Supporting Information

An organogel formed from a cyclic β-aminoalcohol

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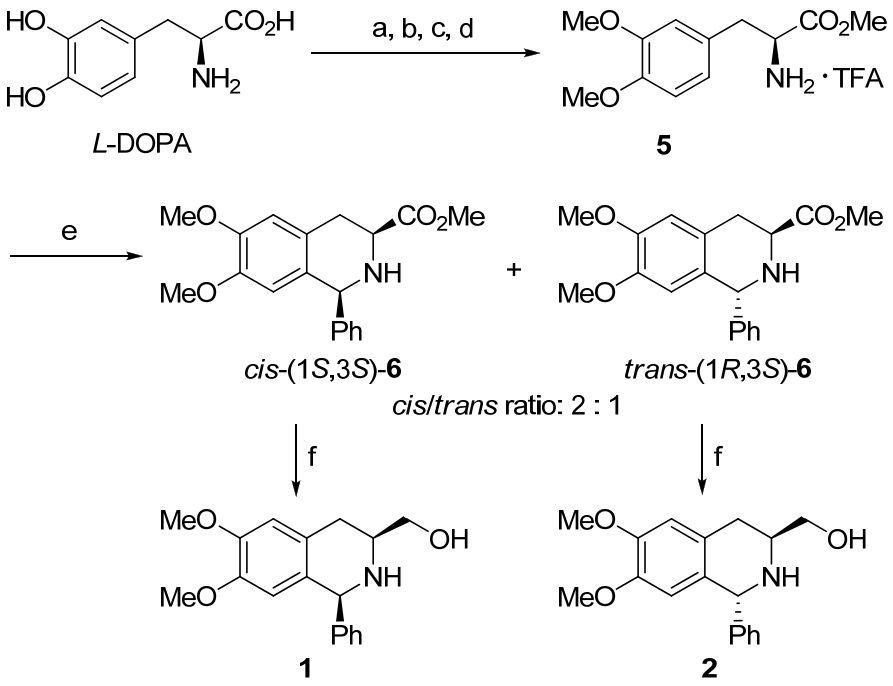
S1. General remarks

All reagents and solvents were obtained from commercial suppliers and used directly without further purification unless otherwise stated. Chromatographic purification was conducted using 100-200 mesh silica gel. TLC was performed on aluminum TLC plate with silica gel GF_{254} and visualized using UV light.

Melting points were measured with a hot-stage XT-4 melting point meter with microscope and thermometer was not corrected. Optical rotations were measured on a Perkin Elmer 341LC polarimeter. HPLC analysis was performed with a Shimadzu Class-VP system on Chiralcel AD-H analytical column with hexane/isopropanol/triethylamine (95/5/0.1) as eluent. 1H NMR and 13C NMR spectra were recorded on a Bruker AV400 or AV600 spectrometer at 300K unless otherwise stated. Chemical shifts were reported in ppm with tetramethylsilane ($\delta = 0.00$) for ^{1}H NMR and with deuterated solvents (for deuterium chloride, $\delta = 77.00$) for ^{13}C NMR. 2D NOESY experiment was performed on a Bruke AV600 spectrometer with a mixing time of 600 ms. MALDI-TOF-MS were recorded with Bruker Reflex III in positive-ion mode at an accelerating voltage of 20 kV equipped with a 337-nm nitrogen laser. Elemental analyses (EA) for C, H and N were carried out with a VarioEL instrument. FTIR spectra were performed on a Bio-Rad FTS135 infrared spectrometer with KBr pellets or with a cell for solution. UV-Vis spectra were recorded on a Shimidzu UV-2550 UV-vis spectrophotometer using a 0.5 mm cuvette. Scanning electronic microscopy (SEM) photo were taken using an XL 30 ESEM FEG field emission scanning electron microscope with 15 kV or 25 kV operating voltage. Powder XRD patterns were recorded by Rigaku D/max 2000 X-ray diffractometer with CuKα1 radiation source. X-ray crystallographic analysis was performed on a Bruker SMART APEX □ CCD diffractometer with graphite-monochromatic MoKα radiation ($\lambda = 0.71073$ Å) operated at 2.0 kW (50 kV, 40 mA). The structures were solved by direct methods using the program SHELXL-97 and refined with anisotropic thermal parameters by full matrix least squares on F^2 values with SHELXL-97. Hydrogen atoms were located from the expected geometry and were refined only with isotropic parameters.

S2. Synthesis and characterization

Synthesis of compound 1 and 2: As shown in scheme S1, both compounds **1** and **2** were prepared by reduction of corresponding ester *cis*-(1*S*, 3*S*)-**6** and *trans*-(1*R*, 3*S*)-**6** with LAH, respectively, and structures were confirmed with NMR spectra, MALDI-TOF MS and EA. The ester precursors *cis*-(1*S*, 3*S*)-**6** and *trans*-(1*R*, 3*S*)-**6** were prepared from *L*-DOPA according to procedures in literature with small modifications at the stage of Pictet-Spengler cyclization.[S1] Methyl *L*-3,4-dimethoxyphenylalaninate trifluoroacetic acid salt **5** was neutrialized with sodium bicarbonate to acid-free form before used in the Pictet-Spengler reaction. The ^{1}H and ^{13}C NMR spectra of both diastereomer **6**s are in consistent with report,[S2] but the optical rotations are not in agreement with that literature. Hitherto we confirm the structures with 2D NOESY, MALDI-TOF MS and EA, and the purity with chiral HPLC.



Scheme S1 Synthesis of compound **1** and **2**. Conditions: a) methanol, $SOCl_2$, reflux, 90%; b) Boc_2O, TEA, MeOH, r.t., 95%; c) MeI, K_2CO_3, butanone, reflux, 98%; d) TFA-DCM (5%), r.t., 80%; e) $NaHCO_3$; PhCHO, MS 3A, DCM, r.t.; TFA, reflux, 85%; f) LAH, THF, 0 ^oC-r.t., 87-89%.

Methyl *cis*-(1*S*, 3*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylate, *cis*-(1*S*, 3*S*)-6 and methyl *trans*-(1*R*, 3*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylate, *trans*-(1*R*, 3*S*)-6: A solution of **5** (23.76 g, 99.3 mmol) in dichloromethane (240 ml) was washed with aqueous saturated sodium bicarbonate and saturated brine and dried with magnesium sulfate, to which was added MS 3A (36.0 g) and phenylaldehyde (11.1 ml, 109.2 mmol) at 0 ^oC with ice-water bath under argon atmosphere. The reaction mixture was then stirred at room temperature overnight. The MS 3A was removed by filtration followed by evaporation to remove solvent. The residues were dissolved in TFA (350 ml) and heated to reflux for more than 8 hr under argon atmosphere. TFA was removed by distillation before addition of dichloromethane. The dichloromethane solution was then washed with aqueous saturated sodium bicarbonate (twice) and saturated brine, dried with magnesium sulfate and concentrated to dryness to give crude diastereomeric mixture (*cis*/*trans* ratio: 2/1 by ^1H NMR). The two isomers were separated by silica gel column with ethyl acetate/petroleum ether as eluent (1/5-2/5) to give *cis*-(1*S*, 3*S*)-**6** (16.10 g) and *trans*-(1*R*, 3*S*)-**6** (6.95 g), yield 49% and 21% respectively.

cis-(1*S*, 3*S*)-**6**: optical purity >99.9% ee, white powder, mp 112-114 ^oC, $[\alpha]_D^{25}$ = -47.2° (c = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 5H, 1-ArH), 6.64 (s, 1H, 5-H), 6.17 (s, 1H, 8-H), 5.10 (s, 1H, 1-H), 3.90 (t, J = 5.2 Hz, 1H, 3-H), 3.86 (s, 3H, 6-CH_3O), 3.77 (s, 3H, 3-CO_2CH_3), 3.59 (s, 3H, 7-CH_3O), 3.08 (m, 4-CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.88, 147.69, 147.33, 143.80, 130.15, 128.96, 128.25, 127.77, 125.99, 111.25, 110.49, 62.79, 56.47, 55.81, 55.77, 52.11, 32.14. MALDI-TOF MS: 328 ($[M-H]^+$) and 330 ($[M+H]^+$). EA: calculated C 69.71, H

6.47, N 4.28; found C 69.70, H 6.48, N 4.27.

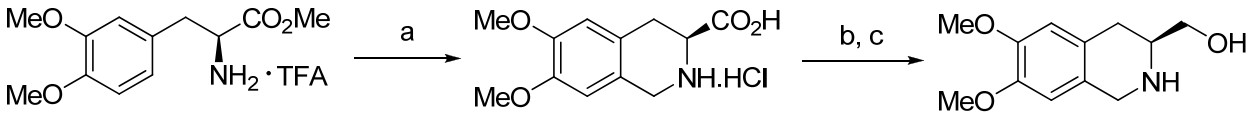
trans-(1*R,* 3*S*)-**6**: optical purity 98.8%, pale yellow bulk, mp 58-61 ^{o}C, $[\alpha]_D^{25}$ = -50.8° (c = 0.35, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): 7.30 (m, 3H, 1-ArH), 7.19 (d, J = 7.2 Hz, 2H, 1-ArH), 6.66 (s, 1H, 5-H), 6.34 (s, 1H, 8-H), 5.26 (s, 1H, 1-H), 3.88 (s, 3H, 6-CH_3O), 3.80 (t, *J* = 5.2 Hz, 1H, 3-H), 3.71 (s, 3H, 3-CO_2CH_3) 3.68 (s, 3H, 7-CH_3O), 3.16 (dd, *J* = 16.0 Hz, 5.2 Hz, 1H, 4-H_β), 3.01 (dd, *J* = 16.0 Hz, 8.8 Hz, 1H, 4-H_α). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.82, 147.91, 147.44, 144.53, 128.67, 128.37, 127.95, 127.35, 125.65, 111.14, 110.85, 58.85, 55.82, 52.05, 51.38, 31.04. MALDI-TOF MS: 327 ($[M-H]^+$) and 328 ($[M+H]^+$). EA: calculated C 69.71, H 6.47, N 4.28; found C 69.69, H 6.49, N 4.27.

***cis*-(1S, 3S)-6,7-Dimethoxy-1-phenyl-3-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline, 1 and *trans*-(1S, 3S)-6,7-Dimethoxy-1-phenyl-3-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline, 2**: To a suspension of LAH (1.08 g, 27.1 mmol) in THF (10 ml), was added dropwise a solution of *cis*-(1*S*, 3*S*)-**6** (5.85 g, 24.6 mmol) in THF (60 ml) at 0 °C. The reaction mixture was then stirred overnight at room temperature followed by cooled to 0 °C and quenched with water. The insoluble precipitates were removed by filtration through celite and the mother liquid was concentrated. The residues was dissolved in dichloromethane and washed with saturated sodium bicarbonate and brine before dried with magnesium sulfate. Solvent was removed by evaporation to give compound **1**, yield 89%. Optical purity >98.5% ee, offwhite powder, mp 165-167 °C, $[\alpha]_D^{25}$ = 22.8° (c = 0.5, THF). ^{1}H NMR ($CDCl_3$): δ 7.32 (m, 5H: 1-ArH), 6.61 (s, 1H, 5-H), 6.17 (s, 1H, 8-H), 5.06 (s, 1H, 1-H), 3.86 (s, 3H, 6-CH_3O), 3.80 (dd, *J* = 10.69 Hz, 3.56 Hz, 1H, one of 3-CH_2OH), 3.59 (s, 3H, 7-CH_3O), 3.56 (dd, *J* = 10.84 Hz, 7.85 Hz, 1H, one of 3-CH_2OH), 3.25 (m, 1H, 3-H), 2.70 (m, 2H, 4-CH_2); ^{13}C NMR (150 MHz, $CDCl_3$): δ 147.69, 147.14, 144.31, 130.59, 128.93, 128.56, 127.66, 126.87, 111.44, 110.70, 66.21, 62.72, 55.86, 55.83, 55.61, 31.52. MALDI-TOF MS: 298 ($[M-H]^+$) and 300 ($[M+H]^+$). EA: calculated: C 72.22, H 7.07, N 4.68; Found: C 72.20, H 7.09, N 4.69.

2: This compound was prepared from *trans*-(1*R*, 3*S*)-**6** by reduction with LAH in similar procedure for synthesis of **1**, yield 87%. Optical purity >97% ee, pale yellow powder, mp 114-116 °C, $[\alpha]_D^{25}$ = -21.3° (c = 0.5, THF). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 3H, 1-ArH), 7.16 (d, *J* = 8.10 Hz, 2H, 1-ArH), 6.62 (s, 1H, 5-H), 6.41 (s, 1H, 8-H), 5.22(s, 1H, 1-H), 3.88 (s, 3H, 6-CH_3O), 3.72 (s, 3H, 7-CH_3O), 3.66 (dd, *J* = 10.74 Hz, 3.77 Hz, one of 3-CH_2OH), 3.48 (dd, *J* = 10.92 Hz, 7.53 Hz, one of 3-CH_2OH), 3.09 (m, 1H, 3-H), 2.66 (m, 2H, 4-CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.98, 147.26, 144.59, 128.70, 128.23, 128.15, 127.11, 126.75, 111.50, 110.95, 65.64, 58.92, 55.88, 55.84, 48.83, 30.55. MALDI-TOF MS: 298 ($[M-H]^+$) and 300 ($[M+H]^+$). EA: calculated: C 72.22, H 7.07, N 4.68; Found: C 72.18, H 7.08, N 4.67.

Synthesis of 3 and 4: (*S*)-6,7-Dimethoxy-3-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline **3** was prepared from **7** by esterification and reduction as shown in Scheme S2.[S2] Compound **7** was derived from compound **5** in same

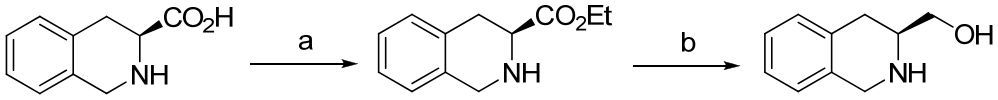
procedure reported by O'Reilly and Lin.[S3] Characterizations were in consistent with those literatures.



5 **7** **3**

Scheme S2 Synthesis of (S)-6,7-dimethoxy-3-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline **2**. Conditions: a) CH_2O, 37% HCl, H_2O, reflux, 57%; b) methanol, $SOCl_2$, reflux, 87%; c) LAH, THF, 0 ^oC-r.t., 89%.

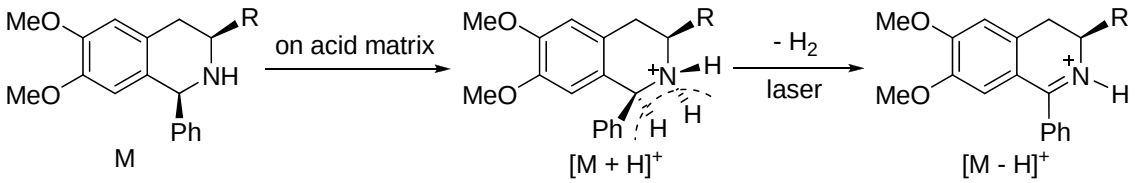
As shown in scheme S3, (*S*)-3-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline **4** was prepared from corresponding carboxylic acid **8** in same procedures for synthesis of **3** and characterizations were in consistent with the literature.[S4]



8 **9** **4**

Scheme S3 Synthesis of (*S*)-3-hydroxymethyl-1, 2, 3, 4-tetrahydroisoquinoline **1**. Conditions: a) ethanol, $SOCl_2$, reflux, 91%; b) LAH, THF, 78%.

MALDI-TOF MS spectra: The cyclic amines **1**, **2** and **6** show two molecular ion peaks corresponding to $[M-H]^+$ and $[M+H]^+$. This unexpected condition is less noticed except sole systematic report by Lou.[S5] The ammonium, protonated amine by matrix, suffers 1, 2-dehydrogenation under laser irradiation to produce protonated imine as shown in the Scheme S4. The presence of two aryl groups on the methylene directly connected to amine should have played important role of promoting dehydrogenation and stabilizing result iminium ion. The MALDI-TOF spectra are shown in Fig. S1-4.



M $[M + H]^+$ $[M - H]^+$

Scheme S4 Dehydrogenation of amines by laser irradiation in MALDI-TOF MS.[S5]

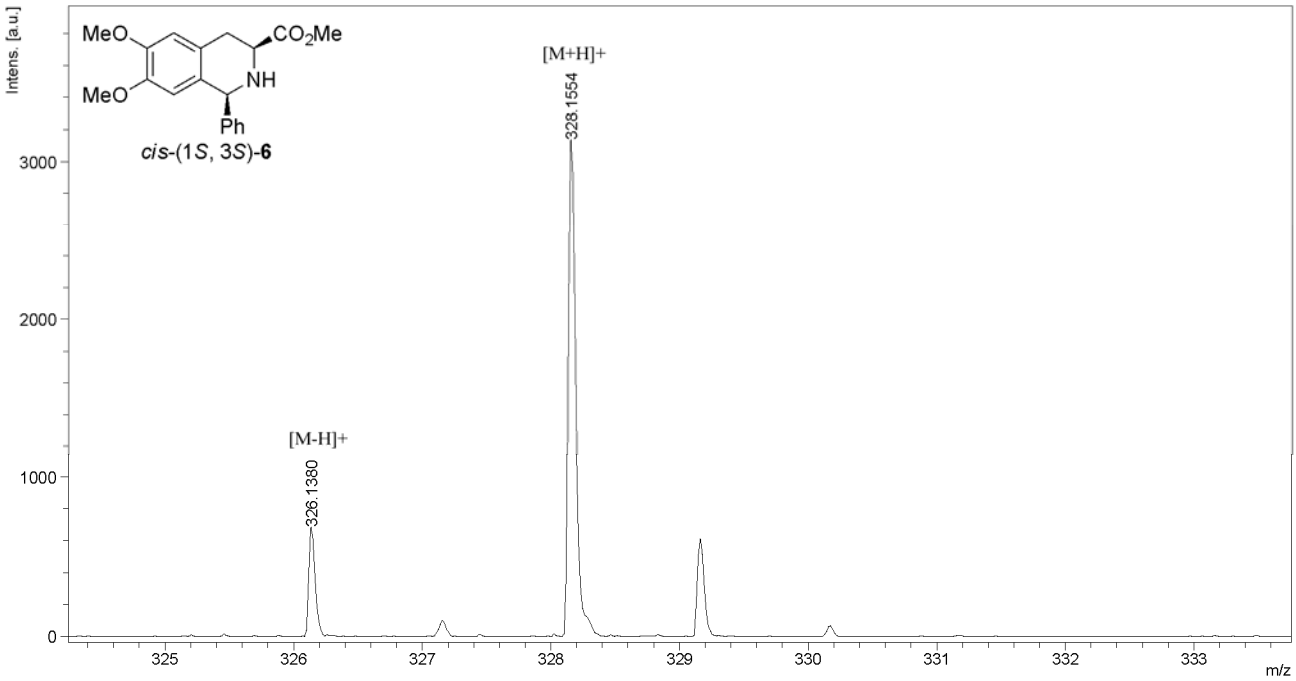


Figure S1 MALDI-TOF spectra of *cis*-(1*S*, 3*S*)-**6**

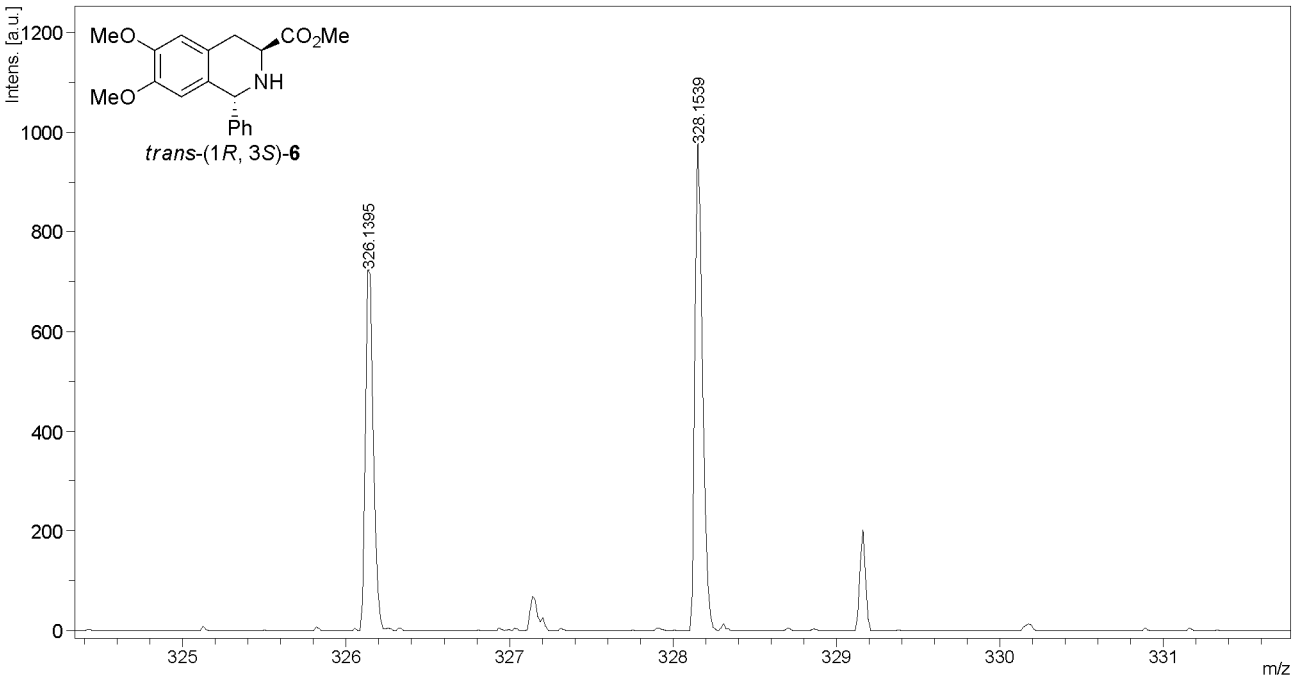


Figure S2 MALDI-TOF spectra of *trans*-(1*R*, 3*S*)-**6**

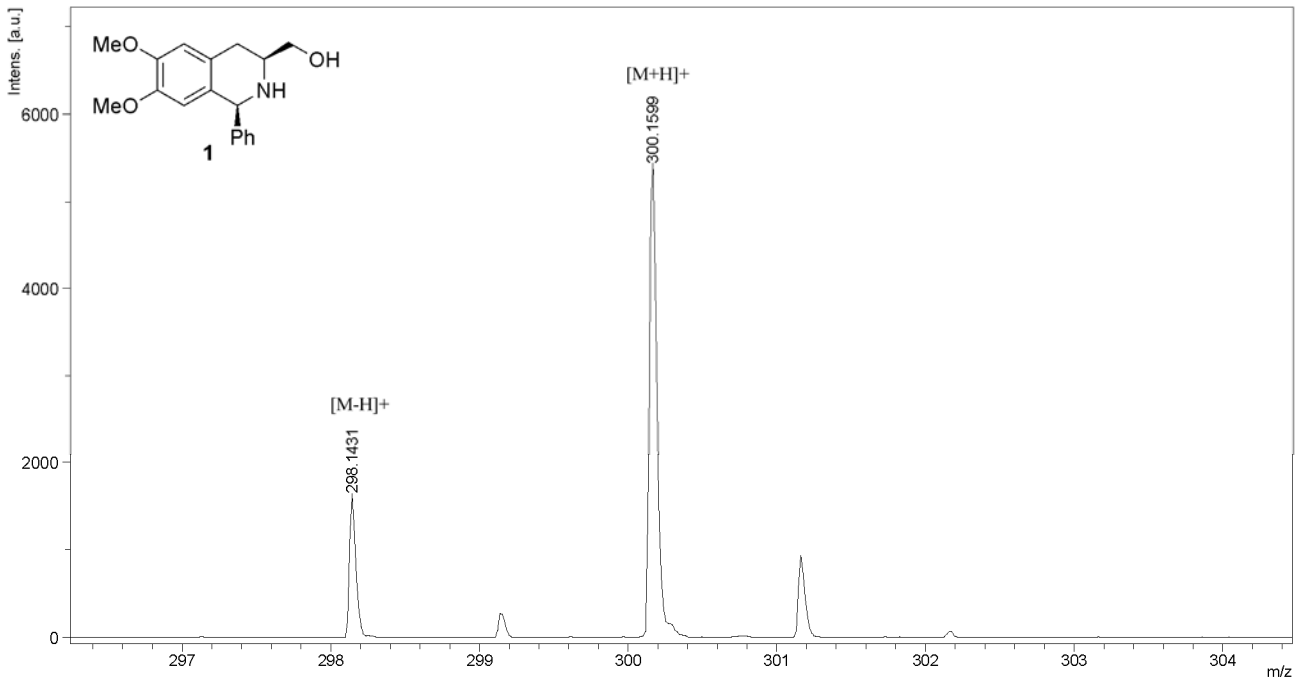


Figure S3 MALDI-TOF spectra of **1**

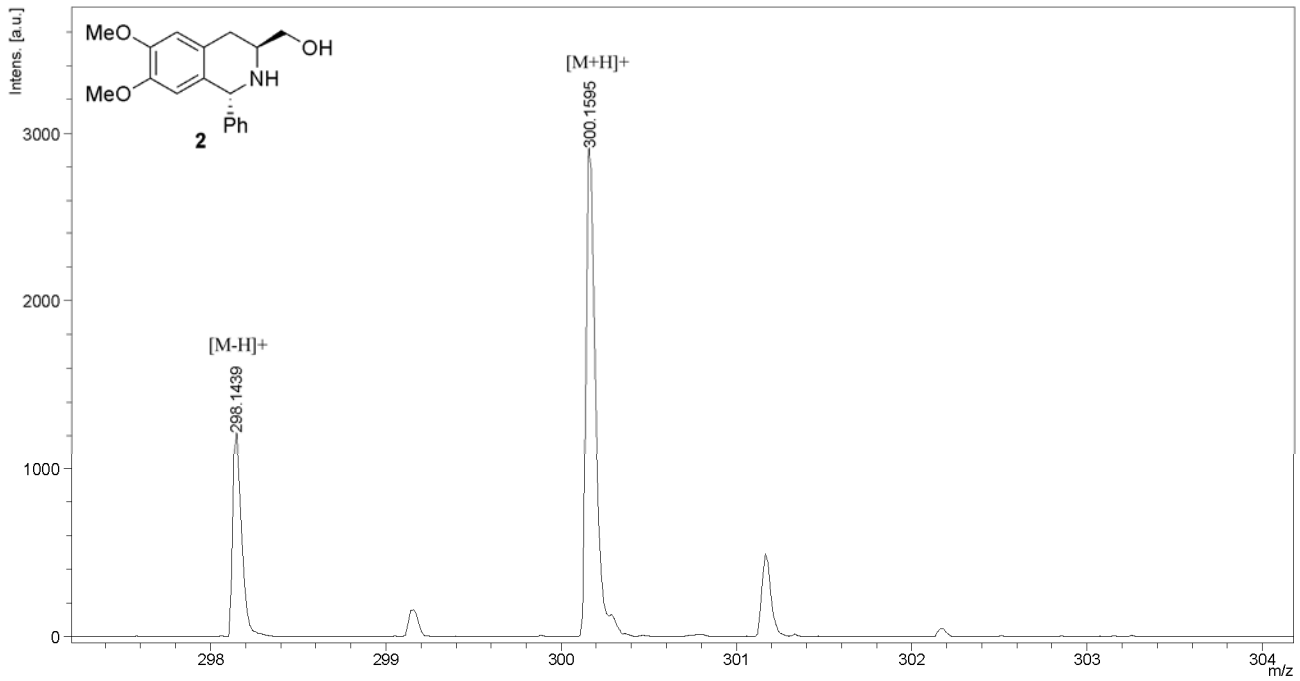


Figure S4 MALDI-TOF spectra of **2**

NMR spectra: The structures of **1**, **2** and **6** are assigned with ^{1}H, ^{13}C and 2D NMR. The ^{1}H and ^{13}C NMR spectra of both epimers of **6** are in agreement with literature.[S2] The *cis* configuration of **6** and **1** are confirmed with 2D NOESY experiments in which a cross peak ascribed to two chiral center can be observed.

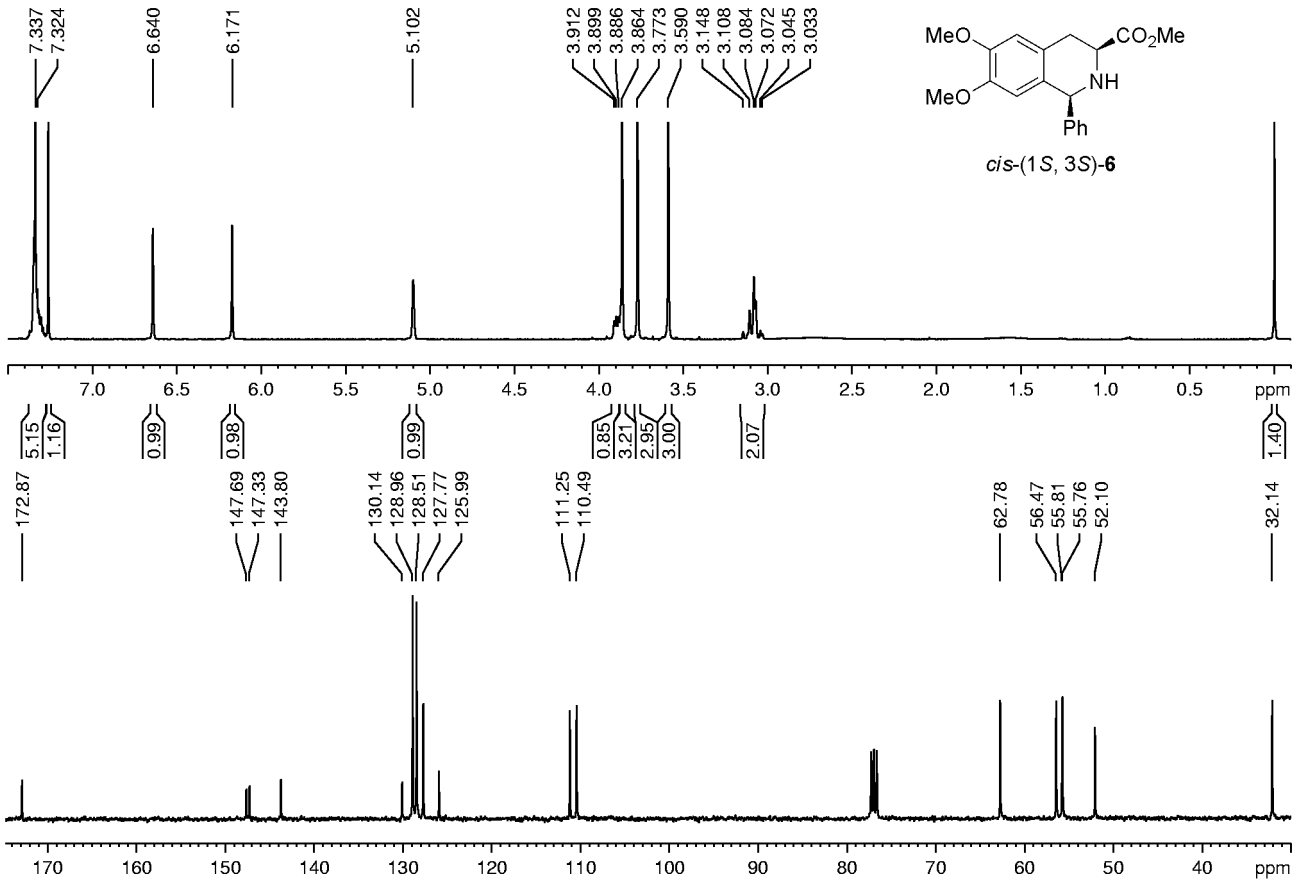


Figure S5 ^{1}H and ^{13}C NMR of *cis*-(1*S*, 3*S*)-**6**

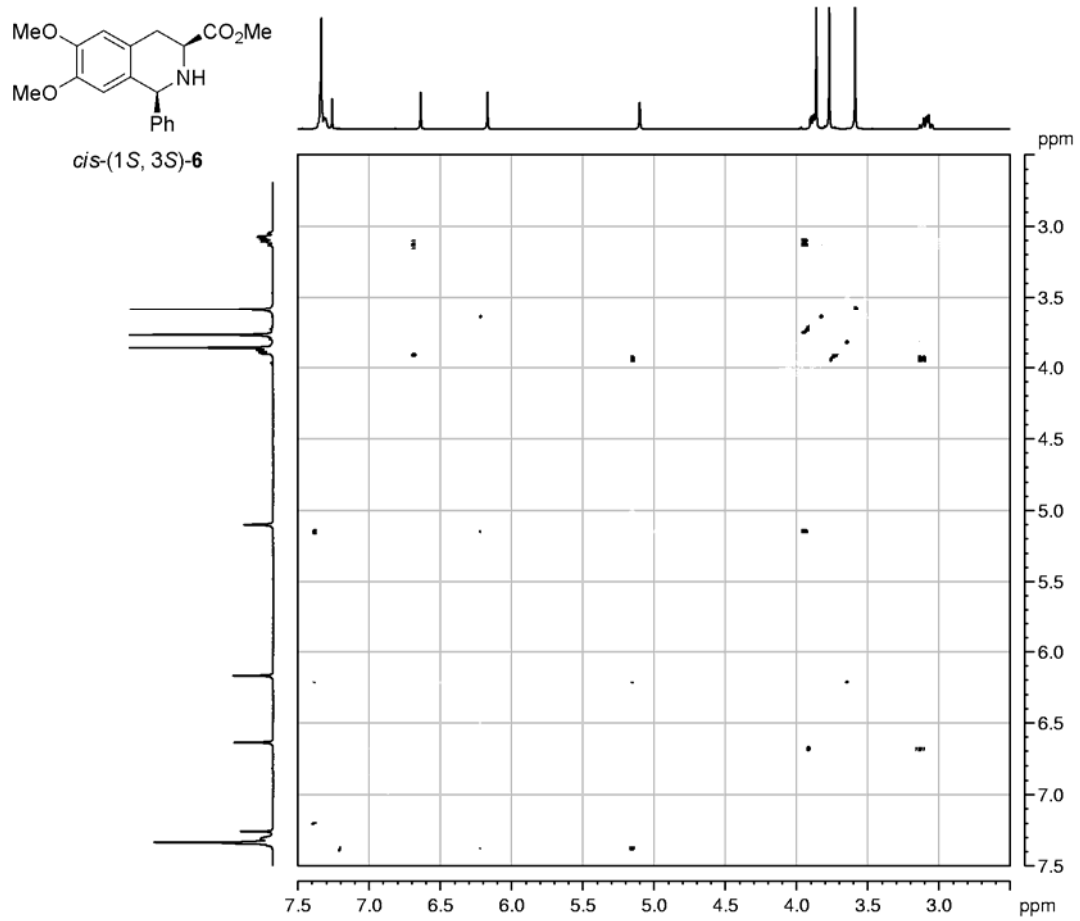


Figure S6 2D NOESY of *cis*-(1*S*, 3*S*)-**6**

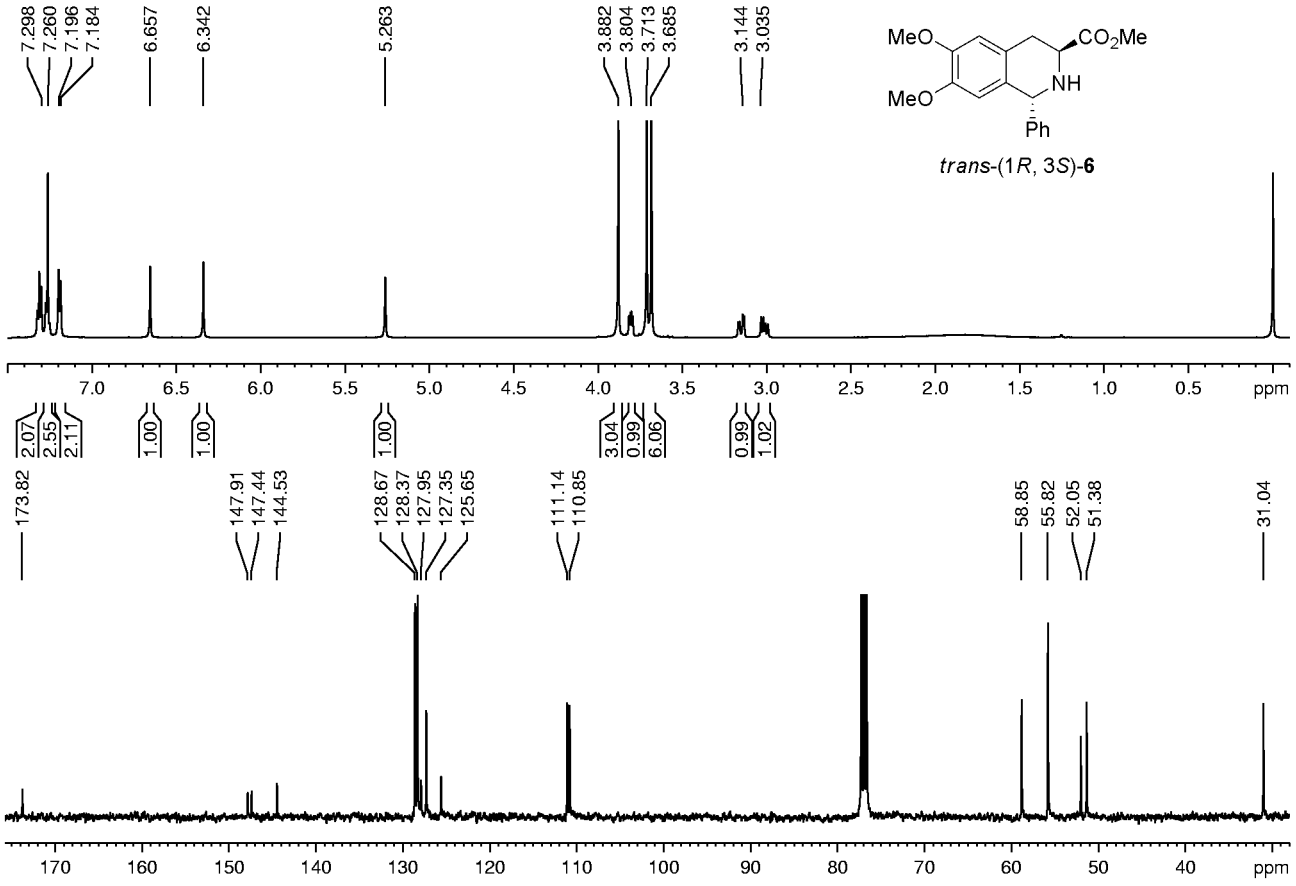


Figure S7 ^{1}H and ^{13}C NMR of *trans*-(1*R*, 3*S*)-**6**

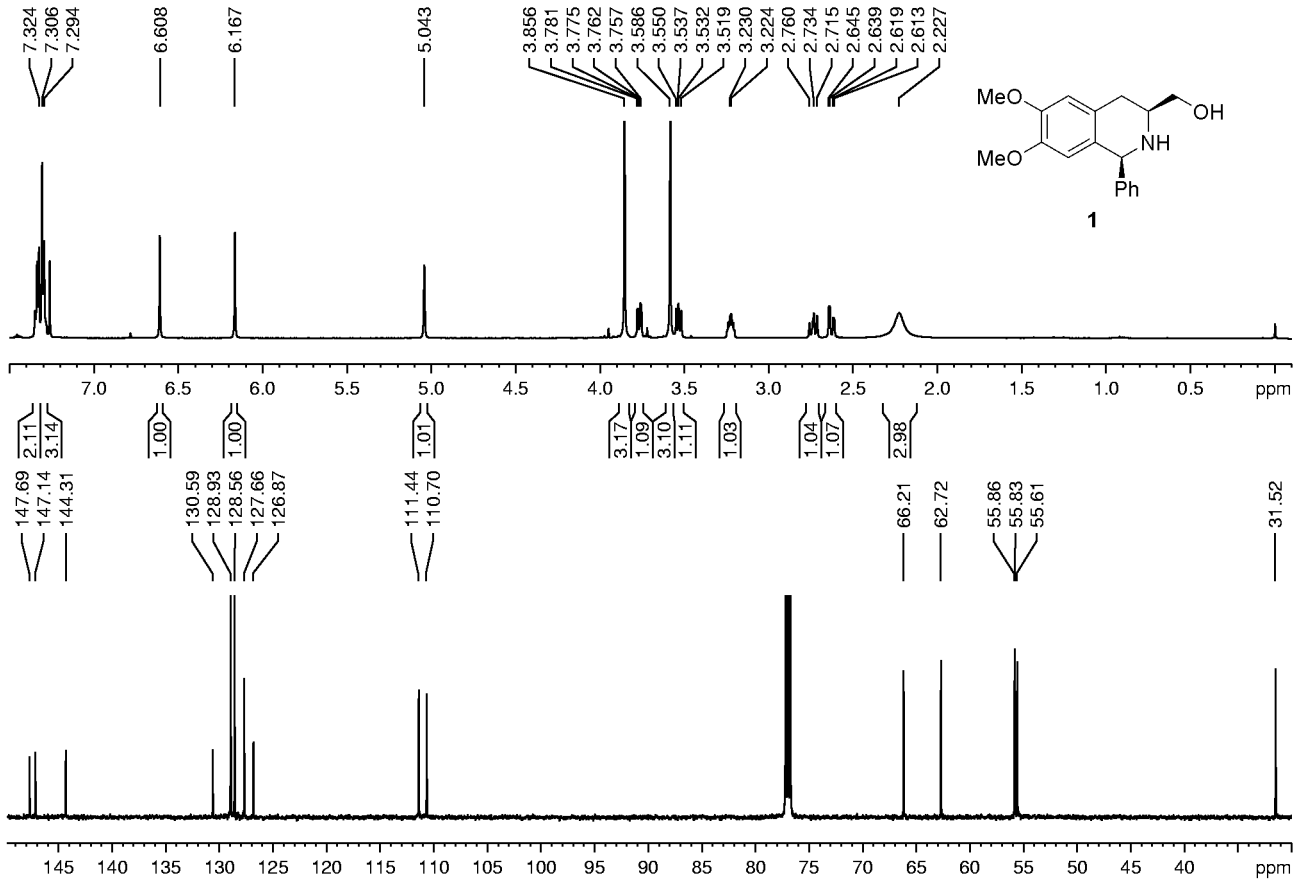


Figure S8 ^{1}H and ^{13}C NMR of **1**

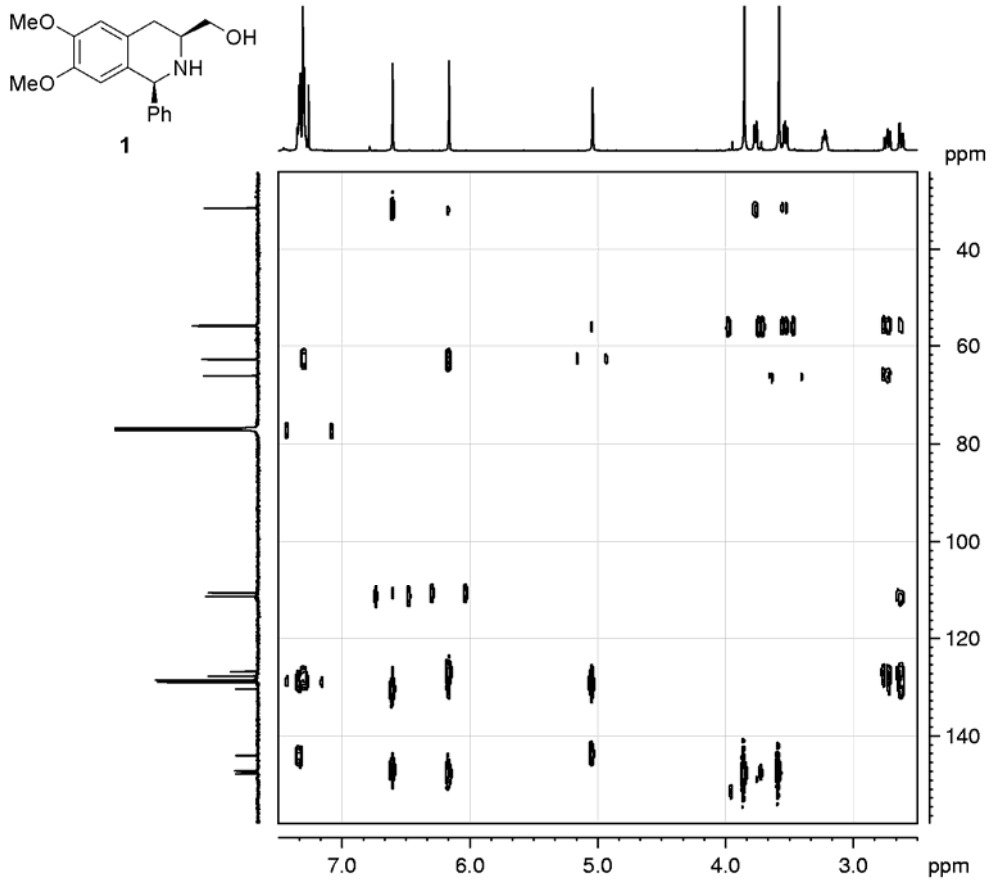


Figure S9 2D HMBC of **1**

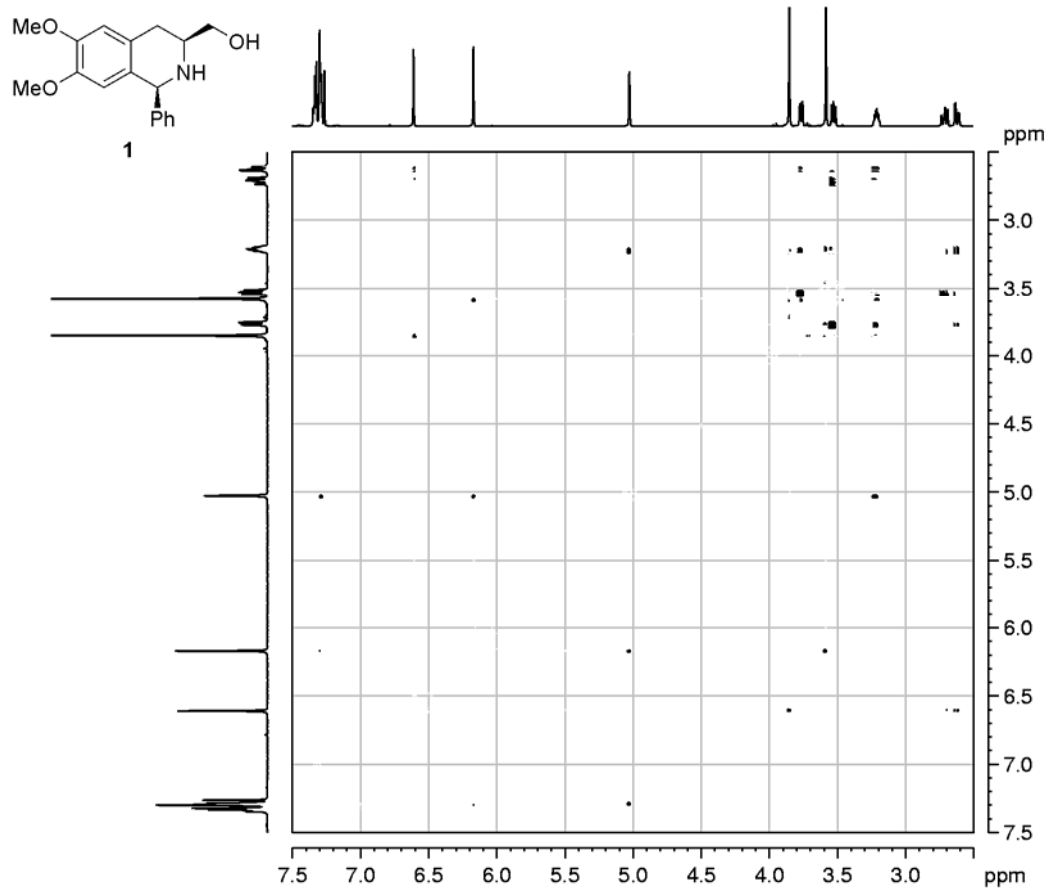


Figure S10 2D NOESY of **1** (mixing time 600 ms)

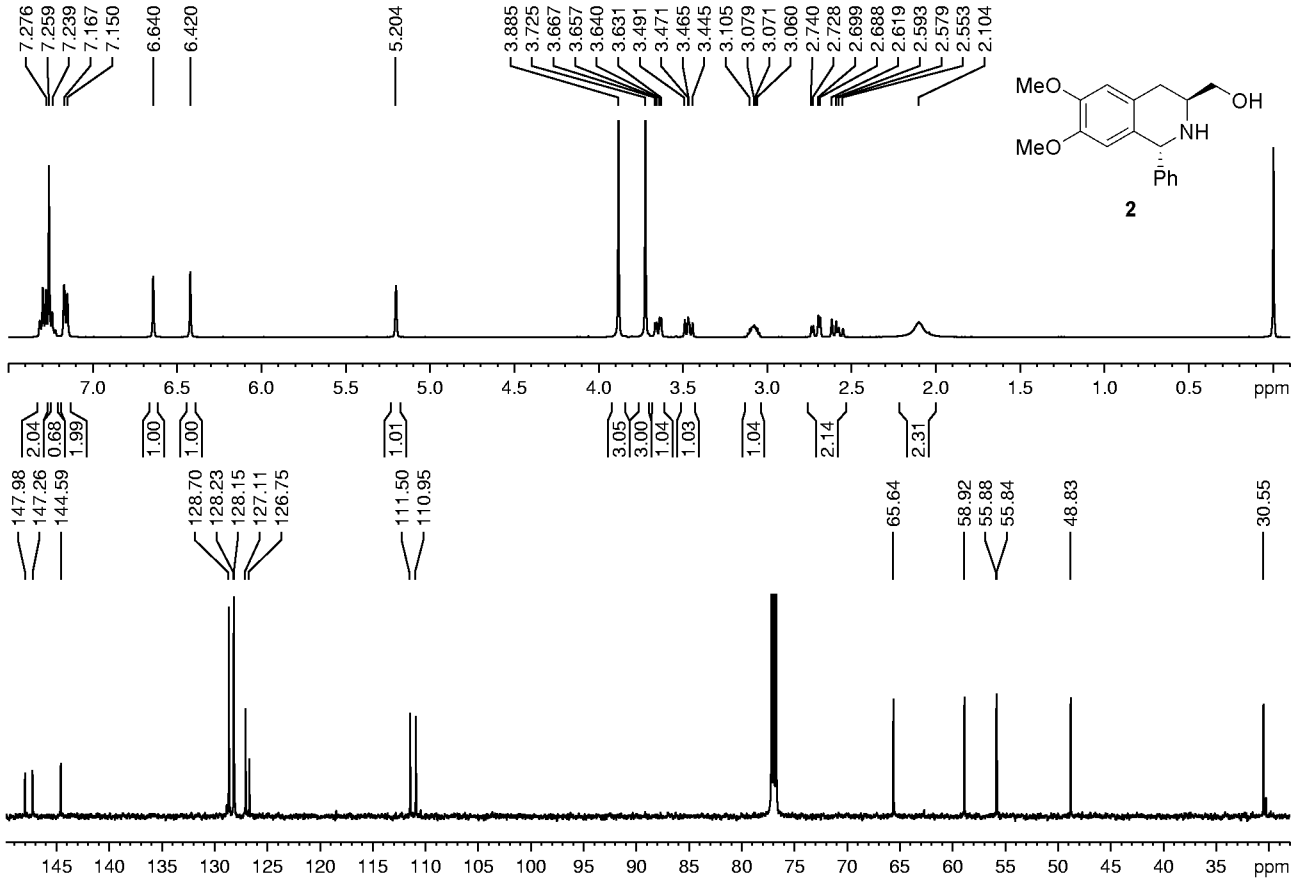


Figure S11 ^{1}H and ^{13}C NMR of **2**

S3. Gel tests

Preparation of gels: A suspension of **1** in a given solvent (1 ml) was heated to form a solution in a vial followed by cooling to room temperature. The solution in the vial was standing for about 30 minutes at room temperature. Gel formation was determined by inversed tube method. The gelation of various solvent by **1** was summarized in Table S1. Other compounds were not listed in the table for no gelation ability.

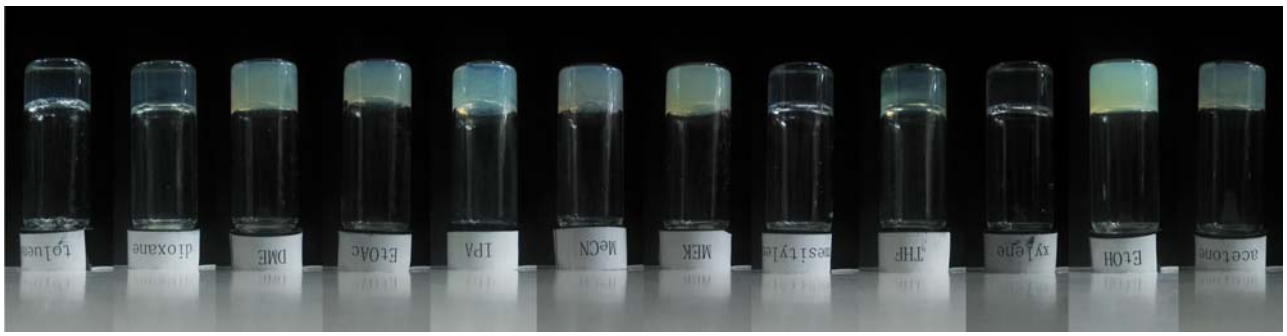


Figure S12 Gels of compound **1**. The bottom labels on caps are solvents for gelation: toluene, dioxane, dimethoxyethane, ethyl acetate, isopropanol, acetonitrile, methyl ethyl ketone, mesitylene, THF, *o*-xylene, ethanol and acetone from left to right.

Table S1. Gelation by **1** [a]

Solvent	C_{gel} (g ml^{-1})	transparency	T_{gel} (°C)[b]
toluene	0.8%	transparent	65
xylene	0.7%	transparent	74
mesitylene	0.7%	transparent	76
butanone	3.0%	opaque	38
isopropanol	3.6%	opaque	68
dioxane	4.1%	transparent	48
acetonitrile	4.7%	opaque	76
THF	5.7%	translucent	52
ethyl acetate	5.8%	opaque	82
acetone	6.7%	opaque	>70
DME	9.4%	opaque	78
ethanol	5.8%	translucent	67
methanol	PG (>10%)	-	-
MTBE	I	-	-
hexane	I	-	-

a) C_{gel} = minimal concentration for gelation; T_{gel} = sol-gel transition temperature; PG = partial gelation; I = insoluble or precipitate. b) measured by inverse tube method

S4. SEM pictures of xerogels

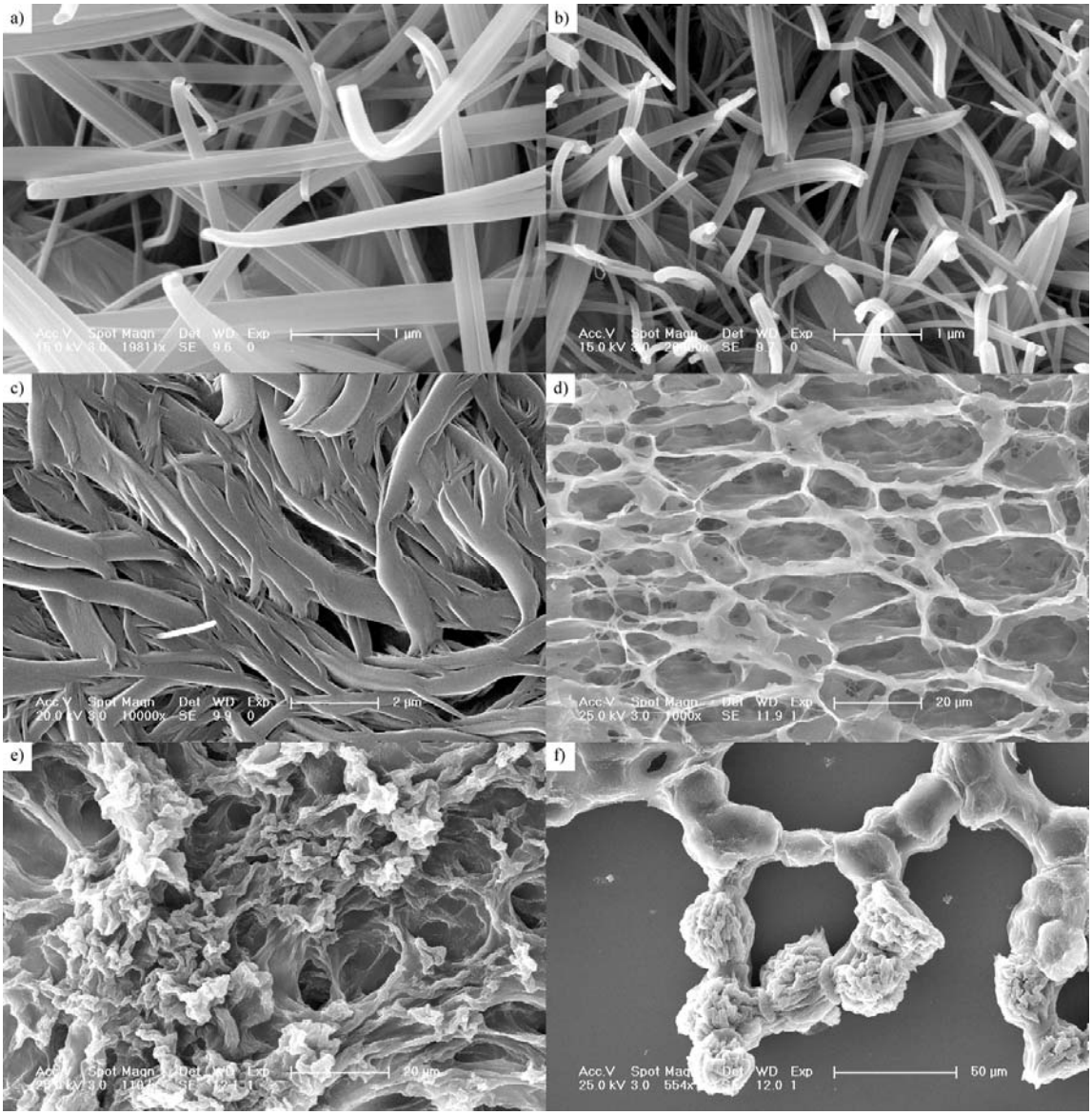


Figure S13 SEM pictures of xerogels from toluene (a), THF (b), mesitylene (c), dioxane (d), acetonitrile (e) and butanone (f).

S5. Gel stability to cations

The tests of gel stability to cations were carried out by covering a toluene gel of **1** (1 ml, 0.8% wt/vol) with a fresh solution of given cation (0.1 mmol in 1 ml water by metal ion) at room temperature. The two-layer sample (aqueous at upper layer) was standing for one week. The gels covered with $FeCl_3$, $CuCl_2$ and $AgNO_2$ were collapsed within 10 hours and displayed phase inversion that aqueous layer immersed at bottom and toluene solution at upper layer. Gels covered with other cations did not show any morphological change after one week. The results are summaried in Table S2.

Table S2. Cation response of toluene gel of **1** to cations

Metal Salt	Morphological change or phase inversion
HCl (PH = 2.5)	NO[a]
LiCl	NO
$LiNO_3$	NO
NaCl	NO
KCl	NO
$MgCl_2$	NO
$CaCl_2$	NO
$Mn(OAc)_2$	NO
$CoCl_2$	NO
$NiCl_2$	NO
$ZnCl_2$	NO
$CdCl_2$	NO
$Yb(OTf)_3$	NO
$FeCl_3$	YES, within 8 hour[b)]
$CuCl_2$	YES, within 10 hour [b)]
$AgNO_2$	YES, within 6 hour [b)]

a) No change after 6 months. b) Morphorlogical change started within 1 hour and completed at time indicated.

S6. FTIR spectroscopies

FTIR measurement and data processing: The xerogel **1** was measured with KBr pellete and the data was used directly without further processing. The dichloromethane solution of **1** (2% g ml^{-1}) was measured with 10 mm cell and the data was processed by substrate of blank solvent. Since the signals are weak for the dilute solution, the resulted FTIR spectroscopy was gained for 15 times for convenience in comparison with that of xerogel.

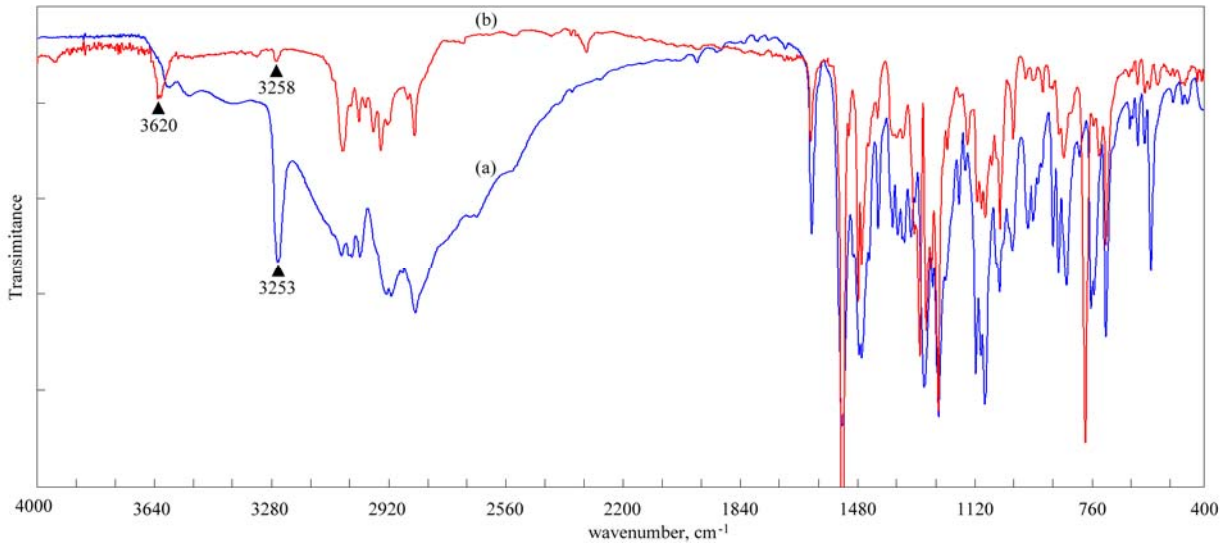


Figure S14 FTIR spectra of xerogel **1** from toluene (a) and dilute solution of **1** in dichloromethane (b)

S7. Single crystal of compound 4

Compounds	**4**
Empirical formula	C10H13NO
Formula weight	163.21
Temperature (K)	295(2)
Crystal system, Space group	Monoclinic, $P2_1$
Unit cell dimensions	a = 9.6435(14) Å, b = 6.500(1) Å, c = 14.390(2) Å α = 90°, β = 106.698(2)°, γ = 90°
Volume (Å^3)	864.0(2)
Z, Calculated density (Mg/m^3)	4, 1.255
Absorption coefficient (mm^{-1})	0.081
F(000)	352
Crystal size (mm)	0.32 x 0.18 x 0.10
θ range for data collection (°)	2.20 to 26.21
Limiting indices	$-11 \le h \le 8$, $-8 \le k \le 7$, $-17 \le l \le 17$
Reflections collected / unique	4797/1863[R_{int} = 0.0295]
Completeness to θ	98.5%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9919 and 0.9745
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1863/1/220
Goodness-of-fit on F^2	1.052
Final R indices [$I > 2\sigma$(I)]	R_1 = 0.0321. wR_2 = 0.0793
R indices (all data)	R_1 = 0.0362, wR_2 = 0.0820
Largest diff. peak and hole (e.Å^{-3})	0.162 and -0.137
CCDC	823631

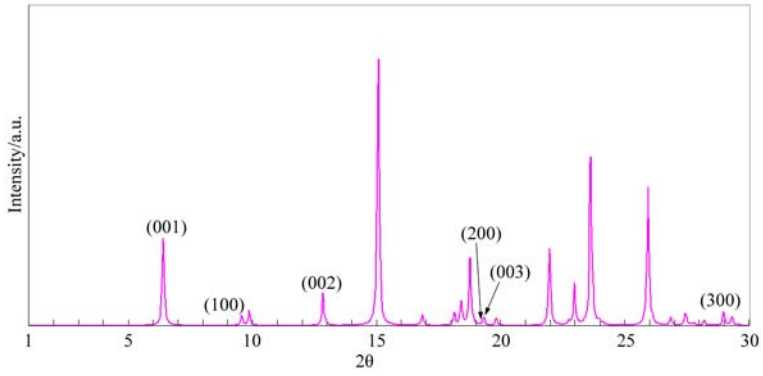


Figure S15 Simulated powder XRD from single crystal **4**

S8. Geometry optimization of 1

The van der Waals size of molecule **1** is determined through geometry (energy) optimization with Gaussian 03 program through CS Chem3D. The Gaussian optimization is performed at the HF level with basic set 6-31G and R-closed shell wave function.[S6] As shown in Fig. S16, the optimized geometry displays that the 1, 2, 3, 4-tetrahydroisoquinoline scaffold and hydroxymethyl at 3-position and methoxys on phenyl are located within an approximate plane. The distance of two far atoms (O<u>H</u> and C<u>H</u>$_3$) on each side is 10.8 Å, while that of O<u>H</u> and CH$_3$<u>O</u> is 9.4 Å. Thus, the long-axis length of **1** is estimated to be about 10 Å.

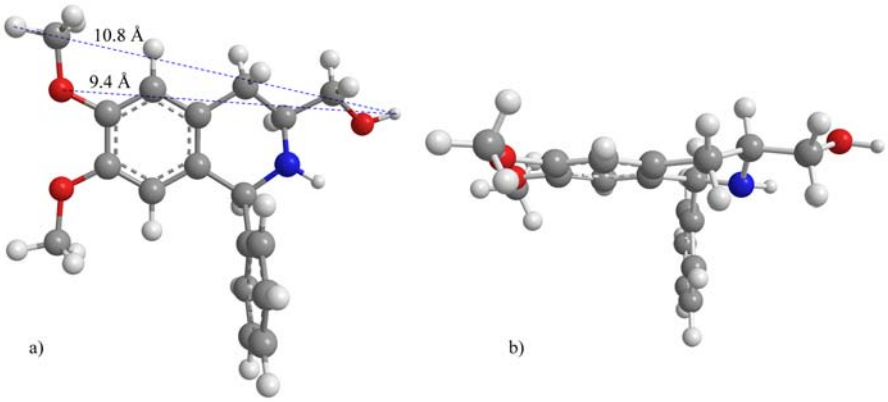


Figure S16 Geometry(energy) optimized **1** by gaussian with HF/6-31G of the theory.

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