Supporting Information

Divergent Stereoselectivity in Phosphothreonine (pThr)-Catalyzed Reductive Aminations of 3-Amidocyclohexanones

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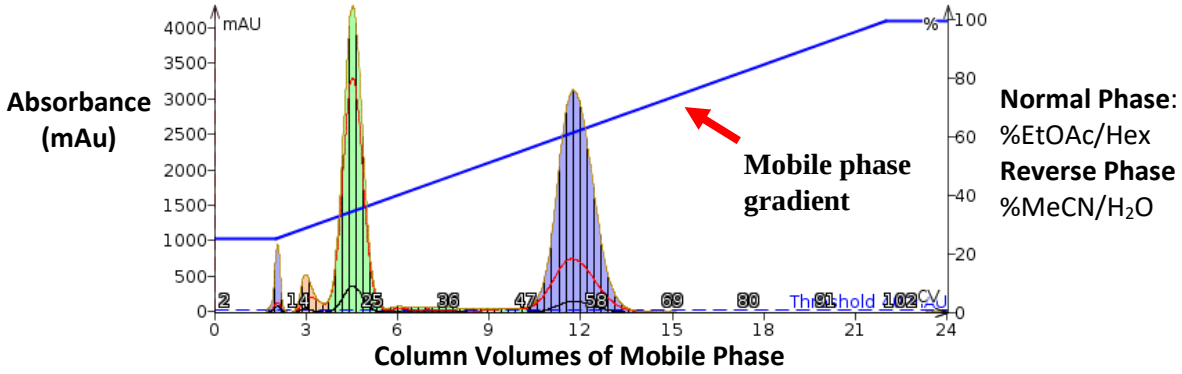
1. General Information

Example Automatic Chromatography Trace



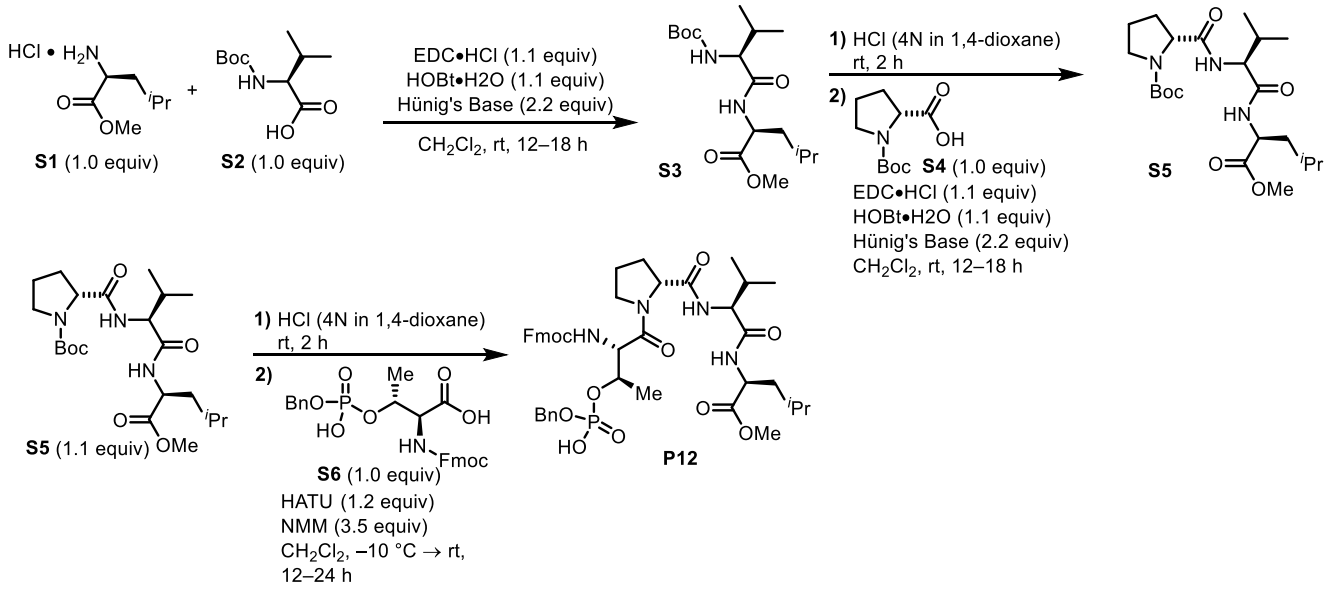
Abbreviations:

AcOH	Acetic Acid
Acpc	1-Aminocyclopropane-1-carboxylic acid
Bz	Benzoyl
C_6H_6	Benzene
$CaSO_4$	Calcium Sulfate
Cbz	Carboxybenzyl
Cha	L-Cyclohexylalanine
Chg	Cyclohexylglycine
CH_2Cl_2	Methylene Chloride
$CHCl_3$	Chloroform
Chg	L-Cyclohexylglycine
Cl-HOBt	6-Chloro-1-hydroxybenzotriazole
Dba	Dibenzylideneacetone
DFT	Density Functional Theory
DPP	Diphenyl Phosphate
DMF	*N*,*N*-dimethylformamide
EDC	*N*-(3-Dimethylaminopropyl)-*N*′-ethylcarbodiimide
EtOAc	Ethyl Acetate
Fmoc	Fluorenylmethyloxycarbonyl
HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate,*N*-[(Dimethylamino)-1H-1,2,3-triazolo-[4,5-b]pyridin-1-ylmethylene]-N-methylmethanaminium hexafluorophosphate *N*-oxide
HCTU	*O*-(1H-6-Chlorobenzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
Hex	Hexanes
HOBt	1-Hydroxybenzotriazole
HPLC	High-performance liquid chromatography
MeCN	Acetonitrile
MeOH	Methanol
MS	Mass Spectrometry
NMM	*N*-Methylmorpholine
NMP	*N*-Methyl-2-pyrrolidone
Phg	L-Phenylglycine
PhH	Benzene
PhMe	Toluene
p-Meo-Bz	*para*-methoxy benzoyl
p-O_2N-Bz	*para*-nitro benzoyl

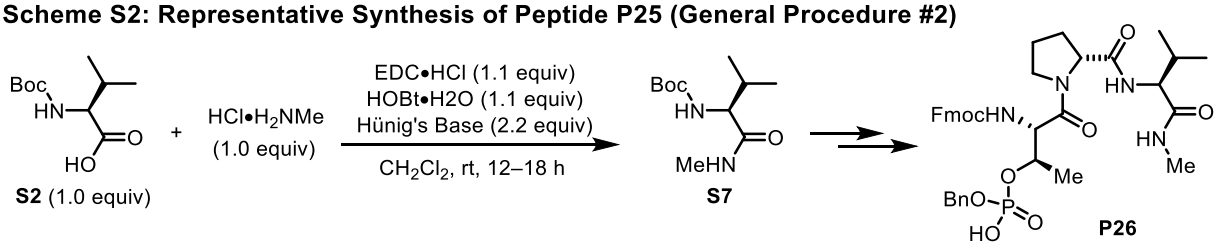
RF	Retention factor
RRF	Relative response factor
rt	Room temperature
THF	Tetrahydrofuran
TMS	Trimethylsilyl
TFA	Trifluoroacetic acid
Tle	L-*tert*-Leucine
UPLC-MS	Ultra-performance liquid chromatography – tandem mass spectrometry

2. Synthesis of pThr-Embedded Peptides

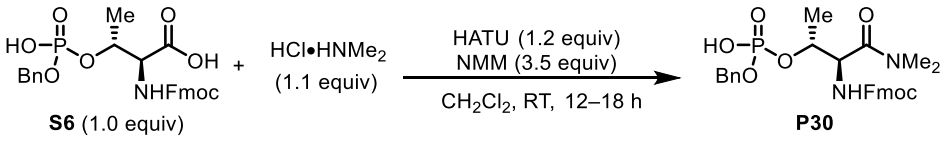
Scheme S1: Representative Synthesis and Characterization of Peptide P12 (General Procedure #1)



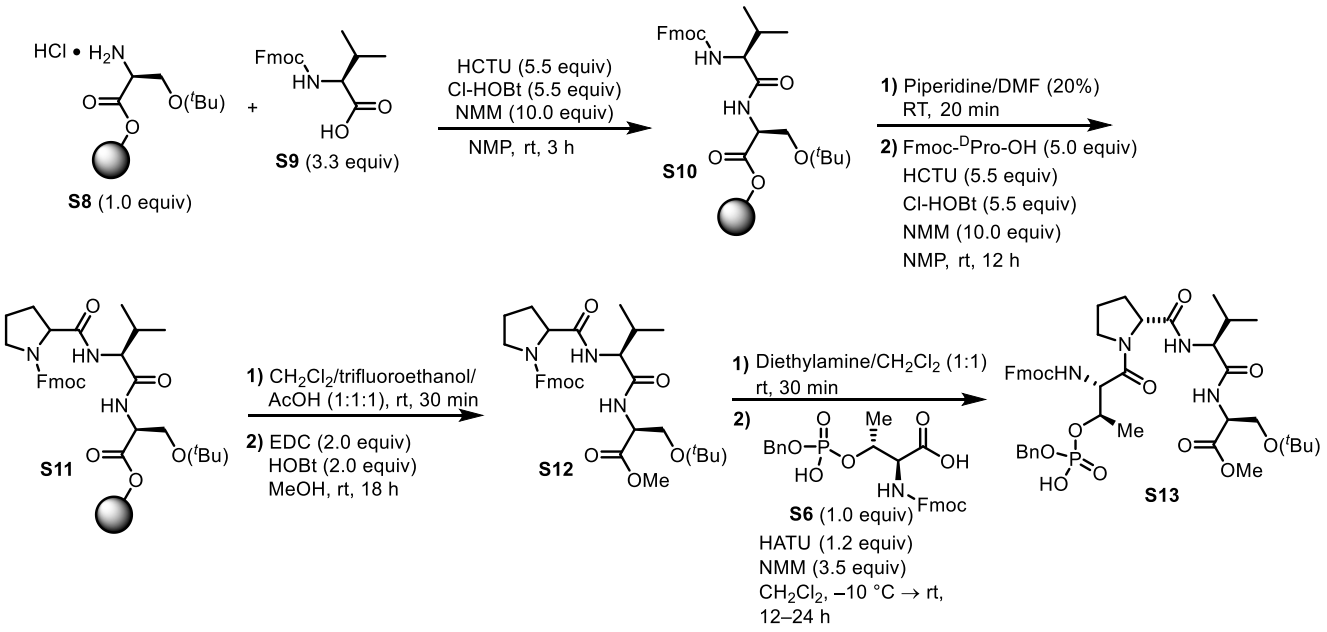
Scheme S2: Representative Synthesis of Peptide P25 (General Procedure #2)



Scheme S3: Synthesis of Peptide P30 (Procedure #3)

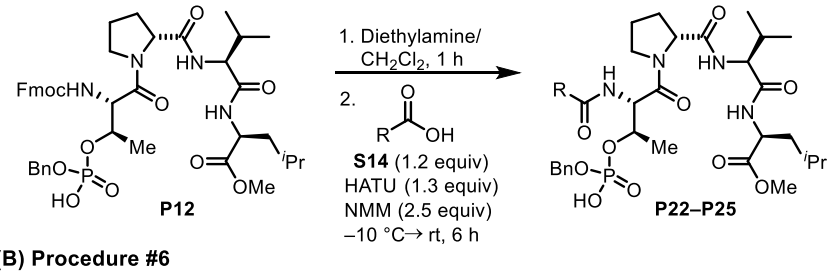


Scheme S4: Representative Synthesis and Characterization S13, a Precursor to Peptide P32 (General Procedure #4)

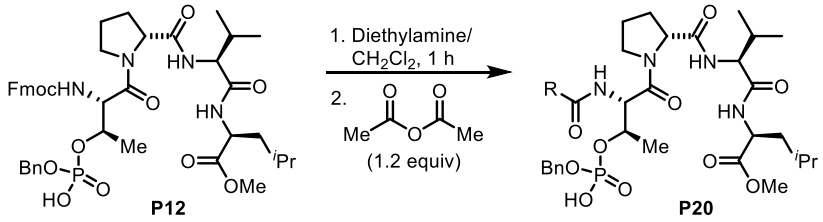


Scheme S5: Variation of *N*-Terminal Protecting Group

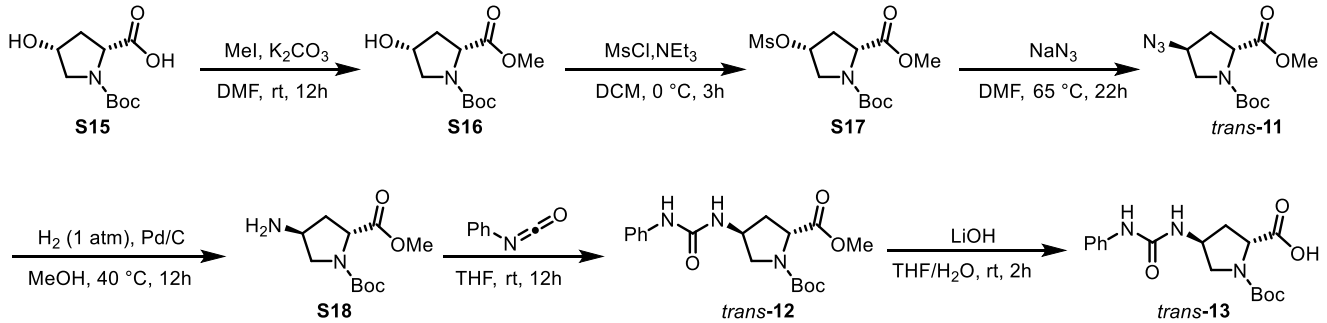
(A) General Procedure #5



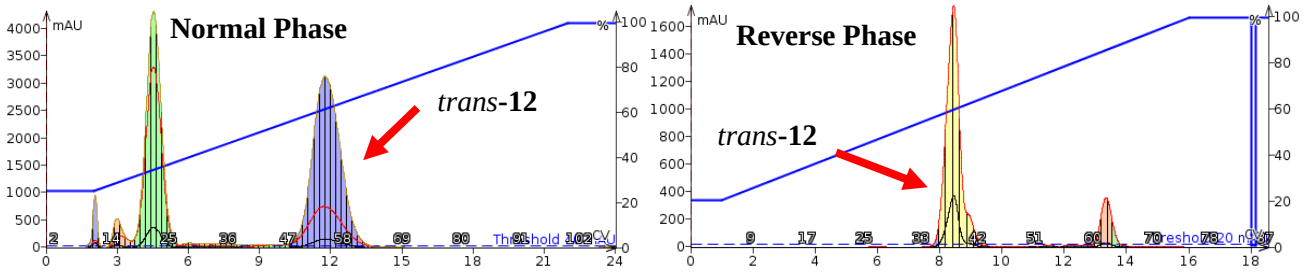
(B) Procedure #6

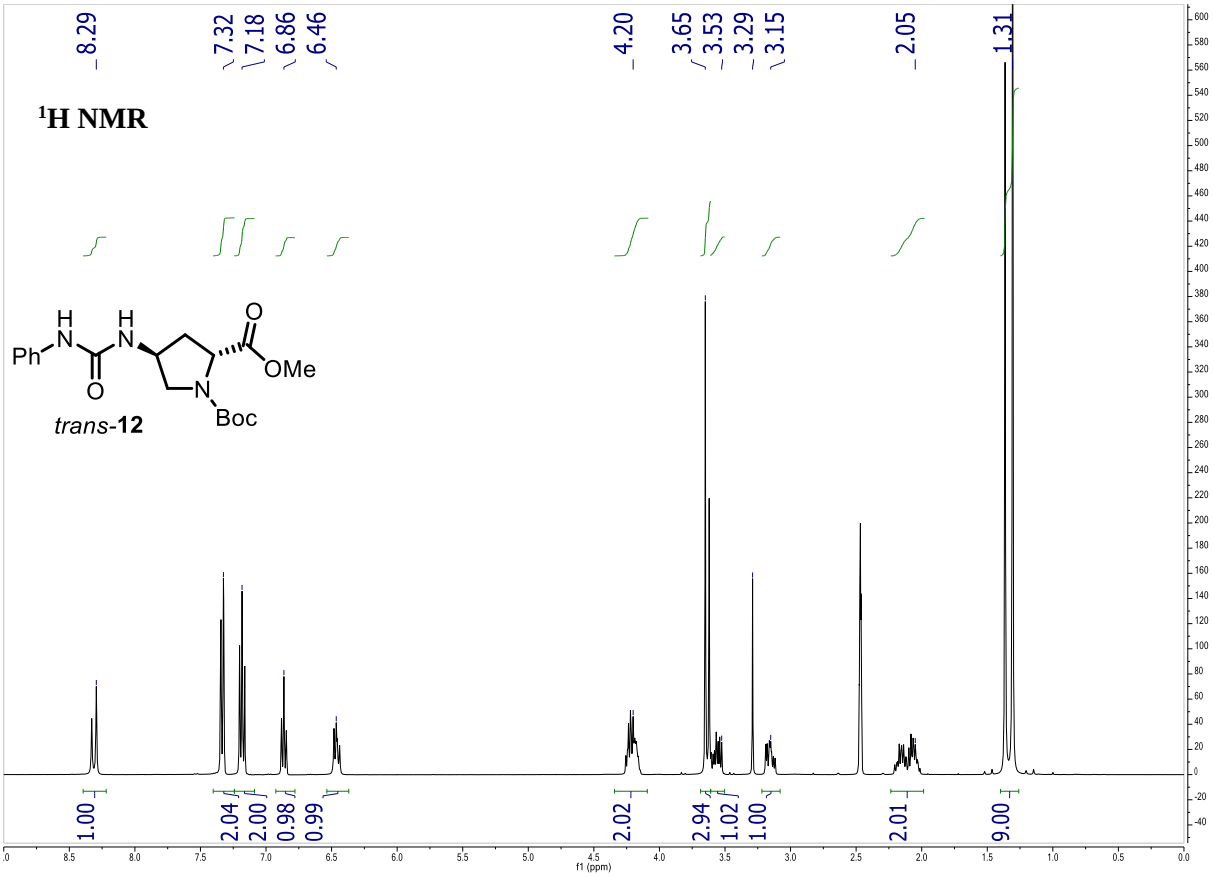


Scheme S6: Synthesis of *trans*-4-Amidoproline Residue (Procedure #7)

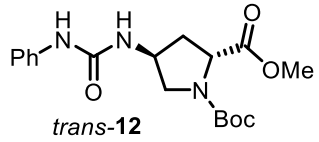


1-(*tert*-butyl) 2-methyl (2*R*,4*S*)-4-(3-phenylureido)pyrrolidine-1,2-dicarboxylate (*trans*-12).
Automatic Chromatography Traces:



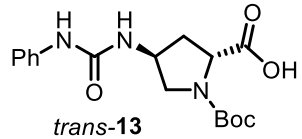


^{13}C NMR

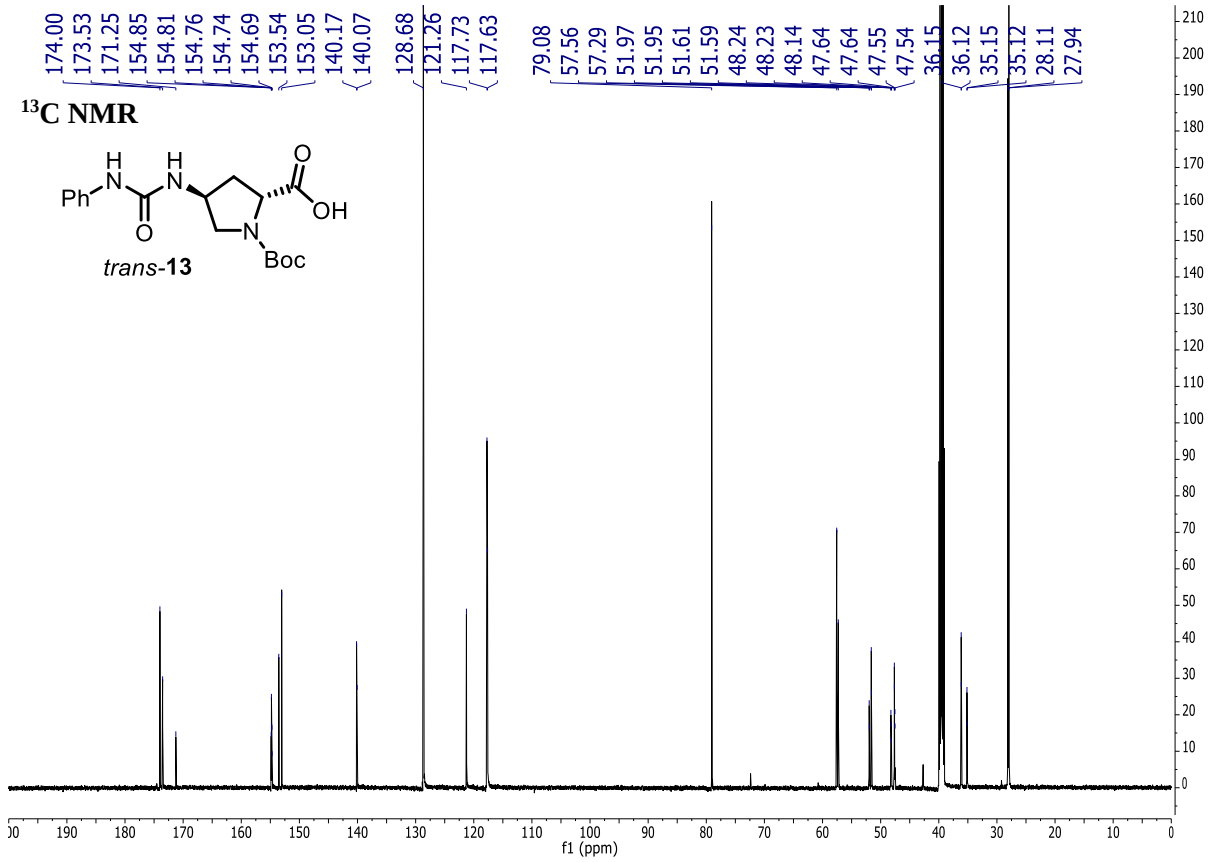


trans-**12**

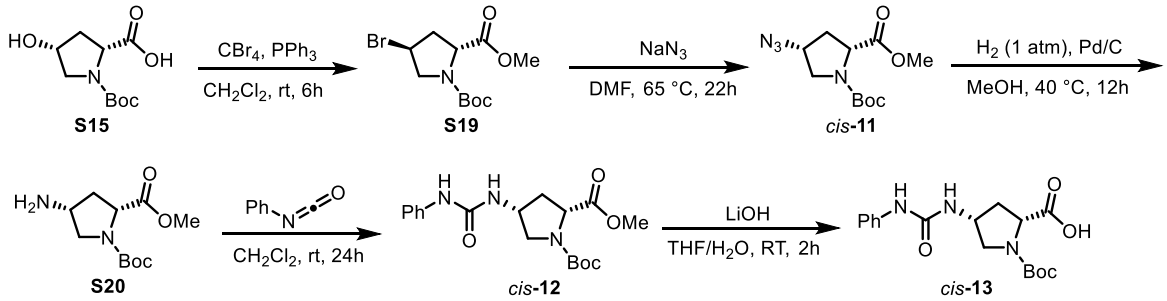
^{1}H NMR



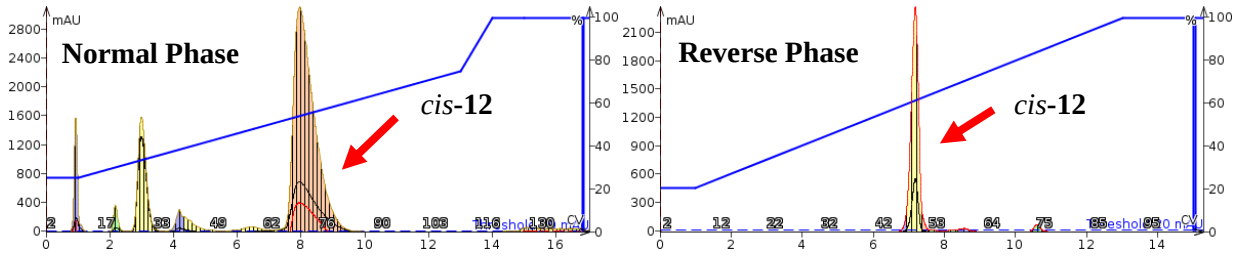
trans-**13**



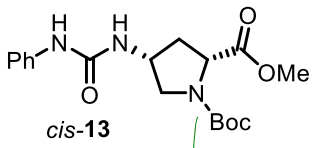
Scheme S7: Synthesis of *cis*-4-Amidoproline Residue (Procedure #8)



1-(*tert*-butyl) 2-methyl (2*R*,4*R*)-4-(3-phenylureido)pyrrolidine-1,2-dicarboxylate (*cis*-12).
Automatic Chromatography Traces:

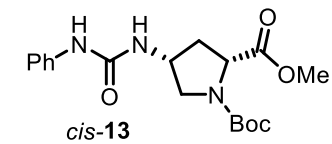


^{1}H NMR



cis-**13**

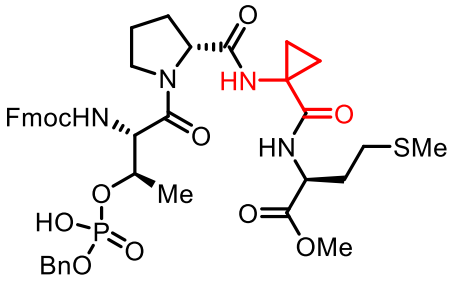
^{13}C NMR



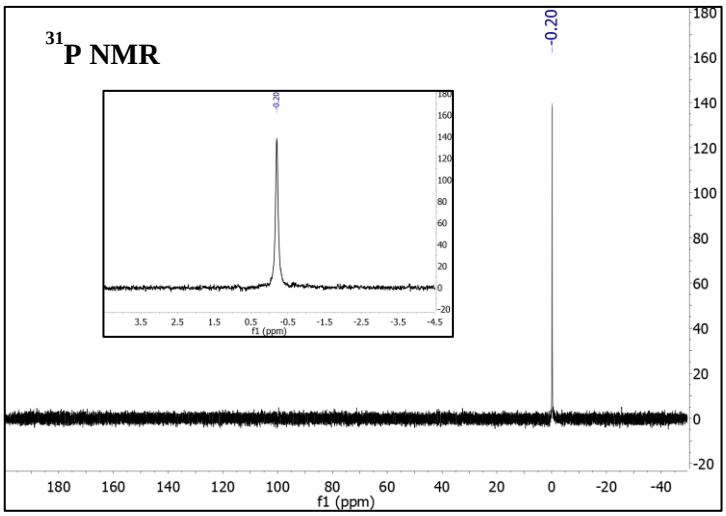
cis-**13**

Additional peaks in ^{31}P NMR of Peptides are presumably either different conformations of peptides or diastereomers of the P-atom.

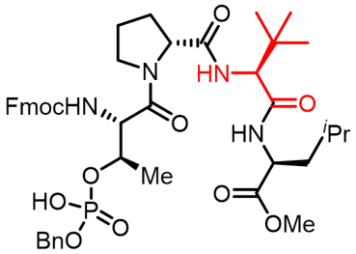
Fmoc-pThr(Bn)-*D*Pro-Acpc-Met-OMe (P1)



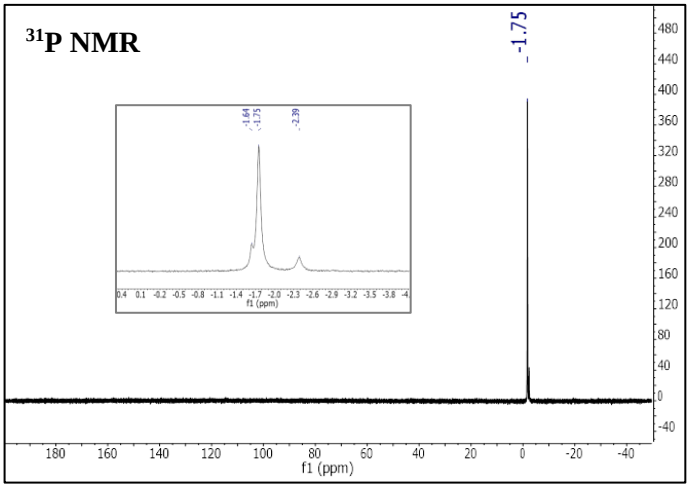
Synthesis: General Procedure #1
Scale: 0.600 mmol wrt **S6**
Yield: 502 mg white solid (63% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.20.



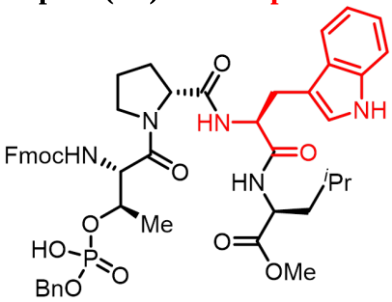
Fmoc-pThr(Bn)-*D*Pro-Tle-Leu-OMe (P2)



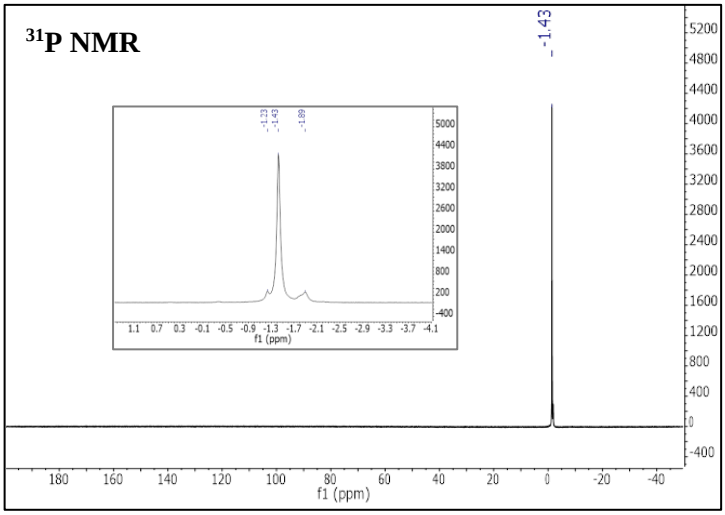
Synthesis: General Procedure #1
Scale: 0.606 mmol wrt **S6**
Yield: 221 mg white solid (43% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.75.



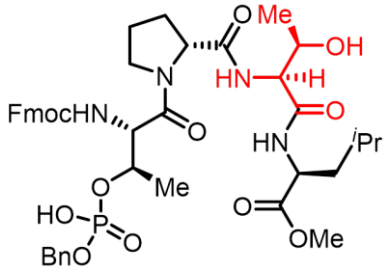
Fmoc-pThr(Bn)-*D*Pro-Trp-Leu-OMe (P3)



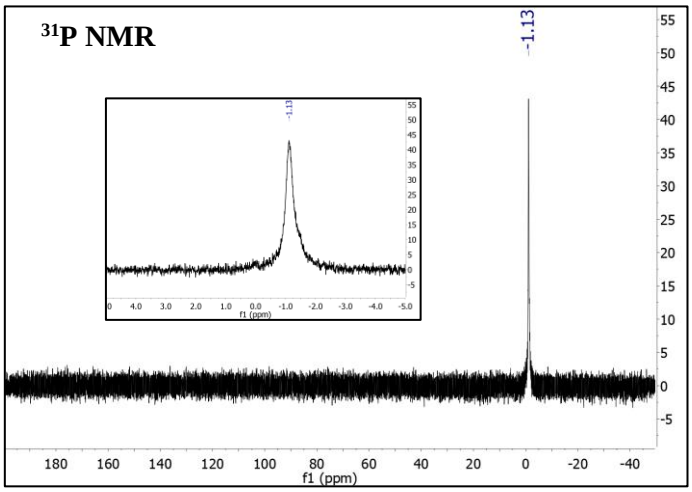
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 228 mg white solid (38% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.43.



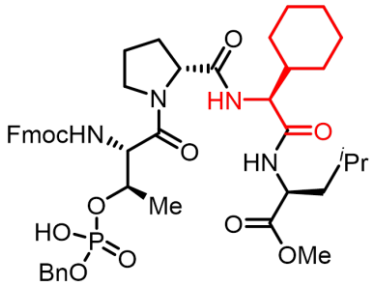
Fmoc-pThr(Bn)-^{D}Pro-Thr(Me)-Leu-OMe (P4)



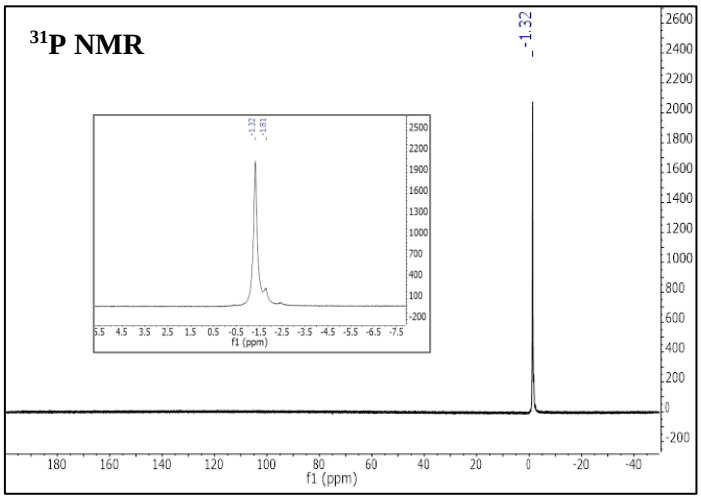
Synthesis: General Procedure #1
Scale: 0.780 mmol wrt **S6**
Yield: 296 mg white solid (51% yield)
^{31}P NMR: (202 MHz, $CDCl_3$) δ –1.13.



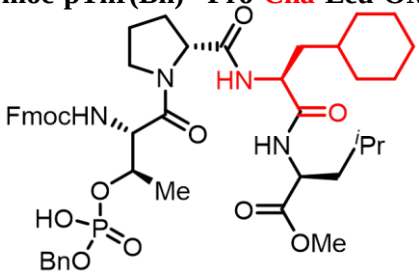
Fmoc-pThr(Bn)-^{D}Pro-Chg-Leu-OMe (P5)



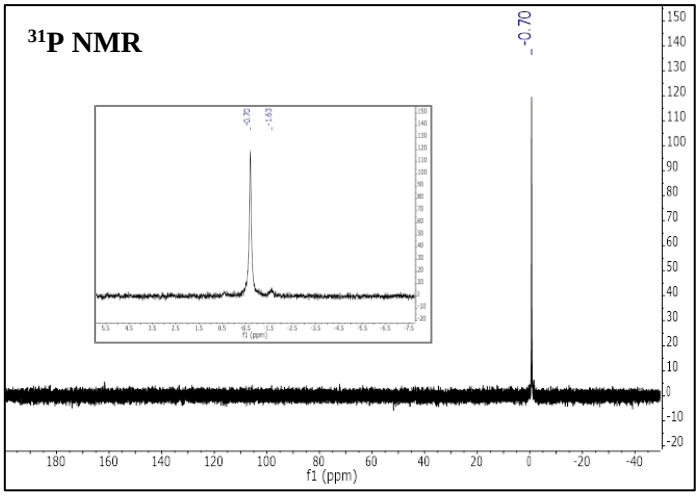
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 407 mg white solid (71% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.32.



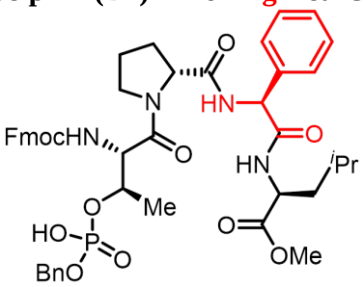
Fmoc-pThr(Bn)-^{D}Pro-Cha-Leu-OMe (P6)



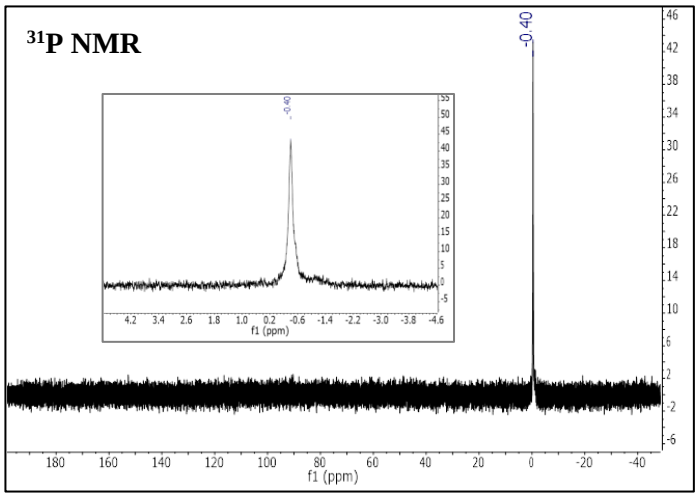
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 379 mg white solid (66% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.70.



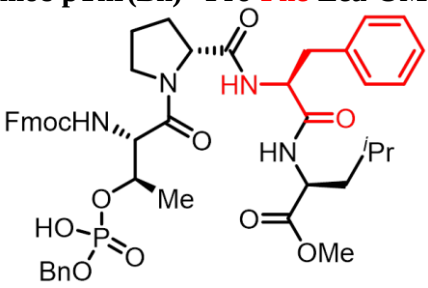
Fmoc-pThr(Bn)-^{D}Pro-Phg-Leu-OMe (P7)



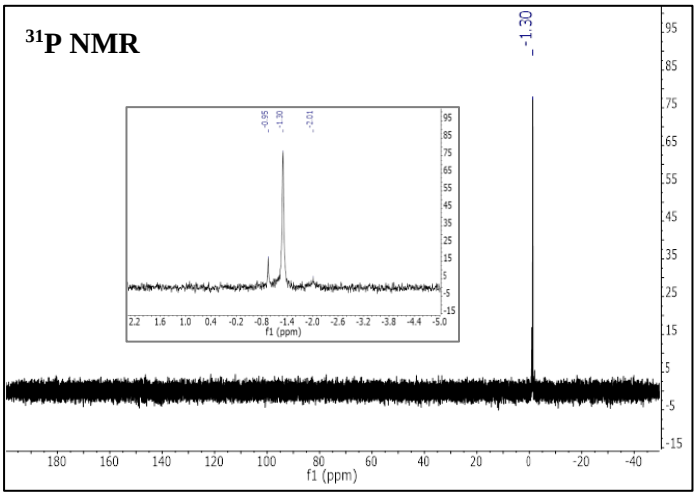
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 347 white solid (62% yield)
^{31}P NMR: (202 MHz, $CDCl_3$) δ –0.40.



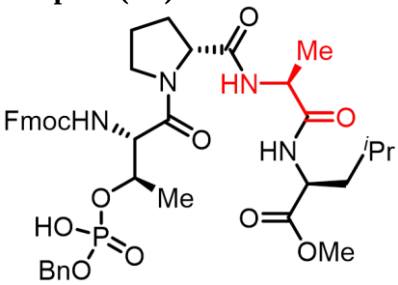
Fmoc-pThr(Bn)-^{D}Pro-Phe-Leu-OMe (P8)



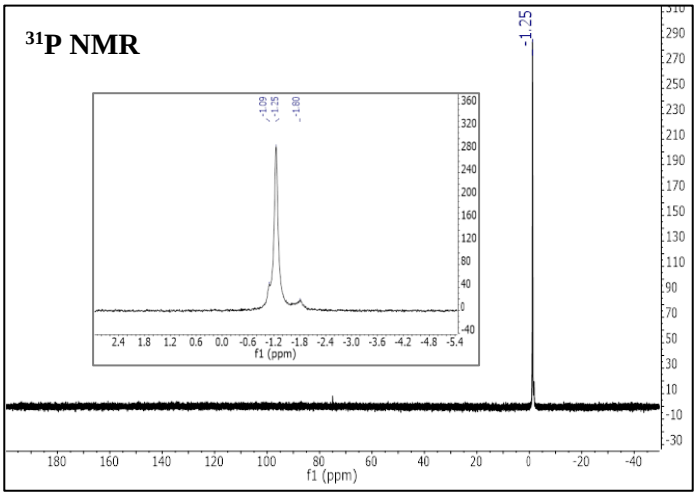
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 210 mg white solid (37% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.30.



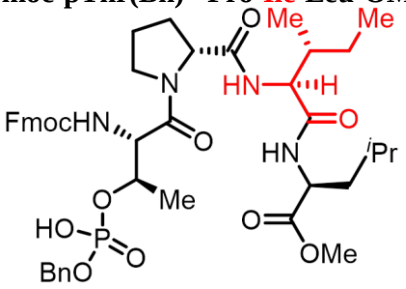
Fmoc-pThr(Bn)-^{D}Pro-Ala-Leu-OMe (P9)



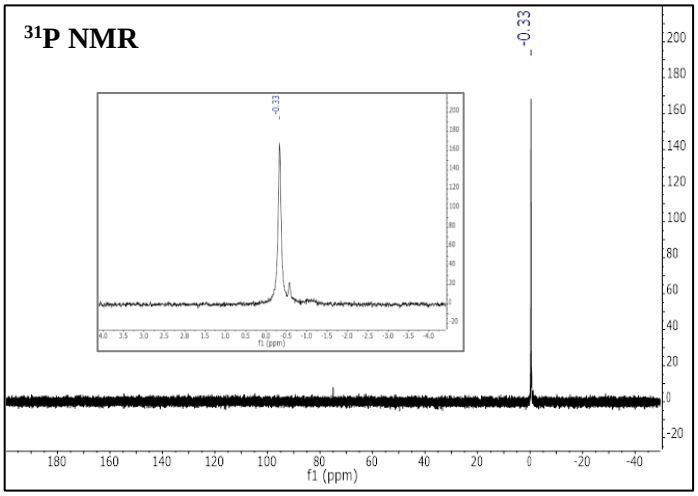
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 309 mg white solid (59% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.25.



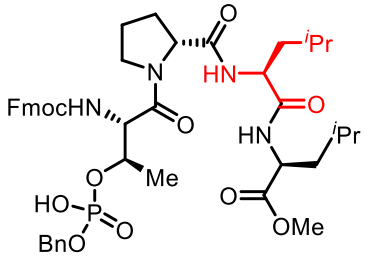
Fmoc-pThr(Bn)-^{D}Pro-Ile-Leu-OMe (P10)



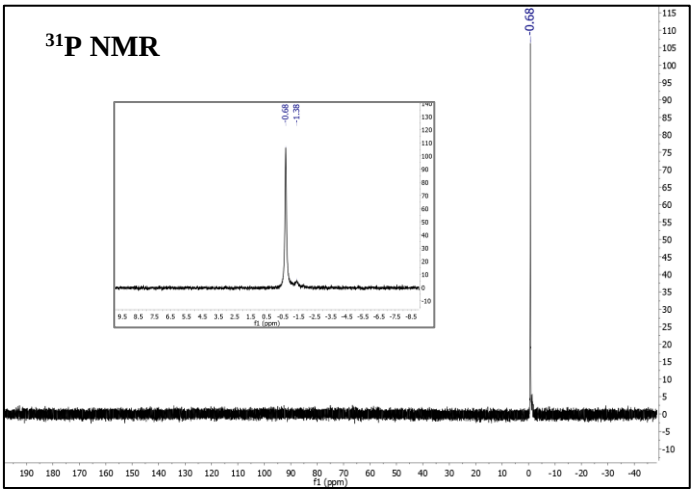
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 424 mg white solid (77% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.33.



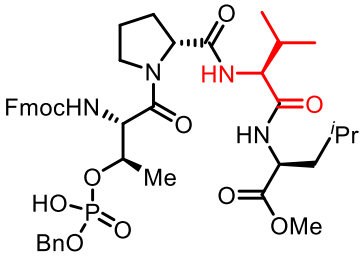
Fmoc-pThr(Bn)-^{D}Pro-Leu-Leu-OMe (P11)



Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 406 mg white solid (56% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.68.



Fmoc-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P12)



Synthesis: General Procedure #1
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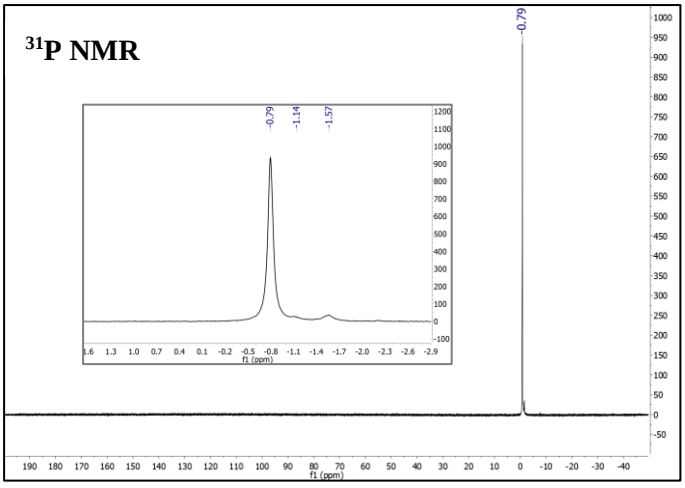
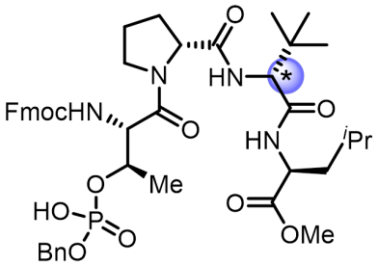
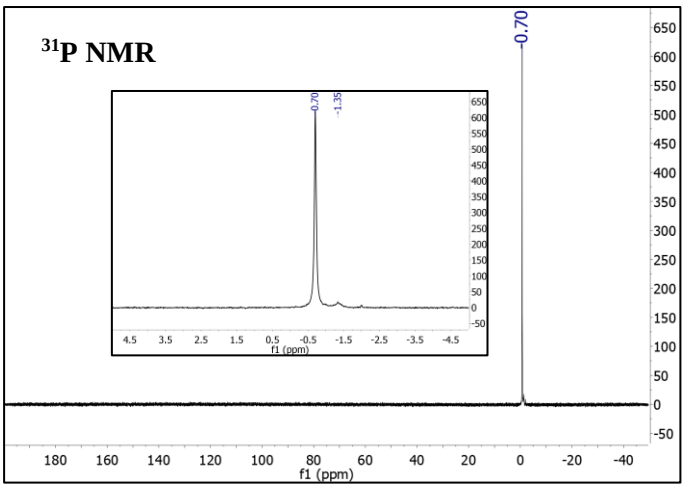
Yield: 874 mg white solid (86% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.79.



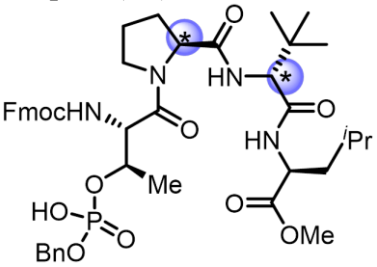
Fmoc-pThr(Bn)-^{D}Pro-^{D}Tle-Leu-OMe (P13)



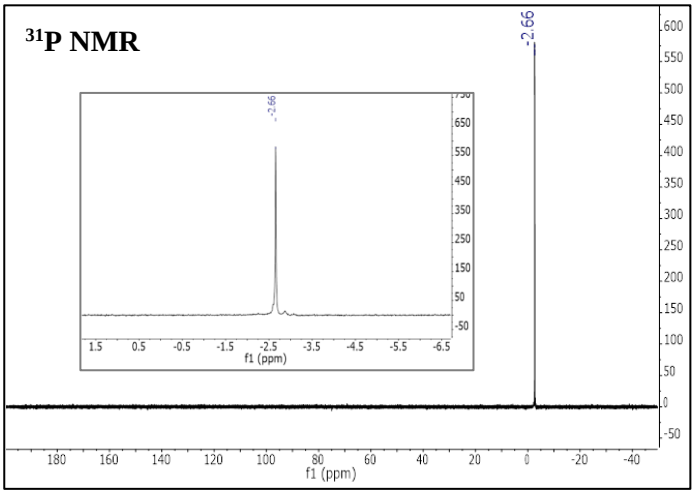
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 223 mg white solid (41% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.44.



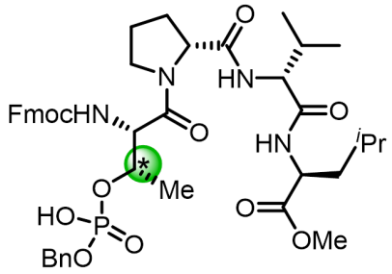
Fmoc-pThr(Bn)-Pro-^{D}Tle-Leu-OMe (P14)



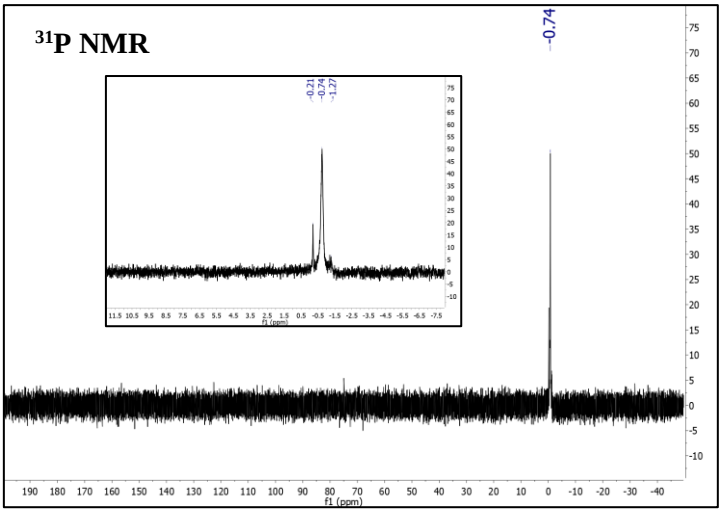
Synthesis: General Procedure #1
Scale: 0.648 mmol wrt **S6**
Yield: 378 mg white solid (69% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –2.66.



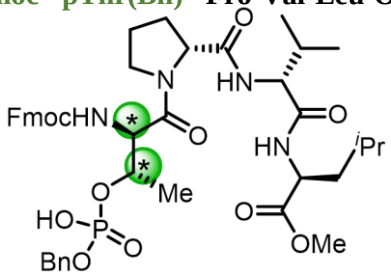
Fmoc-*allo*-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P15)



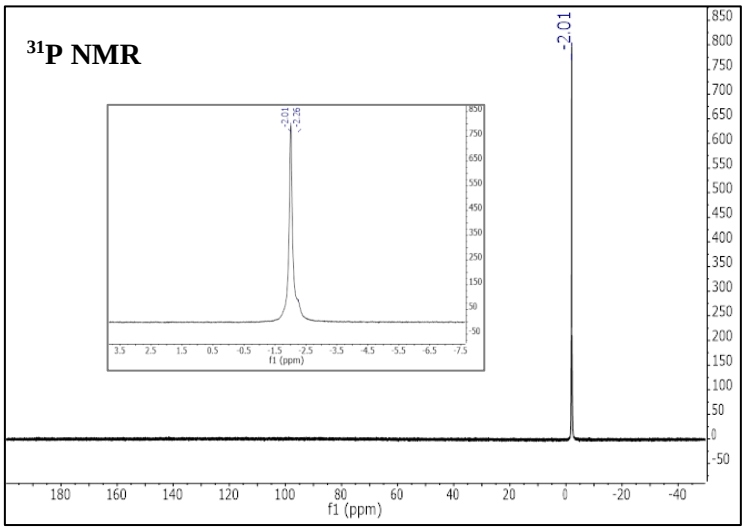
Synthesis: General Procedure #1
Scale: 0.293 mmol wrt *diast*-**S6**
Yield: 210 mg white solid (86% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.74.



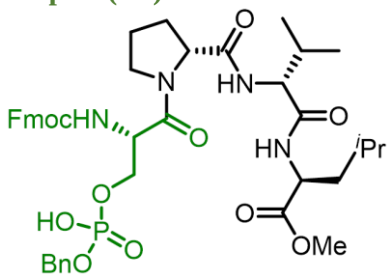
Fmoc-^{D}pThr(Bn)-^{D}Pro-Val-Leu-OMe (P16)



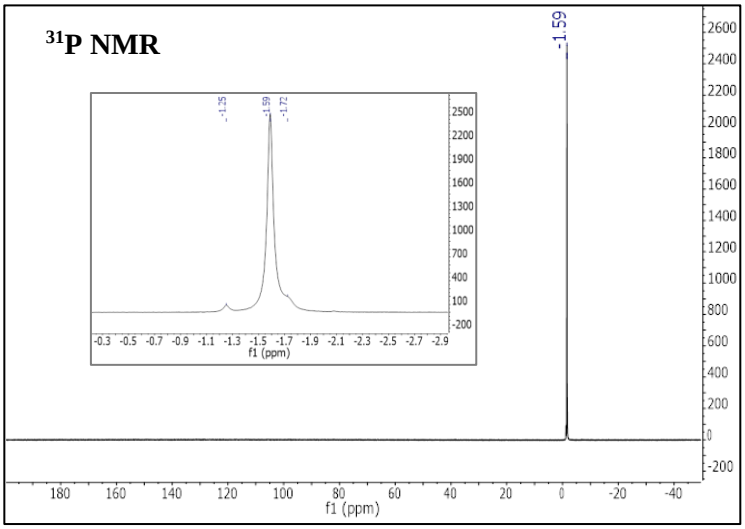
Synthesis: General Procedure #1
Scale: 0.196 mmol wrt *ent*-**S6**
Yield: 108 mg white solid (66% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –2.01.



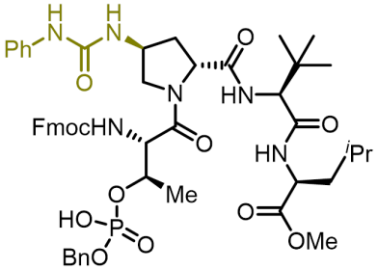
Fmoc-pSer(Bn)-^{D}Pro-Val-Leu-OMe (P17)



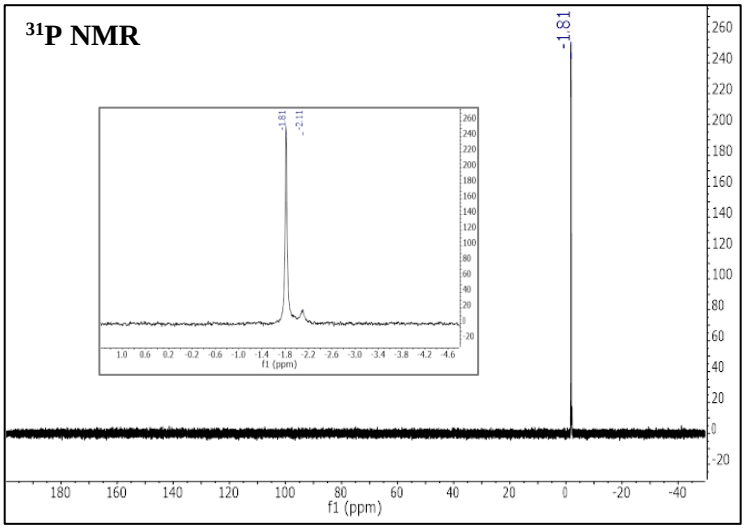
Synthesis: General Procedure #1
Scale: 0.606 mmol wrt pSer monomer
Yield: yield not reported
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.59.



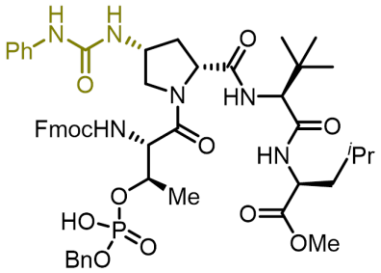
Fmoc-pThr(Bn)-^{D}Pro(4-*trans*-Ph-urea)-Val-Leu-OMe (P18)



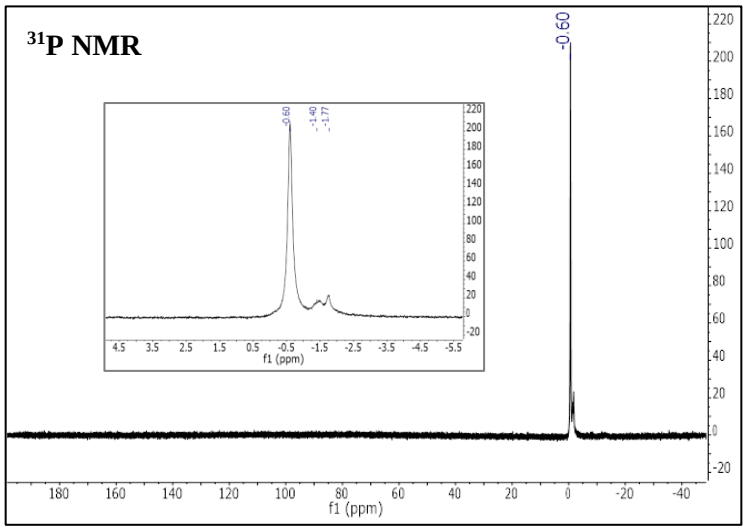
Synthesis: General Procedures #1 and #7
Scale: 0.614 mmol wrt **S6**
Yield: 440 mg white solid (73% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.81.



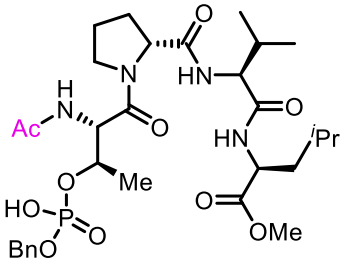
Fmoc-pThr(Bn)-^{D}Pro(4-*cis*-Ph-urea)-Val-Leu-OMe (P19)



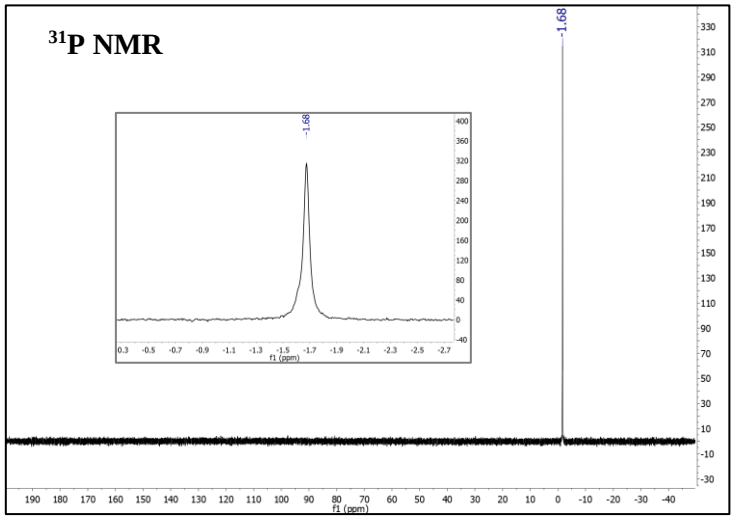
Synthesis: General Procedures #1 and #8
Scale: 0.244 mmol wrt **S6**
Yield: 188 mg white solid (78% yield)
^{31}P NMR: (202 MHz, $CDCl_3$) δ –0.60.



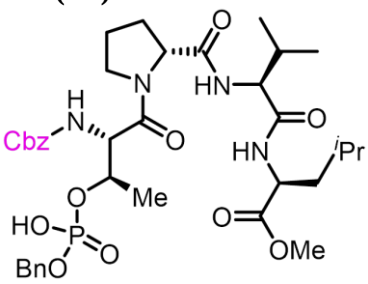
Ac-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P20)



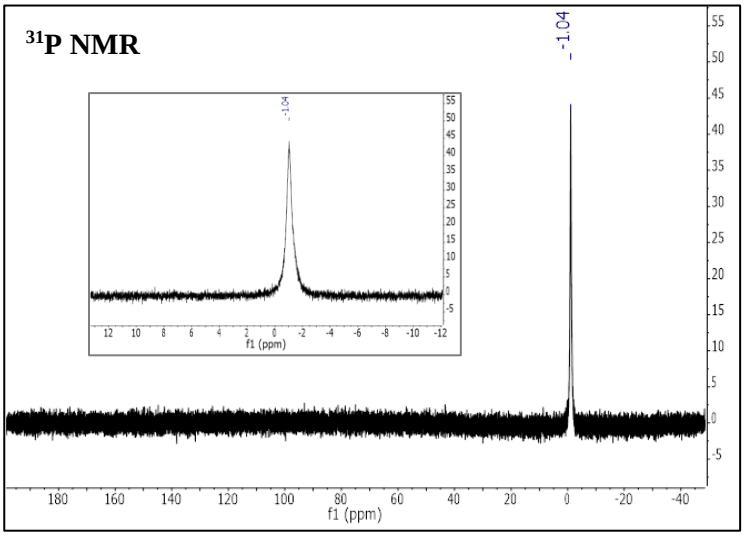
Synthesis: General Procedures #1 and #6
Scale: 0.240 mmol wrt **P11**
Yield: 56.5 mg white solid (36% yield)
^{31}P NMR: (202 MHz, $CDCl_3$) δ –1.68.



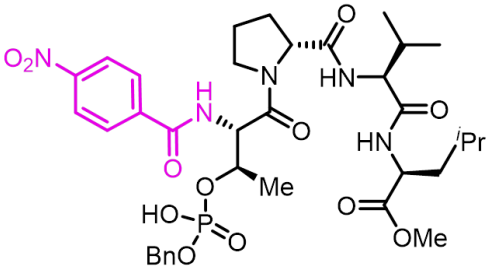
Cbz-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P21)



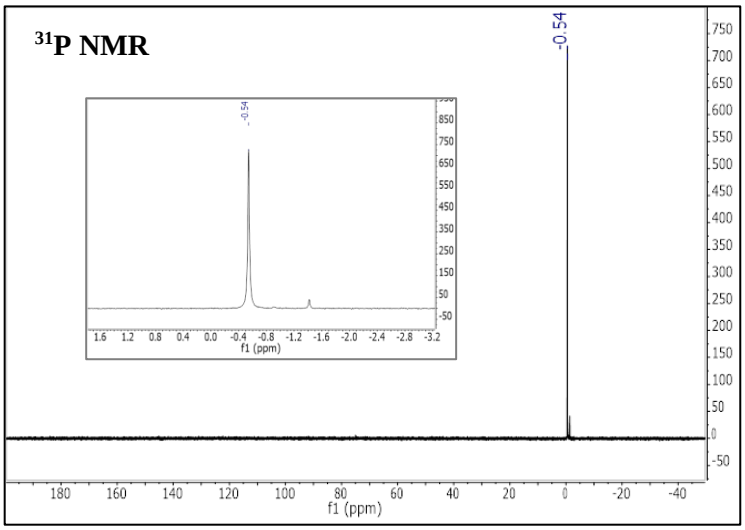
Synthesis: General Procedures #1
Scale: 0.228 mmol wrt **P11**
Yield: not determined
^{31}P NMR: (202 MHz, $CDCl_3$) δ –1.84.



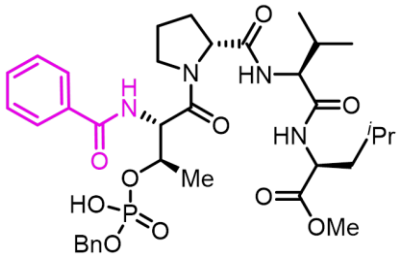
p-O$_2$N-Bz-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P22)



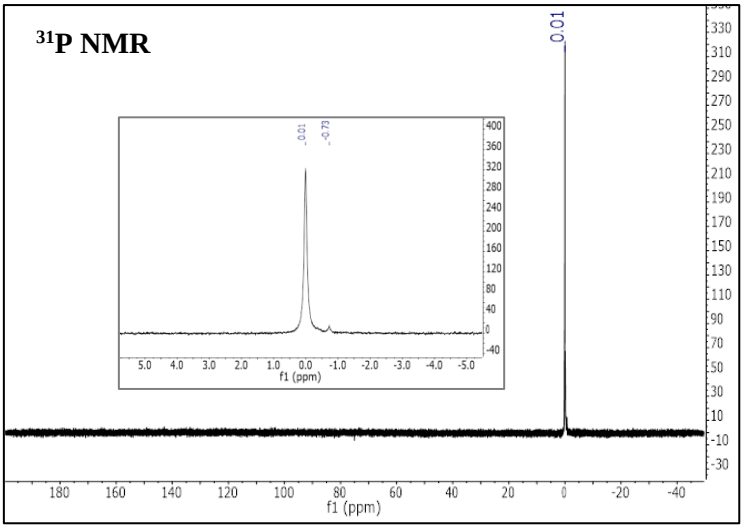
Synthesis: General Procedures #1 and #5
Scale: 0.240 mmol wrt **P11**
Yield: 72.2 mg white solid (39% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.54.



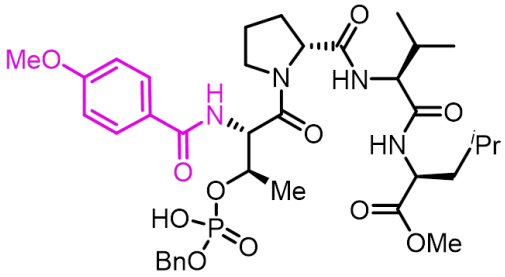
Bz-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P23)



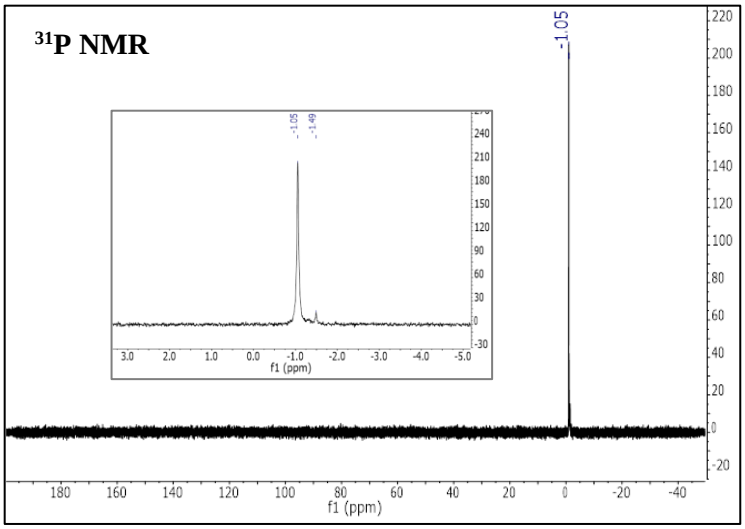
Synthesis: General Procedures #1 and #5
Scale: 0.400 mmol wrt **P11**
Yield: 143 mg white solid (50 % yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ 0.01.



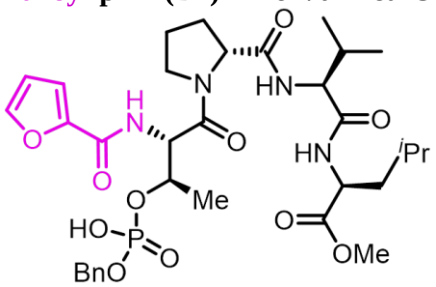
p-MeO-Bz-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P24)



Synthesis: General Procedures #1 and #5
Scale: 0.240 mmol wrt **P11**
Yield: 150 mg white solid (84 % yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.05.

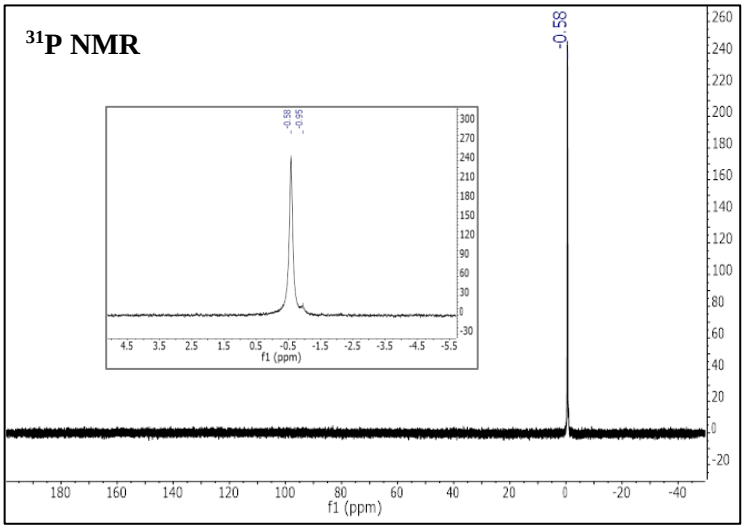


Furanoyl-pThr(Bn)-^{D}Pro-Val-Leu-OMe (P25)



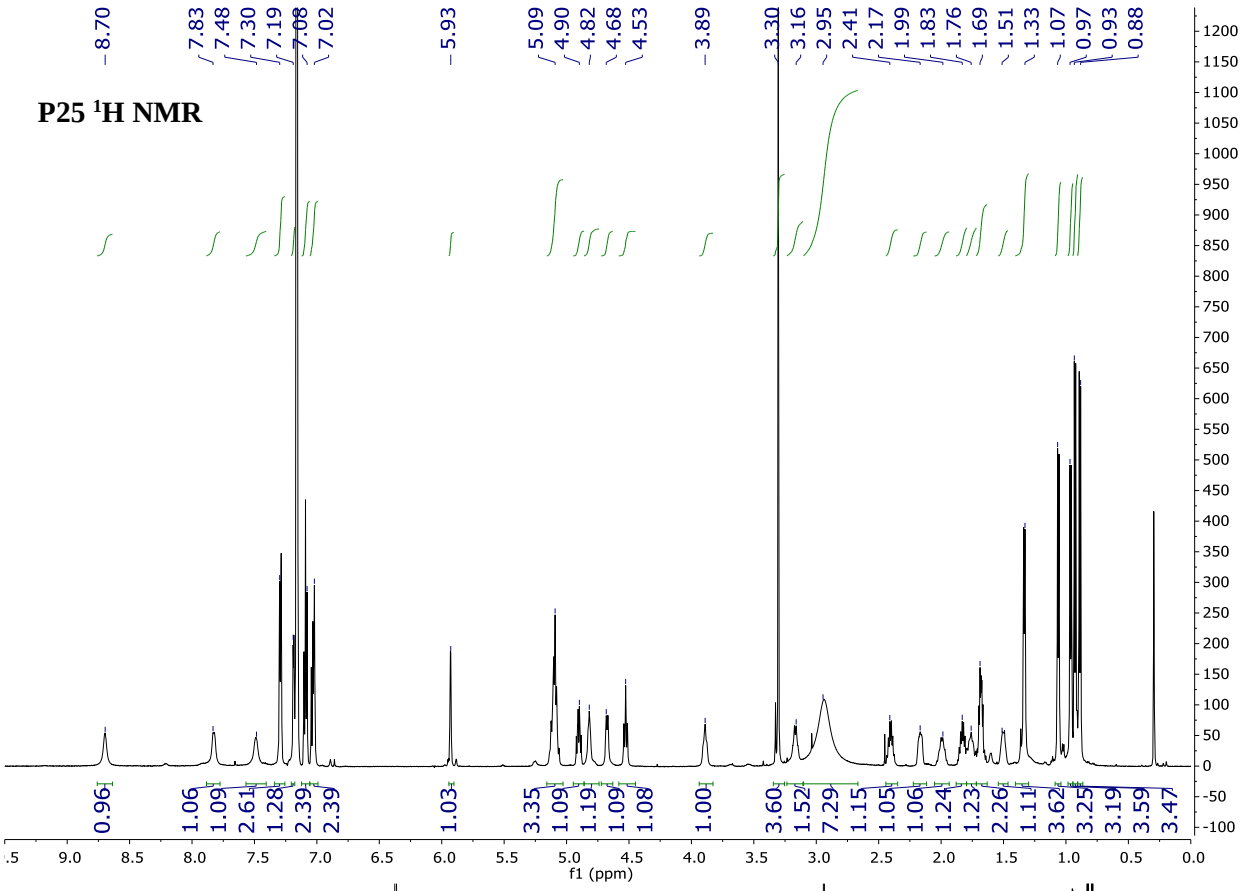
Synthesis: General Procedures #1 and #5
Scale: 0.400 mmol wrt **P11**
Yield: 136 mg white solid (48% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.58.

^{31}P NMR

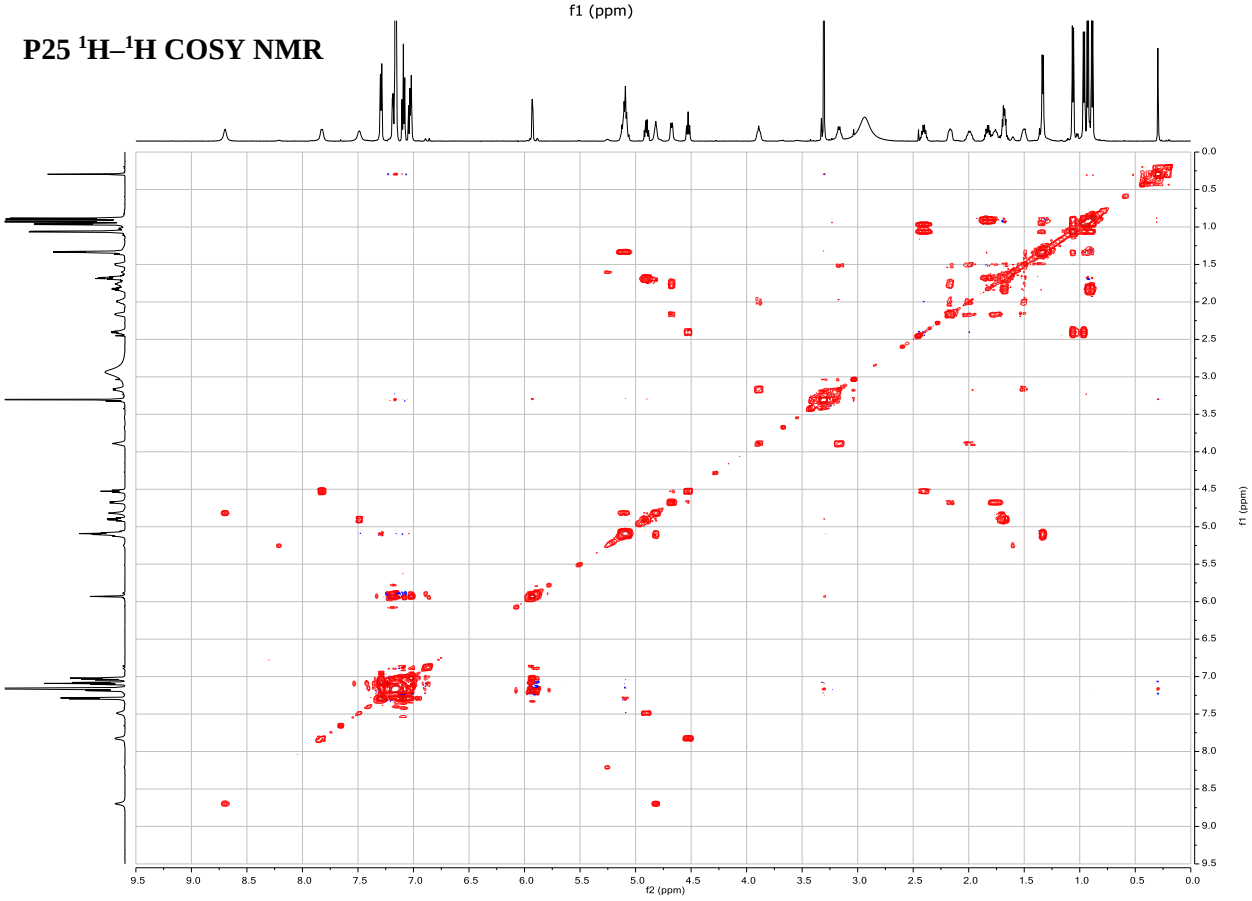


2D NMR Details: Spectra were acquired on Agilent 600 MHz spectrometers at ambient temperature in C_6D_6.
^{1}H NMR: scans = 64, pulse width = 8.75, spectral width = 16.0, d1 relaxation delay = 22.02 s.
^{1}H–^{1}H COSY: scans per t1 = 2, t1 increments = 512, pulse width = 8.75, d1 = 5 s, spectral width = 18.
^{1}H–^{13}C HSQC: scans per t1 = 4, t1 increments = 256, pulse width = 8.5, d1 = 3.74.
^{1}H–^{1}H NOESY: scans = 8, t1 increments = 400, pulse width = 8.75, mixing time = 300 ms, d1 = 5.0 s, spectral width = 18.

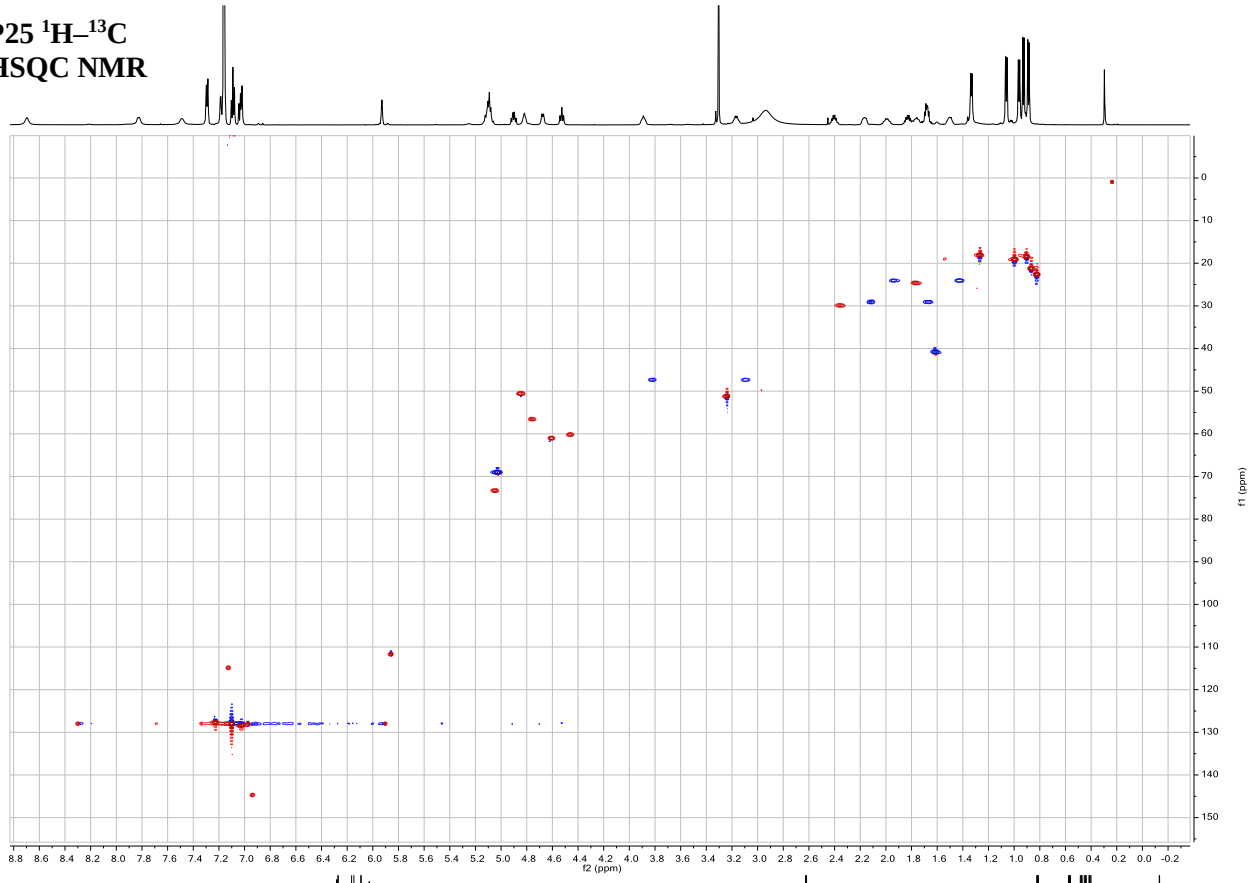
P25 ^{1}H NMR



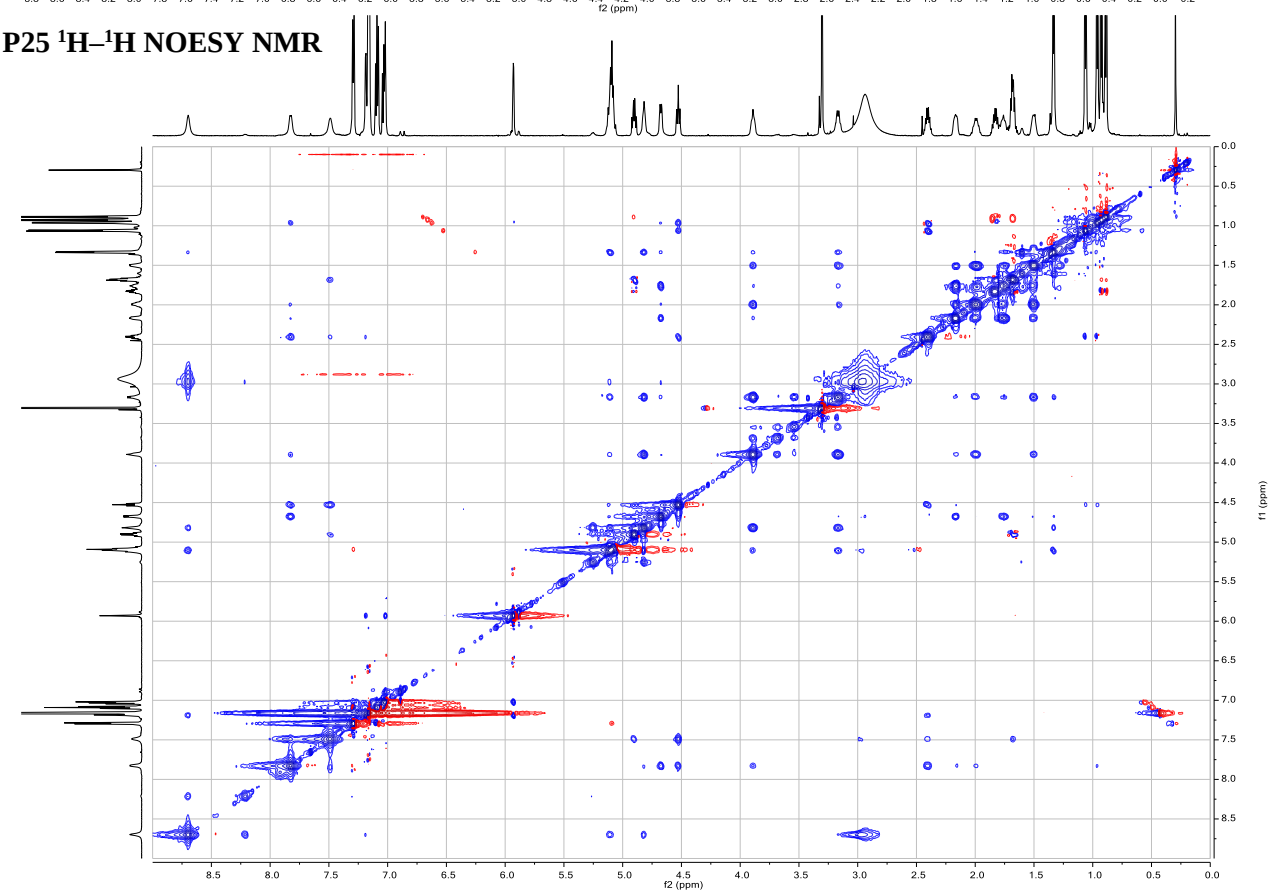
P25 ^{1}H–^{1}H COSY NMR



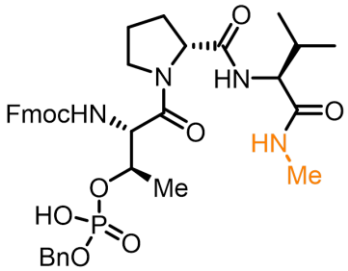
P25 ^{1}H–^{13}C HSQC NMR



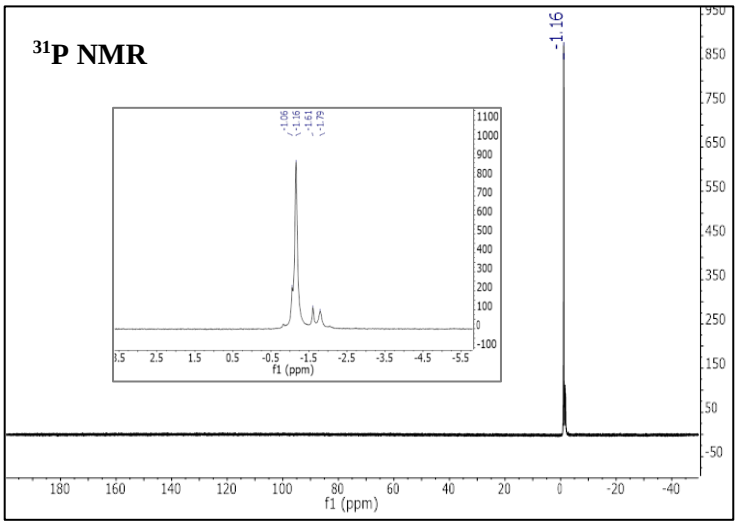
P25 ^{1}H–^{1}H NOESY NMR



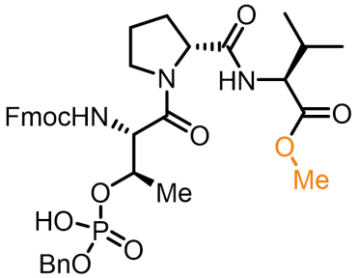
Fmoc-pThr(Bn)-^{D}Pro-Val-NHMe (P26)



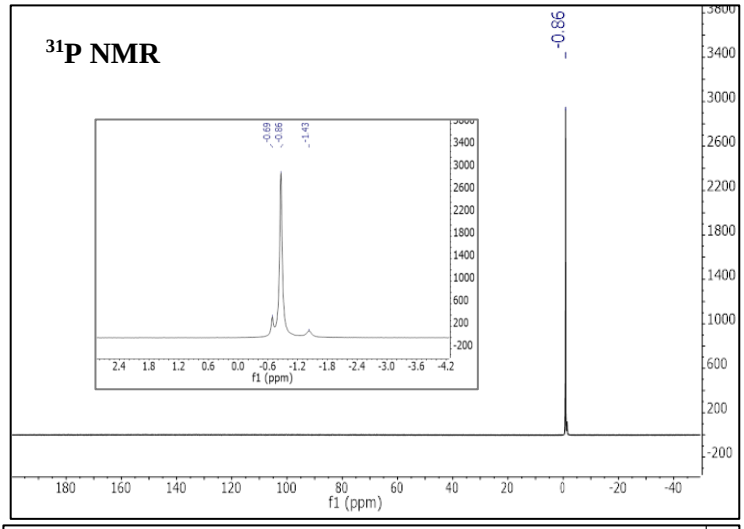
Synthesis: General Procedures #1 and #2
Scale: 1.47 mmol wrt **S6**
Yield: 997 mg white solid (94% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.16.



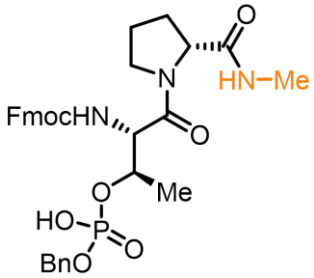
Fmoc-pThr(Bn)-^{D}Pro-Val-OMe (P27)



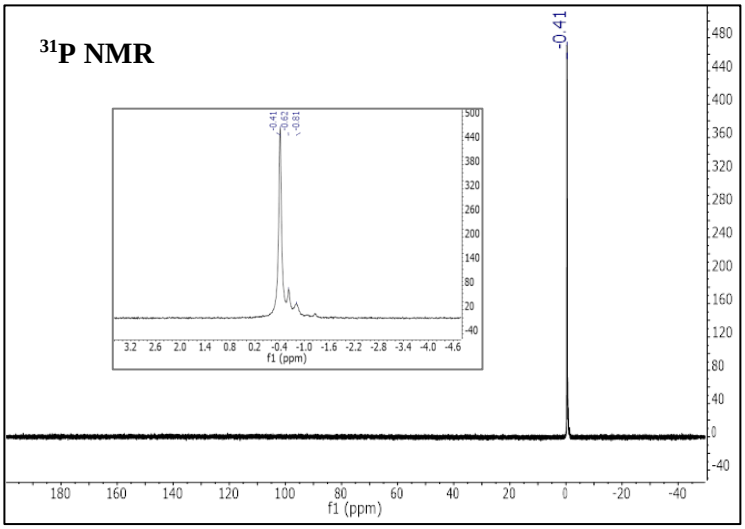
Synthesis: General Procedure #1
Scale: 2.77 mmol wrt **S6**
Yield: 1.63 g white solid (82% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.86.



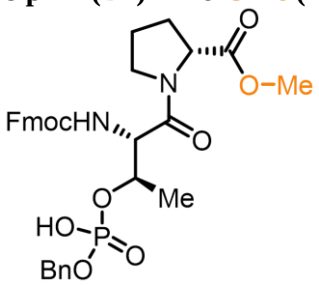
Fmoc-pThr(Bn)-^{D}Pro-NHMe (P28)



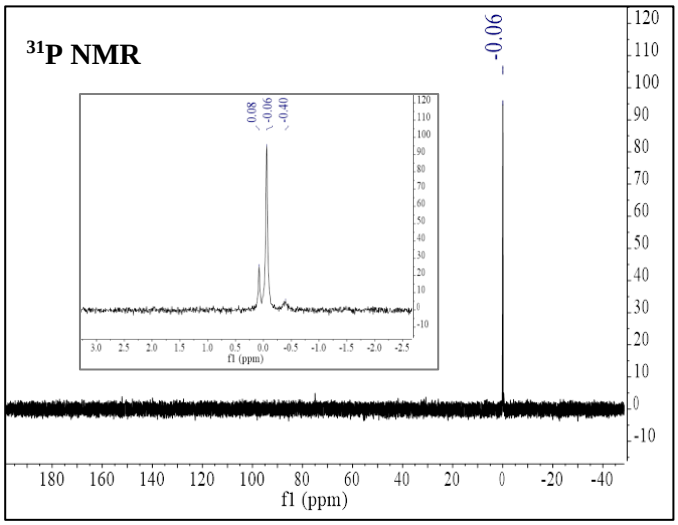
Synthesis: General Procedures #1 and #2
Scale: 2.16 mmol wrt **S6**
Yield: 1.07 g white solid (80 % yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.41.



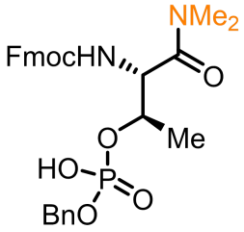
Fmoc-pThr(Bn)-^{D}Pro-OMe (P29)



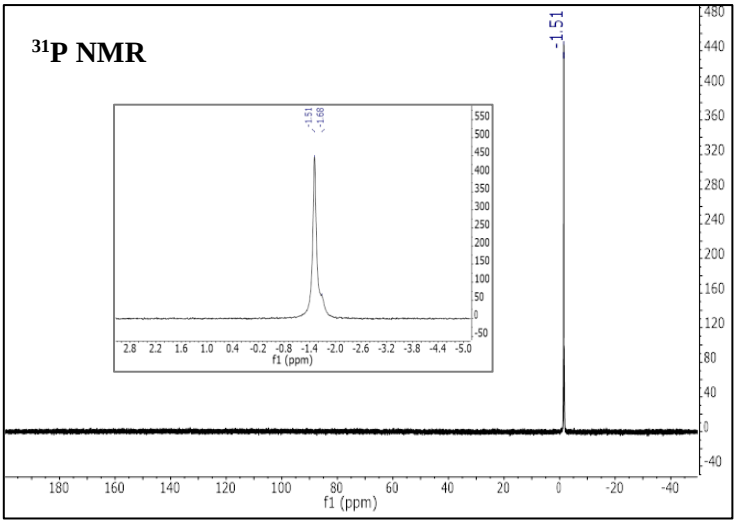
Synthesis: General Procedure #1
Scale: 0.250 mmol wrt **S6**
Yield: 50.2 mg white solid (32% yield)
^{31}P NMR: (202 MHz, $CDCl_3$) δ –0.06.



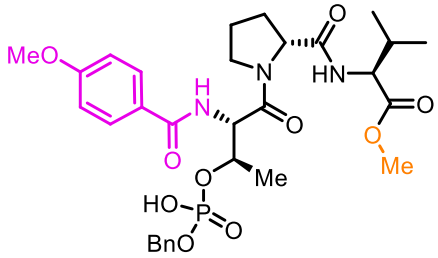
Fmoc-pThr(Bn)-NMe$_2$ (P30)



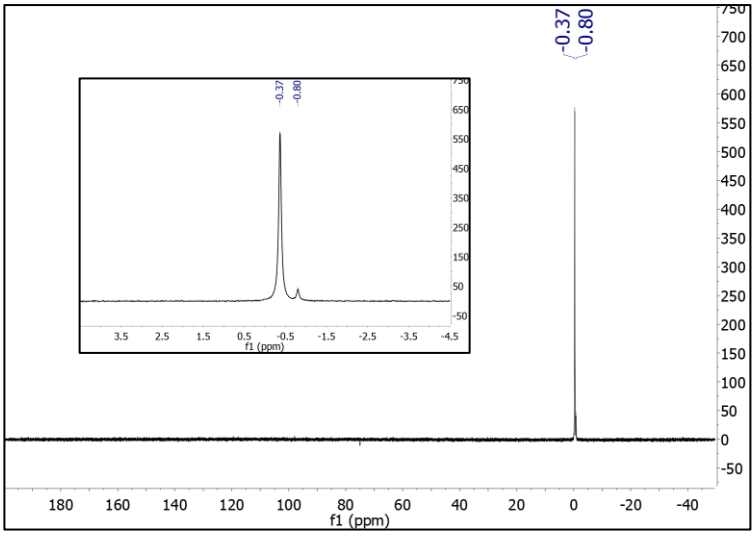
Synthesis: Procedure #3
Scale: 1.00 mmol wrt **S6**
Yield: 353 mg white solid (66% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –1.51.



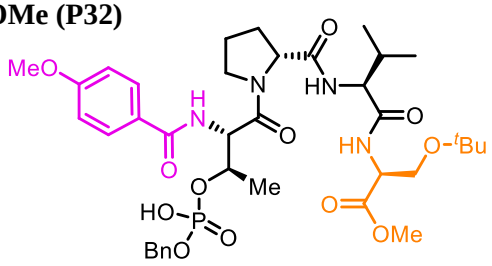
***p*-MeO-Bz-pThr(Bn)-^{D}Pro-Val-OMe (P31)**



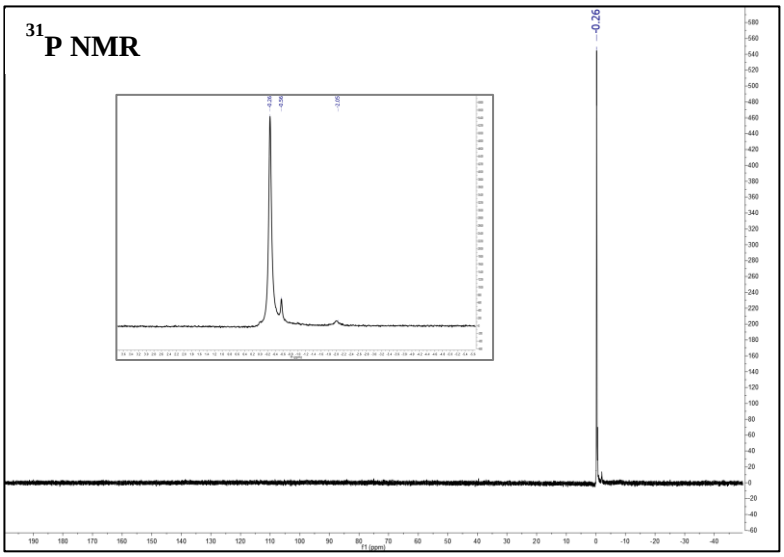
Synthesis: Procedure #1 and #5
Scale: 0.240 mmol wrt **P25**
Yield: 62.6 mg white solid (41% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.37.



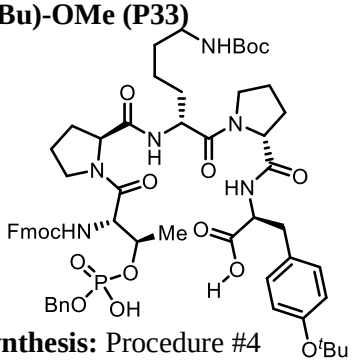
_p_-MeO-Bz-pThr(Bn)-^{D}Pro-Val-Ser(^{t}Bu)-OMe (P32)



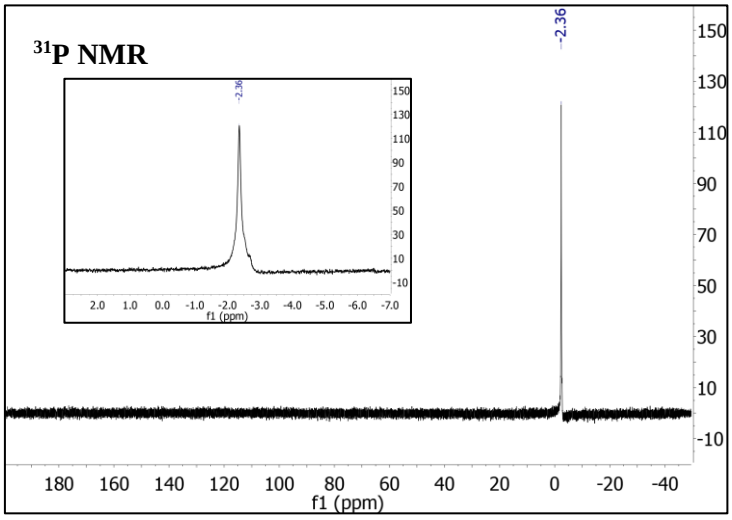
Synthesis: Procedure #4 and #5
Scale: 0.173 mmol wrt **S6**
Yield: 94.0 mg white solid (70% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –0.27.



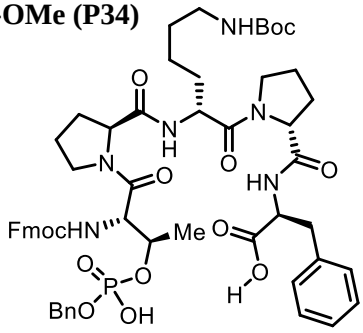
Fmoc-pThr(Bn)-Pro-^{D}Lys(Boc)-^{D}Pro-Tyr(^{t}Bu)-OMe (P33)



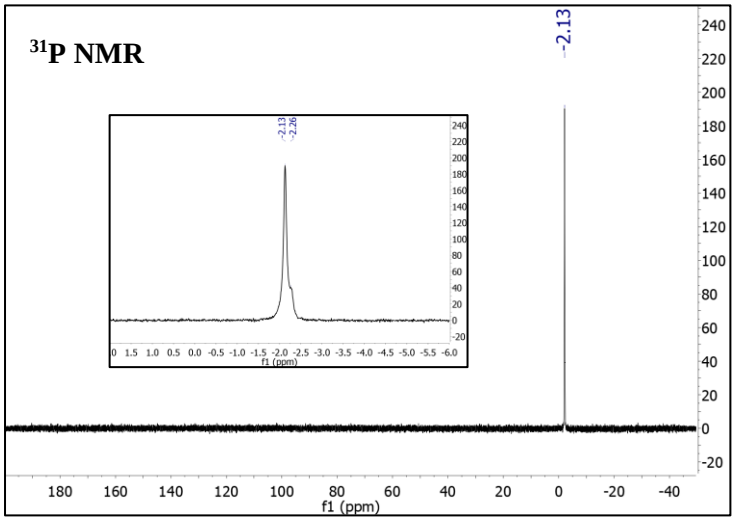
Synthesis: Procedure #4
Scale: 0.433 mmol wrt **S6**
Yield: 339 mg white solid (67% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –2.26.



Fmoc-pThr(Bn)-Pro-^{D}Lys(Boc)-^{D}Pro-Phe-OMe (P34)

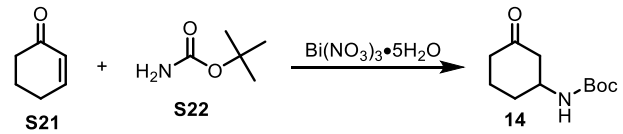


Synthesis: Procedure #4
Scale: 0.621 mmol wrt **S6**
Yield: 429 mg white solid (57% yield)
^{31}P NMR: (162 MHz, $CDCl_3$) δ –2.13.

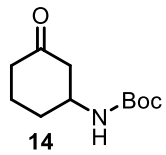


3. Characterization of 3-Amidocyclohexanones

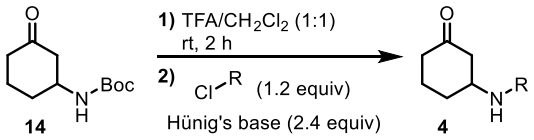
Scheme S8: Synthesis of Boc-Protected Precursor (Procedure #9)



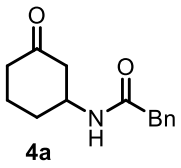
^{1}H NMR



Scheme S9: Variation of N-Protecting Group of 3-Amidocylohexanones (General Procedure #10)

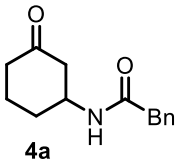


^{1}H NMR



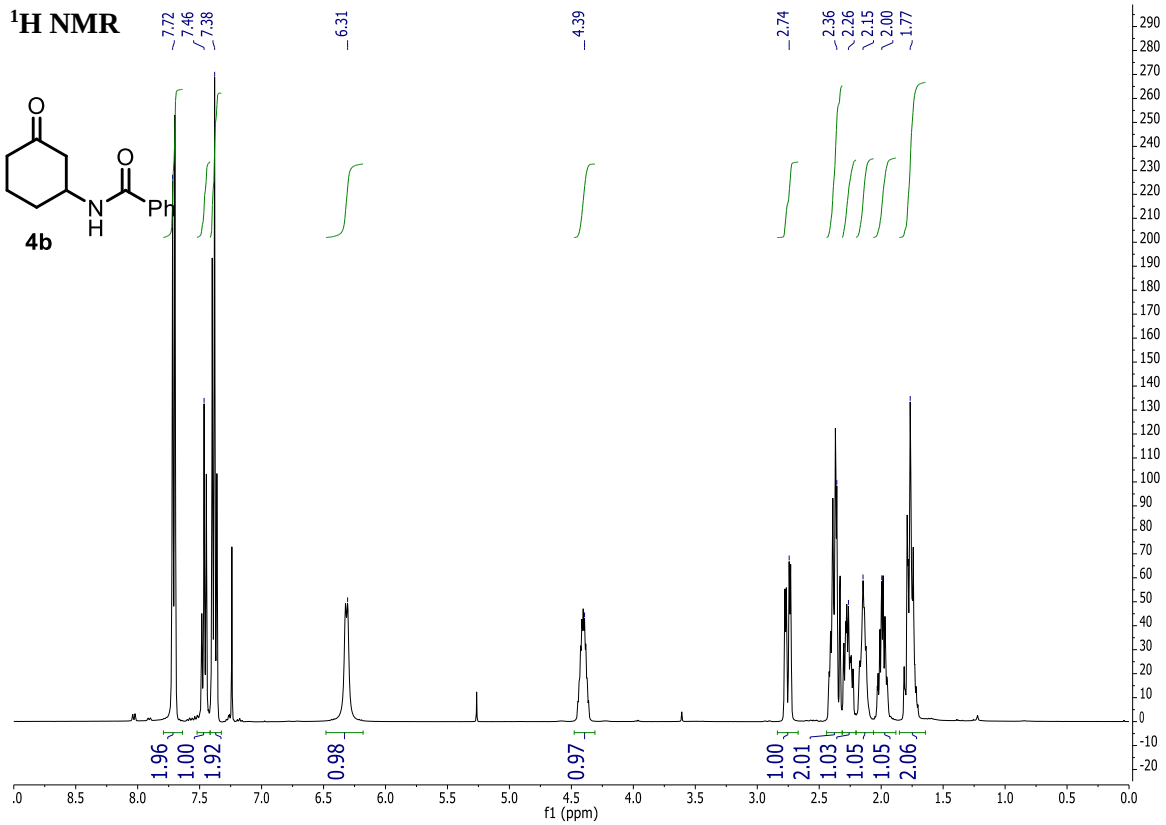
4a

^{13}C NMR



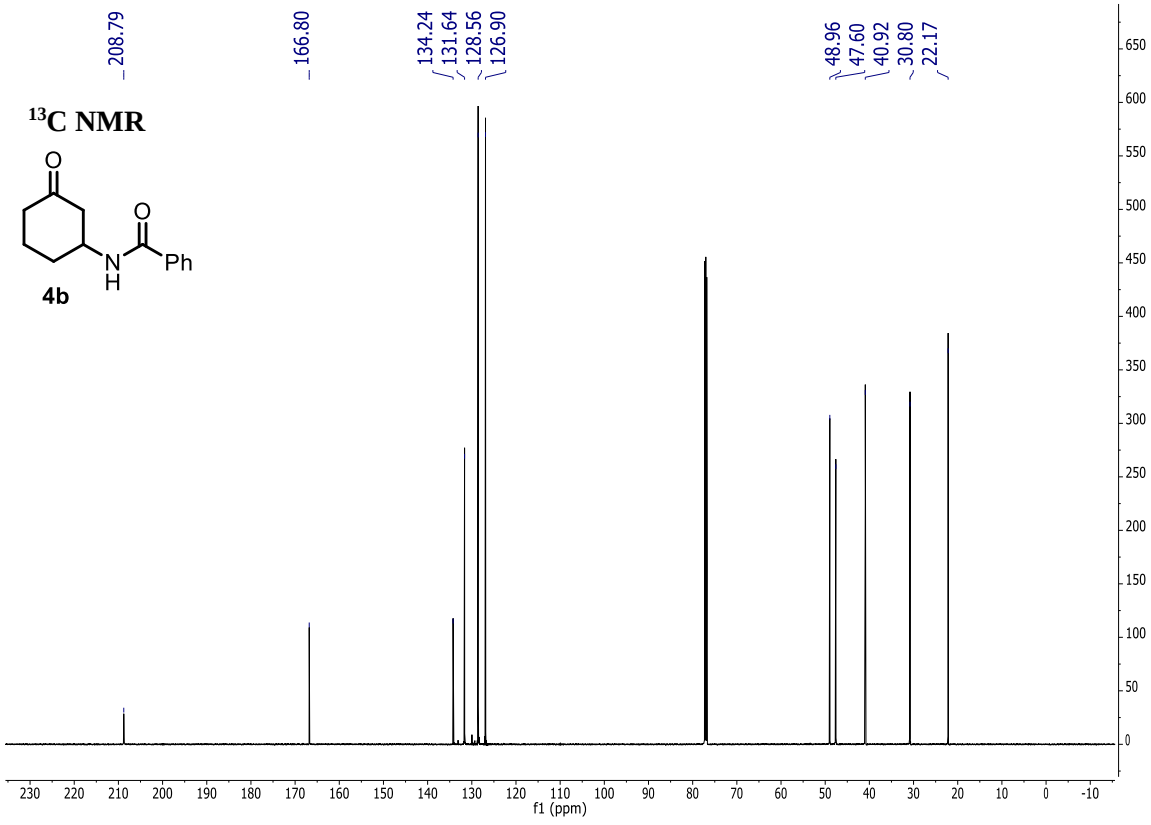
4a

^{1}H NMR

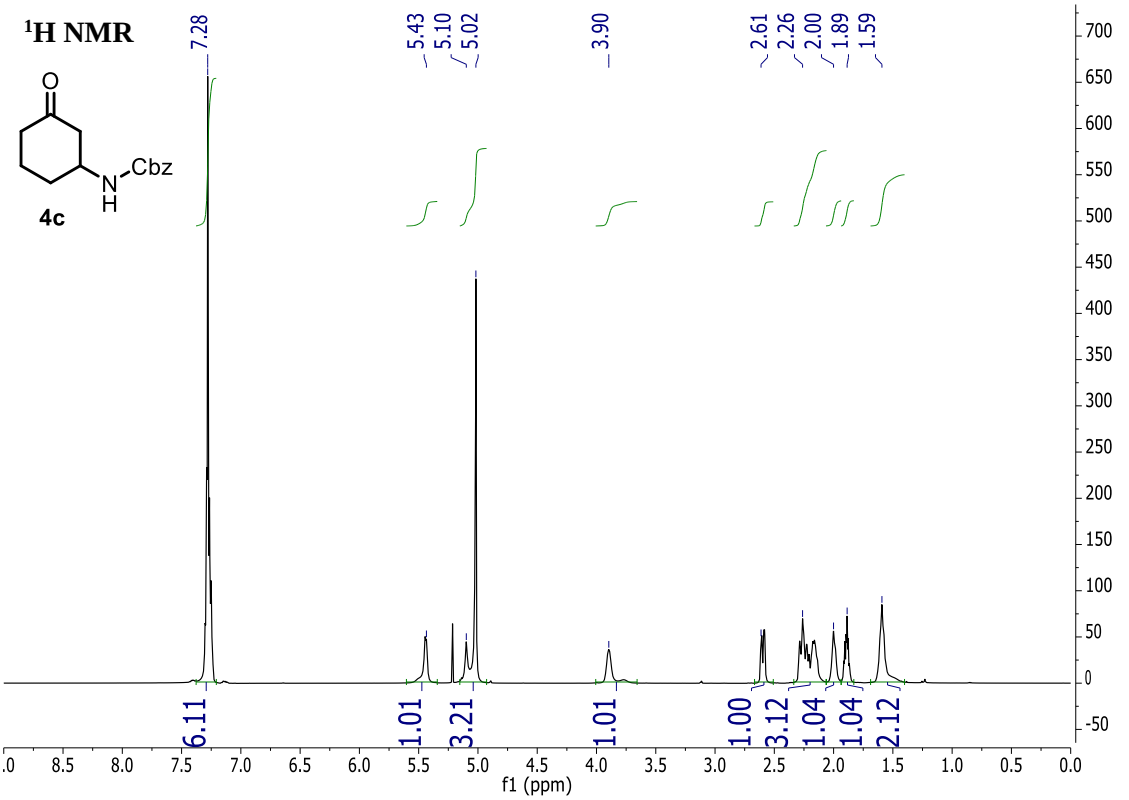


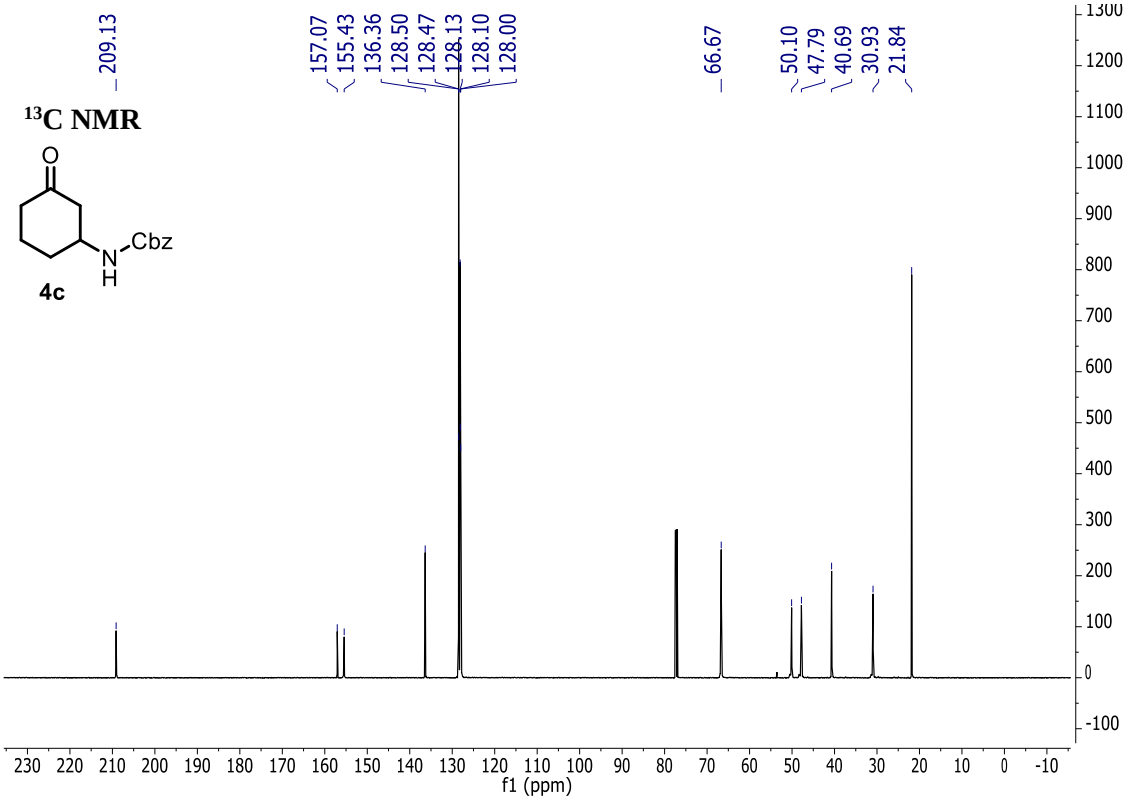
4b

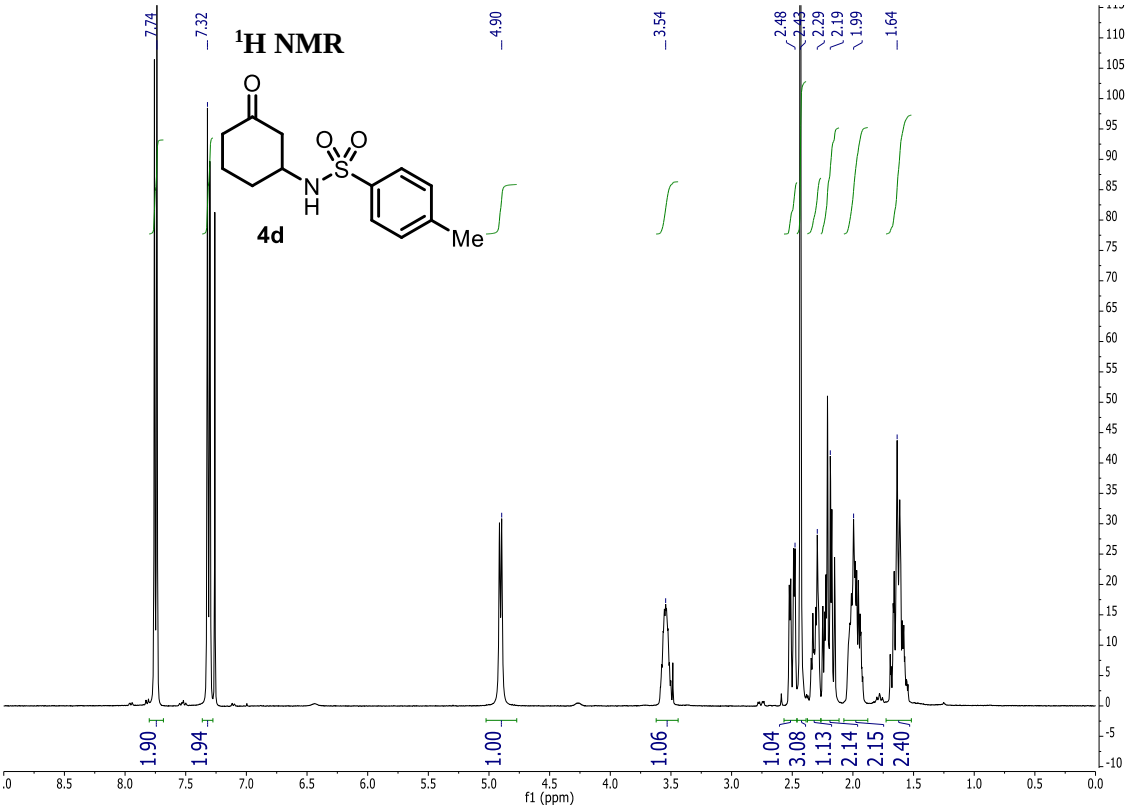
^{13}C NMR

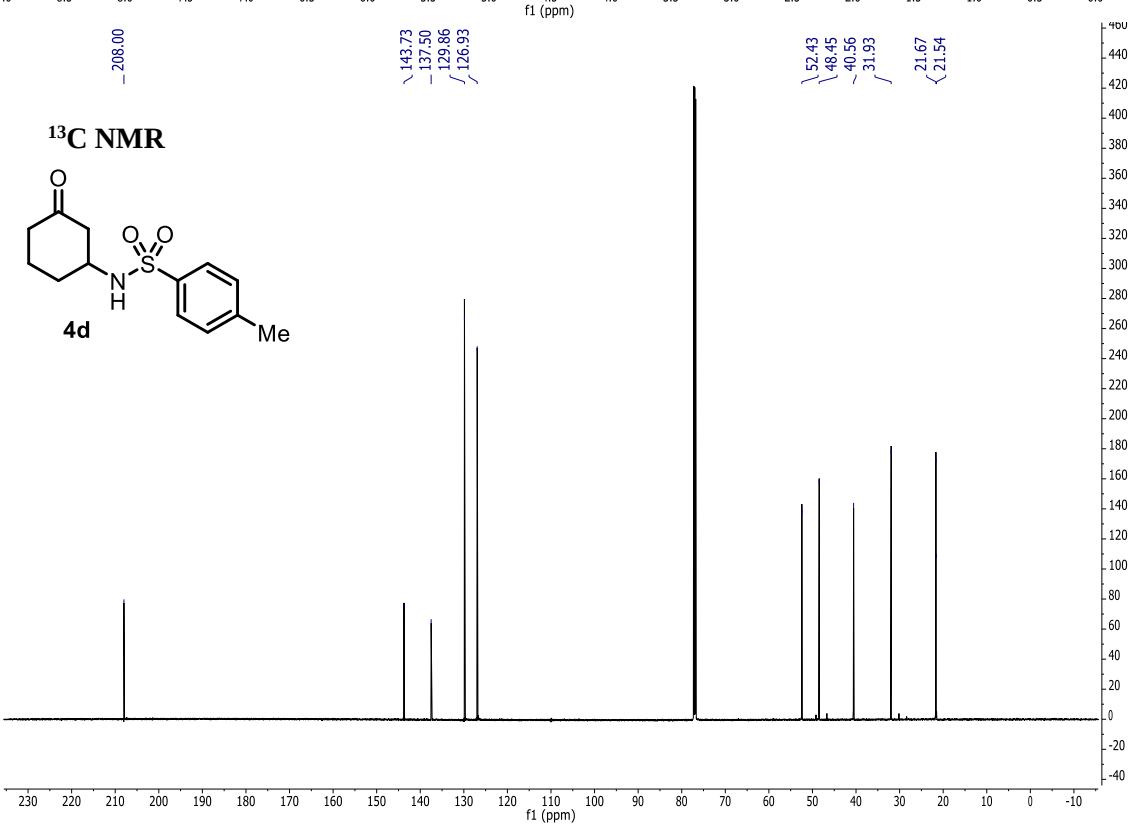


4b


^{1}H NMR
7.28
5.43
5.10
5.02
3.90
2.61
2.26
2.00
1.89
1.59
Cbz
N
H
4c
6.11
1.01
3.21
1.01
1.00
3.12
1.04
1.04
2.12
f1 (ppm)


^{13}C NMR
209.13
157.07
155.43
136.36
128.50
128.47
128.13
128.10
128.00
66.67
50.10
47.79
40.69
30.93
21.84
Cbz
N
H
4c
f1 (ppm)

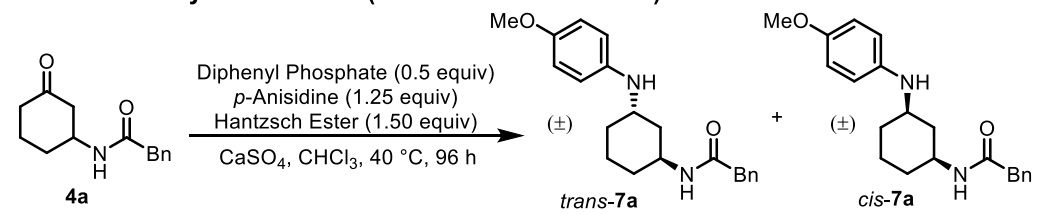

^{1}H NMR
4d
Me
7.74
7.32
4.90
3.54
2.48
2.43
2.29
2.19
1.99
1.64
1.90
1.94
1.00
1.06
1.04
3.08
1.13
2.14
2.15
2.40
f1 (ppm)

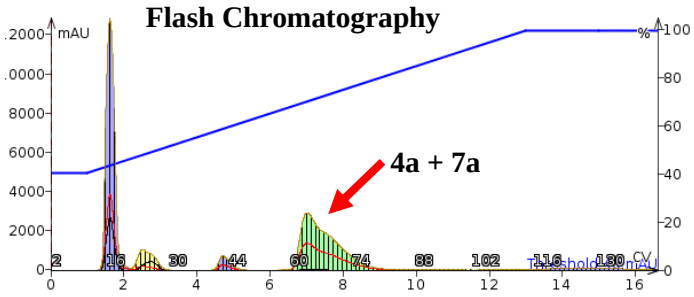

^{13}C NMR
4d
Me
208.00
143.73
137.50
129.86
126.93
52.43
48.45
40.56
31.93
21.67
21.54
f1 (ppm)

4. Purification and Characterization of Racemic Reductive Aminations

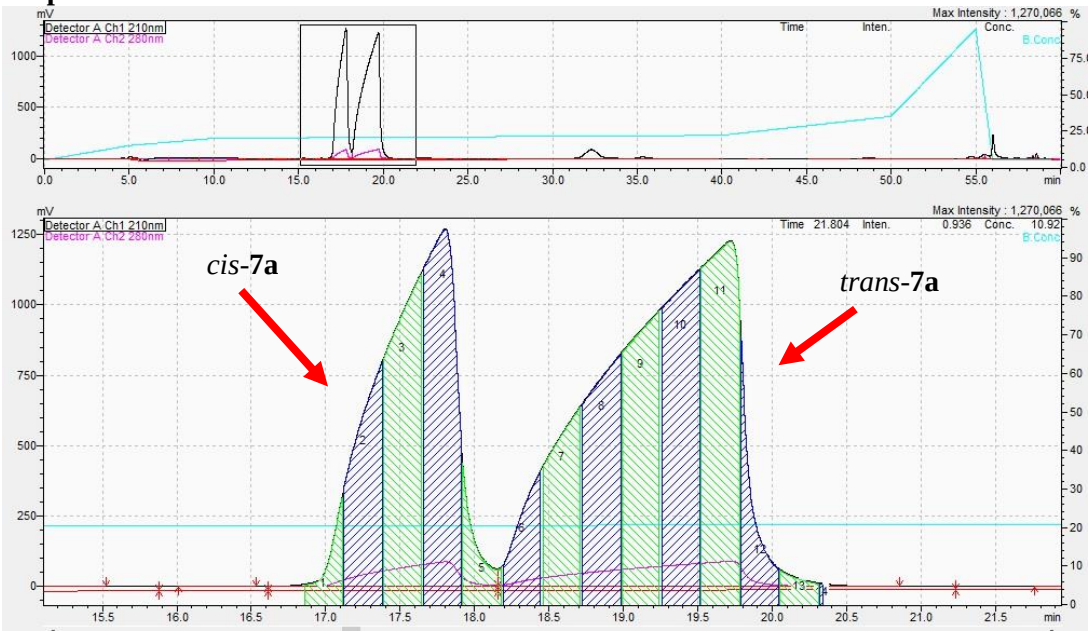
Trans- and *cis*-3-((4-methoxyphenyl)amino)cyclohexyl)-2-phenylacetamide (7a)

Scheme S10: Synthesis of 7a (General Procedure #11)

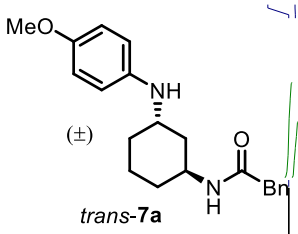




Preparative HPLC:

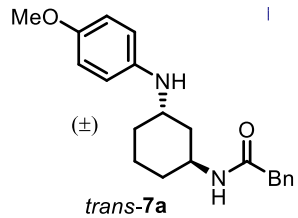


^{1}H NMR



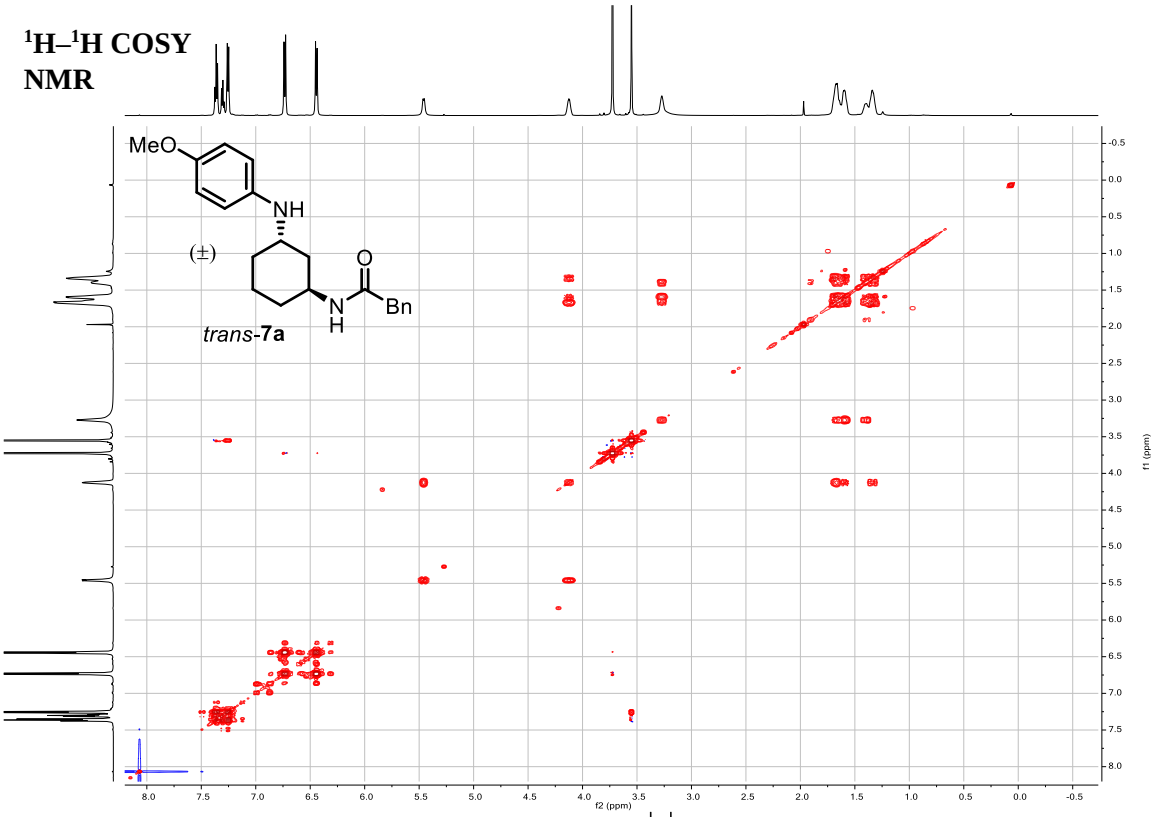
trans-**7a**

^{13}C NMR

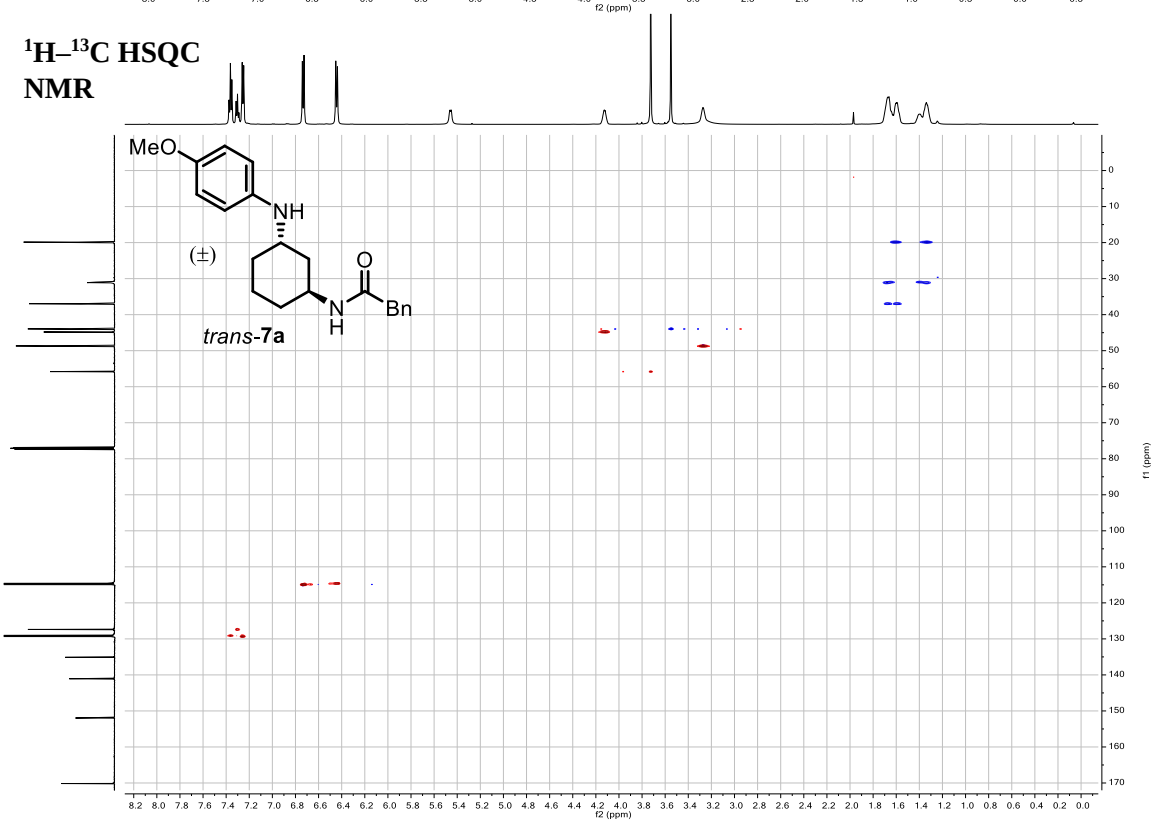


trans-**7a**

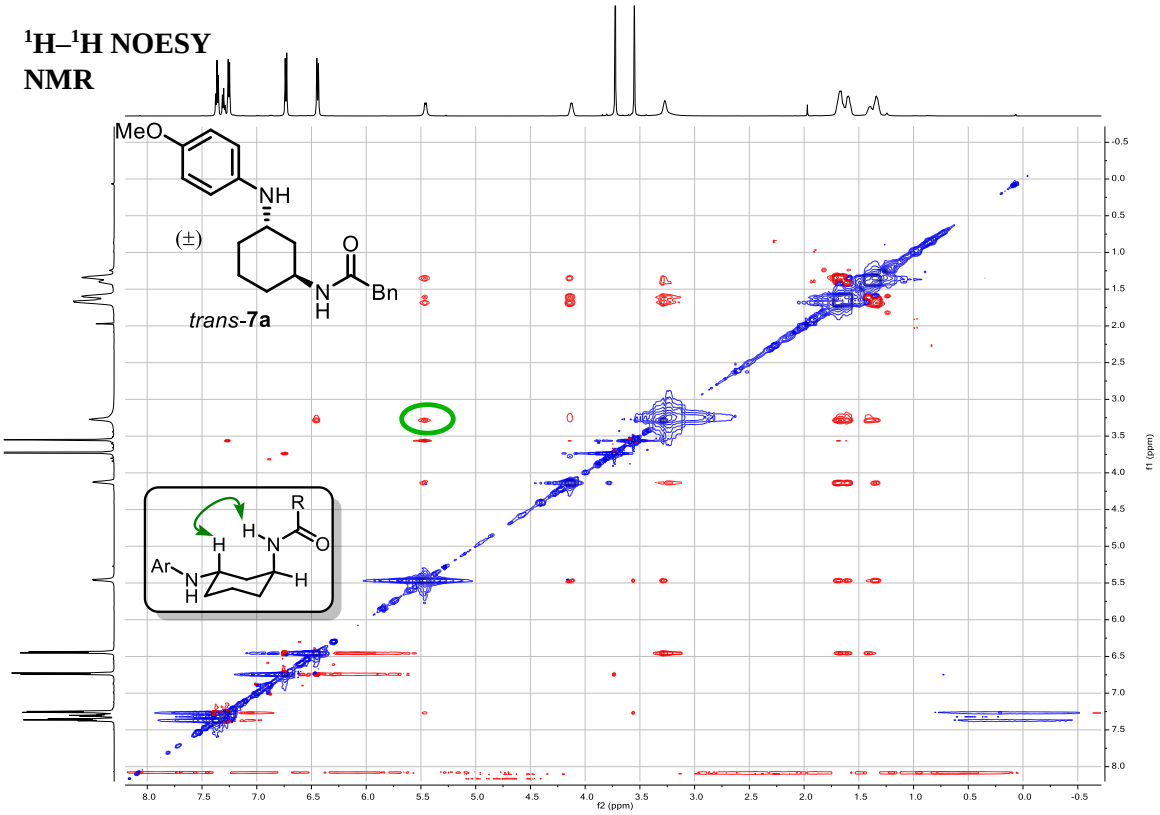
^{1}H–^{1}H COSY NMR



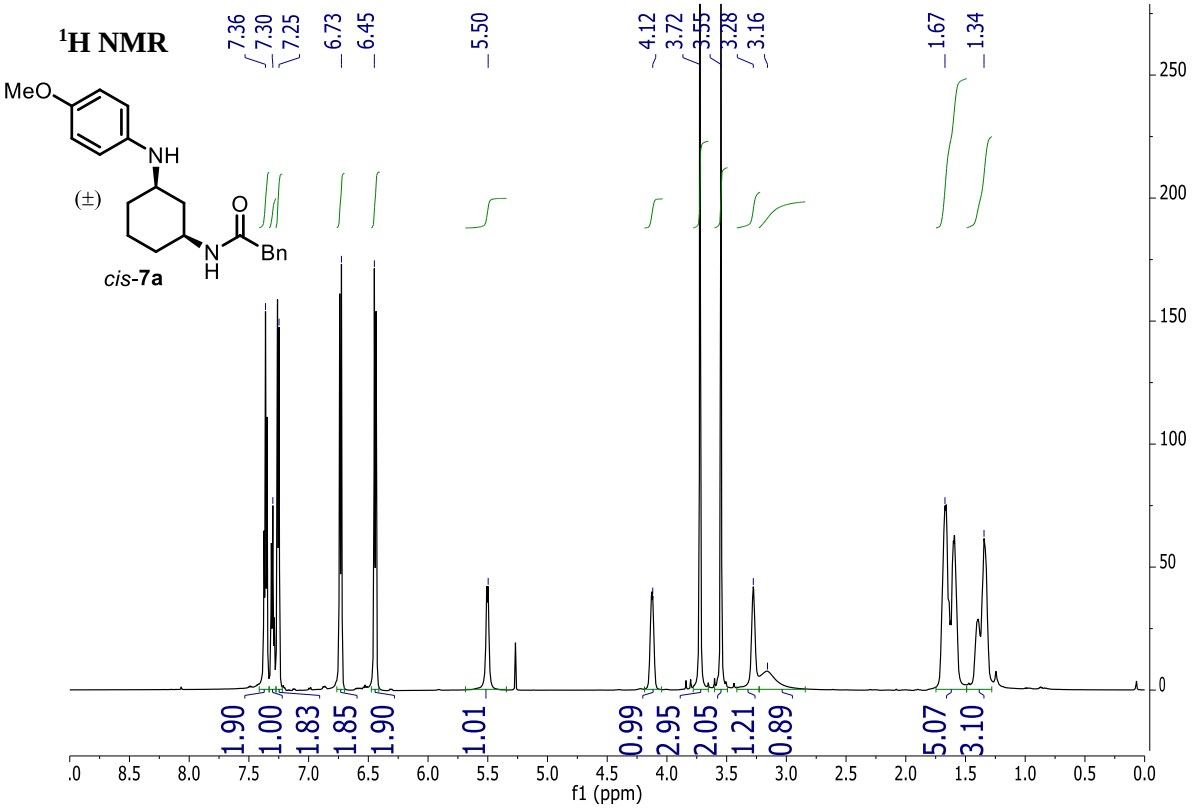
^{1}H–^{13}C HSQC NMR



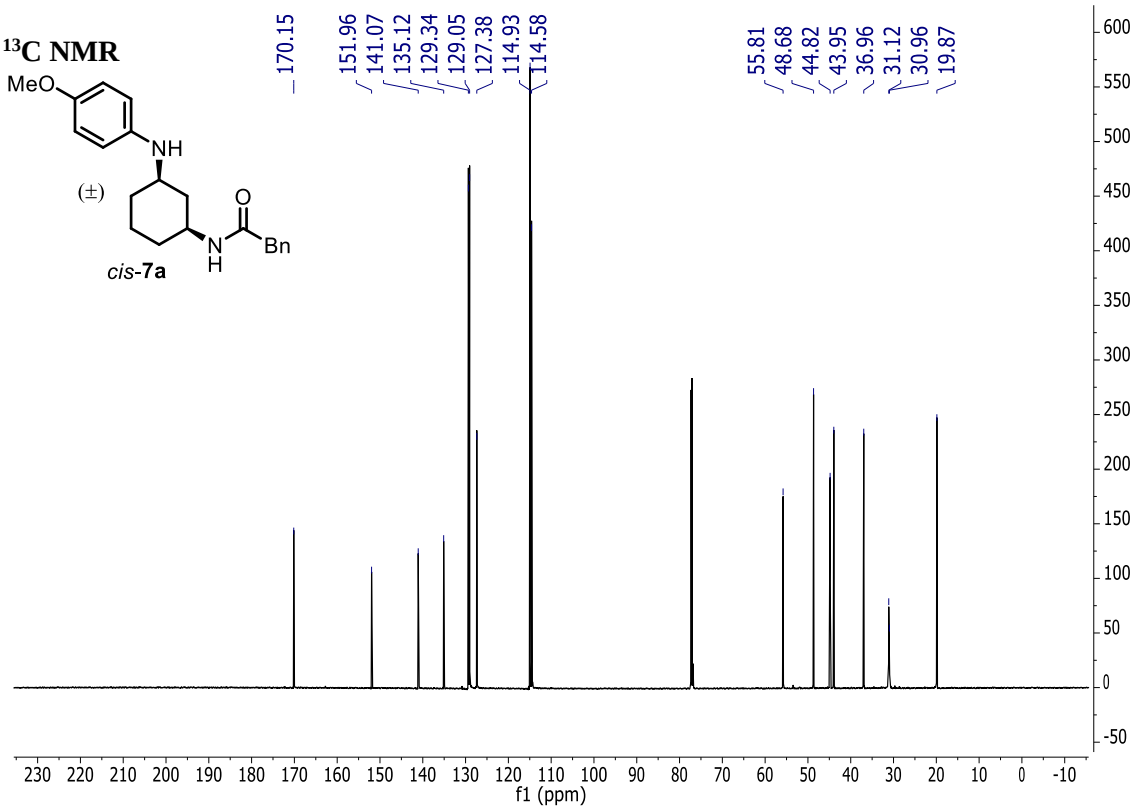
^{1}H–^{1}H NOESY NMR



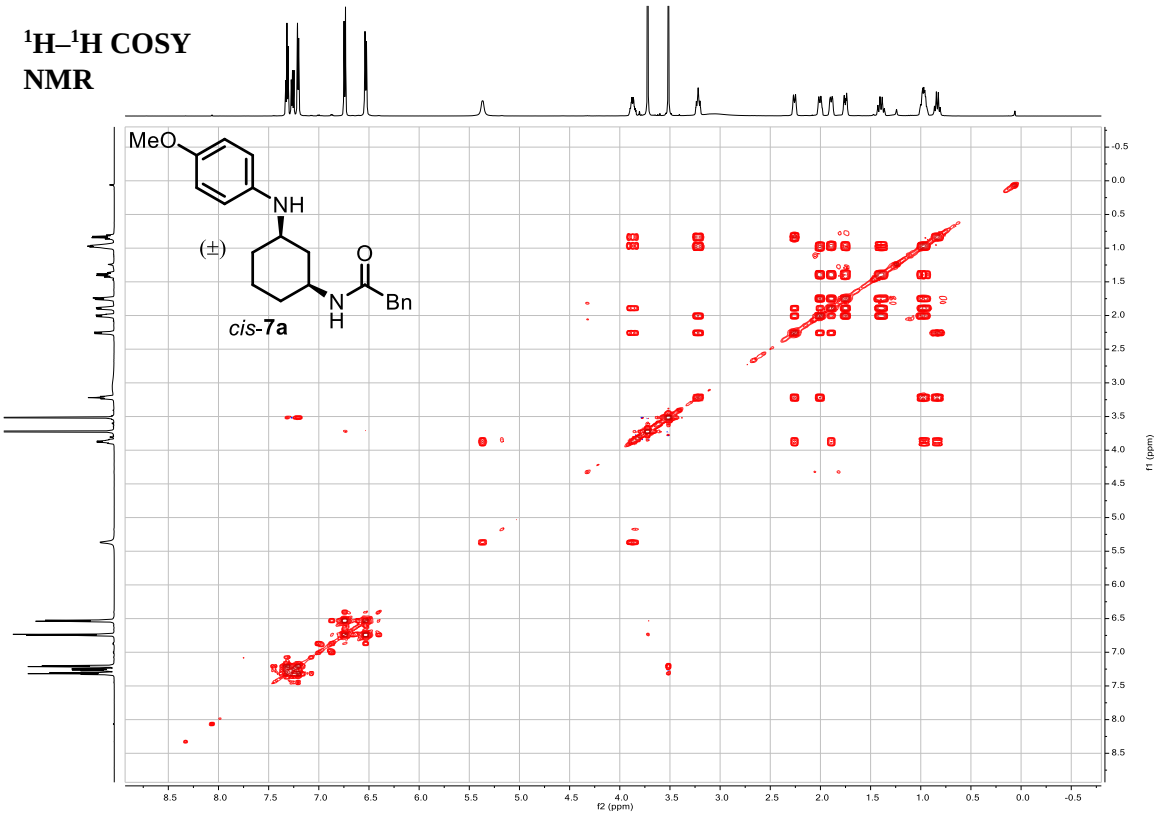
^{1}H NMR



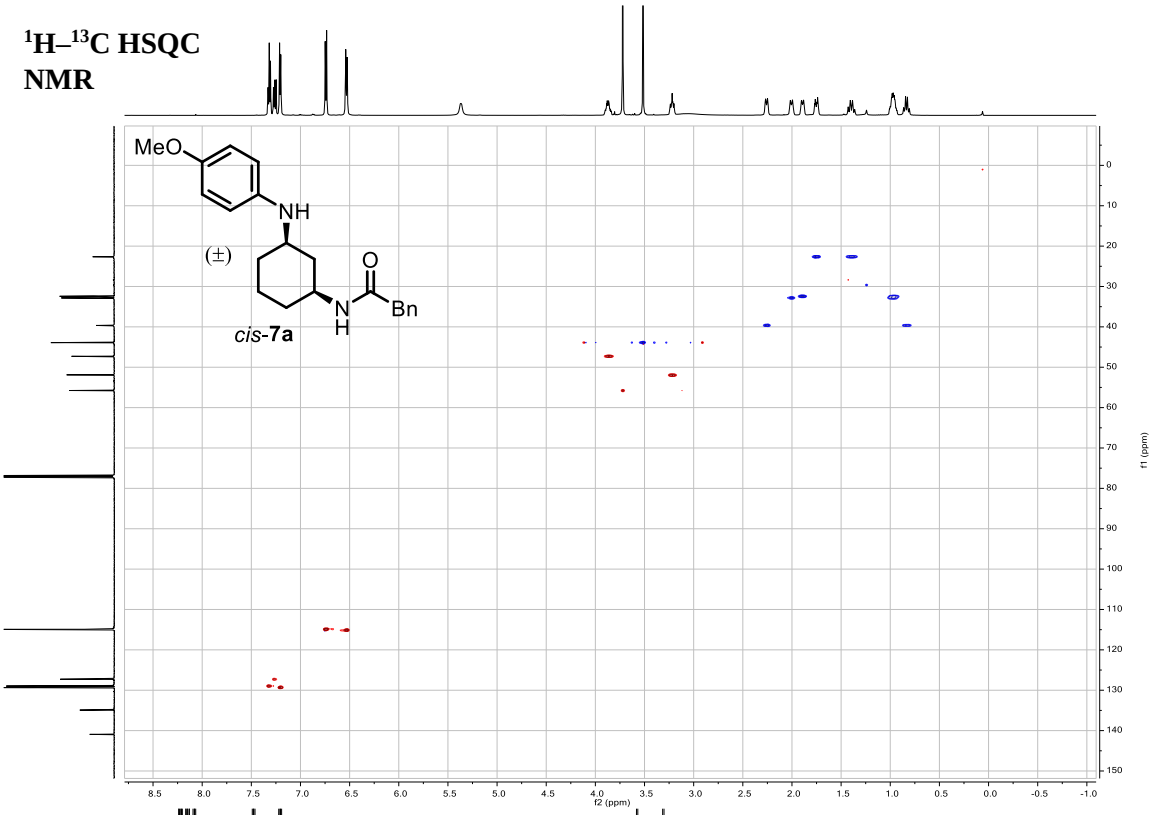
^{13}C NMR



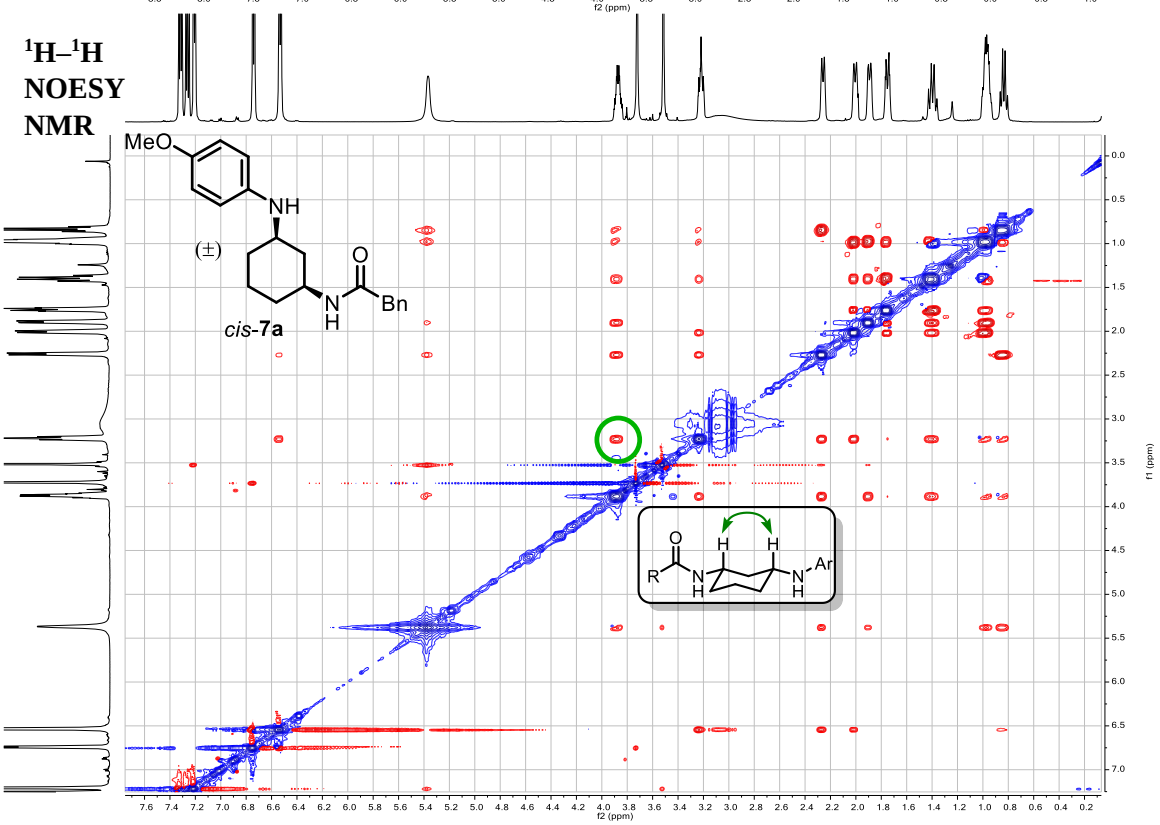
^{1}H–^{1}H COSY NMR



^{1}H–^{13}C HSQC NMR

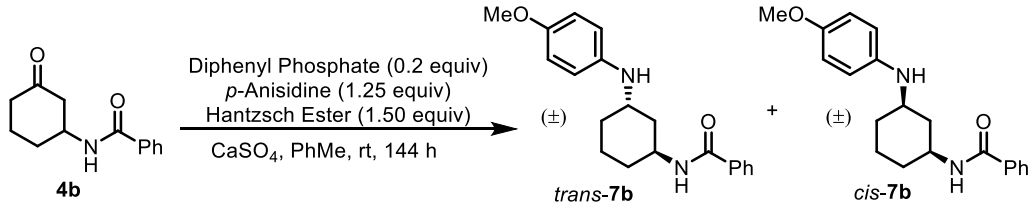


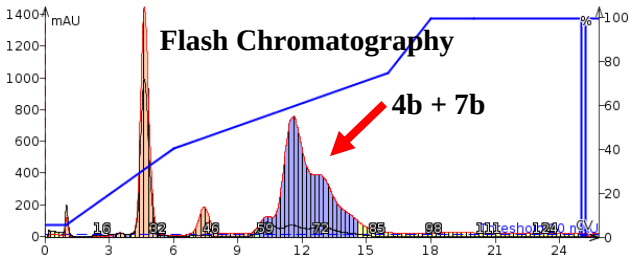
^{1}H–^{1}H NOESY NMR



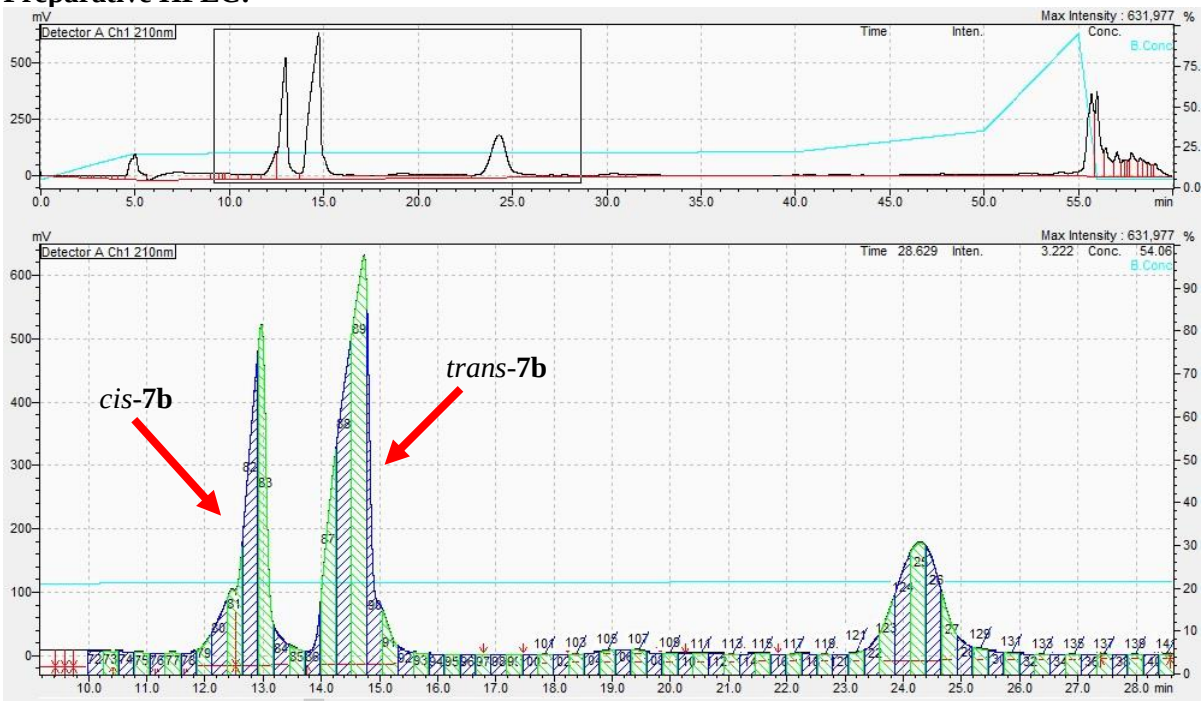
***Trans*- and *Cis*-*N*-(3-((4-methoxyphenyl)amino)cyclohexyl)benzamide (7b).**

Scheme S11: Synthesis 7b (General Procedure #11)

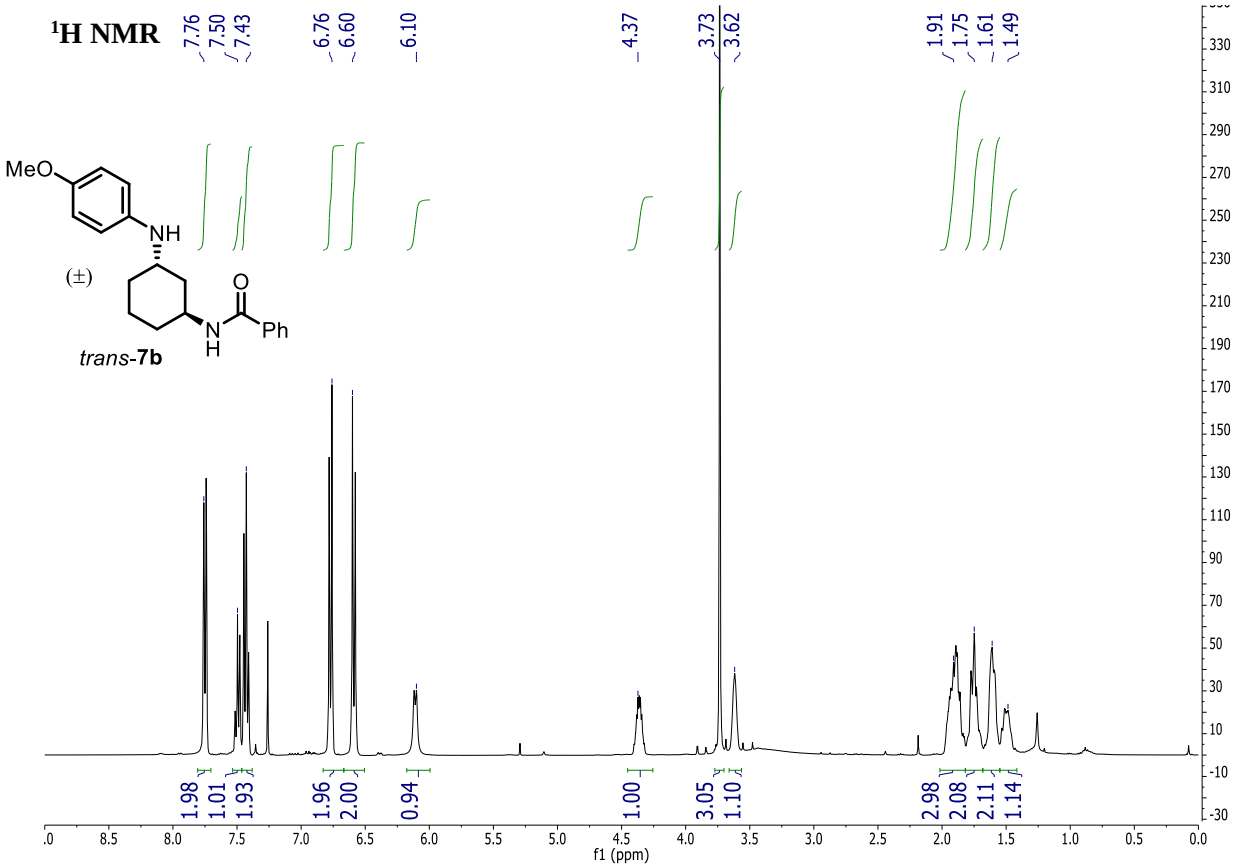




Preparative HPLC:

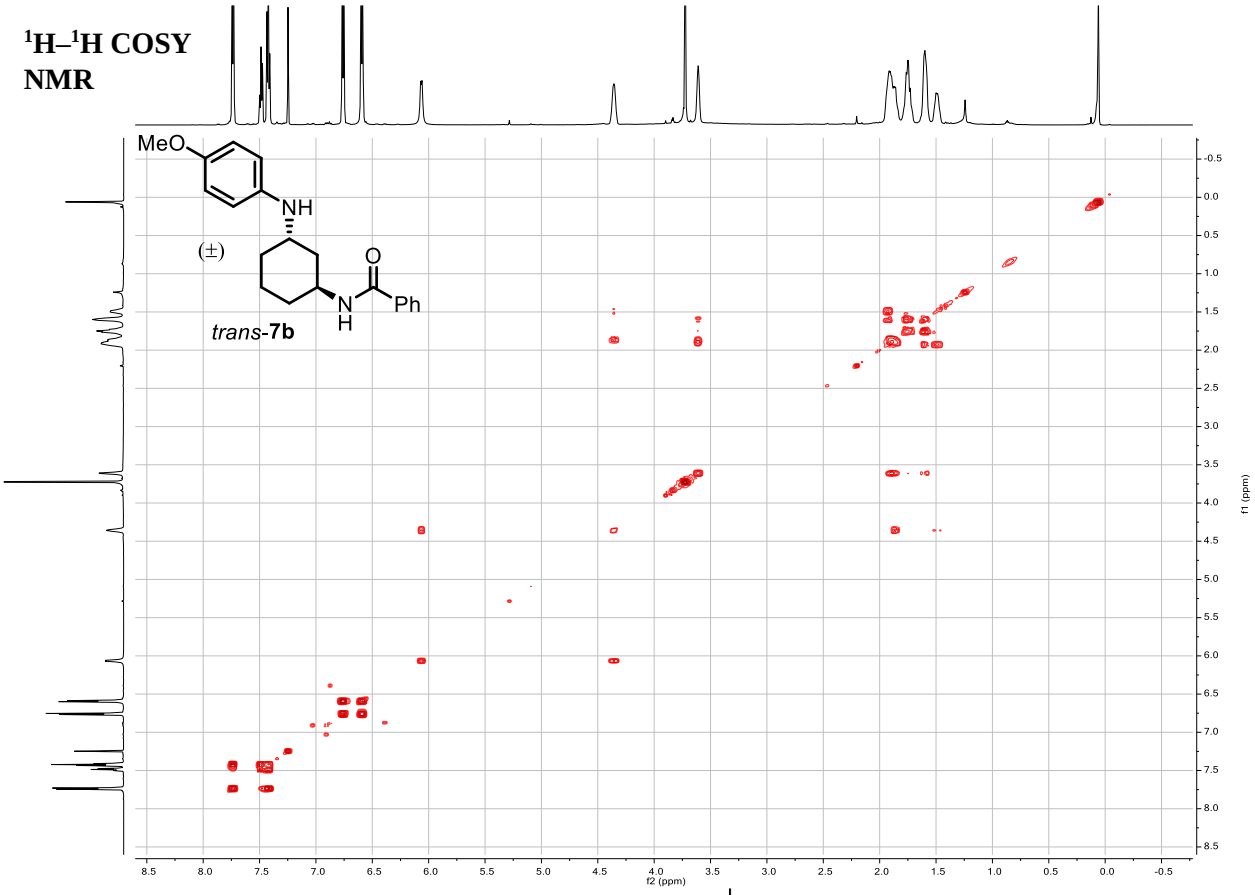


^{1}H NMR

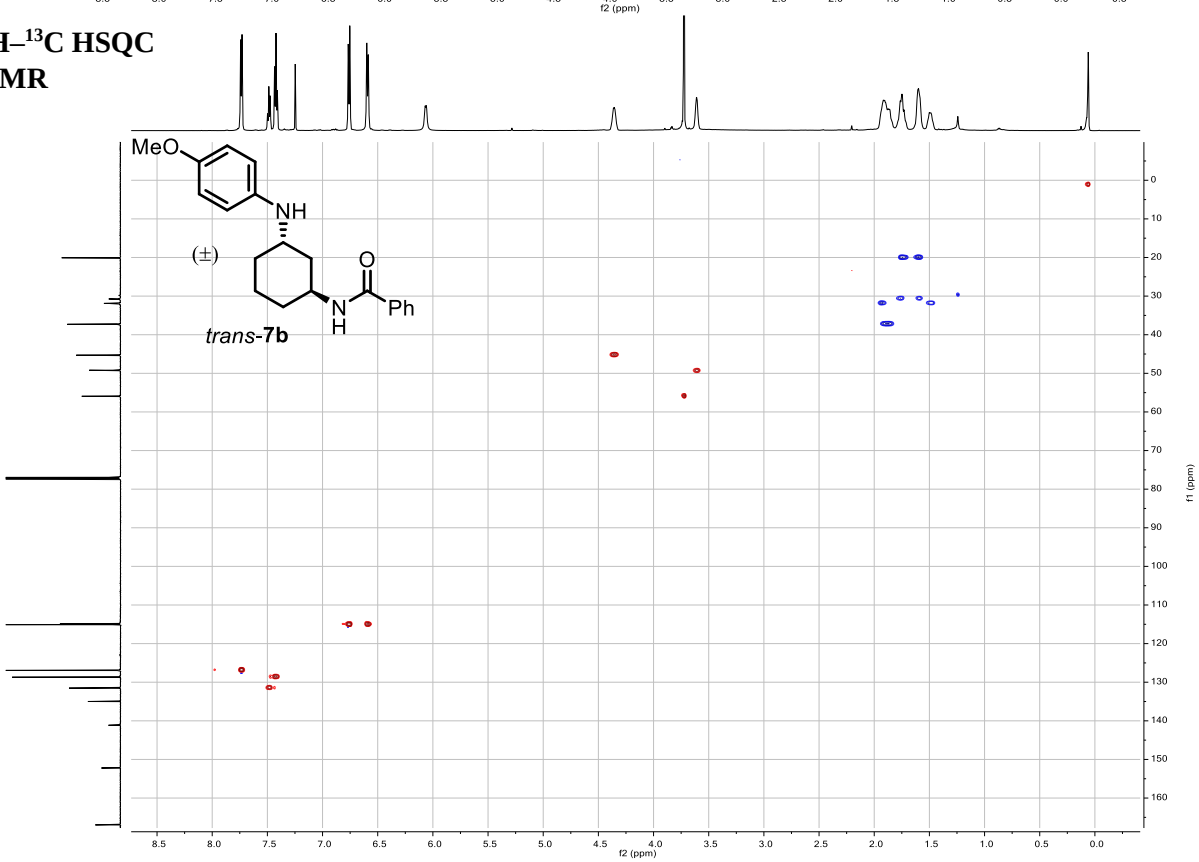


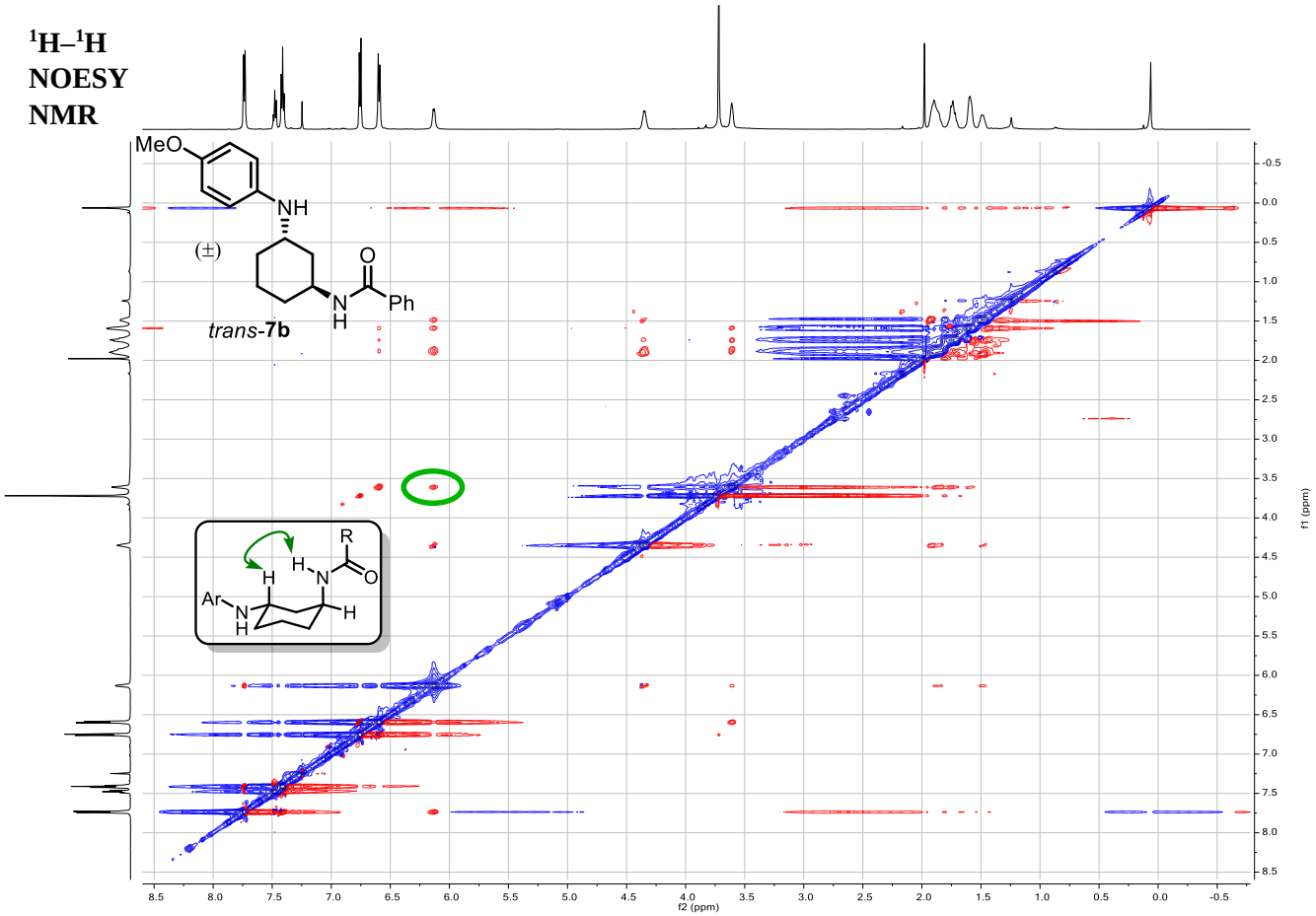
^{13}C NMR

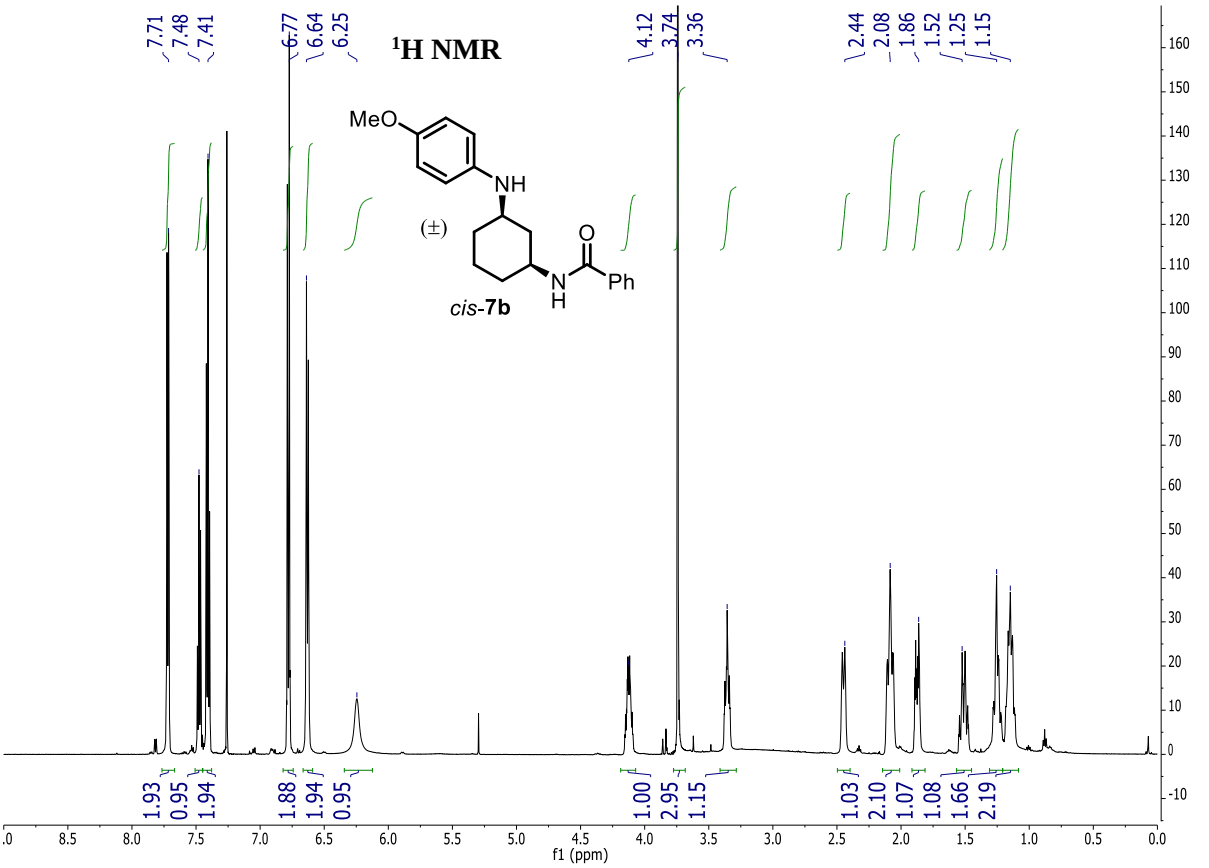
^{1}H–^{1}H COSY NMR

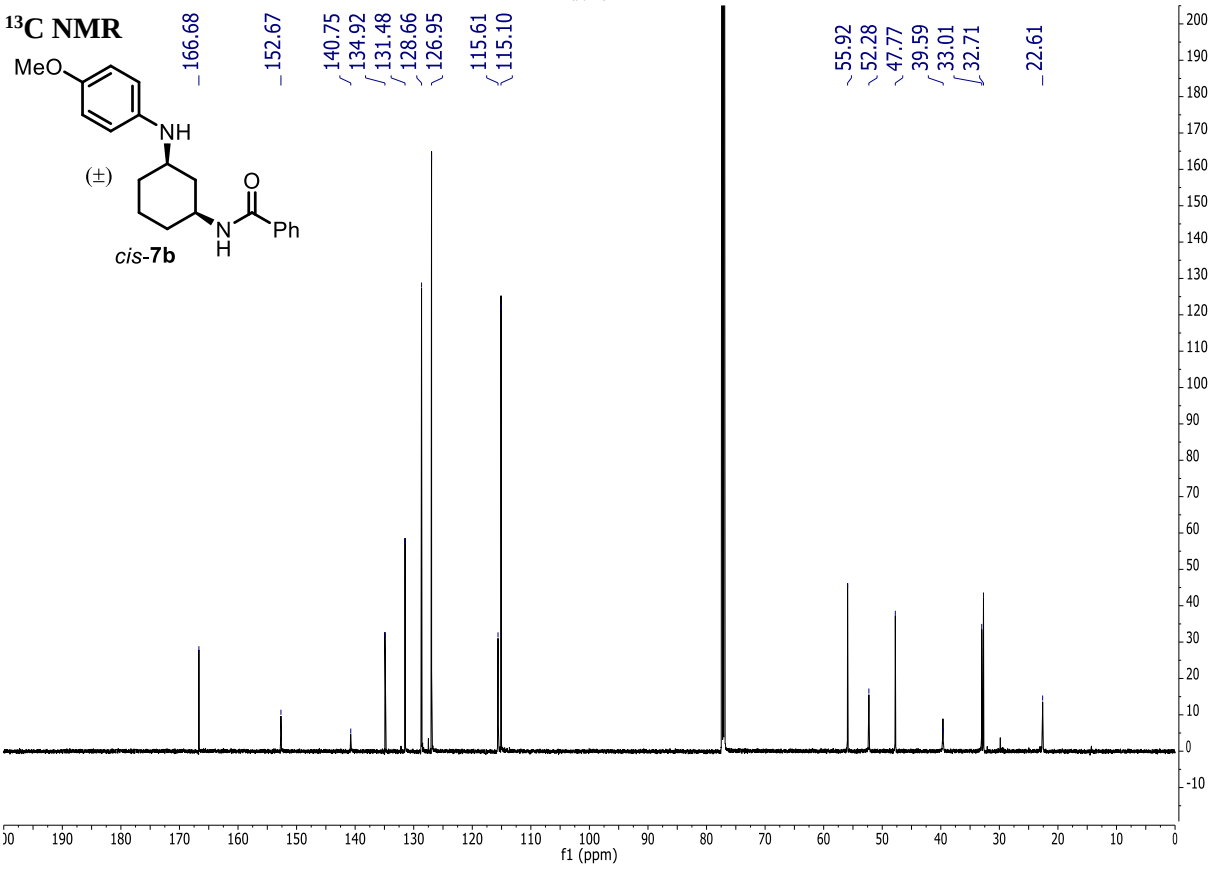


^{1}H–^{13}C HSQC NMR

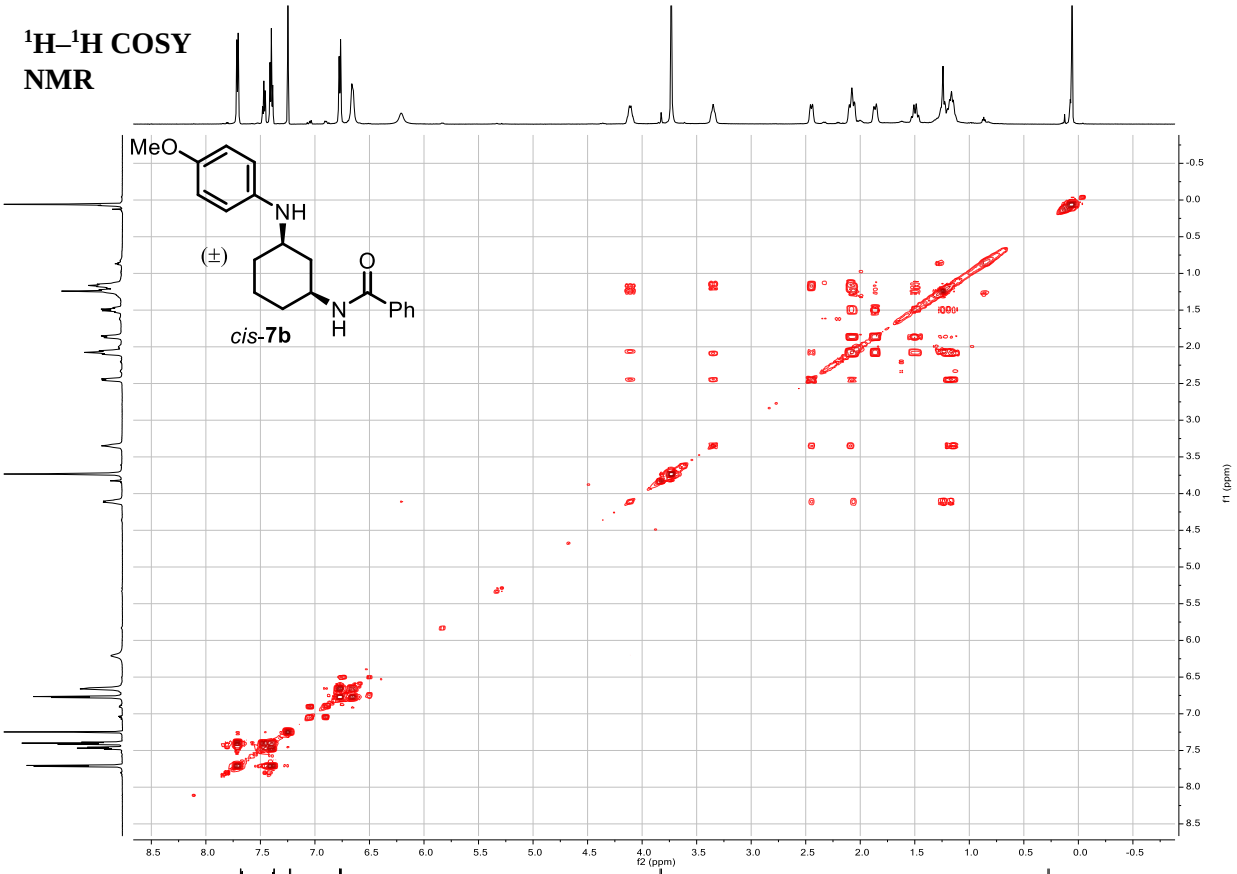



^{1}H–^{1}H
NOESY
NMR
MeO
NH
(±)
O
N
H
Ph
trans-7b
R
H
H
N
O
Ar
N
H
H
f2 (ppm)
f1 (ppm)

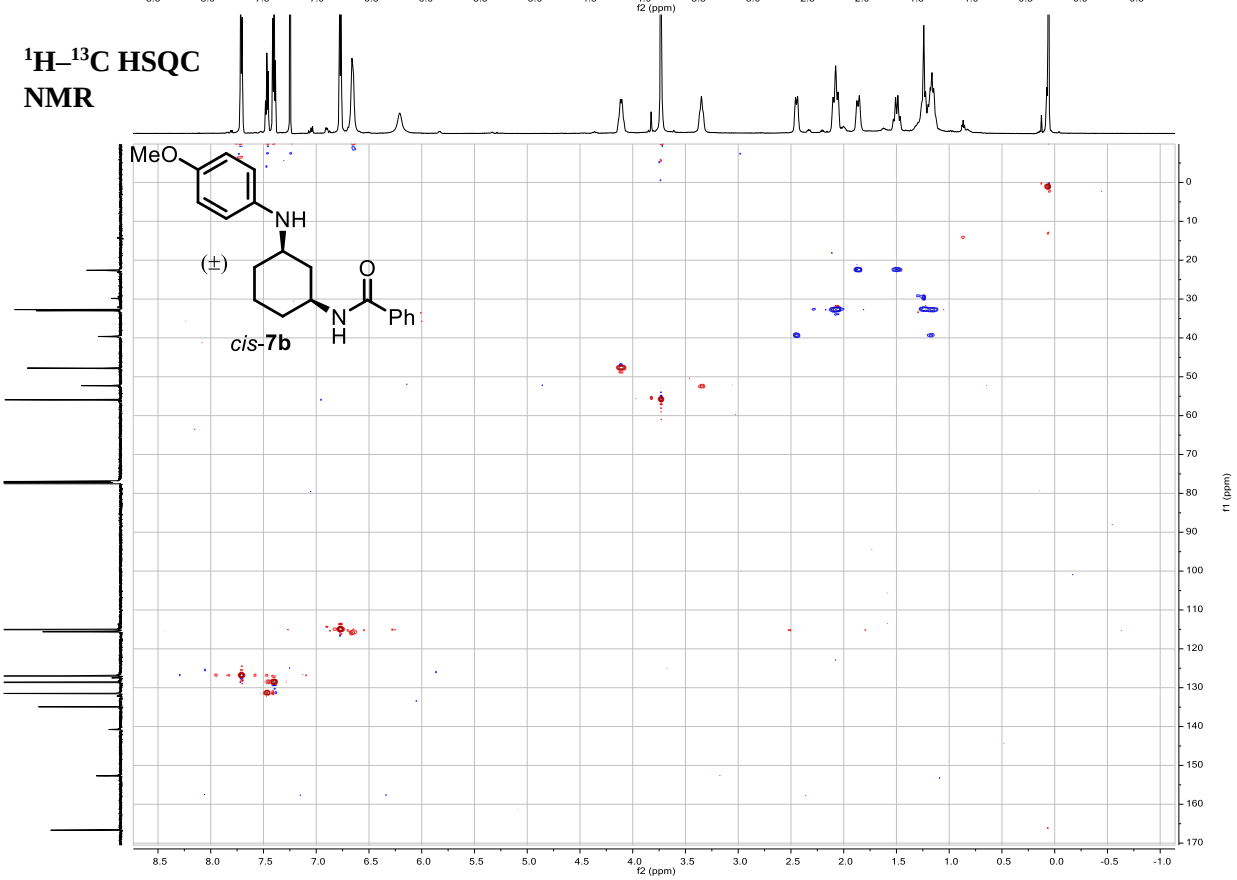

^{1}H NMR
7.71
7.48
7.41
6.77
6.64
6.25
4.12
3.74
3.36
2.44
2.08
1.86
1.52
1.25
1.15
1.93
0.95
1.94
1.88
1.94
0.95
1.00
2.95
1.15
1.03
2.10
1.07
1.08
1.66
2.19
MeO
NH
(±)
O
N
H
Ph
cis-7b
f1 (ppm)

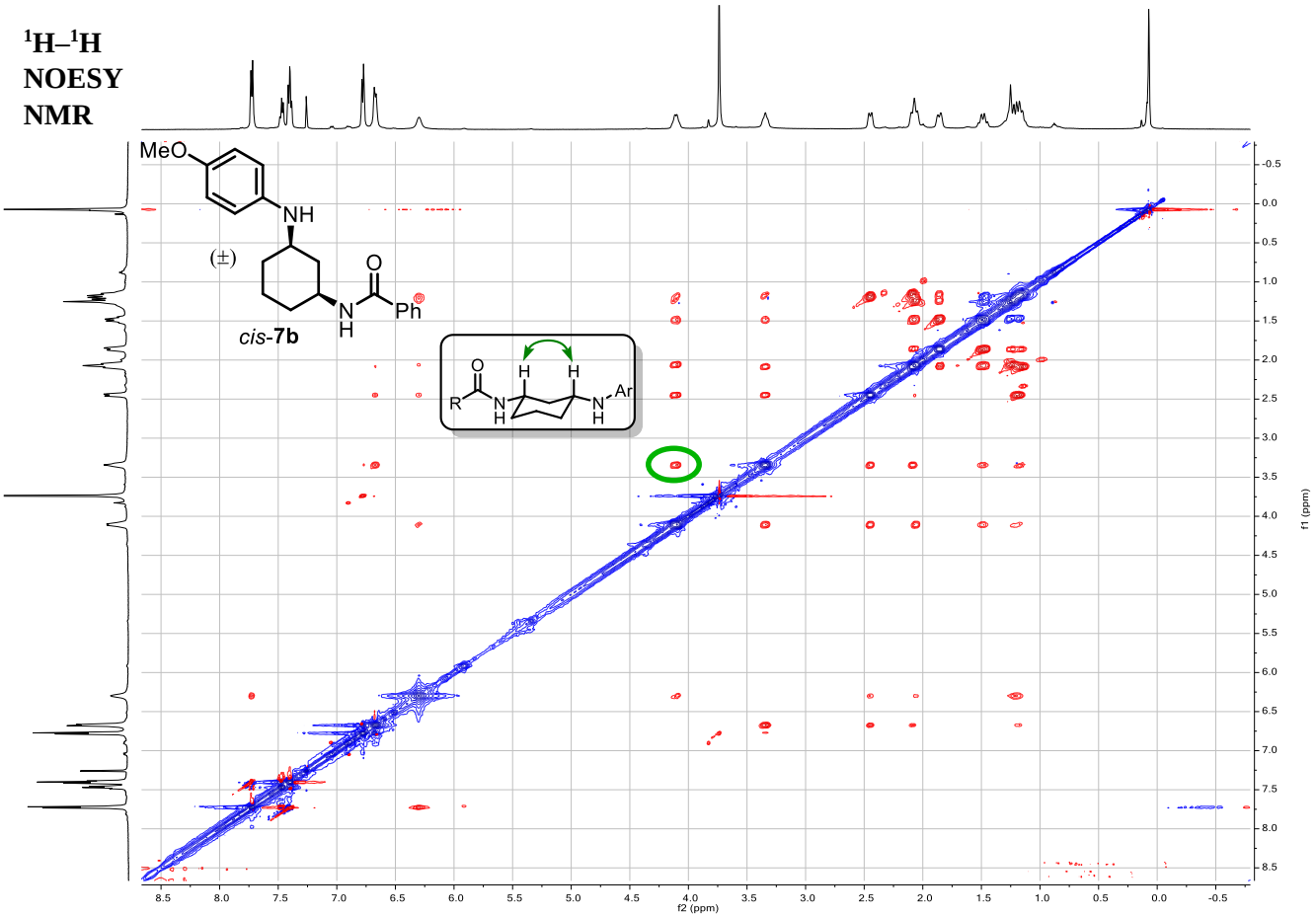

^{13}C NMR
166.68
152.67
140.75
134.92
131.48
128.66
126.95
115.61
115.10
55.92
52.28
47.77
39.59
33.01
32.71
22.61
MeO
NH
(±)
O
N
H
Ph
cis-7b
f1 (ppm)

^{1}H–^{1}H COSY NMR



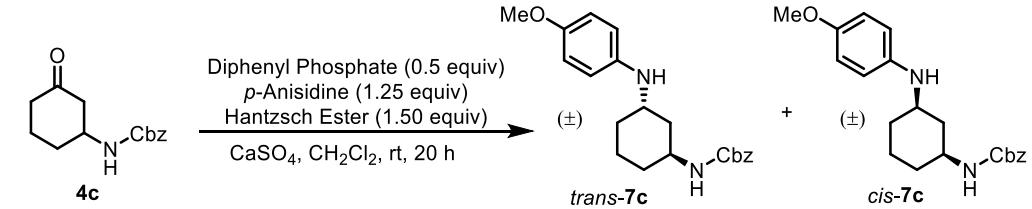
^{1}H–^{13}C HSQC NMR

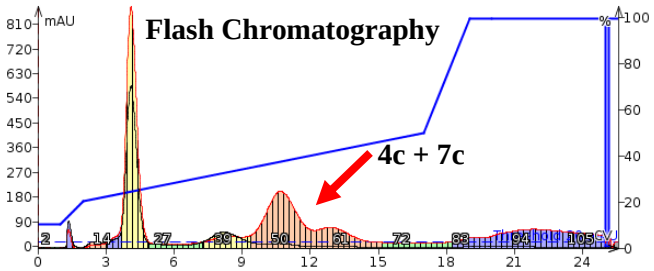




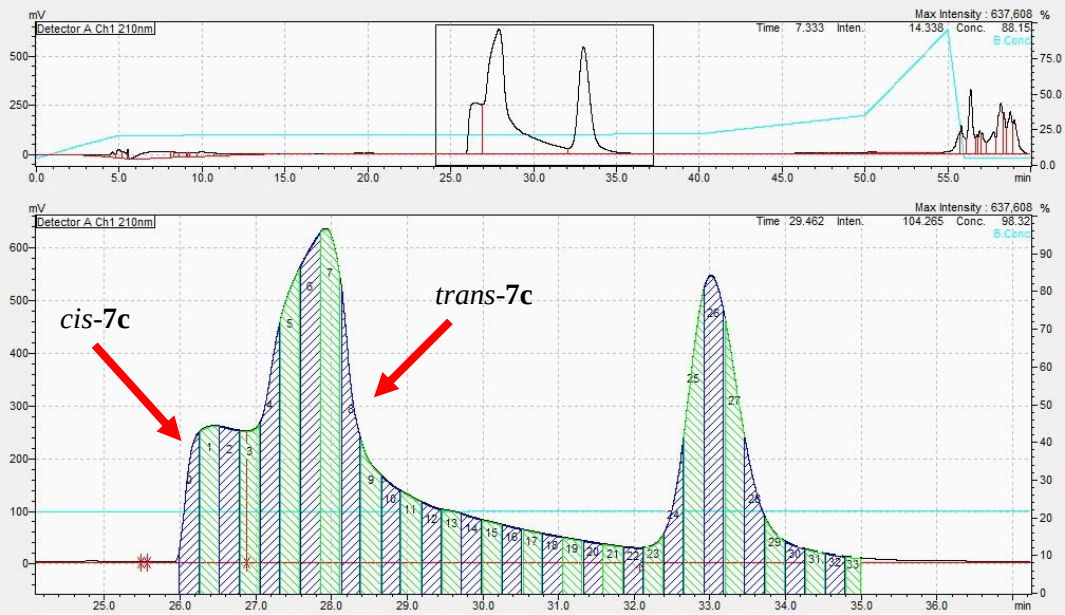
Trans- and *cis*-Benzyl (3-((4-methoxyphenyl)amino)cyclohexyl)carbamate (7c)

Scheme S12: Synthesis 7c (General Procedure #11)

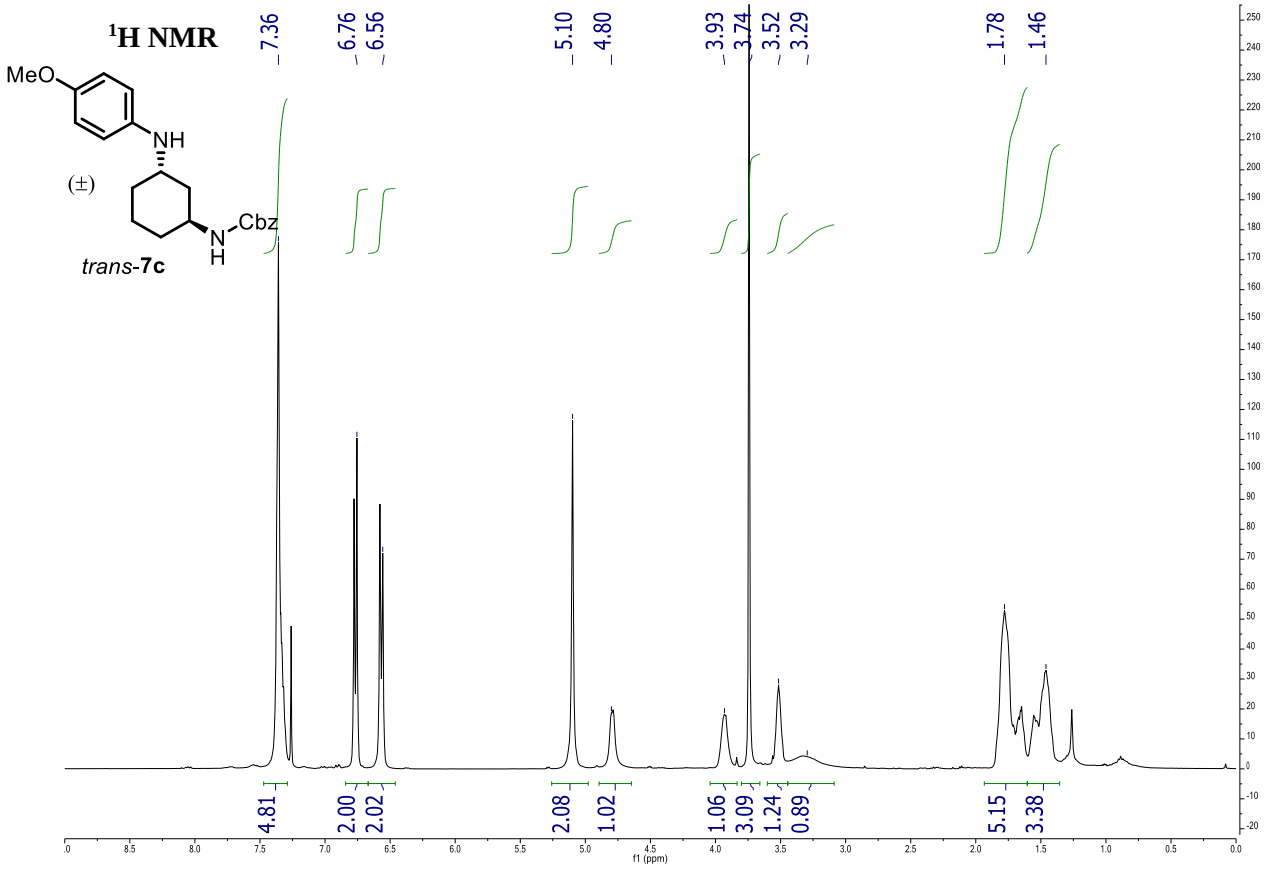


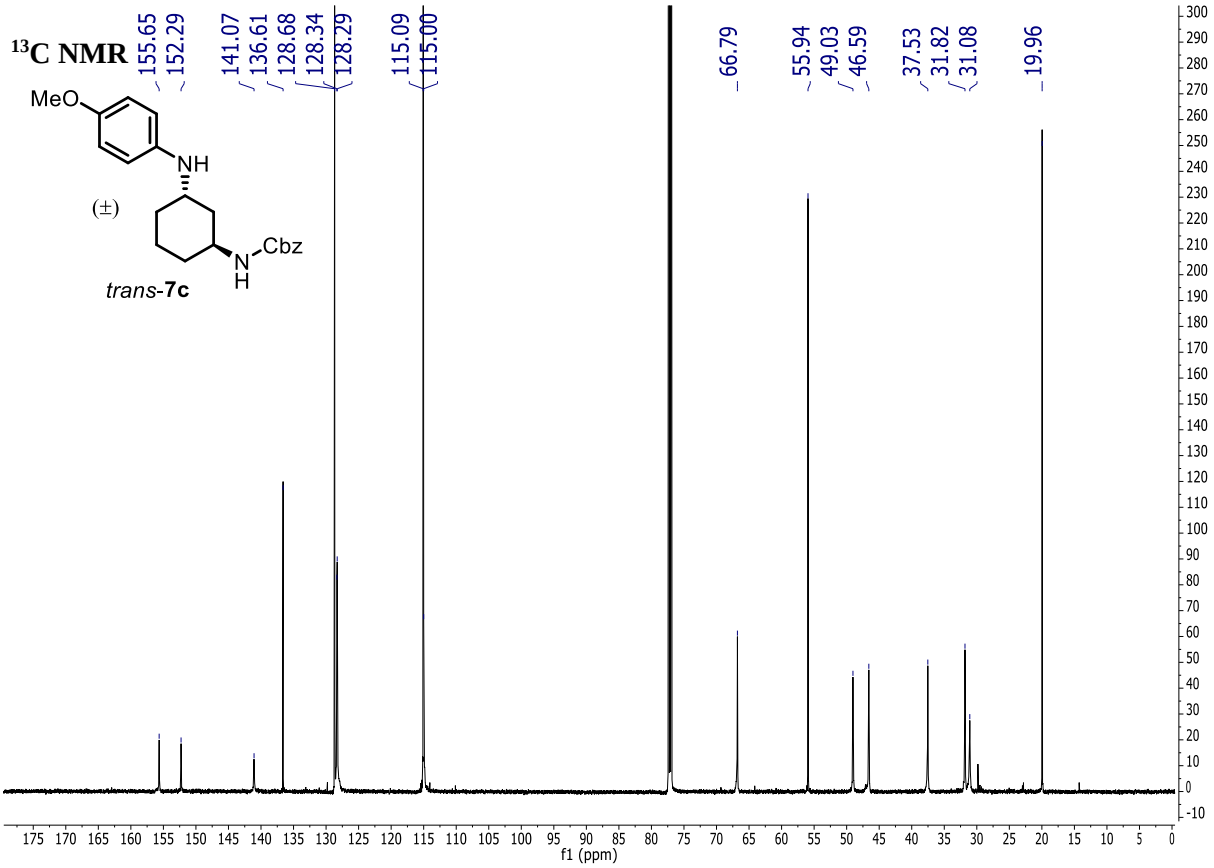


Preparative HPLC:

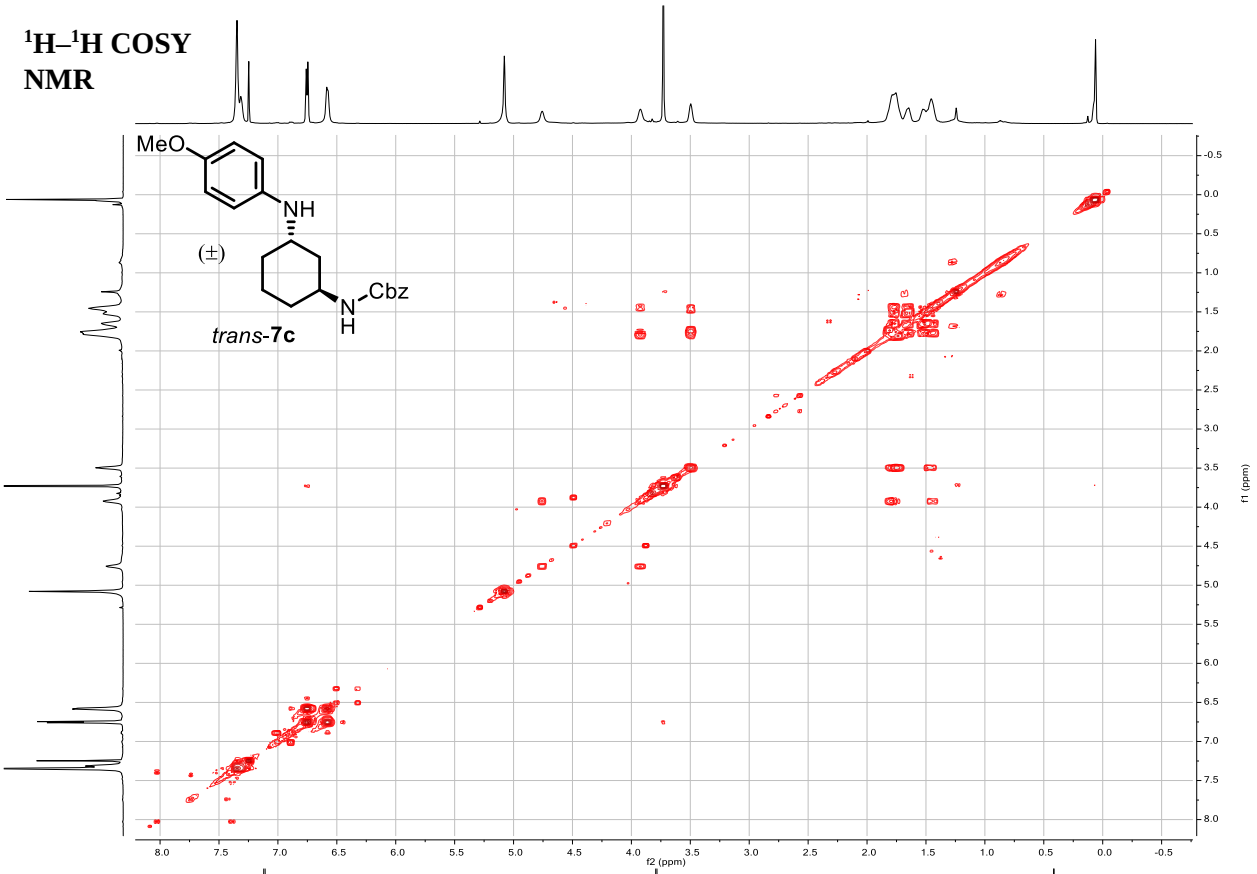


^{1}H NMR

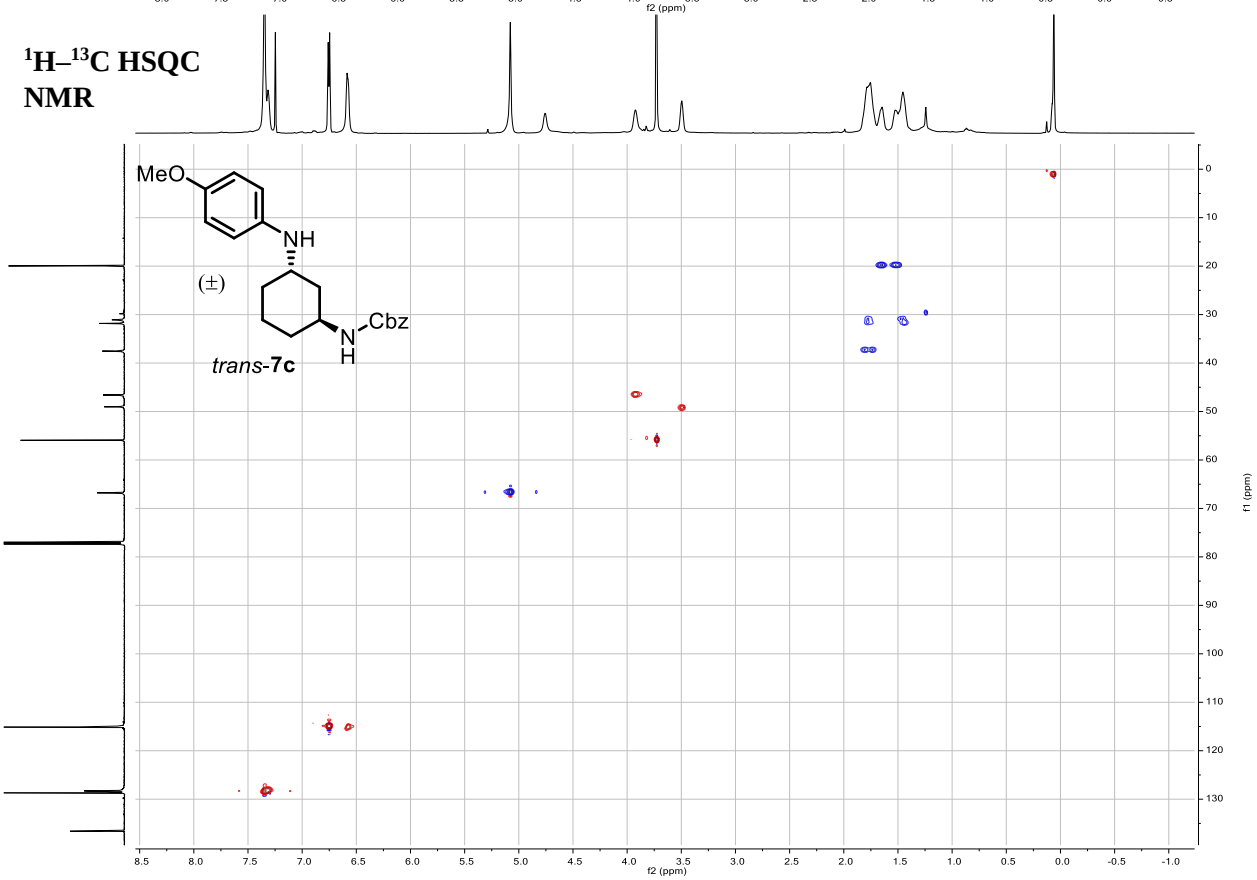



13C NMR
155.65
152.29
141.07
136.61
128.68
128.34
128.29
115.09
115.00
66.79
55.94
49.03
46.59
37.53
31.82
31.08
19.96
MeO
NH
(±)
N
H
Cbz
trans-7c
f1 (ppm)

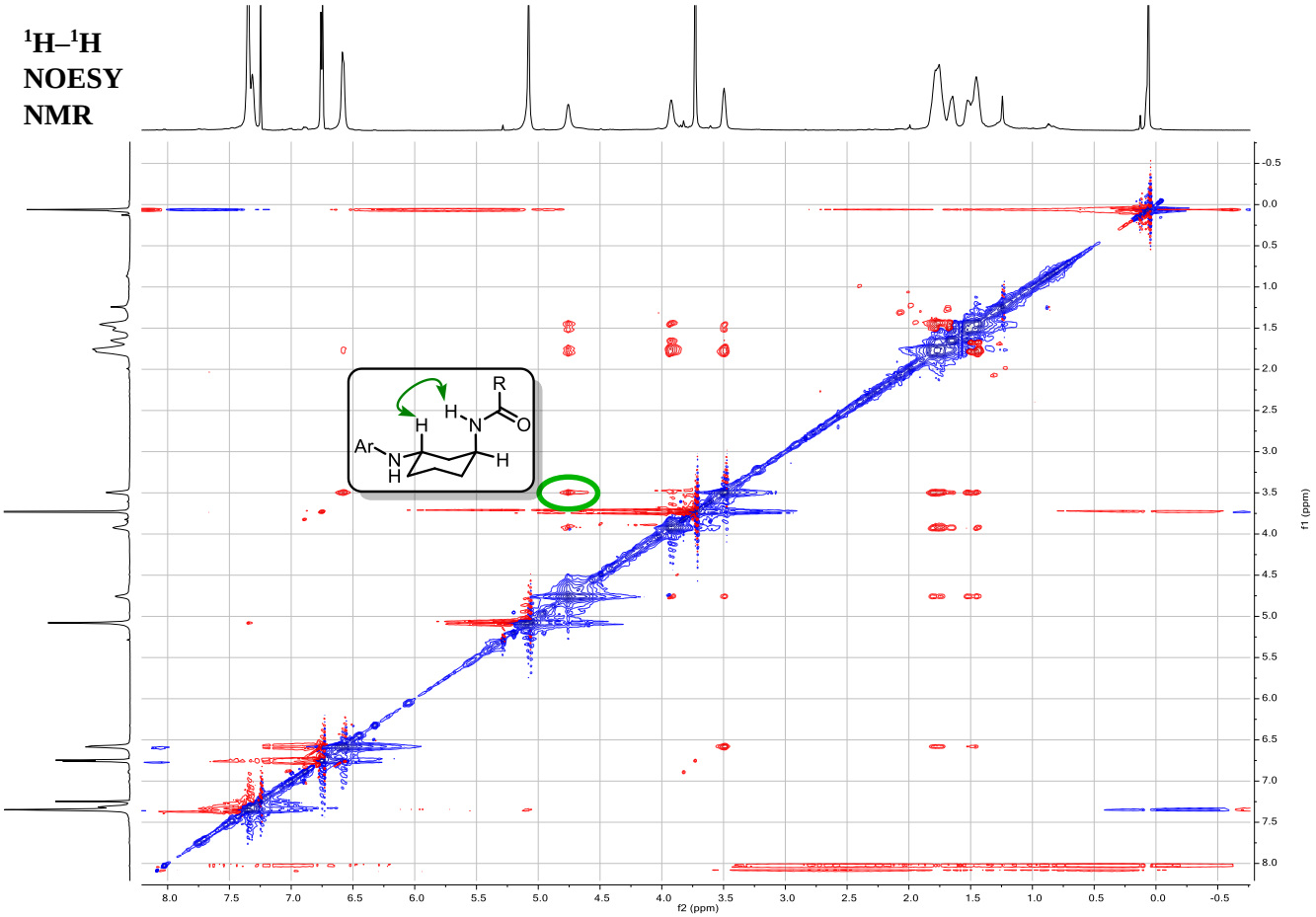
^{1}H–^{1}H COSY NMR

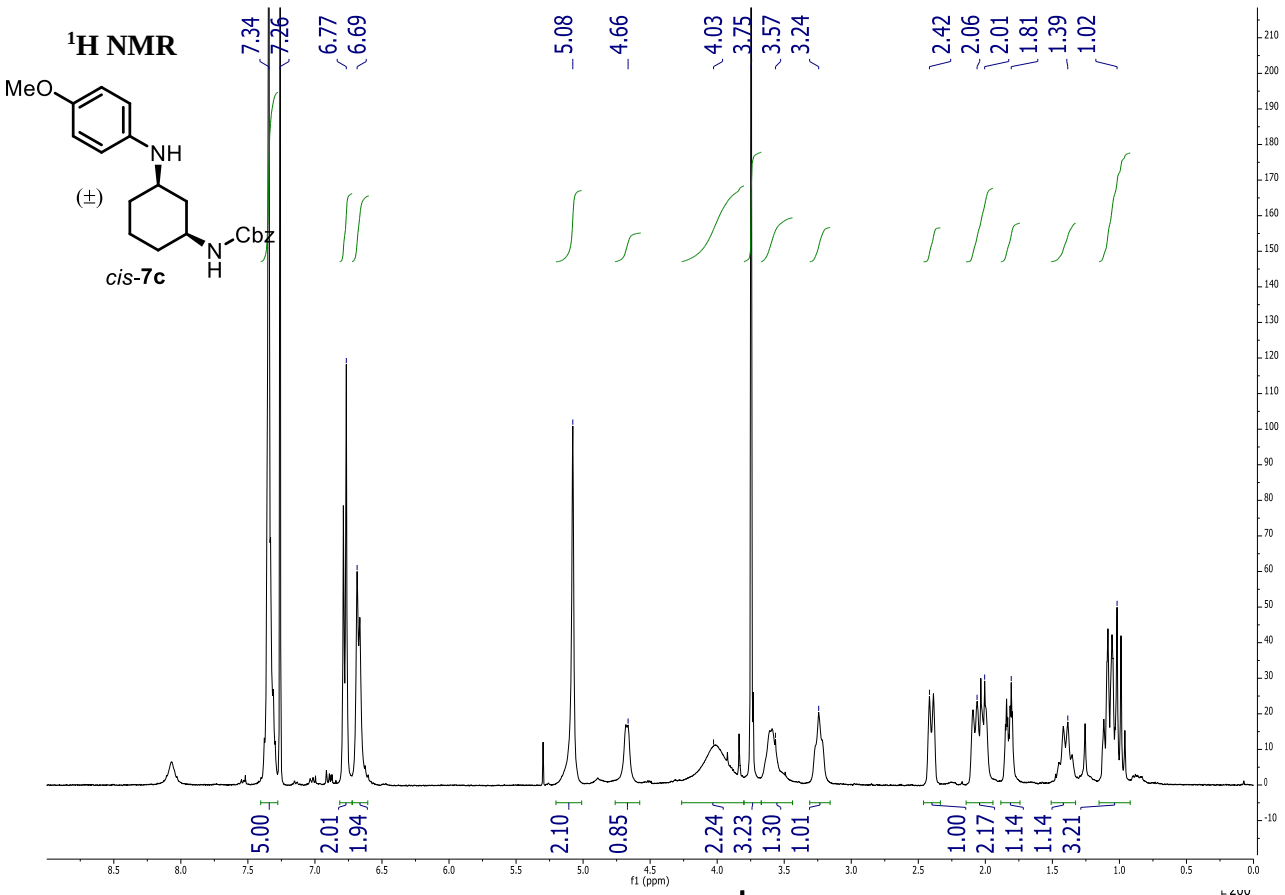


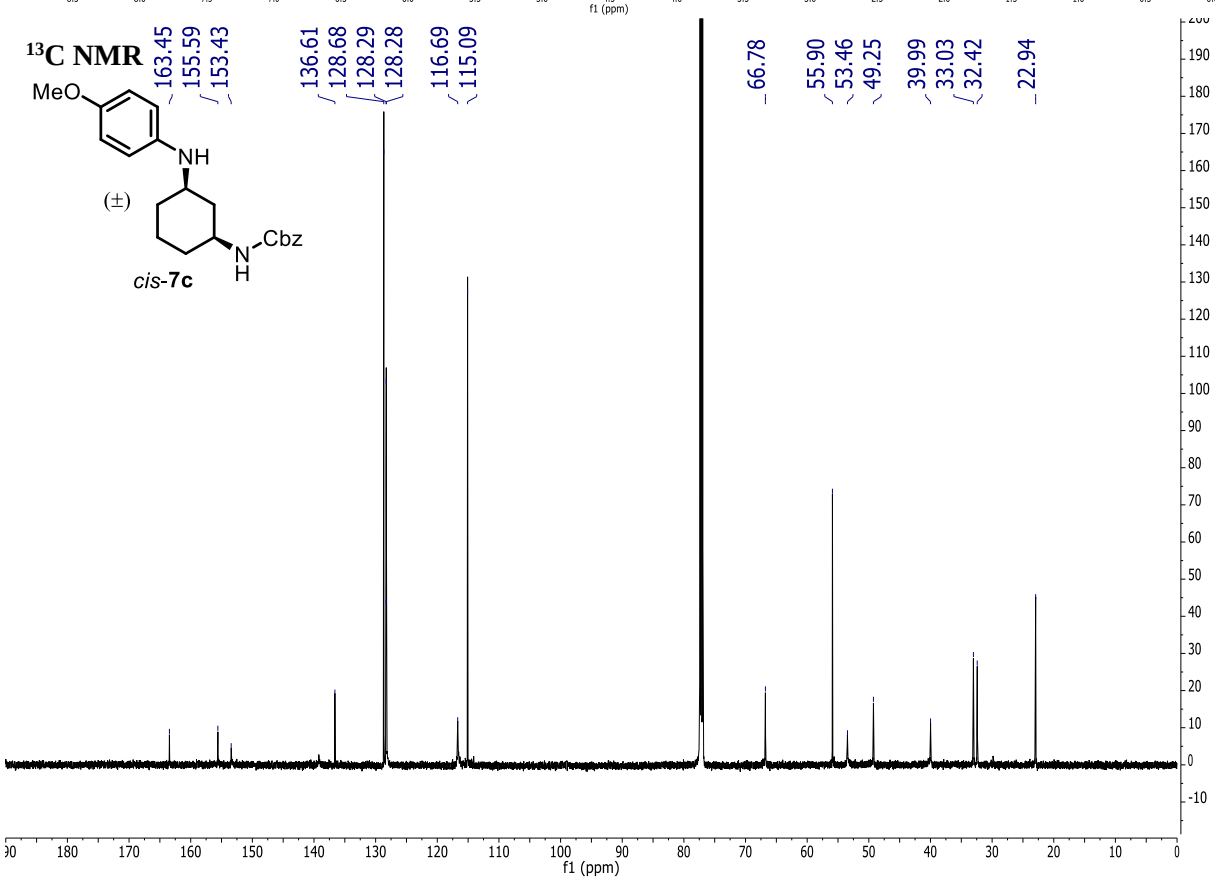
^{1}H–^{13}C HSQC NMR



^{1}H–^{1}H NOESY NMR



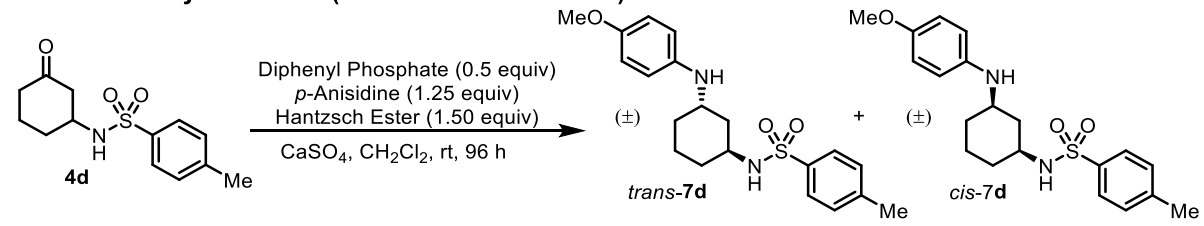


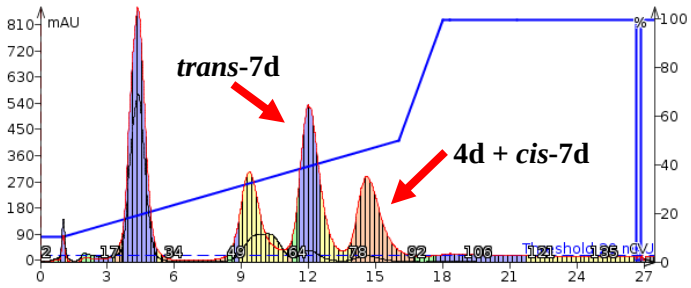


The identify of *cis*-**7c** was confirmed without a NOESY as *trans*-**7c** was analyzed with 2D methods.

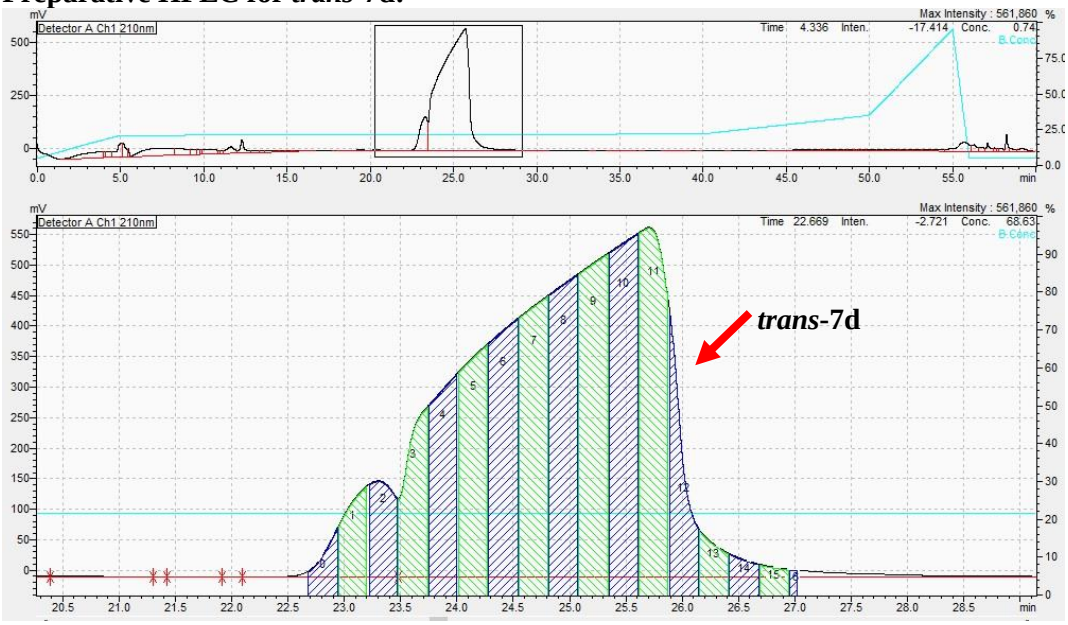
Trans- and *cis*-*N*-(3-((4-methoxyphenyl)amino)cyclohexyl)-4-methylbenzenesulfonamide (7f)

Scheme S13: Synthesis 7d (General Procedure #11)

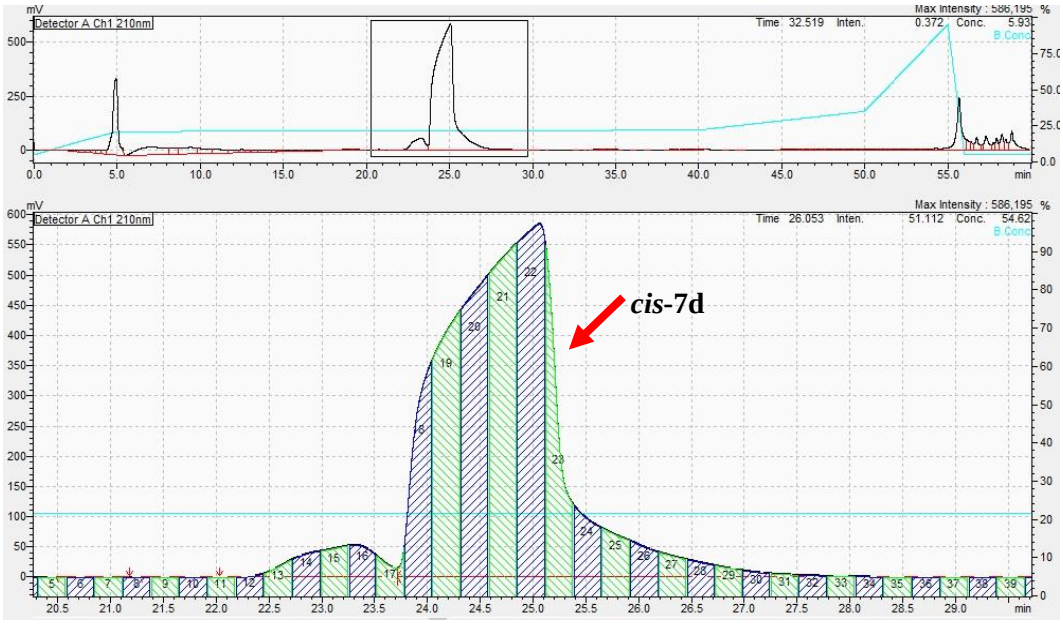


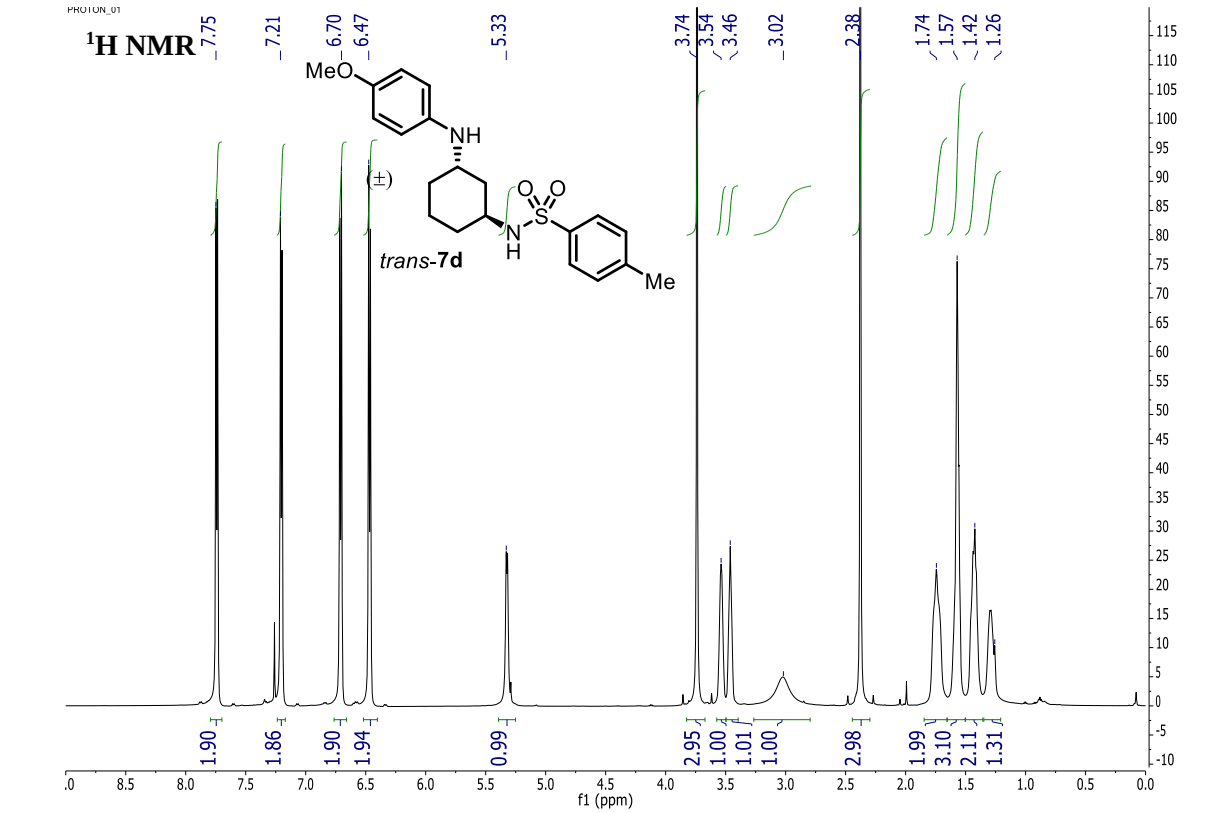


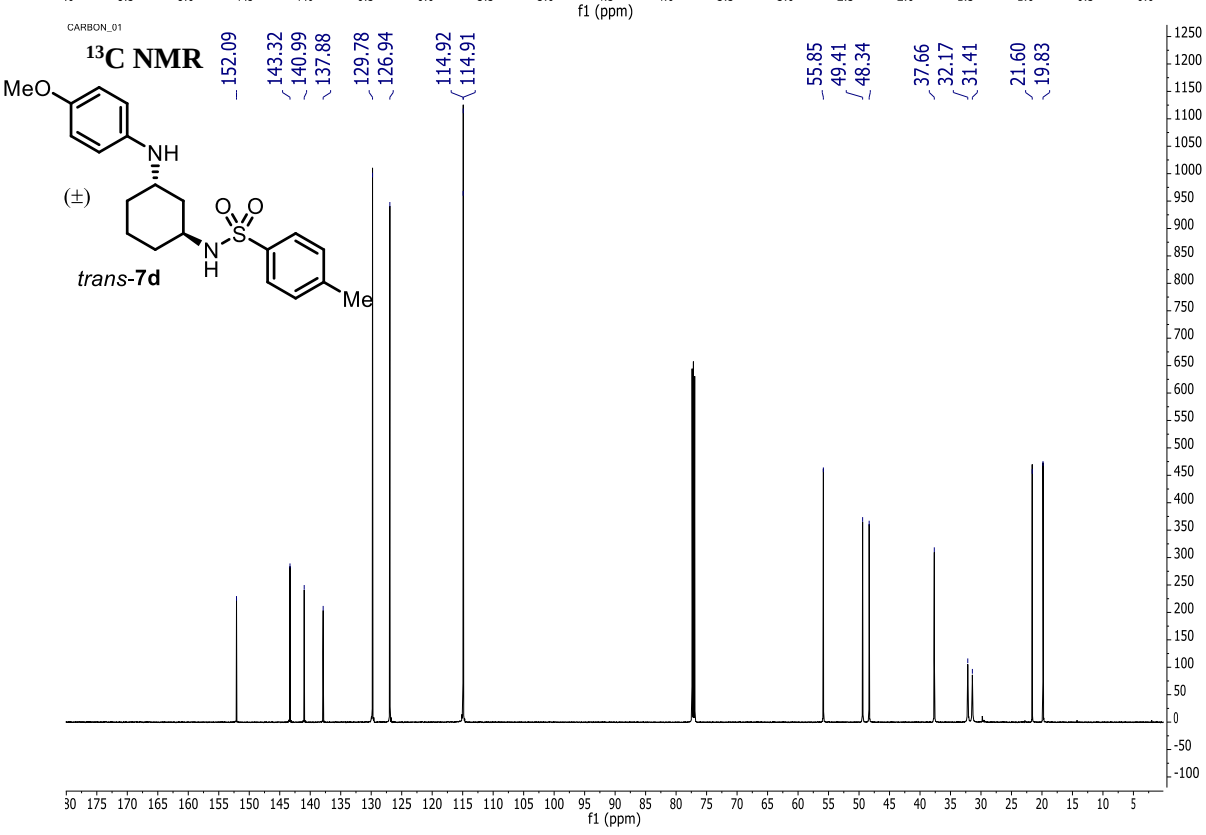
Preparative HPLC for *trans*-7d:

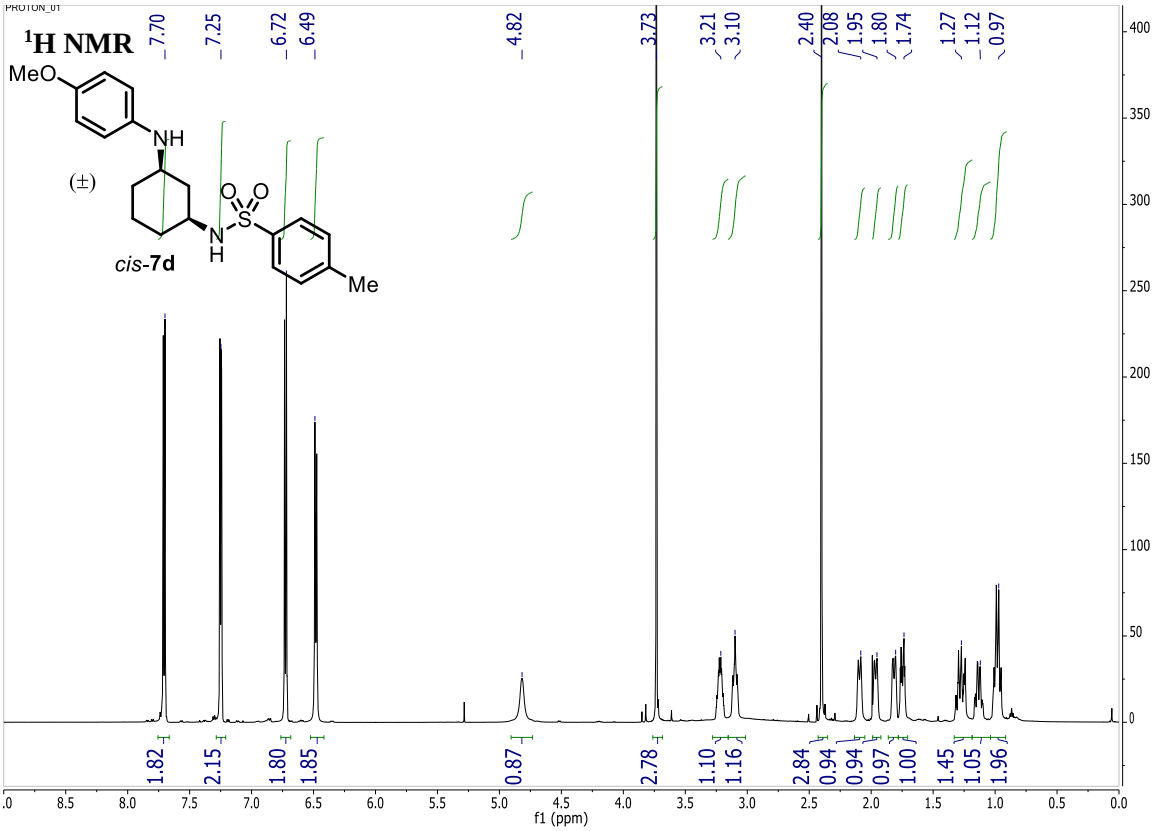


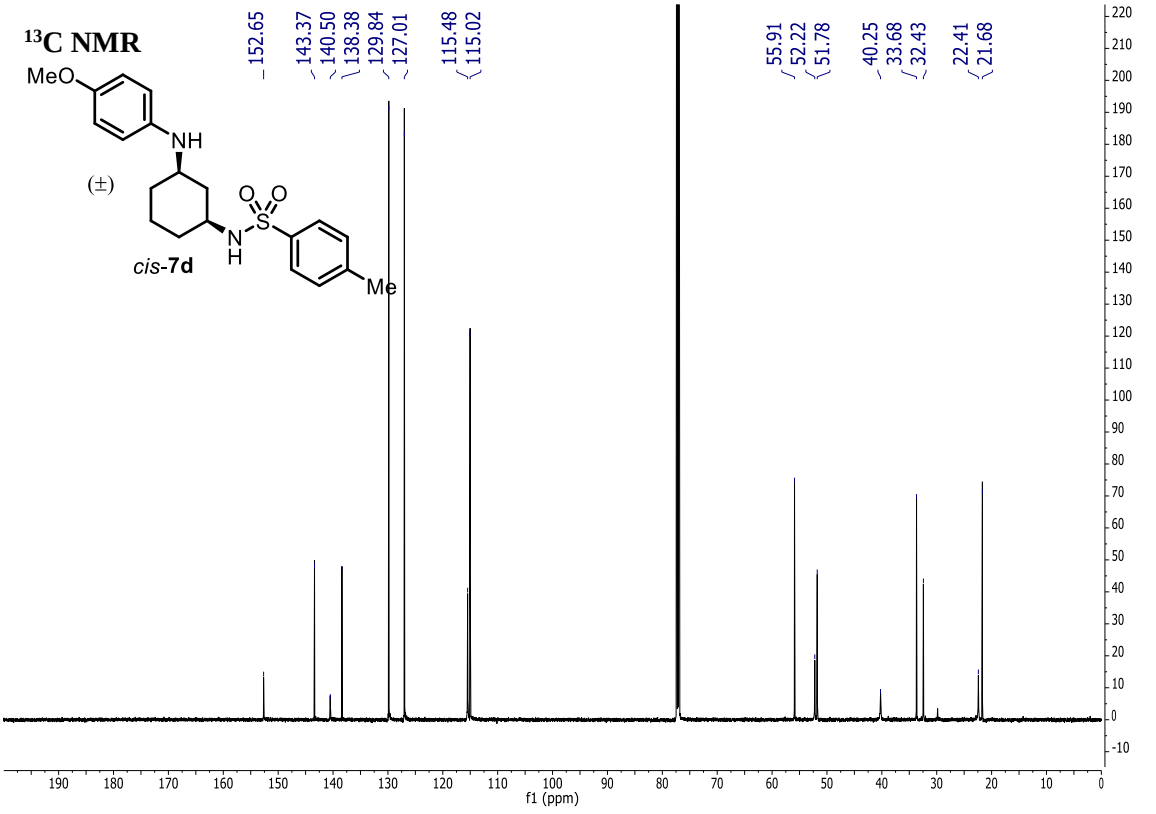
Preparative HPLC for *cis*-7d:



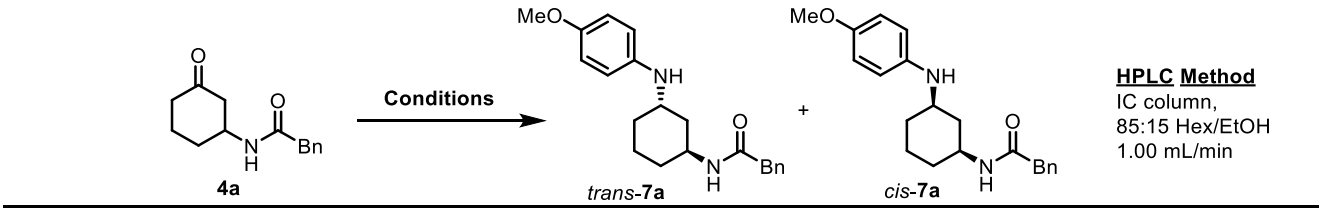

PROTON_01
^{1}H NMR
7.75
7.21
6.70
6.47
5.33
3.74
3.54
3.46
3.02
2.38
1.74
1.57
1.42
1.26
MeO
NH
(±)
trans-7d
Me
1.90
1.86
1.90
1.94
0.99
2.95
1.00
1.01
1.00
2.98
1.99
3.10
2.11
1.31
f1 (ppm)

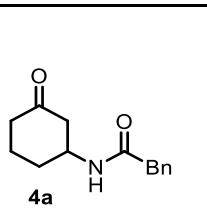

CARBON_01
^{13}C NMR
152.09
143.32
140.99
137.88
129.78
126.94
114.92
114.91
55.85
49.41
48.34
37.66
32.17
31.41
21.60
19.83
MeO
NH
(±)
trans-7d
Me
f1 (ppm)

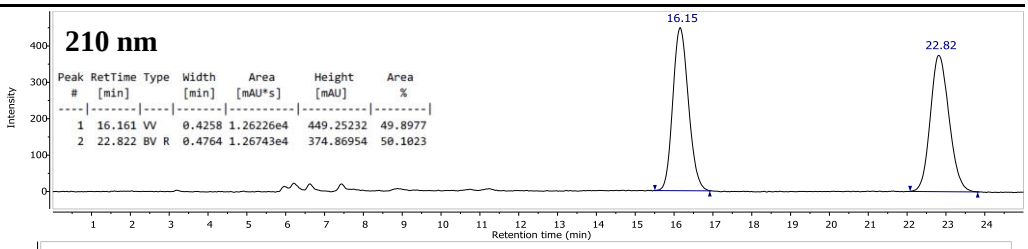

^{1}H NMR
MeO
NH
(±)
cis-7d
Me
7.70
7.25
6.72
6.49
4.82
3.73
3.21
3.10
2.40
2.08
1.95
1.80
1.74
1.27
1.12
0.97
1.82
2.15
1.80
1.85
0.87
2.78
1.10
1.16
2.84
0.94
0.94
0.97
1.00
1.45
1.05
1.96
f1 (ppm)

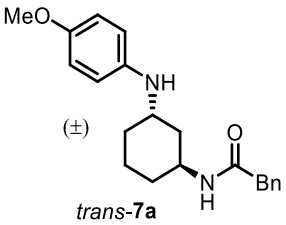

^{13}C NMR
MeO
NH
(±)
cis-7d
Me
152.65
143.37
140.50
138.38
129.84
127.01
115.48
115.02
55.91
52.22
51.78
40.25
33.68
32.43
22.41
21.68
f1 (ppm)

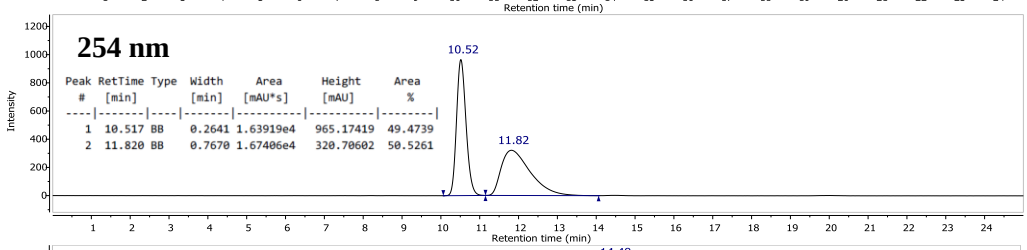
5. HPLC Traces

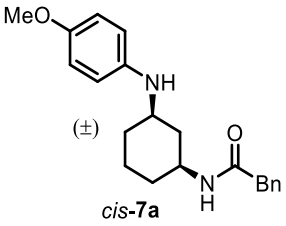


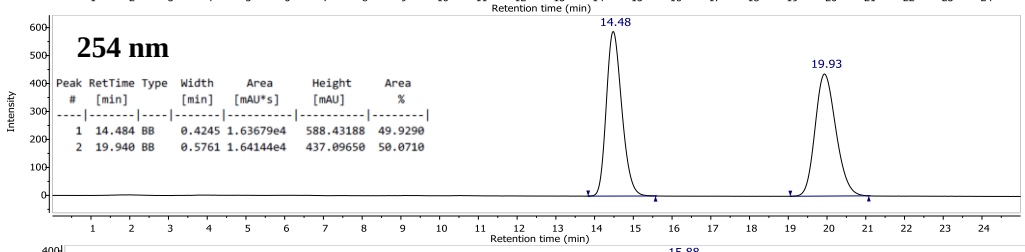




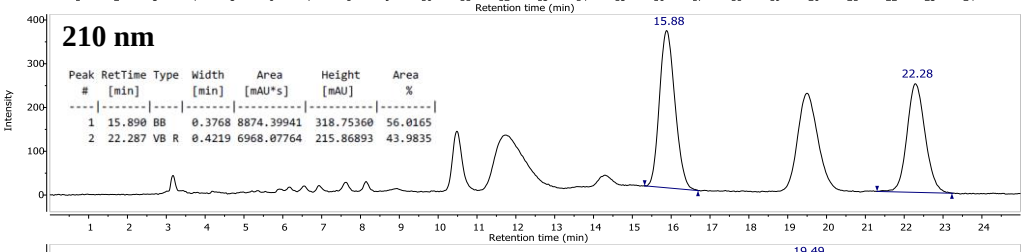


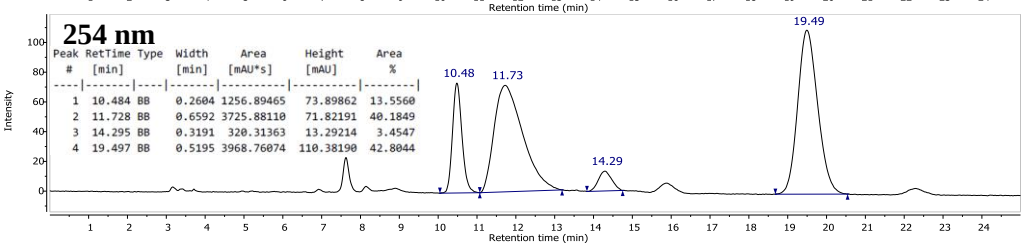


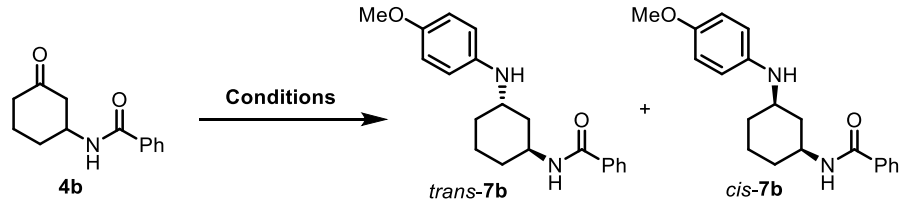




P32-Catalyzed Table 1, entry 33 (one run, 2 wavelengths reported)

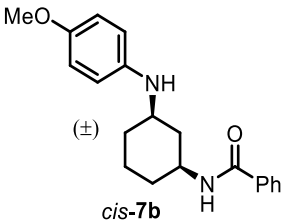




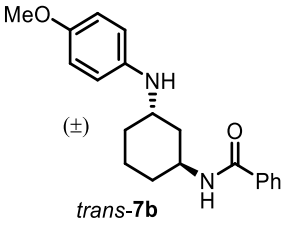


HPLC Methods
For *cis*-**7b**,
OD-H column, 80:20
Hex/IPA, 1.00 mL/min

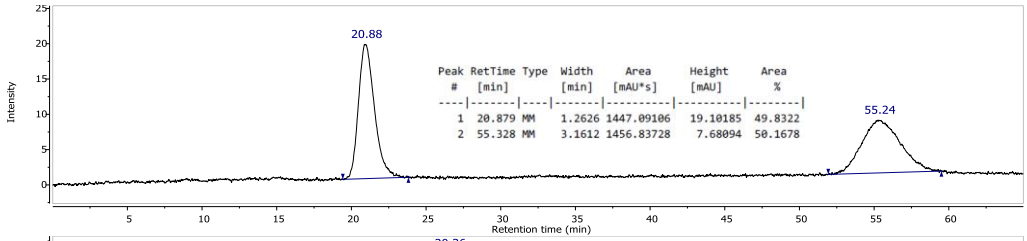
For *trans*-**7b**,
IC column, 80:20
Hex/IPA, 1.00 mL/min



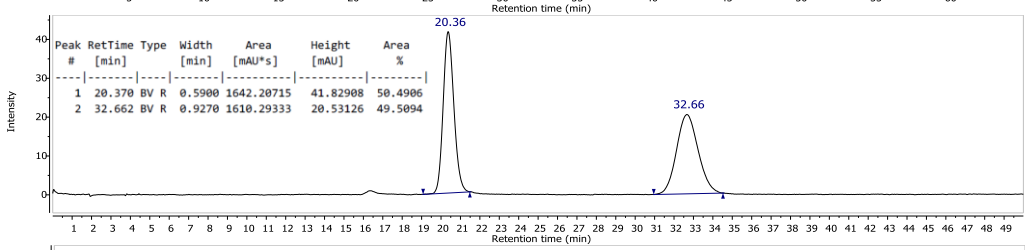
cis-**7b**

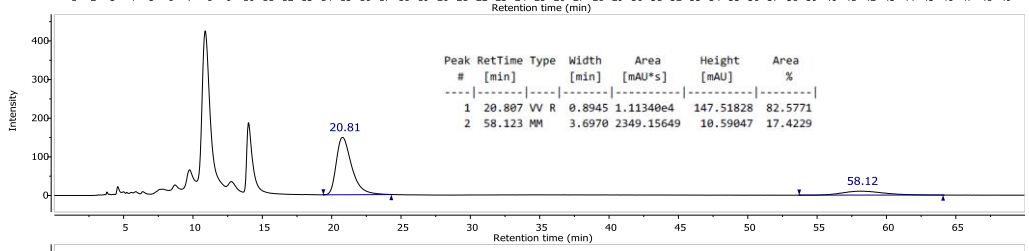


trans-**7b**

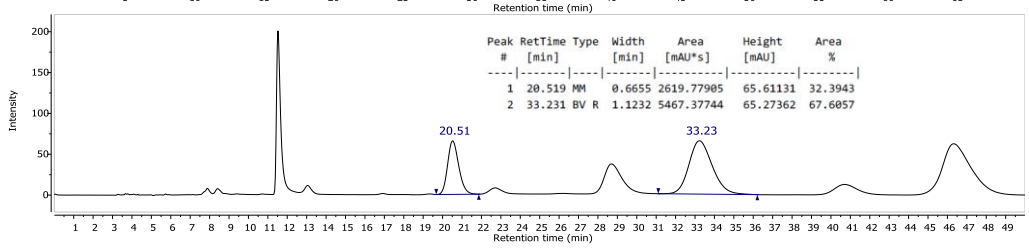


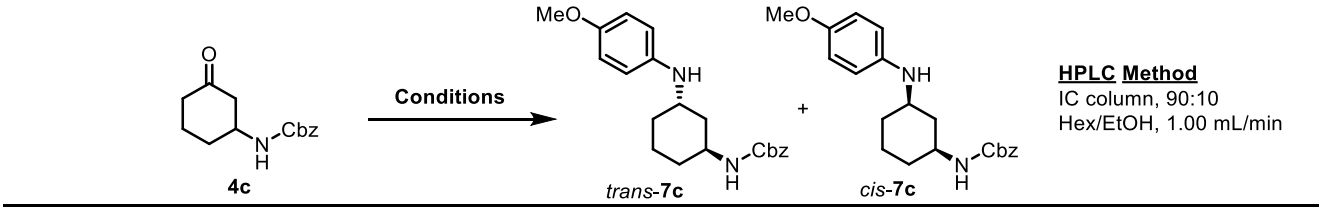
P32-Catalyzed Table 3, entry 4 (OD-H Method for *trans*-**7b**)



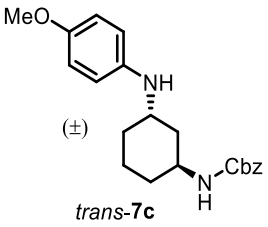


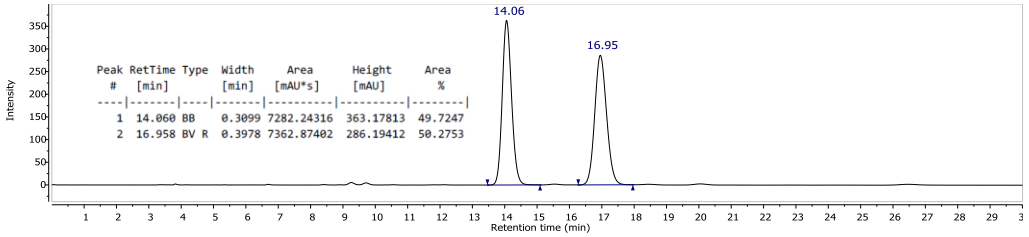
P32-Catalyzed Table 3, entry 4 (IC Method for *cis*-**7b**)

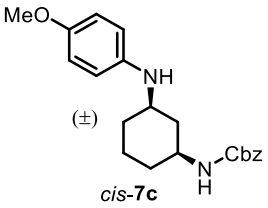


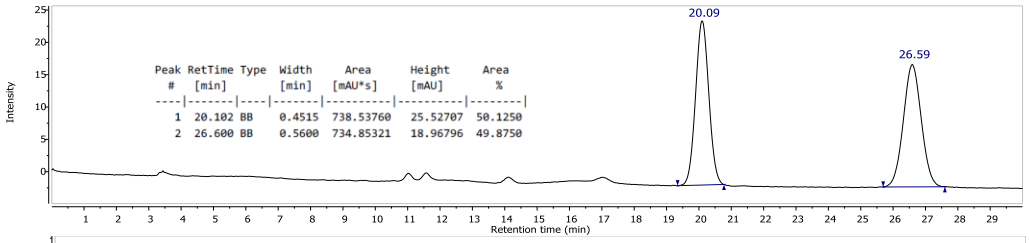


HPLC Method
IC column, 90:10
Hex/EtOH, 1.00 mL/min

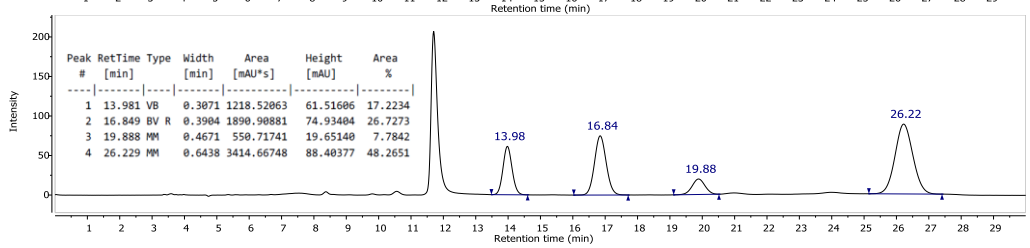


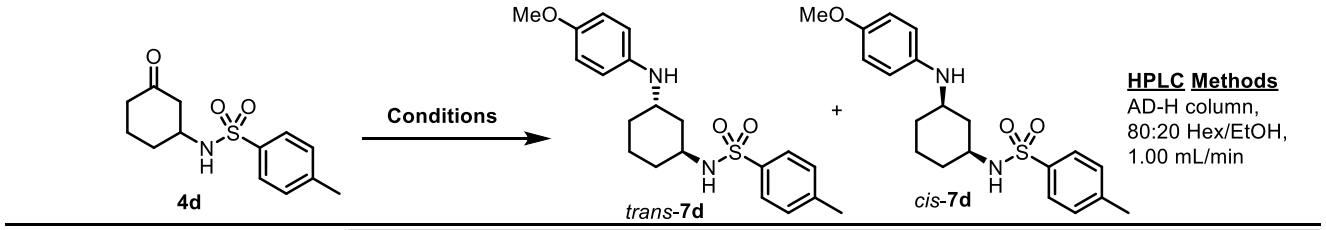


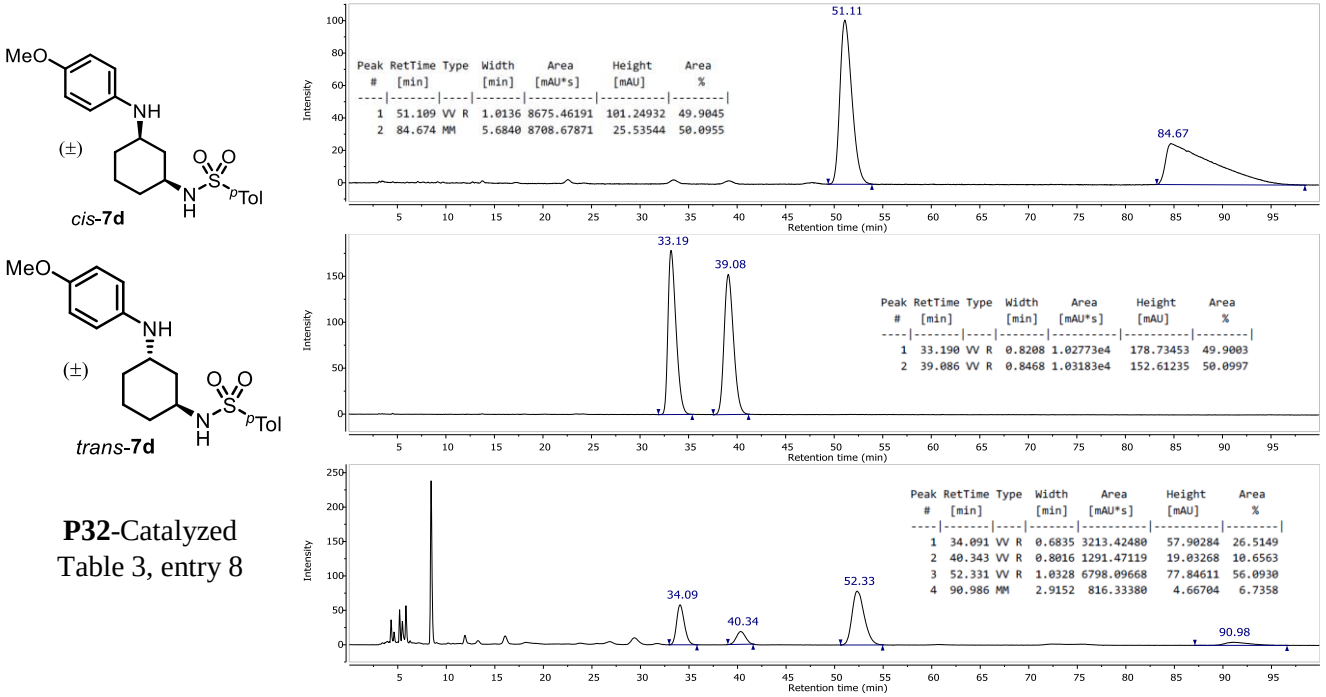




P32-Catalyzed
Table 3, entry 6



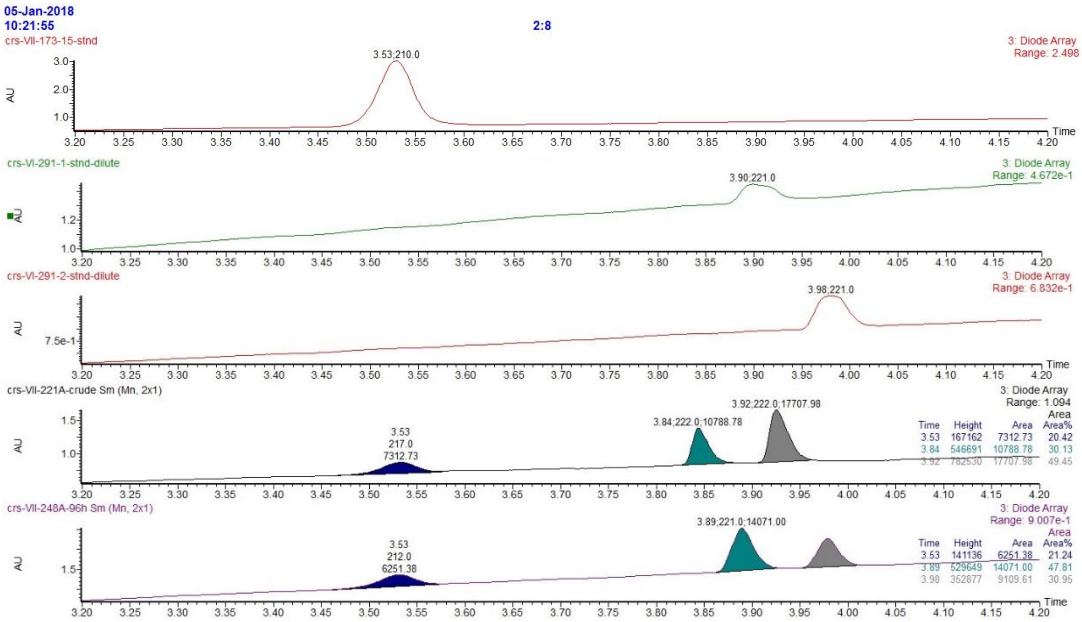




P32-Catalyzed
Table 3, entry 8

6. RRF Measurements by LC/MS

4a/7a:



4a

Cis-**7a**

Trans-**7a**

DPP-Catalyzed
Table 3, entry 1

P32-Catalyzed
Table 3, entry 2

An additional LC/MS method on a Waters ACQUITY column was used for a number of screens in Table 1. An average of the RRF values for *cis*-**7a** and *trans*-**7a** was utilized (2.54), as the two peaks co-eluted. However, during the preparation of this manuscript, the column reached the end of its suggested lifetime, and secondary amines were not tolerated anymore.

4b/7b:

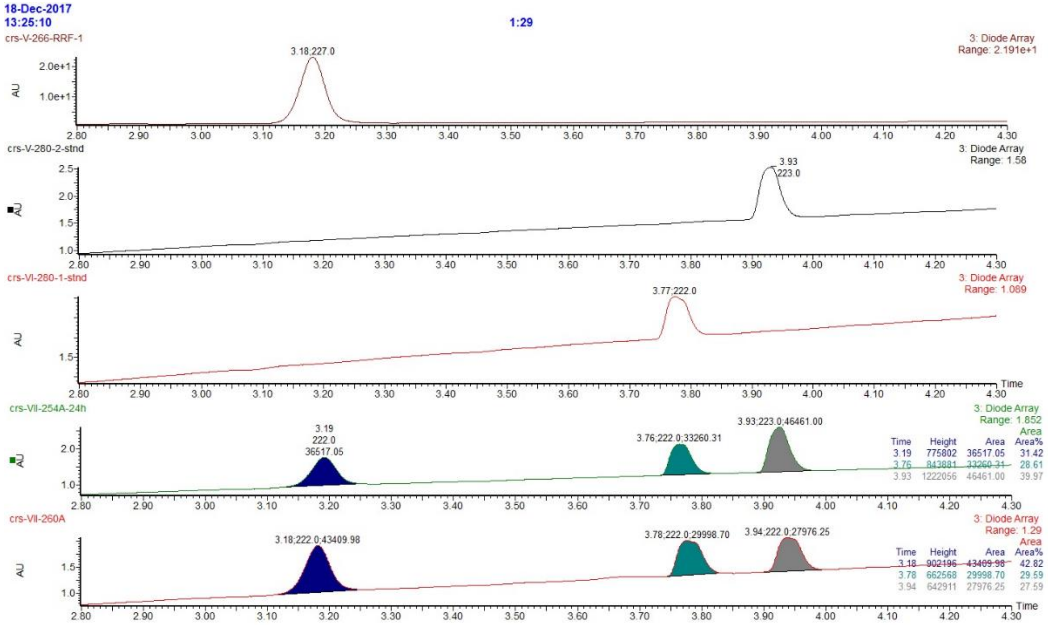
4b

Trans-**7b**

Cis-**7b**

DPP-Catalyzed
Table 3, entry 3

P32-Catalyzed
Table 3, entry 4



4c/7c:

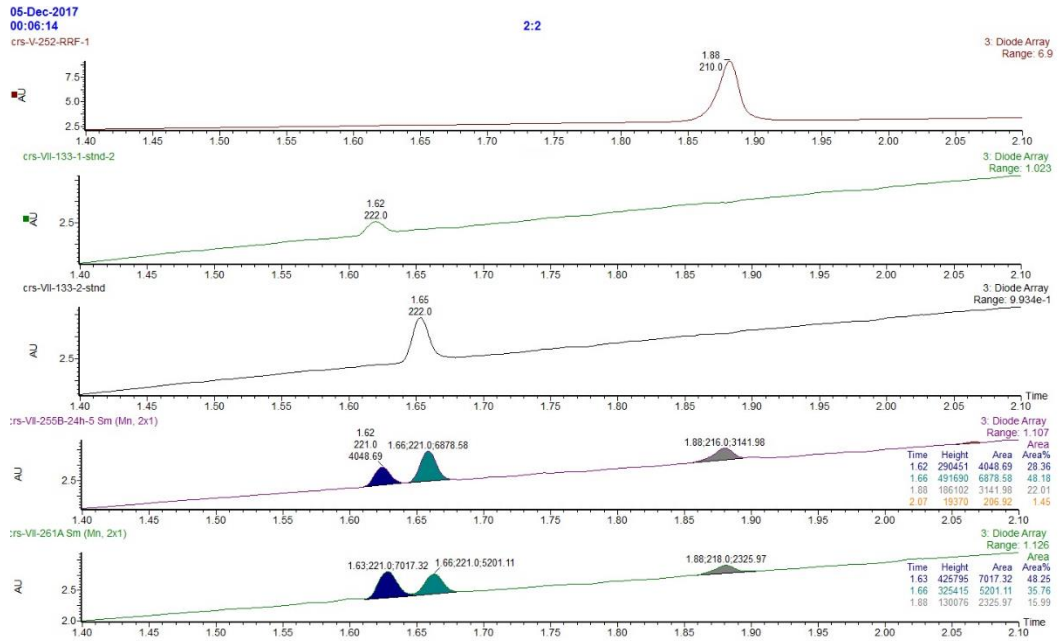
4c

Cis-**7c**

Trans-**7c**

DPP-Catalyzed
Table 3, entry 5

P32-Catalyzed
Table 3, entry 6



4d/7d:

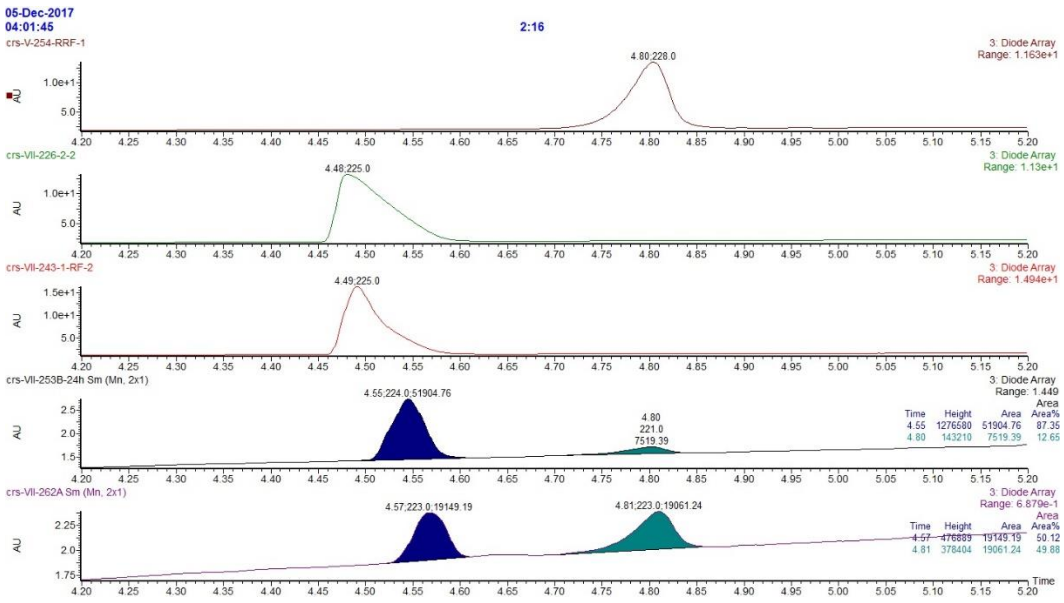
4d

Cis-**7d**

Trans-**7d**

DPP-Catalyzed
Table 3, entry 7

P32-Catalyzed
Table 3, entry 8



7. Crystallographic Data

7.1. (±)-*trans*-7d

Low-temperature diffraction data (ω-scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Dectris Pilatus3R detector with Mo Kα (λ = 0.71073 Å) for the structure of (±)-*trans*-**7d**. The diffraction images were processed and scaled using Rigaku Oxford Diffraction software.[1] The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL.[2] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups). The only exceptions are H1, H2, H3a, and H4 which were found in the difference map and semi-freely refined with the aid of N-H distance restraints set to a value of 0.88(2). The hydrogen atoms associated with C13 appeared to be disordered and were geometrically generated to reflect an equal occupancy, positional disorder. The CH_3 groups is rotated 60 degrees about the C-C bond. The atoms were then refined as riding atoms on C13. Several reflections were affected by detector artifacts and subsequently omitted from the least square refinement. The full numbering scheme of compound (±)-*trans*-**7d** can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC number 1818211 ((±)-*trans*-**7d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

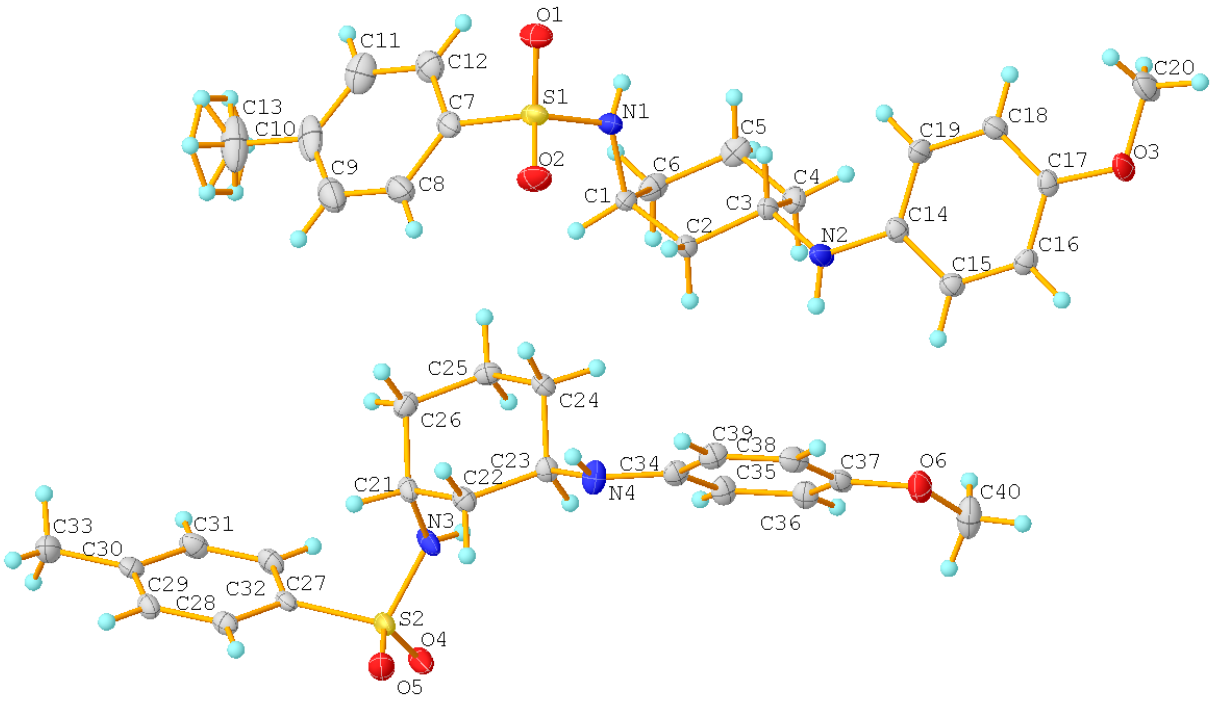


Figure S1. The complete numbering scheme of (±)-*trans*-**7d** with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S1. Crystal data and structure refinement for (±)-*trans*-7d.

Identification code	(±)-*trans*-**7d**	
Empirical formula	C20 H26 N2 O3 S	
Formula weight	374.49	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.0230(3) Å	α= 92.890(2)°.
	b = 10.6673(3) Å	β= 93.940(2)°.
	c = 19.6393(6) Å	γ = 110.439(3)°.
Volume	1956.73(11) $Å^3$	
Z	4	
Density (calculated)	1.271 Mg/m^3	
Absorption coefficient	0.187 mm^{-1}	
F(000)	800	
Crystal size	0.200 x 0.120 x 0.040 mm^3	
Crystal color and habit	Colorless Plate	
Diffractometer	Dectris Pilatus 3R	
Theta range for data collection	2.873 to 27.482°.	
Index ranges	-13<=h<=13, -13<=k<=13, -25<=l<=25	
Reflections collected	49939	
Independent reflections	8954 [R(int) = 0.1164]	
Observed reflections (I > 2sigma(I))	6970	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.46225	
Solution method	SHELXT-2014/5 (Sheldrick, 2014)	
Refinement method	SHELXL-2014/7 (Sheldrick, 2014)	
Data / restraints / parameters	8954 / 4 / 489	
Goodness-of-fit on F^2	1.031	
Final R indices [I>2sigma(I)]	R1 = 0.0510, wR2 = 0.1177	
R indices (all data)	R1 = 0.0710, wR2 = 0.1255	
Largest diff. peak and hole	0.417 and -0.446 e.$Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (±)-*trans*-7d. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	6202(1)	3655(1)	9621(1)	20(1)
O(1)	6055(2)	4114(1)	10304(1)	26(1)
O(2)	7554(2)	3585(2)	9461(1)	30(1)
O(3)	11164(2)	13307(1)	8480(1)	25(1)
N(1)	5810(2)	4649(2)	9122(1)	21(1)
N(2)	8784(2)	7721(2)	8046(1)	24(1)
C(1)	5887(2)	4456(2)	8374(1)	18(1)
C(2)	7314(2)	5416(2)	8174(1)	19(1)
C(3)	7397(2)	6873(2)	8243(1)	18(1)
C(4)	6139(2)	7030(2)	7818(1)	23(1)
C(5)	4705(2)	6112(2)	8029(1)	26(1)
C(6)	4612(2)	4648(2)	7982(1)	25(1)
C(7)	4920(2)	2025(2)	9444(1)	23(1)
C(8)	5323(3)	1002(2)	9156(1)	32(1)
C(9)	4328(3)	-282(2)	9047(1)	38(1)
C(10)	2942(3)	-584(2)	9212(1)	40(1)
C(11)	2544(3)	464(2)	9494(1)	38(1)
C(12)	3526(2)	1759(2)	9610(1)	29(1)
C(13)	1867(3)	-1997(2)	9100(2)	56(1)
C(14)	9292(2)	9119(2)	8157(1)	19(1)
C(15)	10441(2)	9878(2)	7806(1)	20(1)
C(16)	11035(2)	11254(2)	7929(1)	20(1)
C(17)	10495(2)	11929(2)	8404(1)	19(1)
C(18)	9356(2)	11202(2)	8753(1)	21(1)
C(19)	8755(2)	9801(2)	8628(1)	22(1)
C(20)	10686(3)	14014(2)	8989(1)	32(1)
S(2)	5907(1)	-1660(1)	5357(1)	19(1)
O(4)	5339(2)	-1457(1)	4693(1)	27(1)
O(5)	7357(2)	-1626(1)	5438(1)	26(1)
O(6)	11344(2)	8414(1)	6338(1)	27(1)
N(3)	5696(2)	-561(2)	5883(1)	22(1)
N(4)	9010(2)	3053(2)	6920(1)	24(1)

C(21)	6197(2)	-447(2)	6613(1)	19(1)
C(22)	7665(2)	668(2)	6777(1)	20(1)
C(23)	7584(2)	2066(2)	6715(1)	18(1)
C(24)	6455(2)	2254(2)	7154(1)	19(1)
C(25)	4982(2)	1152(2)	6996(1)	20(1)
C(26)	5088(2)	-238(2)	7054(1)	22(1)
C(27)	4814(2)	-3242(2)	5594(1)	16(1)
C(28)	5428(2)	-4151(2)	5819(1)	18(1)
C(29)	4552(2)	-5403(2)	5987(1)	21(1)
C(30)	3071(2)	-5764(2)	5937(1)	21(1)
C(31)	2477(2)	-4831(2)	5710(1)	24(1)
C(32)	3336(2)	-3579(2)	5542(1)	22(1)
C(33)	2119(3)	-7123(2)	6119(1)	31(1)
C(34)	9435(2)	4402(2)	6783(1)	20(1)
C(35)	8826(2)	4877(2)	6245(1)	22(1)
C(36)	9416(2)	6215(2)	6081(1)	22(1)
C(37)	10629(2)	7098(2)	6467(1)	21(1)
C(38)	11204(2)	6647(2)	7028(1)	24(1)
C(39)	10624(2)	5330(2)	7186(1)	23(1)
C(40)	10892(3)	8868(2)	5721(1)	38(1)

Table S3. Bond lengths [Å] and angles [°] for (±)-*trans*-7d.

S(1)-O(2)	1.4369(15)
S(1)-O(1)	1.4412(14)
S(1)-N(1)	1.6068(17)
S(1)-C(7)	1.765(2)
O(3)-C(17)	1.381(2)
O(3)-C(20)	1.428(2)
N(1)-C(1)	1.483(2)
N(1)-H(1)	0.855(16)
N(2)-C(14)	1.397(2)
N(2)-C(3)	1.460(3)
N(2)-H(2)	0.874(16)
C(1)-C(6)	1.527(3)
C(1)-C(2)	1.531(3)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.526(2)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.526(3)
C(3)-H(3)	1.0000
C(4)-C(5)	1.529(3)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.529(3)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(12)	1.391(3)
C(7)-C(8)	1.396(3)
C(8)-C(9)	1.380(3)
C(8)-H(8)	0.9500
C(9)-C(10)	1.378(4)
C(9)-H(9)	0.9500
C(10)-C(11)	1.412(4)
C(10)-C(13)	1.511(3)
C(11)-C(12)	1.385(3)
C(11)-H(11)	0.9500
C(12)-H(12)	0.9500
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(13)-H(13D)	0.9800
C(13)-H(13E)	0.9800
C(13)-H(13F)	0.9800
C(14)-C(19)	1.397(3)
C(14)-C(15)	1.403(3)
C(15)-C(16)	1.378(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.399(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.384(3)
C(18)-C(19)	1.404(3)
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
S(2)-O(5)	1.4383(15)
S(2)-O(4)	1.4437(14)
S(2)-N(3)	1.6028(16)
S(2)-C(27)	1.7679(19)
O(6)-C(37)	1.381(2)
O(6)-C(40)	1.430(3)
N(3)-C(21)	1.470(2)
N(3)-H(3A)	0.850(16)
N(4)-C(34)	1.397(2)
N(4)-C(23)	1.463(2)
N(4)-H(4)	0.853(16)
C(21)-C(26)	1.524(3)

C(21)-C(22)	1.536(3)	C(38)-C(39)	1.380(3)
C(21)-H(21)	1.0000	C(38)-H(38)	0.9500
C(22)-C(23)	1.532(2)	C(39)-H(39)	0.9500
C(22)-H(22A)	0.9900	C(40)-H(40A)	0.9800
C(22)-H(22B)	0.9900	C(40)-H(40B)	0.9800
C(23)-C(24)	1.530(3)	C(40)-H(40C)	0.9800
C(23)-H(23)	1.0000	O(2)-S(1)-O(1)	119.14(9)
C(24)-C(25)	1.532(3)	O(2)-S(1)-N(1)	108.20(9)
C(24)-H(24A)	0.9900	O(1)-S(1)-N(1)	105.98(8)
C(24)-H(24B)	0.9900	O(2)-S(1)-C(7)	106.89(10)
C(25)-C(26)	1.533(3)	O(1)-S(1)-C(7)	107.30(9)
C(25)-H(25A)	0.9900	N(1)-S(1)-C(7)	109.06(9)
C(25)-H(25B)	0.9900	C(17)-O(3)-C(20)	116.64(16)
C(26)-H(26A)	0.9900	C(1)-N(1)-S(1)	119.31(13)
C(26)-H(26B)	0.9900	C(1)-N(1)-H(1)	117.0(17)
C(27)-C(28)	1.392(2)	S(1)-N(1)-H(1)	114.3(17)
C(27)-C(32)	1.392(3)	C(14)-N(2)-C(3)	122.67(16)
C(28)-C(29)	1.388(3)	C(14)-N(2)-H(2)	115.9(16)
C(28)-H(28)	0.9500	C(3)-N(2)-H(2)	113.5(16)
C(29)-C(30)	1.392(3)	N(1)-C(1)-C(6)	110.07(16)
C(29)-H(29)	0.9500	N(1)-C(1)-C(2)	109.82(15)
C(30)-C(31)	1.403(3)	C(6)-C(1)-C(2)	111.93(16)
C(30)-C(33)	1.508(3)	N(1)-C(1)-H(1A)	108.3
C(31)-C(32)	1.383(3)	C(6)-C(1)-H(1A)	108.3
C(31)-H(31)	0.9500	C(2)-C(1)-H(1A)	108.3
C(32)-H(32)	0.9500	C(3)-C(2)-C(1)	111.74(16)
C(33)-H(33A)	0.9800	C(3)-C(2)-H(2A)	109.3
C(33)-H(33B)	0.9800	C(1)-C(2)-H(2A)	109.3
C(33)-H(33C)	0.9800	C(3)-C(2)-H(2B)	109.3
C(34)-C(35)	1.389(3)	C(1)-C(2)-H(2B)	109.3
C(34)-C(39)	1.411(3)	H(2A)-C(2)-H(2B)	107.9
C(35)-C(36)	1.404(3)	N(2)-C(3)-C(4)	113.11(16)
C(35)-H(35)	0.9500	N(2)-C(3)-C(2)	108.40(16)
C(36)-C(37)	1.393(3)	C(4)-C(3)-C(2)	110.15(15)
C(36)-H(36)	0.9500	N(2)-C(3)-H(3)	108.4
C(37)-C(38)	1.392(3)	C(4)-C(3)-H(3)	108.4

C(2)-C(3)-H(3)	108.4	C(7)-C(12)-H(12)	120.4
C(3)-C(4)-C(5)	111.78(16)	C(10)-C(13)-H(13A)	109.5
C(3)-C(4)-H(4A)	109.3	C(10)-C(13)-H(13B)	109.5
C(5)-C(4)-H(4A)	109.3	H(13A)-C(13)-H(13B)	109.5
C(3)-C(4)-H(4B)	109.3	C(10)-C(13)-H(13C)	109.5
C(5)-C(4)-H(4B)	109.3	H(13A)-C(13)-H(13C)	109.5
H(4A)-C(4)-H(4B)	107.9	H(13B)-C(13)-H(13C)	109.5
C(6)-C(5)-C(4)	110.77(17)	C(10)-C(13)-H(13D)	109.5
C(6)-C(5)-H(5A)	109.5	H(13A)-C(13)-H(13D)	141.1
C(4)-C(5)-H(5A)	109.5	H(13B)-C(13)-H(13D)	56.3
C(6)-C(5)-H(5B)	109.5	H(13C)-C(13)-H(13D)	56.3
C(4)-C(5)-H(5B)	109.5	C(10)-C(13)-H(13E)	109.5
H(5A)-C(5)-H(5B)	108.1	H(13A)-C(13)-H(13E)	56.3
C(1)-C(6)-C(5)	112.48(15)	H(13B)-C(13)-H(13E)	141.1
C(1)-C(6)-H(6A)	109.1	H(13C)-C(13)-H(13E)	56.3
C(5)-C(6)-H(6A)	109.1	H(13D)-C(13)-H(13E)	109.5
C(1)-C(6)-H(6B)	109.1	C(10)-C(13)-H(13F)	109.5
C(5)-C(6)-H(6B)	109.1	H(13A)-C(13)-H(13F)	56.3
H(6A)-C(6)-H(6B)	107.8	H(13B)-C(13)-H(13F)	56.3
C(12)-C(7)-C(8)	120.5(2)	H(13C)-C(13)-H(13F)	141.1
C(12)-C(7)-S(1)	119.79(15)	H(13D)-C(13)-H(13F)	109.5
C(8)-C(7)-S(1)	119.70(18)	H(13E)-C(13)-H(13F)	109.5
C(9)-C(8)-C(7)	119.3(2)	N(2)-C(14)-C(19)	122.93(18)
C(9)-C(8)-H(8)	120.4	N(2)-C(14)-C(15)	119.03(17)
C(7)-C(8)-H(8)	120.4	C(19)-C(14)-C(15)	117.97(17)
C(10)-C(9)-C(8)	121.7(2)	C(16)-C(15)-C(14)	121.15(18)
C(10)-C(9)-H(9)	119.1	C(16)-C(15)-H(15)	119.4
C(8)-C(9)-H(9)	119.1	C(14)-C(15)-H(15)	119.4
C(9)-C(10)-C(11)	118.4(2)	C(15)-C(16)-C(17)	120.55(18)
C(9)-C(10)-C(13)	121.3(2)	C(15)-C(16)-H(16)	119.7
C(11)-C(10)-C(13)	120.3(3)	C(17)-C(16)-H(16)	119.7
C(12)-C(11)-C(10)	120.9(2)	O(3)-C(17)-C(18)	125.16(17)
C(12)-C(11)-H(11)	119.6	O(3)-C(17)-C(16)	115.50(17)
C(10)-C(11)-H(11)	119.6	C(18)-C(17)-C(16)	119.34(17)
C(11)-C(12)-C(7)	119.3(2)	C(17)-C(18)-C(19)	120.06(18)
C(11)-C(12)-H(12)	120.4	C(17)-C(18)-H(18)	120.0

C(19)-C(18)-H(18)	120.0	N(4)-C(23)-C(22)	107.70(15)
C(14)-C(19)-C(18)	120.93(18)	C(24)-C(23)-C(22)	110.30(16)
C(14)-C(19)-H(19)	119.5	N(4)-C(23)-H(23)	108.8
C(18)-C(19)-H(19)	119.5	C(24)-C(23)-H(23)	108.8
O(3)-C(20)-H(20A)	109.5	C(22)-C(23)-H(23)	108.8
O(3)-C(20)-H(20B)	109.5	C(23)-C(24)-C(25)	113.24(15)
H(20A)-C(20)-H(20B)	109.5	C(23)-C(24)-H(24A)	108.9
O(3)-C(20)-H(20C)	109.5	C(25)-C(24)-H(24A)	108.9
H(20A)-C(20)-H(20C)	109.5	C(23)-C(24)-H(24B)	108.9
H(20B)-C(20)-H(20C)	109.5	C(25)-C(24)-H(24B)	108.9
O(5)-S(2)-O(4)	118.54(9)	H(24A)-C(24)-H(24B)	107.7
O(5)-S(2)-N(3)	110.46(9)	C(24)-C(25)-C(26)	110.64(16)
O(4)-S(2)-N(3)	105.99(8)	C(24)-C(25)-H(25A)	109.5
O(5)-S(2)-C(27)	106.70(8)	C(26)-C(25)-H(25A)	109.5
O(4)-S(2)-C(27)	108.21(9)	C(24)-C(25)-H(25B)	109.5
N(3)-S(2)-C(27)	106.32(9)	C(26)-C(25)-H(25B)	109.5
C(37)-O(6)-C(40)	117.35(16)	H(25A)-C(25)-H(25B)	108.1
C(21)-N(3)-S(2)	121.03(13)	C(21)-C(26)-C(25)	111.85(16)
C(21)-N(3)-H(3A)	125.7(17)	C(21)-C(26)-H(26A)	109.2
S(2)-N(3)-H(3A)	113.2(17)	C(25)-C(26)-H(26A)	109.2
C(34)-N(4)-C(23)	123.94(16)	C(21)-C(26)-H(26B)	109.2
C(34)-N(4)-H(4)	113.1(15)	C(25)-C(26)-H(26B)	109.2
C(23)-N(4)-H(4)	113.2(16)	H(26A)-C(26)-H(26B)	107.9
N(3)-C(21)-C(26)	110.27(16)	C(28)-C(27)-C(32)	120.42(18)
N(3)-C(21)-C(22)	111.64(16)	C(28)-C(27)-S(2)	120.10(15)
C(26)-C(21)-C(22)	111.58(15)	C(32)-C(27)-S(2)	119.48(14)
N(3)-C(21)-H(21)	107.7	C(29)-C(28)-C(27)	119.37(18)
C(26)-C(21)-H(21)	107.7	C(29)-C(28)-H(28)	120.3
C(22)-C(21)-H(21)	107.7	C(27)-C(28)-H(28)	120.3
C(23)-C(22)-C(21)	111.98(15)	C(28)-C(29)-C(30)	121.24(18)
C(23)-C(22)-H(22A)	109.2	C(28)-C(29)-H(29)	119.4
C(21)-C(22)-H(22A)	109.2	C(30)-C(29)-H(29)	119.4
C(23)-C(22)-H(22B)	109.2	C(29)-C(30)-C(31)	118.37(18)
C(21)-C(22)-H(22B)	109.2	C(29)-C(30)-C(33)	121.30(18)
H(22A)-C(22)-H(22B)	107.9	C(31)-C(30)-C(33)	120.33(19)
N(4)-C(23)-C(24)	112.26(15)	C(32)-C(31)-C(30)	121.05(19)

C(32)-C(31)-H(31)	119.5	C(37)-C(36)-H(36)	120.0
C(30)-C(31)-H(31)	119.5	C(35)-C(36)-H(36)	120.0
C(31)-C(32)-C(27)	119.54(18)	O(6)-C(37)-C(38)	115.66(17)
C(31)-C(32)-H(32)	120.2	O(6)-C(37)-C(36)	125.35(18)
C(27)-C(32)-H(32)	120.2	C(38)-C(37)-C(36)	118.99(18)
C(30)-C(33)-H(33A)	109.5	C(39)-C(38)-C(37)	120.85(18)
C(30)-C(33)-H(33B)	109.5	C(39)-C(38)-H(38)	119.6
H(33A)-C(33)-H(33B)	109.5	C(37)-C(38)-H(38)	119.6
C(30)-C(33)-H(33C)	109.5	C(38)-C(39)-C(34)	121.07(19)
H(33A)-C(33)-H(33C)	109.5	C(38)-C(39)-H(39)	119.5
H(33B)-C(33)-H(33C)	109.5	C(34)-C(39)-H(39)	119.5
C(35)-C(34)-N(4)	124.09(17)	O(6)-C(40)-H(40A)	109.5
C(35)-C(34)-C(39)	117.63(18)	O(6)-C(40)-H(40B)	109.5
N(4)-C(34)-C(39)	118.11(18)	H(40A)-C(40)-H(40B)	109.5
C(34)-C(35)-C(36)	121.37(18)	O(6)-C(40)-H(40C)	109.5
C(34)-C(35)-H(35)	119.3	H(40A)-C(40)-H(40C)	109.5
C(36)-C(35)-H(35)	119.3	H(40B)-C(40)-H(40C)	109.5
C(37)-C(36)-C(35)	119.95(18)		

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (±)-*trans*-7d. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	23(1)	25(1)	18(1)	2(1)	5(1)	14(1)
O(1)	29(1)	34(1)	18(1)	0(1)	2(1)	17(1)
O(2)	26(1)	41(1)	32(1)	6(1)	10(1)	22(1)
O(3)	21(1)	13(1)	39(1)	0(1)	10(1)	2(1)
N(1)	26(1)	20(1)	20(1)	3(1)	8(1)	12(1)
N(2)	23(1)	15(1)	30(1)	-3(1)	12(1)	2(1)
C(1)	23(1)	14(1)	17(1)	0(1)	5(1)	4(1)
C(2)	20(1)	14(1)	21(1)	1(1)	6(1)	5(1)
C(3)	18(1)	14(1)	21(1)	2(1)	5(1)	4(1)
C(4)	28(1)	21(1)	21(1)	5(1)	3(1)	10(1)
C(5)	20(1)	33(1)	25(1)	7(1)	0(1)	10(1)
C(6)	18(1)	27(1)	22(1)	0(1)	1(1)	-2(1)
C(7)	34(1)	22(1)	18(1)	5(1)	2(1)	14(1)
C(8)	48(2)	29(1)	28(1)	5(1)	10(1)	22(1)
C(9)	60(2)	26(1)	32(1)	3(1)	2(1)	19(1)
C(10)	61(2)	24(1)	29(1)	10(1)	-16(1)	10(1)
C(11)	32(1)	37(1)	41(1)	12(1)	-6(1)	7(1)
C(12)	31(1)	29(1)	31(1)	7(1)	1(1)	15(1)
C(13)	68(2)	29(1)	55(2)	12(1)	-25(1)	4(1)
C(14)	17(1)	16(1)	23(1)	0(1)	1(1)	4(1)
C(15)	17(1)	20(1)	22(1)	0(1)	3(1)	6(1)
C(16)	14(1)	20(1)	23(1)	5(1)	4(1)	3(1)
C(17)	15(1)	14(1)	25(1)	2(1)	1(1)	3(1)
C(18)	19(1)	18(1)	26(1)	-2(1)	5(1)	6(1)
C(19)	18(1)	18(1)	26(1)	1(1)	8(1)	2(1)
C(20)	30(1)	18(1)	45(1)	-5(1)	10(1)	4(1)
S(2)	27(1)	15(1)	17(1)	2(1)	3(1)	11(1)
O(4)	49(1)	22(1)	16(1)	2(1)	3(1)	18(1)
O(5)	24(1)	23(1)	33(1)	5(1)	9(1)	9(1)
O(6)	24(1)	18(1)	38(1)	4(1)	5(1)	4(1)
N(3)	38(1)	17(1)	17(1)	-1(1)	-4(1)	17(1)

N(4)	18(1)	21(1)	31(1)	7(1)	-4(1)	4(1)
C(21)	28(1)	14(1)	16(1)	2(1)	0(1)	9(1)
C(22)	20(1)	19(1)	22(1)	2(1)	1(1)	10(1)
C(23)	16(1)	17(1)	22(1)	2(1)	1(1)	5(1)
C(24)	21(1)	17(1)	20(1)	-2(1)	1(1)	8(1)
C(25)	17(1)	25(1)	19(1)	2(1)	4(1)	8(1)
C(26)	22(1)	20(1)	20(1)	3(1)	4(1)	4(1)
C(27)	24(1)	14(1)	13(1)	-1(1)	1(1)	10(1)
C(28)	21(1)	20(1)	17(1)	0(1)	-1(1)	11(1)
C(29)	30(1)	18(1)	19(1)	2(1)	2(1)	12(1)
C(30)	28(1)	18(1)	19(1)	-2(1)	5(1)	9(1)
C(31)	20(1)	25(1)	30(1)	-2(1)	4(1)	10(1)
C(32)	25(1)	22(1)	24(1)	0(1)	0(1)	15(1)
C(33)	35(1)	22(1)	37(1)	4(1)	14(1)	9(1)
C(34)	14(1)	20(1)	26(1)	3(1)	5(1)	5(1)
C(35)	15(1)	20(1)	29(1)	2(1)	0(1)	3(1)
C(36)	18(1)	22(1)	28(1)	4(1)	3(1)	9(1)
C(37)	18(1)	16(1)	30(1)	1(1)	9(1)	6(1)
C(38)	17(1)	24(1)	26(1)	-5(1)	2(1)	2(1)
C(39)	18(1)	27(1)	22(1)	2(1)	2(1)	6(1)
C(40)	30(1)	25(1)	57(2)	15(1)	3(1)	7(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (±)-*trans*-7d.

	x	y	z	U(eq)
H(1)	5150(20)	4910(20)	9249(12)	34(7)
H(2)	9040(20)	7400(20)	7680(9)	27(6)
H(1A)	5839	3515	8264	22
H(2A)	8106	5320	8471	23
H(2B)	7432	5172	7695	23
H(3)	7337	7122	8734	21
H(4A)	6203	6816	7328	27
H(4B)	6194	7974	7877	27
H(5A)	4593	6386	8505	31
H(5B)	3917	6203	7727	31
H(6A)	3721	4090	8166	30
H(6B)	4565	4335	7494	30
H(8)	6272	1189	9036	39
H(9)	4606	-977	8853	46
H(11)	1589	278	9605	45
H(12)	3251	2458	9801	35
H(13A)	947	-2013	9247	67
H(13B)	1748	-2301	8613	67
H(13C)	2209	-2594	9368	67
H(13D)	2322	-2593	8905	67
H(13E)	1521	-2305	9539	67
H(13F)	1060	-2012	8785	67
H(15)	10816	9437	7479	24
H(16)	11817	11747	7689	23
H(18)	8981	11652	9076	25
H(19)	7971	9310	8869	26
H(20A)	9675	13875	8872	48
H(20B)	11253	14974	9007	48
H(20C)	10801	13677	9436	48
H(3A)	5240(30)	-110(20)	5699(12)	36(7)

H(4)	9370(20)	2930(20)	7308(9)	25(6)
H(21)	6303	-1316	6719	23
H(22A)	8043	609	7249	23
H(22B)	8337	534	6460	23
H(23)	7311	2157	6226	22
H(24A)	6368	3134	7078	23
H(24B)	6778	2269	7643	23
H(25A)	4589	1212	6527	24
H(25B)	4320	1283	7321	24
H(26A)	5348	-341	7538	26
H(26B)	4143	-935	6910	26
H(28)	6437	-3918	5857	22
H(29)	4971	-6025	6138	25
H(31)	1468	-5063	5670	29
H(32)	2920	-2953	5394	27
H(33A)	1590	-7659	5702	47
H(33B)	1442	-7011	6433	47
H(33C)	2705	-7581	6341	47
H(35)	7994	4285	5981	27
H(36)	8987	6517	5708	27
H(38)	12005	7253	7306	28
H(39)	11033	5044	7571	27
H(40A)	10908	8269	5329	56
H(40B)	11539	9781	5666	56
H(40C)	9917	8866	5746	56

Table S6. Torsion angles [°] for (±)-*trans*-7d.

O(2)-S(1)-N(1)-C(1)	50.04(17)
O(1)-S(1)-N(1)-C(1)	178.89(14)
C(7)-S(1)-N(1)-C(1)	-65.89(17)
S(1)-N(1)-C(1)-C(6)	138.66(15)
S(1)-N(1)-C(1)-C(2)	-97.67(17)
N(1)-C(1)-C(2)-C(3)	-69.0(2)
C(6)-C(1)-C(2)-C(3)	53.5(2)
C(14)-N(2)-C(3)-C(4)	68.3(2)
C(14)-N(2)-C(3)-C(2)	-169.28(17)
C(1)-C(2)-C(3)-N(2)	179.79(15)
C(1)-C(2)-C(3)-C(4)	-56.0(2)
N(2)-C(3)-C(4)-C(5)	179.05(16)
C(2)-C(3)-C(4)-C(5)	57.6(2)
C(3)-C(4)-C(5)-C(6)	-56.0(2)
N(1)-C(1)-C(6)-C(5)	70.4(2)
C(2)-C(1)-C(6)-C(5)	-52.0(2)
C(4)-C(5)-C(6)-C(1)	52.9(2)
O(2)-S(1)-C(7)-C(12)	174.13(16)
O(1)-S(1)-C(7)-C(12)	45.26(18)
N(1)-S(1)-C(7)-C(12)	-69.11(18)
O(2)-S(1)-C(7)-C(8)	-4.14(19)
O(1)-S(1)-C(7)-C(8)	-133.01(16)
N(1)-S(1)-C(7)-C(8)	112.62(17)
C(12)-C(7)-C(8)-C(9)	-1.0(3)
S(1)-C(7)-C(8)-C(9)	177.21(17)
C(7)-C(8)-C(9)-C(10)	0.3(3)
C(8)-C(9)-C(10)-C(11)	0.6(3)
C(8)-C(9)-C(10)-C(13)	-179.1(2)
C(9)-C(10)-C(11)-C(12)	-0.9(3)
C(13)-C(10)-C(11)-C(12)	178.8(2)
C(10)-C(11)-C(12)-C(7)	0.2(3)
C(8)-C(7)-C(12)-C(11)	0.8(3)
S(1)-C(7)-C(12)-C(11)	-177.50(16)
C(3)-N(2)-C(14)-C(19)	19.2(3)

C(3)-N(2)-C(14)-C(15)	-164.00(18)
N(2)-C(14)-C(15)-C(16)	-176.13(18)
C(19)-C(14)-C(15)-C(16)	0.8(3)
C(14)-C(15)-C(16)-C(17)	-0.5(3)
C(20)-O(3)-C(17)-C(18)	3.9(3)
C(20)-O(3)-C(17)-C(16)	-176.73(18)
C(15)-C(16)-C(17)-O(3)	-179.38(17)
C(15)-C(16)-C(17)-C(18)	0.0(3)
O(3)-C(17)-C(18)-C(19)	179.48(18)
C(16)-C(17)-C(18)-C(19)	0.1(3)
N(2)-C(14)-C(19)-C(18)	176.16(19)
C(15)-C(14)-C(19)-C(18)	-0.6(3)
C(17)-C(18)-C(19)-C(14)	0.2(3)
O(5)-S(2)-N(3)-C(21)	-48.60(18)
O(4)-S(2)-N(3)-C(21)	-178.20(15)
C(27)-S(2)-N(3)-C(21)	66.80(18)
S(2)-N(3)-C(21)-C(26)	-137.90(15)
S(2)-N(3)-C(21)-C(22)	97.46(17)
N(3)-C(21)-C(22)-C(23)	68.9(2)
C(26)-C(21)-C(22)-C(23)	-55.0(2)
C(34)-N(4)-C(23)-C(24)	-73.7(2)
C(34)-N(4)-C(23)-C(22)	164.71(18)
C(21)-C(22)-C(23)-N(4)	176.77(16)
C(21)-C(22)-C(23)-C(24)	53.9(2)
N(4)-C(23)-C(24)-C(25)	-174.41(16)
C(22)-C(23)-C(24)-C(25)	-54.3(2)
C(23)-C(24)-C(25)-C(26)	54.3(2)
N(3)-C(21)-C(26)-C(25)	-69.90(19)
C(22)-C(21)-C(26)-C(25)	54.8(2)
C(24)-C(25)-C(26)-C(21)	-53.9(2)
O(5)-S(2)-C(27)-C(28)	1.20(17)
O(4)-S(2)-C(27)-C(28)	129.80(15)
N(3)-S(2)-C(27)-C(28)	-116.72(15)
O(5)-S(2)-C(27)-C(32)	-177.69(14)
O(4)-S(2)-C(27)-C(32)	-49.09(17)
N(3)-S(2)-C(27)-C(32)	64.40(16)

C(32)-C(27)-C(28)-C(29)	0.5(3)
S(2)-C(27)-C(28)-C(29)	-178.37(13)
C(27)-C(28)-C(29)-C(30)	-0.3(3)
C(28)-C(29)-C(30)-C(31)	0.2(3)
C(28)-C(29)-C(30)-C(33)	-179.97(17)
C(29)-C(30)-C(31)-C(32)	-0.4(3)
C(33)-C(30)-C(31)-C(32)	179.79(18)
C(30)-C(31)-C(32)-C(27)	0.6(3)
C(28)-C(27)-C(32)-C(31)	-0.7(3)
S(2)-C(27)-C(32)-C(31)	178.20(15)
C(23)-N(4)-C(34)-C(35)	-25.3(3)
C(23)-N(4)-C(34)-C(39)	159.48(19)
N(4)-C(34)-C(35)-C(36)	-171.84(19)
C(39)-C(34)-C(35)-C(36)	3.4(3)
C(34)-C(35)-C(36)-C(37)	-0.5(3)
C(40)-O(6)-C(37)-C(38)	172.80(19)
C(40)-O(6)-C(37)-C(36)	-6.7(3)
C(35)-C(36)-C(37)-O(6)	176.81(18)
C(35)-C(36)-C(37)-C(38)	-2.6(3)
O(6)-C(37)-C(38)-C(39)	-176.63(18)
C(36)-C(37)-C(38)-C(39)	2.9(3)
C(37)-C(38)-C(39)-C(34)	0.1(3)
C(35)-C(34)-C(39)-C(38)	-3.1(3)
N(4)-C(34)-C(39)-C(38)	172.36(19)

Table S7. Hydrogen bonds for (±)-*trans*-7d [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...O(1)#1	0.855(16)	2.055(17)	2.892(2)	166(2)
N(3)-H(3A)...O(4)#2	0.850(16)	2.111(17)	2.938(2)	164(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+2 #2 -x+1,-y,-z+1

7.2. (±)-*cis*-7d

Low-temperature diffraction data (ω-scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Dectris Pilatus3R detector with Mo Kα (λ = 0.71073 Å) for the structure of (±)-*cis*-**7d**. The diffraction images were processed and scaled using Rigaku Oxford Diffraction software.[1] The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL.[2] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups). The only exceptions are H1 and H2, which were found in the difference map and freely refined (see Table 7). The full numbering scheme of compound (±)-*cis*-**7d** can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC number 1818210 ((±)-*cis*-**7d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

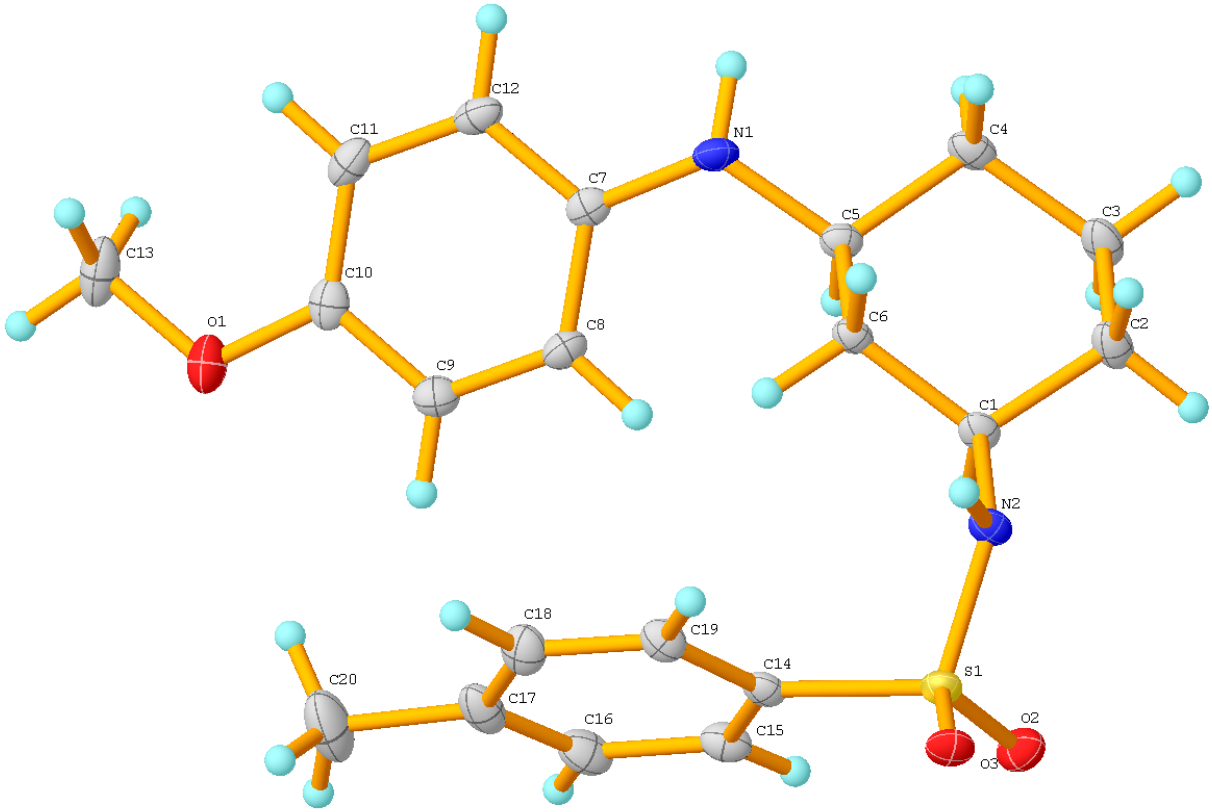


Figure S2. The complete numbering scheme of (±)-*cis*-7d with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S8. Crystal data and structure refinement for (±)-*cis*-7d.

Identification code	(±)-*cis*-**7d**	
Empirical formula	C20 H26 N2 O3 S	
Formula weight	374.49	
Temperature	93(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.7341(3) Å	α= 108.030(4)°.
	b = 10.0802(5) Å	β= 96.352(3)°.
	c = 10.7645(4) Å	γ = 102.318(3)°.
Volume	963.33(7) $Å^3$	
Z	2	
Density (calculated)	1.291 Mg/m^3	
Absorption coefficient	0.190 mm^{-1}	
F(000)	400	
Crystal size	0.200 x 0.100 x 0.040 mm^3	
Crystal color and habit	Colorless Plate	
Diffractometer	Dectris Pilatus 3R	
Theta range for data collection	3.134 to 27.483°.	
Index ranges	-12<=h<=12, -13<=k<=13, -13<=l<=13	
Reflections collected	22946	
Independent reflections	4400 [R(int) = 0.0271]	
Observed reflections (I > 2sigma(I))	3841	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.57899	
Solution method	SHELXT-2014/5 (Sheldrick, 2014)	
Refinement method	SHELXL-2014/7 (Sheldrick, 2014)	
Data / restraints / parameters	4400 / 0 / 245	
Goodness-of-fit on F^2	1.029	
Final R indices [I>2sigma(I)]	R1 = 0.0334, wR2 = 0.0854	
R indices (all data)	R1 = 0.0400, wR2 = 0.0886	
Largest diff. peak and hole	0.381 and -0.391 $e.Å^{-3}$	

Table S9. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (±)-*cis*-7d. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	9852(1)	6086(1)	8444(1)	15(1)
O(1)	2113(1)	711(1)	2854(1)	25(1)
O(2)	10313(1)	7264(1)	7977(1)	22(1)
O(3)	10934(1)	5614(1)	9108(1)	18(1)
N(1)	3553(1)	4891(1)	7967(1)	18(1)
N(2)	8830(1)	6525(1)	9509(1)	16(1)
C(1)	7512(1)	6920(1)	9083(1)	15(1)
C(2)	7379(1)	8272(1)	10156(1)	21(1)
C(3)	6005(1)	8675(1)	9760(1)	22(1)
C(4)	4666(1)	7414(1)	9413(1)	20(1)
C(5)	4837(1)	6094(1)	8324(1)	16(1)
C(6)	6176(1)	5676(1)	8798(1)	15(1)
C(7)	3193(1)	3842(1)	6686(1)	16(1)
C(8)	4172(1)	3662(1)	5822(1)	18(1)
C(9)	3765(1)	2602(1)	4567(1)	19(1)
C(10)	2380(1)	1708(1)	4126(1)	20(1)
C(11)	1392(1)	1863(1)	4968(1)	21(1)
C(12)	1809(1)	2914(1)	6234(1)	19(1)
C(13)	662(2)	-119(2)	2307(2)	30(1)
C(14)	8832(1)	4582(1)	7062(1)	16(1)
C(15)	8582(1)	4709(2)	5811(1)	20(1)
C(16)	7867(2)	3480(2)	4722(1)	24(1)
C(17)	7389(2)	2142(2)	4867(1)	24(1)
C(18)	7596(1)	2058(1)	6149(1)	23(1)
C(19)	8319(1)	3262(1)	7242(1)	19(1)
C(20)	6676(2)	795(2)	3675(2)	39(1)

Table S10. Bond lengths [Å] and angles [°] for (±)-*cis*-7d.

S(1)-O(2)	1.4338(9)
S(1)-O(3)	1.4507(9)
S(1)-N(2)	1.6210(10)
S(1)-C(14)	1.7696(13)
O(1)-C(10)	1.3820(16)
O(1)-C(13)	1.4317(17)
N(1)-C(7)	1.4048(17)
N(1)-C(5)	1.4633(16)
N(1)-H(1)	0.898(17)
N(2)-C(1)	1.4882(15)
N(2)-H(2)	0.869(16)
C(1)-C(6)	1.5280(17)
C(1)-C(2)	1.5301(17)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.5325(17)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.5319(19)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.5313(17)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.5349(16)
C(5)-H(5)	1.0000
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(12)	1.4008(18)
C(7)-C(8)	1.4042(17)
C(8)-C(9)	1.3896(18)
C(8)-H(8)	0.9500
C(9)-C(10)	1.3897(18)
C(9)-H(9)	0.9500
C(10)-C(11)	1.3927(19)
C(11)-C(12)	1.3943(19)
C(11)-H(11)	0.9500
C(12)-H(12)	0.9500
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-C(15)	1.3918(17)
C(14)-C(19)	1.3985(17)
C(15)-C(16)	1.3948(19)
C(15)-H(15)	0.9500
C(16)-C(17)	1.393(2)
C(16)-H(16)	0.9500
C(17)-C(18)	1.403(2)
C(17)-C(20)	1.515(2)
C(18)-C(19)	1.3857(19)
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
O(2)-S(1)-O(3)	118.32(5)
O(2)-S(1)-N(2)	108.86(6)
O(3)-S(1)-N(2)	105.39(5)
O(2)-S(1)-C(14)	107.72(6)
O(3)-S(1)-C(14)	107.70(5)
N(2)-S(1)-C(14)	108.53(6)
C(10)-O(1)-C(13)	116.92(11)
C(7)-N(1)-C(5)	120.04(10)
C(7)-N(1)-H(1)	112.8(11)
C(5)-N(1)-H(1)	113.2(11)
C(1)-N(2)-S(1)	118.91(8)
C(1)-N(2)-H(2)	115.6(11)
S(1)-N(2)-H(2)	111.9(10)

N(2)-C(1)-C(6)	111.34(9)	C(12)-C(7)-C(8)	117.48(12)
N(2)-C(1)-C(2)	109.77(10)	C(12)-C(7)-N(1)	119.71(11)
C(6)-C(1)-C(2)	110.33(10)	C(8)-C(7)-N(1)	122.81(11)
N(2)-C(1)-H(1A)	108.4	C(9)-C(8)-C(7)	120.57(11)
C(6)-C(1)-H(1A)	108.4	C(9)-C(8)-H(8)	119.7
C(2)-C(1)-H(1A)	108.4	C(7)-C(8)-H(8)	119.7
C(1)-C(2)-C(3)	110.83(10)	C(8)-C(9)-C(10)	121.19(12)
C(1)-C(2)-H(2A)	109.5	C(8)-C(9)-H(9)	119.4
C(3)-C(2)-H(2A)	109.5	C(10)-C(9)-H(9)	119.4
C(1)-C(2)-H(2B)	109.5	O(1)-C(10)-C(9)	115.28(12)
C(3)-C(2)-H(2B)	109.5	O(1)-C(10)-C(11)	125.52(12)
H(2A)-C(2)-H(2B)	108.1	C(9)-C(10)-C(11)	119.20(12)
C(4)-C(3)-C(2)	112.53(11)	C(10)-C(11)-C(12)	119.52(12)
C(4)-C(3)-H(3A)	109.1	C(10)-C(11)-H(11)	120.2
C(2)-C(3)-H(3A)	109.1	C(12)-C(11)-H(11)	120.2
C(4)-C(3)-H(3B)	109.1	C(11)-C(12)-C(7)	122.03(12)
C(2)-C(3)-H(3B)	109.1	C(11)-C(12)-H(12)	119.0
H(3A)-C(3)-H(3B)	107.8	C(7)-C(12)-H(12)	119.0
C(5)-C(4)-C(3)	110.17(10)	O(1)-C(13)-H(13A)	109.5
C(5)-C(4)-H(4A)	109.6	O(1)-C(13)-H(13B)	109.5
C(3)-C(4)-H(4A)	109.6	H(13A)-C(13)-H(13B)	109.5
C(5)-C(4)-H(4B)	109.6	O(1)-C(13)-H(13C)	109.5
C(3)-C(4)-H(4B)	109.6	H(13A)-C(13)-H(13C)	109.5
H(4A)-C(4)-H(4B)	108.1	H(13B)-C(13)-H(13C)	109.5
N(1)-C(5)-C(4)	110.67(10)	C(15)-C(14)-C(19)	120.79(12)
N(1)-C(5)-C(6)	111.47(10)	C(15)-C(14)-S(1)	120.18(10)
C(4)-C(5)-C(6)	109.44(10)	C(19)-C(14)-S(1)	119.00(9)
N(1)-C(5)-H(5)	108.4	C(14)-C(15)-C(16)	118.97(12)
C(4)-C(5)-H(5)	108.4	C(14)-C(15)-H(15)	120.5
C(6)-C(5)-H(5)	108.4	C(16)-C(15)-H(15)	120.5
C(1)-C(6)-C(5)	110.35(9)	C(17)-C(16)-C(15)	121.31(12)
C(1)-C(6)-H(6A)	109.6	C(17)-C(16)-H(16)	119.3
C(5)-C(6)-H(6A)	109.6	C(15)-C(16)-H(16)	119.3
C(1)-C(6)-H(6B)	109.6	C(16)-C(17)-C(18)	118.52(12)
C(5)-C(6)-H(6B)	109.6	C(16)-C(17)-C(20)	121.27(13)
H(6A)-C(6)-H(6B)	108.1	C(18)-C(17)-C(20)	120.21(14)

C(19)-C(18)-C(17)	121.06(12)
C(19)-C(18)-H(18)	119.5
C(17)-C(18)-H(18)	119.5
C(18)-C(19)-C(14)	119.25(12)
C(18)-C(19)-H(19)	120.4
C(14)-C(19)-H(19)	120.4
C(17)-C(20)-H(20A)	109.5
C(17)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(17)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5

Table S11. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (±)-*cis*-7d. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	12(1)	16(1)	18(1)	6(1)	4(1)	6(1)
O(1)	27(1)	19(1)	22(1)	3(1)	-3(1)	1(1)
O(2)	20(1)	19(1)	29(1)	12(1)	7(1)	6(1)
O(3)	13(1)	24(1)	22(1)	9(1)	4(1)	9(1)
N(1)	11(1)	23(1)	20(1)	7(1)	5(1)	6(1)
N(2)	14(1)	19(1)	16(1)	6(1)	3(1)	9(1)
C(1)	13(1)	18(1)	17(1)	5(1)	1(1)	8(1)
C(2)	18(1)	20(1)	22(1)	0(1)	-1(1)	10(1)
C(3)	20(1)	19(1)	24(1)	1(1)	1(1)	11(1)
C(4)	17(1)	24(1)	21(1)	6(1)	5(1)	12(1)
C(5)	12(1)	19(1)	17(1)	6(1)	3(1)	7(1)
C(6)	13(1)	17(1)	16(1)	5(1)	4(1)	7(1)
C(7)	14(1)	18(1)	20(1)	10(1)	2(1)	6(1)
C(8)	12(1)	21(1)	21(1)	8(1)	2(1)	3(1)
C(9)	18(1)	21(1)	20(1)	9(1)	5(1)	6(1)
C(10)	22(1)	15(1)	21(1)	7(1)	-1(1)	4(1)
C(11)	15(1)	17(1)	31(1)	11(1)	0(1)	2(1)
C(12)	13(1)	20(1)	28(1)	12(1)	6(1)	6(1)
C(13)	28(1)	17(1)	36(1)	4(1)	-11(1)	2(1)
C(14)	14(1)	18(1)	17(1)	5(1)	5(1)	9(1)
C(15)	21(1)	25(1)	20(1)	10(1)	7(1)	11(1)
C(16)	24(1)	33(1)	17(1)	7(1)	4(1)	14(1)
C(17)	22(1)	26(1)	23(1)	0(1)	1(1)	14(1)
C(18)	22(1)	18(1)	28(1)	6(1)	2(1)	9(1)
C(19)	20(1)	20(1)	19(1)	7(1)	4(1)	9(1)
C(20)	42(1)	33(1)	30(1)	-6(1)	-7(1)	15(1)

Table S12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (±)-*cis*-7d.

	x	y	z	U(eq)
H(1)	2791(19)	5162(18)	8257(17)	28(4)
H(2)	8734(17)	5973(17)	9990(16)	22(4)
H(1A)	7596	7144	8247	19
H(2A)	8219	9087	10285	26
H(2B)	7369	8093	11009	26
H(3A)	5903	9497	10504	26
H(3B)	6084	8994	8982	26
H(4A)	4513	7166	10217	24
H(4B)	3817	7702	9102	24
H(5)	4974	6362	7518	19
H(6A)	6075	5439	9615	18
H(6B)	6275	4808	8104	18
H(8)	5121	4270	6099	22
H(9)	4446	2487	4001	23
H(11)	442	1258	4683	26
H(12)	1133	3003	6808	23
H(13A)	600	-757	1395	46
H(13B)	48	534	2300	46
H(13C)	344	-703	2851	46
H(15)	8894	5618	5700	24
H(16)	7703	3558	3863	29
H(18)	7235	1163	6269	27
H(19)	8464	3190	8104	22
H(20A)	7052	-9	3755	58
H(20B)	6876	972	2859	58
H(20C)	5639	550	3640	58

Table S13. Torsion angles [°] for (±)-*cis*-7d.

O(2)-S(1)-N(2)-C(1)	58.24(10)
O(3)-S(1)-N(2)-C(1)	-173.88(9)
C(14)-S(1)-N(2)-C(1)	-58.74(10)
S(1)-N(2)-C(1)-C(6)	102.19(10)
S(1)-N(2)-C(1)-C(2)	-135.36(10)
N(2)-C(1)-C(2)-C(3)	-178.26(10)
C(6)-C(1)-C(2)-C(3)	-55.20(14)
C(1)-C(2)-C(3)-C(4)	53.73(15)
C(2)-C(3)-C(4)-C(5)	-55.15(14)
C(7)-N(1)-C(5)-C(4)	152.88(11)
C(7)-N(1)-C(5)-C(6)	-85.07(13)
C(3)-C(4)-C(5)-N(1)	-178.94(10)
C(3)-C(4)-C(5)-C(6)	57.83(13)
N(2)-C(1)-C(6)-C(5)	-178.48(9)
C(2)-C(1)-C(6)-C(5)	59.38(13)
N(1)-C(5)-C(6)-C(1)	176.54(9)
C(4)-C(5)-C(6)-C(1)	-60.70(12)
C(5)-N(1)-C(7)-C(12)	-163.98(11)
C(5)-N(1)-C(7)-C(8)	16.71(17)
C(12)-C(7)-C(8)-C(9)	0.30(17)
N(1)-C(7)-C(8)-C(9)	179.63(11)
C(7)-C(8)-C(9)-C(10)	0.86(19)
C(13)-O(1)-C(10)-C(9)	-173.19(11)
C(13)-O(1)-C(10)-C(11)	7.35(18)
C(8)-C(9)-C(10)-O(1)	179.37(11)
C(8)-C(9)-C(10)-C(11)	-1.13(18)
O(1)-C(10)-C(11)-C(12)	179.68(11)
C(9)-C(10)-C(11)-C(12)	0.24(18)
C(10)-C(11)-C(12)-C(7)	0.95(19)
C(8)-C(7)-C(12)-C(11)	-1.20(18)
N(1)-C(7)-C(12)-C(11)	179.44(11)
O(2)-S(1)-C(14)-C(15)	-1.62(12)
O(3)-S(1)-C(14)-C(15)	-130.27(10)
N(2)-S(1)-C(14)-C(15)	116.10(10)
O(2)-S(1)-C(14)-C(19)	176.58(9)

O(3)-S(1)-C(14)-C(19)	47.92(11)
N(2)-S(1)-C(14)-C(19)	-65.70(11)
C(19)-C(14)-C(15)-C(16)	-2.93(18)
S(1)-C(14)-C(15)-C(16)	175.23(10)
C(14)-C(15)-C(16)-C(17)	0.7(2)
C(15)-C(16)-C(17)-C(18)	2.2(2)
C(15)-C(16)-C(17)-C(20)	-177.03(13)
C(16)-C(17)-C(18)-C(19)	-3.0(2)
C(20)-C(17)-C(18)-C(19)	176.25(13)
C(17)-C(18)-C(19)-C(14)	0.84(19)
C(15)-C(14)-C(19)-C(18)	2.17(18)
S(1)-C(14)-C(19)-C(18)	-176.01(10)

Table S14. Hydrogen bonds for (±)-*cis*-7d [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...O(3)#1	0.898(17)	2.185(18)	3.0769(13)	172.2(15)
N(2)-H(2)...O(3)#2	0.869(16)	2.172(16)	3.0075(14)	161.2(14)

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z #2 -x+2,-y+1,-z+2

7.3. (1*R*,3*S*)-*cis*-7d

Low-temperature diffraction data (ω-scans) were collected on a Rigaku MicroMax-007HF diffractometer coupled to a Saturn994+ CCD detector with Cu Kα (λ = 1.54178 Å) for the structure (1*R*,3*S*)-*cis*-**7d**. The diffraction images were processed and scaled using Rigaku Oxford Diffraction software.[1] The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL.[2] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups). The only exceptions were H1, H2, H3, and H4, which were semi-freely refined with the aid of a N-H distance restraint of 0.88(2) Å. This value is similar to the N-H distance suggested by the Fourier difference map. The full numbering scheme of compound (1*R*,3*S*)-*cis*-**7d** can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC number 1818209 ((1*R*,3*S*)-*cis*-**7d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

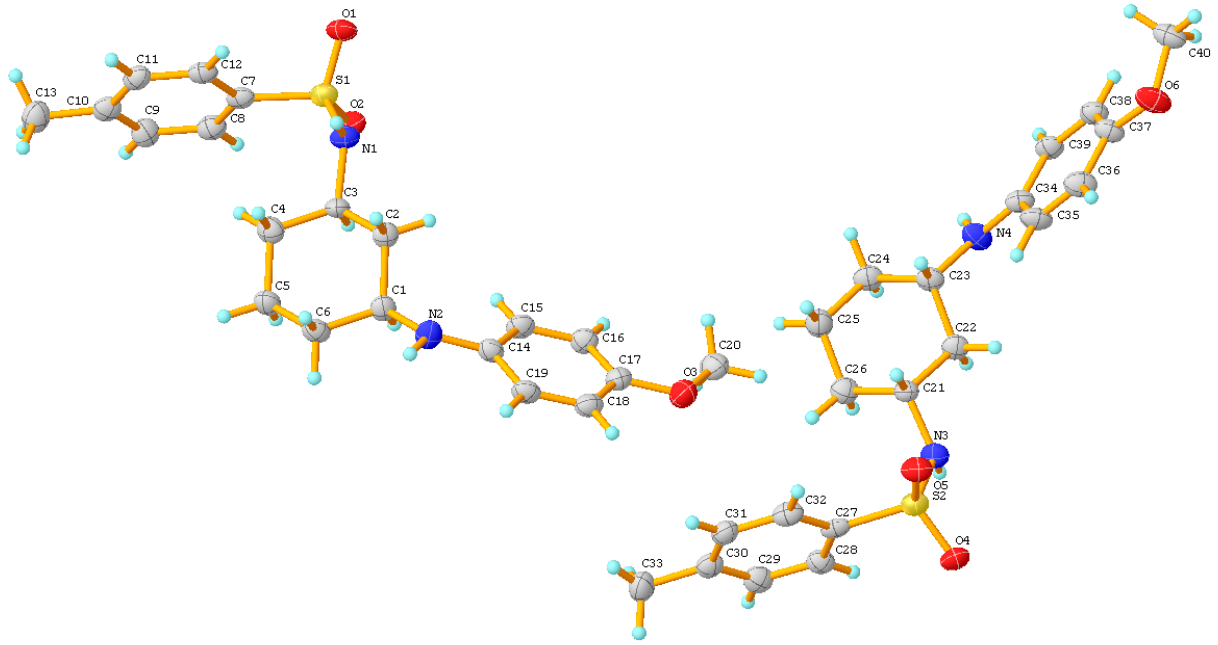


Figure S3. The complete numbering scheme of (1*R*,3*S*)-*cis*-7d with 50% thermal ellipsoid probability levels. The hydrogen atoms are shown as circles for clarity.

Table S15. Crystal data and structure refinement for (1*R*,3*S*)-*cis*-7d.

Identification code	(1*R*,3*S*)-*cis*-**7d**	
Empirical formula	C20 H26 N2 O3 S	
Formula weight	374.49	
Temperature	93(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 9.4315(2) Å	α= 90°.
	b = 9.5202(2) Å	β= 98.443(3)°.
	c = 21.4109(6) Å	γ = 90°.
Volume	1901.64(8) $Å^3$	
Z	4	
Density (calculated)	1.308 Mg/m^3	
Absorption coefficient	1.692 mm^{-1}	
F(000)	800	
Crystal size	0.200 x 0.020 x 0.020 mm^3	
Crystal color and habit	Colorless Needle	
Diffractometer	Rigaku Saturn 944+ CCD	
Theta range for data collection	2.086 to 67.178°.	
Index ranges	-11<=h<=11, -11<=k<=11, -25<=l<=25	
Reflections collected	13138	
Independent reflections	13138 [R(int) = 0.0989]	
Observed reflections (I > 2sigma(I))	10457	
Completeness to theta = 67.178°	99.4 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.92899	
Solution method	SHELXT-2014/5 (Sheldrick, 2014)	
Refinement method	SHELXL-2014/7 (Sheldrick, 2014)	
Data / restraints / parameters	13138 / 5 / 490	
Goodness-of-fit on F^2	1.138	
Final R indices [I>2sigma(I)]	R1 = 0.0630, wR2 = 0.1621	
R indices (all data)	R1 = 0.0902, wR2 = 0.1888	
Absolute structure parameter	0.01(2)	
Largest diff. peak and hole	0.485 and -0.649 $e.Å^{-3}$	

Table S16. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (1*R*,3*S*)-*cis*-7d. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	4211(2)	8641(2)	10127(1)	31(1)
O(1)	3151(7)	9599(7)	9820(3)	35(2)
O(2)	3992(7)	7152(7)	10019(3)	35(2)
O(3)	10196(7)	4799(7)	7019(3)	41(2)
N(1)	5702(8)	9058(9)	9894(4)	30(2)
N(2)	10347(8)	7800(9)	9266(4)	35(2)
C(1)	9398(9)	7585(11)	9736(4)	32(2)
C(2)	8024(9)	8472(10)	9588(4)	31(2)
C(3)	7049(10)	8250(11)	10085(4)	31(2)
C(4)	7824(10)	8617(11)	10735(4)	35(2)
C(5)	9189(9)	7745(11)	10889(4)	36(2)
C(6)	10174(9)	7942(11)	10390(4)	33(2)
C(7)	4374(9)	8924(10)	10944(4)	30(2)
C(8)	4343(9)	7808(11)	11361(4)	35(2)
C(9)	4565(10)	8060(11)	12009(4)	38(2)
C(10)	4831(10)	9417(11)	12249(4)	35(2)
C(11)	4814(10)	10523(11)	11824(4)	35(2)
C(12)	4603(9)	10289(10)	11178(4)	32(2)
C(13)	5122(12)	9670(12)	12948(5)	45(3)
C(14)	10278(9)	6980(10)	8728(4)	31(2)
C(15)	9094(9)	6170(10)	8496(4)	34(2)
C(16)	9032(10)	5407(10)	7935(4)	34(2)
C(17)	10160(10)	5455(10)	7599(4)	33(2)
C(18)	11384(10)	6211(10)	7838(4)	34(2)
C(19)	11453(9)	6953(11)	8393(4)	35(2)
C(20)	8946(11)	4027(11)	6769(5)	44(3)
S(2)	10811(2)	947(2)	5111(1)	31(1)
O(4)	11656(7)	-58(7)	4832(3)	34(2)
O(5)	10907(7)	2405(6)	4930(3)	34(2)
O(6)	2987(7)	5009(8)	2100(3)	43(2)
N(3)	9163(8)	466(9)	4933(4)	30(2)
N(4)	4120(8)	1729(9)	4274(4)	35(2)

C(21)	7963(9)	1317(10)	5106(4)	29(2)
C(22)	6652(9)	1069(11)	4612(4)	32(2)
C(23)	5382(9)	1953(11)	4745(4)	32(2)
C(24)	5033(10)	1644(11)	5403(4)	34(2)
C(25)	6349(10)	1850(11)	5901(4)	39(2)
C(26)	7617(10)	986(11)	5763(4)	35(2)
C(27)	11291(9)	855(10)	5932(4)	29(2)
C(28)	11245(10)	-459(10)	6231(4)	33(2)
C(29)	11583(10)	-538(11)	6880(5)	36(2)
C(30)	11978(9)	647(10)	7245(4)	34(2)
C(31)	12020(10)	1936(11)	6947(4)	37(2)
C(32)	11681(10)	2048(10)	6291(5)	36(2)
C(33)	12377(11)	542(13)	7953(4)	45(3)
C(34)	3823(9)	2578(10)	3740(4)	32(2)
C(35)	4879(9)	3344(10)	3506(5)	37(2)
C(36)	4564(11)	4134(11)	2964(5)	40(2)
C(37)	3173(10)	4183(10)	2640(5)	34(2)
C(38)	2120(9)	3425(10)	2862(4)	34(2)
C(39)	2434(9)	2631(10)	3407(4)	32(2)
C(40)	1539(11)	5414(11)	1863(5)	42(2)

Table S17. Bond lengths [Å] and angles [°] for (1*R*,3*S*)-*cis*-7d.

S(1)-O(1)	1.439(7)
S(1)-O(2)	1.446(7)
S(1)-N(1)	1.609(8)
S(1)-C(7)	1.754(10)
O(3)-C(17)	1.393(11)
O(3)-C(20)	1.425(12)
N(1)-C(3)	1.490(12)
N(1)-H(1)	0.85(4)
N(2)-C(14)	1.385(12)
N(2)-C(1)	1.458(11)
N(2)-H(2)	0.88(4)
C(1)-C(6)	1.519(12)
C(1)-C(2)	1.541(13)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.518(12)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.515(12)
C(3)-H(3)	1.0000
C(4)-C(5)	1.527(13)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.528(12)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(8)	1.391(13)
C(7)-C(12)	1.398(13)
C(8)-C(9)	1.393(13)
C(8)-H(8)	0.9500
C(9)-C(10)	1.399(14)
C(9)-H(9)	0.9500
C(10)-C(11)	1.390(14)
C(10)-C(13)	1.501(14)
C(11)-C(12)	1.385(13)
C(11)-H(11)	0.9500
C(12)-H(12)	0.9500
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-C(15)	1.387(13)
C(14)-C(19)	1.405(12)
C(15)-C(16)	1.399(13)
C(15)-H(15)	0.9500
C(16)-C(17)	1.369(13)
C(16)-H(16)	0.9500
C(17)-C(18)	1.393(13)
C(18)-C(19)	1.376(13)
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
S(2)-O(4)	1.431(7)
S(2)-O(5)	1.448(7)
S(2)-N(3)	1.611(8)
S(2)-C(27)	1.752(9)
O(6)-C(37)	1.389(12)
O(6)-C(40)	1.438(12)
N(3)-C(21)	1.483(12)
N(3)-H(3A)	0.88(4)
N(4)-C(34)	1.395(12)
N(4)-C(23)	1.459(11)
N(4)-H(4)	0.89(4)
C(21)-C(26)	1.523(12)
C(21)-C(22)	1.523(12)
C(21)-H(21)	1.0000
C(22)-C(23)	1.525(13)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900

C(23)-C(24)	1.521(12)	O(1)-S(1)-O(2)	118.4(4)
C(23)-H(23)	1.0000	O(1)-S(1)-N(1)	106.4(4)
C(24)-C(25)	1.524(13)	O(2)-S(1)-N(1)	107.7(4)
C(24)-H(24A)	0.9900	O(1)-S(1)-C(7)	108.1(4)
C(24)-H(24B)	0.9900	O(2)-S(1)-C(7)	107.4(4)
C(25)-C(26)	1.516(14)	N(1)-S(1)-C(7)	108.6(4)
C(25)-H(25A)	0.9900	C(17)-O(3)-C(20)	116.1(7)
C(25)-H(25B)	0.9900	C(3)-N(1)-S(1)	122.4(7)
C(26)-H(26A)	0.9900	C(3)-N(1)-H(1)	108(6)
C(26)-H(26B)	0.9900	S(1)-N(1)-H(1)	118(6)
C(27)-C(32)	1.391(13)	C(14)-N(2)-C(1)	122.5(8)
C(27)-C(28)	1.409(13)	C(14)-N(2)-H(2)	120(9)
C(28)-C(29)	1.381(13)	C(1)-N(2)-H(2)	113(9)
C(28)-H(28)	0.9500	N(2)-C(1)-C(6)	110.1(7)
C(29)-C(30)	1.392(13)	N(2)-C(1)-C(2)	111.4(8)
C(29)-H(29)	0.9500	C(6)-C(1)-C(2)	110.1(8)
C(30)-C(31)	1.387(14)	N(2)-C(1)-H(1A)	108.4
C(30)-C(33)	1.509(13)	C(6)-C(1)-H(1A)	108.4
C(31)-C(32)	1.397(13)	C(2)-C(1)-H(1A)	108.4
C(31)-H(31)	0.9500	C(3)-C(2)-C(1)	110.9(7)
C(32)-H(32)	0.9500	C(3)-C(2)-H(2A)	109.5
C(33)-H(33A)	0.9800	C(1)-C(2)-H(2A)	109.5
C(33)-H(33B)	0.9800	C(3)-C(2)-H(2B)	109.5
C(33)-H(33C)	0.9800	C(1)-C(2)-H(2B)	109.5
C(34)-C(35)	1.387(13)	H(2A)-C(2)-H(2B)	108.0
C(34)-C(39)	1.397(12)	N(1)-C(3)-C(4)	114.2(8)
C(35)-C(36)	1.379(14)	N(1)-C(3)-C(2)	108.4(7)
C(35)-H(35)	0.9500	C(4)-C(3)-C(2)	110.5(8)
C(36)-C(37)	1.392(13)	N(1)-C(3)-H(3)	107.8
C(36)-H(36)	0.9500	C(4)-C(3)-H(3)	107.8
C(37)-C(38)	1.368(13)	C(2)-C(3)-H(3)	107.8
C(38)-C(39)	1.384(13)	C(3)-C(4)-C(5)	110.6(8)
C(38)-H(38)	0.9500	C(3)-C(4)-H(4A)	109.5
C(39)-H(39)	0.9500	C(5)-C(4)-H(4A)	109.5
C(40)-H(40A)	0.9800	C(3)-C(4)-H(4B)	109.5
C(40)-H(40B)	0.9800	C(5)-C(4)-H(4B)	109.5
C(40)-H(40C)	0.9800	H(4A)-C(4)-H(4B)	108.1

C(4)-C(5)-C(6)	111.2(8)	N(2)-C(14)-C(19)	119.3(8)
C(4)-C(5)-H(5A)	109.4	C(15)-C(14)-C(19)	117.5(8)
C(6)-C(5)-H(5A)	109.4	C(14)-C(15)-C(16)	121.7(8)
C(4)-C(5)-H(5B)	109.4	C(14)-C(15)-H(15)	119.1
C(6)-C(5)-H(5B)	109.4	C(16)-C(15)-H(15)	119.1
H(5A)-C(5)-H(5B)	108.0	C(17)-C(16)-C(15)	119.7(9)
C(1)-C(6)-C(5)	110.9(7)	C(17)-C(16)-H(16)	120.1
C(1)-C(6)-H(6A)	109.5	C(15)-C(16)-H(16)	120.1
C(5)-C(6)-H(6A)	109.5	C(16)-C(17)-C(18)	119.4(9)
C(1)-C(6)-H(6B)	109.5	C(16)-C(17)-O(3)	125.1(9)
C(5)-C(6)-H(6B)	109.5	C(18)-C(17)-O(3)	115.6(8)
H(6A)-C(6)-H(6B)	108.0	C(19)-C(18)-C(17)	121.0(9)
C(8)-C(7)-C(12)	119.7(9)	C(19)-C(18)-H(18)	119.5
C(8)-C(7)-S(1)	121.1(7)	C(17)-C(18)-H(18)	119.5
C(12)-C(7)-S(1)	119.1(7)	C(18)-C(19)-C(14)	120.6(8)
C(7)-C(8)-C(9)	119.6(9)	C(18)-C(19)-H(19)	119.7
C(7)-C(8)-H(8)	120.2	C(14)-C(19)-H(19)	119.7
C(9)-C(8)-H(8)	120.2	O(3)-C(20)-H(20A)	109.5
C(8)-C(9)-C(10)	121.1(9)	O(3)-C(20)-H(20B)	109.5
C(8)-C(9)-H(9)	119.4	H(20A)-C(20)-H(20B)	109.5
C(10)-C(9)-H(9)	119.4	O(3)-C(20)-H(20C)	109.5
C(11)-C(10)-C(9)	118.3(9)	H(20A)-C(20)-H(20C)	109.5
C(11)-C(10)-C(13)	121.0(9)	H(20B)-C(20)-H(20C)	109.5
C(9)-C(10)-C(13)	120.7(9)	O(4)-S(2)-O(5)	117.9(4)
C(12)-C(11)-C(10)	121.2(9)	O(4)-S(2)-N(3)	106.8(4)
C(12)-C(11)-H(11)	119.4	O(5)-S(2)-N(3)	107.8(4)
C(10)-C(11)-H(11)	119.4	O(4)-S(2)-C(27)	107.9(4)
C(11)-C(12)-C(7)	120.0(9)	O(5)-S(2)-C(27)	107.5(4)
C(11)-C(12)-H(12)	120.0	N(3)-S(2)-C(27)	108.7(4)
C(7)-C(12)-H(12)	120.0	C(37)-O(6)-C(40)	116.3(7)
C(10)-C(13)-H(13A)	109.5	C(21)-N(3)-S(2)	122.1(7)
C(10)-C(13)-H(13B)	109.5	C(21)-N(3)-H(3A)	110(7)
H(13A)-C(13)-H(13B)	109.5	S(2)-N(3)-H(3A)	116(7)
C(10)-C(13)-H(13C)	109.5	C(34)-N(4)-C(23)	121.8(8)
H(13A)-C(13)-H(13C)	109.5	C(34)-N(4)-H(4)	117(6)
H(13B)-C(13)-H(13C)	109.5	C(23)-N(4)-H(4)	114(6)
N(2)-C(14)-C(15)	123.2(8)	N(3)-C(21)-C(26)	113.1(8)

N(3)-C(21)-C(22)	108.3(7)	C(28)-C(27)-S(2)	118.7(7)
C(26)-C(21)-C(22)	110.3(8)	C(29)-C(28)-C(27)	119.2(9)
N(3)-C(21)-H(21)	108.3	C(29)-C(28)-H(28)	120.4
C(26)-C(21)-H(21)	108.3	C(27)-C(28)-H(28)	120.4
C(22)-C(21)-H(21)	108.3	C(28)-C(29)-C(30)	121.6(9)
C(21)-C(22)-C(23)	111.4(8)	C(28)-C(29)-H(29)	119.2
C(21)-C(22)-H(22A)	109.4	C(30)-C(29)-H(29)	119.2
C(23)-C(22)-H(22A)	109.4	C(31)-C(30)-C(29)	118.8(8)
C(21)-C(22)-H(22B)	109.4	C(31)-C(30)-C(33)	120.1(9)
C(23)-C(22)-H(22B)	109.4	C(29)-C(30)-C(33)	121.1(9)
H(22A)-C(22)-H(22B)	108.0	C(30)-C(31)-C(32)	120.9(9)
N(4)-C(23)-C(24)	110.2(7)	C(30)-C(31)-H(31)	119.6
N(4)-C(23)-C(22)	111.9(8)	C(32)-C(31)-H(31)	119.6
C(24)-C(23)-C(22)	110.4(8)	C(27)-C(32)-C(31)	119.8(9)
N(4)-C(23)-H(23)	108.1	C(27)-C(32)-H(32)	120.1
C(24)-C(23)-H(23)	108.1	C(31)-C(32)-H(32)	120.1
C(22)-C(23)-H(23)	108.1	C(30)-C(33)-H(33A)	109.5
C(23)-C(24)-C(25)	110.9(8)	C(30)-C(33)-H(33B)	109.5
C(23)-C(24)-H(24A)	109.5	H(33A)-C(33)-H(33B)	109.5
C(25)-C(24)-H(24A)	109.5	C(30)-C(33)-H(33C)	109.5
C(23)-C(24)-H(24B)	109.5	H(33A)-C(33)-H(33C)	109.5
C(25)-C(24)-H(24B)	109.5	H(33B)-C(33)-H(33C)	109.5
H(24A)-C(24)-H(24B)	108.0	C(35)-C(34)-N(4)	122.2(8)
C(26)-C(25)-C(24)	112.3(8)	C(35)-C(34)-C(39)	117.7(9)
C(26)-C(25)-H(25A)	109.2	N(4)-C(34)-C(39)	120.0(8)
C(24)-C(25)-H(25A)	109.2	C(36)-C(35)-C(34)	120.9(9)
C(26)-C(25)-H(25B)	109.2	C(36)-C(35)-H(35)	119.5
C(24)-C(25)-H(25B)	109.2	C(34)-C(35)-H(35)	119.5
H(25A)-C(25)-H(25B)	107.9	C(35)-C(36)-C(37)	120.6(9)
C(25)-C(26)-C(21)	110.5(8)	C(35)-C(36)-H(36)	119.7
C(25)-C(26)-H(26A)	109.6	C(37)-C(36)-H(36)	119.7
C(21)-C(26)-H(26A)	109.6	C(38)-C(37)-O(6)	125.4(8)
C(25)-C(26)-H(26B)	109.6	C(38)-C(37)-C(36)	119.2(9)
C(21)-C(26)-H(26B)	109.6	O(6)-C(37)-C(36)	115.3(8)
H(26A)-C(26)-H(26B)	108.1	C(37)-C(38)-C(39)	120.3(8)
C(32)-C(27)-C(28)	119.7(8)	C(37)-C(38)-H(38)	119.9
C(32)-C(27)-S(2)	121.5(7)	C(39)-C(38)-H(38)	119.9

C(38)-C(39)-C(34)	121.2(8)	H(40A)-C(40)-H(40B)	109.5
C(38)-C(39)-H(39)	119.4	O(6)-C(40)-H(40C)	109.5
C(34)-C(39)-H(39)	119.4	H(40A)-C(40)-H(40C)	109.5
O(6)-C(40)-H(40A)	109.5	H(40B)-C(40)-H(40C)	109.5
O(6)-C(40)-H(40B)	109.5		

Table S18. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (1*R*,3*S*)-*cis*-7d. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	21(1)	32(1)	39(1)	-2(1)	4(1)	-1(1)
O(1)	21(3)	37(4)	46(4)	0(3)	1(3)	5(3)
O(2)	27(3)	31(4)	47(4)	-7(3)	7(3)	-5(3)
O(3)	36(4)	46(4)	41(4)	-7(3)	6(3)	2(3)
N(1)	23(4)	25(5)	42(5)	3(3)	7(3)	-1(3)
N(2)	24(4)	45(5)	37(4)	-6(4)	7(3)	-8(4)
C(1)	23(5)	43(6)	32(5)	-1(4)	6(4)	-3(4)
C(2)	25(4)	36(5)	33(5)	0(4)	7(4)	-4(4)
C(3)	26(5)	36(6)	31(5)	-1(4)	2(4)	12(4)
C(4)	30(5)	37(5)	37(5)	-2(4)	1(4)	-4(5)
C(5)	25(5)	49(6)	34(5)	1(4)	3(4)	3(5)
C(6)	22(5)	42(6)	35(5)	6(4)	4(4)	1(4)
C(7)	17(4)	32(5)	41(5)	-3(4)	3(4)	0(4)
C(8)	27(5)	36(5)	44(5)	-2(4)	7(4)	-1(4)
C(9)	33(5)	46(6)	37(5)	2(5)	10(4)	-4(5)
C(10)	21(4)	42(6)	42(5)	-3(4)	8(4)	-1(4)
C(11)	24(5)	38(6)	41(5)	-9(4)	5(4)	0(4)
C(12)	20(4)	34(5)	44(5)	-1(4)	5(4)	2(4)
C(13)	40(6)	56(7)	40(6)	-6(5)	11(5)	-4(5)
C(14)	22(4)	37(5)	33(5)	2(4)	2(4)	0(4)
C(15)	22(4)	40(6)	41(5)	-1(4)	9(4)	-1(4)
C(16)	25(5)	37(5)	39(5)	-4(4)	4(4)	-3(4)
C(17)	30(5)	35(5)	35(5)	-2(4)	5(4)	5(4)
C(18)	28(5)	38(6)	38(5)	5(4)	9(4)	5(4)
C(19)	21(4)	43(6)	40(5)	3(4)	4(4)	1(4)
C(20)	40(6)	43(6)	46(6)	-9(5)	2(5)	6(5)

S(2)	24(1)	30(1)	38(1)	2(1)	7(1)	1(1)
O(4)	27(4)	35(4)	42(4)	0(3)	11(3)	5(3)
O(5)	29(4)	28(4)	45(4)	8(3)	10(3)	-1(3)
O(6)	24(3)	52(4)	52(4)	19(3)	2(3)	-2(3)
N(3)	24(4)	27(5)	39(4)	0(3)	4(3)	-5(4)
N(4)	22(4)	44(5)	40(4)	6(4)	3(3)	-7(4)
C(21)	27(5)	29(5)	31(5)	-1(4)	2(4)	5(4)
C(22)	22(4)	37(5)	36(5)	-1(4)	6(4)	-3(4)
C(23)	20(4)	36(5)	38(5)	0(4)	3(4)	-2(4)
C(24)	24(5)	37(6)	43(5)	1(4)	8(4)	-2(4)
C(25)	32(5)	49(6)	37(5)	-3(5)	5(4)	0(5)
C(26)	31(5)	37(5)	37(5)	3(4)	7(4)	-1(5)
C(27)	17(4)	26(4)	45(5)	-1(4)	10(4)	1(4)
C(28)	23(5)	38(5)	38(5)	0(4)	5(4)	0(4)
C(29)	27(5)	43(6)	41(5)	4(5)	10(4)	-3(5)
C(30)	26(5)	40(6)	37(5)	-2(4)	9(4)	1(4)
C(31)	29(5)	43(6)	39(5)	-9(5)	6(4)	4(4)
C(32)	28(5)	31(5)	50(6)	-2(4)	8(4)	1(4)
C(33)	40(6)	62(8)	34(5)	-6(5)	9(4)	3(5)
C(34)	24(5)	32(5)	41(5)	1(4)	6(4)	2(4)
C(35)	20(4)	43(6)	48(6)	6(4)	3(4)	4(4)
C(36)	28(5)	41(6)	51(6)	9(5)	9(4)	0(4)
C(37)	22(5)	37(5)	41(5)	5(4)	0(4)	0(4)
C(38)	22(5)	40(6)	41(5)	-1(4)	3(4)	1(4)
C(39)	20(4)	38(5)	40(5)	-1(4)	6(4)	0(4)
C(40)	31(5)	41(6)	51(6)	4(5)	-7(5)	3(5)

Table S19. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for (1*R*,3*S*)-*cis*-7d.

	x	y	z	U(eq)
H(1)	5920(90)	9930(40)	9880(40)	10(20)
H(2)	11150(90)	8220(130)	9420(60)	80(40)
H(1A)	9120	6571	9732	39
H(2A)	8283	9478	9575	37
H(2B)	7508	8207	9169	37
H(3)	6795	7230	10085	37
H(4A)	7186	8437	11054	42
H(4B)	8071	9629	10750	42
H(5A)	8933	6740	10912	44
H(5B)	9702	8029	11307	44
H(6A)	10508	8929	10395	40
H(6B)	11026	7330	10490	40
H(8)	4172	6880	11205	42
H(9)	4535	7298	12293	46
H(11)	4950	11455	11978	41
H(12)	4613	11055	10895	39
H(13A)	6132	9922	13070	67
H(13B)	4910	8814	13171	67
H(13C)	4514	10438	13058	67
H(15)	8304	6134	8725	41
H(16)	8211	4857	7787	41
H(18)	12183	6214	7615	41
H(19)	12302	7453	8551	41
H(20A)	9040	3696	6343	65
H(20B)	8102	4634	6750	65
H(20C)	8838	3219	7042	65
H(3A)	8990(100)	-430(50)	4980(40)	30(30)
H(4)	3380(70)	1370(100)	4430(40)	30(30)
H(21)	8232	2332	5093	35
H(22A)	6387	62	4611	38
H(22B)	6887	1308	4189	38

H(23)	5660	2965	4730	38
H(24A)	4690	664	5420	41
H(24B)	4256	2276	5495	41
H(25A)	6616	2856	5918	47
H(25B)	6108	1581	6319	47
H(26A)	7393	-26	5792	42
H(26B)	8461	1196	6082	42
H(28)	10985	-1281	5990	40
H(29)	11546	-1423	7082	43
H(31)	12282	2753	7191	44
H(32)	11717	2936	6092	43
H(33A)	13285	33	8053	68
H(33B)	11623	37	8130	68
H(33C)	12482	1488	8134	68
H(35)	5834	3324	3722	45
H(36)	5302	4650	2810	47
H(38)	1170	3443	2642	41
H(39)	1691	2114	3557	39
H(40A)	1545	6120	1530	63
H(40B)	1086	5810	2207	63
H(40C)	998	4588	1690	63

Table S20. Torsion angles [°] for (1*R*,3*S*)-*cis*-7d.

O(1)-S(1)-N(1)-C(3)	-176.7(7)
O(2)-S(1)-N(1)-C(3)	-48.9(8)
C(7)-S(1)-N(1)-C(3)	67.2(8)
C(14)-N(2)-C(1)-C(6)	147.1(9)
C(14)-N(2)-C(1)-C(2)	-90.5(11)
N(2)-C(1)-C(2)-C(3)	-179.5(8)
C(6)-C(1)-C(2)-C(3)	-57.1(10)
S(1)-N(1)-C(3)-C(4)	-80.9(10)
S(1)-N(1)-C(3)-C(2)	155.4(7)
C(1)-C(2)-C(3)-N(1)	-176.3(8)
C(1)-C(2)-C(3)-C(4)	57.9(11)
N(1)-C(3)-C(4)-C(5)	-179.8(8)
C(2)-C(3)-C(4)-C(5)	-57.3(11)
C(3)-C(4)-C(5)-C(6)	56.6(11)
N(2)-C(1)-C(6)-C(5)	179.1(8)
C(2)-C(1)-C(6)-C(5)	56.0(11)
C(4)-C(5)-C(6)-C(1)	-56.3(11)
O(1)-S(1)-C(7)-C(8)	131.4(7)
O(2)-S(1)-C(7)-C(8)	2.6(8)
N(1)-S(1)-C(7)-C(8)	-113.6(8)
O(1)-S(1)-C(7)-C(12)	-51.5(8)
O(2)-S(1)-C(7)-C(12)	179.7(7)
N(1)-S(1)-C(7)-C(12)	63.5(8)
C(12)-C(7)-C(8)-C(9)	-1.1(13)
S(1)-C(7)-C(8)-C(9)	176.0(7)
C(7)-C(8)-C(9)-C(10)	-0.6(14)
C(8)-C(9)-C(10)-C(11)	2.5(14)
C(8)-C(9)-C(10)-C(13)	-177.7(9)
C(9)-C(10)-C(11)-C(12)	-2.8(14)
C(13)-C(10)-C(11)-C(12)	177.4(9)
C(10)-C(11)-C(12)-C(7)	1.2(14)
C(8)-C(7)-C(12)-C(11)	0.7(13)
S(1)-C(7)-C(12)-C(11)	-176.4(7)
C(1)-N(2)-C(14)-C(15)	18.6(14)
C(1)-N(2)-C(14)-C(19)	-161.5(9)

N(2)-C(14)-C(15)-C(16)	176.9(9)
C(19)-C(14)-C(15)-C(16)	-3.0(14)
C(14)-C(15)-C(16)-C(17)	-0.3(14)
C(15)-C(16)-C(17)-C(18)	3.1(14)
C(15)-C(16)-C(17)-O(3)	-176.6(9)
C(20)-O(3)-C(17)-C(16)	0.0(13)
C(20)-O(3)-C(17)-C(18)	-179.8(8)
C(16)-C(17)-C(18)-C(19)	-2.6(14)
O(3)-C(17)-C(18)-C(19)	177.2(9)
C(17)-C(18)-C(19)-C(14)	-0.8(14)
N(2)-C(14)-C(19)-C(18)	-176.3(9)
C(15)-C(14)-C(19)-C(18)	3.5(14)
O(4)-S(2)-N(3)-C(21)	-175.7(7)
O(5)-S(2)-N(3)-C(21)	-48.1(8)
C(27)-S(2)-N(3)-C(21)	68.1(8)
S(2)-N(3)-C(21)-C(26)	-87.2(10)
S(2)-N(3)-C(21)-C(22)	150.2(7)
N(3)-C(21)-C(22)-C(23)	-177.9(8)
C(26)-C(21)-C(22)-C(23)	57.8(11)
C(34)-N(4)-C(23)-C(24)	143.9(9)
C(34)-N(4)-C(23)-C(22)	-92.8(11)
C(21)-C(22)-C(23)-N(4)	179.8(8)
C(21)-C(22)-C(23)-C(24)	-57.0(10)
N(4)-C(23)-C(24)-C(25)	179.1(8)
C(22)-C(23)-C(24)-C(25)	54.9(11)
C(23)-C(24)-C(25)-C(26)	-55.1(11)
C(24)-C(25)-C(26)-C(21)	55.7(11)
N(3)-C(21)-C(26)-C(25)	-177.9(8)
C(22)-C(21)-C(26)-C(25)	-56.5(11)
O(4)-S(2)-C(27)-C(32)	127.9(7)
O(5)-S(2)-C(27)-C(32)	-0.3(8)
N(3)-S(2)-C(27)-C(32)	-116.7(7)
O(4)-S(2)-C(27)-C(28)	-53.6(8)
O(5)-S(2)-C(27)-C(28)	178.2(7)
N(3)-S(2)-C(27)-C(28)	61.9(8)
C(32)-C(27)-C(28)-C(29)	0.4(13)
S(2)-C(27)-C(28)-C(29)	-178.2(7)

C(27)-C(28)-C(29)-C(30)	-0.5(14)
C(28)-C(29)-C(30)-C(31)	0.5(14)
C(28)-C(29)-C(30)-C(33)	-178.6(9)
C(29)-C(30)-C(31)-C(32)	-0.4(14)
C(33)-C(30)-C(31)-C(32)	178.7(8)
C(28)-C(27)-C(32)-C(31)	-0.3(13)
S(2)-C(27)-C(32)-C(31)	178.3(7)
C(30)-C(31)-C(32)-C(27)	0.3(13)
C(23)-N(4)-C(34)-C(35)	22.3(14)
C(23)-N(4)-C(34)-C(39)	-160.3(9)
N(4)-C(34)-C(35)-C(36)	177.6(9)
C(39)-C(34)-C(35)-C(36)	0.2(15)
C(34)-C(35)-C(36)-C(37)	0.2(16)
C(40)-O(6)-C(37)-C(38)	18.6(14)
C(40)-O(6)-C(37)-C(36)	-162.4(9)
C(35)-C(36)-C(37)-C(38)	-0.7(15)
C(35)-C(36)-C(37)-O(6)	-179.8(9)
O(6)-C(37)-C(38)-C(39)	179.7(9)
C(36)-C(37)-C(38)-C(39)	0.7(15)
C(37)-C(38)-C(39)-C(34)	-0.3(15)
C(35)-C(34)-C(39)-C(38)	-0.2(14)
N(4)-C(34)-C(39)-C(38)	-177.7(9)

Table S21. Hydrogen bonds for (1*R*,3*S*)-*cis*-7d [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...O(2)#1	0.85(4)	2.13(4)	2.962(11)	165(8)
N(2)-H(2)...O(1)#2	0.88(4)	2.35(4)	3.227(10)	173(13)
N(3)-H(3A)...O(5)#3	0.88(4)	2.07(5)	2.931(10)	167(9)
N(4)-H(4)...O(4)#4	0.89(4)	2.37(4)	3.245(10)	168(9)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+2 #2 x+1,y,z #3 -x+2,y-1/2,-z+1

#4 x-1,y,z

8. Computational Data

8.1. General Computational Information

All calculations were carried out on the supercomputer clusters provided by the Yale University Faculty of Arts and Science High Performance Computing Center.[3] These calculations were performed using Gaussian 09 revision C.01,[4] and the all input and output files were created and visualized using GaussView 5.0. All calculations were carried out at 25 °C and 1 atm of pressure in the gas phase.[5,6]

In order to determine the Gibbs free energy difference (ΔG°) between the four conformers of the imine intermediates, the optimized geometries of the *Z*- and *E*-imine and axial and equatorial directing group conformations were found. First, potential energy scans were performed on the axial and equatorial phenyl-acetamide substituent, along with the aniline using B3LYP/6-31+G(d,p) in order to determine the preferred dihedral angles of the compounds. The relevant dihedral angles were defined as constrained coordinates and a scan from 0° to 360° at 10° increments was performed for each, with the structure of each increment being subjected to a geometry optimization and frequency calculation. On the scans shown below, the positive direction represents clockwise rotation of the functional group and the negative direction represents counterclockwise rotation. Red numbers on the y-axis of the dihedral scans below represent the energy maximum. Red numbers on the x-axis represent the lowest energy dihedral angle. Using these minimized dihedral angles, the compounds were then submitted for unconstrained geometry optimization and vibrational frequency calculation using B3LYP/6-311+G(d,p). As a control, some dihedral angles of each compound were varied outside their absolute minimum and submitted for the same optimization and frequency calculation to ensure the previously calculated structures were the true energy minimum. Finally, single-point energies for the optimized geometries were calculated using M06-2X/6-311++G(2d,3p), B3LYP/6-311++G(2d,3p), or MP2/6-311+G(2d,3p).[7,8] The dipole moments from these single-point energy calculation were utilized in the paper.

The energies derived from these calculations are expressed as total energy (E°) in Hartree atomic units (a.u.). Each calculation performing a frequency calculation also contained a thermal correction of the total energy value to a Gibbs free energy value (G°).[9] These values can be used to calculate the change in Gibbs free energy (ΔG°) between the chair conformers in kilocalories per mole using the following equation:

$$\Delta G^\circ = \left(G^\circ_{axial} - G^\circ_{equatorial}\right)\left(\frac{627.51\ kcal}{mol{\cdot}a.u.}\right) \quad (1)$$

Using 0.001987 kcal·mol^{-1}·K^{-1} as the gas constant (R) and 298 K as temperature (T), the equilibrium constant can then be derived from this value by:

$$\Delta G^\circ = -RTlnK \quad (2)$$

The equilibrium ratio of the two conformers can be obtained by the following equation [major:minor]:

$$\left[\left(100 - \frac{100}{1+K}\right) : \left(\frac{100}{1+K}\right)\right] \quad (3)$$

The calculation of equilibrium ratios becomes more complicated when there are greater than two competing conformations, such as when a compound such as **7a** can exist with an equatorial or axial amido group and with an *E* or *Z* imine, resulting in four accessible conformations. In this case, the lowest energy conformer (**A**) is determined, and each of the remaining three conformations is presumed to be in equilibrium with conformer **A** **(Figure SI-15)**. The individual ΔG° and K are determined between **A** and each conformer using equations 1 and 2.[9,10]

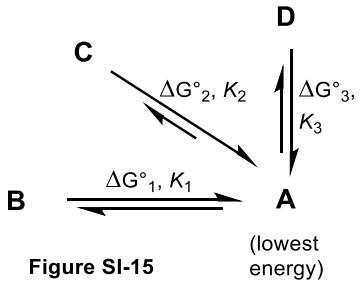


Figure SI-15

The individual K values can be summed to yield K_{TOT} using equation 4. As a note, K_A is the equilibrium constant of A to itself, meaning $K_A = 1$.[12,13]

$$K_{TOT} = K_1 + K_2 + K_3 + K_A = \frac{[B]}{[A]} + \frac{[C]}{[A]} + \frac{[D]}{[A]} + \frac{[A]}{[A]} = \frac{[A] + [B] + [C] + [D]}{[A]} \quad (4)$$

Calculation of the equilibrium percentages of each species can be performed using equation 5.

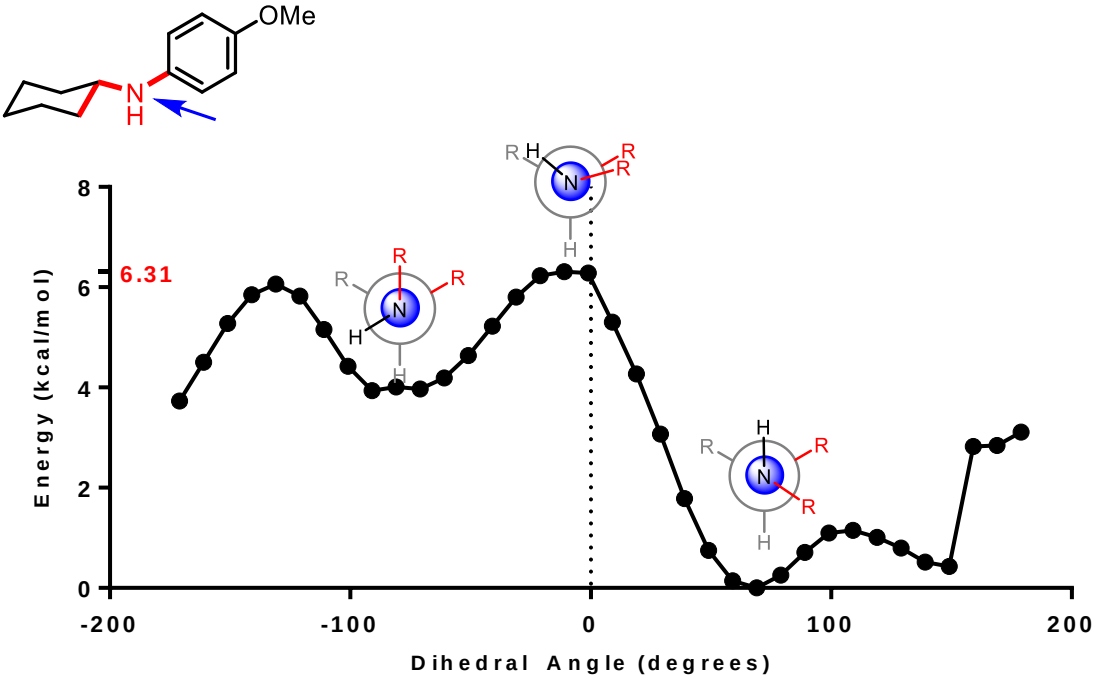
$$\%_B = \frac{K_1}{K_{TOT}} \bullet 100 = \frac{[B]}{[A]} \bullet \frac{[A]}{[A] + [B] + [C] + [D]} = \frac{[B]}{[A] + [B] + [C] + [D]} \quad (5)$$

It is important to note that this method is an estimation of the equilibrium percentages, as it does not take into account equilibration between other conformers not including A, such as B to C. Furthermore, this does not take into account potential stereoselectivity in catalyst controlled imine formation. However, this method can effectively determine whether particular conformers alone are vastly more stable or unstable than others.

8.2. Potential Energy Scans for Structure Optimization Calculations

Prior to submission of geometry optimization and frequency calculations on substrates, a number of potential energy scans were performed on appended groups to determine the preferred dihedral angles in the complexes and prevent any geometry optimization calculations to find a local, as opposed to the desired absolute, energy minimum. DFT calculations were performed at the B3LYP/6-31+G (d,p) level of theory in the gas phase.

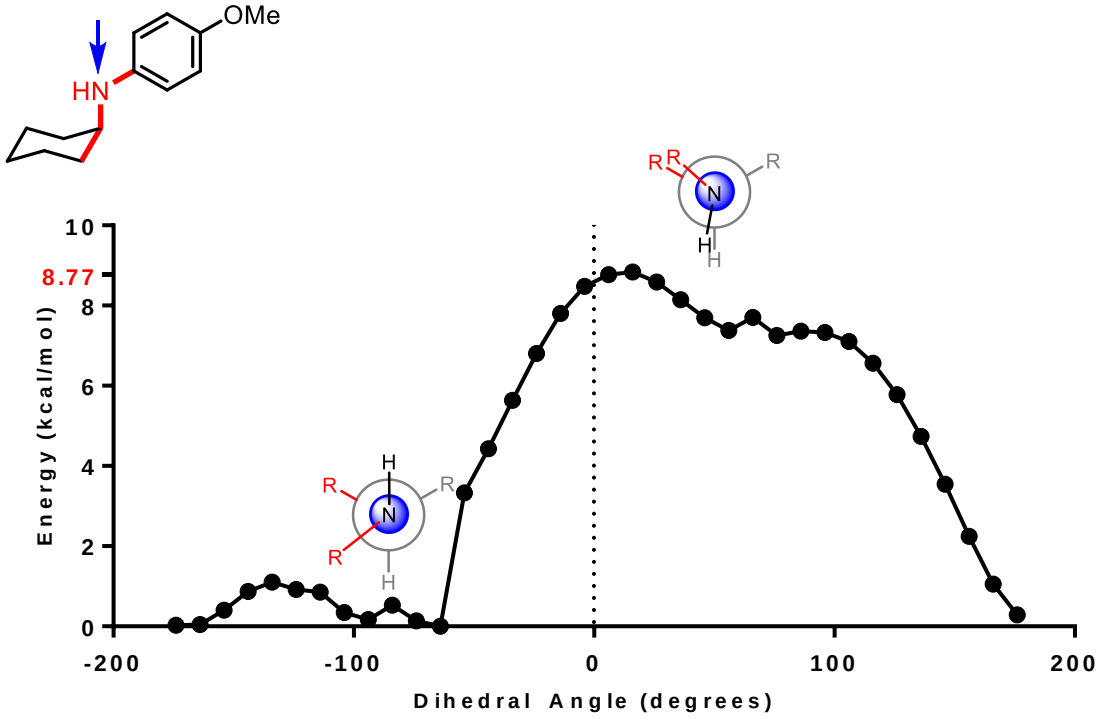
_N_-Cyclohexyl-4-methoxyaniline (10-_eq_, Ring Connection, Equatorial)



As a note, the nitrogen center inverts over the course of this scan. The dihedral is between the red groups.

C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)
-171	3.728418	-41	5.222918	89	0.707388
-161	4.505208	-31	5.802968	99	1.099118
-151	5.276978	-21	6.229238	109	1.150468
-141	5.849788	-11	6.313128	119	1.010658
-131	6.064288	-1	6.28334	129	0.793538
-121	5.822448	9	5.306038	139	0.516488
-111	5.159988	19	4.267258	149	0.433095
-101	4.424838	29	3.066668	159	2.822758
-91	3.938538	39	1.785238	169	2.840598
-81	4.011488	49	0.749098	179	3.112358
-71	3.967708	59	0.146147	89	0.707388
-61	4.189108	69	0		
-51	4.634308	79	0.257544		

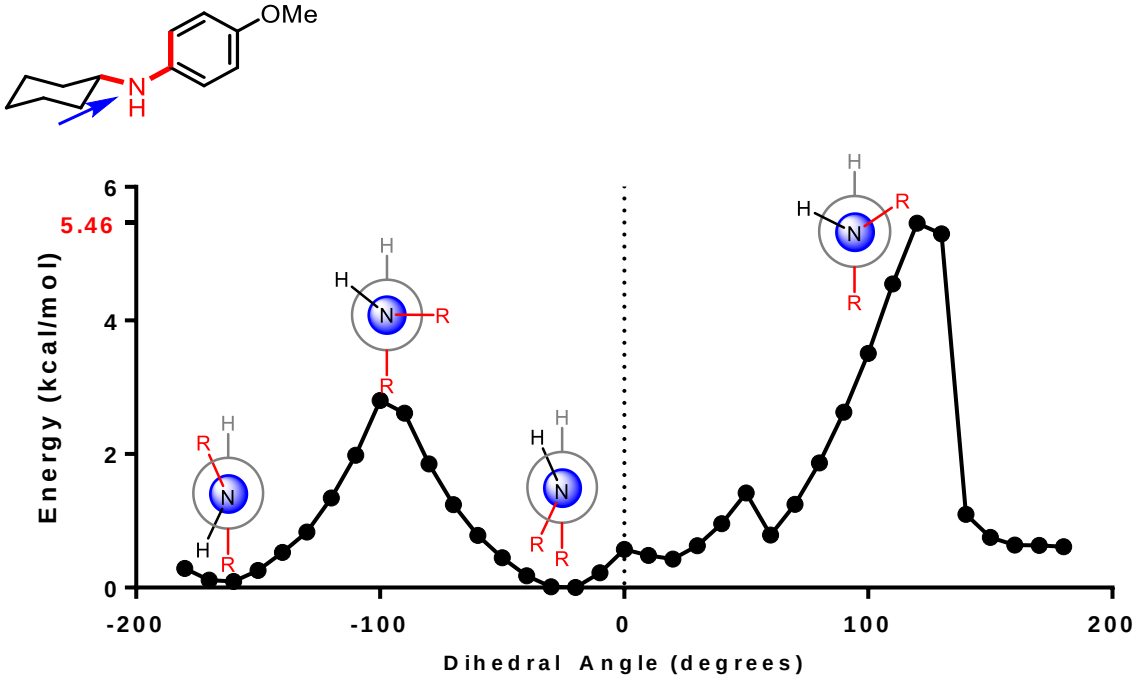
_N_-Cyclohexyl-4-methoxyaniline (10-_ax_, Ring Connection, Axial)



As a note, the nitrogen center inverts over the course of this scan. The dihedral is between the red groups.

C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)
-174	0.026684	-44	4.42992	86	7.35971
-164	0.04473	-34	5.6386	96	7.32869
-154	0.403874	-24	6.80499	106	7.10678
-144	0.86812	-14	7.80238	116	6.55886
-134	1.10599	-4	8.47822	126	5.78316
-124	0.92129	6	8.77203	136	4.73862
-114	0.85118	16	8.83345	146	3.54604
-104	0.34711	26	8.59144	156	2.24387
-94	0.173662	36	8.14842	166	1.05213
-84	0.529116	46	7.6986	176	0.283866
-74	0.134637	56	7.37744	86	7.35971
-64	0	66	7.70592		
-54	3.32692	76	7.25574		

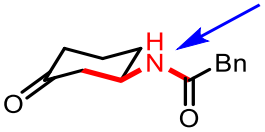
_N_-Cyclohexyl-4-methoxyaniline (10-_eq_, Pendant Group, Equatorial)

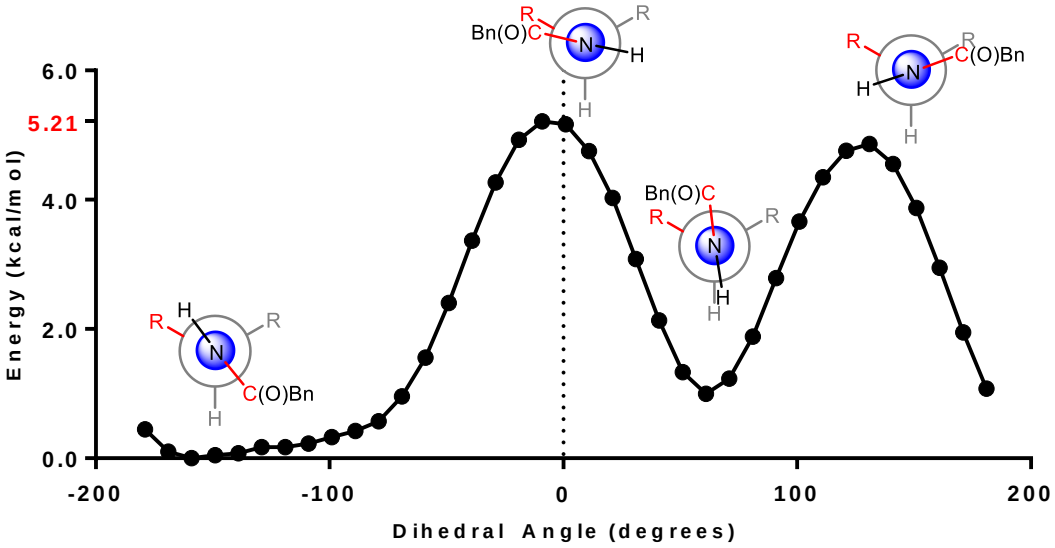


As a note, the nitrogen center inverts over the course of this scan. The dihedral is between the red groups.

C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)
-171	3.728418	-41	5.222918	89	0.707388
-161	4.505208	-31	5.802968	99	1.099118
-151	5.276978	-21	6.229238	109	1.150468
-141	5.849788	-11	6.313128	119	1.010658
-131	6.064288	-1	6.28334	129	0.793538
-121	5.822448	9	5.306038	139	0.516488
-111	5.159988	19	4.267258	149	0.433095
-101	4.424838	29	3.066668	159	2.822758
-91	3.938538	39	1.785238	169	2.840598
-81	4.011488	49	0.749098	179	3.112358
-71	3.967708	59	0.146147	89	0.707388
-61	4.189108	69	0		
-51	4.634308	79	0.257544		

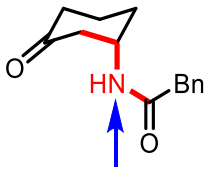
3-Phenylacetamidocyclohexanone (4a-*eq*, Ring Connection, Equatorial)

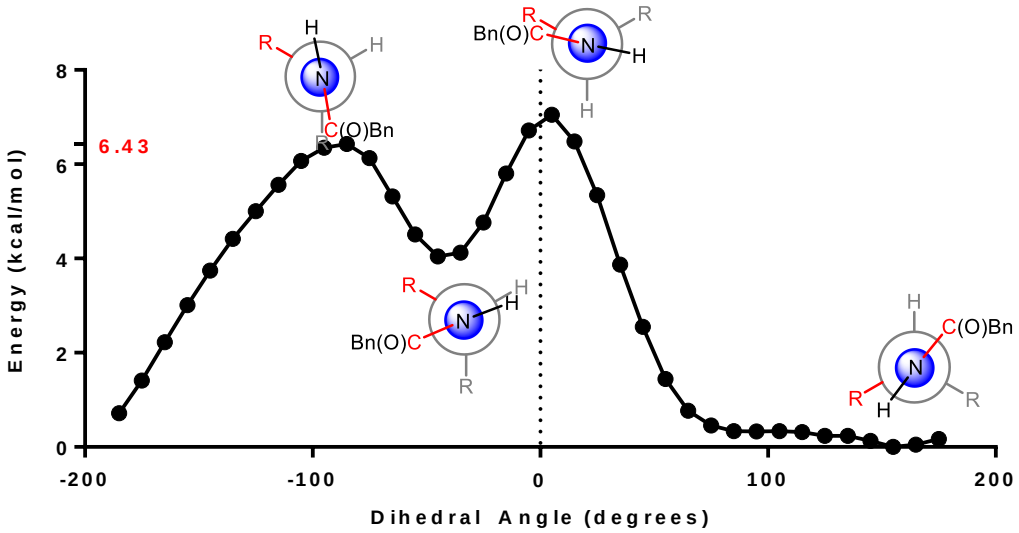




C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)
181	1.07759	51	1.33124	-79	0.57439
171	1.9453	41	2.13148	-89	0.420537
161	2.94592	31	3.08265	-99	0.329924
151	3.87012	21	4.02968	-109	0.227092
141	4.55274	11	4.75236	-119	0.172461
131	4.86062	1	5.16659	-129	0.172524
121	4.75769	-9	5.21122	-139	0.075323
111	4.34699	-19	4.9273	-149	0.049563
101	3.66222	-29	4.26766	-159	0
91	2.78655	-39	3.3655	-169	0.1025
81	1.88347	-49	2.40003	-179	0.445313
71	1.23013	-59	1.55708		
61	0.99762	-69	0.95876		

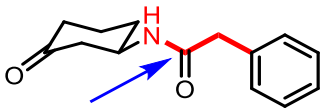
3-Phenylacetamidocyclohexanone (4a-*ax*, Ring Connection, Axial)

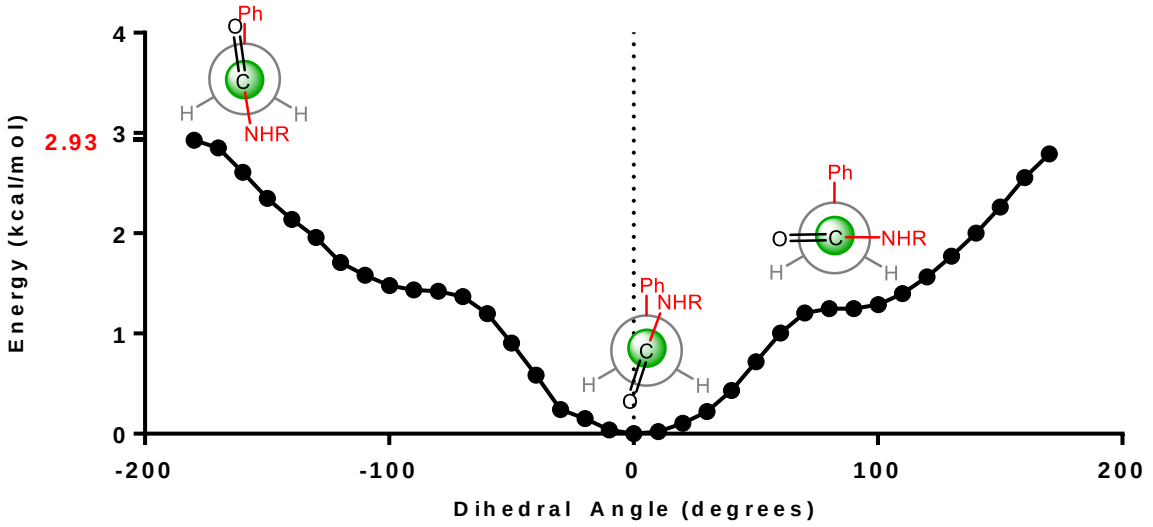




C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)
175	0.168812	45	2.548687	-85	6.432337
165	0.050373	35	3.867727	-95	6.351657
155	0	25	5.345097	-105	6.068087
145	0.130946	15	6.484757	-115	5.563577
135	0.23707	5	7.048567	-125	5.001067
125	0.236933	-5	6.713727	-135	4.416177
115	0.314085	-15	5.802997	-145	3.741057
105	0.336201	-25	4.761987	-155	3.008137
95	0.328625	-35	4.123757	-165	2.224157
85	0.337794	-45	4.045967	-175	1.408567
75	0.458013	-55	4.508897	-185	0.719983
65	0.770948	-65	5.316027		
55	1.446497	-75	6.132267		

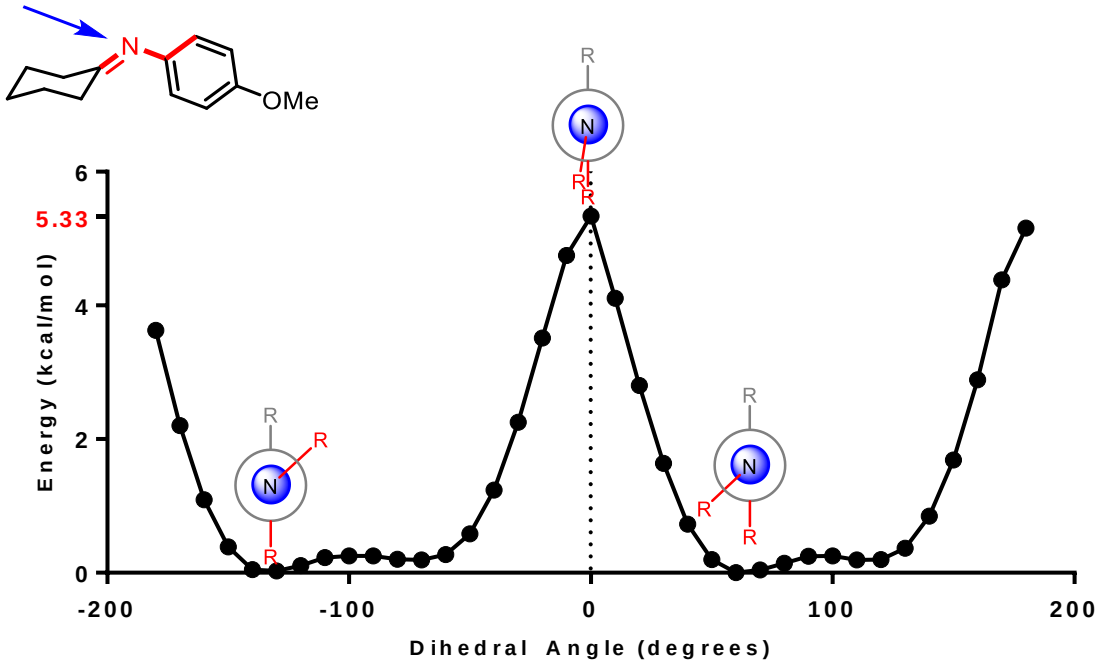
3-Phenylacetamido-Cyclohexanone (4a-*eq*, Pendant Group, Equatorial)





C-C Dihedral (°)	Total Energy (kcal/mol)	C-C Dihedral (°)	Total Energy (kcal/mol)	C-C Dihedral (°)	Total Energy (kcal/mol)
170.1	2.790515	40.1	0.432175	-89.9	1.434145
160.1	2.555405	30.1	0.222193	-99.9	1.478445
150.1	2.262865	20.1	0.10659	-109.9	1.581435
140.1	2.001495	10.1	0.020838	-119.9	1.707785
130.1	1.770075	0.1	0	-129.9	1.956845
120.1	1.566395	-9.9	0.039291	-139.9	2.138395
110.1	1.398525	-19.9	0.151717	-149.9	2.346875
100.1	1.287545	-29.9	0.243295	-159.9	2.609415
90.1	1.249075	-39.9	0.585865	-169.9	2.851165
80.1	1.248485	-49.9	0.906105	-179.9	2.928945
70.1	1.205515	-59.9	1.199115		
60.1	1.005125	-69.9	1.367945		
50.1	0.718015	-79.9	1.420815		

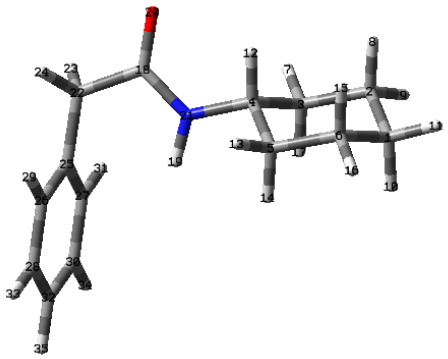
3-Phenylacetamido-Cycloheximine (S20)



C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)	C-N Dihedral (°)	Total Energy (kcal/mol)
-180	3.629519	-50	0.580009	80	0.144708
-170	2.201559	-40	1.235449	90	0.249572
-160	1.091568	-30	2.250619	100	0.253882
-150	0.388648	-20	3.510339	110	0.192838
-140	0.048023	-10	4.747619	120	0.196424
-130	0.027703	0	5.338299	130	0.368868
-120	0.10566	10	4.108809	140	0.848257
-110	0.227405	20	2.803499	150	1.688439
-100	0.253547	30	1.639299	160	2.887369
-90	0.253553	40	0.728078	170	4.384389
-80	0.204877	50	0.199626	180	5.156599
-70	0.194703	60	0		
-60	0.271299	70	0.043169		

8.3. Calculation of Relative Energies of Phenylcyclohexane Conformers (10-*eq*, 10-*ax*)

8.3.1. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [**10**-eq-PhMe, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-4.200613	-1.355929	0.229370	19	H	0.262171	-0.216118	-0.017560
2	C	-3.876256	-0.186003	1.168440	20	O	-0.433911	2.845425	-0.314841
3	C	-2.367204	0.094031	1.218784	21	N	-0.350184	0.577534	-0.143850
4	C	-1.792688	0.335735	-0.188073	22	C	1.747229	1.876208	-0.098736
5	C	-2.112837	-0.836754	-1.126749	23	H	1.956829	2.512945	0.765374
6	C	-3.621638	-1.122040	-1.172808	24	H	2.069835	2.441491	-0.977120
7	H	-2.156857	0.963074	1.848914	25	C	2.510335	0.576863	0.005500
8	H	-4.398185	0.714190	0.819785	26	C	2.948819	-0.092173	-1.144599
9	H	-4.249900	-0.390688	2.176612	27	C	2.786764	0.004549	1.254089
10	H	-3.780588	-2.281176	0.645268	28	C	3.639399	-1.299431	-1.051296
11	H	-5.283524	-1.504304	0.169292	29	H	2.751084	0.339678	-2.120539
12	H	-2.234067	1.250198	-0.592441	30	C	3.476731	-1.203128	1.351462
13	H	-1.732551	-0.617061	-2.129027	31	H	2.463551	0.512800	2.157107
14	H	-1.584438	-1.733225	-0.773616	32	C	3.904645	-1.859530	0.198063
15	H	-4.133538	-0.270052	-1.637886	33	H	3.974961	-1.799083	-1.953244
16	H	-3.814298	-1.987623	-1.814332	34	H	3.685277	-1.627105	2.327466
17	H	-1.849443	-0.762938	1.670098	35	H	4.445453	-2.796166	0.272350
18	C	0.212447	1.808441	-0.195252					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –675.13604022 a.u.
RMS Gradient Norm= 0.00000217 a.u.
Imaginary Freq= 0
Dipole Moment= 4.5348 Debye
Point Group= C1
Job cpu time= 8 hours 4 minutes 5.6 seconds

Zero-point correction= 0.305403 (Hartree/Particle)
Thermal correction to Energy= 0.320223
Thermal correction to Enthalpy= 0.321167
Thermal correction to Gibbs Free Energy= 0.260410
Sum of electronic and zero-point Energies= -674.830637
Sum of electronic and thermal Energies= -674.815817
Sum of electronic and thermal Enthalpies= -674.814873
Sum of electronic and thermal Free Energies= -674.875630

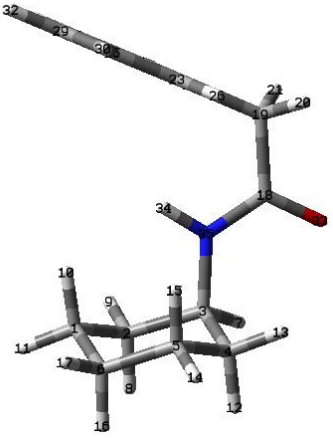
8.3.2. *Single Point Energy Calculation in PhMe [**10**-eq, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –674.86312761 a.u.
Dipole Moment= 4.5168 Debye
Point Group= C1
Job cpu time= 1 hours 50 minutes 54.1 seconds

From **Section 8.3.1.**:
Thermal correction to Gibbs free energy= 0.260410

Sum of electronic and thermal free energies= –674.86312761 + 0.260410 = **–674.602718 a.u**.

8.3.3. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [**10**-ax, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	2.107154	-1.874740	-0.892920	19	C	-1.448886	2.001486	0.240404
2	C	2.333576	-0.495732	-1.534188	20	H	-1.584724	2.456688	1.225253
3	C	2.086447	0.667787	-0.559268	21	H	-1.861358	2.712561	-0.480557
4	C	2.895602	0.476419	0.740191	22	C	-2.176290	0.680831	0.160636
5	C	2.654240	-0.895643	1.384231	23	C	-2.316406	-0.131965	1.293015
6	C	2.927669	-2.038720	0.395425	24	C	-2.714177	0.228243	-1.051091
7	H	2.394349	1.606940	-1.022888	25	C	-2.967897	-1.361827	1.216722
8	H	3.373992	-0.429529	-1.872421	26	H	-1.915678	0.205568	2.243733
9	H	1.706099	-0.371925	-2.422454	27	C	-3.366546	-1.000817	-1.131613
10	H	1.042545	-2.018372	-0.664796	28	H	-2.623971	0.847855	-1.937736
11	H	2.364385	-2.659413	-1.611414	29	C	-3.493978	-1.801049	0.002779
12	H	3.959372	0.579613	0.491971	30	H	-3.070138	-1.973492	2.106284
13	H	2.653770	1.286083	1.433194	31	H	-3.779985	-1.330140	-2.078437
14	H	3.284505	-1.004672	2.272418	32	H	-4.004834	-2.755348	-0.057139
15	H	1.616649	-0.958007	1.735678	33	O	0.695927	3.055467	0.054438
16	H	3.995912	-2.047448	0.141748	34	H	0.061663	-0.009386	-0.305356
17	H	2.710578	-3.005678	0.860606	35	N	0.650164	0.809624	-0.291675
18	C	0.072544	2.005227	-0.006235					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –675.13360998 a.u.
RMS Gradient Norm= 0.00000732 a.u.
Imaginary Freq= 0
Dipole Moment= 4.6895 Debye
Point Group= C1
Job cpu time= 9 hours 42 minutes 25.5 seconds

Zero-point correction= 0.305668 (Hartree/Particle)
Thermal correction to Energy= 0.320323
Thermal correction to Enthalpy= 0.321267
Thermal correction to Gibbs Free Energy= 0.262023
Sum of electronic and zero-point Energies= -674.827942
Sum of electronic and thermal Energies= -674.813287
Sum of electronic and thermal Enthalpies= -674.812343
Sum of electronic and thermal Free Energies= -674.871587

8.3.4. *Single Point Energy Calculation in PhMe [**10**-ax-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x

Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –674.86247942 a.u.
Dipole Moment= 4.6721 Debye
Point Group= C1
Job cpu time= 1 hours 59 minutes 34.3 seconds

From **Section 3.3.3.**:
Thermal correction to Gibbs free energy= 0.262023

Sum of electronic and thermal free energies= –674.86247942 + 0.262023 = **–674.600456 a.u**.

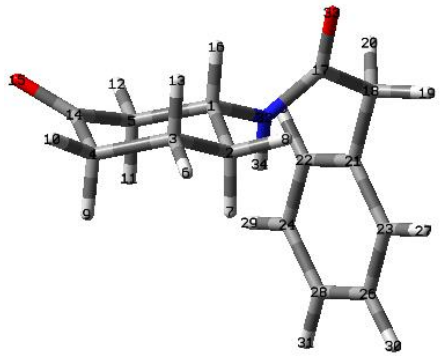
8.3.5. *Calculation of ΔG°, K, and Equilibrium Ratio Between **10**-eq and **10**-ax using M06-2X/6-311++G(2d,3p) Single-point Energies:*

10-*eq*: From **Section 8.3.2.**: $G^{\circ}_{eq} = -674.602718$
10-*ax*: From **Section 8.3.4.**: $G^{\circ}_{ax} = -674.600456$

Using Equation 1: $\Delta G^{\circ} = (-674.600456 + 674.602718)\left(\frac{627.51\ kcal}{mol \cdot a.u.}\right) = -1.42\ kcal/mol$
Using Equation 2: $K = 0.0911$
Using Equation 3: **10**-*eq* : **10**-*ax* → **92**:**8**

8.4. Calculation of Relative Energies of 3-Phenylacetamidocyclohexanone Conformers (4a-*eq*, 4a-*ax*)

8.4.1. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [**4a**-eq-PhMe, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-1.560582	0.477193	-0.044498	18	C	2.032218	1.792837	-0.515529
2	C	-2.088885	0.552095	1.396654	19	H	2.344068	2.593316	0.161013
3	C	-3.611833	0.379247	1.432188	20	H	2.300041	2.125501	-1.522009
4	C	-4.055749	-0.946487	0.783176	21	C	2.743292	0.504208	-0.175239
5	C	-1.970351	-0.848081	-0.719409	22	C	3.031419	-0.440120	-1.169413
6	H	-3.971797	0.417528	2.463376	23	C	3.120514	0.219248	1.143451
7	H	-1.608364	-0.229610	1.999106	24	C	3.672883	-1.637012	-0.854700
8	H	-1.805449	1.514197	1.831017	25	H	2.755560	-0.233261	-2.198580
9	H	-3.698979	-1.784874	1.397031	26	C	3.762239	-0.976975	1.461861
10	H	-5.141609	-1.026124	0.713017	27	H	2.915985	0.943716	1.925424
11	H	-1.450271	-1.677378	-0.218781	28	C	4.039157	-1.909684	0.463057
12	H	-1.688847	-0.861193	-1.773200	29	H	3.891646	-2.353073	-1.638966
13	H	-4.084995	1.215378	0.905138	30	H	4.052220	-1.176325	2.487483
14	C	-3.461861	-1.125785	-0.600821	31	H	4.542104	-2.838222	0.708142
15	O	-4.122592	-1.480191	-1.556345	32	N	-0.112320	0.639911	-0.115949
16	H	-1.979225	1.311598	-0.612058	33	O	-0.120566	2.816341	-0.777313
17	C	0.495067	1.798461	-0.480498	34	H	0.474245	-0.144606	0.132074

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –749.17359328 a.u.
RMS Gradient Norm= 0.00000858 a.u.
Imaginary Freq= 0
Dipole Moment= 6.0272 Debye
Point Group= C1
Job cpu time= 8 hours 44 minutes 38.2 seconds

Zero-point correction= 0.286418 (Hartree/Particle)
Thermal correction to Energy= 0.301926
Thermal correction to Enthalpy= 0.302870
Thermal correction to Gibbs Free Energy= 0.240667
Sum of electronic and zero-point Energies= -748.887176
Sum of electronic and thermal Energies= -748.871667
Sum of electronic and thermal Enthalpies= -748.870723
Sum of electronic and thermal Free Energies= -748.932926

8.4.2. *Single Point Energy Calculation in PhMe [**4a**-eq-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

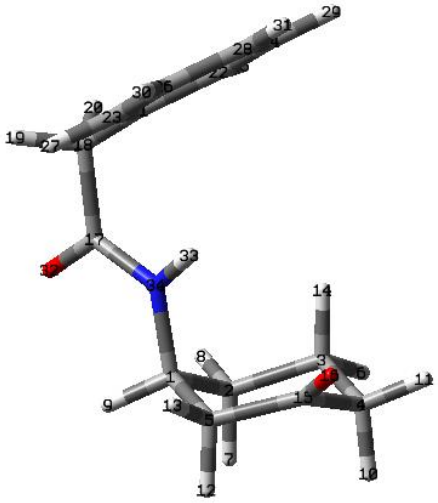
Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)

Charge= 0
Spin= Singlet
E(RM062x)= –748.88205751 a.u.
Dipole Moment= 5.9610 Debye
Point Group= C1
Job cpu time= 1 hours 47 minutes 41.7 seconds

From **Section 8.4.1.**:
Thermal correction to Gibbs free energy= 0.240667

Sum of electronic and thermal free energies= –748.88205751 + 0.240667 = **–748.641391 a.u**.

8.4.3. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [**4a**-ax-PhMe, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	1.955393	0.830796	-0.641624	18	C	-1.619239	2.056034	0.128129
2	C	2.828760	0.928315	0.623732	19	H	-2.074749	2.705753	-0.624172
3	C	2.677130	-0.299134	1.527665	20	H	-1.753473	2.563474	1.087587
4	C	2.990132	-1.607128	0.772355	21	C	-2.295706	0.705446	0.143195
5	C	2.241495	-0.474830	-1.409662	22	C	-2.416504	-0.024777	1.332475
6	H	3.337296	-0.213642	2.394682	23	C	-2.809232	0.148906	-1.035446
7	H	3.874311	1.031889	0.309328	24	C	-3.026498	-1.278384	1.343367
8	H	2.568470	1.841542	1.163088	25	H	-2.035529	0.395343	2.258044
9	H	2.179457	1.681917	-1.287272	26	C	-3.418881	-1.104438	-1.028236
10	H	4.055756	-1.620406	0.505696	27	H	-2.734206	0.704382	-1.964973
11	H	2.788162	-2.492089	1.377930	28	C	-3.528154	-1.822642	0.161940
12	H	3.255899	-0.403965	-1.820113	29	H	-3.113192	-1.827300	2.274404
13	H	1.552983	-0.609888	-2.245695	30	H	-3.811102	-1.517954	-1.950551
14	H	1.655507	-0.344606	1.919909	31	H	-4.002712	-2.797181	0.169062
15	C	2.206688	-1.711024	-0.521958	32	O	0.474230	3.179438	-0.210478
16	O	1.595996	-2.712389	-0.841173	33	H	-0.030544	0.071227	-0.293383
17	C	-0.109198	2.101690	-0.153843	34	N	0.524107	0.914590	-0.330414

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –749.17216200 a.u.
RMS Gradient Norm= 0.00000878 a.u.
Imaginary Freq= 0
Dipole Moment= 1.7764 Debye
Point Group= C1
Job cpu time= 9 hours 59 minutes 21.8 seconds

Zero-point correction= 0.286463 (Hartree/Particle)
Thermal correction to Energy= 0.301888
Thermal correction to Enthalpy= 0.302832
Thermal correction to Gibbs Free Energy= 0.241144
Sum of electronic and zero-point Energies= -748.885699
Sum of electronic and thermal Energies= -748.870274
Sum of electronic and thermal Enthalpies= -748.869330
Sum of electronic and thermal Free Energies= -748.931018

8.4.4. *Single Point Energy Calculation in PhMe [**4a**-ax-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)

Charge= 0
Spin= Singlet
E(RM062x)= –748.88256752 a.u.
Dipole Moment= 1.7871 Debye
Point Group= C1
Job cpu time= 2 hours 1 minute 32.6 seconds

From **Section 8.4.1.**:
Thermal correction to Gibbs free energy= 0.241144

Sum of electronic and thermal free energies= –748.88256752 + 0.241144 = **–748.641424 a.u**.

8.4.5. *Calculation of ΔG°, K, and Equilibrium Ratio Between **4a**-eq and **4a**-ax using M06-2X/6-311++G(2d,3p) Single-point Energies:*

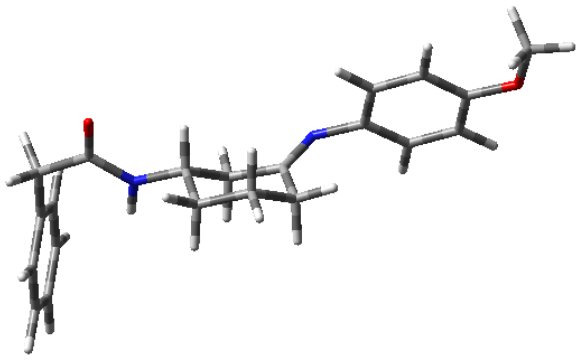
4a-*eq*: From **Section 8.4.2.**: $G^\circ_{eq} = -748.641391$
4a-*ax*: From **Section 8.4.4.**: $G^\circ_{ax} = -748.641424$

Using Equation 1: $\Delta G^\circ = (-748.641424 + 748.641391)\left(\frac{627.51\ kcal}{mol \cdot a.u.}\right) = -0.0207\ kcal/mol$
Using Equation 2: $K = 1.04$
Using Equation 3: **4a**-*eq* : **4a**-*ax*→ **49**:**51**

8.5. Overview of Calculations of the Relative Energies of 3-Amidocycloheximine Conformers [*E*-8a-*eq*, *Z*-8a-*eq*, *E*-8a-*ax*, *Z*-8a-*ax*]

8.5.1. Calculations for Equatorial (*E*)-3-Phenylacetamidocyclohexanone [*E*-8a-*eq*]

8.5.1.1. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [E-**8a**-eq-gas, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-1.383504	-0.390603	1.572420	26	O	-7.464421	0.660892	-0.018723
2	C	-0.642278	-1.737481	1.693808	27	C	-8.222072	-0.513839	-0.263018
3	C	0.862211	-1.587431	1.439736	28	H	-9.261840	-0.240440	-0.089626
4	C	1.129773	-0.940284	0.071161	29	H	-8.106730	-0.858585	-1.296938
5	C	0.409273	0.415462	-0.052409	30	H	-7.941834	-1.322147	0.422127
6	H	-0.816436	-2.161575	2.686805	31	N	-1.900138	0.772204	-0.579990
7	H	-1.041752	0.273399	2.378450	32	C	3.318659	-1.716165	-0.791162
8	H	-2.458980	-0.519568	1.693288	33	C	4.804703	-1.376726	-1.009756
9	H	1.312919	-0.964381	2.223456	34	O	2.874923	-2.792131	-1.163760
10	H	1.356236	-2.561588	1.475865	35	H	4.959703	-1.443024	-2.090442
11	H	0.760619	-1.614654	-0.706700	36	H	5.361621	-2.209823	-0.573280
12	H	0.855774	1.117220	0.667992	37	C	5.315260	-0.057815	-0.480063
13	H	0.530032	0.835080	-1.051868	38	C	5.247866	1.104737	-1.259042
14	H	-1.063663	-2.447965	0.973248	39	C	5.854417	0.037759	0.809205
15	C	-1.067690	0.294862	0.258094	40	C	5.699253	2.326737	-0.763466
16	C	-3.299188	0.685676	-0.387827	41	H	4.842225	1.050044	-2.264400
17	C	-4.001466	-0.492044	-0.646146	42	C	6.308147	1.257653	1.307806
18	C	-4.027446	1.833270	-0.038583	43	H	5.924846	-0.853413	1.425020
19	C	-5.393989	-0.542539	-0.535505	44	C	6.230452	2.407107	0.522891
20	H	-3.458658	-1.379284	-0.952575	45	H	5.642056	3.213823	-1.384409
21	C	-5.407494	1.787825	0.085410	46	H	6.727017	1.308833	2.306700
22	H	-3.496934	2.762635	0.134375	47	H	6.586266	3.355942	0.907997
23	C	-6.103830	0.598692	-0.161434	48	N	2.555244	-0.764069	-0.190338
24	H	-5.902537	-1.473510	-0.747856	49	H	3.004447	0.086421	0.117071
25	H	-5.970503	2.670411	0.365126					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.93768906 a.u.
RMS Gradient Norm= 0.00000330 a.u.
Imaginary Freq= 0
Dipole Moment= 3.3110 Debye
Point Group= C1
Job cpu time= 1 day 17 hours 47 minutes 15.5 seconds

Zero-point correction= 0.411025 (Hartree/Particle)
Thermal correction to Energy= 0.434045
Thermal correction to Enthalpy= 0.434989
Thermal correction to Gibbs Free Energy= 0.353194
Sum of electronic and zero-point Energies= -1074.526664
Sum of electronic and thermal Energies= -1074.503644

Sum of electronic and thermal Enthalpies= -1074.502700
Sum of electronic and thermal Free Energies= -1074.584495

8.5.1.2. *Single Point Energy Calculation in the Gas Phase [E-***8a***-eq-gas, M06-2x/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.52784267 a.u.
Dipole Moment= 3.3268 Debye
Point Group= C1
Job cpu time= 4 hours 38 minutes 36.2 seconds

From **Section 8.5.1.1.**:
Thermal correction to Gibbs free energy= 0.353194

Sum of electronic and thermal free energies= –1074.52784267 + 0.353194 = **–1074.174649 a.u**.

8.5.1.3. *Single Point Energy Calculation in the Gas Phase [E-***8a***-eq-gas, B3LYP/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.97514250 a.u.
Dipole Moment= 3.6837 Debye
Point Group= C1
Job cpu time= 4 hours 25 minutes 48.5 seconds

From **Section 8.5.1.1.**:
Thermal correction to Gibbs free energy= 0.353194

Sum of electronic and thermal free energies= –1074.97514250 + 0.353194 = **–1074.621949 a.u**.

8.5.1.4. *Single Point Energy Calculation in the Gas Phase [E-***8a***-eq-gas, MP2/6-311+G(2d,3p)]*

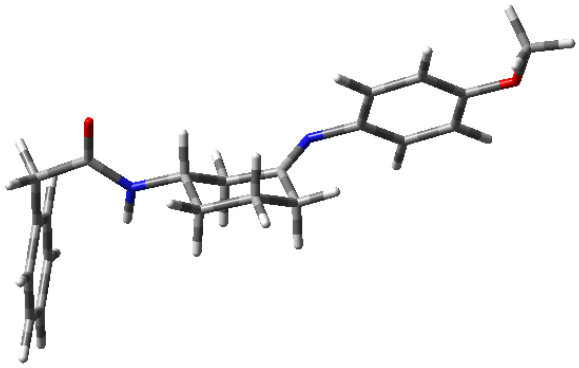
Calculation Type= SP
Calculation Method= RMP2–FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

Spin= Singlet
E(MP2)= – 1072.05755474 a.u.
Dipole Moment= 4.1450 Debye
Point Group= C1
Job cpu time= 20 hours 25 minutes 21.4 seconds

From **Section 8.5.1.1.**:
Thermal correction to Gibbs free energy= 0.353194

Sum of electronic and thermal free energies= – 1072.05755474 + 0.353194 = **–1071.704361 a.u**.

8.5.1.5. *Geometry Optimization and Vibrational Frequency Calculation in PhMe [E-***8a***-eq-PhMe, B3LYP/6-311+G(d,p), IEF-PCM Solvation Model]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-1.367431	-0.312174	1.601522	26	O	-7.466715	0.651051	-0.055322
2	C	-0.636149	-1.659695	1.768415	27	C	-8.214454	-0.552051	-0.190002
3	C	0.867114	-1.532219	1.494403	28	H	-9.257481	-0.272206	-0.052335
4	C	1.127721	-0.936533	0.101354	29	H	-8.085689	-0.992944	-1.184231
5	C	0.413861	0.419752	-0.064159	30	H	-7.932068	-1.285072	0.573233
6	H	-0.802678	-2.040436	2.779805	31	N	-1.899007	0.756709	-0.597437
7	H	-1.007257	0.381425	2.373427	32	C	3.287521	-1.687061	-0.865320
8	H	-2.441569	-0.427105	1.744109	33	C	4.777802	-1.364628	-1.067032
9	H	1.329929	-0.885513	2.251102	34	O	2.818237	-2.721808	-1.327631
10	H	1.352152	-2.509395	1.564751	35	H	4.937649	-1.399583	-2.148226
11	H	0.751153	-1.632508	-0.652328	36	H	5.321097	-2.218095	-0.652556
12	H	0.866837	1.141636	0.630799	37	C	5.306682	-0.070502	-0.494671
13	H	0.536663	0.803180	-1.077631	38	C	5.243012	1.118688	-1.233112
14	H	-1.070972	-2.394741	1.081514	39	C	5.862154	-0.027040	0.790564
15	C	-1.061371	0.315016	0.257065	40	C	5.713868	2.317751	-0.700713
16	C	-3.298188	0.673405	-0.400679	41	H	4.825092	1.103284	-2.234713
17	C	-3.990939	-0.530290	-0.542606	42	C	6.335058	1.170453	1.325939
18	C	-4.037326	1.844417	-0.171915	43	H	5.930504	-0.940024	1.373668
19	C	-5.383876	-0.580297	-0.436366	44	C	6.260615	2.347358	0.581922
20	H	-3.440837	-1.440738	-0.752781	45	H	5.659375	3.226569	-1.289583
21	C	-5.418218	1.801002	-0.050679	46	H	6.766257	1.182422	2.320778
22	H	-3.515418	2.790923	-0.088493	47	H	6.631134	3.278447	0.995503
23	C	-6.104570	0.587367	-0.182120	48	N	2.553351	-0.780281	-0.173447
24	H	-5.884734	-1.531472	-0.557524	49	H	3.028025	0.032476	0.193856
25	H	-5.987070	2.704214	0.136826					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.94582698 a.u.
RMS Gradient Norm= 0.00000178 a.u.
Imaginary Freq= 0
Dipole Moment= 4.2899 Debye
Point Group= C1
Job cpu time= 2 days 0 hours 3 minutes 59.7 seconds

Zero-point correction= 0.410975 (Hartree/Particle)
Thermal correction to Energy= 0.433945
Thermal correction to Enthalpy= 0.434889
Thermal correction to Gibbs Free Energy= 0.353483
Sum of electronic and zero-point Energies= -1074.534852
Sum of electronic and thermal Energies= -1074.511882

Sum of electronic and thermal Enthalpies= -1074.510938
Sum of electronic and thermal Free Energies= -1074.592344

8.5.1.6. *Single Point Energy Calculation in PhMe [E-***8a-***eq-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.53549318 a.u.
Dipole Moment= 4.2875 Debye
Point Group= C1
Job cpu time= 4 hours 52 minutes 30.3 seconds

From **Section 8.5.1.5.**:
Thermal correction to Gibbs free energy= 0.353483

Sum of electronic and thermal free energies= –1074.53549318 +0.353483 = **–1074.182010 a.u**.

8.5.1.7. *Single Point Energy Calculation in PhMe [E-***8a-***eq-PhMe, B3LYP/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.98295081 a.u.
Dipole Moment= 4.2480 Debye
Point Group= C1
Job cpu time= 4 hours 24 minutes 35.3 seconds

From **Section 8.5.1.5.**:
Thermal correction to Gibbs free energy= 0.353483

Sum of electronic and thermal free energies= –1074.98295081 + 0.353483 = **–1074.629468 a.u**.

8.5.1.8. *Single Point Energy Calculation in PhMe [E-***8a-***eq-PhMe, MP2/6-311+G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RMP2–FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

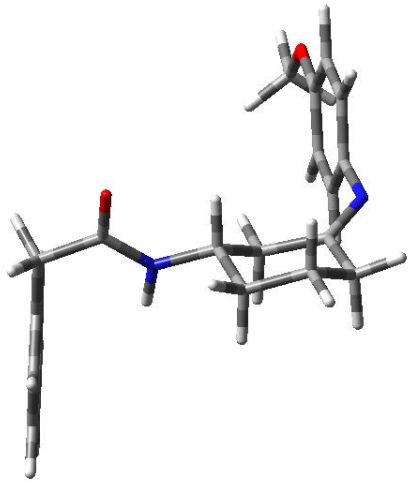
Spin= Singlet
E(MP2)= –1072.06505596 a.u.
Dipole Moment= 4.7210 Debye
Point Group= C1
Job cpu time= 18 hours 3 minutes 23.6 seconds

From **Section 8.5.1.5.**:
Thermal correction to Gibbs free energy= 0.353483

Sum of electronic and thermal free energies= –1072.06505596 + 0.353483 = **–1071.711573 a.u**.

8.5.2. Calculations for Equatorial (*Z*)-3-Phenylacetamidocyclohexanone [*Z*-8a-*eq*]

8.5.2.1. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [Z-**8a**-eq-gas, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-0.645815	3.547072	-1.424423	26	O	-5.265393	-2.449473	0.803205
2	C	0.454681	4.084401	-0.491580	27	C	-5.303650	-3.628834	0.015064
3	C	1.541793	3.033506	-0.241185	28	H	-5.935501	-4.330518	0.557536
4	C	0.933995	1.740898	0.324682	29	H	-5.739855	-3.437785	-0.972010
5	C	-0.165646	1.176472	-0.599642	30	H	-4.304624	-4.062757	-0.107580
6	H	0.894546	4.988528	-0.922035	31	N	-2.470631	2.117590	-0.803522
7	H	-0.214100	3.381168	-2.421764	32	C	2.562038	0.550411	1.765742
8	H	-1.466170	4.257308	-1.534831	33	C	3.604925	-0.579035	1.858335
9	H	2.063523	2.804557	-1.180113	34	O	2.317410	1.239048	2.744675
10	H	2.290229	3.410861	0.460505	35	H	3.244282	-1.241011	2.650666
11	H	0.498203	1.965013	1.301880	36	H	4.510994	-0.107560	2.247702
12	H	0.301529	0.847300	-1.539375	37	C	3.909343	-1.366032	0.606010
13	H	-0.629222	0.302906	-0.140814	38	C	3.176252	-2.514908	0.281732
14	H	0.005559	4.379432	0.463845	39	C	4.922468	-0.955921	-0.270216
15	C	-1.207344	2.232600	-0.931697	40	C	3.443215	-3.229694	-0.884702
16	C	-3.099543	0.916750	-0.408358	41	H	2.393222	-2.854473	0.952401
17	C	-3.096286	-0.225732	-1.210661	42	C	5.192823	-1.668282	-1.437262
18	C	-3.861005	0.897872	0.771438	43	H	5.508681	-0.073949	-0.031750
19	C	-3.810074	-1.370536	-0.844746	44	C	4.452272	-2.807542	-1.748977
20	H	-2.548710	-0.218512	-2.146691	45	H	2.867824	-4.119644	-1.114424
21	C	-4.554264	-0.239526	1.152043	46	H	5.985205	-1.337074	-2.099269
22	H	-3.898694	1.789573	1.386392	47	H	4.663857	-3.365121	-2.654273
23	C	-4.536800	-1.384717	0.345948	48	N	1.942175	0.712824	0.565081
24	H	-3.789972	-2.232190	-1.498816	49	H	2.233210	0.128410	-0.205373
25	H	-5.131240	-0.259289	2.068967					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.93757447 a.u.
RMS Gradient Norm= 0.00000307 a.u.
Imaginary Freq= 0
Dipole Moment= 5.5514 Debye
Point Group= C1
Job cpu time= 1 day 21 hours 25 minutes 42.2 seconds

Zero-point correction= 0.411029 (Hartree/Particle)
Thermal correction to Energy= 0.434011
Thermal correction to Enthalpy= 0.434956
Thermal correction to Gibbs Free Energy= 0.353995
Sum of electronic and zero-point Energies= -1074.526545
Sum of electronic and thermal Energies= -1074.503563

Sum of electronic and thermal Enthalpies= -1074.502619
Sum of electronic and thermal Free Energies= -1074.583579

8.5.2.2. *Single Point Energy Calculation in the Gas Phase [Z-***8a-***eq-gas, M06-2x/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.52754083 a.u.
Dipole Moment= 5.4525 Debye
Point Group= C1
Job cpu time= 4 hours 59 minutes 34.2 seconds

From **Section 8.5.2.1.**:
Thermal correction to Gibbs free energy= 0.353995

Sum of electronic and thermal free energies= –1074.52754083 + 0.353995 = **–1074.173546 a.u**.

8.5.2.3. *Single Point Energy Calculation in the Gas Phase [Z-***8a-***eq-gas, B3LYP/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= – 1074.97505935 a.u.
Dipole Moment= 5.4471 Debye
Point Group= C1
Job cpu time= 4 hours 46 minutes 34.7 seconds

From **Section 8.5.2.1.**:
Thermal correction to Gibbs free energy= 0.353995

Sum of electronic and thermal free energies= – 1074.97505935 + 0.353995 = **–1074.621064 a.u**.

8.5.2.4. *Single Point Energy Calculation in the Gas Phase [Z-***8a-***eq-gas, MP2/6-311+G(2d,3p)]*

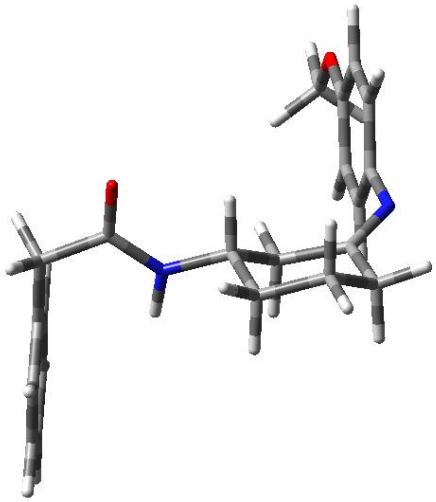
Calculation Type= SP
Calculation Method= RMP2–FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

Spin= Singlet
E(MP2)= – 1072.05775965 a.u.
Dipole Moment= 6.1586 Debye
Point Group= C1
Job cpu time= 19 hours 26 minutes 31.4 seconds

From **Section 8.5.2.1.**:
Thermal correction to Gibbs free energy= 0.353995

Sum of electronic and thermal free energies= –1072.05775965 + 0.353995 = **–1071.703765 a.u**.

8.5.2.5. *Geometry Optimization and Vibrational Frequency Calculation in PhMe [Z-***8a***-eq-PhMe, B3LYP/6-311+G(d,p), IEF-PCM Solvation Model]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-0.634175	3.557761	-1.418426	26	O	-5.244101	-2.458160	0.783267
2	C	0.466935	4.098568	-0.488458	27	C	-5.285354	-3.632599	-0.018994
3	C	1.553646	3.048246	-0.234460	28	H	-5.915258	-4.339247	0.518595
4	C	0.944707	1.760377	0.340097	29	H	-5.725057	-3.429171	-1.001186
5	C	-0.157905	1.192232	-0.579900	30	H	-4.286740	-4.063481	-0.148359
6	H	0.907105	4.999271	-0.925022	31	N	-2.462329	2.127126	-0.803241
7	H	-0.202310	3.384911	-2.414203	32	C	2.511472	0.498430	1.795511
8	H	-1.451292	4.271095	-1.533424	33	C	3.564922	-0.619845	1.870676
9	H	2.072744	2.814329	-1.173229	34	O	2.211443	1.124487	2.806438
10	H	2.304322	3.431229	0.462020	35	H	3.206973	-1.304202	2.644702
11	H	0.511316	1.987113	1.317086	36	H	4.464507	-0.148095	2.275380
12	H	0.307871	0.855501	-1.516951	37	C	3.886953	-1.375260	0.602808
13	H	-0.621857	0.322889	-0.113870	38	C	3.161274	-2.519401	0.246102
14	H	0.018993	4.398870	0.465757	39	C	4.909752	-0.942652	-0.251185
15	C	-1.197203	2.246289	-0.921468	40	C	3.445378	-3.208855	-0.931655
16	C	-3.087023	0.921594	-0.409548	41	H	2.371130	-2.875396	0.899506
17	C	-3.083810	-0.215809	-1.219654	42	C	5.196738	-1.629723	-1.430047
18	C	-3.842983	0.892749	0.773387	43	H	5.490253	-0.064345	0.013138
19	C	-3.793999	-1.364694	-0.859569	44	C	4.463959	-2.764948	-1.774432
20	H	-2.536539	-0.202857	-2.155763	45	H	2.876014	-4.095565	-1.187304
21	C	-4.534195	-0.249011	1.147878	46	H	5.996067	-1.282074	-2.074995
22	H	-3.878903	1.777970	1.397983	47	H	4.688867	-3.302778	-2.688443
23	C	-4.518163	-1.388401	0.333126	48	N	1.953158	0.731896	0.581109
24	H	-3.772565	-2.222217	-1.518865	49	H	2.281072	0.186300	-0.203613
25	H	-5.106805	-0.274105	2.067606					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.94572757 a.u.
RMS Gradient Norm= 0.00000310 a.u.
Imaginary Freq= 0
Dipole Moment= 6.5238 Debye
Point Group= C1
Job cpu time= 2 days 2 hours 31 minutes 2.7 seconds

Zero-point correction= 0.411045 (Hartree/Particle)
Thermal correction to Energy= 0.433977
Thermal correction to Enthalpy= 0.434921
Thermal correction to Gibbs Free Energy= 0.354235
Sum of electronic and zero-point Energies= -1074.534682
Sum of electronic and thermal Energies= -1074.511751

Sum of electronic and thermal Enthalpies= -1074.510807
Sum of electronic and thermal Free Energies= -1074.591493

8.5.2.6. *Single Point Energy Calculation in PhMe [Z-***8a-***eq-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.53530951 a.u.
Dipole Moment= 6.4058 Debye
Point Group= C1
Job cpu time= 5 hours 14 minutes 25.7 seconds

From **Section 8.5.2.5.**:
Thermal correction to Gibbs free energy= 0.354235

Sum of electronic and thermal free energies= –1074.53530951 + 0.354235 = **–1074.181075 a.u**.

8.5.2.7. *Single Point Energy Calculation in PhMe [Z-***8a-***eq-PhMe, B3LYP/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.98286924 a.u.
Dipole Moment= 6.3276 Debye
Point Group= C1
Job cpu time= 5 hours 2 minutes 8.4 seconds

From **Section 8.5.2.5.**:
Thermal correction to Gibbs free energy= 0.354235

Sum of electronic and thermal free energies= –1074.98286924 + 0.354235 = **–1074.628634 a.u**.

8.5.2.8. *Single Point Energy Calculation in PhMe [Z-***8a-***eq-PhMe, MP2/6-311+G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RMP2–FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

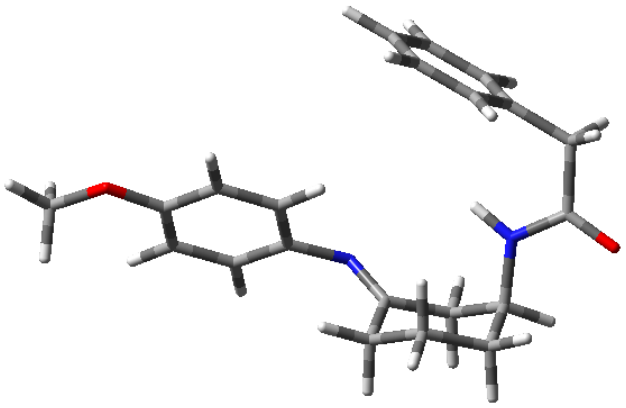
Spin= Singlet
E(MP2)= –1072.06526480 a.u.
Dipole Moment= 7.0588 Debye
Point Group= C1
Job cpu time= 20 hours 10 minutes 34.5 seconds

From **Section 8.5.2.5.**:
Thermal correction to Gibbs free energy= 0.354235

Sum of electronic and thermal free energies= –1072.06526480 + 0.354235 = **–1071.711030 a.u**.

8.5.3. Calculations for Axial (*E*)-3-Phenylacetamidocyclohexanone [*E*-8a-*ax*-PhMe]

8.5.3.1. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [E-**8a**-ax-gas, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-1.276133	-2.449160	1.242776	26	O	5.569939	0.890926	-0.763286
2	C	-2.504649	-2.190505	0.348914	27	C	6.828479	0.472391	-0.257958
3	C	-2.299453	-2.804968	-1.049173	28	H	7.575617	1.046352	-0.804077
4	C	-0.996555	-2.333719	-1.705345	29	H	6.921978	0.684398	0.813180
5	C	0.229434	-2.588416	-0.801445	30	H	6.995649	-0.596616	-0.432246
6	H	-3.387817	-2.645727	0.802414	31	N	0.778905	-1.212401	1.219181
7	H	-1.220157	-3.529909	1.421206	32	C	-4.000880	-0.251809	0.012020
8	H	-1.377055	-1.954554	2.210225	33	C	-4.163300	1.277922	0.057004
9	H	-2.284187	-3.896573	-0.940143	34	O	-4.962867	-0.965678	-0.234192
10	H	-3.161837	-2.561524	-1.673407	35	H	-4.765240	1.482774	0.948042
11	H	-0.853016	-2.840263	-2.664143	36	H	-4.794004	1.527470	-0.799041
12	H	-1.063950	-1.263061	-1.926762	37	C	-2.909428	2.119921	0.062779
13	H	0.360244	-3.672962	-0.684296	38	C	-2.320875	2.530031	-1.140477
14	H	1.141820	-2.197623	-1.251964	39	C	-2.298163	2.499313	1.264216
15	C	0.012228	-2.007570	0.581190	40	C	-1.155150	3.293005	-1.143381
16	C	1.995160	-0.731942	0.677729	41	H	-2.786004	2.255145	-2.081983
17	C	3.208700	-1.162692	1.215880	42	C	-1.128868	3.258763	1.265164
18	C	2.021166	0.259723	-0.314849	43	H	-2.744153	2.201141	2.208002
19	C	4.424791	-0.655862	0.753879	44	C	-0.553445	3.657728	0.060711
20	H	3.201226	-1.904073	2.006681	45	H	-0.719325	3.607073	-2.085503
21	C	3.225462	0.777643	-0.770206	46	H	-0.670230	3.540009	2.206334
22	H	1.088145	0.638222	-0.716740	47	H	0.354363	4.250019	0.060079
23	C	4.438221	0.319923	-0.245056	48	H	-2.019221	-0.102298	0.499062
24	H	5.344776	-1.023158	1.188883	49	N	-2.764886	-0.748962	0.284369
25	H	3.247207	1.544990	-1.535051					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.93715038 a.u.
RMS Gradient Norm= 0.00000384 a.u.
Imaginary Freq= 0
Dipole Moment= 3.8089 Debye
Point Group= C1
Job cpu time= 2 days 7 hours 1 minute 39.0 seconds

Zero-point correction= 0.411457 (Hartree/Particle)
Thermal correction to Energy= 0.434239
Thermal correction to Enthalpy= 0.435183
Thermal correction to Gibbs Free Energy= 0.355119
Sum of electronic and zero-point Energies= -1074.525693

Sum of electronic and thermal Energies= -1074.502911
Sum of electronic and thermal Enthalpies= -1074.501967
Sum of electronic and thermal Free Energies= -1074.582032

8.5.3.2. *Single Point Energy Calculation in the Gas Phase [E-***8a***-ax-gas, M06-2x/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.53026985 a.u.
Dipole Moment= 3.7430 Debye
Point Group= C1
Job cpu time= 5 hours 34 minutes 56.7 seconds

From **Section 8.5.3.1.**:
Thermal correction to Gibbs free energy= 0.355119

Sum of electronic and thermal free energies= –1074.97438976 + 0.355119 = **–1074.175151 a.u**.

8.5.3.3. *Single Point Energy Calculation in the Gas Phase [E-***8a***-ax-gas, B3LYP/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.97438976 a.u.
Dipole Moment= 3.8107 Debye
Point Group= C1
Job cpu time= 5 hours 20 minutes 20.1 seconds

From **Section 3.5.3.1.**:
Thermal correction to Gibbs free energy= 0.355119

Sum of electronic and thermal free energies= –1074.97438976 + 0.355119 = **–1074.619271 a.u**.

8.5.3.4. *Single Point Energy Calculation in the Gas Phase [E-***8a***-ax-gas, MP2/6-311+G(2d,3p)]*

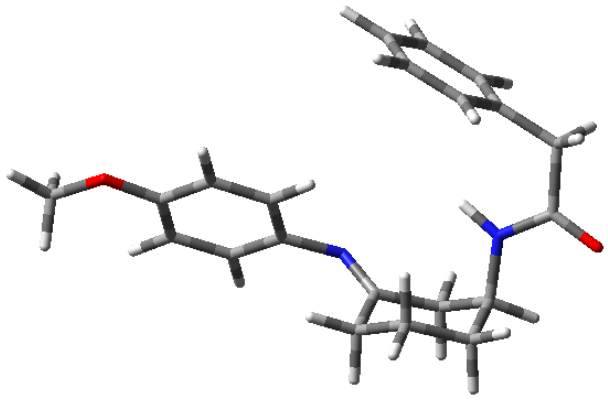
Calculation Type= SP
Calculation Method= RMP2-FC
Basis Set= 6-311+G(2d,3p)

Charge= 0
Spin= Singlet
E(MP2)= –1072.06282823 a.u.
Dipole Moment= 3.8196 Debye
Point Group= C1
Job cpu time= 1 day 1 hour 40 minutes 14.9 seconds

From **Section 8.5.3.1.**:
Thermal correction to Gibbs free energy= 0.355119

Sum of electronic and thermal free energies= –1072.06282823 + 0.355199 = **–1071.707709 a.u**.

8.5.3.5. *Geometry Optimization and Vibrational Frequency Calculation in PhMe [E-***8a***-ax-PhMe, B3LYP/6-311+G(d,p), IEF-PCM Solvation Model]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	1.247850	-2.434511	-1.238177	26	O	-5.603619	0.912443	0.752463
2	C	2.478710	-2.203650	-0.339446	27	C	-6.863320	0.505520	0.230149
3	C	2.260815	-2.821853	1.054636	28	H	-7.611408	1.079054	0.774767
4	C	0.962808	-2.336104	1.709480	29	H	-6.943300	0.728930	-0.838982
5	C	-0.263207	-2.575325	0.801942	30	H	-7.036781	-0.563423	0.393530
6	H	3.351443	-2.672583	-0.797605	31	N	-0.807973	-1.196908	-1.217445
7	H	1.180676	-3.512191	-1.429669	32	C	4.020651	-0.292643	-0.035968
8	H	1.360274	-1.930413	-2.199339	33	C	4.203479	1.233561	-0.048036
9	H	2.230701	-3.912141	0.940105	34	O	4.986904	-1.025354	0.154150
10	H	3.122957	-2.592928	1.684976	35	H	4.817231	1.448205	-0.928307
11	H	0.810752	-2.844800	2.665499	36	H	4.827632	1.459121	0.819807
12	H	1.041743	-1.267016	1.935185	37	C	2.961937	2.094424	-0.048792
13	H	-0.402614	-3.657876	0.678365	38	C	2.357985	2.474888	1.156900
14	H	-1.172581	-2.180062	1.254200	39	C	2.382354	2.524992	-1.248779
15	C	-0.040180	-1.991052	-0.577479	40	C	1.206026	3.259099	1.163320
16	C	-2.025958	-0.717053	-0.677070	41	H	2.799381	2.160191	2.097354
17	C	-3.238725	-1.137389	-1.226289	42	C	1.227765	3.307140	-1.246062
18	C	-2.053565	0.265885	0.324225	43	H	2.840998	2.249175	-2.193131
19	C	-4.455648	-0.628017	-0.768584	44	C	0.635637	3.675876	-0.039531
20	H	-3.231589	-1.873692	-2.021971	45	H	0.757057	3.549084	2.106919
21	C	-3.258581	0.786695	0.775823	46	H	0.793881	3.629825	-2.185710
22	H	-1.121582	0.634204	0.737765	47	H	-0.260739	4.285396	-0.036082
23	C	-4.470628	0.340122	0.238298	48	H	2.029263	-0.103282	-0.431106
24	H	-5.374459	-0.987096	-1.212592	49	N	2.771737	-0.767909	-0.265053
25	H	-3.278799	1.547701	1.547240					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.94470654 a.u.
RMS Gradient Norm= 0.00000405 a.u.
Imaginary Freq= 0
Dipole Moment= 4.4063 Debye
Point Group= C1
Job cpu time= 1 day 18 hours 38 minute 48.6 seconds

Zero-point correction= 0.411235 (Hartree/Particle)
Thermal correction to Energy= 0.434081
Thermal correction to Enthalpy= 0.435025
Thermal correction to Gibbs Free Energy= 0.354317
Sum of electronic and zero-point Energies= -1074.533472
Sum of electronic and thermal Energies= -1074.510626

Sum of electronic and thermal Enthalpies= -1074.509682
Sum of electronic and thermal Free Energies= -1074.590389

8.5.3.6. *Single Point Energy Calculation in PhMe [E-***8a-***ax-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.53722972 a.u.
Dipole Moment= 4.3479 Debye
Point Group= C1
Job cpu time= 5 hours 50 minutes 5.5 seconds

From **Section 8.5.3.5.**:
Thermal correction to Gibbs free energy= 0.354317

Sum of electronic and thermal free energies= –1074.53722972 + 0.354317 = **–1074.182913 a.u**.

8.5.3.7. *Single Point Energy Calculation in PhMe [E-***8a-***ax-PhMe, B3LYP/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.98163782 a.u.
Dipole Moment= 4.3128 Debye
Point Group= C1
Job cpu time= 5 hours 35 minutes 6.1 seconds

From **Section 8.5.3.5.**:
Thermal correction to Gibbs free energy= 0.354317

Sum of electronic and thermal free energies= –1074.98163782 + 0.354317 = **–1074.627321 a.u**.

8.5.3.8. *Single Point Energy Calculation in PhMe [E-***8a-***ax-PhMe, MP2/6-311+G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RMP2-FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

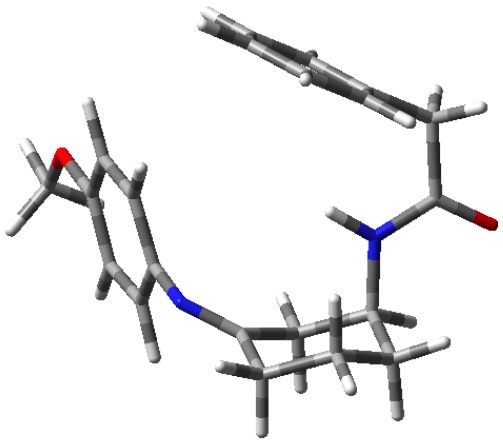
Spin= Singlet
E(MP2)= –1072.06980022 a.u.
Dipole Moment= 4.2719 Debye
Point Group= C1
Job cpu time= 21 hours 51 minutes 31.4 seconds

From **Section 8.5.3.5.**:
Thermal correction to Gibbs free energy= 0.354317

Sum of electronic and thermal free energies= –1072.06980022 + 0.354317 = **–1071.715483 a.u**.

8.5.4. Calculations for Axial (*Z*)-3-Phenylacetamidocyclohexanone [*Z*-8a-*ax*]

8.5.4.1. *Geometry Optimization and Vibrational Frequency Calculation in the Gas Phase [Z-**8a**-ax-gas, B3LYP/6-311+G(d,p)]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-0.109158	-2.360014	0.403634	26	O	5.192293	1.259098	0.701409
2	C	-1.542521	-2.137250	0.932905	27	C	6.208008	0.562897	1.407952
3	C	-2.575037	-2.910918	0.092828	28	H	6.907974	1.323229	1.750982
4	C	-2.476942	-2.559473	-1.394838	29	H	5.799815	0.029621	2.273964
5	C	-1.051414	-2.785010	-1.933695	30	H	6.734279	-0.146338	0.759260
6	H	-1.597551	-2.486321	1.965254	31	N	0.866274	-1.364848	-1.675965
7	H	0.147906	-3.410355	0.587630	32	C	-2.677854	-0.174261	1.915884
8	H	0.598567	-1.749873	0.965243	33	C	-2.903957	1.346866	1.868080
9	H	-2.395466	-3.984318	0.232095	34	O	-3.215358	-0.847343	2.783639
10	H	-3.574822	-2.704142	0.482079	35	H	-2.381967	1.750701	2.741076
11	H	-3.187125	-3.157462	-1.973248	36	H	-3.970167	1.484192	2.062763
12	H	-2.760445	-1.511868	-1.546398	37	C	-2.489553	2.087444	0.618372
13	H	-0.837951	-3.863609	-1.919992	38	C	-3.333390	2.123949	-0.500182
14	H	-0.947417	-2.444699	-2.964954	39	C	-1.260339	2.752720	0.544399
15	C	0.001217	-2.099074	-1.090246	40	C	-2.958572	2.800706	-1.658175
16	C	1.944664	-0.751488	-1.002609	41	H	-4.295699	1.623218	-0.458398
17	C	2.931247	-1.481769	-0.335709	42	C	-0.882707	3.433562	-0.612782
18	C	2.106954	0.639713	-1.107298	43	H	-0.595135	2.743615	1.401991
19	C	4.035662	-0.849961	0.242048	44	C	-1.730131	3.458671	-1.718137
20	H	2.853416	-2.561958	-0.283415	45	H	-3.627517	2.820422	-2.511374
21	C	3.187384	1.276563	-0.518995	46	H	0.070596	3.949112	-0.645873
22	H	1.367315	1.212567	-1.654377	47	H	-1.439463	3.990082	-2.617209
23	C	4.162020	0.537377	0.163393	48	H	-1.461077	-0.090019	0.275127
24	H	4.781906	-1.452222	0.742987	49	N	-1.841382	-0.703235	0.981777
25	H	3.306801	2.351454	-0.587246					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.93639794 a.u.
RMS Gradient Norm= 0.00000378 a.u.
Imaginary Freq= 0
Dipole Moment= 2.1076 Debye
Point Group= C1
Job cpu time= 2 days 4 hours 24 minute 15.3 seconds

Zero-point correction= 0.411250 (Hartree/Particle)
Thermal correction to Energy= 0.434061
Thermal correction to Enthalpy= 0.435005
Thermal correction to Gibbs Free Energy= 0.354808
Sum of electronic and zero-point Energies= -1074.525148
Sum of electronic and thermal Energies= -1074.502337

Sum of electronic and thermal Enthalpies= -1074.501393
Sum of electronic and thermal Free Energies= -1074.581589

8.5.4.2. *Single Point Energy Calculation in the Gas Phase [Z-***8a-***ax-gas, M06-2x/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.52906559 a.u.
Dipole Moment= 2.0474 Debye
Point Group= C1
Job cpu time= 5 hours 39 minutes 36.3 seconds

From **Section 8.5.4.1.**:
Thermal correction to Gibbs free energy= 0.354808

Sum of electronic and thermal free energies= –1074.52906559 + 0.354808 = **–1074.174258 a.u**.

8.5.4.3. *Single Point Energy Calculation in the Gas Phase [Z-***8a-***ax-gas, B3LYP/6-311++G(2d,3p)]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.97365512 a.u.
Dipole Moment= 2.0790 Debye
Point Group= C1
Job cpu time= 5 hours 24 minutes 12.0 seconds

From **Section 8.5.4.1.**:
Thermal correction to Gibbs free energy= 0.354808

Sum of electronic and thermal free energies= –1074.97365512 + 0.354808 = **–1074.618847 a.u**.

8.5.4.4. *Single Point Energy Calculation in the Gas Phase [Z-***8a-***ax-gas, MP2/6-311+G(2d,3p)]*

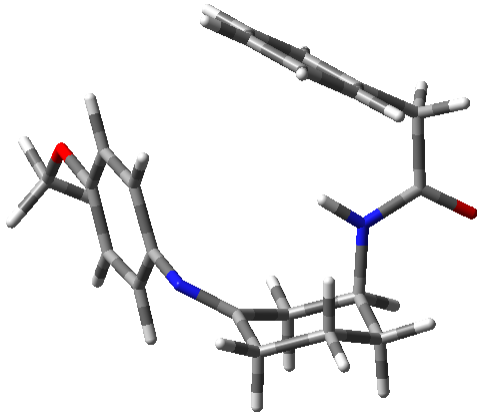
Calculation Type= SP
Calculation Method= RMP2-FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

Spin= Singlet
E(MP2)= –1072.06194618 a.u.
Dipole Moment= 1.9607 Debye
Point Group= C1
Job cpu time= 1 day 2 hours 25 minutes 16.9 seconds

From **Section 8.5.4.1.**:
Thermal correction to Gibbs free energy= 0.354808

Sum of electronic and thermal free energies= –1072.06194618 + 0.354808 = **–1071.707138 a.u**.

8.5.4.5. *Geometry Optimization and Vibrational Frequency Calculation in PhMe [Z-***8a***-ax-PhMe, B3LYP/6-311+G(d,p), IEF-PCM Solvation Model]*



Tag	Atom	X	Y	Z	Tag	Atom	X	Y	Z
1	C	-0.111573	-2.337202	0.404051	26	O	5.197805	1.254673	0.704140
2	C	-1.547291	-2.132003	0.933995	27	C	6.212733	0.553317	1.414236
3	C	-2.570515	-2.920190	0.096675	28	H	6.914063	1.311471	1.758297
4	C	-2.477046	-2.571230	-1.391748	29	H	5.799728	0.022253	2.278405
5	C	-1.050021	-2.785513	-1.930618	30	H	6.736218	-0.156455	0.765168
6	H	-1.592203	-2.479865	1.966771	31	N	0.870063	-1.364610	-1.681480
7	H	0.160241	-3.382093	0.595863	32	C	-2.680615	-0.166223	1.924362
8	H	0.587413	-1.713404	0.961330	33	C	-2.935912	1.347756	1.852752
9	H	-2.377099	-3.990383	0.238937	34	O	-3.187132	-0.830395	2.823448
10	H	-3.573936	-2.724963	0.482840	35	H	-2.445687	1.771651	2.734326
11	H	-3.180571	-3.178889	-1.967653	36	H	-4.009805	1.467082	2.016319
12	H	-2.771665	-1.527256	-1.546900	37	C	-2.504507	2.084296	0.606035
13	H	-0.826834	-3.861764	-1.911846	38	C	-3.323414	2.099609	-0.531503
14	H	-0.952554	-2.449850	-2.964117	39	C	-1.284544	2.769136	0.556811
15	C	-0.001101	-2.089947	-1.091456	40	C	-2.932518	2.775059	-1.685582
16	C	1.948166	-0.749694	-1.005493	41	H	-4.278311	1.583850	-0.508806
17	C	2.932867	-1.481688	-0.336999	42	C	-0.891258	3.448640	-0.596174
18	C	2.111618	0.641348	-1.108589	43	H	-0.639775	2.776489	1.429813
19	C	4.037432	-0.851640	0.242569	44	C	-1.713461	3.452515	-1.721365
20	H	2.852457	-2.561516	-0.281700	45	H	-3.581656	2.778221	-2.554127
21	C	3.193204	1.276869	-0.519221	46	H	0.054321	3.978987	-0.611230
22	H	1.372624	1.218088	-1.652667	47	H	-1.410343	3.982514	-2.617165
23	C	4.166424	0.535930	0.163879	48	H	-1.511280	-0.090129	0.258312
24	H	4.781228	-1.455053	0.745541	49	N	-1.866407	-0.701139	0.980169
25	H	3.310452	2.352150	-0.586940					

Calculation Type= OPT+FREQ
Calculation Method= RB3LYP
Basis Set= 6-311+G(d,p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.94418700 a.u.
RMS Gradient Norm= 0.00000455 a.u.
Imaginary Freq= 0
Dipole Moment= 2.3991 Debye
Point Group= C1
Job cpu time= 2 days 6 hours 37 minute 28.2 seconds

Zero-point correction= 0.411121 (Hartree/Particle)
Thermal correction to Energy= 0.433938
Thermal correction to Enthalpy= 0.434883
Thermal correction to Gibbs Free Energy= 0.354862
Sum of electronic and zero-point Energies= -1074.533066
Sum of electronic and thermal Energies= -1074.510249

Sum of electronic and thermal Enthalpies= -1074.509304
Sum of electronic and thermal Free Energies= -1074.589325

8.5.4.6. *Single Point Energy Calculation in PhMe [Z-***8a-***ax-PhMe, M06-2x/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RM062x
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RM062x)= –1074.53643923 a.u.
Dipole Moment= 2.3422 Debye
Point Group= C1
Job cpu time= 5 hours 56 minutes 47.3 seconds

From **Section 8.5.4.5.**:
Thermal correction to Gibbs free energy= 0.354862

Sum of electronic and thermal free energies= –1074.53643923 + 0.354862 = **–1074.181577 a.u**.

8.5.4.7. *Single Point Energy Calculation in PhMe [Z-***8a-***ax-PhMe, B3LYP/6-311++G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RB3LYP
Basis Set= 6-311++G(2d,3p)
Charge= 0
Spin= Singlet
E(RB3LYP)= –1074.98110154 a.u.
Dipole Moment= 2.3621 Debye
Point Group= C1
Job cpu time= 5 hours 39 minutes 35.3 seconds

From **Section 8.5.4.5.**:
Thermal correction to Gibbs free energy= 0.354862

Sum of electronic and thermal free energies= –1074.98110154 + 0.354862 = **–1074.626240 a.u**.

8.5.4.8. *Single Point Energy Calculation in PhMe [Z-***8a-***ax-PhMe, MP2/6-311+G(2d,3p), IEF-PCM Solvation Model]*

Calculation Type= SP
Calculation Method= RMP2-FC
Basis Set= 6-311+G(2d,3p)
Charge= 0

Spin= Singlet
E(MP2)= –1072.06911047 a.u.
Dipole Moment= 2.1946 Debye
Point Group= C1
Job cpu time= 23 hours 47 minutes 33.5 seconds

From **Section 8.5.4.5.**:
Thermal correction to Gibbs free energy= 0.354862

Sum of electronic and thermal free energies= –1072.06911047 + 0.354862 =
–1071.714248 a.u.

8.5.5. Calculation of ΔG°, K, and Equilibrium Ratio Between [*E*-8a-*eq*, *Z*-8a-*eq*, *E*-8a-*ax*, *Z*-8a-*ax*] using Single-point Energies:

These values are taken at the M062x level of theory, with the IEF-PCM solvation model using PhMe and equilibrium ratios are determined using equations 1–5.

E-**8a**-*ax*: From **Section 8.5.3.6.**: $G^\circ_A = -1074.182913$
E-**8a**-*eq*: From **Section 8.5.1.6.**: $G^\circ_B = -1074.182010$
Z-**8a**-*ax*: From **Section 8.5.4.6.**: $G^\circ_C = -1074.181577$
Z-**8a**-*eq*: From **Section 8.5.2.6.**: $G^\circ_D = -1074.181075$

Eq 1: $\Delta G^\circ_{B/A} = (-1074.182010 + 1074.182913)\left(\frac{627.51\ kcal}{mol \cdot a.u.}\right) = -0.567\ kcal/mol$
$\Delta G^\circ_{C/A} = (-1074.181577 + 1074.182913)\left(\frac{627.51\ kcal}{mol \cdot a.u.}\right) = -0.838\ kcal/mol$
$\Delta G^\circ_{D/A} = (-1074.181075 + 1074.182913)\left(\frac{627.51\ kcal}{mol \cdot a.u.}\right) = -1.15\ kcal/mol$

Eq 2: $K_{A/A} = 1$
$K_{B/A} = 0.384$
$K_{C/A} = 0.243$
$K_{D/A} = 0.143$

Eq 4: $K_{TOT} = 0.384 + 0.243 + 0.143 + 1 = 1.77$

Eq. 5: $\%_A = \frac{K_{A/A}}{K_{TOT}} \bullet 100 = \frac{1}{1.77} \bullet 100 = 56\%$
$\%_B = \frac{K_{B/A}}{K_{TOT}} \bullet 100 = \frac{0.384}{1.77} \bullet 100 = 22\%$
$\%_C = \frac{K_{C/A}}{K_{TOT}} \bullet 100 = \frac{0.243}{1.77} \bullet 100 = 14\%$
$\%_D = \frac{K_{D/A}}{K_{TOT}} \bullet 100 = \frac{0.143}{1.77} \bullet 100 = 8\%$

A summary of all the calculated equilibrium percentages at various levels of theory and phases is shown below.

Phase	Theory	*E*-8a-ax	*E*-8a-eq	*Z*-8a-ax	*Z*-8a-eq
Gas	M062x	46	27	18	9
	B3LYP	4	67	3	26
	MP2	71	0.5	28	0.5
PhMe	M062x	56	22	14	8
	B3LYP	6	65	2	27
	MP2	77	1	21	1

Table S22: Summary of values indicate equilibrium percentages of each species, depending on theory and solvation model.

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