

Supporting Information

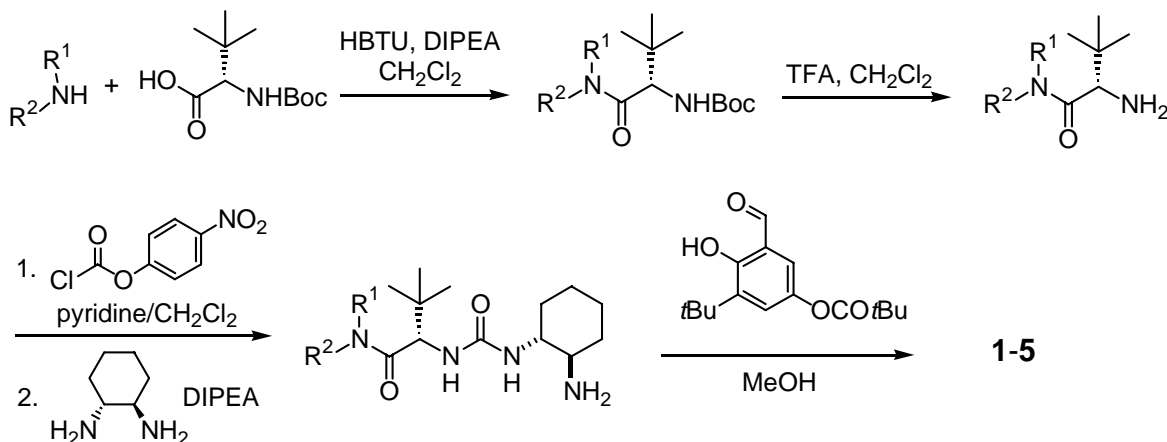
Structure-Based Analysis and Optimization of a Highly Enantioselective Catalyst for the Strecker Reaction

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General: Boc-*L*-*tert*-leucine was purchased from Fluka, O-Benztriazole-1-*N,N,N',N'*-tetraethyluronium hexafluorophosphate (HBTU) from Advanced ChemTech, (*S*)-*N*-*tert*-Butoxycarbonyl-2-amino-3-methyl-3-phenylbutyric acid *tert*-butylamine salt was purchased from ChiroTech; unless stated otherwise, all other chemicals were purchased from Aldrich or Alfa Aesar and used without purification. (*R,R*)-1,2-Diaminocyclohexane was resolved by literature methods.¹ Imine substrates and Strecker adducts were prepared according to published procedures.² ¹⁵N-Benzylamine for the synthesis of isotopically labeled ¹⁵N-2,2-dimethylpropylidene benzylamine was prepared in two steps from ¹⁵N-ammonium chloride according to literature procedure.³ 2-Hydroxy-5-pivaloyloxy-3-*tert*-butylbenzaldehyde was prepared according to published procedure.²

General Procedure for the Preparation of the Urea Catalysts (Illustrated for **1**)⁴



Coupling of Boc-L-tert-leucine with benzylamine, followed by deprotection: A 1000-mL round bottom flask equipped with a stirbar was charged with 5.00 g (21.6 mmol) of Boc-*L*-*tert*-leucine. Dichloromethane (170 mL) and HBTU (8.21 g, 1.0 eq.) were added with stirring. After 2 min, DIPEA (7.55 mL, 2 eq.) and benzylamine (2.37

mL, 1.0 eq.) were added sequentially and the reaction was stirred for 90 min. The mixture was combined with dichloromethane (250 mL) and water (250 mL) and the organic layer was separated, washed three times with 1N hydrochloric acid (250 mL), and dried over sodium sulfate. Solvents were removed in vacuo to afford crude Boc-protected amide as colorless oil. The oil was dissolved in dichloromethane (110 mL); then trifluoroacetic acid (25 mL, 15 eq.) was added in one portion and the reaction was stirred at rt for 1 hour. The reaction mixture was then cooled to 0°C and a 20% aqueous solution of sodium carbonate (250 mL) was added slowly. The resulting biphasic mixture was transferred to a separatory funnel, diluted with chloroform (140 mL), and the organic and aqueous layers were separated. The organic layer was washed with a 20% aqueous solution of sodium carbonate (250 mL). The combined aqueous layers were washed with chloroform (3 x 150 mL). All organic phases were combined, dried over sodium sulfate and concentrated to afford a mixture of product and tetramethylurea as a white solid (4.71 g, 21.4 mmol, 99% over two steps based on crude mass and ¹H NMR analysis). The mixture was carried on to the next step without further purification. The spectral properties are as follows: mp 53-54 °C: IR (KBr) 3303, 1650 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.33 (m, 5H), 7.05 (s, 1H), 4.45 (d, *J* = 0.9 Hz, 1H), 4.43 (d, *J* = 0.9 Hz, 1H), 3.14 (s, 1H), 1.41 (s, 2H), 1.01 (s, 9H); ¹³C NMR {¹H} (100 MHz, CDCl₃) δ 173.4, 138.5, 128.5, 127.8, 127.3, 64.3, 43.0, 34.1, 26.7; HRMS (*M* + *H*) calcd 221.1654, obsd 221.1658.

Carbamate and urea formation: A 500mL-round-bottom flask equipped with a stir bar was flame-dried and charged with the entire amount of crude amine obtained from the previous step (4.71 g, 21.4 mmol) dissolved in freshly distilled dichloromethane (50 mL). Freshly distilled pyridine (3.49 mL, 2 equiv.) was added via syringe to the stirred solution; after 2 min, 4-nitrophenylchloroformate (4.44 g, 1.02 equiv.) was added in one portion. After the reaction was stirred for 10 min, (*R,R*)-1,2-diaminocyclohexane (7.40 g, 3 equiv.) was added in one portion, followed by addition of DIPEA (4.2 mL, 1.1 equiv.) via syringe, and the reaction mixture was stirred for an additional 10 min. The resulting mixture was then combined with dichloromethane (500 mL) and 0.5 M sodium hydroxide solution (120 mL). The organic layer was separated, washed with another portion of 0.5 M sodium hydroxide solution (120 mL), and dried over sodium sulfate. The organic layer was concentrated to afford viscous oil, which was suspended in hexanes (500 mL). The resulting mixture was allowed to stand for 30 min, and then filtered, with the collected solids then washed with (3 x 125 mL) hexanes. The product was obtained as a white powder (6.25 g, 17.3 mmol, 82% yield over 2 steps) with no impurities detectable by ¹H NMR analysis (for some urea catalysts, the amine product was purified by flash chromatography on silica gel; eluent: 2M solution of ammonia in methanol/dichloromethane = 1/9): IR (thin film) 3284, 2934, 2858, 1631, 1555 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.28 (m, 5H), 7.08 (s, 1H), 6.11 (s, 1H), 5.31 (s, 1H), 4.48 (dd, *J*₁ = 14.9 Hz, *J*₂ = 6.1 Hz, 1H), 4.26 (dd, *J*₁ = 14.9 Hz, *J*₂ = 5.1 Hz, 1H), 4.20 (d, *J* = 8.8 Hz, 1H), 3.20 (m, 1H), 2.31 (m, 1H), 1.98 (d, *J* = 11.7 Hz, 1H), 1.85 (m, 2H), 1.68 (d, *J* = 11.2 Hz, 2H), 1.16 (m, 5H), 1.03 (s, 9H); ¹³C NMR {¹H} (100 MHz, CDCl₃) δ 172.7, 159.0, 138.5, 128.5, 127.5, 127.1, 61.3, 57.0, 55.1, 43.1, 35.0, 34.7, 33.4, 27.1, 25.3, 25.1.

Schiff base formation: A 1L-round-bottom flask equipped with a stirbar was charged with 6.25 g of amine prepared in the previous step and anhydrous methanol (40 mL) was added with stirring. Once the solution became homogeneous, sodium sulfate

(10 g) was added. In a separate flask, 2-hydroxy-5-pivaloyloxy-3-*tert*-butylbenzaldehyde (4.73 g, 0.98 eq.) was dissolved in anhydrous methanol (40 mL), then transferred to the reaction mixture. An additional 30 mL of methanol was used to effect quantitative transfer of the aldehyde into the reaction mixture. The reaction mixture was stirred for 90 min, then concentrated under reduced pressure with the sodium sulfate still present. The resulting mixture was combined with hexanes (250 mL) and filtered through a Buchner funnel, and the solids were rinsed with hexanes (250 mL). The filtrate was concentrated under reduced pressure to yield 10.55 g of **1** as a yellow solid (17.0 mmol, 98% yield, 80% overall yield from Boc-*L*-*tert*-leucine): IR (KBr) 3309, 2960, 1752, 1684, 1550, 1437, 1270, 1150, 1116 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 14.32 (s, 1H), 8.08 (s, 1H), 7.23 (d, *J* = 2.6 Hz, 1H), 7.12 (m, 2H), 7.08 (m, 2H), 7.02 (d, *J* = 2.6 Hz, 1H), 7.00 (t, *J* = 7.1 Hz, 1H), 6.67 (m, 1H), 5.63 (m, 1H), 4.59 (m, 1H), 4.37 (dd, *J* = 14.8, 6.6 Hz, 1H), 4.29 (d, *J* = 9.1 Hz, 1H), 3.86 (dd, *J* = 14.8, 4.6 Hz, 1H), 3.43 (m, 1H), 3.15 (m, 1H), 1.95 (m, 1H), 1.68- 1.0 (m, 7H), 1.51 (s, 9H), 1.30 (s, 9H), 1.05 (s, 9H); ¹³C NMR {¹H} (100 MHz, CDCl₃) δ 177.4, 172.0, 164.3, 158.1, 157.7, 141.7, 138.5, 130.1, 128.4, 127.4, 127.1, 122.6, 121.2, 118.1, 70.3, 61.5, 54.0, 43.1, 38.9, 34.8, 34.7, 31.5, 29.1, 27.1, 26.7, 24.2, 23.6, 22.6; HRMS (ES) (M)⁺ calcd 621.4016, obsd 621.3986.

2: Catalyst was prepared in 50% overall yield according to the general procedure for the synthesis of urea catalysts. The spectral properties are as follows: IR (thin film) 3368, 1750, 1633, 1550cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 14.22 (s, 1H), 8.22 (s, 1H), 7.24 (m, 3H), 7.14 (m, 2H), 6.94 (d, *J* = 6 Hz, 1H), 6.76 (d, *J* = 6 Hz, 1H), 5.38 (d, *J* = 9 Hz, 1H), 5.33 (d, *J* = 8 Hz, 1H), 4.81 (m, 1H), 4.70 (m, 1H), 4.38 (d, *J* = 15 Hz, 0.3H), 4.10 (d, *J* = 15 Hz, 0.7H), 3.34 (m, 1H), 3.17 (m, 1H), 2.91 (s, 0.7x3H), 2.79 (s, 0.3x3H), 1.99 (d, *J* = 12Hz, 1H), 1.81 (d, 12Hz, 1H), 1.69 (m, 2H), 1.21-1.50 (m, 4H), 1.40 (s, 0.7x9H), 1.39 (s, 0.3x9H), 1.34 (s, 0.7x9H), 1.33 (s, 0.3x9H), 0.91 (s, 0.7x9H), 0.86 (s, 0.3x9H); ¹³C NMR {¹H} (100 MHz, CDCl₃) δ 177.4, 173.01, 164.1, 158.2, 141.8, 138.6, 136.9, 129.9, 128.2, 128.1, 127.8, 127.3, 126.4, 122.6, 121.2, 118.2, 72.0, 69.0, 55.2, 49.2, 38.9, 36.4, 36.2, 34.9, 33.2, 31.5, 29.2, 27.2, 24.2, 23.8; MS (MH)⁺ 635.6.

3: Catalyst was prepared in 34% overall yield according to the general procedure for the synthesis of urea catalysts. The spectral properties are as follows: IR (thin film) 3370, 1748, 1632, 1550, 1438 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 13.78 (s, 1H), 8.27 (s, 1H), 7.26 (s, 6H), 6.94 (s, 4H), 6.94 (d, *J* = 2.6 Hz, 1H), 6.77 (s, 1H), 5.07 (d, *J* = 14.6 Hz, 1H), 4.88 (d, *J* = 9.2 Hz, 1H), 4.77 (d, *J* = 16.1 Hz, 1H), 4.59 (s, 1H), 4.26 (d, *J* = 16.1 Hz, 1H), 3.90 (d, *J* = 14.6 Hz, 1H), 3.41 (s, 1H), 3.23 (s, 1H), 2.07 (s, 1H), 1.88 (m, 1H), 1.79-1.60 (m, 4H), 1.55-1.36 (m, 2H), 1.39 (s, 9H), 1.33 (s, 9H), 0.89 (s, 9H); ¹³C NMR {¹H} (100 MHz, CDCl₃) δ 177.4, 173.3, 164.3, 158.2, 157.0, 128.7, 128.7, 128.1, 127.8, 127.7, 127.5, 122.6, 121.2, 118.2, 70.3, 55.2, 54.3, 50.8, 47.7, 38.9, 36.0, 34.9, 33.0, 31.1, 29.2, 27.1, 26.9, 26.6, 24.4, 23.5; MS (TOF) m/z (M+H) calcd 711.4, obs 711.6.

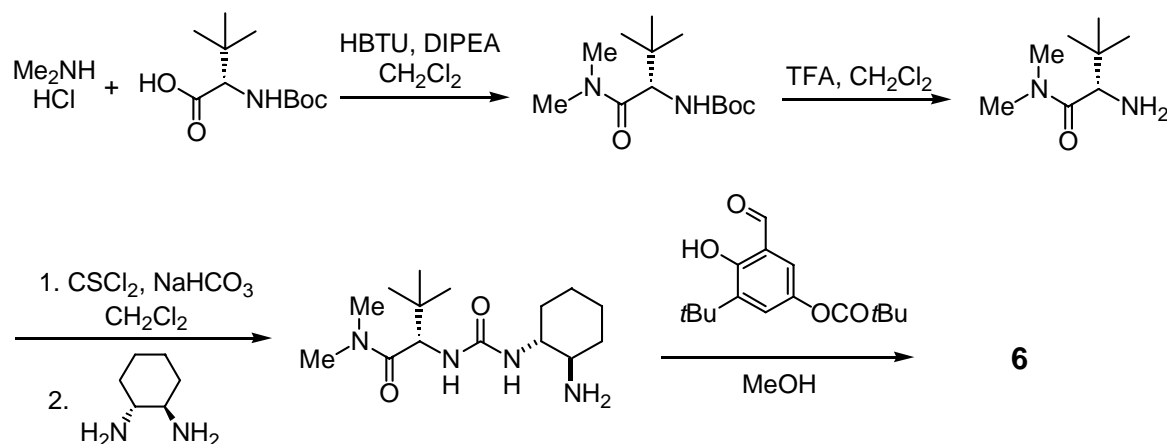
4: *Coupling with Boc-L-tert-leucine* was performed using dimethylamine hydrochloride (1equiv) and DIPEA (3 equiv).

Boc deprotection: A 25-mL, round-bottomed flask equipped with a stirbar was charged with N-(*tert*-Butoxycarbonyl)-*L*-*tert*-Leucine N,N-dimethylamide (2.0 mmol). A

4 M solution of hydrogen chloride in 1,4-dioxane (5 mL) was added at room temperature with stirring. After 2 hours, solvents were removed in vacuo. The product was used as hydrochloric salt in the subsequent step without further purification. The subsequent steps were performed according to the general procedure for urea catalysts (3 equivalents of pyridine were used for the urea formation). The product was isolated as a yellow solid in 16% overall yield. The spectral properties are as follows: IR (thin film) 3400, 1750, 1633, 1557, 1437 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 13.72 (s, 1H), 8.27 (s, 1H), 6.94 (d, J = 2.9 Hz, 1H), 6.79 (d, J = 2.6 Hz, 1H), 5.06 (s, 1H), 4.65 (d, J = 9.2 Hz, 1H), 4.35 (s, 1H), 3.55 (s, 1H), 3.13 (m, 1H), 2.99 (s, 3H), 2.82 (s, 3H), 2.12-2.07 (m, 1H), 1.92-1.84 (m, 1H), 1.82-1.62 (m, 4H), 1.44-1.34 (m, 2H), 1.40 (s, 9H), 1.34 (s, 9H), 0.89 (s, 9H); ^{13}C NMR $\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 177.4, 172.7, 164.0, 158.2, 157.2, 141.7, 138.5, 122.5, 121.1, 118.2, 71.3, 54.9, 54.1, 38.9, 38.2, 35.6, 35.5, 34.8, 33.2, 31.6, 29.2, 27.1, 26.4, 24.6, 23.8; MS (TOF) m/z ($\text{M}+\text{H}$) calcd 559.4, obs 559.5.

5: The catalyst was prepared in 31% overall yield from the Boc-amino acid salt (3 equiv. of DIPEA used for the initial coupling), using the general synthetic protocol for the urea catalysts. The spectral properties of the yellow product are as follows: IR (thin film) 2934, 1751, 1632, 1549, 1439 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 13.72 (s, 1H), 8.31 (s, 1H), 7.37 (d, J = 7.3 Hz, 2H), 7.26 (t, J = 6.7 Hz, 2H), 7.18 (t, J = 7.3 Hz, 1H), 6.93 (d, J = 2.7 Hz, 1H), 6.81 (s, 1H), 5.24 (s, 1H), 4.86 (d, J = 7.9 Hz, 1H), 4.41 (s, 1H), 3.56 (m, 1H), 3.19 (m, 1H), 2.57 (s, 3H), 3.09 (s, 3H), 1.89 (d, J = 11.3 Hz, 1H), 1.77 (m, 3H), 1.67 (d, J = 13.7 Hz, 1H), 1.48-1.33 (m, 3H), 1.39 (s, 9H), 1.35 (s, 3H), 1.33 (s, 12H); ^{13}C NMR $\{^1\text{H}\}$ (100 MHz, CDCl_3) δ 177.4, 171.7, 164.1, 158.2, 157.1, 145.9, 141.7, 138.6, 127.9, 126.8, 126.4, 122.6, 121.1, 118.2, 71.4, 56.1, 54.3, 42.5, 38.9, 36.7, 35.1, 34.9, 33.3, 31.6, 29.2, 27.1, 26.4, 24.7, 23.8, 22.4; MS (TOF) m/z ($\text{M}+\text{H}$) calcd 621.4, obs 621.3.

Synthesis of catalyst 6:

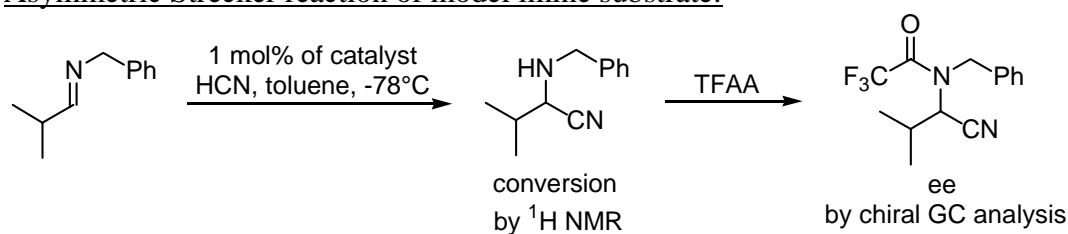


Coupling of Boc-L-tert-leucine with benzylamine, followed by deprotection was performed according to the procedure described for the preparation of 4.

Thiourea formation:⁵ A 500mL-round bottom flask equipped with a stir bar was charged with 1.86 g (9.54 mmol) of crude amine hydrochloride from the deprotection step. To this mixture dichloromethane (50 mL), and saturated aqueous solution of sodium bicarbonate was added. The biphasic mixture is cooled to 0°C and neat thiophosgene (0.80 mL, 1.1 equiv.) was added via syringe with vigorous stirring. The reaction mixture was vigorously stirred at 0°C for additional 30 min, the organic layer was separated, dried over sodium sulfate, and concentrated in vacuo to afford isothiocyanate used immediately without purification. The crude isothiocyanate was dissolved in freshly distilled dichloromethane (30 mL) and (*R,R*)-1,2-diaminocyclohexane (1.20 g, 1.1 equiv.) was added in one portion. The reaction mixture was allowed to stir at room temperature for 30 min and concentrated in vacuo. Crude product was purified by flash chromatography on silica gel (Eluent: 2M solution of ammonia in methanol/dichloromethane = 1/9, stain with ninhydrine) to afford 2.13 g (75% overall from Boc-*L*-*tert*-leucine) of pure amine.

Schiff base formation was performed according to the general procedure for the preparation of urea catalysts (1.00 equivalents of aldehyde used). Catalyst **6** was isolated as a yellow solid in 75% overall yield (from Boc-*L*-*tert*-leucine). The spectral properties are as follows: IR (thin film) 3293, 1750, 1630, 1535cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 13.55 (s, 1H), 8.23 (s, 1H), 6.92 (d, *J* = 8 Hz, 1H), 6.85 (d, *J* = 8 Hz, 1H), 6.55 (s, 1H), 6.44 (d, *J* = 7 Hz, 1H), 5.56 (d, *J* = 9 Hz, 1H), 3.83 (m, 1H), 3.18 (s, 3H), 3.11 (td, *J* = 2, 8Hz, 1H), 2.92 (s, 3H), 2.09 (m, 1H), 1.88 (m, 1H), 1.71 (m, 3H), 1.25-1.44 (m, 3H), 1.40 (s, 9H), 1.34 (s, 9H), 0.90 (s, 9H); ¹³C NMR {¹H} (100 MHz, CDCl₃) δ 177.6, 172.0, 165.0, 157.9, 141.9, 135.5, 123.0, 121.6, 118.2, 60.4, 38.9, 38.4, 36.0, 35.6, 34.9, 29.2, 27.2, 26.6; MS (MH)⁺ 575.6.

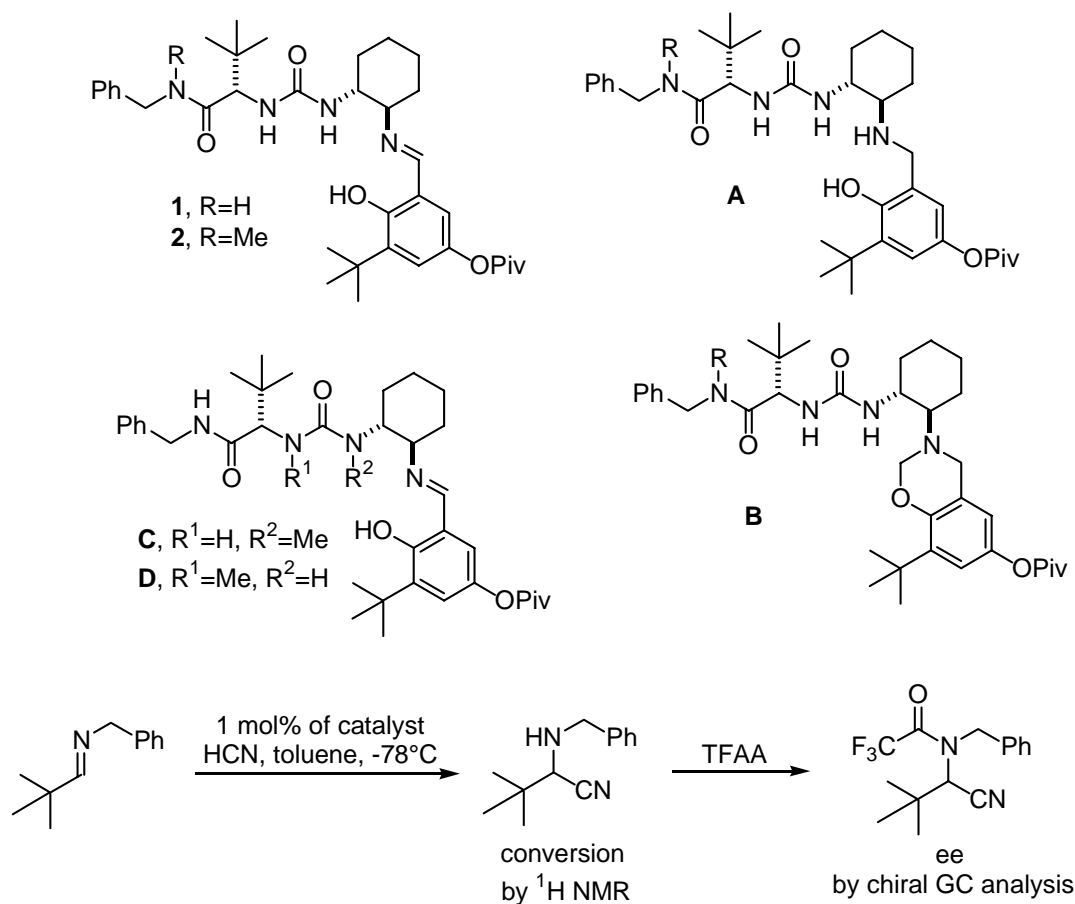
Asymmetric Strecker reaction of model imine substrate:



A flame-dried 10mL-round-bottom flask equipped with a stir bar was charged with 0.003 mmol of a catalyst (0.01 equiv.), 2.5 mL of toluene, and imine (0.3 mmol). The reaction was stirred at ambient temperature until catalyst completely dissolved and then cooled below -70 °C by means of a constant temperature bath. A flame-dried 5mL-recovery-flask was equipped with a stir bar and charged with freshly distilled toluene (0.5 mL) and 50 μL TMSCN (1.25 equiv.). The mixture was cooled to 0°C; to this solution 15 μL of anhydrous methanol (1.25 equiv.) was added via syringe; the solution was allowed to stir at 0°C for 2h and then added to reaction flask containing catalyst and substrate by a syringe addition at -78°C. After 15h, a sample was transferred into a precooled vial via a precooled syringe and the solvents were removed under reduced pressure at low temperature to ensure no reaction progress during this operation. The conversion of the Strecker reaction was determined by ¹H NMR (product/imine). To the NMR sample, an

excess of TFAA (approx. 5 equiv.) was added at room temperature in one portion and the resulting trifluoroacetamide of the Strecker adduct was analyzed by chiral GC analysis.²

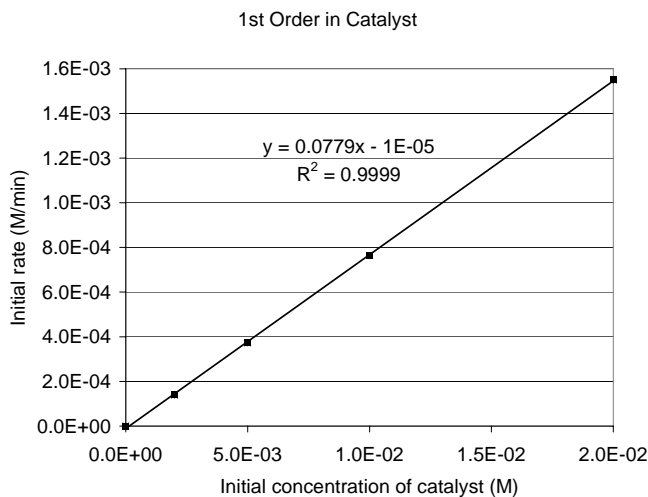
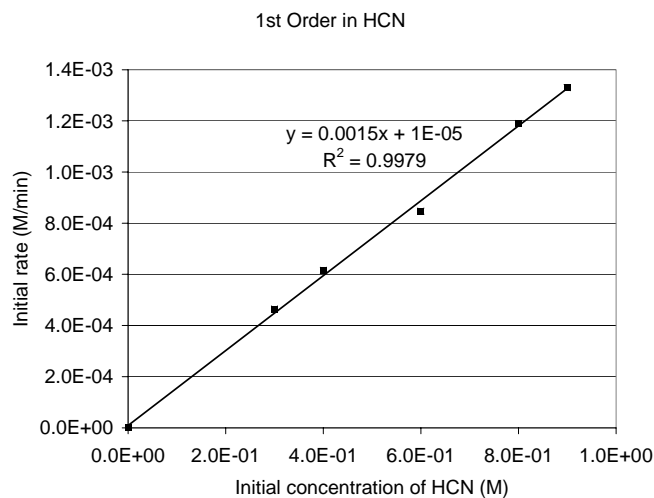
Identification of the active site of the catalyst: Several derivatives of **1** were prepared and tested as catalyst in the asymmetric Strecker reaction of *N*-(2,2-dimethylpropylidene) benzylamine; the screen was conducted according to the general procedure given for *N*-isobutylene benzylamine. The results and comments are summarized in the following Table:

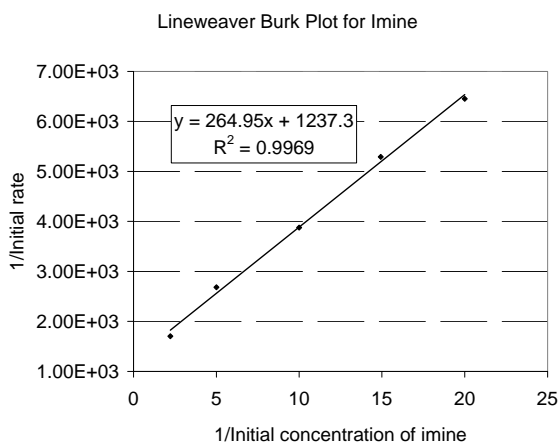
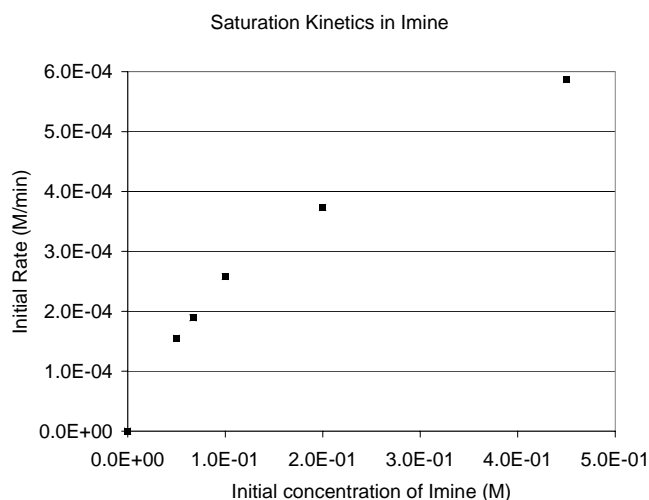


Entry	Catalyst	Conv. ^a (%)	Ee (%)	Comments
1	1	> 99	95.6	
2	2	> 99	96.4	2 even better catalyst than 1 → amide H not active site
3	A	> 99	85	Ee declines from 1 (not surprise: weaker H-bond, etc.)
4	B	> 99	88	B better catalyst than A → phenol H not active site
5	C	83	13	C and D are significantly worse catalysts than 1 → → urea H(s) are important for both rate and ee; might be the active site
6	D	46	27	

^a: in 15h at -78°C

Kinetics, General: Reaction kinetics were investigated using an ASI 1000 React-IR™ instrument equipped with a silicon probe. The probe was dried by heating with a heat gun (<200°C) and allowed to cool under nitrogen atmosphere prior to each run to ensure reproducible results. Rate dependence on the concentration of each reagent was investigated under pseudo-constant concentration of remaining reagents by monitoring the change of the initial rate (10% conversion) as a function of investigated reagent concentration. The Strecker reaction was conducted by the means of the general protocol given for the testing of catalyst derivatives. The observed dependence on the concentration of each reagent is given bellow (Charts 1-3). Saturation kinetics in imine substrate was confirmed by Lineweaver Burk plot (Chart 4):



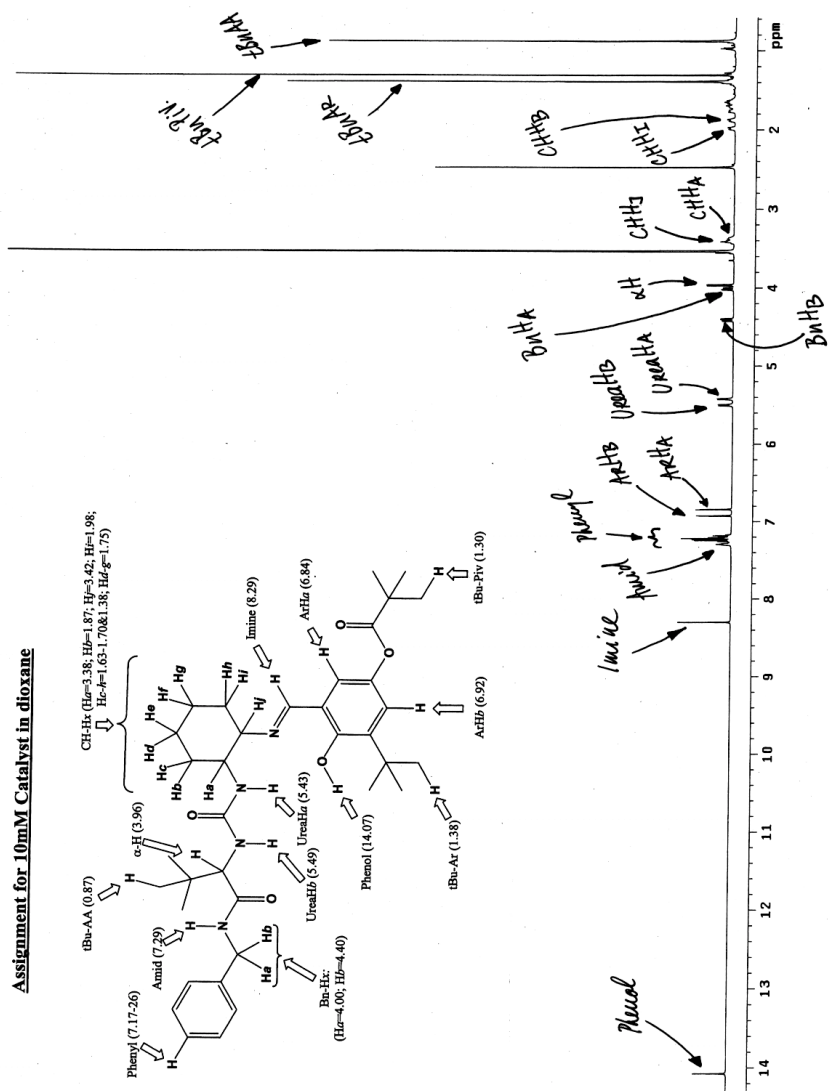


NMR Spectroscopy, General: All experiments were performed using instruments equipped with a Bruker magnet and Varian software. Experiments at room temperature (20°C, regulated) were performed using INOVA 600 MHz instrument. Low temperature (regulated) experiments were performed using INOVA 500 MHz, or MERCURY 400 MHz instruments equipped with an external thermostat filled with liquid nitrogen. All NMR solvents were purchased from Cambridge Isotope Laboratories and used as received. Prior to the ROESY and NOE experiments, the NMR sample was degassed with nitrogen for 10 min.

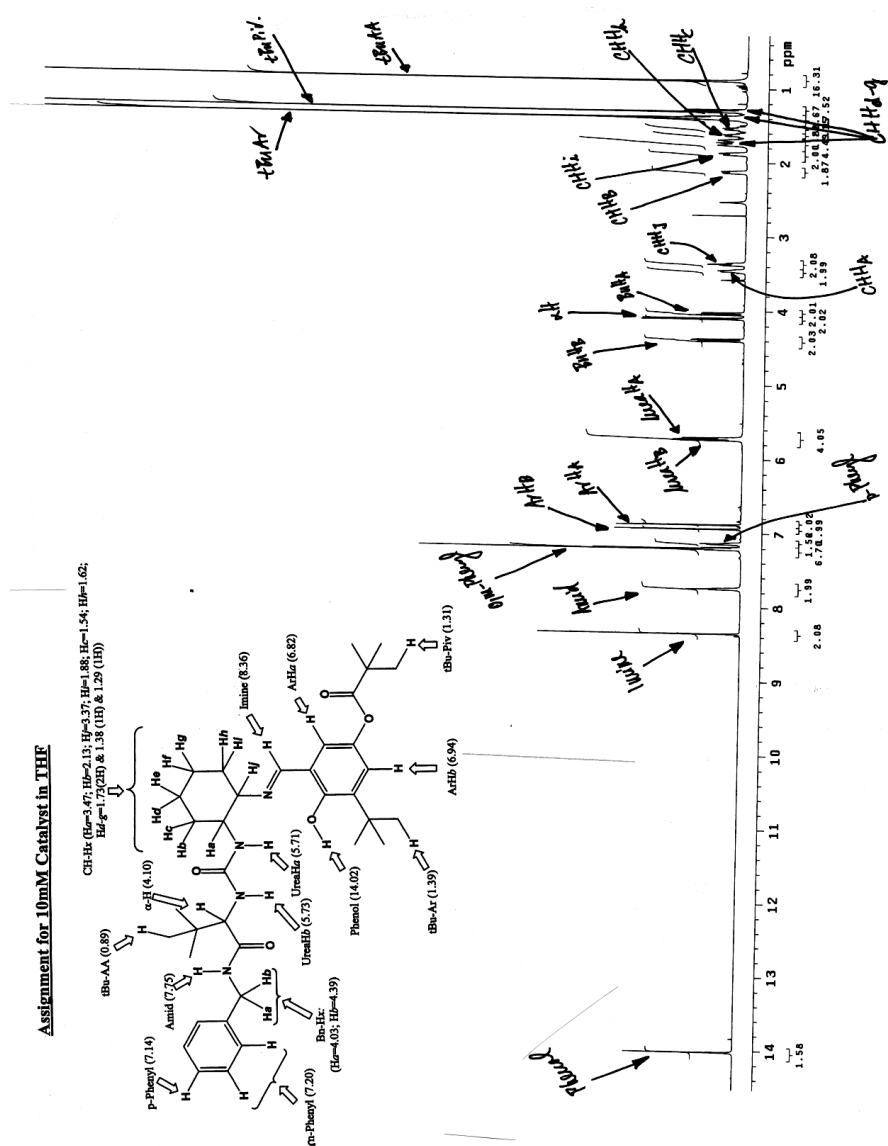
Catalyst 1:

Assignment of H-signals in relevant solvents (THF and dioxane) for ^1H NMR was accomplished by COSY connectivity experiments; tBuPiv, tBuAr, ArHa, and ArHb were assign based on their NOE interactions (NOESY, ROESY):

10mM **1** in d_8 -dioxane:

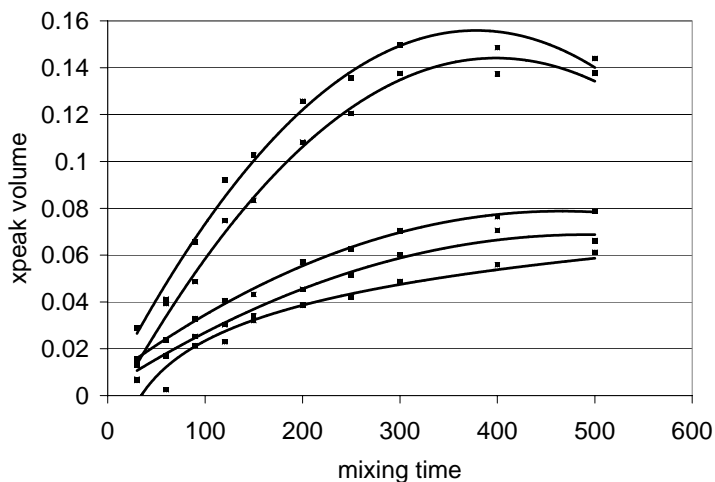


10mM **1** in d_8 -THF:

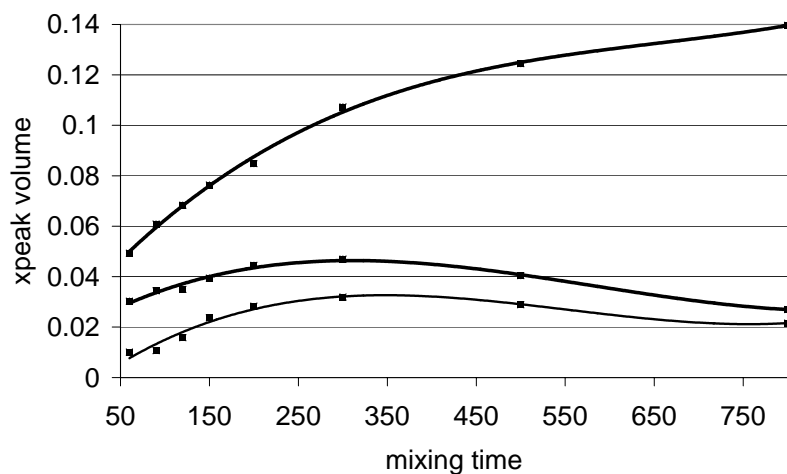


Determination of the correct mixing time for 2D-ROESY experiments was accomplished by monitoring of NOE build-up curves (mix=30-600ms) for significant xpeaks in ROESY. Charts below show selected xpeaks for 10mM **1** in d_8 -dioxane (determined as 120 ms) and 50mM **1** in d_8 -THF (determined as 160ms; unchanged when imine substrate was present); other conditions: i600, d1=2s, t=20°C (regulated), nt=4, ni=350, sw=9000.

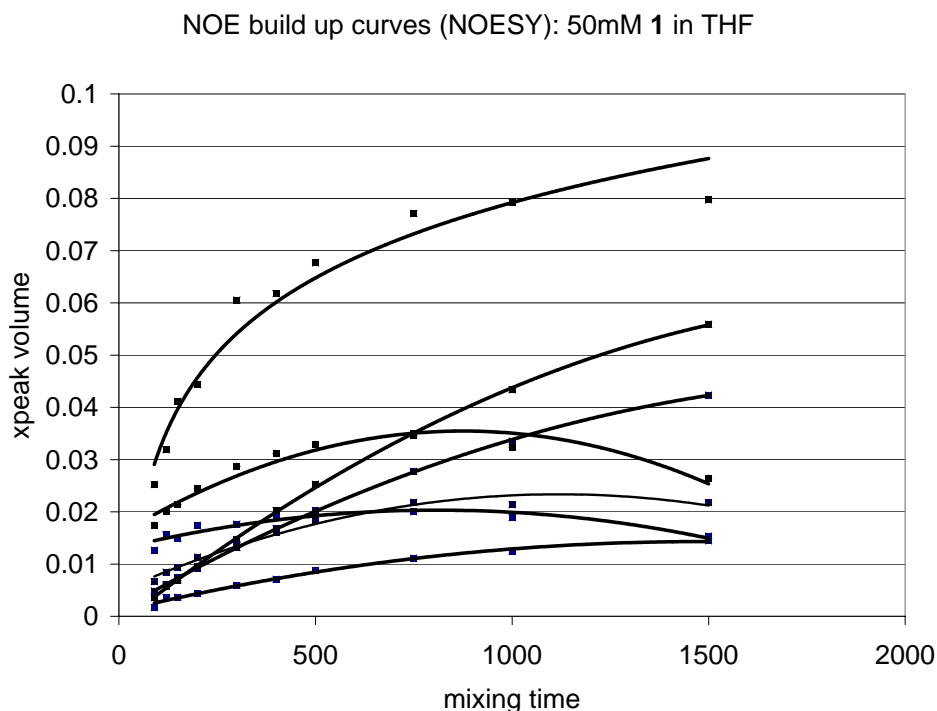
NOE build up curves (ROESY): 10 mM **1** in dioxane



NOE buildup curves (ROESY): 50mM **1** in THF



Determination of the correct mixing time for NOESY, and NOESY1D experiments was accomplished by monitoring NOE build up curves for significant xpeaks in NOESY experiment. Chart below shows selected xpeaks for 50mM **1** in d_8 -THF (determined as 160ms; unchanged if imine substrate was present); other conditions: i600, d1=2s, t=20°C (regulated), nt=4, ni=350, sw=9000.



ROESY Experiment, 50mM **1** in d_8 -THF, 20°C (regulated), i600, d1=1s, ni=1K, sw=9000, nt=16, mix=160ms; distance in Å, compare to calculations (MM2):

Peak1	Peak 2	Xpeak volume	distance, Å (ROESY)	distance, Å (computation)
Phenol	Imine	0.18	3.8	3.9
Phenol	UreaHa	0.09	4.2	4.3
Phenol	CHHa	0.074	4.4	4.0
Phenol	tBuAr	0.351	3.4	4.0
Imine	ArHa	2.26	define as 2.46 (law of cosine)	
Imine	UreaHa	0.242	3.6	3.6
Imine	CHHa	0.714	3.0	2.7
Imine	CHHj	4.15	2.2	2.4
Imine	tBuAA	0.577	3.1	3.5
Amide	α -H	4.13	2.2	2.2
Amide	tBuAA	1.71	2.6	3.7
ArHb	tBuAr	4.61	2.2	2.1
ArHa	tBuAr	3.57	2.3	2.4
UreaHb	UreaHa	3.325	2.3	2.3
UreaHb	tBuAA	3.04	2.3	2.4

UreaHa	CHHa	1.021	2.8	2.8
UreaHa	CHHj	0.959	2.8	2.9
α -H	tBuAA	5.16	2.1	2.3
BnHb	BnHa	3.685	mix w/ cosy	2.2

ROESY Experiment, 10mM 1 in d₈-dioxane, 20°C (regulated), i600, d1=1s, ni=1K, sw=9000, nt=16, mix=120ms:

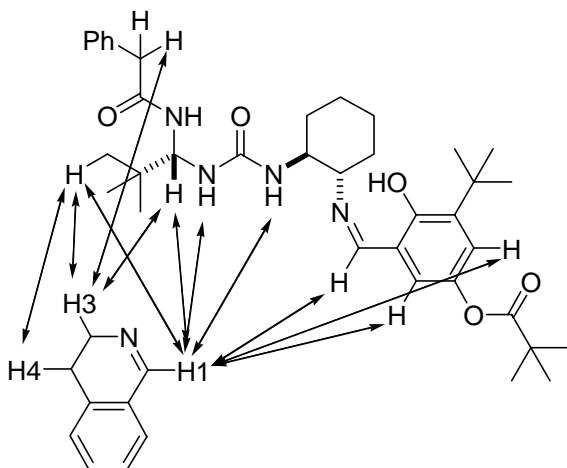
Peak 1	Peak 2	ROESY xpeak volume
Phenol (14.07)	tBu-Ar (1.38)	0.74519854
Phenol (14.07)	CH-Ha (3.38)	1.684133
Phenol (14.07)	Urea-Ha (5.43)	0.200816
Phenol (14.07)	Imine (8.29)	0.97271824
Imine (8.29)	tBu-AA (0.87)	1.7759821
Imine (8.29)	CH-Hb (1.87)	1.97931078
Imine (8.29)	CH-Ha (3.38)	7.86
Imine (8.29)	CH-Hj (3.42)	18.64
Imine (8.29)	Urea-Ha (5.43)	1.442701
Imine (8.29)	Ar-Ha (6.84)	14.717
Imine (8.29)	Ar-Hb (6.92)	5.18
Amid (7.29)	tBu-AA (0.87)	8.62042714
Amid (7.29)	a-H (3.96)	26.14315296
Amid (7.29)	Bn-Hb (4.4)	3.20317565
Phenyl (7.17-7.26)	tBu-AA (0.87)	6.48191987
Ar-Hb (6.92)	tBu-AA (0.87)	2.44275541
Ar-Hb (6.92)	tBu-Ar (1.38)	37.73484386
Ar-Ha (6.84)	tBu-AA (0.87)	4.06189233
Ar-Ha (6.84)	tBu-Ar (1.38)	15.2834654
Urea-Hb (5.49)	tBu-AA (0.87)	15.27080143
Urea-Hb (5.49)	a-H (3.96)	3.77627491
Urea-Hb (5.49)	Urea-Ha (5.43)	15
Urea-Ha (5.43)	tBu-AA (0.87)	2.8687825
Urea-Ha (5.43)	CH-Hc-h (1.63)/ CH-Hc-h (1.70)	3.69794199
Urea-Ha (5.43)	CH-Ha (3.38)	7.04332542
Urea-Ha (5.43)	CH-Hj (3.42)	6.04332542
a-H (3.96)	tBu-AA (0.87)	22.81397889
CH-Hj (3.42)	tBu-Ar (1.38) or CH	7.24282364
CH-Hj (3.42)	CH-Hb (1.87)	5.1718353
CH-Hj (3.42)	CH-Hi (1.98)	0.5
CH-Ha (3.38)	tBu-Ar (1.38) or CH	5.23395427
CH-Ha (3.38)	CH-Hb (1.87)	0.5000001
CH-Ha (3.38)	CH-Hi (1.98)	5.21282502

CH-Hd-g (1.75)	tBu-Ar (1.38) or CH	53.46867114
CH-Hc-h (1.70)	tBu-Ar (1.38) or CH	49.25715698

NOESY1D Experiments, 70mM 1 in d₈-THF, 20°C (regulated), i600, d1=1s, ni=1K, sw=9000, nt=4000-7000, mix=300ms (presence of 3,4-dihydroisoquinoline did not have an influence on the magnitude of intramolecular xpeaks; same relative volumes observed):

Irradiated	Phenol	Imine	Amide	Phenyl	ArHb	ArHa	UreaHb	UreaHa	α -H	BnHb	BnHa	CHHa	CHHj	CHHb	CHHi	tBuAr	tBuPiv	tBuAA
Phenol		0.20														0.99		
Imine	0.19					1.28		0.10				0.24	1.50					0.17
Amide				0.38			0.01		1.66									
ArHb		0.09														4.15	0.13	
ArHa	0.01	0.99														0.05	0.09	0.14
UreaHb		0.10																1.73
UreaHa		0.27										0.86	0.71					
α -H			1.09															2.11
BnHb				0.41												0.03		0.11
BnHa				0.46	0.03											0.03		0.05
CHHa	0.05	0.25						0.64						0.80				
CHHj	0.04	1.67						0.42							0.82			
CHHb		0.02						0.29				1.14	0.24					
CHHi	0.01	0.27										0.22	1.07					
tBuAr	0.06				0.99													
tBuPiv					0.01	0.01										0.14		0.16
tBuAA		0.05	0.12	0.10		0.01	0.34		0.69	0.12	0.15					0.14	0.16	

*Intermolecular xpeaks between catalyst **1** and 3,4-dihydroisoquinoline.* The xpeaks were observed in NOESY1D experiment, 20°C (regulated), nt=4000-12000, d1=0.1-1s, sw=9000, 70mM **1** and 330mM in 3,4-dihydroisoquinoline in *d*₈-THF. Since correct mixing time was not established for catalyst/substrate complex, reported xpeak volumes should be considered as qualitative, not quantitative measure of the distance. Following Figure shows important intermolecular xpeaks; integrated values are given in the Table:



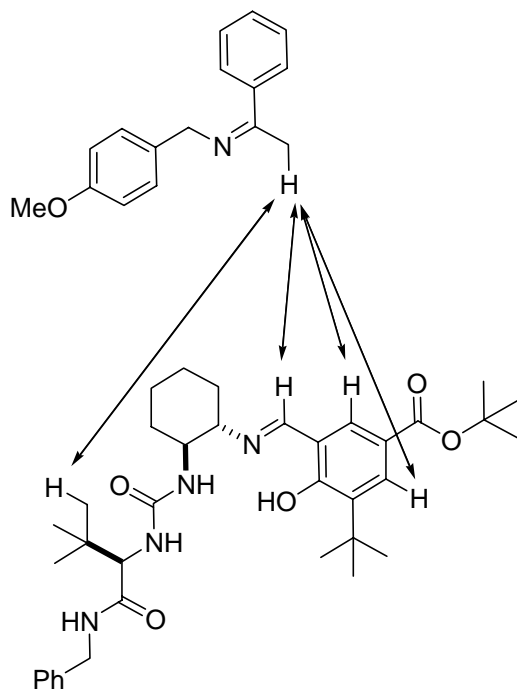
Intermolecular xpeak volume:

	H1	H3	H4
Phenol			
Imine	0.01		
Amide	0.05	0.10	
ArHb	0.02		
ArHa	0.07		
UreaHb	0.12		
UreaHa	0.10		
α-H	0.07	0.08	
BnHb		0.10	
BnHa	0.01	0.03	
CHHa	0.01		
CHHj	0.03	0.02	
CHHb			
CHHi			
tBuAr			
tBuPiv			
tBuAA	0.12	0.13	0.18

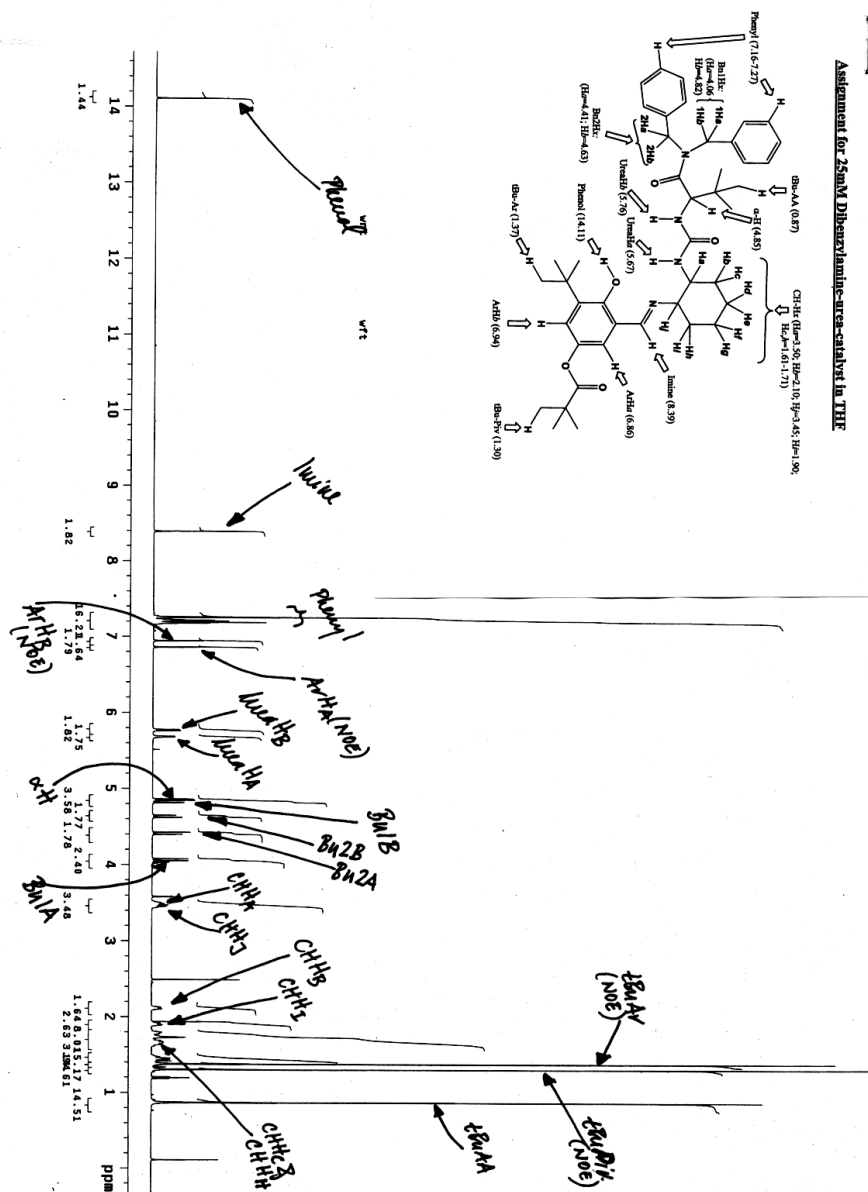
Intermolecular xpeaks between catalyst 1 and a Z-Imine. The xpeaks were observed in NOESY1D experiment, 20°C (regulated), nt=12000-25000, d1=0.1-1s, sw=9000, 100mM **1** and 90mM imine (overall concentration of both isomers) in *d*₈-THF. The intensity of the intermolecular xpeaks was low and a quantitative integration was not possible, therefore qualitative comparison is given instead; four significant xpeaks are shown in the following figure:

Catalyst Peak	Xpeak to α Me (Z-imine)
Phenol	w
Imine	s
Amide	--
ArHb	s
ArHa	s
UreaHb	m
UreaHa	m
α -H	m
BnHb	--
BnHa	--
CHHa	--
CHHj	--
tBuAr	--
tBuPiv	--
tBuAA	s

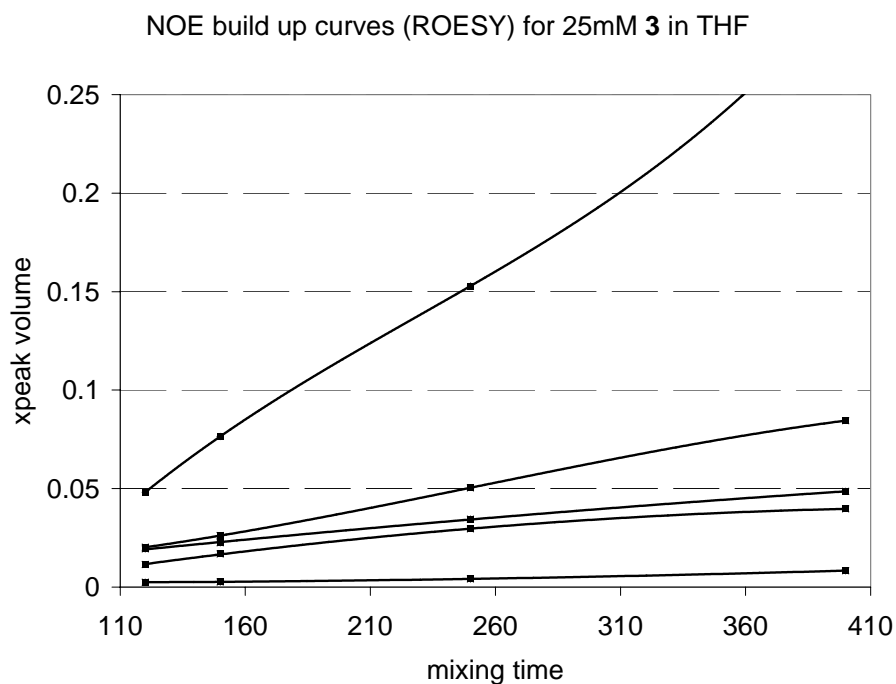
w=weak, m=medium, s=strong



Assignment of H-signals for 25mM **3** in d₈-THF was accomplished by COSY connectivity experiments. tBuPiv, tBuAA, ArHa, and ArHb were assign based on NOE xpeaks (ROESY):



Determination of the correct mixing time for 2D-ROESY experiments was accomplished by monitoring the NOE build up curves (mix=60-400ms) for significant xpeaks in 2D-ROESY. Chart shows selected xpeaks for 25mM **3** in d_8 -THF (determined as 120ms); other conditions: i600, d1=1.5s, t=20°C (regulated), nt=4, ni=350, sw=9000.



ROESY Experiment, 25mM 3 in d_8 -THF, 20°C (regulated), i600, d1=1.7s, ni=1.5K, sw=9000, nt=16, mix=120ms; distance calculated based on the relative xpeak volume related to the standard distance in Å; comments included for an easier data analysis:

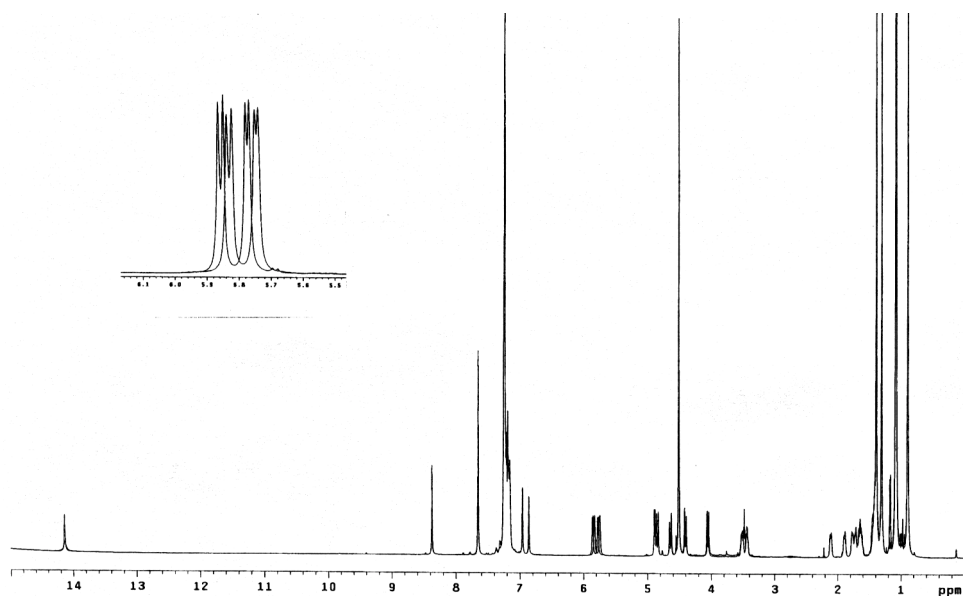
Entry	Peak 1	Peak 2	Xpeak vol.	Dist.	Comments
1	Phenol (14.11)	CHHj (3.45)	half of 0.402	nd	overlap
2	Phenol (14.11)	CHHa (3.50)	half of 0.402	nd	overlap
3	Phenol (14.11)	Imine (8.39)	0.1953	3.5	trivial
4	Imine (8.39)	CHHc&CHHh (1.61-1.71)	0.212	3.4	trivial
5	Imine (8.39)	CHHi (1.90)	0.304	3.2	sets imine-CH ring conformation (Entries 5-8)
6	Imine (8.39)	CHHj (3.45)	2.53	2.3	
7	Imine (8.39)	CHHa (3.50)	1.21 ^a	nd	
8	Imine (8.39)	UreaHa (5.67)	0.251	3.3	imine and urea: same face
9	Imine (8.39)	ArHa (6.86)	1.485	2.5	Standard for distance, 2.46Å
10	Imine (8.39)	ArHb (6.94)	0.8395	2.7	trivial
11	Phenyl (7.15-7.27)	tBuAA (0.87)	2.099	2.3	very strong --> hindered face
12	Phenyl (7.15-7.27)	Bn1Ha (4.06)	1.027	2.6	trivial
13	Phenyl (7.15-7.27)	Bn2Ha (4.41)	1.244	2.5	trivial
14	Phenyl (7.15-7.27)	Bn2Hb (4.63)	0.6665	2.8	trivial

15	Phenyl (7.15-7.27)	α -H (4.85)	1.544	2.4	very strong --> hindered face
16	ArHb (6.94)	tBuAr (1.37)	4.917	2.0	trivial
17	ArHa (6.86)	tBuAr (1.37)	2.262	2.3	trivial
18	Urea Hb (5.76)	tBuAA (0.87)	2.4833	2.3	trivial
19	Urea Hb (5.76)	α -H (4.85)	0.4996	3.0	trivial
20	Urea Hb (5.76)	UreaHa (5.67)	0.617 ^b	nd	trivial
21	UreaHa (5.67)	CHHc&CHHh (1.61-1.71)	0.5958	2.9	sets Urea-CH ring conformation (Entries 21-24)
22	UreaHa (5.67)	CHHb (2.10)	0.2221	3.4	
23	UreaHa (5.67)	CHHj (3.45)	half of 1.8166	nd	
24	UreaHa (5.67)	CHHa (3.50)	half of 1.8166	nd	
25	α -H (4.85)	tBuAA (0.87)	3.887	2.1	trivial
26	α -H (4.85)	Bn2Ha (4.41)	2.002	2.3	confirms rigidity and potential hindrance as origin of enantios.
27	α -H (4.85)	Bn2Hb (4.63)	3.636	2.1	
28	Bn1Hb (4.82)	Bn1Ha (4.06)	9.0699 ^c	nd	trivial
29	Bn2Hb (4.63)	tBuAA (0.87)	1.731	2.4	very strong --> hindered face
30	Bn2Hb (4.63)	Bn1Ha (4.06)	0.3832	3.1	weak --> rigid conf., hind. face
31	Bn2Hb (4.63)	Bn2Ha (4.41)	(-) 5.6384 ^c	nd	trivial
32	Bn2Ha (4.41)	tBuAA (0.87)	1.276	2.5	very strong --> hindered face
33	CHHa (3.50)	CHHb (2.10)	1.2187	2.5	trivial
34	CHHj (3.45)	CHHi (1.90)	1.2007	2.6	trivial

a: volume magnified by overlap with entry 6; b: volume reduced by close proximity to the diagonal peak; c: mixed with cosy.

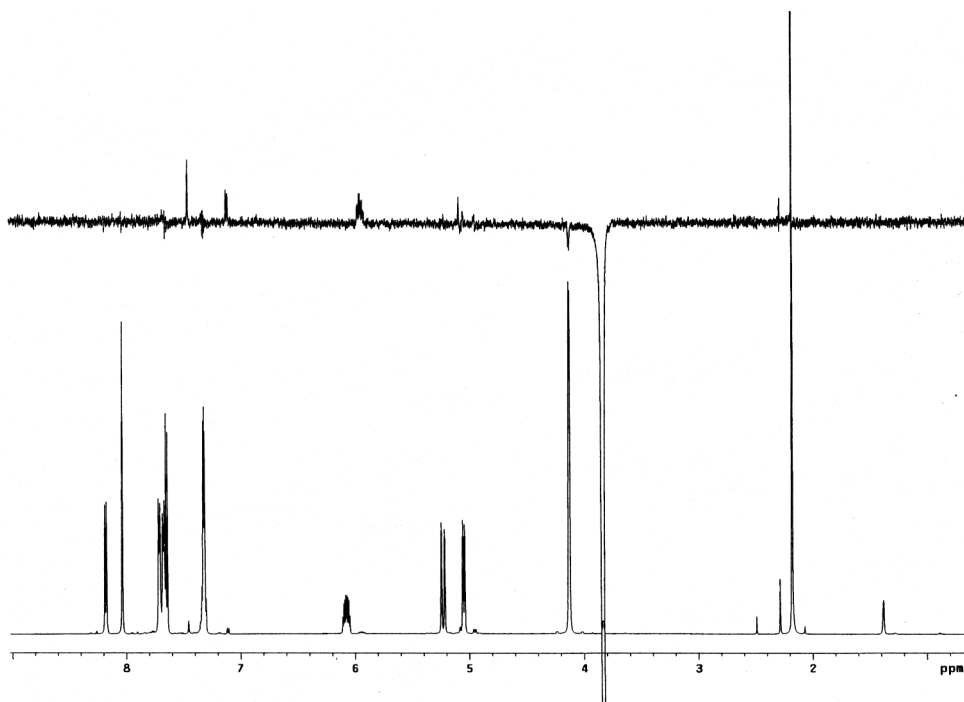
Isotopically labeled imine experiment:

Direct evidence of binding by ¹H NMR: Following Figure represents two ¹H NMR of the mixture of catalyst **3** with 2,2-dimethylpropylidene benzylamine in *d*₈-THF printed on the top of each other. Both samples contain the same amount of **3** (0.162M), and the same amount of imine (0.668M). In case of sample 1, ¹⁴N-imine was used (natural abundance); In case of sample 2, ¹⁵N-imine was used (content of ¹⁵N > 99%). Frequency (δ) of none of the protons of **1** has changed ($\Delta \delta < 1\text{Hz}$) as a function of the isotope content of the imine nitrogen, except for 2 signals: both urea-hydrogens ($\Delta \delta = 16.9\text{Hz}$, and 16.1Hz). Urea region of catalyst **3** is enlarged in the offset. Since the only difference between the two samples is the content of ¹⁵N in the imine substrate, this result represented a direct evidence of imine nitrogen binding to the UreaH's portion of the catalyst.



Equilibrium between E-and Z-stereoisomers of imine substrate by NMR

The sample of α -methylnaphtylidene allylamine that coexists as a mixture of both stereoisomers was irradiated (saturated) with the frequency of the Z-isomer allylic proton in NOESY1D experiment in d_{12} -cyclohexane (top spectrum). Exchanging allylic protons of E-isomer ($\delta = 4.14$ ppm) and Z-isomer ($\delta = 3.84$ ppm) had the same phase (opposite phase to the NOE xpeaks) as they underwent energy transfer due to chemical exchange. The ^1H NMR spectrum of the sample is provided below for clarity (Figure follows).



Computation and Modeling, General: Calculations were performed using standard computational methods. Theoretical calculations on the simplified system were performed using Gaussian 98;⁶ method B3LYP with many available basics sets. Reported data are consistent for all applied basic sets; data shown in Figure 2 of the text relate to 6-31G (d, p) basic set in the gas phase. The strength of the hydrogen bond was calculated as a difference of the energy of the complex and each individual component with dummy-atoms replacing other relevant fragments present in the complex. Calculations of the energy minimum of **1** were performed on Spartan with semi-empirical base, MM2, solvent-free as well as in hexadecane matrix. The 3D pictures of catalyst and catalyst/substrate complex were generated using Spartan and Gaussian 98 and modified in MOLMOL⁷ (see the text of the paper for relevant graphics).

Selected example of the resulting Z-matrix for imine-catalyst complex (*N*-ethylidene methylamine and *N,N'*-dimethylthiourea; Figure 1a of the main text):

```

0 1
C
N      1      B1
C      2      B2 1      A1
H      2      B3 1      A2 3      D1
N      2      B4 1      A3 3      D2
C      5      B5 2      A4 1      D3
N      6      B6 5      A5 2      D4
H      7      B7 6      A6 5      D5
S      6      B8 5      A7 2      D6
C      7      B9 6      A8 5      D7
C      5      B10 2      A9 1      D8
H      1      B11 2      A10 3      D9
H      1      B12 2      A11 3      D10
H      1      B13 2      A12 3      D11
H      3      B14 2      A13 1      D12
H      11     B15 5      A14 2      D13
H      11     B16 5      A15 2      D14
H      11     B17 5      A16 2      D15
H      10     B18 7      A17 6      D16
H      10     B19 7      A18 6      D17
H      10     B20 7      A19 6      D18
C      3      B21 2      A20 1      D19
H      22     B22 3      A21 2      D20
H      22     B23 3      A22 2      D21
H      22     B24 3      A23 2      D22

```

```

B1      1.455741
B2      1.276237
B3      2.239701
B4      3.182107
B5      1.360697
B6      1.360724
B7      1.015077
B8      1.689246
B9      1.449707
B10     1.449708
B11     1.095109
B12     1.095077

```

B13	1.095523
B14	1.095273
B15	1.093754
B16	1.095671
B17	1.093286
B18	1.093715
B19	1.093289
B20	1.095708
B21	1.504538
B22	1.096302
B23	1.096289
B24	1.089971
A1	122.568110
A2	125.590662
A3	132.352264
A4	101.892446
A5	113.793423
A6	117.226997
A7	123.099027
A8	123.695380
A9	134.262370
A10	108.509599
A11	108.503048
A12	115.769535
A13	114.856042
A14	111.033669
A15	111.775786
A16	108.033520
A17	111.016624
A18	108.035103
A19	111.789957
A20	130.784654
A21	109.221987
A22	109.229639
A23	114.402737
D1	145.373132
D2	151.123449
D3	114.066421
D4	-6.217759
D5	-4.120913
D6	173.088171
D7	-177.574987
D8	-70.440674
D9	-122.004795
D10	122.363105
D11	0.180566
D12	-179.995330
D13	-116.416000
D14	123.524546
D15	3.368130
D16	-58.144599
D17	-177.922986
D18	61.914645
D19	0.008921
D20	121.933831
D21	-122.013128

D22 -0.032016

1 2 1.0 12 1.0 13 1.0 14 1.0
 2 3 2.0
 3 15 1.0 22 1.0
 4 5 1.0
 5 6 1.5 11 1.0
 6 7 1.5 9 1.0
 7 8 1.0 10 1.0
 8
 9
 10 19 1.0 20 1.0 21 1.0
 11 16 1.0 17 1.0 18 1.0
 12
 13
 14
 15
 16
 17
 18
 19
 20
 21
 22 23 1.0 24 1.0 25 1.0
 23
 24
 25

Selected example of the resulting Z-matrix for imine-Strecker adduct complex (2-methylamino propionitrile and *N,N'*-dimethylthiourea; Figure 2b in the main text):

0	1				
C					
H	1	B1			
N	1	B2	2	A1	
C	3	B3	1	A2	2
N	4	B4	3	A3	1
H	5	B5	4	A4	3
S	4	B6	3	A5	1
C	5	B7	4	A6	3
C	3	B8	1	A7	2
H	1	B9	2	A8	3
H	1	B10	2	A9	3
H	1	B11	2	A10	3
H	9	B12	3	A11	1
H	9	B13	3	A12	1
H	9	B14	3	A13	1
H	8	B15	5	A14	4
H	8	B16	5	A15	4
H	8	B17	5	A16	4
C	1	B18	2	A17	3
H	19	B19	1	A18	2
H	19	B20	1	A19	2
H	19	B21	1	A20	2
C	19	B22	1	A21	2
H	23	B23	19	A22	1

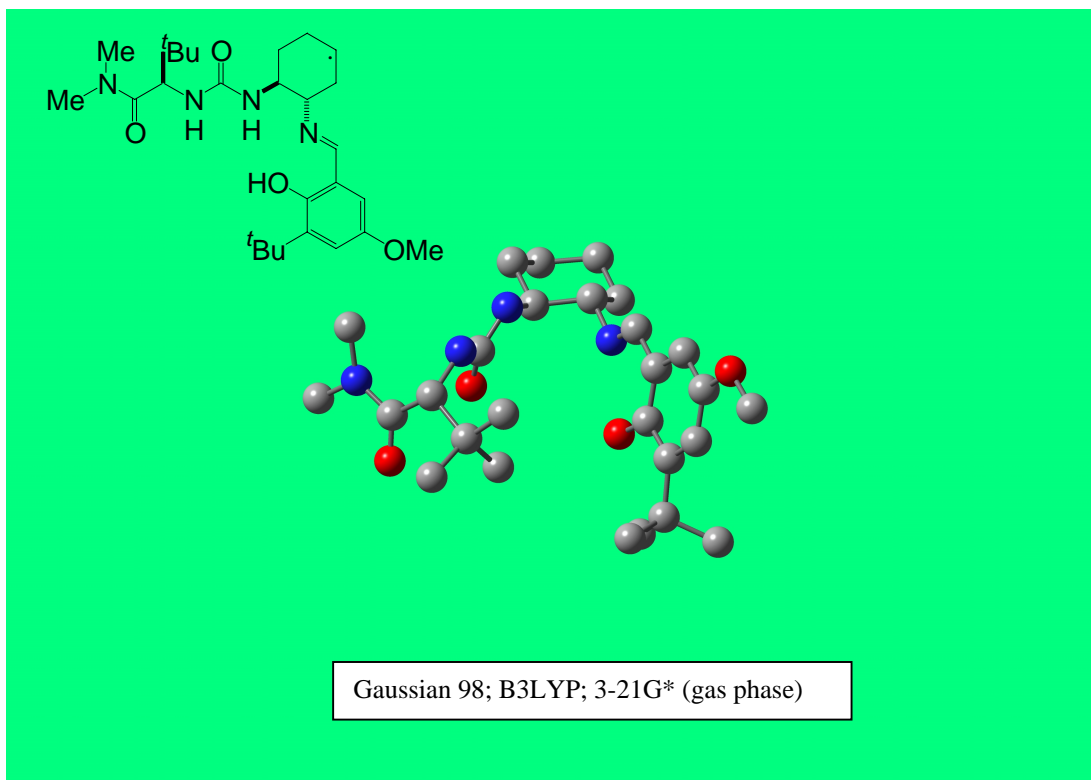
N	1	B24	2	A23	3	D22
H	25	B25	1	A24	2	D23
C	23	B26	19	A25	1	D24
N	27	B27	23	A26	19	D25

B1	3.015224
B2	3.982588
B3	1.358746
B4	1.380058
B5	1.012098
B6	1.681411
B7	1.457016
B8	1.452368
B9	1.092331
B10	1.092583
B11	1.099270
B12	1.092398
B13	1.093065
B14	1.096532
B15	1.093225
B16	1.096564
B17	1.090685
B18	3.073710
B19	1.092105
B20	1.092413
B21	1.092307
B22	1.535576
B23	1.096264
B24	1.472183
B25	1.018212
B26	1.484711
B27	1.161474
A1	5.512924
A2	131.282634
A3	113.197265
A4	114.455632
A5	123.871734
A6	122.064513
A7	101.118426
A8	83.650648
A9	89.853187
A10	152.593929
A11	110.366289
A12	108.053573
A13	112.276654
A14	108.047715
A15	112.514361
A16	109.760351
A17	62.780331
A18	96.404969
A19	154.142282
A20	68.046398
A21	53.704771
A22	107.803439
A23	39.641127
A24	107.966420

A25	110.905524
A26	177.230410
D1	35.971619
D2	-28.271400
D3	-25.964968
D4	151.056784
D5	-172.277881
D6	-168.998991
D7	18.902969
D8	-88.919579
D9	137.675719
D10	146.593476
D11	27.194684
D12	-93.495556
D13	-177.415610
D14	61.540940
D15	-58.412203
D16	85.971445
D17	-29.522778
D18	136.293714
D19	-137.815655
D20	79.665522
D21	-145.725867
D22	151.264711
D23	118.891813
D24	97.026468
D25	-132.139643

1 10 1.0 11 1.0 12 1.0 25 1.0
 2 3 1.0
 3 4 1.5 9 1.0
 4 5 1.5 7 1.0
 5 6 1.0 8 1.0
 6
 7
 8 16 1.0 17 1.0 18 1.0
 9 13 1.0 14 1.0 15 1.0
 10
 11
 12
 13
 14
 15
 16
 17
 18
 19 20 1.0 21 1.0 22 1.0 23 1.0
 20
 21
 22
 23 24 1.0 25 1.0 27 1.0
 24
 25 26 1.0
 26
 27 28 3.0
 28

Optimization to the energy minimum of a catalyst **6** derivative using Gaussian 98; method B3LYP; basis set 3-21G* (gas phase) provided the same structure that was observed by NMR spectroscopy in solution (Figure 1a of the text). Following is the figure (all hydrogens omitted for clarity) of the calculated structure and the resulting Z-matrix (including hydrogens).



Symbolic Z-matrix:

```

0 1
N
C      1  B1
O      2  B2      1  A1
C      2  B3      1  A2      3  D1      0
C      4  B4      2  A3      1  D2      0
N      4  B5      2  A4      1  D3      0
C      5  B6      4  A5      2  D4      0
C      5  B7      4  A6      2  D5      0
C      5  B8      4  A7      2  D6      0
C      6  B9      4  A8      2  D7      0
O     10  B10     6  A9      4  D8      0
N     10  B11     6  A10     4  D9      0
C     12  B12    10  A11     6  D10     0
H      6  B13     4  A12     2  D11     0
H     12  B14    10  A13     6  D12     0
C     13  B15    12  A14    10  D13     0
C     13  B16    12  A15    10  D14     0
C     16  B17    13  A16    12  D15     0
C     13  B18    12  A17    10  D16     0
C     16  B19    13  A18    12  D17     0
N     20  B20    16  A19    13  D18     0

```

C	21	B21	20	A20	16	D19	0
C	22	B22	21	A21	20	D20	0
C	23	B23	22	A22	21	D21	0
C	24	B24	23	A23	22	D22	0
C	25	B25	24	A24	23	D23	0
C	26	B26	25	A25	24	D24	0
C	27	B27	26	A26	25	D25	0
O	25	B28	24	A27	23	D26	0
O	28	B29	27	A28	26	D27	0
C	27	B30	26	A29	25	D28	0
C	31	B31	27	A30	26	D29	0
C	31	B32	27	A31	26	D30	0
H	33	B33	31	A32	27	D31	0
H	4	B34	2	A33	1	D32	0
H	7	B35	5	A34	4	D33	0
H	7	B36	5	A35	4	D34	0
H	7	B37	5	A36	4	D35	0
H	8	B38	5	A37	4	D36	0
H	8	B39	5	A38	4	D37	0
H	8	B40	5	A39	4	D38	0
H	9	B41	5	A40	4	D39	0
H	9	B42	5	A41	4	D40	0
H	9	B43	5	A42	4	D41	0
H	18	B44	16	A43	13	D42	0
H	18	B45	16	A44	13	D43	0
H	19	B46	13	A45	12	D44	0
H	19	B47	13	A46	12	D45	0
H	20	B48	16	A47	13	D46	0
H	22	B49	21	A48	20	D47	0
H	24	B50	23	A49	22	D48	0
H	26	B51	25	A50	24	D49	0
H	30	B52	28	A51	27	D50	0
H	32	B53	31	A52	27	D51	0
H	32	B54	31	A53	27	D52	0
H	33	B55	31	A54	27	D53	0
H	33	B56	31	A55	27	D54	0
H	32	B57	31	A56	27	D55	0
C	31	B58	27	A57	26	D56	0
H	59	B59	31	A58	27	D57	0
H	59	B60	31	A59	27	D58	0
H	59	B61	31	A60	27	D59	0
H	13	B62	12	A61	10	D60	0
H	17	B63	13	A62	12	D61	0
H	17	B64	13	A63	12	D62	0
H	16	B65	13	A64	12	D63	0
H	16	B66	13	A65	12	D64	0
C	1	B67	2	A66	3	D65	0
H	68	B68	1	A67	2	D66	0
H	68	B69	1	A68	2	D67	0
H	68	B70	1	A69	2	D68	0
C	1	B71	2	A70	3	D69	0
H	72	B72	1	A71	2	D70	0
H	72	B73	1	A72	2	D71	0
H	72	B74	1	A73	2	D72	0
C	29	B75	25	A74	24	D73	0
H	76	B76	29	A75	25	D74	0

H	76	B77	29	A76	25	D75	0
H	76	B78	29	A77	25	D76	0

Variables:

B1	1.37791
B2	1.24688
B3	1.55597
B4	1.56422
B5	1.47848
B6	1.54778
B7	1.54895
B8	1.55018
B9	1.38729
B10	1.24336
B11	1.38548
B12	1.46434
B13	1.01527
B14	1.01401
B15	2.53026
B16	2.54031
B17	1.54479
B18	1.54286
B19	1.54554
B20	1.47683
B21	1.29382
B22	1.45107
B23	1.39859
B24	1.38629
B25	1.39909
B26	1.40071
B27	1.41578
B28	1.3935
B29	1.36153
B30	1.54993
B31	1.55589
B32	1.55098
B33	1.08826
B34	1.10009
B35	1.09735
B36	1.0887
B37	1.09283
B38	1.09921
B39	1.09551
B40	1.09531
B41	1.0988
B42	1.09591
B43	1.09017
B44	1.09879
B45	1.09617
B46	1.09994
B47	1.09523
B48	1.10475
B49	1.09757
B50	1.08328
B51	1.0804
B52	1.055
B53	1.09439

B54	1.09523
B55	1.09279
B56	1.09692
B57	1.0961
B58	1.55391
B59	1.09689
B60	1.09564
B61	1.09447
B62	1.094
B63	1.09803
B64	1.09624
B65	1.09681
B66	1.09584
B67	1.47366
B68	1.09641
B69	1.08928
B70	1.09786
B71	1.46721
B72	1.09937
B73	1.08652
B74	1.09772
B75	1.45621
B76	1.09765
B77	1.09757
B78	1.09065
A1	120.72517
A2	117.01515
A3	113.81247
A4	111.00832
A5	113.23394
A6	108.2498
A7	108.23234
A8	121.15722
A9	123.14424
A10	114.12773
A11	119.17522
A12	116.14609
A13	121.48891
A14	146.10246
A15	146.98971
A16	90.31198
A17	112.36749
A18	35.10283
A19	110.03427
A20	119.82911
A21	122.75859
A22	118.95156
A23	120.00438
A24	118.63279
A25	123.49792
A26	117.77938
A27	116.41702
A28	121.9508
A29	117.12898
A30	109.49413
A31	114.88095

A32	111.63737
A33	106.14158
A34	108.32793
A35	109.40145
A36	112.63195
A37	111.32942
A38	109.19633
A39	111.19055
A40	110.77232
A41	109.45774
A42	109.47194
A43	109.24995
A44	109.6469
A45	109.32544
A46	108.55464
A47	109.06709
A48	121.22349
A49	120.99213
A50	118.65008
A51	107.99163
A52	112.33078
A53	110.16859
A54	111.12335
A55	107.79737
A56	109.09485
A57	108.38429
A58	109.77108
A59	111.22957
A60	109.93512
A61	104.3915
A62	91.61034
A63	144.68439
A64	90.01697
A65	144.30072
A66	117.62067
A67	110.01124
A68	107.0382
A69	110.48987
A70	127.17575
A71	110.77438
A72	110.32411
A73	109.28869
A74	117.90664
A75	111.90703
A76	111.90925
A77	104.98726
D1	-174.97216
D2	172.92094
D3	-57.19889
D4	59.89443
D5	-179.02921
D6	-62.01234
D7	-43.70959
D8	3.33987
D9	-177.73844
D10	173.51594

D11	158.16273
D12	-6.73402
D13	-115.98529
D14	112.87055
D15	-134.24379
D16	115.71943
D17	-7.16314
D18	120.09487
D19	114.57599
D20	179.88701
D21	178.35154
D22	-179.67675
D23	1.10892
D24	-0.48953
D25	-1.28705
D26	-179.23457
D27	-177.33593
D28	-179.95149
D29	-50.84911
D30	-170.8978
D31	-62.63932
D32	56.80967
D33	-173.62152
D34	-54.23142
D35	67.57077
D36	56.97602
D37	176.23957
D38	-65.31227
D39	-56.82477
D40	-175.9341
D41	64.0879
D42	93.0285
D43	-149.37133
D44	61.94659
D45	-55.59575
D46	-119.5129
D47	-0.38606
D48	0.31102
D49	179.53152
D50	-176.48374
D51	61.13493
D52	-60.08847
D53	57.84253
D54	177.09801
D55	-179.2681
D56	68.2336
D57	-177.92236
D58	-57.68025
D59	62.70808
D60	-3.05731
D61	-117.3486
D62	6.99653
D63	115.55696
D64	-6.28774
D65	-4.32683
D66	-122.99338

D67	-3.00875
D68	116.57464
D69	170.83295
D70	-107.78505
D71	14.62921
D72	133.33393
D73	-179.81204
D74	-61.34278
D75	61.34813
D76	-179.99249

Z-matrix for the catalyst-imine complex (including hydrogens); Figure 2b-c of the main text:

```

0 1
C
N      1      1.455100
C      2      1.307659      1      120.326986
O      3      1.217380      2      124.951408      1      0.150436
C      3      1.537574      2      113.113208      1      -179.982473
C      5      1.547259      3      111.304327      2      121.863903
N      5      1.464335      3      110.818912      2      -115.964654
C      6      1.537108      5      110.094633      3      61.342520
C      6      1.530865      5      109.663057      3      -178.541730
C      6      1.533359      5      109.590417      3      -58.870713
C      7      1.315610      5      120.314565      3      -10.053245
O      11     1.215877      7      120.721550      5      -0.005474
N      11     1.319129      7      119.034418      5      -179.990229
C      13     1.466249      11     122.751257      7      179.840369
H      7      1.011999      5      119.597747      3      169.883662
N      13     2.904829      11     100.906104      7      -0.019423
C      14     2.503556      13     144.236575      11     -125.366467
C      14     2.493638      13     144.759766      11     115.671826
C      18     1.531964      14     90.072562      13     124.005363
C      14     1.529160      13     109.292019      11     115.369939
C      14     1.529334      13     109.066819      11     -124.952615
C      1      1.436670      2      112.630728      3      176.434088
C      22     1.405807      1      120.034799      2      179.997704
C      23     1.404255      22     119.919026      1      179.993126
C      24     1.404425      23     120.015986      22     -0.009202
C      25     1.404770      24     120.046423      23     -0.081602
C      22     1.403141      1      119.944134      2      -0.069812
N      21     1.431013      14     108.705660      13     60.147439
C      28     1.339587      21     119.989678      14     -119.783391
C      29     1.320516      28     122.036228      21     179.957090
C      30     1.404100      29     120.429102      28     179.974290
C      31     1.405305      30     119.940692      29     179.950946
C      32     1.404137      31     120.067753      30     0.112073
C      33     1.403600      32     119.956263      31     -0.108519
C      34     1.404311      33     120.046419      32     0.101346
O      32     1.392087      31     119.942920      30     179.960959
O      35     1.391273      34     120.038204      33     179.995640
C      36     1.315207      32     106.044677      31     -179.949661
O      38     1.207858      36     119.918747      32     0.134995
C      38     1.448154      36     118.521426      32     -179.912822
C      40     1.544513      38     107.343896      36     -179.762586

```


C	40	1.542914	38	110.411370	36	61.565281
C	40	1.543116	38	110.761871	36	-59.246233
C	34	1.449602	33	118.942088	32	179.978131
C	44	1.542961	34	109.164788	33	-59.938961
C	44	1.544605	34	110.275620	33	59.669479
C	44	1.542991	34	108.950032	33	-178.935849
C	16	1.279505	13	117.405295	11	103.108901
H	13	1.013096	11	118.574677	7	-0.038520
C	16	1.471633	13	117.445992	11	-101.842503
C	48	1.531949	16	119.998372	13	154.970391
C	48	1.530919	16	119.986104	13	-25.104829
C	51	2.771308	16	153.003071	13	138.431560
C	51	1.385864	48	119.979739	16	-0.081275
C	51	1.387154	48	119.957641	16	179.957536
C	55	1.385165	51	119.981485	48	179.989198
C	53	1.385803	51	59.990805	54	0.017075
C	50	1.531473	16	109.436884	13	25.604244
C	58	1.332800	50	119.960560	16	-179.702030
H	1	B1	2	A1	3	D1
H	5	B2	3	A2	2	D2
H	8	B3	6	A3	5	D3
H	8	B4	6	A4	5	D4
H	8	B5	6	A5	5	D5
H	9	B6	6	A6	5	D6
H	9	B7	6	A7	5	D7
H	9	B8	6	A8	5	D8
H	10	B9	6	A9	5	D9
H	10	B10	6	A10	5	D10
H	10	B11	6	A11	5	D11
H	14	B12	13	A12	11	D12
H	17	B13	14	A13	13	D13
H	17	B14	14	A14	13	D14
H	18	B15	14	A15	13	D15
H	18	B16	14	A16	13	D16
H	19	B17	18	A17	14	D17
H	19	B18	18	A18	14	D18
H	20	B19	14	A19	13	D19
H	20	B20	14	A20	13	D20
H	21	B21	14	A21	13	D21
H	23	B22	22	A22	1	D22
H	24	B23	23	A23	22	D23
H	25	B24	24	A24	23	D24
H	26	B25	25	A25	24	D25
H	27	B26	22	A26	1	D26
H	29	B27	28	A27	21	D27
H	31	B28	30	A28	29	D28
H	33	B29	32	A29	31	D29
H	37	B30	35	A30	34	D30
H	41	B31	40	A31	38	D31
H	41	B32	40	A32	38	D32
H	41	B33	40	A33	38	D33
H	42	B34	40	A34	38	D34
H	42	B35	40	A35	38	D35
H	42	B36	40	A36	38	D36
H	43	B37	40	A37	38	D37
H	43	B38	40	A38	38	D38

H	43	B39	40	A39	38	D39
H	45	B40	44	A40	34	D40
H	45	B41	44	A41	34	D41
H	45	B42	44	A42	34	D42
H	46	B43	44	A43	34	D43
H	46	B44	44	A44	34	D44
H	46	B45	44	A45	34	D45
H	47	B46	44	A46	34	D46
H	47	B47	44	A47	34	D47
H	47	B48	44	A48	34	D48
H	50	B49	16	A49	13	D49
H	50	B50	16	A50	13	D50
H	52	B51	48	A51	16	D51
H	52	B52	48	A52	16	D52
H	52	B53	48	A53	16	D53
H	53	B54	57	A54	54	D54
H	54	B55	51	A55	48	D55
H	55	B56	51	A56	48	D56
H	56	B57	55	A57	51	D57
H	57	B58	53	A58	51	D58
H	58	B59	50	A59	16	D59
H	59	B60	58	A60	50	D60
H	59	B61	58	A61	50	D61

B1	1.070000
B2	1.070000
B3	1.070000
B4	1.070000
B5	1.070000
B6	1.070000
B7	1.070000
B8	1.070000
B9	1.070000
B10	1.070000
B11	1.070000
B12	1.070000
B13	1.070000
B14	1.070000
B15	1.070000
B16	1.070000
B17	1.070000
B18	1.070000
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B20	1.070000
B21	1.070000
B22	1.070000
B23	1.070000
B24	1.070000
B25	1.070000
B26	1.070000
B27	1.070000
B28	1.070000
B29	1.070000
B30	0.960000
B31	1.070000
B32	1.070000

B33	1.070000
B34	1.070000
B35	1.070000
B36	1.070000
B37	1.070000
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B39	1.070000
B40	1.070000
B41	1.070000
B42	1.070000
B43	1.070000
B44	1.070000
B45	1.070000
B46	1.070000
B47	1.070000
B48	1.070000
B49	1.070000
B50	1.070000
B51	1.070000
B52	1.070000
B53	1.070000
B54	1.070000
B55	1.070000
B56	1.070000
B57	1.070000
B58	1.070000
B59	1.070000
B60	1.070000
B61	1.070000
A1	123.684636
A2	107.311453
A3	109.471221
A4	109.471221
A5	109.471221
A6	109.471221
A7	109.471221
A8	109.471221
A9	109.471221
A10	109.471221
A11	109.471221
A12	109.866854
A13	141.765216
A14	85.675338
A15	85.029188
A16	142.112676
A17	106.813008
A18	106.813008
A19	106.852493
A20	106.852493
A21	109.971157
A22	120.040487
A23	119.992007
A24	119.976788
A25	120.041946
A26	119.959342
A27	118.981886

A28	120.029654
A29	120.021868
A30	109.471221
A31	109.471221
A32	109.471221
A33	109.471221
A34	109.471221
A35	109.471221
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A38	109.471221
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A47	109.471221
A48	109.471221
A49	106.785975
A50	106.785975
A51	109.471221
A52	109.471221
A53	109.471221
A54	119.991139
A55	120.045682
A56	120.009257
A57	120.007307
A58	119.977930
A59	120.019720
A60	120.000000
A61	120.000000
D1	-3.565912
D2	3.118839
D3	180.000000
D4	60.000000
D5	-60.000000
D6	-180.000000
D7	60.000000
D8	-60.000000
D9	180.000000
D10	-60.000000
D11	60.000000
D12	-4.723939
D13	-7.064176
D14	128.516025
D15	-129.103199
D16	5.765422
D17	-84.663267
D18	145.771523
D19	64.507789
D20	-65.108182
D21	-60.026839
D22	-0.006874

D23	179.990798
D24	179.918398
D25	-179.879157
D26	0.046110
D27	-0.042910
D28	-0.049054
D29	179.891481
D30	-10.884943
D31	-180.000000
D32	-60.000000
D33	60.000000
D34	-180.000000
D35	60.000000
D36	-60.000000
D37	180.000000
D38	-60.000000
D39	60.000000
D40	0.000000
D41	120.000000
D42	-120.000000
D43	0.000000
D44	-120.000000
D45	120.000000
D46	-180.000000
D47	-60.000000
D48	60.000000
D49	140.838962
D50	-89.630475
D51	179.999998
D52	-60.000000
D53	60.000000
D54	179.954276
D55	0.013566
D56	-0.010802
D57	179.960425
D58	179.982915
D59	0.297970
D60	-0.000001
D61	180.000000

Notes and References

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