Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Copper-Catalyzed Enantioselective 1,4-Addition of Alkyl Groups to *N*-Sulfonyl Imines

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1) Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded at 300 or 500 MHz (75.5 or 125 MHz) on a Bruker AV-300, an AV-500, or a DRX-500 instrument in $CDCl_3$, using the residual peak of $CHCl_3$ (^{1}H NMR: δ = 7.26 ppm, ^{13}C NMR: δ = 77.36 ppm) as internal standard. IR spectra were recorded on a Bruker Alpha-P FT-IR spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter, $[\alpha]_D^{20}$ values are given in 10^{-1} deg cm^2 g^{-1}. Electron impact (EI) mass spectra were recorded on a Finnigan MAT 95S spectrometer (70 eV); electrospray ionisation (ESI) mass spectra on a Finnigan LTQ FT spectrometer. Melting points are uncorrected. Gas chromatograms were recorded on a Shimadzu GC-2010 Plus with an AOC-20i autosampler. Enantiomeric excesses were determined with a Chiral-Separations Cyclodextrin TA column (6-TBDMS-2,3-acetyl-β-cyclodextrin, 50% in PS086, 25 m, 0.25 mm i.d., 0.125 μm film). Helium was used as the carrier gas. Method A: 4 min 80 °C isothermal → 10 K min^{-1} to 130 °C → 20 K min^{-1} to 170 °C → 5 min isothermal; 45 cm s^{-1} gas flow. Method B: 2 min 100 °C isothermal → 2 K min^{-1} to 140 °C → 20 min isothermal → 1 K min^{-1} to 160 °C → 50 min isothermal; 45 cm s^{-1} gas flow. Method C: 2 min 100 °C isothermal → 2 K min^{-1} to 140 °C → 20 min isothermal → 0.5 K min^{-1} to 160 °C → 50 min isothermal; 30 cm s^{-1} gas flow. HPLC chromatograms were recorded on a JASCO instrument equipped with a JASCO MD-2010 Plus multiwavelength detector. Method A: Daicel Chiralpak IA column, isocratic elution: *n*-hexane/2-propanol 98:2, flow rate 1.0 mL min^{-1}. Method B: Daicel Chiralpak IC column, isocratic elution: *n*-hexane/2-propanol 95:5, flow rate 1.0 mL min^{-1}. Method C: Daicel Chiralpak IA column coupled with a Daicel Chiralpak IB column, isocratic elution: *n*-hexane/2-propanol 98:2, flow rate 1.0 mL min^{-1}. Method D: Daicel Chiralpak IC column, isocratic elution: *n*-hexane/2-propanol 99:1, flow rate 1.5 mL min^{-1}. Method E: Daicel Chiralpak IC column, isocratic elution: *n*-hexane/2-propanol 98:2, flow rate 1.0 mL min^{-1}. Method F: Daicel Chiralpak IC column, isocratic elution: *n*-hexane/2-propanol 98:2, flow rate 1.5 mL min^{-1}. Method G: Daicel Chiralpak IC column, isocratic elution: *n*-hexane/2-propanol 85:15, flow rate 1.0 mL min^{-1}. Diastereomeric ratios were determined by ^{1}H NMR spectrometry at 300 or 500 MHz; the relative configuration of the products was determined by NOESY. Solvents used for extraction and chromatography were of technical grade and distilled prior to use. All moisture-sensitive reactions were carried out under argon in oven- and/or flame-dried glassware. Column chromatography was carried out on MN Kieselgel 60 M (Machery-Nagel, 0.040-0.063 mm). Diethyl ether, THF, and toluene were distilled from sodium benzophenone ketyl; triethyl amine and CH_2Cl_2 were distilled from CaH_2. *N*-(Cyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1a**),[1] *N*-(4,4-dimethylcyclopent-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1b**),[1] *N*-(4,4-dimethylcyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1c**),[1] (*E*)-*N*-(5,5-dimethylcyclopent-2-en-1-ylidene)-4-

methylbenzenesulfonamide (**1d**),[1] (*E*)-*N*-(6,6-dimethylcyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1e**),[1] *N*-(5,5-dimethylcyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1f**),[1] *N*-(3-methylcyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1g**),[1] *N*-(1,3-diphenylprop-*2E*-en-1-ylidene)-4-methylbenzenesulfonamide (**1h**),[2] *N*-(*5R*-methylcyclohex-2-en-1-ylidene)-4-methylbenzenesulfonamide (**1i**),[1] *N*-(cyclohex-2-en-1-ylidene)-*tert*-butanesulfonamide (**5a**),[1] *N*-(cyclopent-2-en-1-ylidene)-*tert*-butanesulfonamide (**5b**),[1] *N*-(cyclohept-2-en-1-ylidene)-*tert*-butanesulfonamide (**5c**),[1] and *N*-(cyclohex-2-en-1-ylidene)diphenylphosphinamide (**7a**),[1] the racemic ligand *O*,*O*′-(1,1′-dinaphthyl-2,2′-diyl)-*N*,*N*-di-*iso*-propylphosphoramidite,[3] *O*,*O*′-(*S*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*,*N*-di-(*R*,*R*)-1-phenylethylphosphoramidite (**L1**) and *O*,*O*′-(*R*)-(1,1′-dinaphthyl-2,2′-diyl)-*N*,*N*-di-(*S*,*S*)-1-phenylethylphosphoramidite (*ent*-**L1**),[4] RuCl(*p*-cymene)[(*S*,*S*)-Ts-DPEN] (**3**),[5] and copper(I)-thiophen-2-carboxylate (CuTC)[6] were prepared according to literature. All other chemicals were of commercial origin and used as received.

General Procedure for the Optimization of the Conjugate Addition (GP 1):

A mixture of the respective copper salt (10.0 μmol, 2.00 mol%), ligand **L1** (10.8 mg, 20.0 μmol, 4.00 mol%), and ketimine **1a** (125 mg, 501 μmol) was dissolved in the respective solvent (4 mL), stirred for 0.5 h at rt, and then cooled to the given temperature. $ZnEt_2$ (0.50 mL, 0.75 mmol, 1.5 M in toluene) was added slowly, and the resulting yellow solution was stirred for the given time at the given temperature. The solution was then poured into a mixture of methyl *tert*-butyl ether (MTBE, 20 mL), H_2O (0.5 mL), and $NaHCO_3$ (0.5 g), stirred for 10 min, dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

For determination of the yield by ^{1}H NMR spectrometry, a precise amount of diphenylmethane (about 50 mg) was added to the crude enamide **2a**-*Et*, which was then dissolved in CH_2Cl_2 (20 mL). The solvent was then carefully removed under reduced pressure to give the crude product with internal standard, and a ^{1}H NMR spectrum was recorded in $CDCl_3$. Signals at $\delta = 5.37$ (1H, **2a**-*Et*) and $\delta = 3.99$ (2H, diphenylmethane) were used for determination of the yield.

General Procedure for the Hydrolysis of Enamide 2a-*Et* (GP 2):

THF (5 mL) and aqueous HCl (1 mL, 6 M) were added to the crude enamide **2a**-*Et*, and the solution was stirred for 1 h at rt. The reaction mixture was then diluted with pentane (5 mL), and sat. aqueous $NaHCO_3$ solution was added until the gas evolution ceased. The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was performed by column chromatography over silica gel (R_f 0.31, pentane/Et_2O 5:1), and the ee of the 3-ethylcyclohexanone thus obtained was measured by GC, method A, retention times 9.54 min (minor enantiomer), 9.67 min (major enantiomer). The (*S*)-configuration of enamide **2a**-*Et* was

determined by comparison with a sample of authentic (*S*)-3-ethylcyclohexanone, which was prepared according to literature.[7]

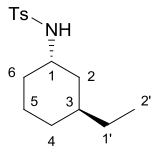
General Procedure for the Asymmetric Conjugate Addition (GP 3):

A mixture of copper(I)-thiophene-2-carboxylate (1.91 mg, 10.0 μmol), ligand **L1** (10.8 mg, 20.0 μmol), and the respective ketimine **1**, **5**, or **7** (500 μmol) was dissolved in toluene (4 mL), stirred for 0.5 h at rt, and then cooled to the given temperature. $ZnEt_2$ (0.50 mL, 0.75 mmol, 1.5 M in toluene) was slowly added, and the resulting yellow solution was stirred for the given time at the given temperature. The reaction mixture was then poured into a mixture of MTBE (20 mL), H_2O (0.5 mL), and $NaHCO_3$ (0.5 g), stirred for 10 min, dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

General Procedure for the Hydrogenation Catalyzed by RuCl(*p*-cymene)[Ts-DPEN] (GP 4)

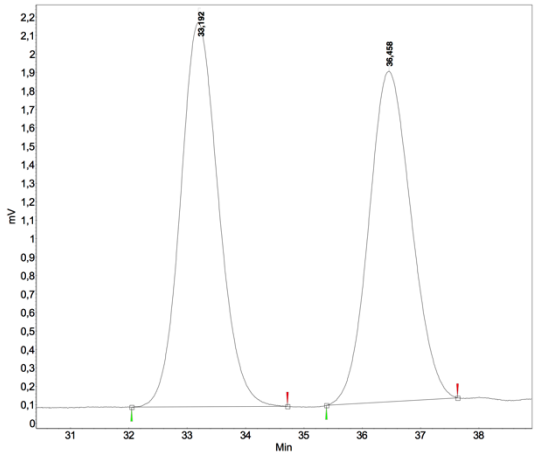
The crude product of the conjugate addition was dissolved in acetonitrile (3 mL), racemic RuCl(*p*-cymene)[Ts-DPEN] (**3**, 15.9 mg, 25.0 μmol) and a 5:2 mixture of formic acid and triethyl amine (314 μL, 0.75 mmol) were added, and the reaction mixture was stirred for 16 h at rt. The solution was then poured into half-saturated brine (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by flash column chromatography over silica gel.

***N*-[(1*S*,3*S*)-3-Ethylcyclohexyl]-4-methylbenzenesulfonamide (*trans*-4a-*Et*)**



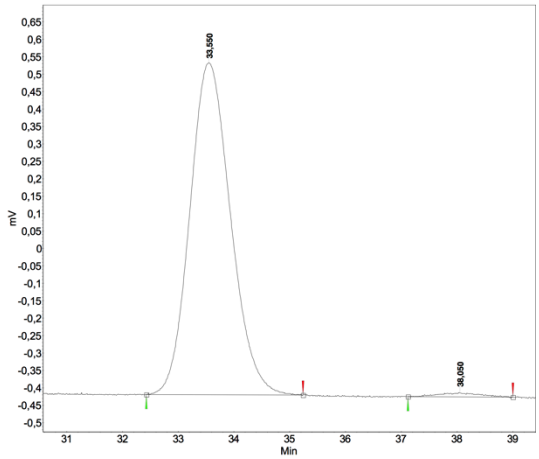
Preparation according to GP 3 and GP 4 using ketimine **1a** (125 mg, 501 μmol), reaction time 1 h at –30 °C, yielded 120 mg (85%) of amide *trans*-**4a**-*Et* as a colorless solid with a dr (*trans*/*cis*) >97:3.

R_f 0.50, CH_2Cl_2. – mp 68 °C. – $[\alpha]_D^{20}$ +7.5 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3277, 2927, 2872, 2850, 1598, 1421, 1322, 1163, 1142, 818, 708, 552, 515. – δ_H (500 MHz; $CDCl_3$) 0.74 (t, ^3J = 7.5 Hz, 3H, 2'-H), 0.86-0.93 (m, 1H, 4-H), 1.07-1.17 (m, 3H, 2-H, 1'-H), 1.32 (m_c, 1H, 3-H), 1.37-1.62 (m, 6H, 2-H, 4-H, 5-H, 6-H), 2.41 (s, 3H, ArCH_3), 3.50 (m_c, 1H, 1-H), 4.89 (d, ^3J = 7.3 Hz, 1H, NH), 7.29 (m_c, 2H, Ar-H), 7.77 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 11.4 (C-2'), 20.4 (C-5), 21.6 (Ar*C*H_3), 28.7 (C-1'), 31.3 (C-4), 31.8 (C-6), 33.7 (C-3), 37.4 (C-2), 49.5 (C-1), 127.1 (C-Ar), 129.7 (C-Ar), 138.4 (C-Ar), 143.2 (C-Ar). – HRMS (ESI) *m*/*z* calcd. for $C_{15}H_{23}NO_2SNa$ $[M+Na]^+$: 304.1342; found 304.1341. – The enantiomeric excess was measured by HPLC, method A, retention times 33.6 min (major enantiomer), 38.1 min (minor enantiomer): 98% ee. The (*S*)-configuration at C-3 was assigned based on the configuration of enamide **2a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	33,192	51,11	2,1	1,6	51,114
2	UNKNOWN	36,458	48,89	1,8	1,5	48,886
Total			100,00	3,9	3,1	100,000



Peak results :

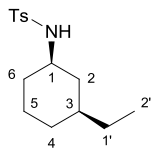
Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	33,550	98,78	1,0	0,8	98,779
2	UNKNOWN	38,050	1,22	0,0	0,0	1,221
Total			100,00	1,0	0,8	100,000

Racemic amide *trans*-**4a**-*Et* was prepared as follows: CuCl (49.5 mg, 500 μmol) was suspended in THF (2 mL), cooled to –30 °C, and treated dropwise with EtMgBr (344 μL, 750 μmol, 2.18 M in Et_2O). The reaction mixture was stirred for 15 min, a solution of ketimine **1a** (125 mg, 501 μmol) in THF (2 mL) was added dropwise, and the reaction mixture was stirred for 1 h at –30 °C. Workup was performed as described in GP 3. Hydrogenation according to GP 4 yielded 42 mg (30%) of the racemic amide *trans*-**4a**-*Et*.

Preparation of Amide *trans*-4a-*Et* with 0.01 mol% Cu-catalyst

A mixture of copper(I)-thiophene-2-carboxylate (1.91 mg, 10.0 μmol) and ligand **L1** (10.8 mg, 20.0 μmol) was dissolved in toluene (50 mL) and stirred for 3 h at rt. In a second flask, ketimine **1a** (125 mg, 501 μmol) was dissolved in toluene (3.75 mL), an aliquot of the catalyst-containing solution (250 μL) was added, and the reaction mixture was cooled to –30 °C. $ZnEt_2$ (0.50 mL, 0.75 mmol, 1.5 M in toluene) was slowly added, and the resulting yellow solution was stirred for 1 h at –30 °C. Workup was performed according to GP 3, and hydrogenation according to GP 4 furnished 125 mg (89%) of amide *trans*-**4a**-*Et*. – 87% ee.

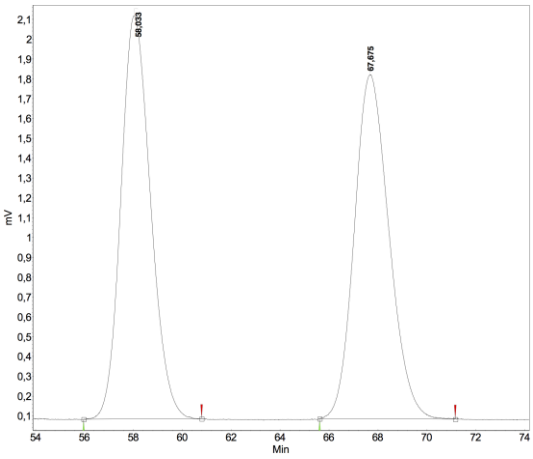
***N*-[(1*R*,3*S*)-3-Ethylcyclohexyl]-4-methylbenzenesulfonamide (*cis*-4a-*Et*)**



Conjugate addition was performed according to GP 3 using ketimine **1a** (125 mg, 501 μmol), reaction time 1 h at –30 °C. After workup, the crude product was cooled to 0 °C, and a solution of *t*$BuNH_2 \cdot BH_3$ (91.3 mg, 1.05 mmol) in CH_2Cl_2 (3 mL) was added. The reaction mixture was stirred for 16 h at 0 °C, then poured into half-saturated aqueous NH_4Cl (2 mL), and extracted with MTBE (3 × 10 mL). The combined organic phases were washed with water (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced

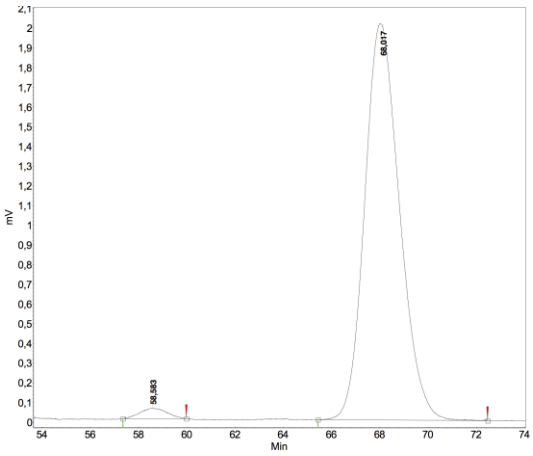
pressure. Purification by flash column chromatography over silica gel furnished 90 mg (64%) of amide *cis*-**4a**-*Et* as a colorless solid. – dr (*trans*/*cis*) before chromatography: 10:90, after chromatography: <3:97.

R_f 0.25, pentane/EtOAc 10:1. – mp 54 °C. – $[\alpha]_D^{20}$ +22.8 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3277, 2927, 2854, 1599, 1448, 1321, 1155, 1093, 813, 662, 568, 547. – δ_H (500 MHz; $CDCl_3$) 0.63-0.74 (m, 2H, 2-H, 5-H), 0.78 (t, *J* = 7.2 Hz, 3H, 2'-H), 1.00 (m_c, 1H, 6-H), 1.07-1.20 (m, 4H, 3-H, 4-H, 1'-H), 1.59-1.68 (m, 2H, 4-H, 5-H), 1.73-1.83 (m, 2H, 2-H, 6-H), 2.41 (s, 3H, ArCH_3), 3.06 (m_c, 1H, 1-H), 4.78 (d, *J* = 7.7 Hz, 1H, NH), 7.28 (m_c, 2H, Ar-H), 7.77 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 11.3 (C-2'), 21.6 (ArCH_3), 24.9 (C-4), 29.6 (C-1'), 31.5 (C-5), 34.3 (C-6), 38.7 (C-3), 40.6 (C-2), 53.3 (C-1), 127.0 (C-Ar), 129.7 (C-Ar), 138.7 (C-Ar), 143.2 (C-Ar). – HRMS (ESI) *m*/*z* calcd for $C_{15}H_{23}NO_2SNa$ $[M+Na]^+$: 304.1342; found 304.1341. – The enantiomeric excess was measured by HPLC, method B, retention times 58.6 min (minor enantiomer), 68.0 min (major enantiomer): 96% ee



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	58,033	50,01	2,0	2,9	50,014
2	UNKNOWN	67,675	49,99	1,7	2,9	49,986
Total			100,00	3,8	5,7	100,000

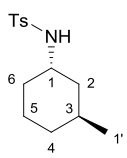


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
2	UNKNOWN	58,583	1,96	0,1	0,1	1,958
1	UNKNOWN	68,017	98,04	2,0	3,4	98,042
Total			100,00	2,1	3,4	100,000

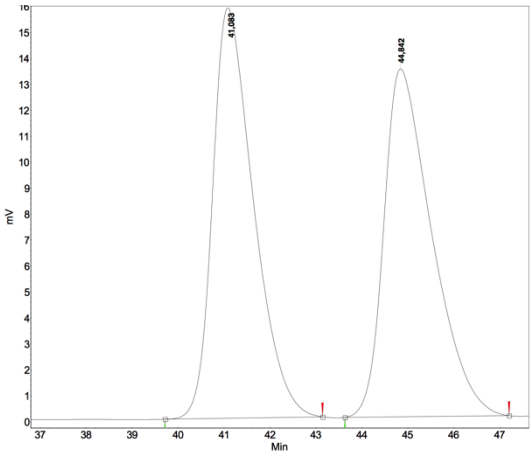
Racemic preparation was performed as described above using racemic *O*,*O*'-(1,1'-dinaphthyl-2,2'-diyl)-*N*,*N*-di-*iso*-propylphosphoramidite (8.30 mg, 20.0 µmol) and yielded 51 mg (36%) of racemic amide *cis*-**4a**-*Et*.

N-[(1*S*,3*S*)-3-Methylcyclohexyl]-4-methylbenzenesulfonamide (4a-*Me*)



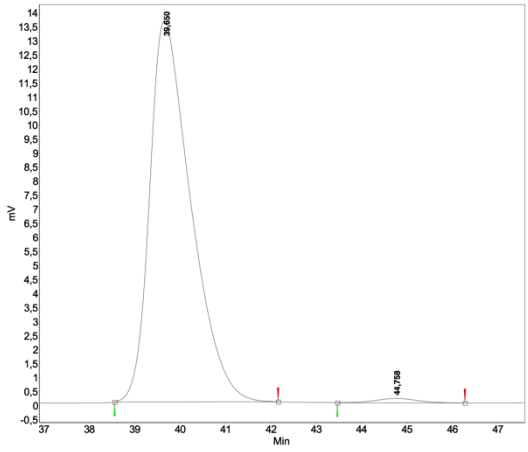
Addition of $ZnMe_2$: Preparation according to GP 3 and GP 4 using ketimine **1a** (125 mg, 501 µmol) and $ZnMe_2$ (0.63 mL, 0.76 mmol, 1.2 M in toluene), reaction time 1 h at –30 °C, yielded 117 mg (87%) of amide **4a**-*Me* as a colorless solid with a dr (*trans*/*cis*) >97:3.

R_f 0.44, CH_2Cl_2. – mp 112 °C. – $[\alpha]_D^{20}$ –0.7 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3282, 2925, 2867, 1599, 1454, 1422, 1323, 1159, 1141, 1092, 813, 672, 549. – δ_H (500 MHz; $CDCl_3$) 0.78 (d, *J* = 6.5 Hz, 3H, 1'-H), 0.84-0.92 (m, 1H, 4-H), 1.09 (ddd, *J* = 13.5, 10.3, 3.4 Hz, 1H, 2-H), 1.33-1.62 (m, 7H, 2-H, 3-H, 4-H, 5-H, 6-H), 2.41 (s, 3H, ArCH_3), 3.49 (m_c, 1H, 1-H), 5.01 (d, *J* = 7.3 Hz, 1H, NH), 7.28 (m_c, 2H, Ar-H), 7.77 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 20.4 (C-5), 21.6 (Ar-CH_3), 21.7 (C-1'), 26.9 (C-3), 31.4 (C-6), 33.7 (C-4), 39.7 (C-2), 49.5 (C-1), 127.1 (C-Ar), 129.7 (C-Ar), 138.3 (C-Ar), 143.2 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{14}H_{21}NO_2SNa$ $[M+Na]^+$: 290.1185; found 290.1183. – The enantiomeric excess was measured by HPLC, method A, retention times 39.7 min (major enantiomer), 44.8 min (minor enantiomer): 98% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	41,083	50,18	15,8	16,3	50,179
2	UNKNOWN	44,842	49,82	13,4	16,2	49,821
Total			100,00	29,2	32,4	100,000



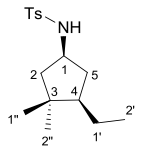
Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	39,650	98,86	13,6	14,2	98,859
2	UNKNOWN	44,758	1,14	0,2	0,2	1,141
Total			100,00	13,7	14,4	100,000

Racemic conjugate addition was performed in analogy to a literature procedure:[8] Ketimine **1a** (125 mg, 501 µmol) and $[Rh(cod)Cl]_2$ (6.16 mg, 12.5 µmol) were dissolved in THF (2 mL), and the resulting yellow solution was cooled to 0 °C. Neat $AlMe_3$ (72 µL, 0.75 mmol) was added dropwise, and the reaction mixture was stirred for 1 h at rt. The reaction mixture was then poured into a mixture of MTBE (20 mL), H_2O (1 mL), and $NaHCO_3$ (0.5 g), stirred for 10 min, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Hydrogenation according to GP 4 yielded 70 mg (52%) of the racemic amide **4a**-*Me*.

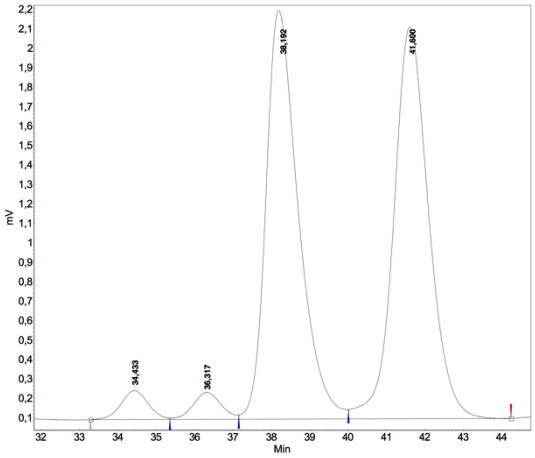
Addition of $AlMe_3$: Conjugate addition according to GP 3 using ketimine **1a** (125 mg, 501 µmol) and $AlMe_3$ (72 µL, 0.75 mmol) in Et_2O (4 mL), reaction time 1.5 h at –30 °C, and hydrogenation according to GP 4 yielded 37 mg (28%) of amide **4a**-*Me* with a dr (*trans/cis*) >97:3. – 96% ee.

***N*-[(1*S*,4*R*)-3,3-Dimethyl-4-ethylcyclopentyl]-4-methylbenzenesulfonamide (4b-*Et*)**



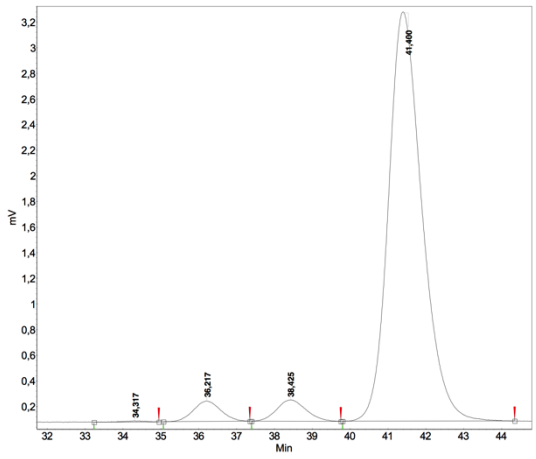
Conjugate addition according to GP 3 using ketimine **1b** (65.8 mg, 250 μmol), CuTC (0.96 mg, 5.0 μmol), ligand **L1** (5.40 mg, 10.0 μmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 5 h at –30 °C. The crude product was dissolved in EtOH (2 mL) and cooled to –15 °C, and $NaBH_4$ (94.5 mg, 2.50 mmol) was added. The solution was stirred for 20 h at this temperature, poured into saturated aqueous NH_4Cl (10 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure; the crude product was purified by flash column chromatography over silica gel. Amide **4b**-*Et* (52 mg, 70%) was obtained as a viscous, colorless oil that crystallized in the freezer. – dr (*trans*/*cis*) before chromatography: 7:93, after chromatography: 7:93.

R_f 0.32, CH_2Cl_2. – mp 74-75 °C. – $[\alpha]_D^{20}$ –11.7 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3274, 2956, 2865, 1598, 1495, 1319, 1304, 1156, 1092, 813, 661, 565, 546. – δ_H (500 MHz; $CDCl_3$) 0.78 (s, 3H, 2"-H), 0.79 (t, ^3J = 7.4 Hz, 3H, 2'-H), 0.87 (s, 3H, 1"-H), 0.96-1.03 (m, 1H, 1'-H), 1.09-1.15 (m, 1H, 5-H), 1.16-1.22 (m, 1H, 4-H), 1.28 (dd, *J* = 13.7, 6.1 Hz, 1H, 2-H), 1.37 (m_c, 1H, 1'-H), 1.72 (dd, *J* = 13.7, 9.2 Hz, 1H, 2-H), 2.12 (m_c, 1H, 5-H), 2.42 (s, 3H, ArC*H*$_3$), 3.54 (m_c, 1H, 1-H), 4.95 (s, 1H, NH), 7.29 (m_c, 2H, Ar-H), 7.75 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 13.6 (C-2'), 21.6 (Ar*C*H$_3$), 22.6 (C-1'), 24.2 (C-2"), 29.2 (C-1"), 39.36 (C-5), 39.40 (C-3), 49.4 (C-2), 50.6 (C-4), 51.9 (C-1), 127.2 (C-Ar), 129.7 (C-Ar), 137.9 (C-Ar), 143.3 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{16}H_{25}NO_2SNa$ $[M+Na]^+$: 318.1498; found 318.1500. – The enantiomeric excesses were measured by HPLC, method A; *cis*-**4b**-*Et*: retention times 38.4 min (minor enantiomer), 41.4 min (major enantiomer): 91% ee; *trans*-**4b**-*Et*: retention times 34.3 min (minor enantiomer), 36.2 min (major enantiomer): 91% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	34,433	2,75	0,1	0,1	2,747
2	UNKNOWN	36,317	2,64	0,1	0,1	2,636
3	UNKNOWN	38,192	46,47	2,1	2,0	46,472
4	UNKNOWN	41,600	48,14	2,0	2,1	48,144
Total			100,00	4,4	4,4	100,000

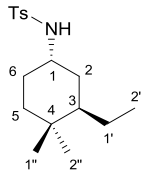


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
4	UNKNOWN	34,317	0,17	0,0	0,0	0,168
3	UNKNOWN	36,217	3,70	0,2	0,1	3,698
1	UNKNOWN	38,425	4,19	0,2	0,1	4,191
2	UNKNOWN	41,400	91,94	3,2	3,3	91,942
Total			100,00	3,5	3,6	100,000

Racemic conjugate addition was performed as follows: CuCl (49.5 mg, 500 µmol) was suspended in THF (2 mL) and cooled to –30 °C, and EtMgBr (344 µL, 750 µmol, 2.18 M in Et_2O) was added dropwise. The reaction mixture was stirred for 15 min, a solution of ketimine **1b** (132 mg, 501 µmol) in THF (2 mL) was added dropwise, and the reaction mixture was stirred for 5 h at –30 °C. Workup was performed according to GP 3; hydrogenation according to GP 4 and repeated column chromatography over silica gel yielded an analytical sample of the racemic amide **4b**-*Et*.

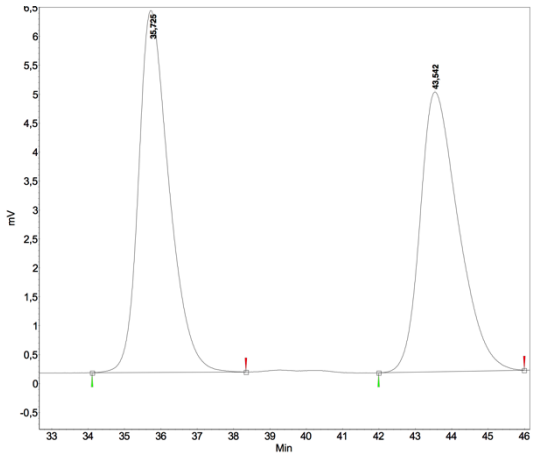
***N*-[(1*S*,3*R*)-4,4-Dimethyl-3-ethylcyclohexyl]-4-methylbenzenesulfonamide (4c-*Et*)**



Conjugate addition according to GP 3 using ketimine **1c** (69.3 mg, 250 µmol), CuTC (0.96 mg, 5.0 µmol), ligand **L1** (5.40 mg, 10.0 µmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 18 h at –10 °C. Hydrogenation according to GP 4 with racemic RuCl(*p*-cymene)[Ts-DPEN] (**3**, 7.95 mg, 12.5 µmol) and a 5:2 mixture of formic acid and triethyl amine (157 µL, 374 µmol) yielded 67 mg (87%) of amide **4c**-*Et* as a colorless solid with a dr (*trans/cis*) >97:3.

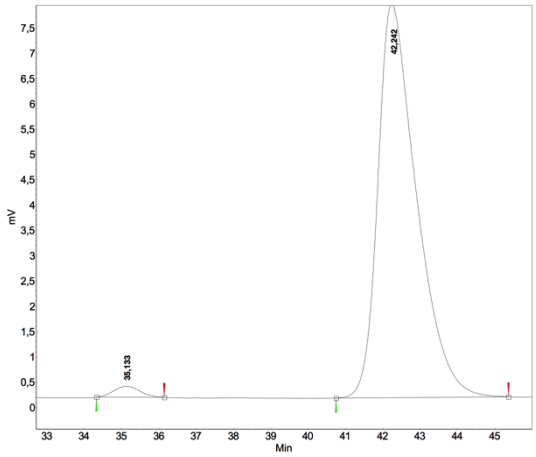
R_f 0.37, pentane/EtOAc 10:1. – mp 100 °C. – $[\alpha]_D^{20}$ –23.1 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3279, 2961, 2939, 2867, 1428, 1325, 1152, 683, 552. – δ_H (500 MHz; $CDCl_3$) 0.69 (t, *J* = 7.4 Hz, 3H, 2'-H), 0.71 (s, 3H, 1''-H*), 0.75-0.84 (m, 1H, 5-H), 0.88 (s, 3H, 2''-H*), 1.02 (m_c, 1H, 3-H), 1.15-1.21 (m, 2H, 1'-H, 2-H), 1.28 (m_c, 1H, 2-H), 1.39-1.44 (m, 1H, 6-H), 1.48-1.60 (m, 3H, 1'-H, 5-H, 6-H), 2.42 (s, 3H, ArCH_3), 3.48 (m_c, 1H, 1-H), 4.66 (d, *J* = 6.4 Hz, 1H, NH), 7.29 (m_c, 2H, Ar-H), 7.77 (m_c, 2H, H-Ar). – δ_C (125 MHz; $CDCl_3$) 12.6 (C-2'), 20.6 (C-2''*), 21.6 (ArCH_3), 22.1

(C-5), 27.8 (C-6), 29.8 (C-1"*), 31.6 (C-1'), 32.9 (C-4), 35.4 (C-2), 43.0 (C-3), 49.4 (C-1), 127.2 (C-Ar), 129.8 (C-Ar), 138.4 (C-Ar), 143.3 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{17}H_{27}NO_2SNa$ $[M+Na]^+$: 332.1655; found 332.1654. – The enantiomeric excess was measured by HPLC, method A, retention times 35.1 min (minor enantiomer), 42.2 min (major enantiomer): 96% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	35,725	50,79	6,3	6,1	50,787
2	UNKNOWN	43,542	49,21	4,8	5,9	49,213
Total			100,00	11,1	12,0	100,000

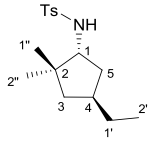


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	35,133	1,87	0,2	0,2	1,867
2	UNKNOWN	42,242	98,13	7,8	9,3	98,133
Total			100,00	8,0	9,5	100,000

Racemic conjugate addition was performed as follows: CuCl (24.8 mg, 251 µmol) was suspended in THF (1 mL) and cooled to –10 °C, and EtMgBr (172 µL, 375 µmol, 2.18 M in Et_2O) was added dropwise. The reaction mixture was stirred for 15 min, a solution of ketimine **1c** (69.3 mg, 250 µmol) in THF (1 mL) was added dropwise, and the reaction mixture was stirred for 18 h at –10 °C. Workup was performed according to GP 3; hydrogenation according to GP 4 and repeated column chromatography over silica gel yielded an analytical sample of the racemic amide **4c**-*Et*.

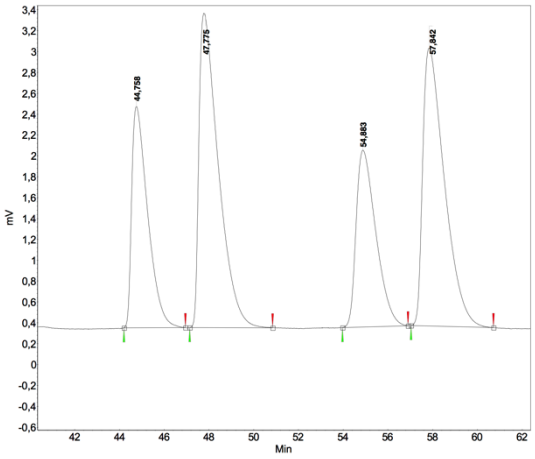
N-[(1*R*,4*S*)-2,2-Dimethyl-4-ethylcyclopentyl]-4-methylbenzenesulfonamide (4d-*Et*)



Conjugate addition according to GP 3 using ketimine **1d** (65.8 mg, 250 µmol), CuTC (0.96 mg, 5.0 µmol), ligand **L1** (5.40 mg, 10.0 µmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 20 h at –30 °C. The crude product was dissolved in EtOH (2 mL) and cooled to 0 °C, and $NaBH_4$ (94.5 mg, 2.50 mmol) was added. The solution was stirred for 16 h at this temperature, poured into saturated aqueous NH_4Cl (10 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography over silica gel yielded 66 mg (89%) of amide **4d**-*Et* as a

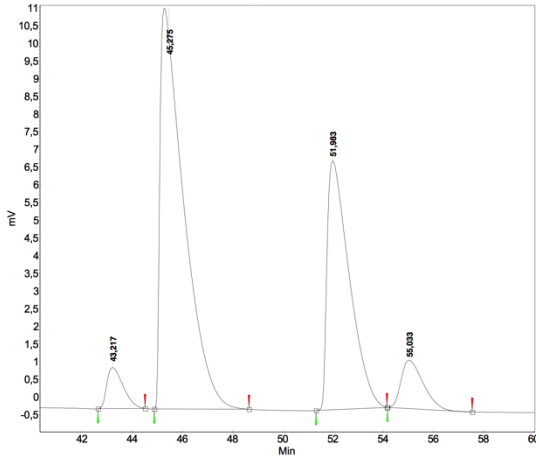
viscous, colorless oil that crystallized in the freezer. – dr (*trans*/*cis*) before chromatography: 64:36, after chromatography: 64:36.

R_f 0.33, CH_2Cl_2. – mp 102 °C. – $[\alpha]_D^{20}$ +0.6 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3256, 2955, 2930, 2872, 1320, 1156, 1084, 809, 669, 570. – δ_H (500 MHz; $CDCl_3$; signals of *cis*-**4d**-*Et* marked with "#") 0.74 (t, *J* = 7.4 Hz, 3H, 2'-H), 0.76 (t, *J* = 7.4 Hz, 3H, 2'-H#), 0.81 (s, 3H, 2"-H), 0.85 (s, 3H, 1"-H#), 0.87 (s, 3H, 1"-H, 2"-H#), 0.89-0.95 (m, 1H, 3-H), 0.98-1.02 (m, 1H, 5-H#), 1.04-1.08 (m, 1H, 3-H#), 1.14-1.25 (m, 2H, 1'-H), 1.34-1.40 (m, 1H, 5-H), 1.45-1.52 (m, 1H, 5-H), 1.57-1.63 (m, 1H, 3-H, 4-H#), 1.79-1.85 (m, 1H, 5-H#, 4-H), 2.41 (s, 3H, ArC*H*$_3$), 3.11-3.18 (m, 1H, 1-H), 4.79 (d, *J* = 9.4 Hz, 1H, NH), 4.84 (d, *J* = 9.4 Hz, 1H, NH#), 7.28 (m_c, 2H, Ar-H), 7.77 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$; signals of *cis*-**4d**-*Et* marked with "#") 12.4 (C-2'), 12.8 (C-2'#), 21.1 (C-2"), 21.6 (Ar*C*H$_3$), 24.5 (C-1"#), 26.8 (C-1"), 28.3 (C-2"#), 29.9 (C-1'#), 30.2 (C-1'), 35.4 (C-4), 36.1 (C-4#), 37.2 (C-5), 38.9 (C-5#), 40.2 (C-2#), 41.8 (C-2), 45.3 (C-3#), 46.1 (C-3), 62.0 (C-1), 63.0 (C-1#), 127.2 (C-Ar), 129.6 (C-Ar), 138.3 (C-Ar), 143.2 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{16}H_{25}NO_2SNa$ $[M+Na]^+$: 318.1498; found 318.1497. – The enantiomeric excesses were measured by HPLC, method C; *trans*-**4d**-*Et*: retention times 45.3 min (major enantiomer), 55.0 min (minor enantiomer): 80% ee; *cis*-**4d**-*Et*: retention times 43.2 min (minor enantiomer), 52.0 min (major enantiomer): 78% ee. The absolute configurations were assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	44,758	18,50	2,1	1,8	18,505
2	UNKNOWN	47,775	31,81	3,0	3,0	31,815
3	UNKNOWN	54,883	18,24	1,7	1,7	18,237
4	UNKNOWN	57,842	31,44	2,7	3,0	31,444
Total			100,00	9,5	9,5	100,000



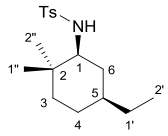
Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	43,217	4,01	1,2	0,9	4,007
2	UNKNOWN	45,275	56,66	11,3	12,4	56,659
3	UNKNOWN	51,983	33,01	7,0	7,2	33,008
4	UNKNOWN	55,033	6,33	1,4	1,4	6,326
Total			100,00	20,9	21,9	100,000

Racemic conjugate addition was performed as follows: CuCl (24.8 mg, 251 µmol) was suspended in THF (1 mL) and cooled to –30 °C, and EtMgBr (172 µL, 375 µmol, 2.18 M in Et_2O) was added dropwise. The reaction mixture was stirred for 15 min, a solution of ketimine **1d** (65.8 mg, 250 µmol) in THF (1 mL) was added dropwise, and the reaction mixture was stirred for 16 h

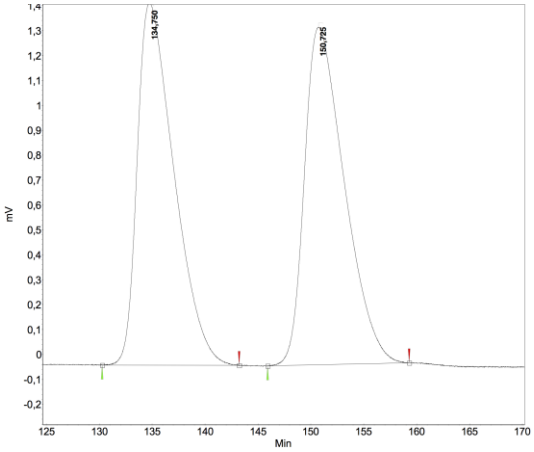
at –30 °C. Workup and hydrogenation were performed as described in GP 3 and GP 4 to yield 20 mg (27%) of the racemic amide **4d**-*Et*.

N-[(1*S*,5*S*)-2,2-Dimethyl-5-ethylcyclohexyl]-4-methylbenzenesulfonamide (4e-*Et*)



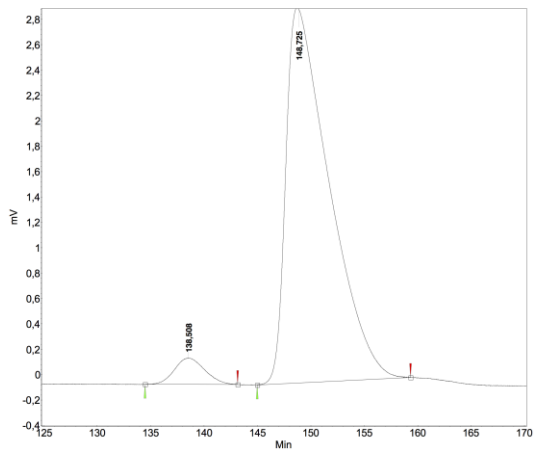
Conjugate addition according to GP 3 using ketimine **1e** (138.7 mg, 500.0 µmol), reaction time 16 h at –30 °C. The crude product was cooled to 0 °C, and a solution of *t*BuNH$_2$·BH$_3$ (91.3 mg, 1.05 mmol) in CH_2Cl_2 (3 mL) was added. The reaction mixture was stirred for 16 h at 0 °C, poured into half-saturated aqueous NH_4Cl (2 mL), and extracted with MTBE (3 × 10 mL). The combined organic phases were washed with water (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography over silica gel furnished 118 mg (76%) of amide **4e**-*Et* as a colorless solid with a dr (*trans/cis*) <3:97.

R_f 0.50, CH_2Cl_2. – mp 136 °C. – $[\alpha]_D^{20}$ +17.7 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3249, 2955, 2920, 2855, 1597, 1451, 1318, 1155, 1092, 812, 660, 573, 549. – δ_H (500 MHz; $CDCl_3$) 0.71 (t, *J* = 7.3 Hz, 3H, 2'-H), 0.76 (s, 3H, 2''-H), 0.79 (s, 3H, 1''-H), 0.84-0.96 (m, 2H, 3-H, 6-H), 1.02-1.21 (m, 4H, 4-H, 5-H, 1'-H), 1.39-1.44 (m, 3H, 3-H, 4-H, 6-H), 2.41 (s, 3H, ArC*H*$_3$), 2.90 (ddd, *J* = 12.2, 9.5, 4.0 Hz, 1H, 1-H), 4.39 (d, *J* = 9.5 Hz, 1H, NH), 7.28 (m$_c$, 2H, Ar-H), 7.76 (m$_c$, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 11.3 (C-2'), 18.7 (C-2''), 21.6 (Ar*C*H$_3$), 27.8 (C-3), 29.32 (C-1'), 29.34 (C-1''), 34.6 (C-2), 36.2 (C-6), 39.5 (C-5), 40.1 (C-4), 60.9 (C-1), 127.2 (C-Ar), 129.6 (C-Ar), 138.6 (C-Ar), 143.2 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{17}H_{27}NO_2SNa$ [M+Na]$^+$: 332.1655; found 332.1652. – The enantiomeric excess was measured by HPLC, method D, retention times 139 min (minor enantiomer), 149 min (major enantiomer): 91% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	134,750	49,68	1,5	5,8	49,676
2	UNKNOWN	150,725	50,32	1,4	5,9	50,324
Total			100,00	2,8	11,8	100,000

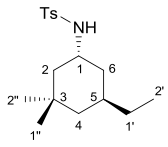


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	138,508	4,67	0,2	0,7	4,668
2	UNKNOWN	148,725	95,33	3,0	13,9	95,332
Total			100,00	3,2	14,5	100,000

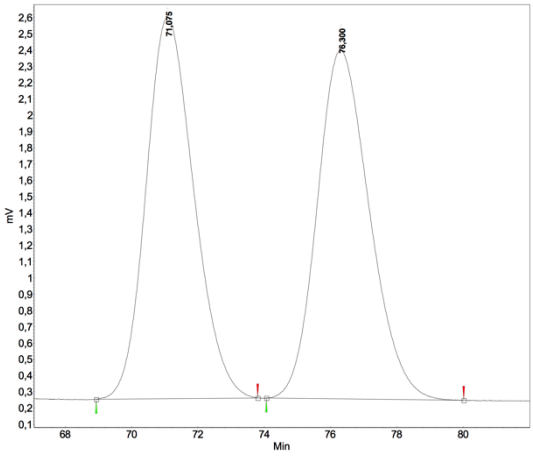
Racemic conjugate addition was performed as follows: CuCl (19.8 mg, 200 μmol) was suspended in THF (1 mL) and cooled to –30 °C, and EtMgBr (138 μL, 301 μmol, 2.18 M in Et_2O) was added dropwise. The reaction mixture was stirred for 15 min, a solution of ketimine **1e** (55.5 mg, 200 μmol) in THF (1 mL) was added dropwise, and the reaction mixture was stirred for 1 h at –30 °C. Workup and hydrogenation were performed according to the preparation of enantiomerically enriched **4e**-*Et* using *t*$BuNH_2 \cdot BH_3$ (36.5 mg, 420 μmol). Purification by column chromatography yielded 39 mg (63%) of the racemic amide **4e**-*Et*.

_N_-[(1*R*,5*S*)-3,3-Dimethyl-5-ethylcyclohexyl]-4-methylbenzenesulfonamide (4f-*Et*)



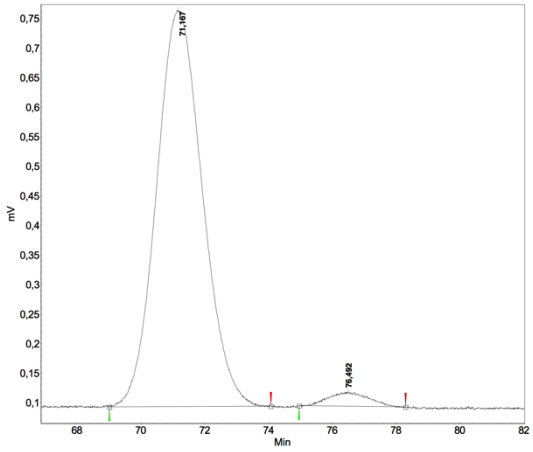
Preparation according to GP 3 and GP 4 using ketimine **1f** (139 mg, 501 μmol), reaction time 1 h at –30 °C, yielded 129 mg (83%) of amide **4f**-*Et* as a colorless solid with a dr (*trans/cis*) >97:3.

R_f 0.39, pentane/EtOAc 10:1. – mp 82 °C. – $[\alpha]_D^{20}$ –5.8 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3255, 2957, 2918, 2873, 1347, 1304, 1152, 1120, 773, 666, 597, 527, 498. – δ_H (500 MHz; $CDCl_3$) 0.72-0.75 (m, 1H, 4-H), 0.76 (t, *J* = 7.4 Hz, 3H, 2'-H), 0.82 (s, 3H, 2''-H), 0.95 (m_c, 1H, 6-H), 0.93 (s, 3H, 1''-H), 1.12 (m_c, 2H, 1'-H), 1.23 (dd, *J* = 14.2, 4.6 Hz, 1H, 2-H), 1.36-1.46 (m, 3H, 2-H, 4-H, 5-H), 1.57-1.64 (m, 1H, 6-H), 2.41 (s, 3H, ArC*H*$_3$), 3.50 (m_c, 1H, 1-H), 4.74 (d, *J* = 6.2 Hz, 1H, NH), 7.29 (m_c, 2H, Ar-H), 7.76 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 11.4 (C-2'), 21.6 (Ar*C*H$_3$), 28.5 (C-1''), 29.4 (C-1'), 30.3 (C-5), 30.8 (C-3), 33.7 (C-2''), 37.1 (C-6), 43.3 (C-2), 45.2 (C-4), 49.8 (C-1), 127.3 (C-Ar), 129.7 (C-Ar), 137.9 (C-Ar), 143.3 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{17}H_{28}NO_2S$ $[M+H]^+$: 310.1835; found 310.1836. – The enantiomeric excess was measured by HPLC, method E, retention times 71.2 min (major enantiomer), 76.5 min (minor enantiomer): 94% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	71,075	49,97	2,3	3,9	49,972
2	UNKNOWN	76,300	50,03	2,1	3,9	50,028
Total			100,00	4,5	7,8	100,000

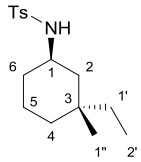


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	71,167	97,03	0,7	1,1	97,029
2	UNKNOWN	76,492	2,97	0,0	0,0	2,971
Total			100,00	0,7	1,1	100,000

Racemic conjugate addition was performed as follows: Ketimine **1f** (139 mg, 501 µmol) and CuCl (49.5 mg, 500 µmol) were dissolved in Et_2O (2 mL) and cooled to –30 °C. EtMgBr (344 µL, 750 µmol, 2.18 M in Et_2O) was added dropwise, and the reaction mixture was stirred for 1 h at –30 °C. Workup and hydrogenation were performed according to the preparation of enantiomerically enriched **4f**-*Et*, and an analytical sample of the racemic compound was obtained by repeated column chromatography.

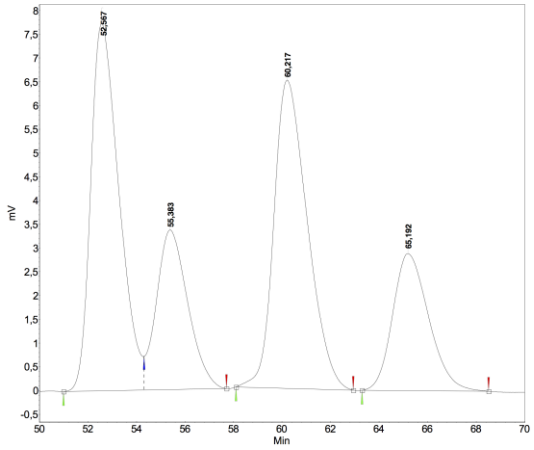
N-[(1*R*,3*R*)-3-Ethyl-3-methylcyclohexyl]-4-methylbenzenesulfonamide (4g-*Et*)



Conjugate addition according to GP 3 using ketimine **1g** (131.7 mg, 500 µmol), CuTC (9.55 mg, 50.1 µmol), and ligand *ent*-**L1** (32.4 mg, 60.0 µmol), reaction time 20 h at –15 °C. Hydrogenation according to GP 4 with RuCl(*p*-cymene)[(*S*,*S*)-Ts-DPEN] and column chromatography furnished 133 mg of **4g**-*Et* with minor impurities from unreacted ketimine **1g**. After repeated column chromatography, 80 mg (54%) of amide **4g**-*Et* were obtained as a colorless oil. – dr (*trans*/*cis*) before chromatography: 82:18, after repeated chromatography: 81:19.

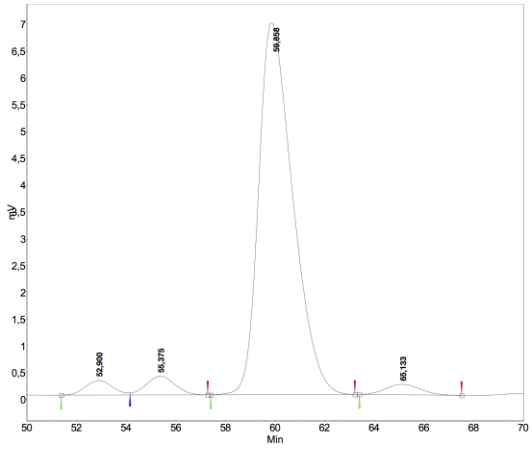
R_f 0.33, pentane/EtOAc 5:1. – mp 55-57 °C. – IR (neat) ν_{max}/cm^{-1} 3247, 2963, 2929, 2865, 1447, 1319, 1164, 811, 659, 569, 548. – δ_H (500 MHz; $CDCl_3$, signals of *cis*-**4g**-*Et* marked with "#") 0.64 (t, *J* = 7.5 Hz, 3H, 2'-H), 0.72 (t, *J* = 7.6 Hz, 3H, 2'-H#), 0.75 (s, 3H, 1''-H), 0.85 (t, *J* = 12.4 Hz, 1H, 2-H), 0.89-1.01 (m, 2H, 5-H, 6-H), 1.11-1.26 (m, 2H, 1'-H), 1.32-1.57 (m, 4H, 2-H, 5-H, 4-H), 1.81 (m_c, 1H, 6-H), 2.42 (s, 3H, ArCH_3), 3.18 (m_c, 1H, 1-H), 3.27 (m_c, 1H, 1-H#), 4.68 (d, *J* = 8.1 Hz, 1H, NH#), 4.71 (d, *J* = 7.7 Hz, 1H, NH), 7.28 (m_c, 2H, Ar-H), 7.76 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$; signals of *cis*-**4g**-*Et* marked with "#") 7.5 (C-2'#), 7.7 (C-2'), 20.8 (C-4), 21.2 (C-4#), 21.4

(C-1"#), 21.6 ($ArCH_3$), 28.3 (C-1'), 28.6 (C-1"), 34.18 (C-6), 34.24 (C-3), 34.4 (C-3#), 34.6 (C-6#), 35.9 (C-5#), 36.3 (C-5), 38.1 (C-1'#), 44.6 (C-2), 44.9 (C-2#), 49.6 (C-1), 50.2 (C-1#), 127.05 (C-Ar#), 127.07 (C-Ar), 129.7 (C-Ar), 138.6 (C-Ar), 138.7 (C-Ar#) 143.2 (C-Ar). – HRMS (ESI) *m/z* calcd for $C_{16}H_{25}NO_2SNa$ $[M+Na]^+$: 318.1498; found 318.1499. – The enantiomeric excesses were measured by HPLC, method B; *trans*-**4g**-*Et*: retention times 52.9 min (minor enantiomer), 59.9 min (major enantiomer): 94% ee; *cis*-**4g**-*Et*: retention times 55.4 min (major enantiomer), 65.1 min (minor enantiomer): 19% ee. The absolute configurations were assigned in analogy to amide **4a**-*Et*.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
2	UNKNOWN	52,567	33,86	7,7	10,4	33,860
3	UNKNOWN	55,383	16,31	3,4	5,0	16,308
4	UNKNOWN	60,217	33,72	6,5	10,4	33,715
1	UNKNOWN	65,192	16,12	2,9	5,0	16,117
Total			100,00	20,5	30,7	100,000

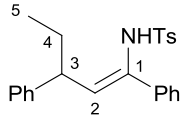


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	52,900	2,84	0,3	0,3	2,839
2	UNKNOWN	55,375	3,85	0,3	0,5	3,849
3	UNKNOWN	59,858	90,70	6,9	11,0	90,701
4	UNKNOWN	65,133	2,61	0,2	0,3	2,611
Total			100,00	7,8	12,2	100,000

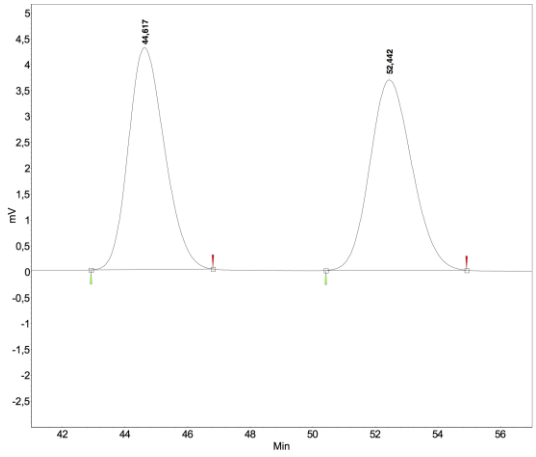
Racemic conjugate addition was performed as follows: Ketimine **1g** (65.8 mg, 250 µmol) and CuCl (18.6 mg, 188 µmol) were dissolved in Et_2O (2 mL) and cooled to –15 °C. EtMgBr (172 µL, 375 µmol, 2.18 M in Et_2O) was added dropwise, and the reaction mixture was stirred for 16 h at –30 °C. Workup was performed according to GP 3. Hydrogenation according to GP 4 with racemic RuCl(*p*-cymene)[Ts-DPEN] (*rac*-**3**, 7.95 mg, 12.5 µmol) and a 5:2 mixture of formic acid and triethyl amine (157 µL, 374 µmol) and repeated column chromatography yielded an analytical sample of the racemic amide **4g**-*Et*.

(Z)-*N*-(1,3-Diphenylpent-1-enyl)-4-methylbenzenesulfonamide (2h-*Et*)



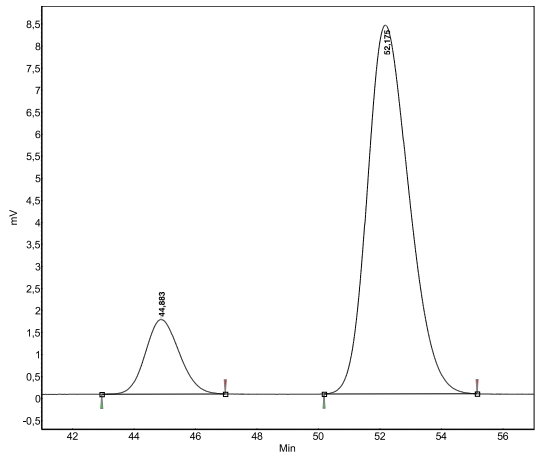
Preparation according to GP 3 from ketimine **1h** (90.4 mg, 250 µmol), CuTC (0.96 mg, 5.0 µmol), ligand **L1** (5.40 mg, 10.0 µmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 2.5 h at –30 °C. The crude product was purified by column chromatography, and 67 mg (68%) of enamide **2h**-*Et* were obtained as a colorless solid.

R_f 0.57, CH_2Cl_2. – mp 144 °C. – $[\alpha]_D^{20}$ –39.3 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3279, 2964, 2927, 1597, 1387, 1305, 1166, 688. – δ_H (500 MHz; $CDCl_3$) 0.66 (t, *J* = 7.4 Hz, 3H, 5-H), 1.41-1.49 (m, 1H, 4-H), 1.53-1.60 (m, 1H, 4-H), 2.37 (s, 3H, ArCH_3), 2.94 (dt, *J* = 9.0, 7.4 Hz, 1H, 3-H), 5.65 (dd, *J* = 9.2, 0.7 Hz, 1H, 2-H), 6.13 (s, 1H, NH), 6.99 (m_c, 2H, Ar-H), 7.17-7.19 (m, 3H, Ar-H), 7.22-7.26 (m, 5H, Ar-H), 7.37-7.40 (m, 2H, Ar-H), 7.56 (m_c, 2H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 11.9 (C-5), 21.6 (Ar*C*H_3), 30.6 (C-4), 45.2 (C-3), 126.7 (C-Ar), 127.39 (C-Ar), 127.41 (C-Ar), 127.5 (C-Ar), 128.1 (C-Ar), 128.4 (C-Ar), 128.9 (C-2), 129.6 (C-Ar), 135.0 (C-1), 136.9 (C-Ar), 137.7 (C-Ar), 143.4 (C-Ar), 143.8 (C-Ar). – HRMS (EI) *m/z* calcd for $C_{24}H_{25}NO_2S$ $[M]^+$: 391.1606; found 391.1608. – The enantiomeric excess was measured by HPLC, method F, retention times 44.9 min (minor enantiomer), 52.2 min (major enantiomer): 72% ee. The absolute configuration was not determined.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	44,617	50,04	4,3	5,8	50,040
2	UNKNOWN	52,442	49,96	3,7	5,8	49,960
Total			100,00	8,0	11,5	100,000

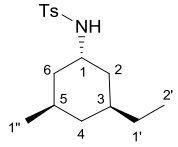


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	44,883	14,15	1,7	2,2	14,148
2	UNKNOWN	52,175	85,85	8,4	13,1	85,852
Total			100,00	10,1	15,3	100,000

Racemic preparation was performed as described above using racemic *O,O'*-(1,1'-dinaphthyl-2,2'-diyl)-*N,N*-di-*iso*-propylphosphoramidite (4.15 mg, 10.0 µmol) and yielded 96 mg (98%) of the racemic enamide **2h**-*Et*, no purification was performed.

N-[(1*S*,3*S*,5*R*)-3-Ethyl-5-methylcyclohexyl]-4-methylbenzenesulfonamide (4i-*Et*)



Conjugate addition according to GP 3 from ketimine (*R*)-**1i** (131.7 mg, 500 µmol), reaction time 1 h at –30 °C, furnished the conjugate addition product **2i**-*Et* with a dr (*trans/cis*) 48:52. Hydrogenation according to GP 4 yielded 53 mg (36%) of amide (1*S*,3*S*,5*R*)-**4i**-*Et* as a colorless solid.

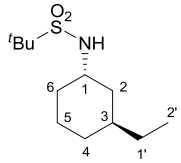
R_f 0.60, pentane/EtOAc 5:1. – mp 116 °C. – $[\alpha]_D^{20}$ –6.2 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3276, 2922, 1495, 1162, 1144, 1092, 817, 684, 553. – δ_H (500 MHz; $CDCl_3$) 0.44 (ddd, *J* = 12.5,

12.3, 12.1 Hz, 1H, 4-H), 0.75 (t, *J* = 7.5 Hz, 3H, 2'-H), 0.79 (d, *J* = 6.5 Hz, 3H, 1''-H), 0.92 (m_c, 2H, 2-H, 6-H), 1.04-1.17 (m, 2H, 1'-H), 1.24-1.33 (m, 1H, 3-H), 1.46-1.55 (m, 1H, 5-H), 1.57-1.64 (m, 2H, 2-H, 6-H), 1.65-1.68 (m, 1H, 4-H), 2.42 (s, 3H, ArC*H*$_3$), 3.60 (m_c, 1H, 1-H), 4.82 (d, *J* = 7.2 Hz, 1H, NH), 7.29 (m_c, 2H, H-Ar), 7.77 (m_c, 2H, H-Ar). – δ_C (125 MHz; $CDCl_3$) 11.2 (C-2'), 21.6 (Ar*C*H$_3$), 22.5 (C-1''), 26.8 (C-5), 29.7 (C-1'), 33.4 (C-3), 36.9 (C-6), 39.6 (C-2), 41.0 (C-4), 50.1 (C-1), 127.2 (C-Ar), 129.7 (C-Ar), 138.3 (C-Ar), 143.3 (C-Ar). – HRMS (EI) *m/z* calcd for $C_{16}H_{25}NO_2S$ $[M]^+$: 295.1606 ; found 295.1601.

Additionally, 51 mg (35%) of *N*-[(3*R*,5*R*)-3-ethyl-5-methylcyclohexyl]-4-methylbenzenesulfonamide were obtained as an oil that crystallized in the freezer. This material is an epimeric mixture at C-1 in a 54:46 ratio.

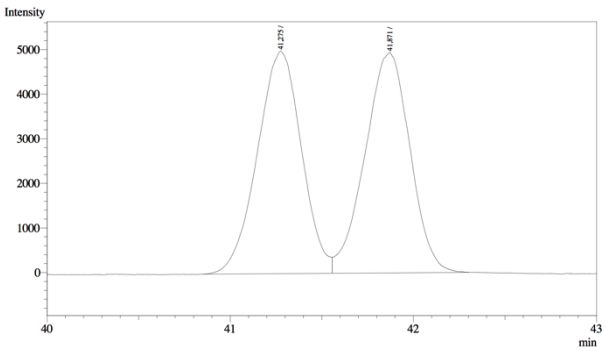
R_f 0.48, pentane/EtOAc 5:1. – δ_H (500 MHz; $CDCl_3$, signals corresponding to single diastereomers are marked with "#") 0.65-0.81 (m, 7H), 0.86 (d, *J* = 7.3 Hz, 3H#), 0.91-0.98 (m, 1H), 1.08-1.26 (m, 3H), 1.34-1.62 (m, 4H), 1.82 (m_c, 1H), 1.98 (m_c, 1H#), 2.42 (s, 3H), 3.22 (m_c, 1H#), 3.31 (m_c, 1H#), 4.59 (m, 1H), 7.29 (m_c, 2H), 7.76 (m_c, 2H). – δ_C (125 MHz; $CDCl_3$) 11.4, 12.4, 18.6, 21.6, 22.5, 24.8, 26.5, 27.9, 29.7, 32.9, 35.4, 37.0, 37.3, 37.6, 39.7, 41.0, 43.3, 49.0, 127.1, 129.7, 138.6, 138.7, 143.2.

_N_-[(1*S*,3*S*)-3-Ethylcyclohexyl]-*tert*-butylsulfonamide (6a-*Et*)

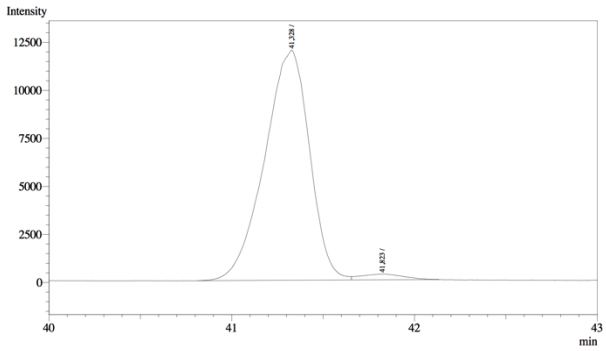


Conjugate addition according to GP 3 using ketimine **5a** (53.8 mg, 250 μmol), CuTC (0.96 mg, 5.0 μmol), ligand **L1** (5.40 mg, 10.0 μmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2mL), reaction time 20 h at –30 °C. Hydrogenation according to GP 4 with racemic RuCl(*p*-cymene)[Ts-DPEN] (*rac*-**3**, 7.95 mg, 12.5 μmol) and a 5:2 mixture of formic acid and triethyl amine (157 μL, 374 μmol) yielded 37 mg (60%) of amide **6a**-*Et* as a colorless oil that crystallized in the freezer. – dr (*trans/cis*) >97:3.

R_f 0.30, CH_2Cl_2. – mp 54 °C. – $[\alpha]_D^{20}$ +1.3 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3290, 2958, 2927, 2873, 1478, 1294, 1124, 677, 514. – δ_H (500 MHz; $CDCl_3$) 0.87 (t, *J* = 7.4 Hz, 3H, 2'-H), 0.97-1.05 (m, 1H, 5-H), 1.21-1.27 (m, 2H, 1'-H), 1.38-1.47 (m, 12H, 2-H, 3-H, 4-H, C(C*H*$_3$)$_3$), 1.56-1.65 (m, 4H, 4-H, 5-H, 6-H), 1.69-1.74 (m, 1H, 2-H), 3.67 (m_c, 1H, 1-H), 4.16 (d, *J* = 9.3 Hz, 1H, NH). – δ_C (125 MHz; $CDCl_3$) 11.6 (C-2'), 20.6 (C-4), 24.5 (C(*C*H$_3$)$_3$), 28.3 (C-1'), 31.0 (C-5), 33.3 (C-6), 34.2 (C-3), 38.8 (C-2), 50.7 (C-1), 59.7 (*C*(CH$_3$)$_3$). – HRMS (ESI) *m/z* calcd for $C_{12}H_{25}NO_2SNa$ $[M+Na]^+$: 270.1498; found 270.1497. – The enantiomeric excess was measured by GC, method B, retention times 41.3 min (major enantiomer), 41.8 min (minor enantiomer): 95% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



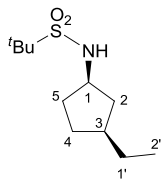
Peak#	Ret.Time	Area	Area%	Height	Cmpd Name
1	41,275	83635	49,8018	4986	
2	41,871	84301	50,1982	4936	
Total		167936	100,0000	9922	



Peak#	Ret.Time	Area	Area%	Height	Cmpd Name
1	41,328	204614	97,7171	11970	
2	41,823	4780	2,2829	296	
Total		209394	100,0000	12266	

Racemic conjugate addition was performed as follows: CuCl (24.8 mg, 251 μmol) was suspended in THF (1 mL) and cooled to –30 °C, then EtMgBr (172 μL, 375 μmol, 2.18 M in Et_2O) was added dropwise. The reaction mixture was stirred for 15 min, a solution of ketimine **5a** (53.8 mg, 250 μmol) in THF (1 mL) was added dropwise, and the reaction mixture was stirred for 1 h at –30 °C. Workup was performed according to GP 3. Hydrogenation according to GP 4 with racemic RuCl(*p*-cymene)[Ts-DPEN] (*rac*-**3**, 7.95 mg, 12.5 μmol) and a 5:2 mixture of formic acid and triethyl amine (157 μL, 374 μmol) yielded 13 mg (21%) of the racemic amide **6a**-*Et*.

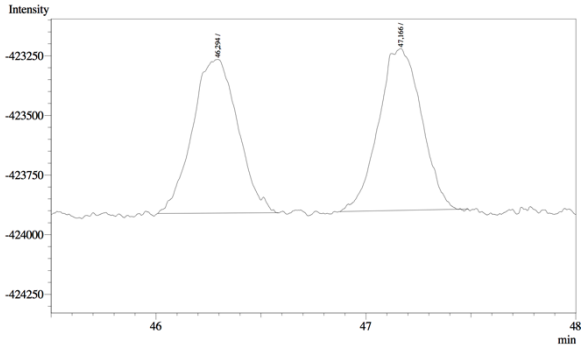
N-[(1*R*,3*S*)-3-Ethylcyclopentyl]-*tert*-butylsulfonamide (6b-*Et*)



Conjugate addition according to GP 3 using ketimine **5b** (50.3 mg, 250 μmol), CuTC (0.96 mg, 5.0 μmol), ligand **L1** (5.40 mg, 10.0 μmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 20 h at –30 °C. Hydrogenation according to GP 4 with RuCl(*p*-cymene)[(*S*,*S*)-Ts-DPEN] ((*S*,*S*)-**3**, 7.95 mg, 12.5 μmol) and a 5:2 mixture of formic acid and triethyl amine (157 μL, 374 μmol) yielded 42 mg (72%) of amide **6b**-*Et* as a colorless oil that crystallized in the freezer. – dr (*trans*/*cis*) before chromatography: 23:77, after chromatography: 23:77.

R_f 0.15, CH_2Cl_2. – mp 47–49 °C. – $[\alpha]_D^{20}$ +1.3 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3289, 2958, 2931, 2873, 1477, 1297, 1116, 933, 667. – δ_H (500 MHz; $CDCl_3$, signals of the minor diastereomer marked with "#") 0.86 (t, *J* = 7.4 Hz, 3H, 2'-H), 1.02 (ddd, *J* = 12.5, 9.7, 9.7 Hz, 1H, 2-H), 1.09 (ddd, *J* = 9.5, 8.1, 4.2 Hz, 1H, 2-H#), 1.23-1.35 (m, 3H, 1'-H, 4-H), 1.37 (s, 9H, C(C*H*$_3$)$_3$), 1.44-1.54 (m, 1H, 5-H), 1.59 (dt, *J* = 13.4, 7.7 Hz, 1H, 2-H#), 1.67-1.78 (m, 2H, 3-H, 4-H), 1.88 (m_c, 2H, 3-H#), 1.98-2.05 (m, 1H, 5-H), 2.07-2.13 (m, 1H, 5-H#), 2.25 (ddd, *J* = 12.5, 6.8, 6.8 Hz, 1H, 2-H), 3.75 (m_c, 1H, 1-H), 3.83 (m_c, 1H, 1-H#), 4.09 (d, *J* = 9.2 Hz, 1H, NH), 4.14 (d, *J* = 9.2 Hz, 1H, NH#). – δ_C (125 MHz; $CDCl_3$, signals of the minor diastereomer marked with "#") 12.8 (C-2'), 24.5 (C(*C*H$_3$)$_3$), 29.1 (C-1'#), 29.3 (C-1'), 29.7 (C-4), 30.6 (C-4#), 33.9 (C-5), 35.1 (C-5#), 39.4 (C-3#), 39.8 (C-3), 40.7 (C-2#), 41.8 (C-2), 56.1 (C-1#), 56.4 (C-1), 59.61 (*C*(CH$_3$)$_3$), 59.63 (*C*(CH$_3$)$_3$#). –

HRMS (ESI) *m/z* calcd for $C_{11}H_{23}NO_2SNa$ $[M+Na]^+$: 256.1342; found 256.1339. – The enantiomeric excess was measured by GC, method B, retention times 46.2 min (major enantiomer), 47.1 min (minor enantiomer): 69% ee. Enantiomers of the minor diastereomer could not be separated; the absolute configuration was assigned in analogy to amide **4a**-*Et*.



Peak#	Ret.Time	Area	Area%	Height	Cmpd Name
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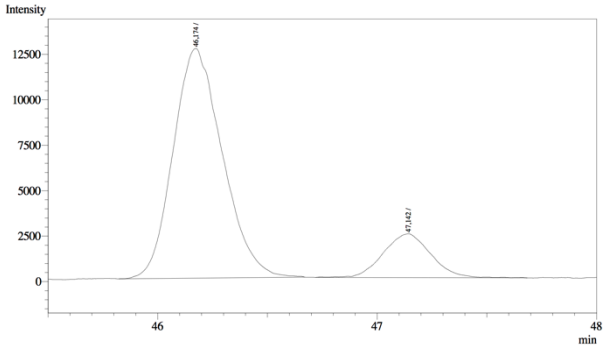
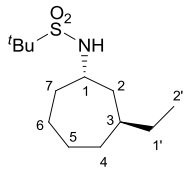
2	47,166	9703	49,9281	678	
Total		19434	100,0000	1323	



Peak#	Ret.Time	Area	Area%	Height	Cmpd Name
1	46,174	197392	84,4600	12634	
2	47,142	36318	15,5400	2409	
Total		233710	100,0000	15043	

Racemic conjugate addition was performed as described above using racemic *O,O*'-(1,1'-dinaphthyl-2,2'-diyl)-*N,N*-di-*iso*-propylphosphoramidite (4.15 mg, 10.0 μmol). The crude conjugate addition product was dissolved in EtOH (2 mL), $NaBH_4$ (94.5 mg, 2.50 mmol) was added, and the reaction mixture was stirred for 16 h at rt. The reaction mixture was then poured into saturated aqueous NH_4Cl (10 mL), extracted with CH_2Cl_2 (3 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography over silica gel yielded 17 mg (29%) of the racemic amide **6b**-*Et*.

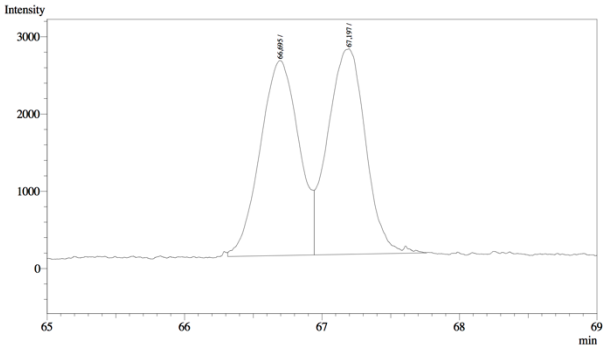
N-[(1*S*,3*S*)-3-Ethylcycloheptyl]-*tert*-butylsulfonamide (6c-*Et*)



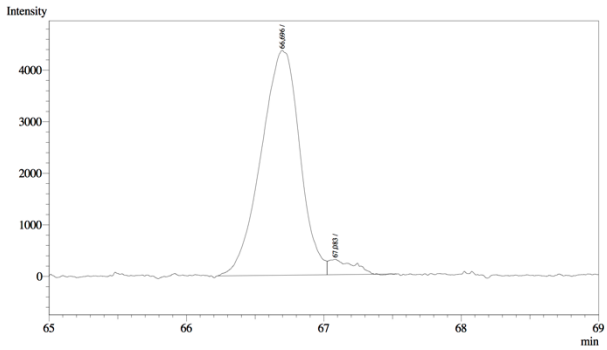
Conjugate addition according to GP 3 using ketimine **5c** (57.3 mg, 250 μmol), CuTC (0.96 mg, 5.0 μmol), ligand **L1** (5.40 mg, 10.0 μmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 16 h at –30 °C. Hydrogenation according to GP 4 with racemic RuCl(*p*-cymene)[Ts-DPEN] (*rac*-**3**, 7.95 mg, 12.5 μmol) and a 5:2 mixture of formic acid and triethyl amine (157 μL, 374 μmol) yielded 43 mg (66%) of amide **6c**-*Et* as a colorless oil that crystallized in the freezer. – dr (*trans*/*cis*) before chromatography: 96:4, after chromatography: 97:3.

R_f 0.17, pentane/EtOAc 15:1. – mp 35 °C. – $[\alpha]_D^{20}$ –9.2 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3268, 2921, 2855, 1440, 1306, 1125, 1048, 666. – δ_H (500 MHz; $CDCl_3$) 0.88 (t, *J* = 7.4 Hz, 3H, 2'-H), 1.09-1.17 (m, 1H, 4-H), 1.24-1.46 (m, 14H, 1'-H, 3-H, 5-H, 6-H, C(CH_3)$_3$), 1.53-1.60 (m, 1H, 7-H), 1.65-1.82 (m, 5H, 2-H, 4-H, 5-H, 6-H), 2.01 (m_c, 1H, 7-H), 3.62 (m_c, 1H, 1-H), 3.99 (d, *J* = 9.8 Hz, 1H, NH). – δ_C (125 MHz; $CDCl_3$) 11.9 (C-2'), 24.4 (C(*C*H_3)$_3$), 25.5 (C-5), 28.3 (C-6),

30.5 (C-1'), 34.4 (C-4), 36.2 (C-3), 37.3 (C-7), 42.1 (C-2), 54.2 (C-1), 59.7 ($C(CH_3)_3$). – HRMS (ESI) *m/z* calcd for $C_{13}H_{27}NO_2SNa$ $[M+Na]^+$: 284.1655; found 284.1651. – The enantiomeric excess was measured by GC, method C, retention times 66.7 min (major enantiomer), 67.1 min (minor enantiomer): ~92% ee. The absolute configuration was assigned in analogy to amide **4a**-*Et*.



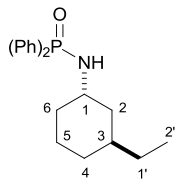
Peak#	Ret.Time	Area	Area%	Height	Cmpd Name
1	66,695	49496	49,4116	2524	
2	67,197	50675	50,5884	2658	
Total		100171	100,0000	5182	



Peak#	Ret.Time	Area	Area%	Height	Cmpd Name
1	66,696	85449	95,8059	4360	
2	67,083	3741	4,1941	296	
Total		89190	100,0000	4656	

Racemic preparation was performed as described above using racemic *O,O*'-(1,1'-dinaphthyl-2,2'-diyl)-*N,N*-di-*iso*-propylphosphoramidite (4.15 mg, 10.0 μmol) and yielded 30 mg (46%) of the racemic amide **6c**-*Et*.

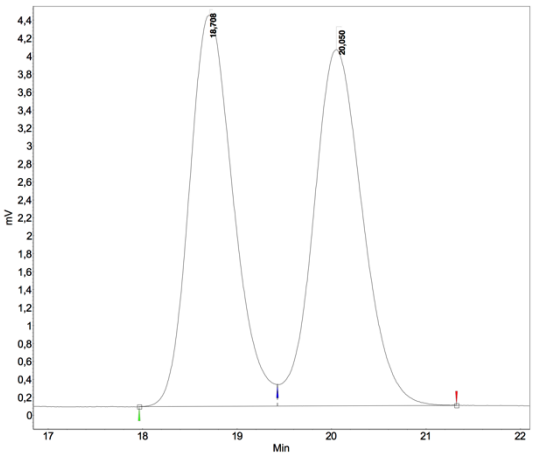
_N_-Diphenylphosphinoyl-(1*S,3*S**)-3-ethylcyclohexylamide (8a-*Et*)**



Conjugate addition according to GP 3 using ketimine **7a** (73.8 mg, 250 μmol), CuTC (0.96 mg, 5.0 μmol), ligand **L1** (5.40 mg, 10.0 μmol), and $ZnEt_2$ (0.25 mL, 0.38 mmol, 1.5 M in toluene) in toluene (2 mL), reaction time 20 h at –30 °C. The crude product was dissolved in THF (2.5 mL), and L-Selectride® (0.55 mL, 0.55 mmol, 1.0 M in THF) was added. The solution was stirred for 2.5 h and cooled to 0 °C, and H_2O (0.5 mL), aqueous NaOH (0.1 mL, 15 w/w), and H_2O_2 (0.1 mL, 30 w/w in H_2O) were added subsequently. The mixture was stirred for 0.5 h at 0 °C and poured onto a mixture of H_2O (10 mL) and MTBE (10 mL). The organic phase was separated, and the aqueous phase was extracted with MTBE (2 × 10 mL). The combined organic phases were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography over silica gel yielded 51 mg (62%) of amide **8a**-*Et* as a colorless solid. – dr (*trans/cis*) >97:3.

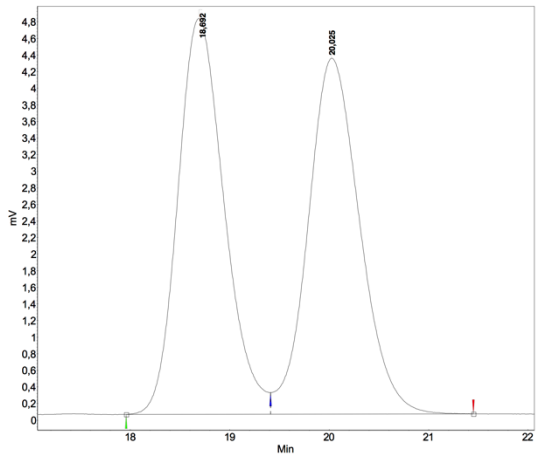
R_f 0.35, CH_2Cl_2/THF 85:15. – mp 117-118°C. – IR (neat) ν_{max}/cm^{-1} 3199, 2924, 1437, 1186, 1121, 1109, 748, 721, 693, 555, 526. – δ_H (500 MHz; $CDCl_3$) 0.83 (t, J = 7.4 Hz, 3H, 2'-H), 0.95-1.02 (m, 1H, 4-H), 1.15-1.24 (m, 2H, 1'-H), 1.30-1.36 (m, 1H, 2-H), 1.42-1.74 (m, 7H, 2-H, 3-H, 4-H, 5-H, 6-H), 3.44 (m_c, 1H, 1-H), 7.42-7.46 (m, 4H, Ar-H), 7.47-7.51 (m, 2H, Ar-H), 7.88-7.94 (m, 4H, Ar-H). – δ_C (125 MHz; $CDCl_3$) 11.6 (C-2'), 20.5 (C-5), 28.5 (C-1'), 31.2 (C-4), 34.0 (C-6), 34.1

(C-3), 39.7 (d, $J_{C,P}$ = 4.8 Hz, C-2), 46.9 (C-1), 128.6 (d, $J_{C,P}$ = 12.5 Hz, C-Ar), 131.9 (C-Ar), 132.2 (d, $J_{C,P}$ = 9.5 Hz, C-Ar), 132.4 (d, $J_{C,P}$ = 9.4 Hz, C-Ar). – HRMS (ESI) *m/z* calcd for $C_{20}H_{26}NOPNa$ $[M+Na]^+$: 350.1644; found 350.1633. – The enantiomeric excess was measured by HPLC, method G, retention times 18.7 min (first enantiomer), 20.0 min (second enantiomer): 0% ee.



Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	18,708	49,59	4,4	2,3	49,591
2	UNKNOWN	20,050	50,41	4,0	2,4	50,409
Total			100,00	8,3	4,7	100,000

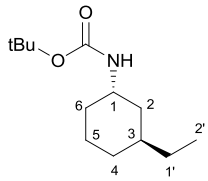


Peak results :

Index	Name	Time [Min]	Quantity [% Area]	Height [mV]	Area [mV.Min]	Area % [%]
1	UNKNOWN	18,692	49,98	4,8	2,6	49,975
2	UNKNOWN	20,025	50,02	4,3	2,6	50,025
Total			100,00	9,1	5,1	100,000

Racemic preparation was performed as described above using racemic *O,O'*-(1,1'-dinaphthyl-2,2'-diyl)-*N,N*-di-*iso*-propylphosphoramidite (4.15 mg, 10.0 μmol) and yielded 44 mg (54%) of the racemic amide **8a**-*Et*.

tert-Butyl-(1*S*,3*S*)-3-ethylcyclohexylcarbamat (9a-*Et*)



A solution of amide **4a**-*Et* (84 mg, 0.30 mmol) in CH_3CN (1 mL) was treated with di-*tert*-butyldicarbonate (97.7 mg, 448 μmol) and 4-(dimethylamino)pyridine (3.65 mg, 29.9 μmol) and stirred for 1 h at rt. The reaction mixture was poured onto MTBE (5 mL), washed subsequently with saturated aqueous NH_4Cl (5 mL), saturated aqueous $NaHCO_3$ (5 mL), and brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dissolved in MeOH (4 mL), Mg powder (36.3 mg, 1.49 mmol) was added, and the suspension was stirred at rt under ultrasonication. After 48 min, the suspension was filtered through a pad of celite, and the solvent was removed under reduced pressure. Purification by flash column chromatography over silica gel furnished 57 mg (84%) of carbamate **9a**-*Et* as a colorless solid.

R_f 0.58, CH_2Cl_2. – mp 45 °C. – $[\alpha]_D^{20}$ +2.5 (*c* 1.0 in $CHCl_3$). – IR (neat) ν_{max}/cm^{-1} 3369, 2924, 1681, 1517, 1162, 1047, 1020, 609. – δ_H (500 MHz; $CDCl_3$) 0.84 (t, *J* = 7.4 Hz, 3H, 2'-H), 0.96-1.03 (m, 1H, 4-H), 1.20-1.39 (m, 6H, 1'-H, 2-H, 3-H, 5-H, 6-H), 1.43 (s, 9H, $C(CH_3)_3$), 1.51-1.58

(m, 2H, 5-H, 6-H), 1.60-1.66 (m, 2H, 2-H, 4-H), 3.80, (m_c, 1H, 1-H), 4.63 (bs, 1H, NH). – δ_C (125 MHz; $CDCl_3$) 11.6 (C-2'), 20.7 (C-5), 28.6 (C(*C*H_3)$_3$, C-1'), 31.4 (C-4), 31.5 (C-6), 34.3 (C-3), 37.2 (C-2), 45.9 (C-1), 79.0 (*C*(CH_3)$_3$), 155.3 (CO). – HRMS (ESI) *m/z* calcd for $C_{13}H_{25}NO_2Na$ $[M+Na]^+$: 250.1778; found 250.1780.

2) Monitoring of the 1,4-Addition by Continuous IR Detection

A 10 mL three-necked flask, equipped with the probe of a Mettler-Toledo ReactIR® device, was charged with a mixture of copper(I)-thiophene-2-carboxylate (3.82 mg, 20.0 μmol), ligand **L1** (21.6 mg, 40.0 μmol), and ketimine **1a** (249 mg, 0.999 mmol). Toluene (8 mL) was added, and the solution was stirred for 0.5 h at rt and then cooled to –30 °C. $ZnEt_2$ (1.0 mL, 1.5 mmol, 1.5 M in toluene) was added rapidly, and simultaneously, data collection was started (t = 0 min). Then, the resulting yellow solution was stirred at –30 °C for 24 min.

Data analysis was performed using the decreasing IR band at 1320 cm^{-1} to determine conversion and the increasing IR band at 1129 cm^{-1} to determine product formation. Raw data is plotted in Fig. 1, while Fig. 2 gives an overview of all IR absorptions within the monitored reaction time.

We are indebted to Dr. Jennifer A. Allen, application specialist at Mettler-Toledo, for technical advisory concerning data acquisition and analysis.

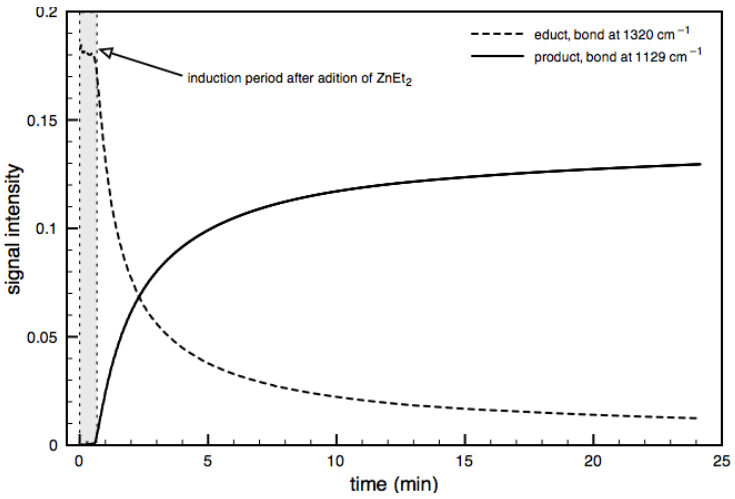


Figure 1: Monitoring of the 1,4-addition by continuous IR detection, sampling rate >5 Hz.

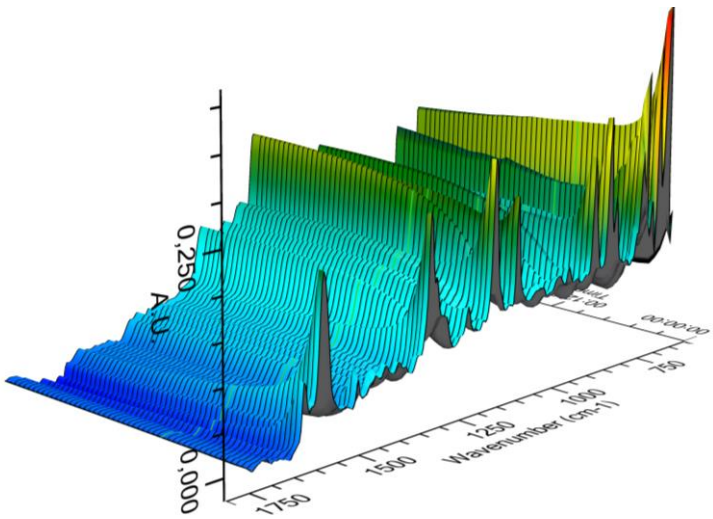
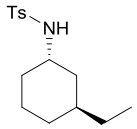
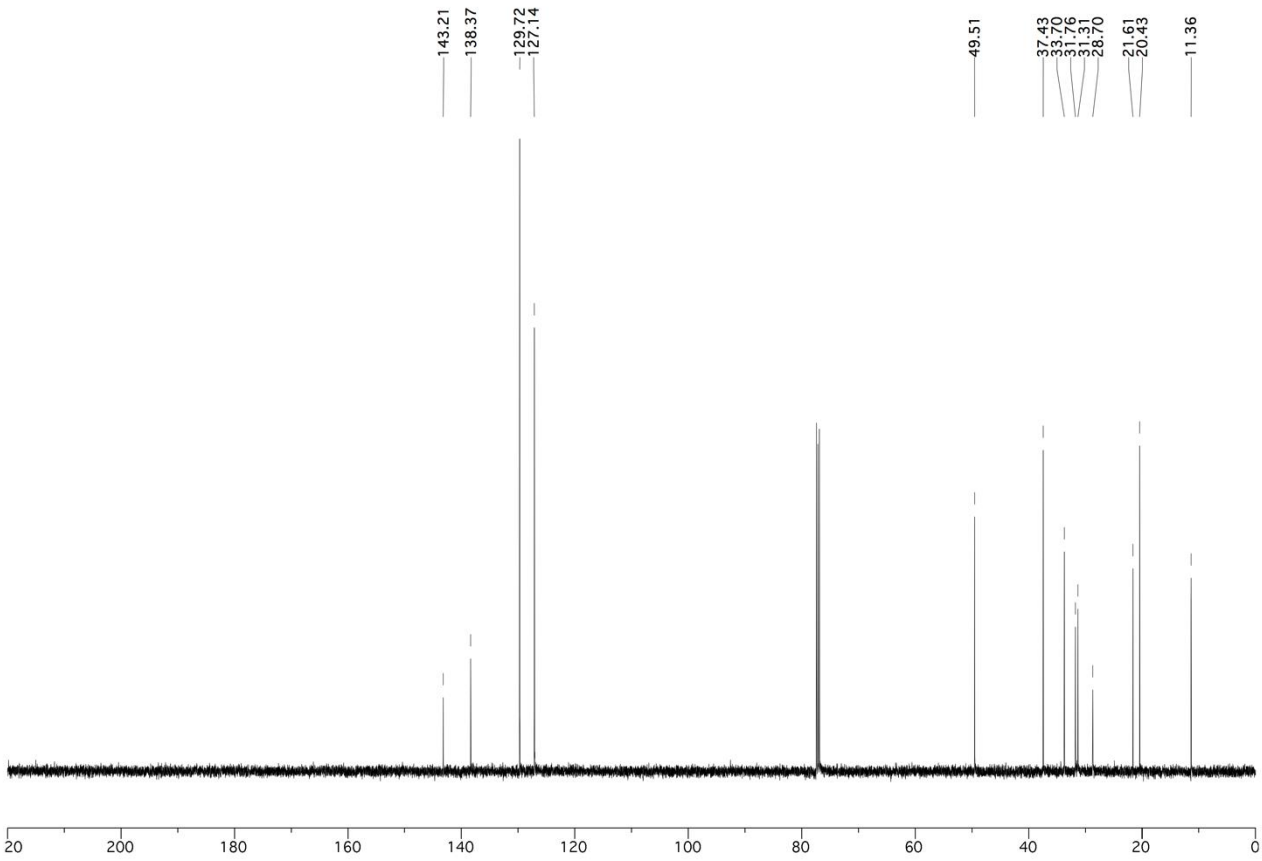


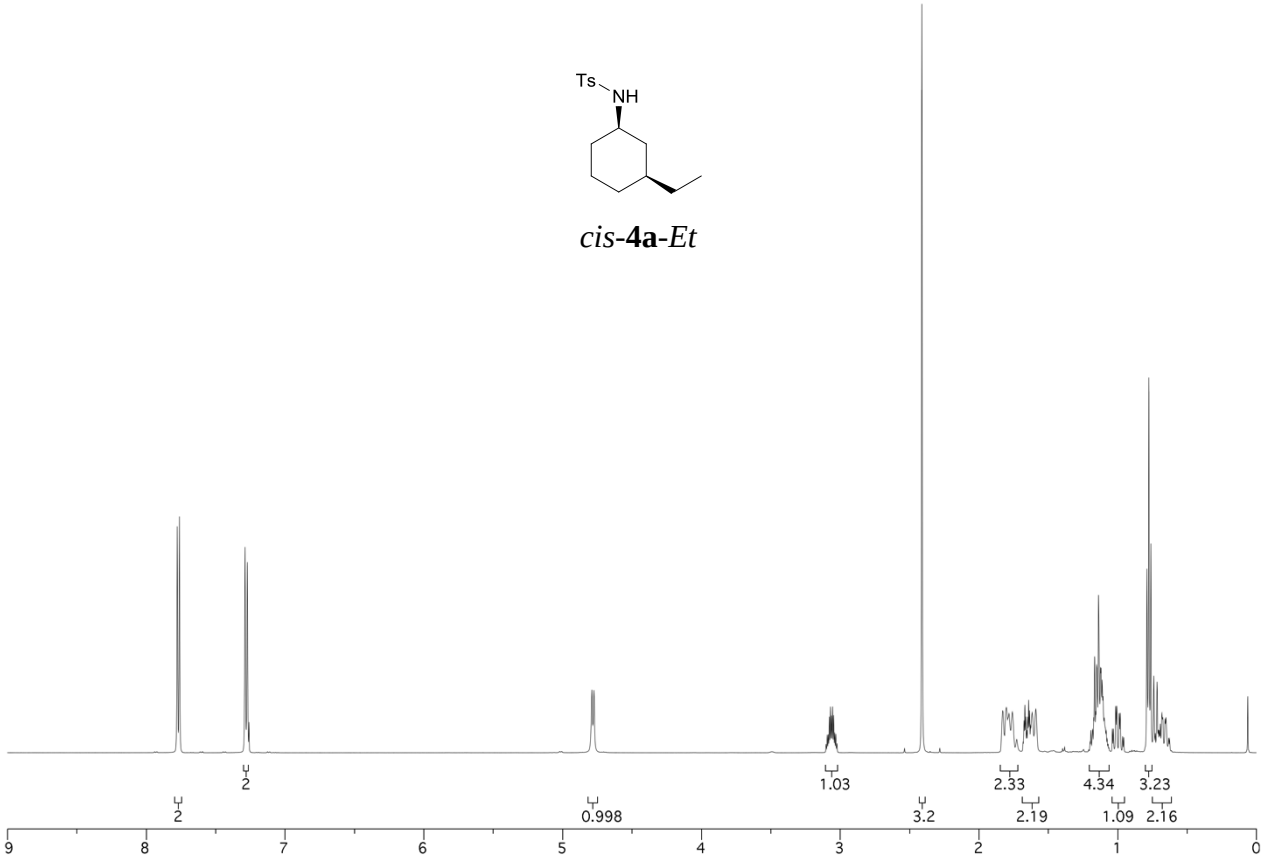
Figure 2: Overview of all IR band intensities over time.

3) ^{1}H and ^{13}C NMR spectra

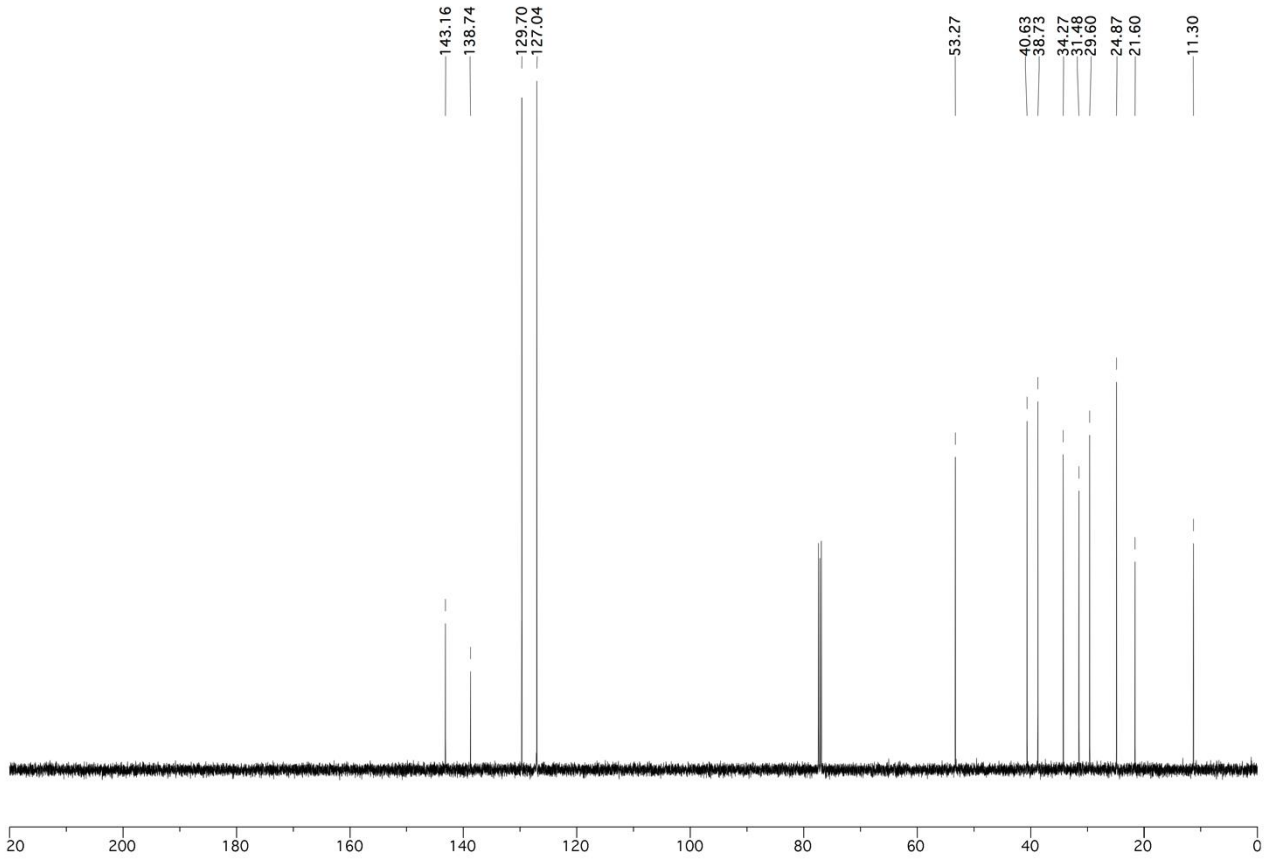


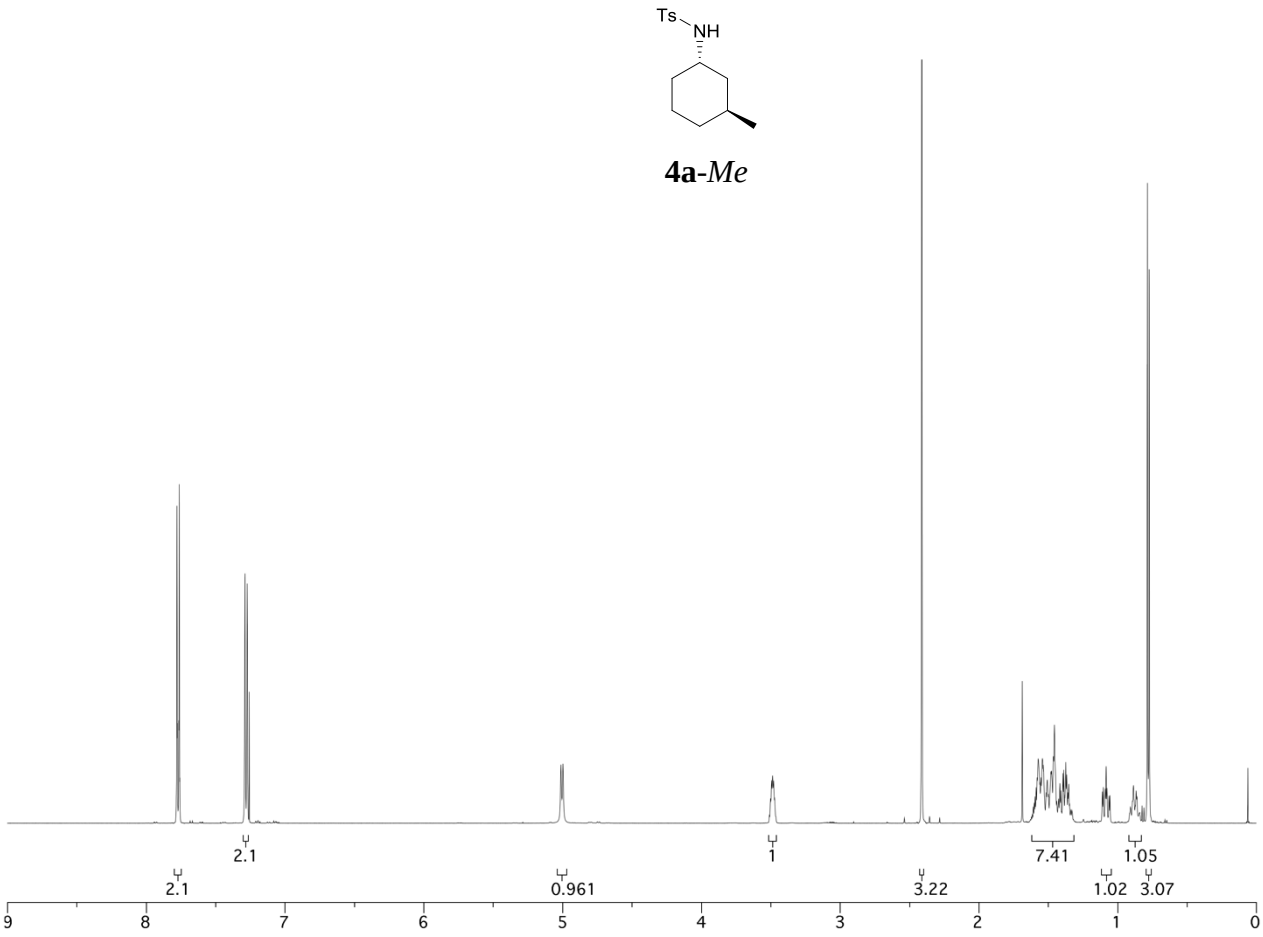
trans-**4a**-*Et*



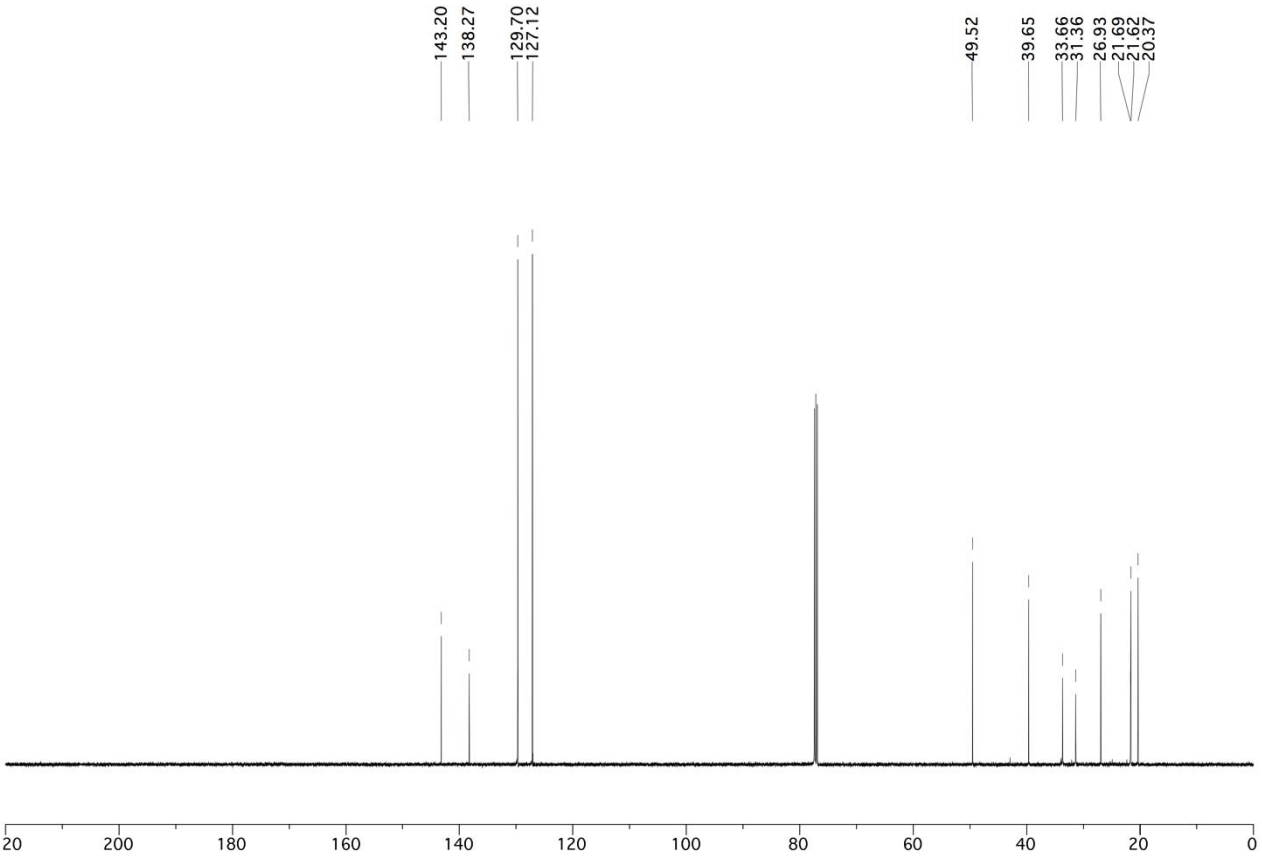

Ts
NH
2
2
0.998
1.03
3.2
2.33
2.19
4.34
1.09
3.23
2.16
9
8
7
6
5
4
3
2
1
0

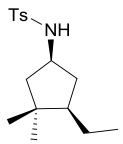
cis-**4a**-*Et*


143.16
138.74
129.70
127.04
53.27
40.63
38.73
34.27
31.48
29.60
24.87
21.60
11.30
220
200
180
160
140
120
100
80
60
40
20
0

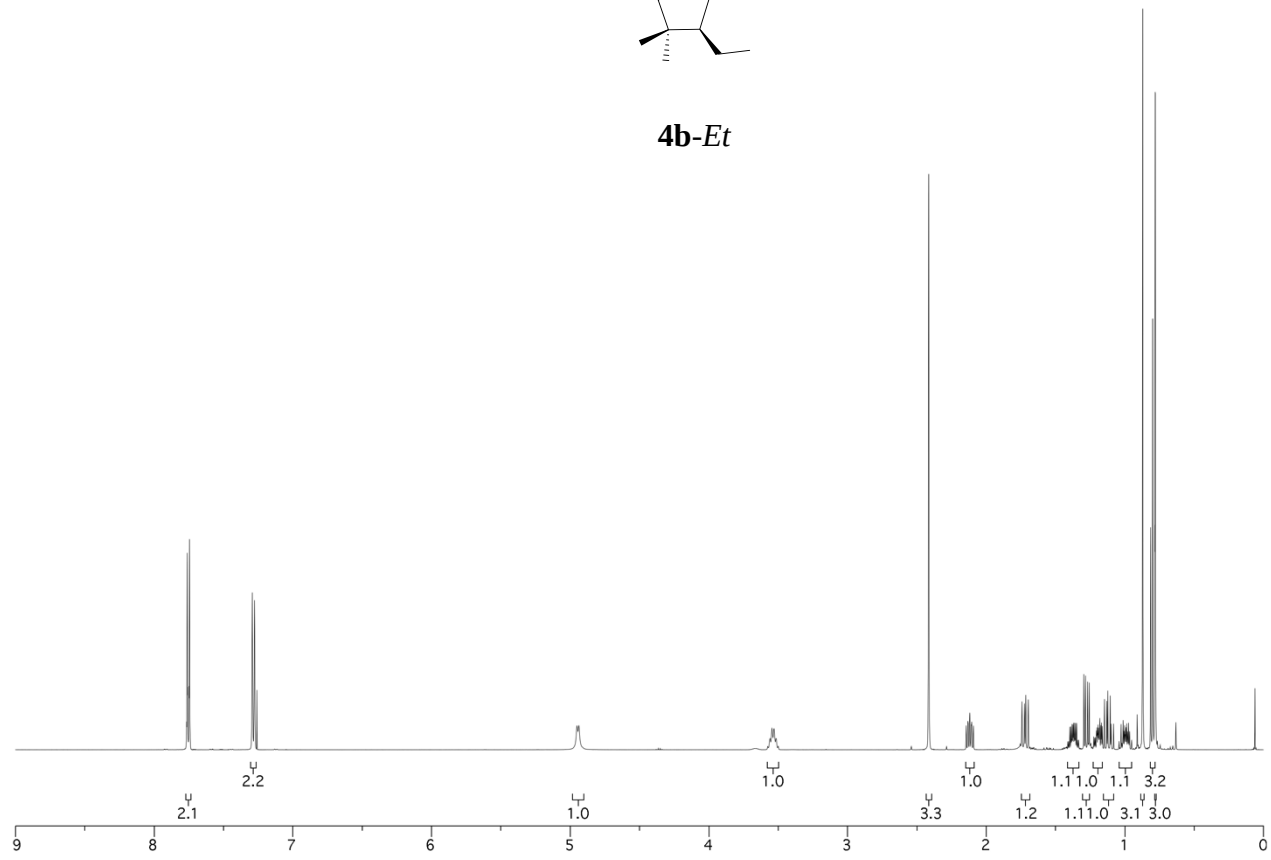

Ts
NH
2.1
1
7.41
1.05
2.1
0.961
3.22
1.02
3.07
9
8
7
6
5
4
3
2
1
0

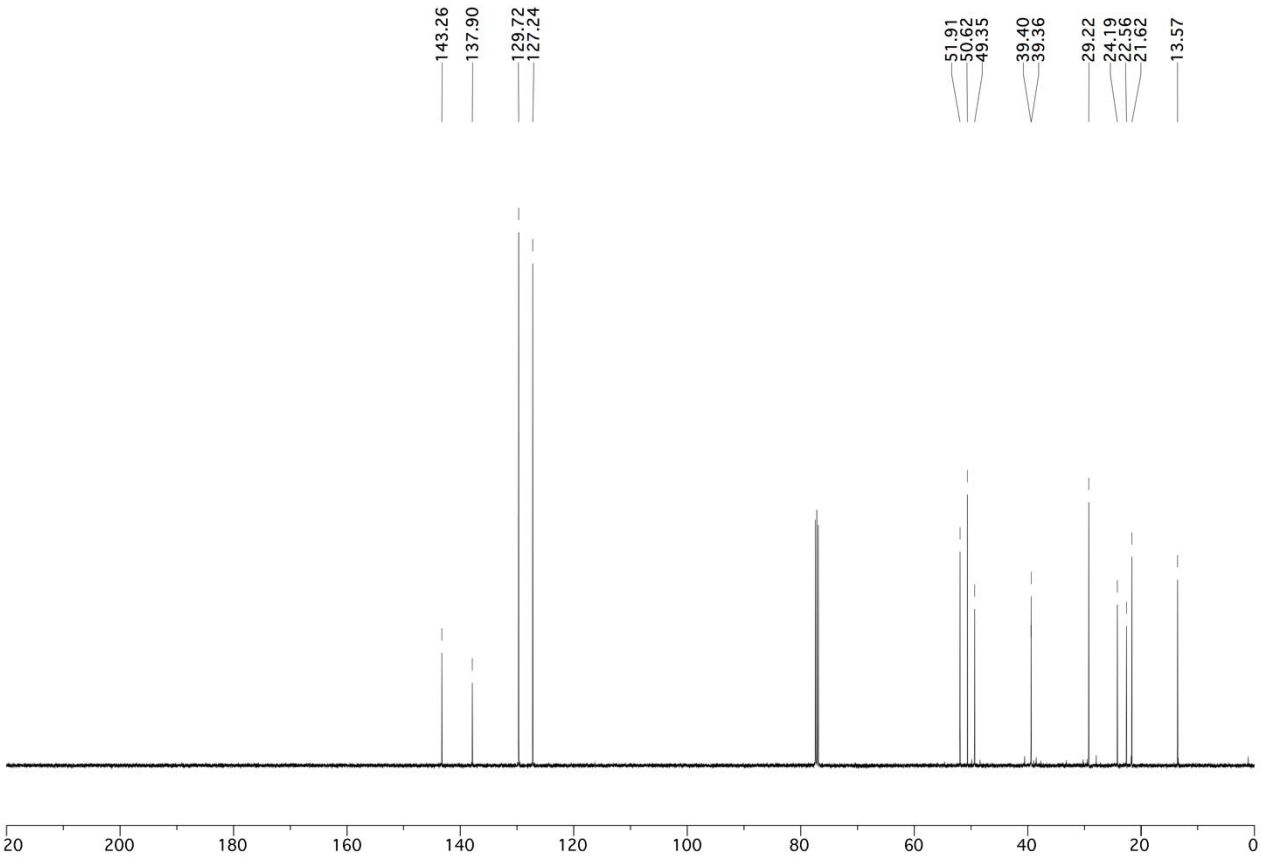
4a-*Me*

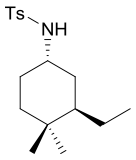

143.20
138.27
129.70
127.12
49.52
39.65
33.66
31.36
26.93
21.69
21.62
20.37
220
200
180
160
140
120
100
80
60
40
20
0


Ts
NH

4b-*Et*


2.2
1.0
1.0
1.1 1.0 1.1 3.2
2.1
1.0
3.3
1.2
1.1 1.0 3.1 3.0
9
8
7
6
5
4
3
2
1
0


143.26
137.90
129.72
127.24
51.91
50.62
49.35
39.40
39.36
29.22
24.19
22.56
21.62
13.57
200
180
160
140
120
100
80
60
40
20
0


Ts
NH

4c-*Et*

1.96
1.01
4.02
1.22
1.06
1.26
3.2
1.93
1
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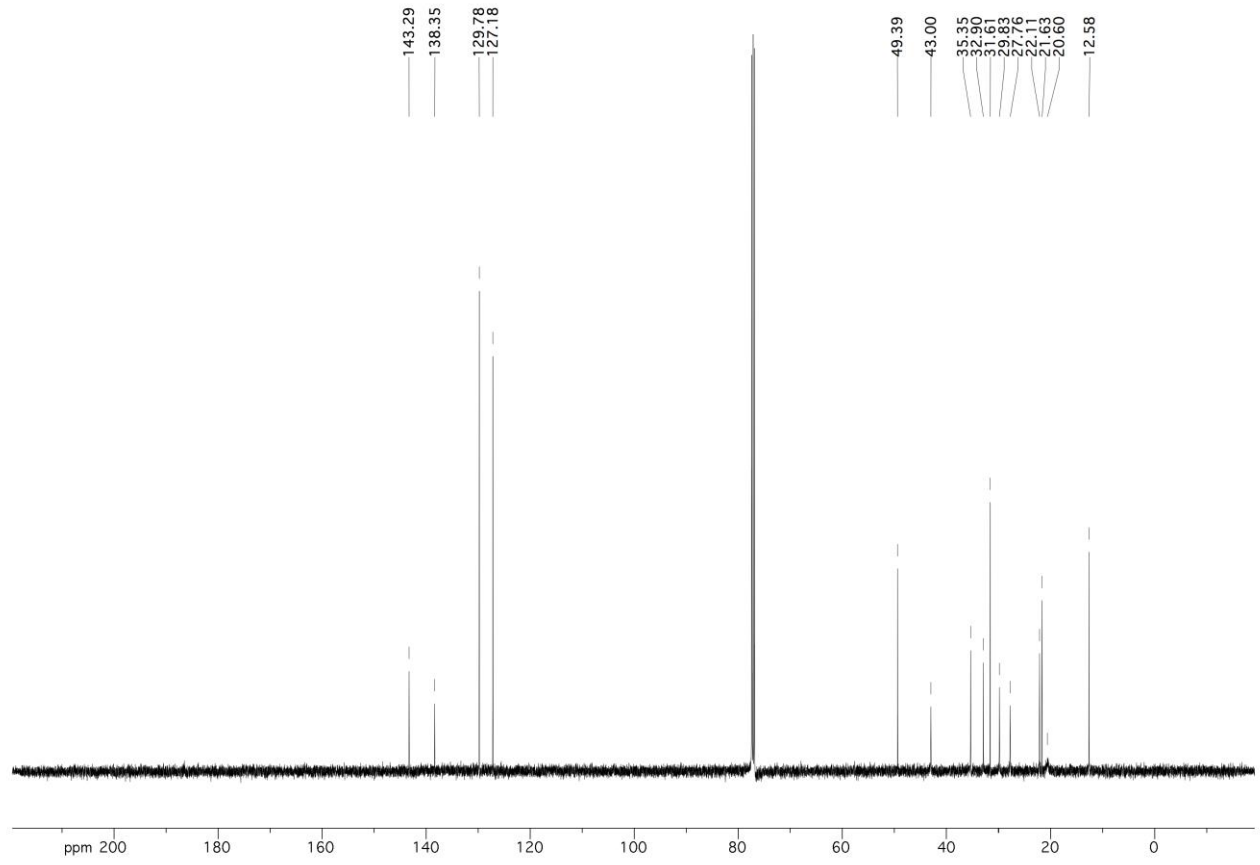
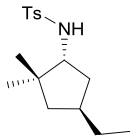
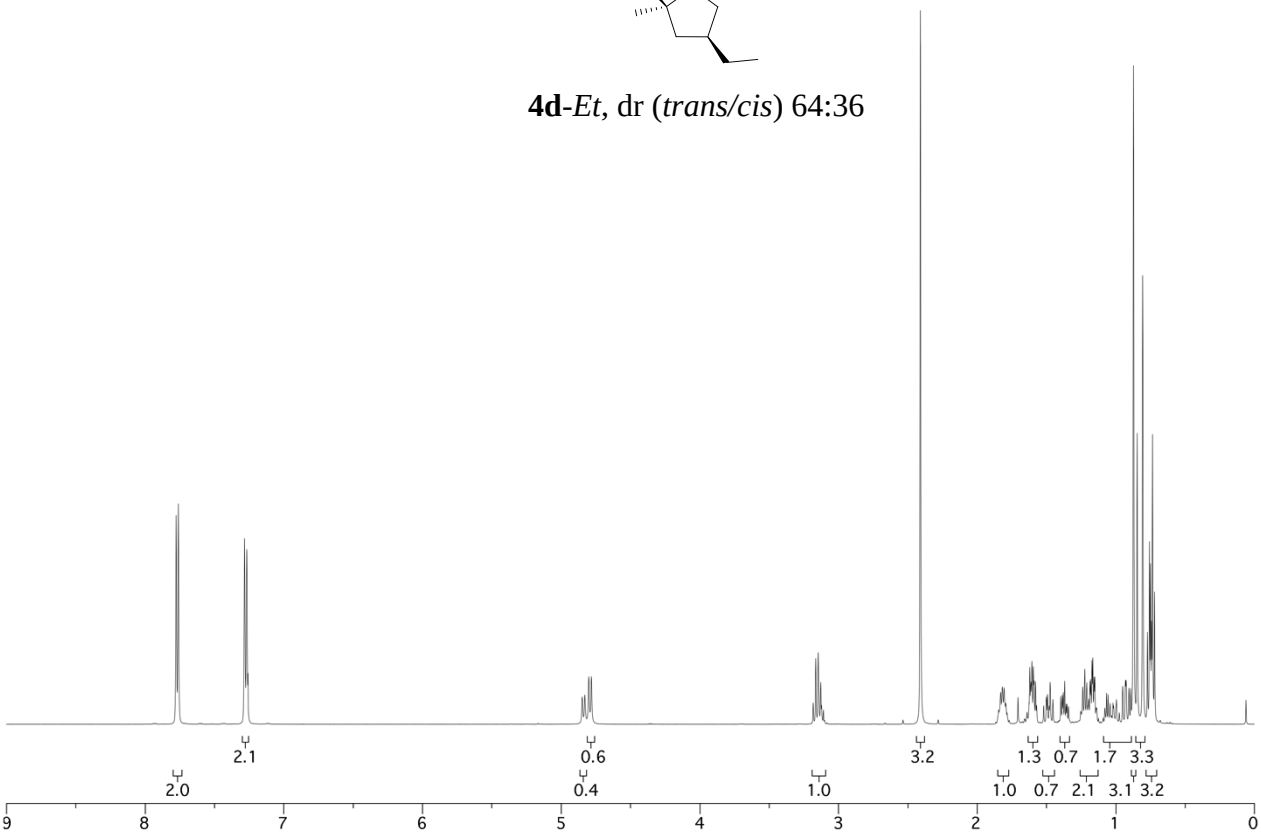
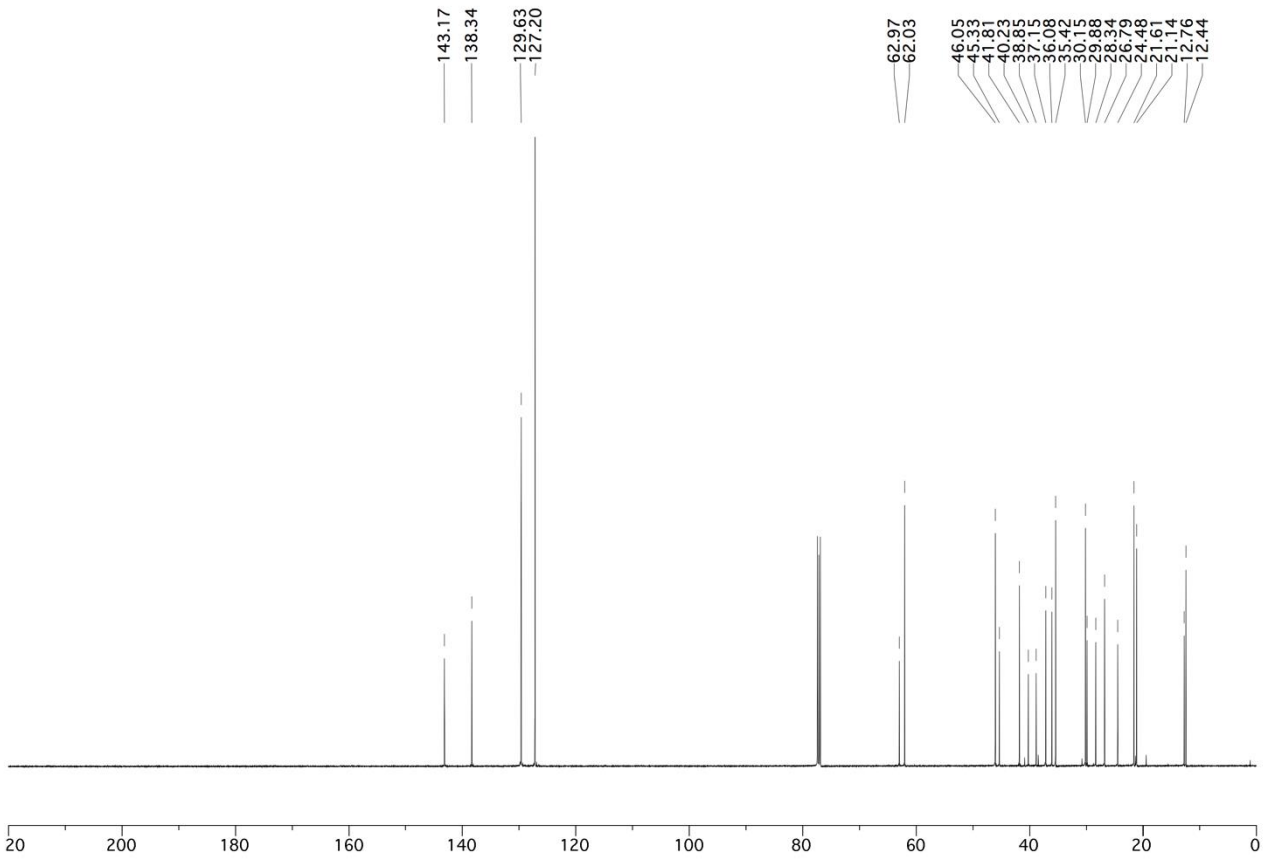
1.06
2.04
3.22
2.91
8
7
6
5
4
3
2
1
0

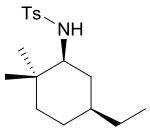

143.29
138.35
129.78
127.18
49.39
43.00
35.35
32.90
31.61
29.83
27.76
22.11
21.63
20.60
12.58
ppm 200
180
160
140
120
100
80
60
40
20
0



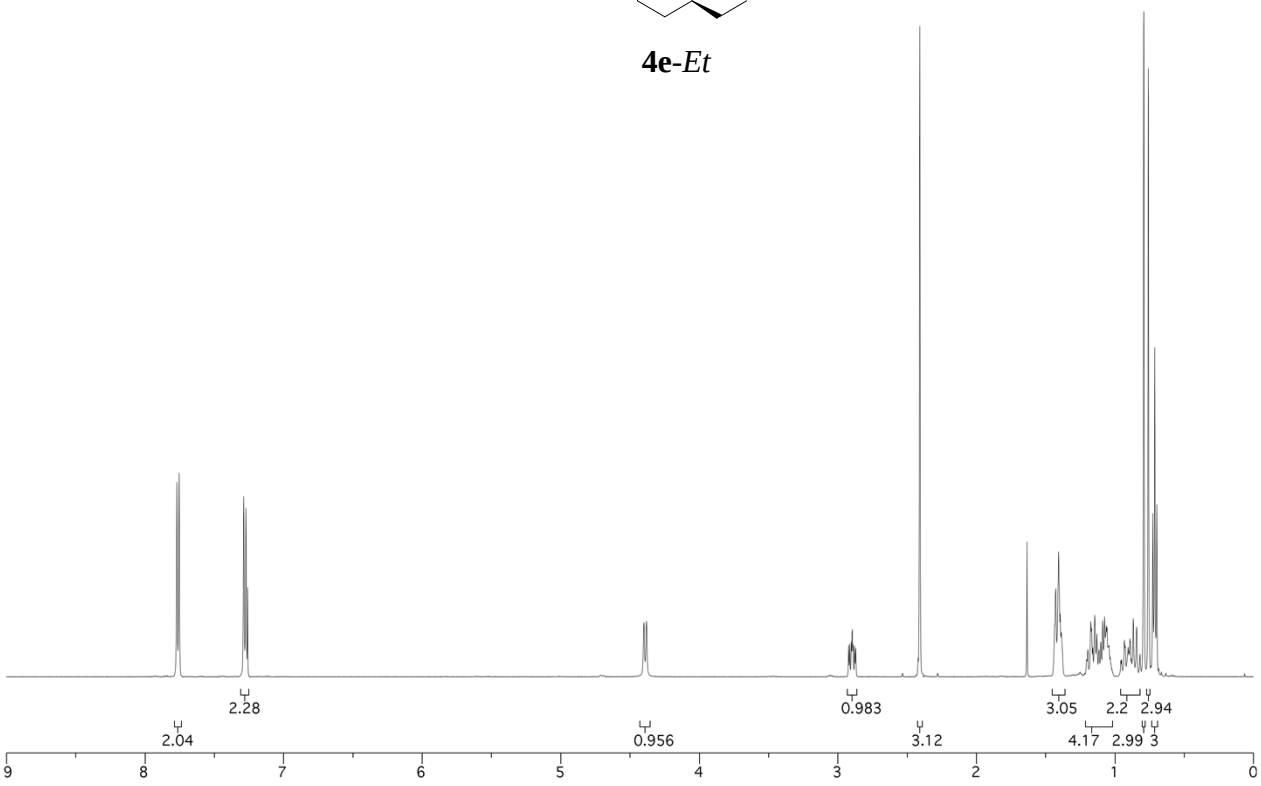
4d-*Et*, dr (*trans/cis*) 64:36






Ts
NH

4e-*Et*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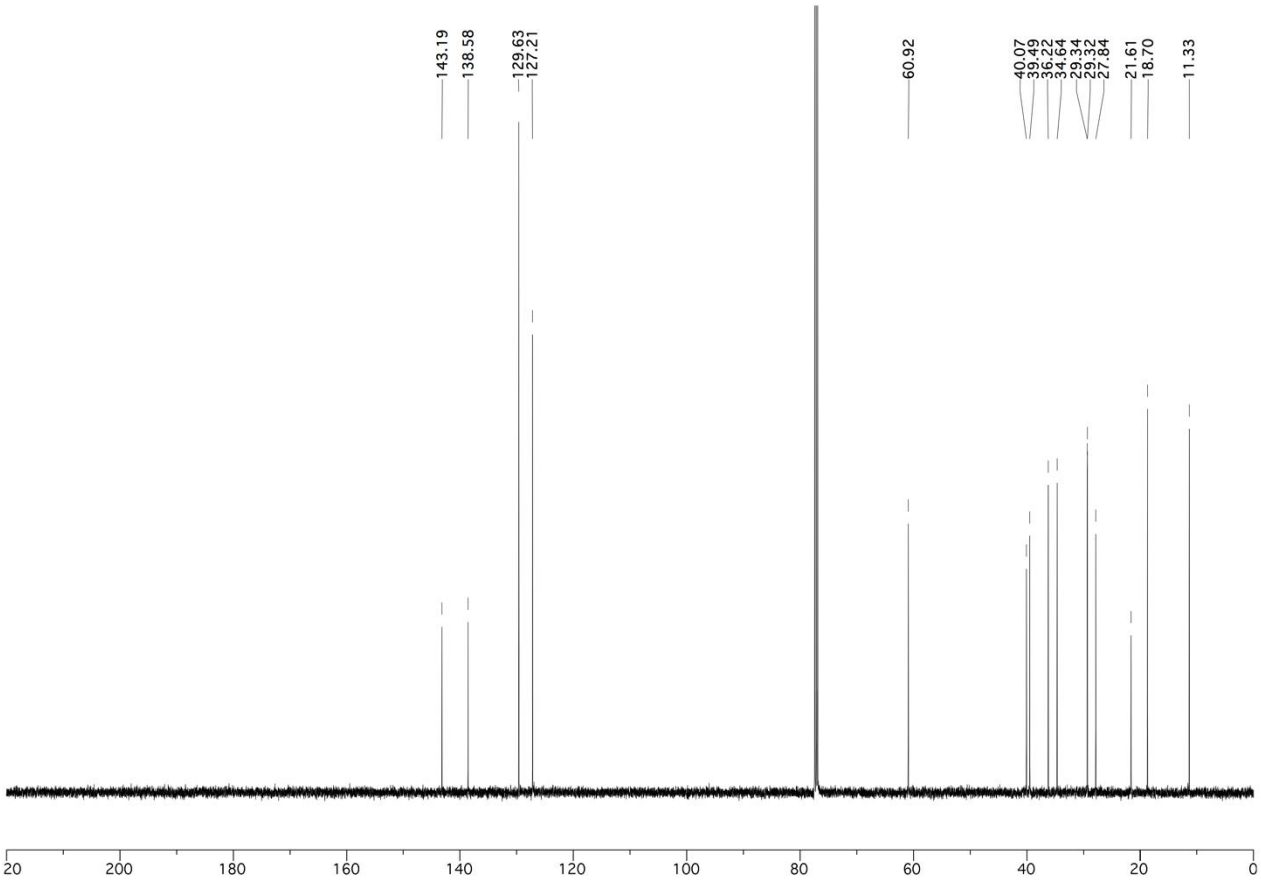
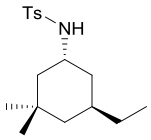
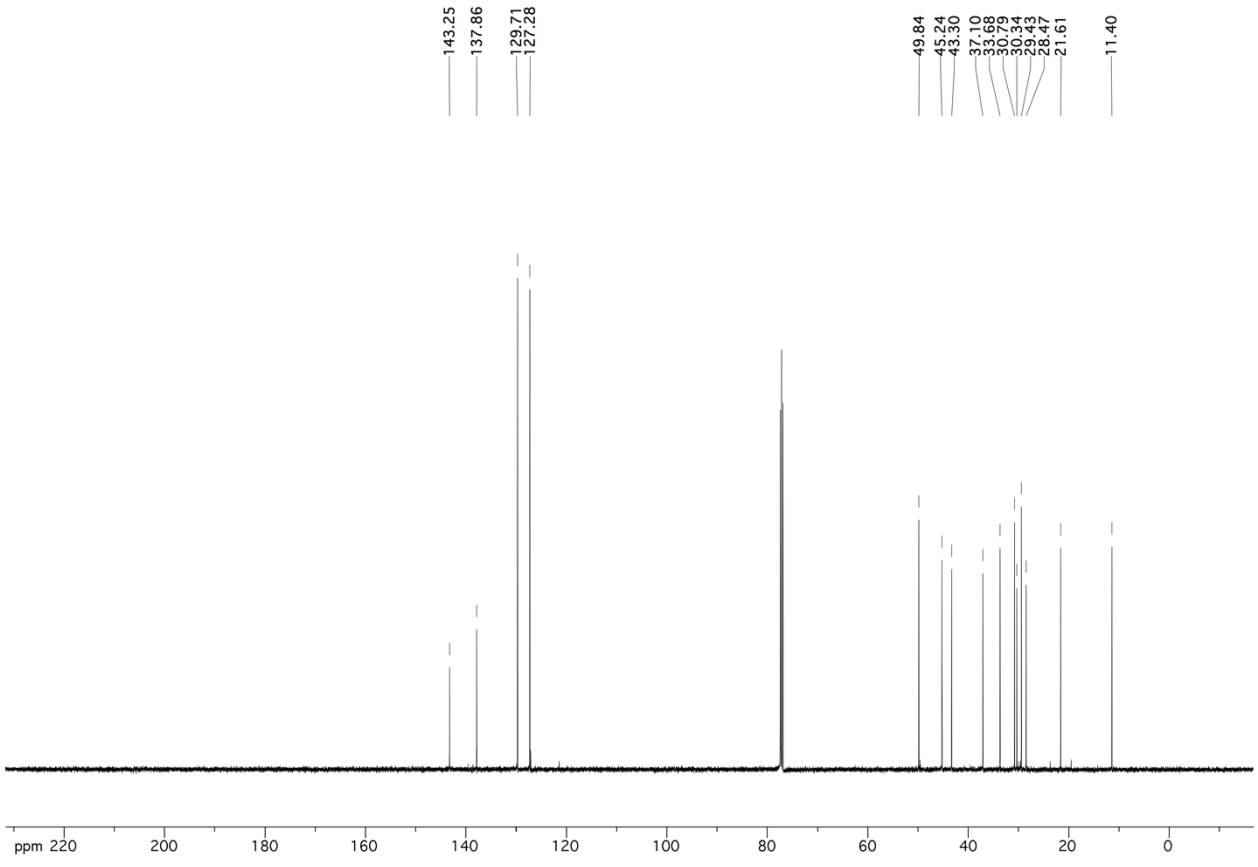
0.983
3.05
2.2
2.94
2.04
0.956
3.12
4.17
2.99
3
9
8
7
6
5
4
3
2
1
0

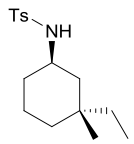

143.19
138.58
129.63
127.21
60.92
40.07
39.49
36.22
34.64
29.34
29.32
27.84
21.61
18.70
11.33
20
200
180
160
140
120
100
80
60
40
20
0


Ts
NH

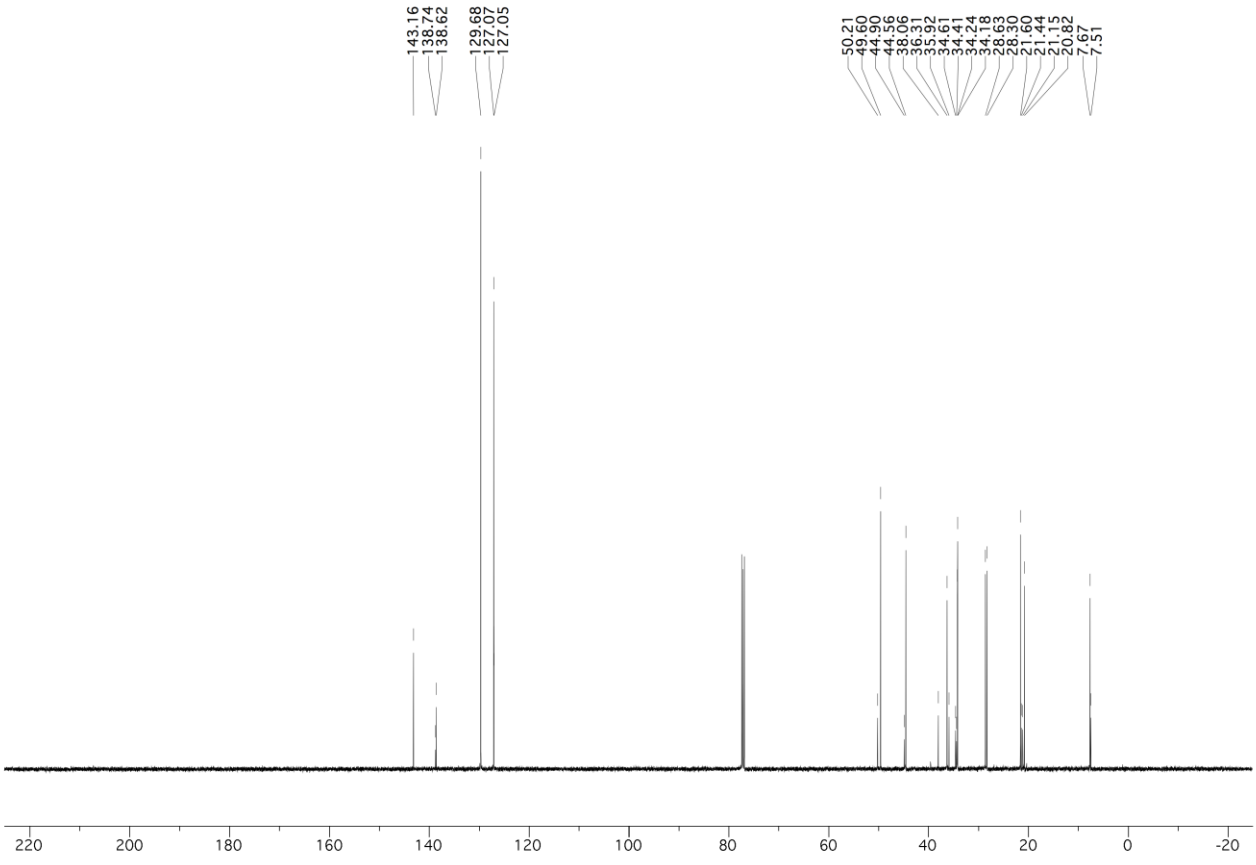
4f-*Et*

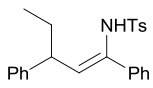
2.07
1
1.18
1.09
3.15
3.02
2.06
0.951
3.18
3.05
2.08
3.793
4.04
9
8
7
6
5
4
3
2
1
0


143.25
137.86
129.71
127.28
49.84
45.24
43.30
37.10
33.68
30.79
30.34
29.43
28.47
21.61
11.40
ppm 220
200
180
160
140
120
100
80
60
40
20
0



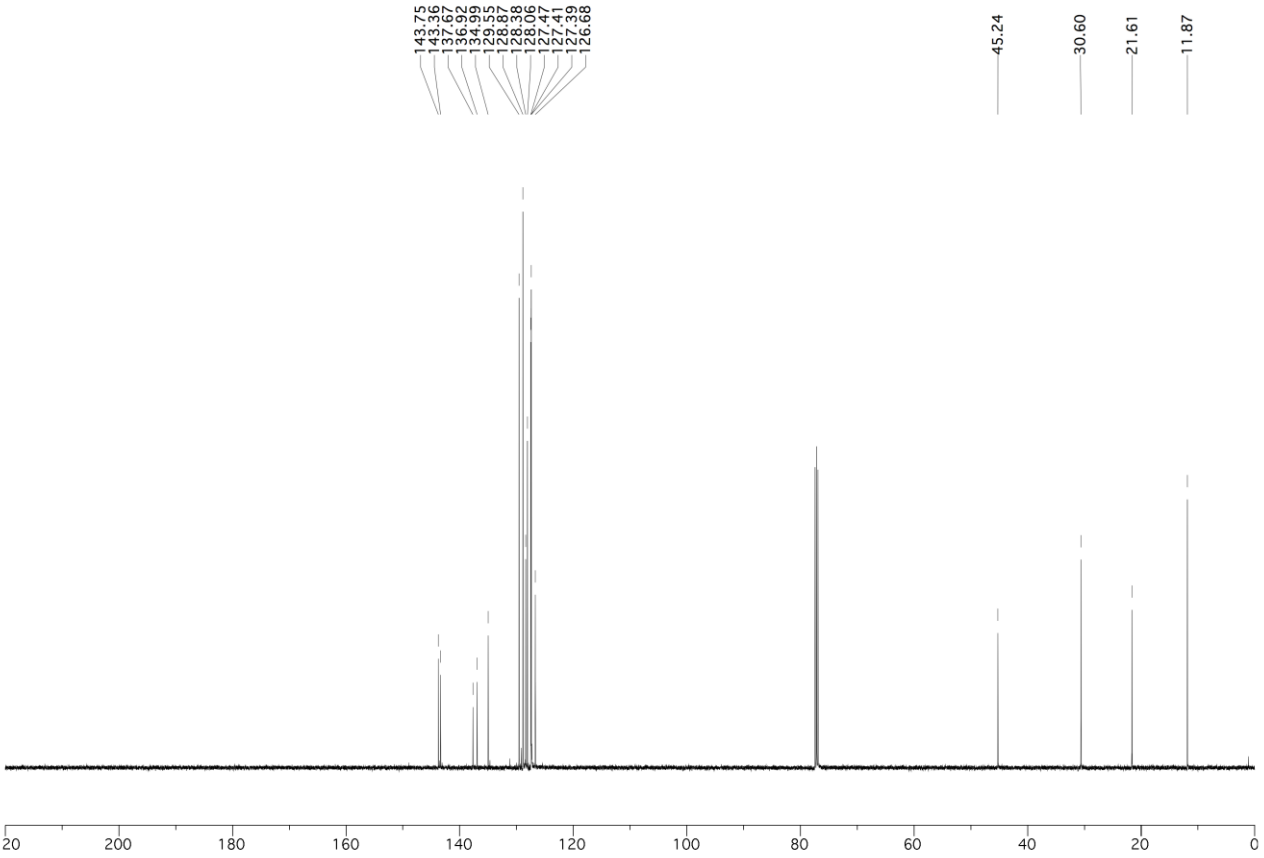
4g-*Et*, dr (*trans/cis*) 71:29

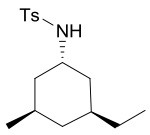



NHTs
Ph
Ph

2h-*Et*

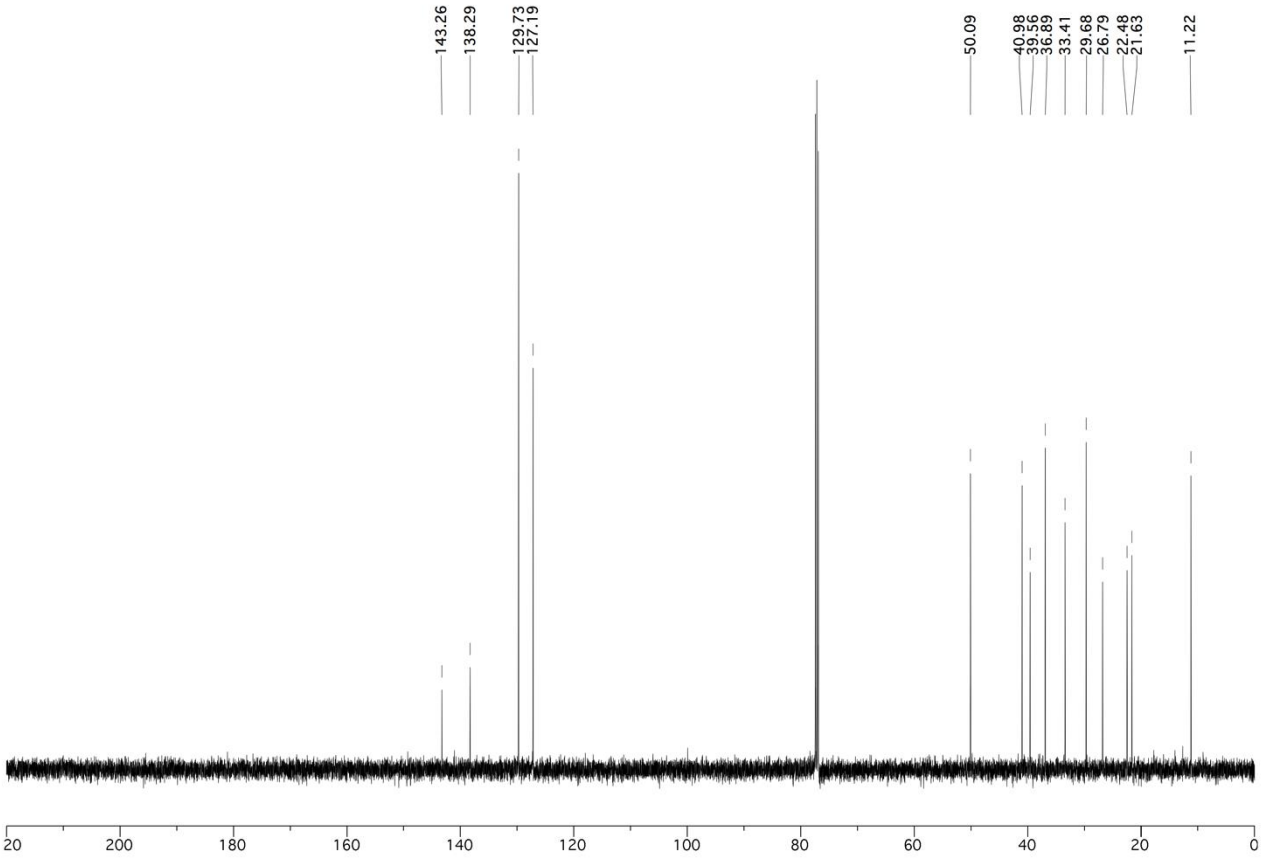
2.19
3
0.956
0.987
1.15
3
2.06
5.33
1.98
0.985
2.95
0.998
9
8
7
6
5
4
3
2
1
0

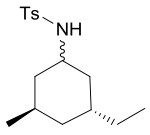

143.75
143.36
137.67
136.92
134.99
128.87
128.38
128.06
127.47
127.41
127.39
126.68
45.24
30.60
21.61
11.87
200
180
160
140
120
100
80
60
40
20
0


Ts
NH

(1*S*,3*S*,5*R*)-**4i**-*Et*

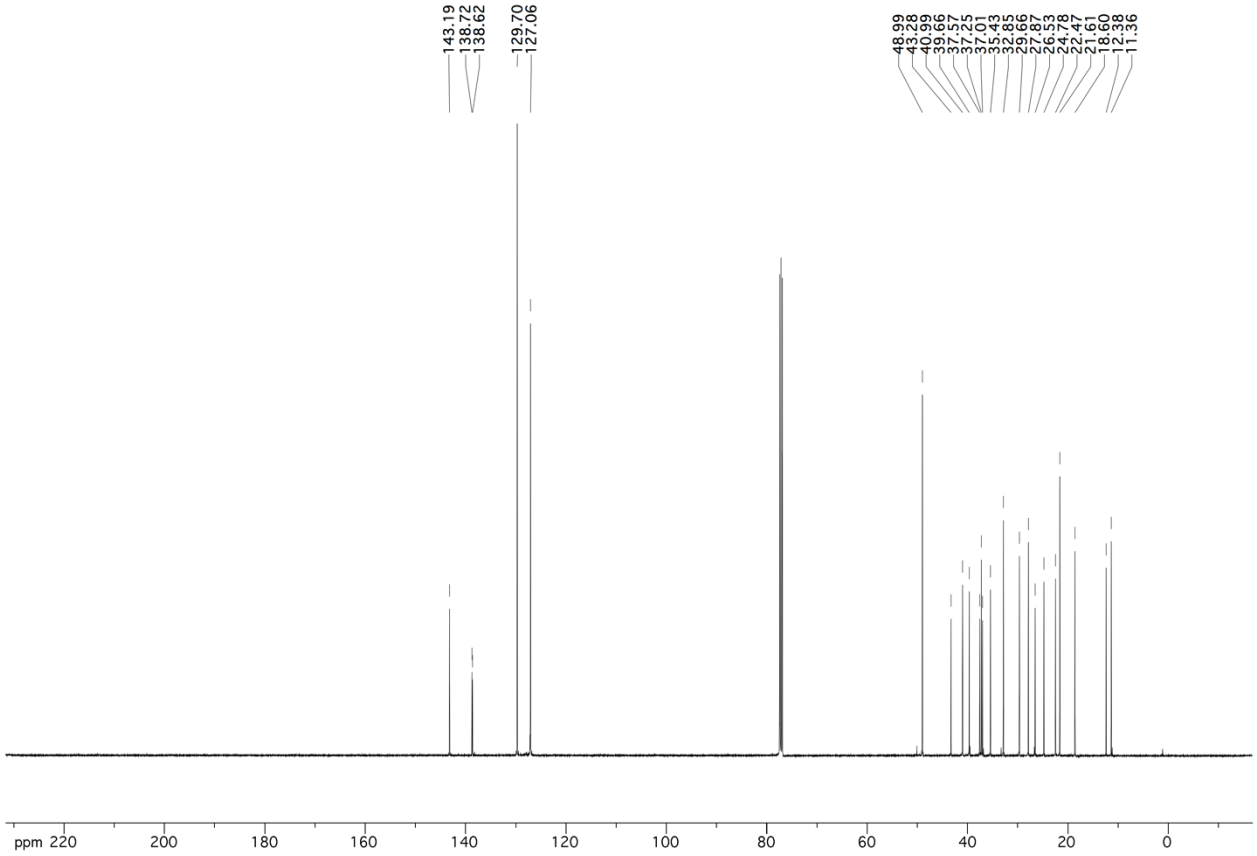
2.0
2.0
1.0
1.0
3.1
1.1
1.1
2.2
3.2
1.1
2.5
1.2
2.4
3.2
9
8
7
6
5
4
3
2
1
0

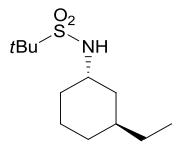

143.26
138.29
129.73
127.19
50.09
40.98
39.56
36.89
33.41
29.68
26.79
22.48
21.63
11.22
220
200
180
160
140
120
100
80
60
40
20
0


Ts
NH

(3*R*,5*R*)-**4i**-*Et*

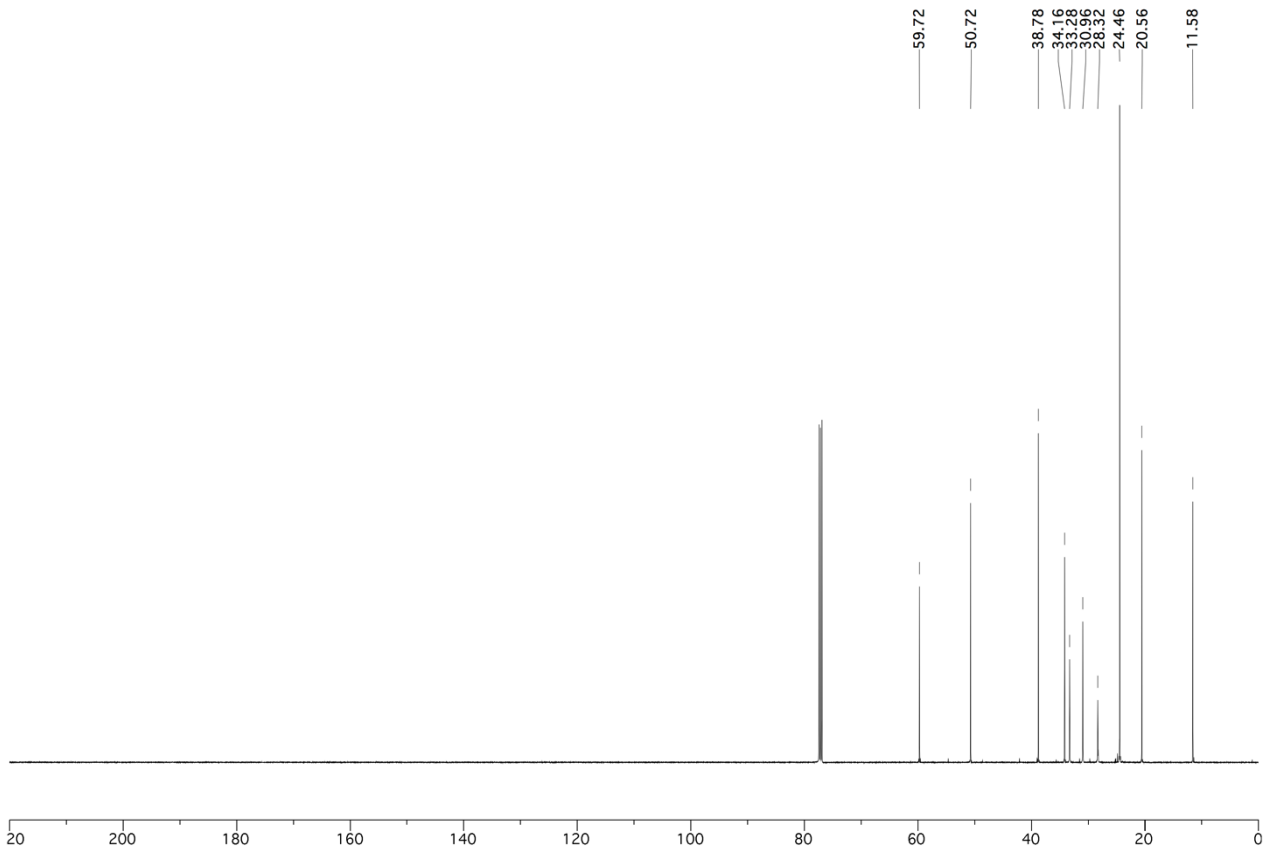
2.07
2.05
0.993
0.54
0.46
3.14
1.06
0.554
3.21
3.72
0.989
1.67
5.66
9
8
7
6
5
4
3
2
1
0

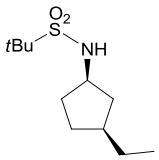

143.19
138.72
138.62
129.70
127.06
48.99
43.28
40.99
39.66
37.57
37.25
37.01
35.43
32.85
29.66
27.87
26.53
24.78
22.47
21.61
18.60
12.38
11.36
ppm 220
200
180
160
140
120
100
80
60
40
20
0


O2
S
tBu
NH

6a-*Et*

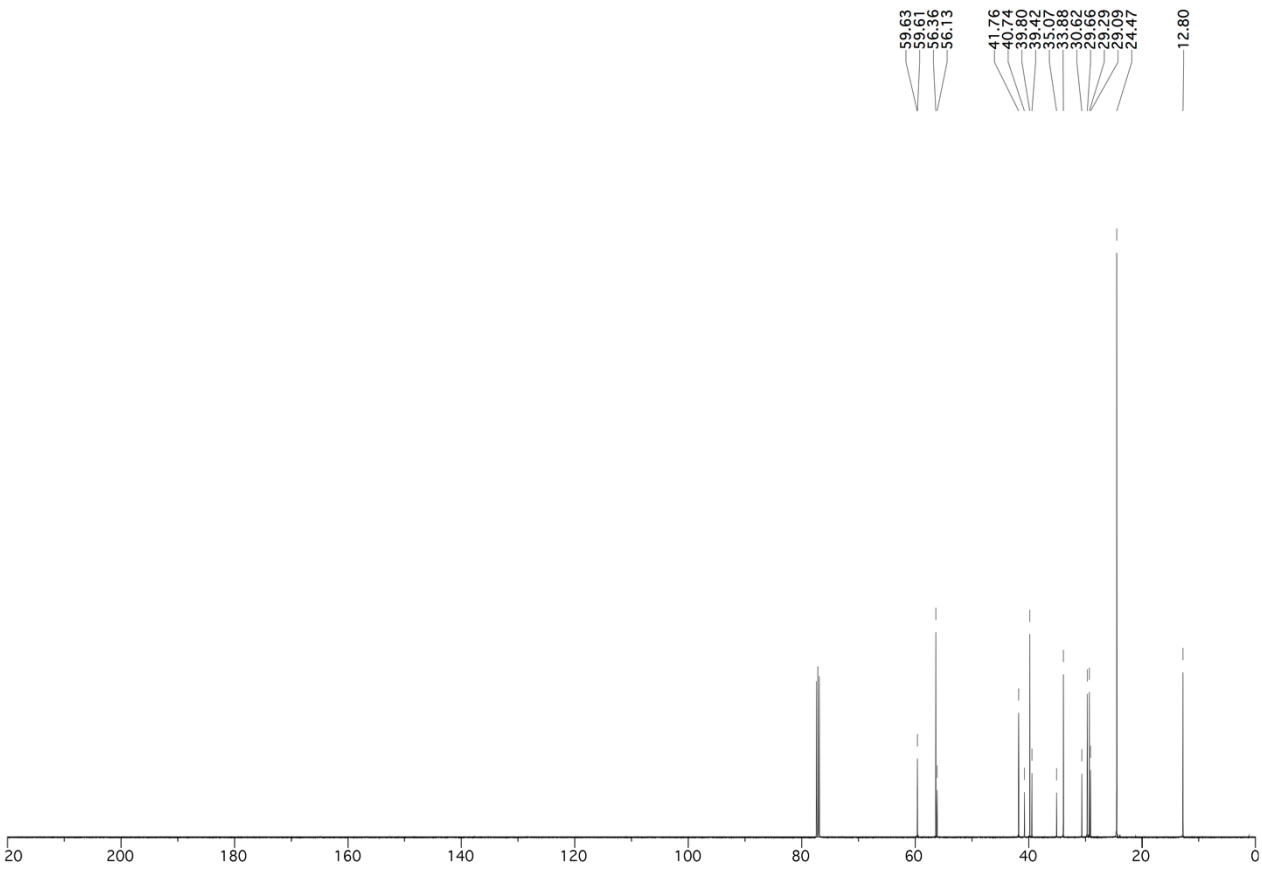
1.0
1.0
4.1
2.2
3.1
1.3
12.6
1.0
9
8
7
6
5
4
3
2
1
0

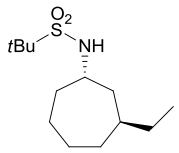

59.72
50.72
38.78
34.16
33.28
30.96
28.32
24.46
20.56
11.58
20
200
180
160
140
120
100
80
60
40
20
0



6b-*Et*

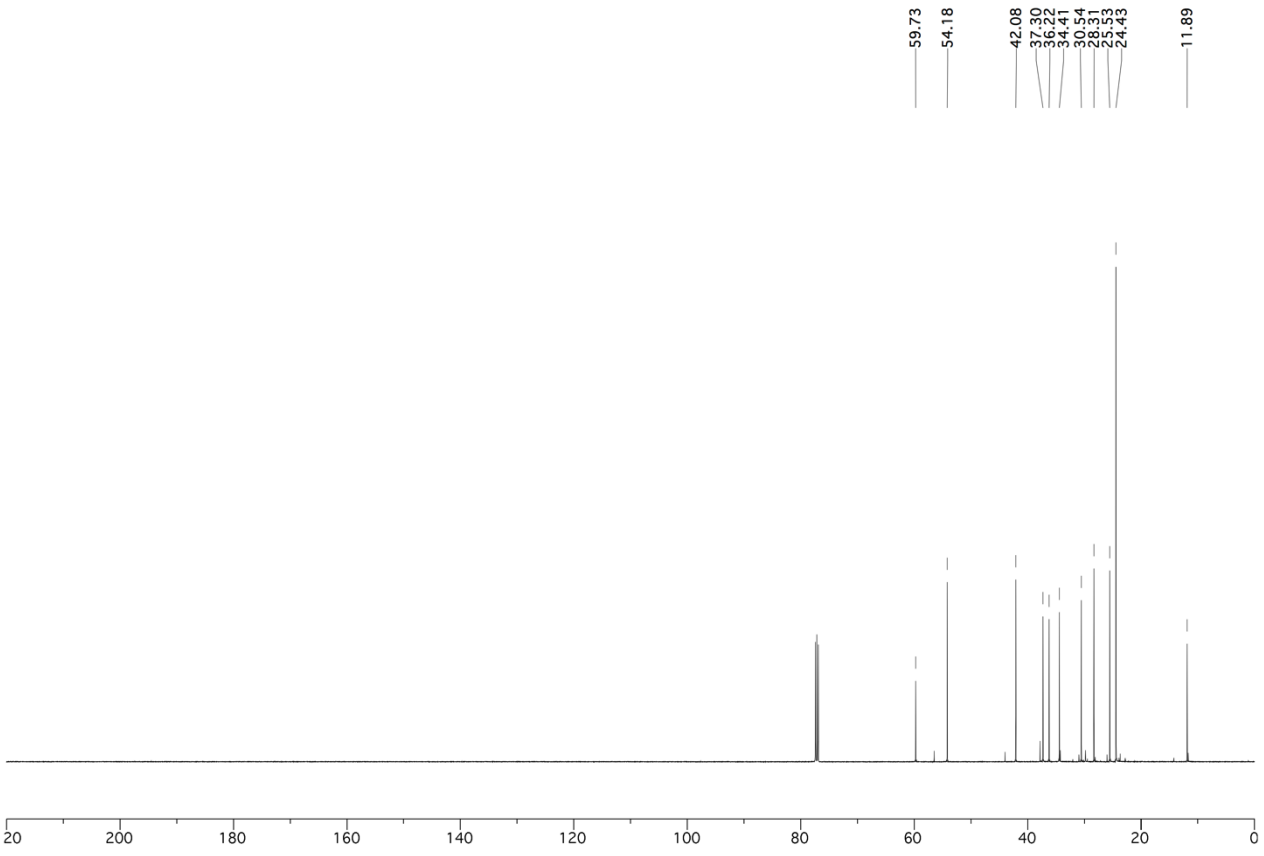
dr (*trans/cis*) 23:77

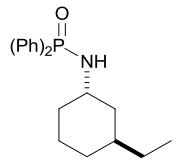



O2
S
tBu
NH

6c-*Et*

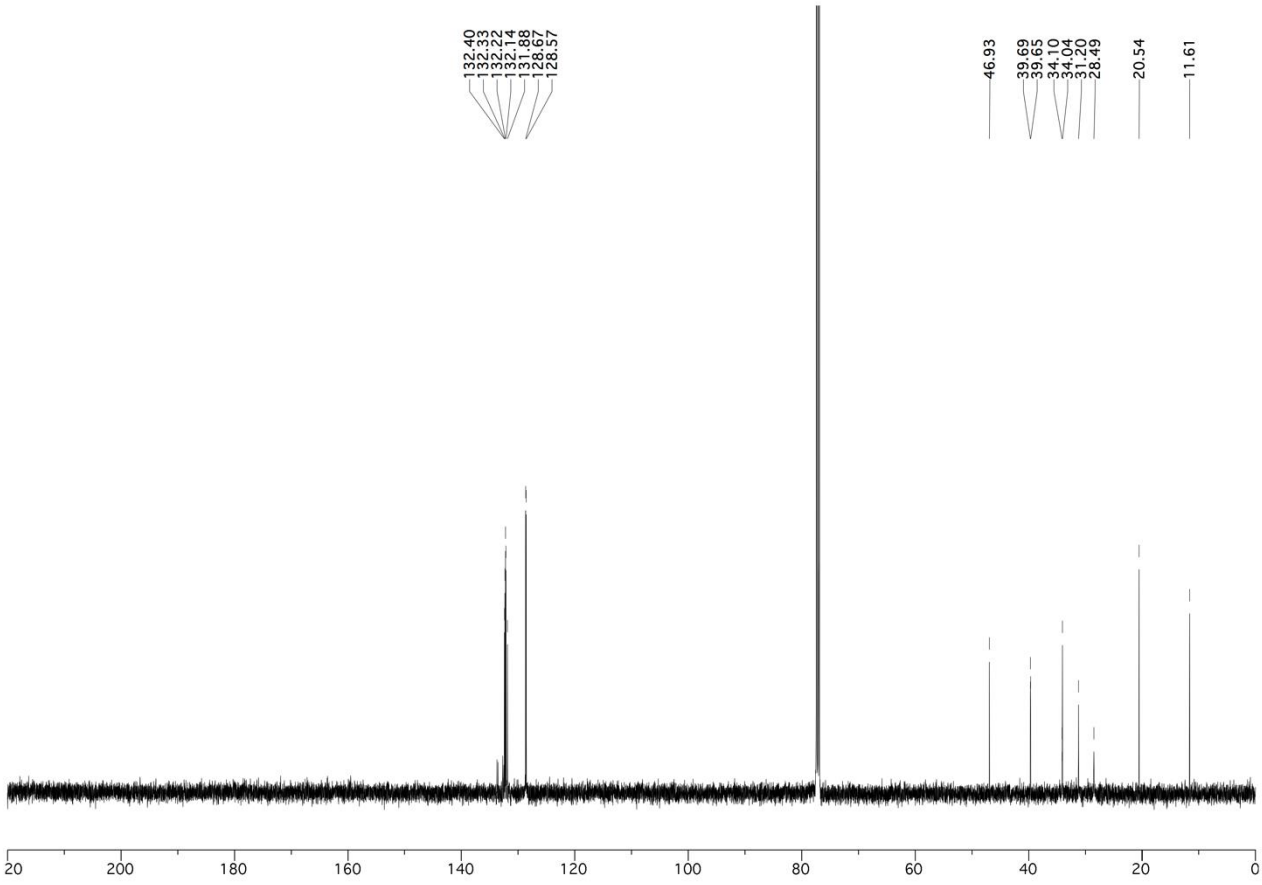
1.0
5.3
16.3
3.2
1.0
1.1
1.3
1.2
9
8
7
6
5
4
3
2
1
0

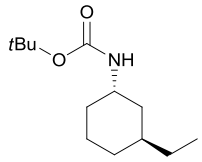

59.73
54.18
42.08
37.30
36.32
34.41
30.54
28.31
25.53
24.43
11.89
220
200
180
160
140
120
100
80
60
40
20
0


O
(Ph)2P
NH

8a-*Et*

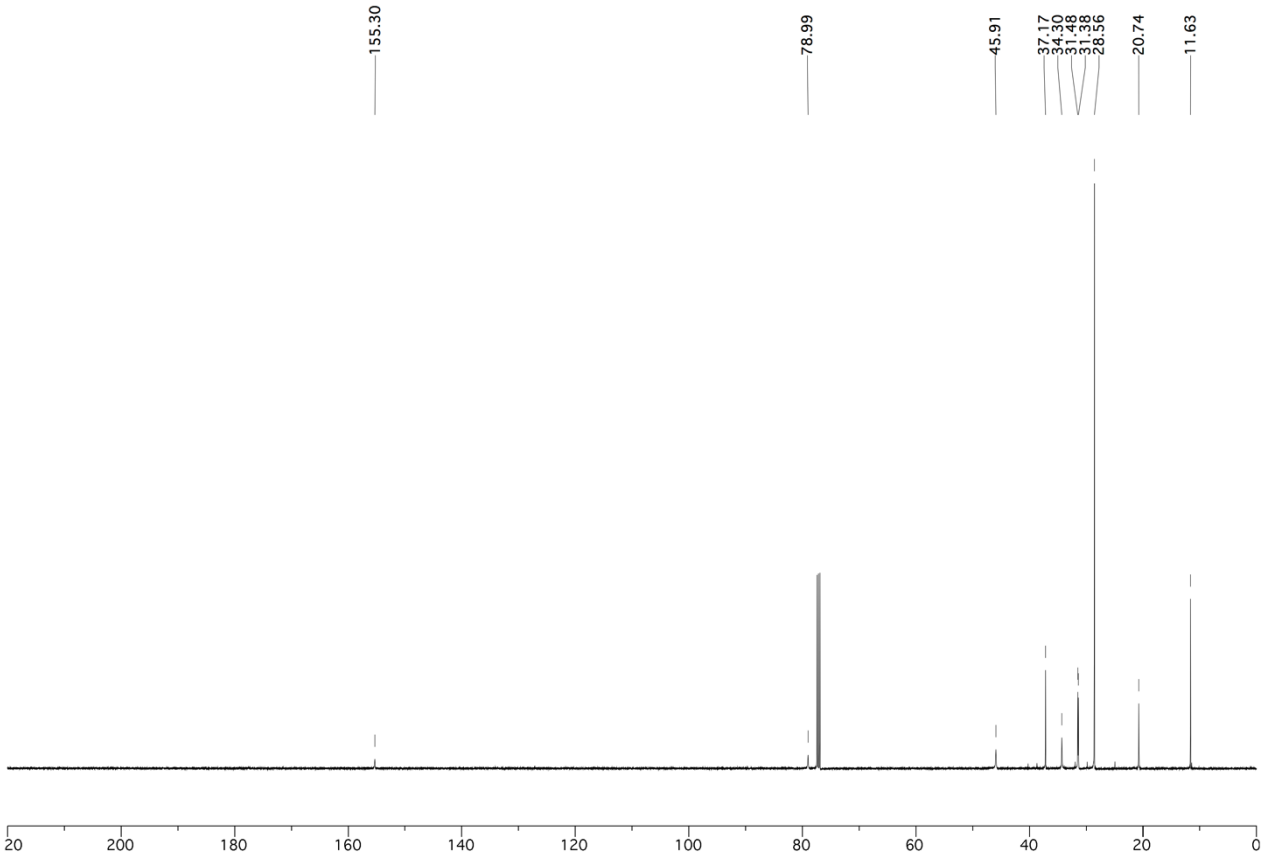
2.0
1.0
1.0
1.0
4.0
4.0
7.0
2.3
3.0
9
8
7
6
5
4
3
2
1
0


132.40
132.33
132.22
132.14
131.88
128.67
128.57
46.93
39.69
39.65
34.10
34.04
31.20
28.49
20.54
11.61
200
180
160
140
120
100
80
60
40
20
0


O
tBu
O
NH

9a-*Et*

0.9
0.9
2.8
5.2
3.0
2.0
9.2
1.0
9
8
7
6
5
4
3
2
1
0


155.30
78.99
45.91
37.17
34.30
31.48
31.38
28.56
20.74
11.63
20
200
180
160
140
120
100
80
60
40
20
0

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