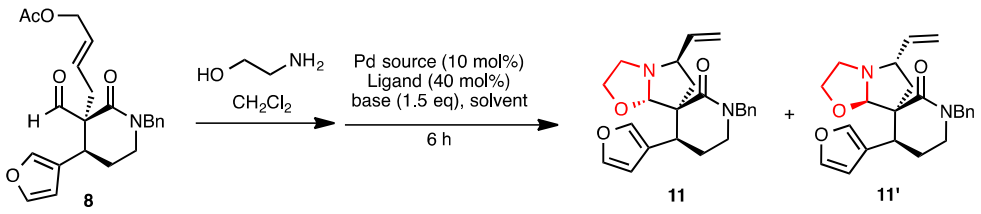


4. Epimerization experiment of 11/11' in acidic conditions



Judging from these experiments, **11'** turned out to be the thermodynamically favored product.

5. Optimization of the diastereoselective allylic amination



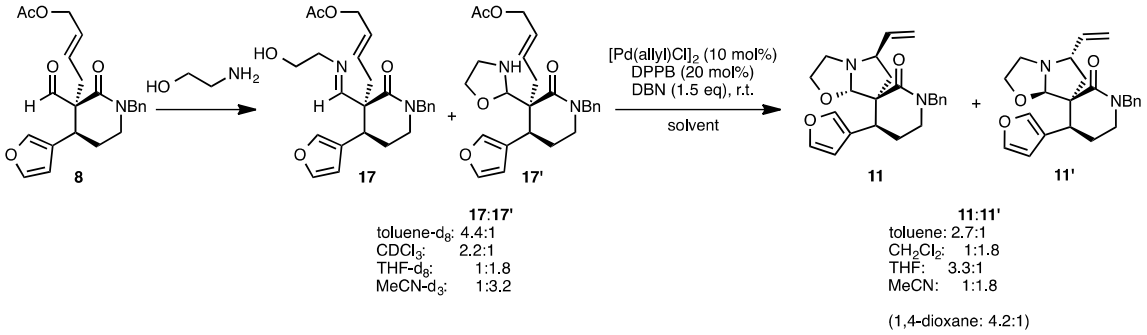
Entry	Pd source	Ligand	Base	Solvent	Temp. (°C)	conv (%)	d.r. (**11:11'**)[*a]
1	$Pd(PPh_3)_4$	-	NaOAc	DMF	60	100	1:3.1
2	$Pd(PPh_3)_4$	-	-	THF	60	100	1:2.0
3	$Pd(PPh_3)_4$	-	K_2CO_3	THF	60	63	1:2.0
4	$Pd(PPh_3)_4$	-	NEt_3	THF	60	73	1:1.2
5	$Pd(PPh_3)_4$	-	DBU	THF	60	100	1.5:1
6	$Pd(PPh_3)_4$	-	-	1,4-dioxane	60	87	1:2.0
7	$Pd(PPh_3)_4$	-	NEt_3	1,4-dioxane	60	73	1:1.2
8	$Pd(PPh_3)_4$	-	DBU	1,4-dioxane	60	100	1.5:1
9	$Pd(PPh_3)_4$	-	DBN	1,4-dioxane	60	100	4.8:1
10	$Pd(OAc)_2$	Xantphos	-	1,4-dioxane	60	93	1:3.0
11	$Pd(OAc)_2$	-	DBN	1,4-dioxane	60	0	-
12	-	-	DBN	1,4-dioxane	60	0	-
13	$Pd(dba)_2$	-	DBN	1,4-dioxane	60	93	2.8:1
14	$Pd(dba)_2$	DPPP*	DBN	1,4-dioxane	60	100	1.7:1
15	$Pd(dba)_2$	DPEPhos*	DBN	1,4-dioxane	60	100	3.3:1
16	$[Pd(allyl)Cl]_2$	DPEPhos*	DBN	1,4-dioxane	r.t.	100	2.0:1

17	$[Pd(allyl)Cl]_2$	DPPM*	DBN	1,4-dioxane	r.t.	100	1.2:1
18	$[Pd(allyl)Cl]_2$	DPPB*	DBN	1,4-dioxane	r.t.	100	4.0:1
19	$[Pd(allyl)Cl]_2$	Xantphos*	DBN	1,4-dioxane	r.t.	100	1.1:1
20	$[Pd(allyl)Cl]_2$	P(*p*-tol)$_3$	DBN	1,4-dioxane	r.t.	100	4.3:1
21	$[Pd(allyl)Cl]_2$	P(4-methoxyphenyl)$_3$	DBN	1,4-dioxane	r.t.	100	3.3:1
22	$[Pd(allyl)Cl]_2$	P(4-chlorophenyl)$_3$	DBN	1,4-dioxane	r.t.	100	1:1.1
23	$[Pd(allyl)Cl]_2$	$P(C_6F_5)_3$	DBN	1,4-dioxane	r.t.	66	1:2
24	$[Pd(allyl)Cl]_2$	P(*p*-tol)$_3$	DBN	THF	r.t.	100	2.5:1
25	$[Pd(allyl)Cl]_2$	DPPB*	DBN	THF	r.t.	100	3.3:1
26	$[Pd(allyl)Cl]_2$	DPPB*	DBN	Toluene	r.t.	100	2.7:1
27	$[Pd(allyl)Cl]_2$	DPPB*	DBN	MeCN	r.t.	100	1:1.8
28	$[Pd(allyl)Cl]_2$	DPPB*	DBN	CH_2Cl_2	r.t.	100	1:1.8
29	$Pd(dba)_2$	DPPP*	DBN	Toluene	60	100	1.4:1
30	$Pd(dba)_2$	DPPB*	DBN	Toluene	60	100	2.0:1
31	$Pd(dba)_2$	DPPF*	DBN	Toluene	60	100	1.6:1
32	$Pd(dba)_2$	DPEPhos*	DBN	Toluene	60	100	1:1.1
33	$Pd(dba)_2$	Xantophos*	DBN	Toluene	60	100	1:2.0
34	$Pd(dba)_2$	P(*n*-Bu)$_3$	DBN	Toluene	60	100	1:2.0
35	$Pd(dba)_2$	PCy_3	DBN	Toluene	60	0	-
36	$Pd(dba)_2$	P(2-furyl)$_3$	DBN	Toluene	60	70	2.8:1
37	$Pd(dba)_2$	P(2-furyl)$_3$	DBN	Toluene	60	100	2.4:1
38	$Pd(dba)_2$	P(*o*-tol)$_3$	DBN	Toluene	60	100	1.9:1

*20 mol% of ligand was employed.

Solvent effects

- The ratio between 17 and 17' is irrelevant to the diastereoselectivity



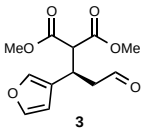
6. references

1. Q. Lin, D. Meloni, Y. Pan, M. Xia, J. Rodgers, S. Shepard, M. Li, L. Galya, B. Metcalf, T-Y. Yue, P. Liu and J. Zhou, *Org. Lett.*, **2009**, *11*, 1999.

2. S. Brandau, A. Landa, J. Franzøn, M. Marigo and K. A. Jørgensen, *Angew. Chem. Int. Ed.,* **2006**. *45*, 4305.

3. A. M. Zawisza and J. Muzart, *J. Organomet. Chem.*, **2010**, *695*, 62

7. Copies of ^{1}H and ^{13}C NMR charts



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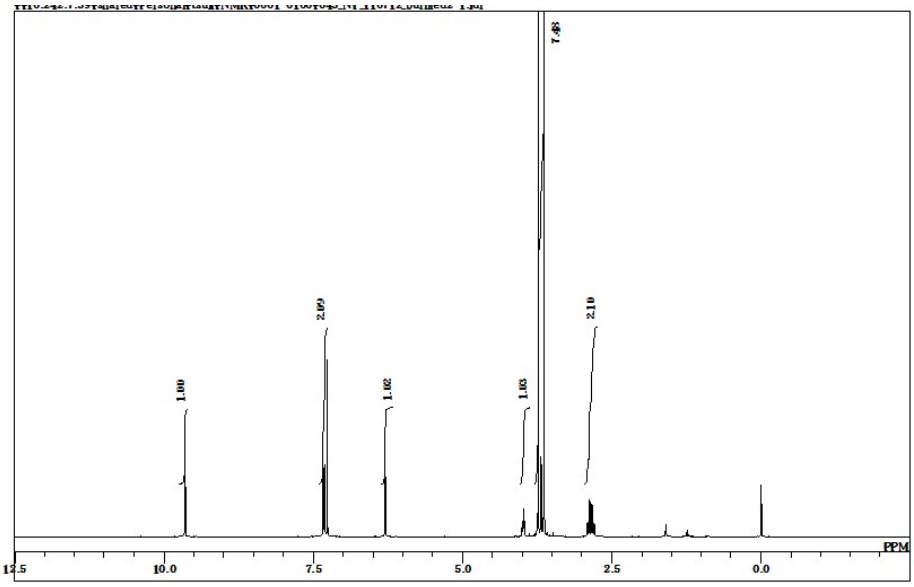


Figure S1. ^{1}H NMR of **3**

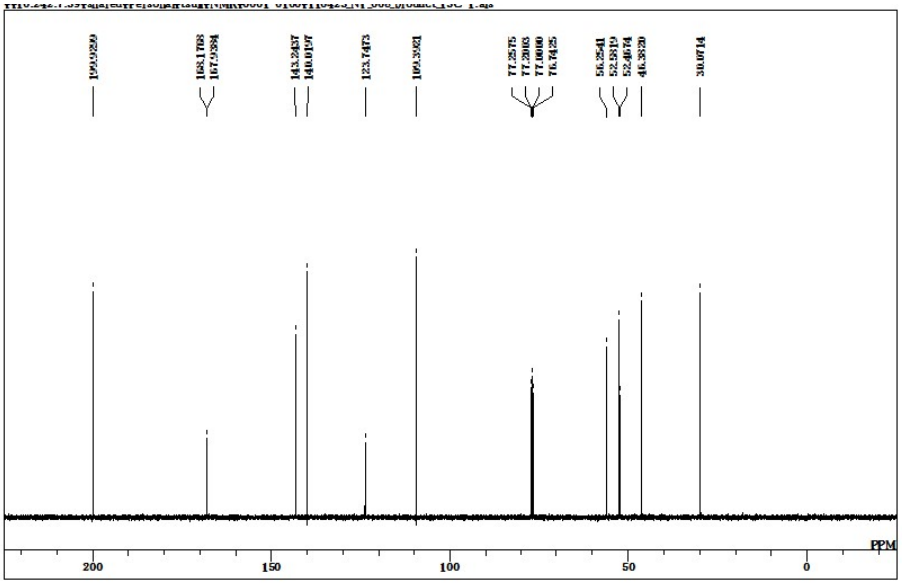
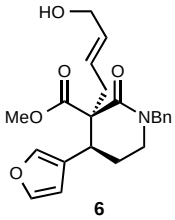


Figure S2. ^{13}C NMR of **3**



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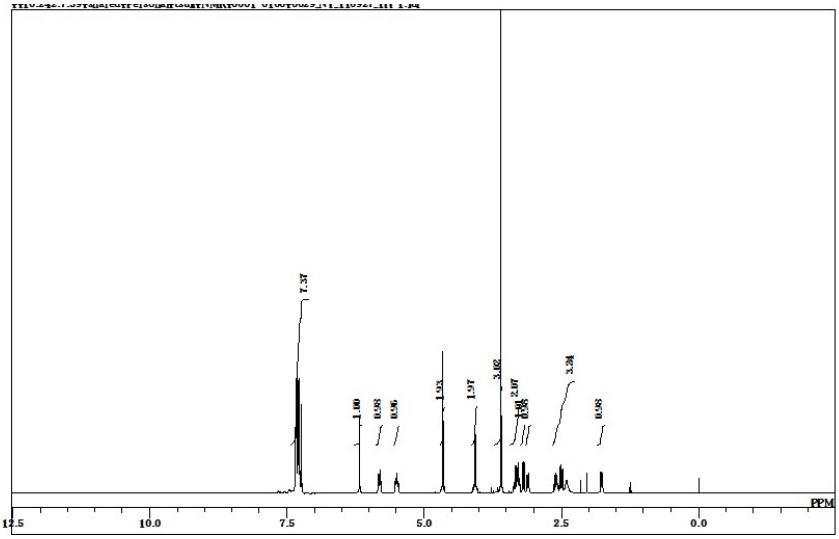


Figure S3. ^{1}H NMR of **6**

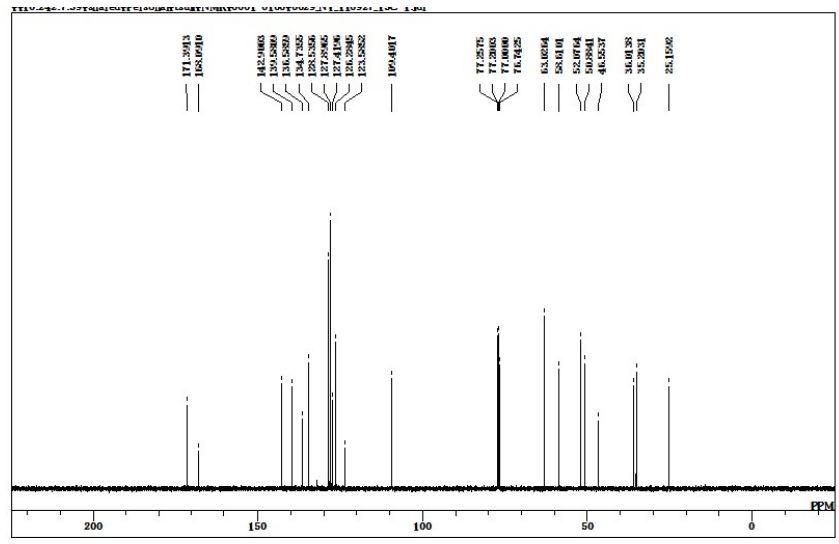
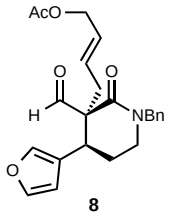


Figure S4. ^{13}C NMR of **6**



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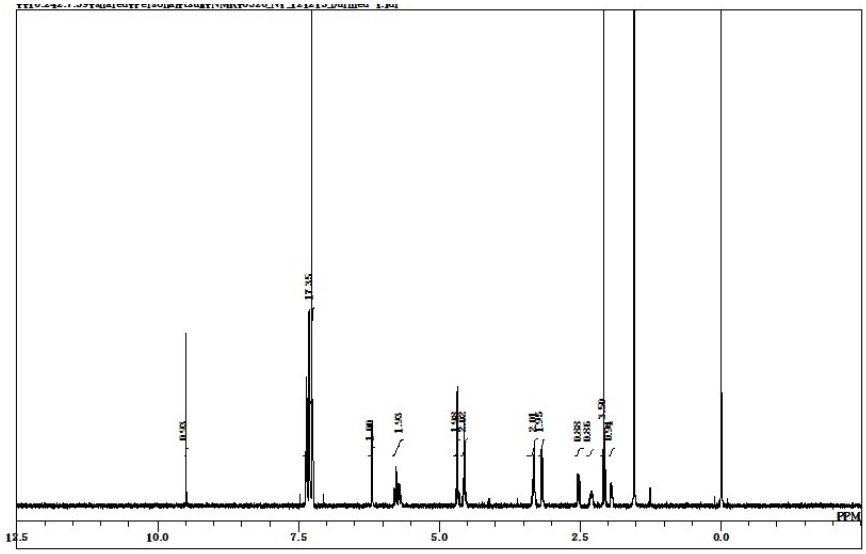


Figure S5. ^{1}H NMR of **8**

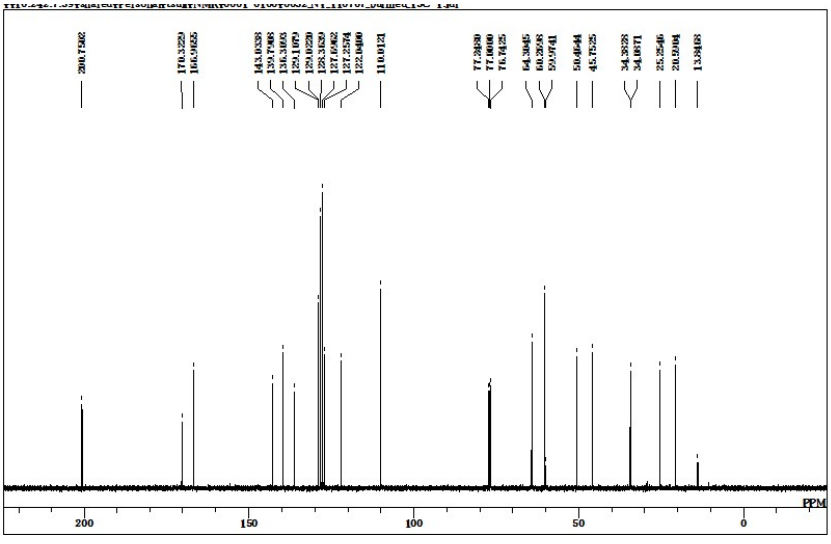
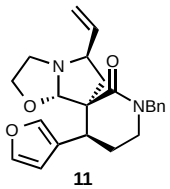


Figure S6. ^{13}C NMR of **8**



11

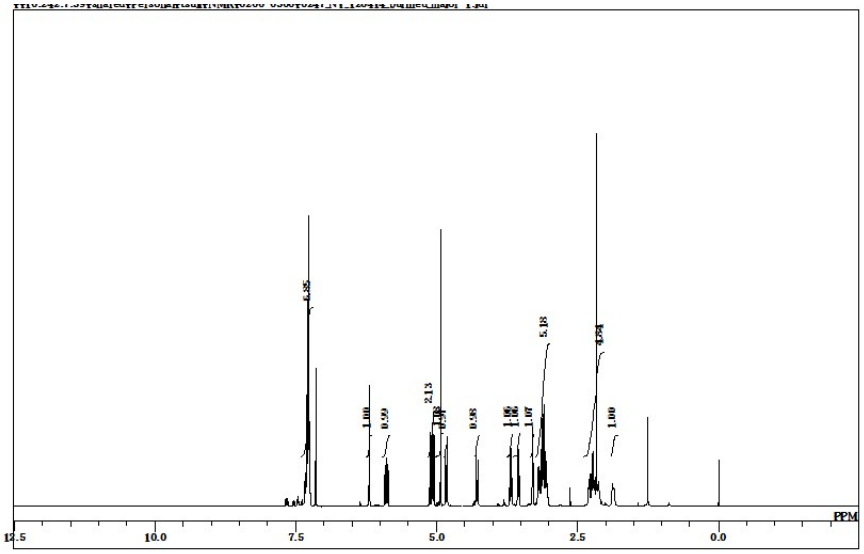


Figure S7. ^{1}H NMR of **11**

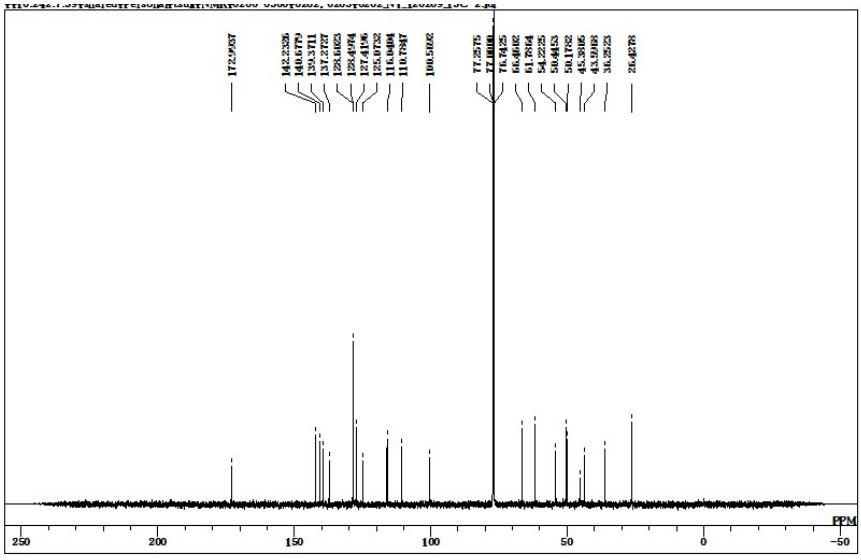
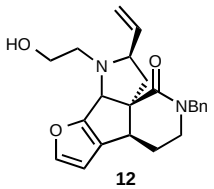


Figure S8. ^{13}C NMR of **11**



12

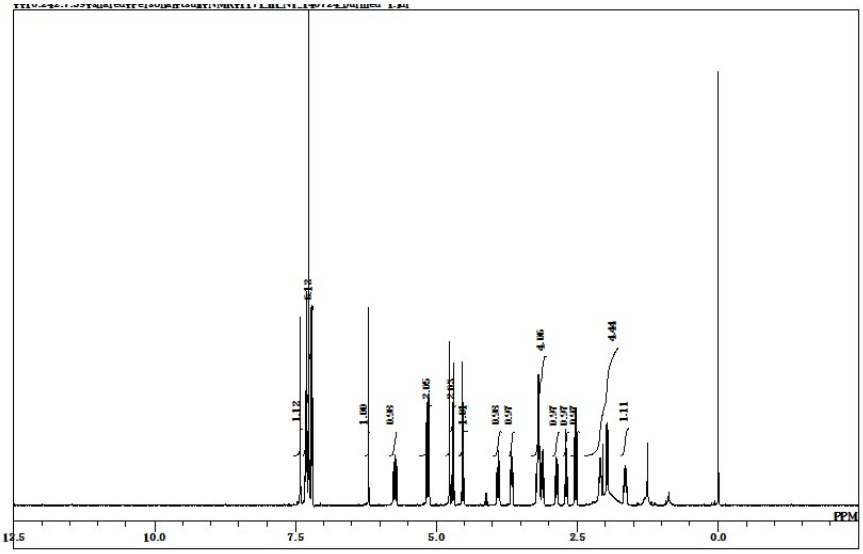


Figure S9. ^{1}H NMR of **12**

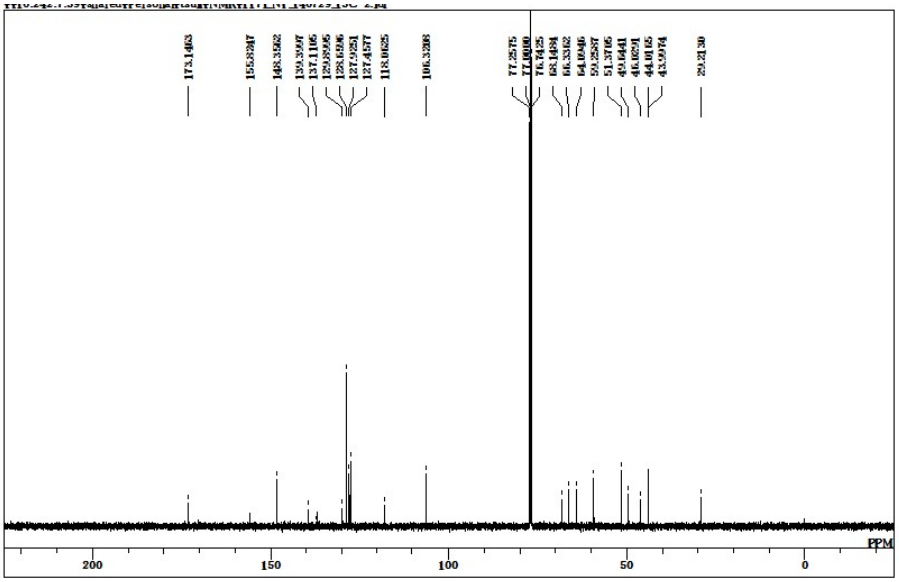
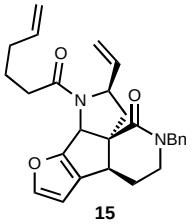


Figure S10. ^{13}C NMR of **12**



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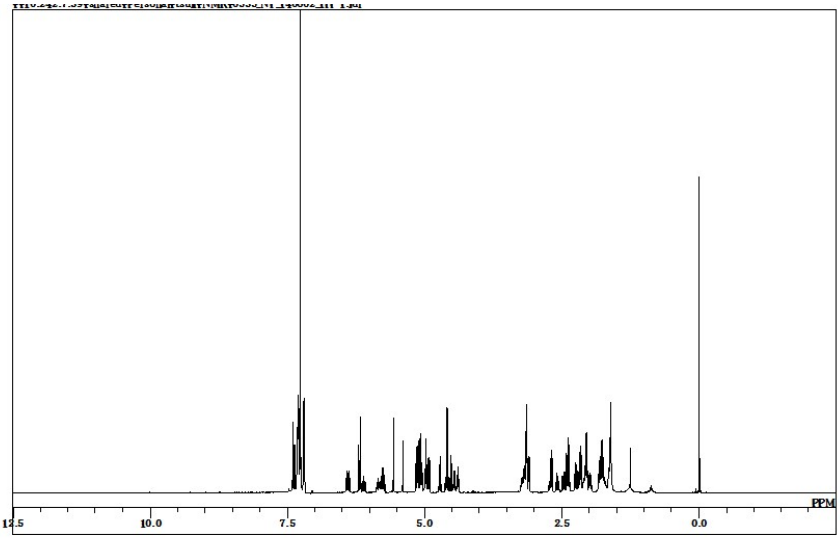


Figure S11. ^{1}H NMR of **15**

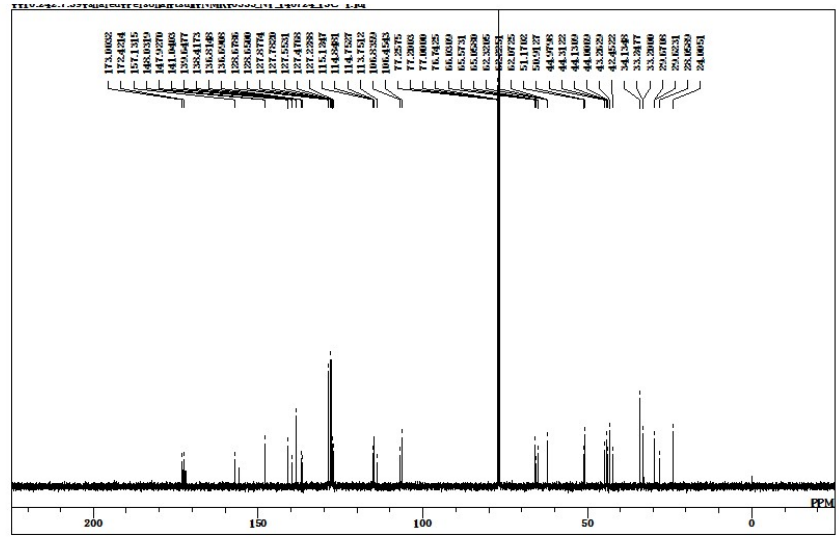
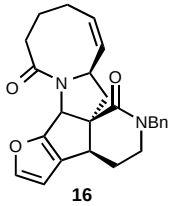


Figure S12. ^{13}C NMR of **15**



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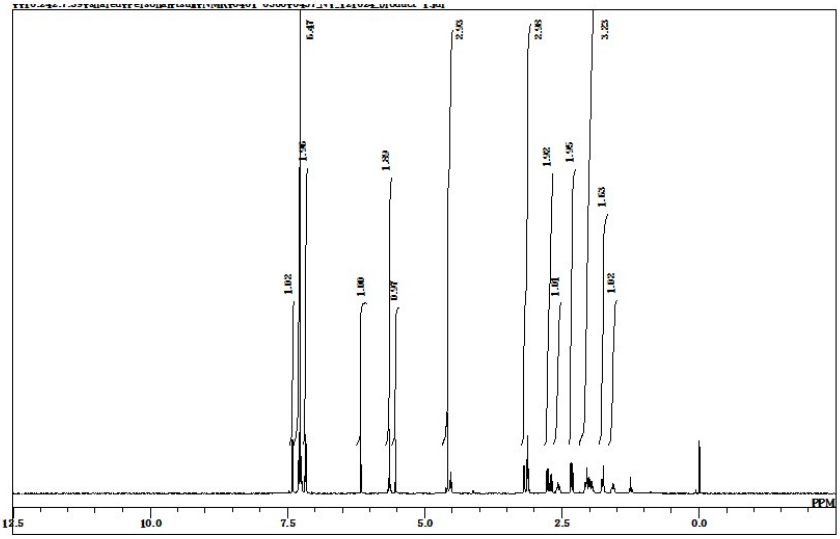


Figure S13. ^{1}H NMR of **16**

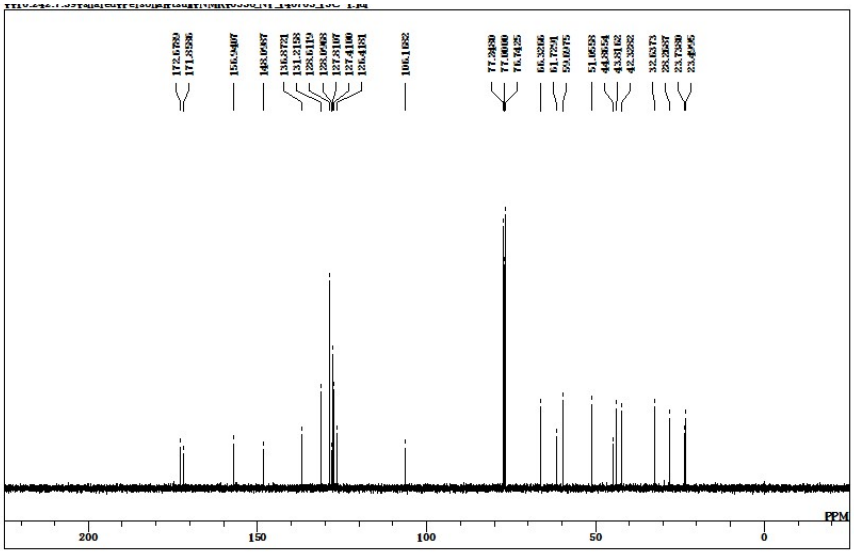


Figure S14. ^{13}C NMR of **16**

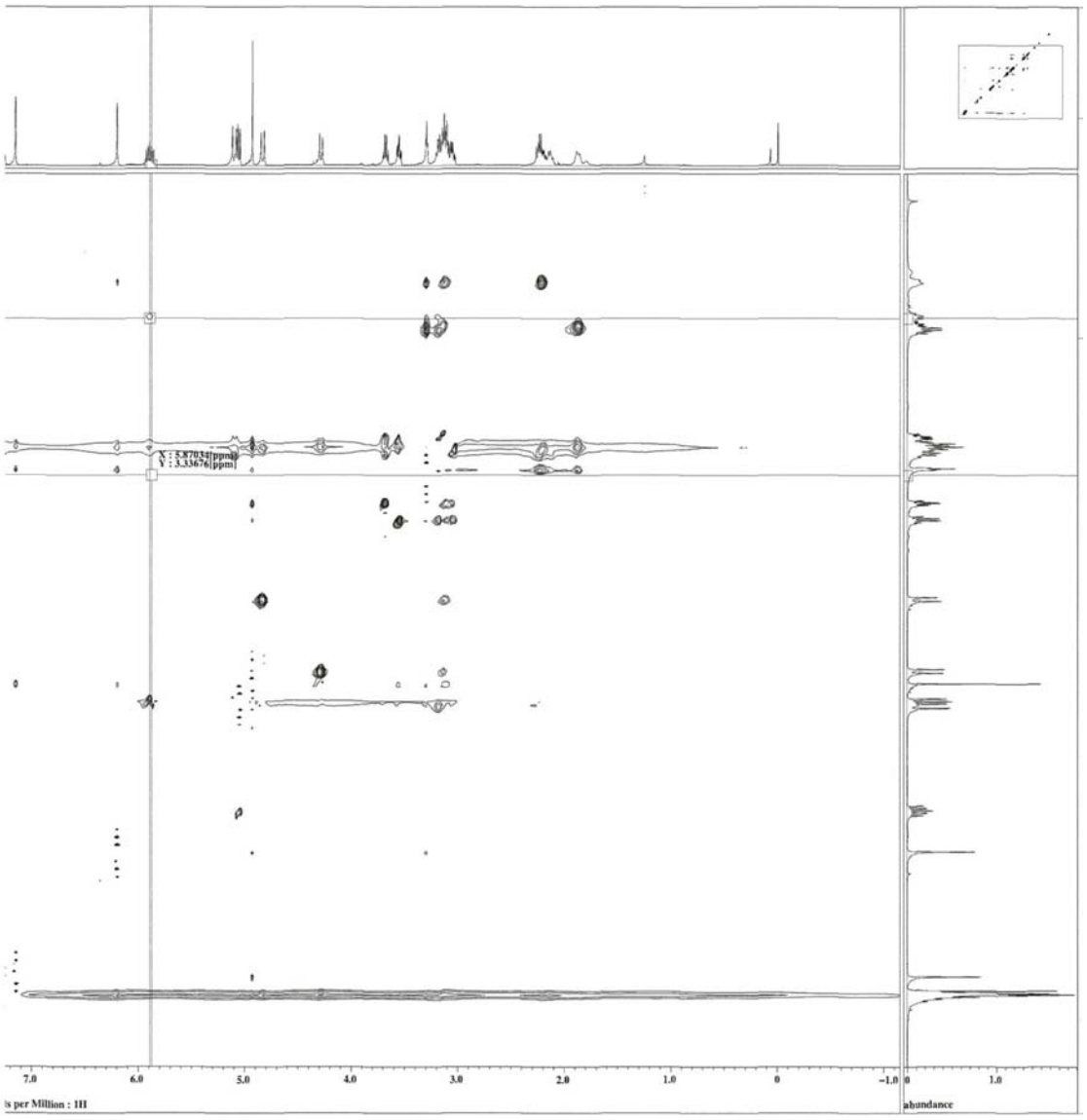


Figure S15. NOESY of **11** in $CDCl_3$

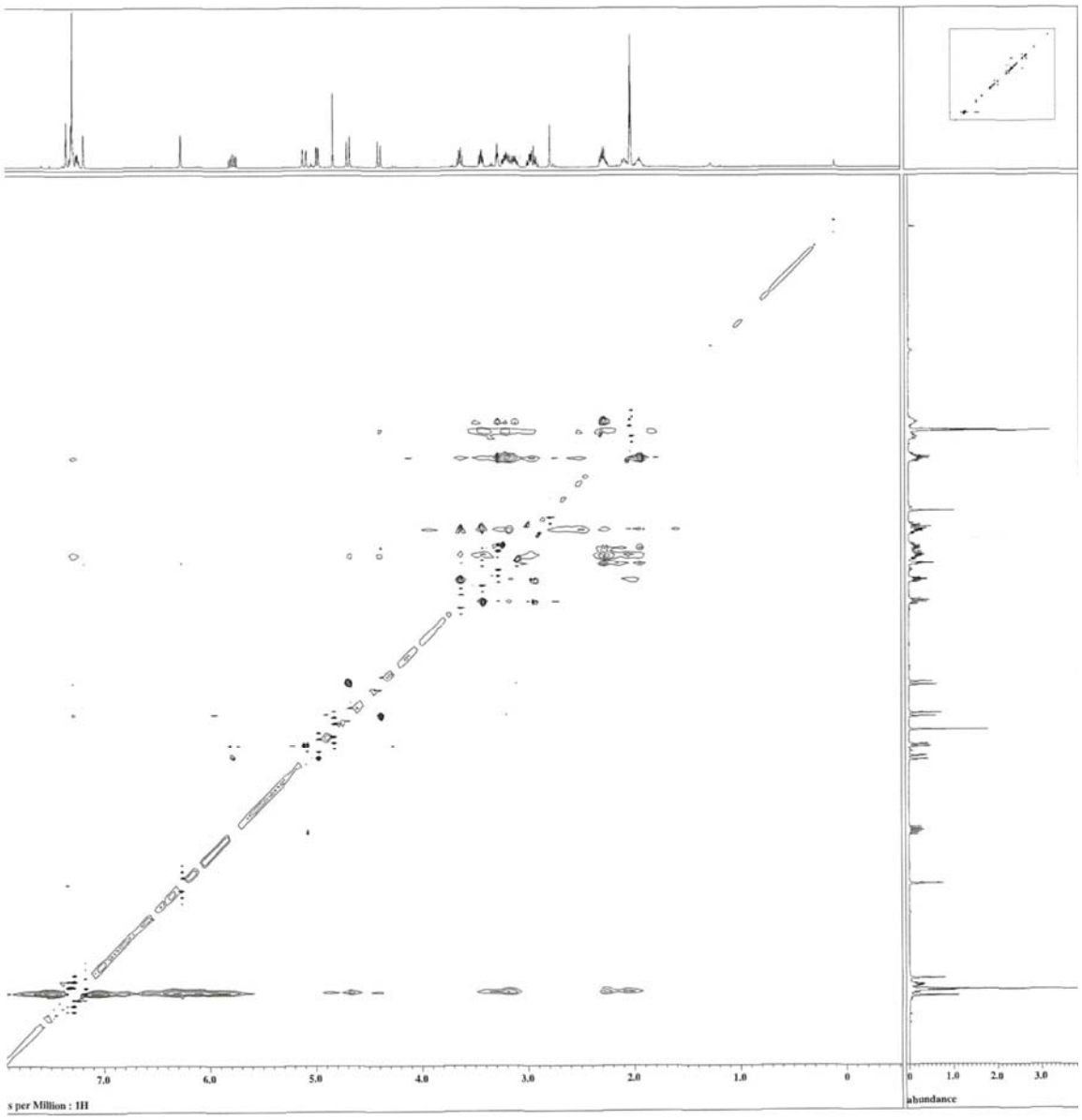


Figure S16. NOESY of **11** in acetone-d_6

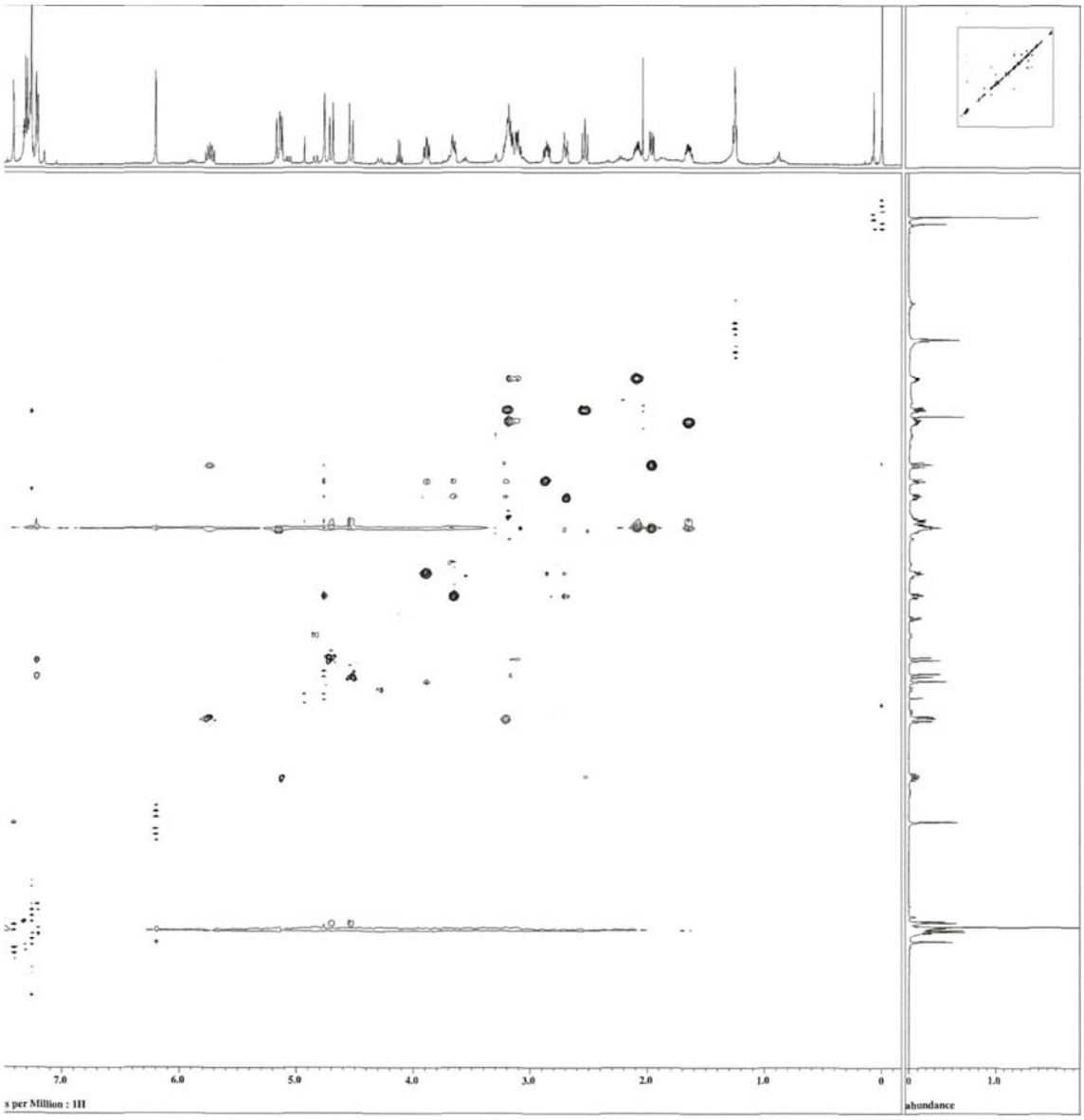


Figure S17. NOESY of **12** in $CDCl_3$

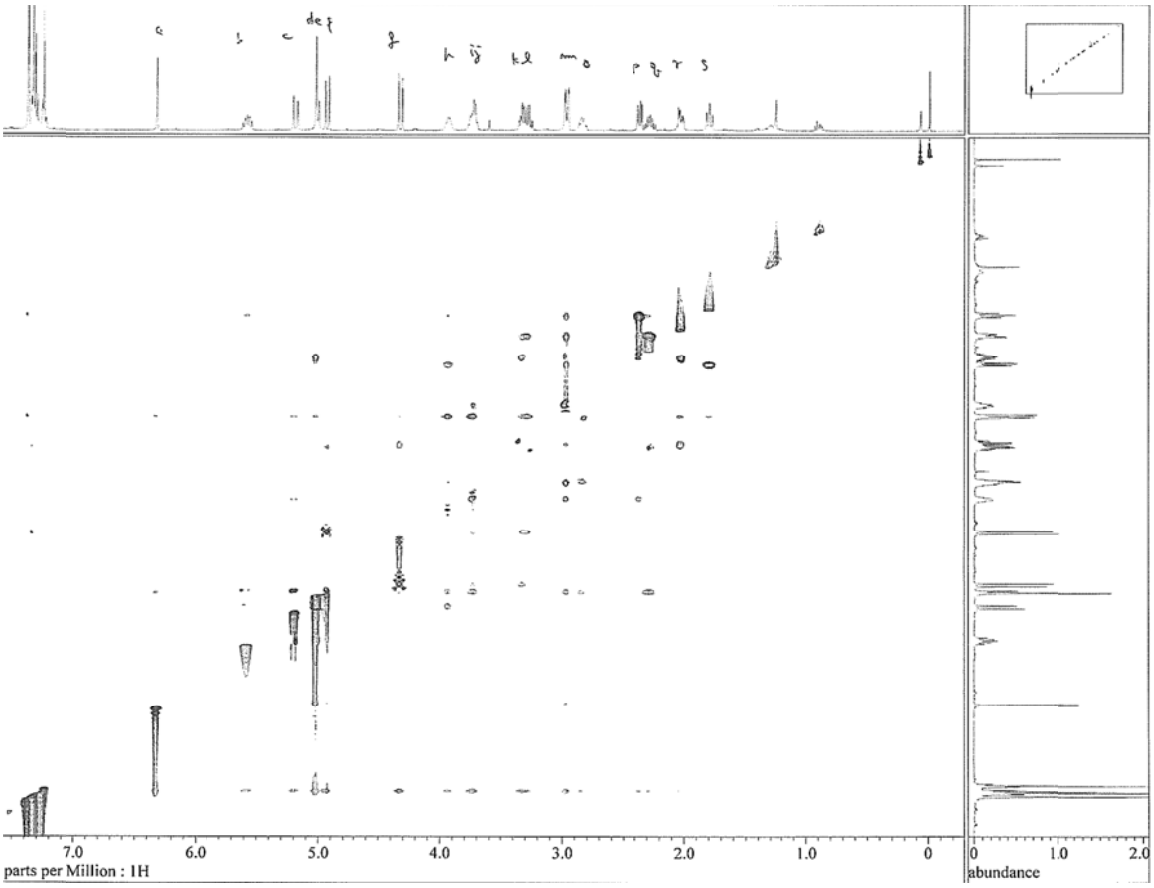
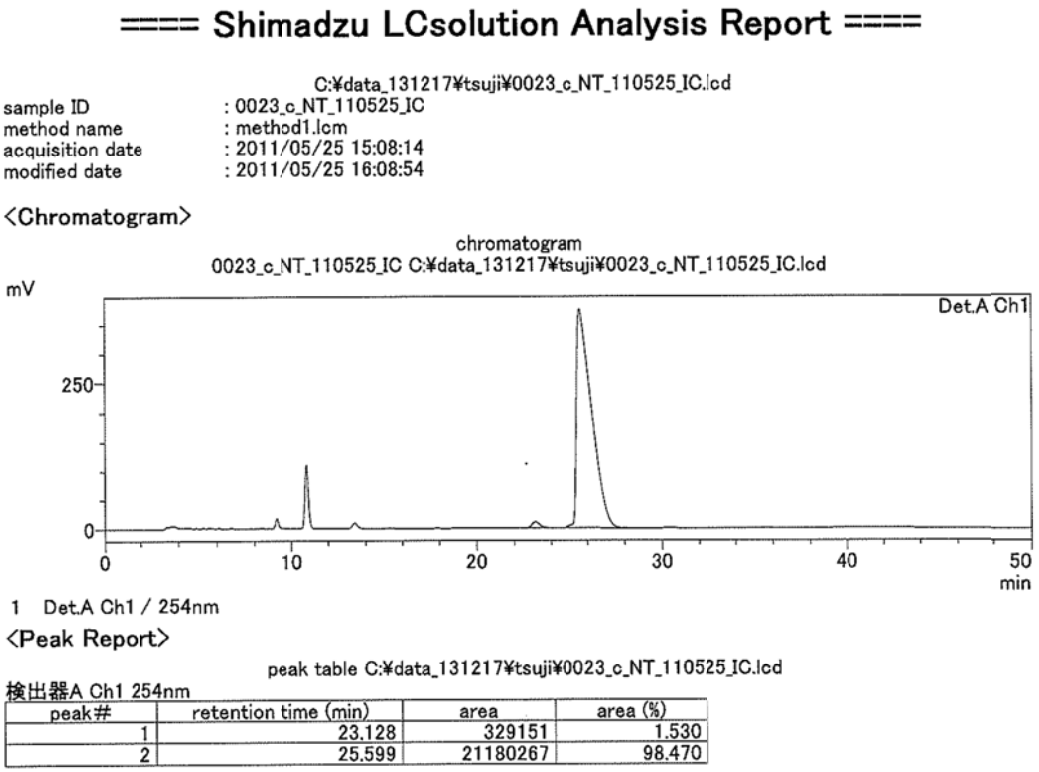


Figure S18. NOESY of **11'** in $CDCl_3$

8. Copies of HPLC charts



==== Shimadzu LCsolution Analysis Report ====

C:¥data_131217¥tsuji¥0023_c_NT_110525_IC.lcd

sample ID : 0023_c_NT_110525_IC
method name : method1.lcm
acquisition date : 2011/05/25 15:08:14
modified date : 2011/05/25 16:08:54

<Chromatogram>

chromatogram
0023_c_NT_110525_IC C:¥data_131217¥tsuji¥0023_c_NT_110525_IC.lcd

1 Det.A Ch1 / 254nm

<Peak Report>

peak table C:¥data_131217¥tsuji¥0023_c_NT_110525_IC.lcd

検出器A Ch1 254nm

peak#	retention time (min)	area	area (%)
1	23.128	329151	1.530
2	25.599	21180267	98.470

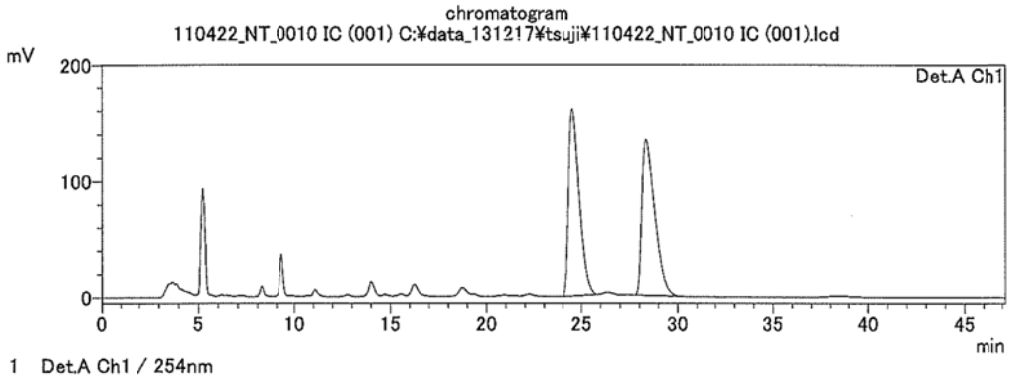
Figure S19. HPLC chart of **S-3**

==== Shimadzu LCsolution Analysis Report ====

C:¥data_131217¥tsuji¥110422_NT_0010 IC (001).lcd

sample ID : 110422_NT_0010 IC (001)
method name : method1.lcm
acquisition date : 2011/04/22 18:53:30
modified date : 2011/04/22 19:42:32

<Chromatogram>



1 Det.A Ch1 / 254nm

<Peak Report>

peak table C:¥data_131217¥tsuji¥110422_NT_0010 IC (001).lcd

検出器A Ch1 254nm

peak#	retention time (min)	area	area (%)
1	24.512	6275589	50.170
2	28.344	6232961	49.830

Figure S19. HPLC chart of (*rac*)-**S-3**