Supplementary Material for Organic & Biomolecular Chemistry


## Supporting Information

# N-Heterocyclic carbene catalysed β-lactam synthesis

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# I. General Experimental Procedures

## General Information

All reactions involving moisture sensitive reagents were performed under an atmosphere of nitrogen *via* standard vacuum line techniques and with freshly dried solvents. All glassware was flame dried and allowed to cool under vacuum. Toluene, tetrahydrofuran (THF), diethyl ether ($Et_2O$) and dichloromethane were obtained dry from a solvent purification system (MBraun, SPS-800). Potassium bis(trimethylsilyl)amide (KHMDS) was supplied as a 0.5M solution in toluene (Aldrich), titrated before use,[1] and used as a 0.45M solution. Petrol is defined as petroleum ether 40-60 ˚C. All solvents and commercial reagents were used as supplied without further purification unless stated otherwise. Room temperature refers to 20-25˚C. Reflux conditions were obtained using an oil bath equipped with a contact thermometer. *In vacuo* refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand $CVC_2$ vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller.

Analytical thin layer chromatography was performed on aluminium sheets coated with 60 $F_{254}$ silica. TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated.

$^1H$ and $^{13}C$ nuclear magnetic resonance (NMR) spectra were acquired on a Bruker Avance II 400 (400 MHz $^1H$, 100 MHz $^{13}C$) spectrometer and in $CDCl_3$ unless stated otherwise. Coupling constants (*J*) are reported in Hz.

Infrared spectra ($\nu_{max}$) were recorded on a Perkin-Elmer Spectrum GX FT-IR Spectrometer using KBr discs (KBr disc) as stated. Only the characteristic peaks are quoted. Microanalyses were carried out on a Carlo Erba CHNS analyser. Melting points were recorded on an Electrothermal apparatus and are uncorrected.

Mass spectrometric (*m/z*) data was acquired by electrospray ionisation (ESI), electron impact (EI) or chemical ionisation (CI), either at the University of St Andrews Mass Spectrometry facility or from the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews low and high resolution ESI MS was carried out on a Micromass LCT spectrometer and low and high resolution CI MS was carried out on a Micromass GCT

[1] L. Duhamel and J.-C. Plaquevent, *J. Organometallic Chem*.,**1993**, *448*, 1.

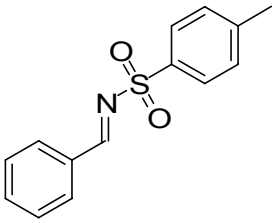
spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low and high resolution EI MS was carried out on a Micromass Quattro II spectrometer.

## II. Synthesis of ketenes

Diphenylketene and isobutylphenylketene were synthesized according to literature procedures.[2,3]

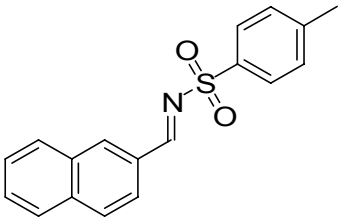
## III. Synthesis of imines

*N*-Tosyl imines were prepared according the procedure described by Proctor.[4] $BF_3.Et_2O$ (0.016 equiv) was added to a refluxing solution of aldehyde (1.0 equiv.) and *para*-toluenesulfonamide (1.0 equiv) in toluene (150 mL) using a Dean-Stark apparatus. The mixture was refluxed until the theoretical amount of water had been collected (20 hours). The solution was then cooled and washed with 2M NaOH solution and water. The organic layer was separated, dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was purified by recrystallisation from EtOAc/hexane unless otherwise noted. The following yields have not been optimised.

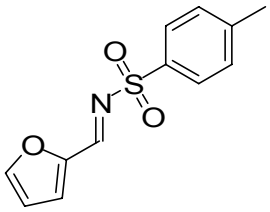


***N*-Benzylidene-4-methylbenzenesulfonamide**. The imine was obtained using benzaldehyde (5.1 mL, 50 mmol) and *para*-toluenesulfonamide (8.56 g, 50 mmol) and following the above general procedure. The residue was purified by recrystallisation to give the title compound (9.83 g, 76% yield) as a white solid. $^1$H NMR $\delta$ 2.44 (3H, s), 7.35 (2H, d, $J$ = 8.0), 7.49 (2H, t, $J$ = 7.8), 7.62 (2H, tt, $J$ = 7.6, 2.8), 7.86-7.97 (4H, m), 9.03 (1H, s).

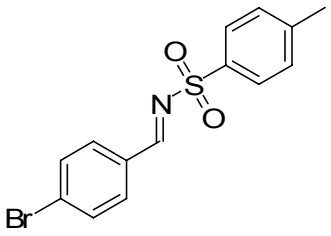
[2] E. C. Taylor, A. McKillop and G. H. Hawks, *Org. Syntheses, Coll. Vol. 6,* **1988***,* 549.
[3] B. L. Houdous and G. C. Fu, *J. Am. Chem. Soc.,* **2002**, *124*, 1578.
[4] W. R. McKay and G. R. Proctor, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 2435-2442.



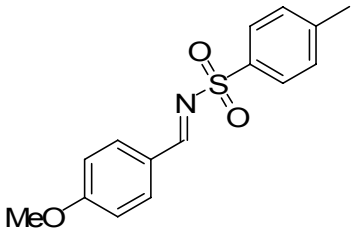
***N*-(2-Naphthylidene)-4-methylbenzenesulfonamide**. The imine was obtained using 2-naphthaldehyde (5 g, 32 mmol) and *para*-toluenesulfonamide (5.48 g, 32 mmol) and following the above general procedure. The residue was purified by recrystallisation to give the title compound (8.41 g, 85% yield) as a white solid. $^1$H NMR $\delta$ 2.44 (3H, s), 7.36 (2H, d, $J$ = 8.4), 7.57 (1H, t, $J$ = 7.2), 7.62 (1H, t, $J$ = 7.0), 7.87 (2H, d, $J$ = 8.8), 7.91-7.98 (3H, m), 8.02 (1H, dd, $J$ = 8.4, 1.2), 8.32 (1H, s), 9.17 (1H, s).



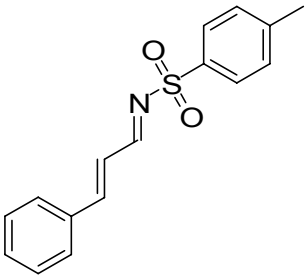
***N*-(2-Furfurylidene)-4-methylbenzenesulfonamide**. The imine was obtained using furfural (4.15 mL, 50 mmol) and *para*-toluenesulfonamide (8.56 g, 50 mmol) and following the above general procedure. The residue was purified by recrystallisation to give the title compound (6.69 g, 54% yield) as a yellowish solid. $^1$H NMR $\delta$2.42 (3H, s), 6.64 (1H, dd, $J$ = 3.6, 1.8), 7.28-7.37 (3H, m), 7.74 (1H, m), 7.86 (2H, d, $J$ = 8.4), 8.81 (1H, s).



***N*-(4-Bromobenzylidene)-4-methylbenzenesulfonamide**. The imine was obtained using 4-bromobenzaldehyde (9.25 g, 50 mmol) and *para*-toluenesulfonamide (8.56 g, 50 mmol) and following the above general procedure. The residue was purified by recrystallisation from THF/hexane to give the title compound (13.20 g, 78% yield) as a white solid. $^1$H NMR $\delta$2.44 (3H, s), 7.35 (2H, d, $J$ = 8.0), 7.63 (2H, d, $J$ = 8.4), 7.78 (2H, d, $J$ = 8.4), 7.88 (2H, d, $J$ = 8.4), 8.98 (1H, s).



***N*-(4-Methoxybenzylidene)-4-methylbenzenesulfonamide**. The imine was obtained using 4-methoxybenzaldehyde (6.1 mL, 50 mmol) and *para*-toluenesulfonamide (8.56 g, 50 mmol) and following the above general procedure. The residue was purified by recrystallisation from THF/hexane to give the title compound (10.89 g, 75% yield) as a white solid. $^1$H NMR $\delta$2.41 (3H, s), 3.86 (3H, s), 6.95 (2H, d, $J$ = 8.7), 7.32 (2H, d, $J$ = 8.1), 7.78-7.97 (4H, m), 8.93 (1H, s).



***N*-(3-Phenyl-allylidene)-4-methylbenzenesulfonamide**. The imine was obtained using cinnamaldehyde (6.3 mL, 50 mmol) and *para*-toluenesulfonamide (8.56 g, 50 mmol) and following the above general procedure. The residue was purified by recrystallisation to give the title compound (10.92 g, 77% yield) as a pale brown solid. $^1$H NMR $\delta$2.43 (3H, s), 6.98 (1H, dd, $J$ = 15.6, 9.3), 7.34 (2H, d, $J$ = 8.1), 7.37-7.60 (6H, m), 7.86 (2H, d, $J$ = 8.1), 8.77 (1H, d, $J$ = 9.3).

## IV. Procedures for the Staudinger reaction promoted by NHC 2 (Figure 2)

**Entry 1:**

A 0.45 M solution of KHMDS in toluene (0.16 mL, 0.0733 mmol, 19 mol%) was added to a suspension of triazolium salt **1** (21.1 mg, 0.0771 mmol, 20 mol%) in toluene (1 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (74.9 mg, 0.386 mmol, 1.0 equiv) in toluene (1 mL) was added, followed by a solution of *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) in toluene (1 mL), then the reaction mixture was stirred for 24 hours at room temperature before concentration. The analysis of the crude product by $^1$H NMR revealed

>95% conversion of the imine to the corresponding β-lactam. The residue was purified by column chromatography (EtOAc/petroleum ether 10:90 → 30:70) to give β-lactam **(±)-5** (103.1 mg, 59% yield) as a white solid.

**Entries 2 and 3:**

A 0.45 M solution of KHMDS in toluene (0.16 mL, 0.0733 mmol, 19 mol%) was added to a suspension of triazolium salt **1** (21.1 mg, 0.0771 mmol, 20 mol%) in toluene (1 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in toluene (1 mL) was added, followed by a solution of *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) in toluene (1 mL), then the reaction mixture was stirred for 24 hours at room temperature before concentration. The reaction mixture was sampled after 1 hour and 24 hours and the $^1$H NMR spectroscopic analysis revealed 66% and >95% conversion of the imine to the corresponding β-lactam, respectively. The residue was purified by column chromatography (EtOAc/petroleum ether 10:90 → 30:70) to give β-lactam **(±)-5** (146.3 mg, 84% yield) as a white solid.

**Entries 4 and 5:**

Same procedure as above, except that $CH_2Cl_2$ and THF were used as solvent instead of toluene.

**Entry 6:**

A 0.45 M solution of KHMDS in toluene (0.16 mL, 0.0733 mmol, 19 mol%) was added to a suspension of triazolium salt **1** (21.1 mg, 0.0771 mmol, 20 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed by *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred for 1 hour at room temperature before concentration. The analysis of the crude product by $^1$H NMR revealed >95% conversion of the imine to the corresponding β-lactam **(±)-5**.

**Entry 7:**

A 0.45M solution of KHMDS in toluene (0.08 mL, 0.0347 mmol, 9 mol%) was added to a suspension of triazolium salt **1** (10.5 mg, 0.0386 mmol, 10 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed by *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred for 1 hour at room temperature before concentration. The analysis of the crude product by $^1$H NMR revealed >95% conversion of the imine to the corresponding β-lactam **(±)-5**.

**Entry 8:**

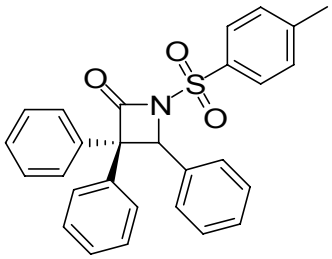
A 0.45 M solution of KHMDS in toluene (0.04 mL, 0.0174 mmol, 4.5 mol%) was added to a suspension of triazolium salt **1** (5.3 mg, 0.0193 mmol, 5 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed by *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred for 1 hour at room temperature before concentration. The analysis of the crude product by $^1$H NMR revealed >95% conversion of the imine to the corresponding β-lactam **(±)-5**. The residue was purified by column chromatography (EtOAc/petroleum ether 10:90 → 30:70) to give β-lactam **(±)-5** (162.6 mg, 93% yield) as a white solid.

**Entry 9:**

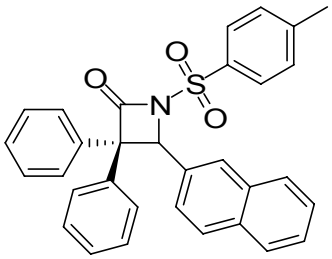
A 0.45 M solution of KHMDS in toluene (0.008 mL, 0.0035 mmol, 0.9 mol%) was added to a suspension of triazolium salt **1** (1.1 mg, 0.0039 mmol, 1 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed by *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred for 24 hours at room temperature before concentration. The analysis of the crude product by $^1$H NMR revealed 60% conversion of the imine to the corresponding β-lactam **(±)-5**.

**V. General procedure for the synthesis of β-lactams 5 and 8-12 (Figure 4).**

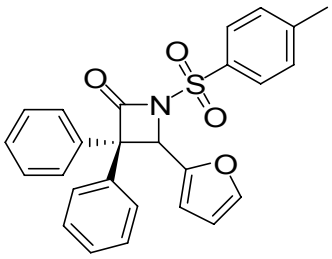
A 0.45 M solution of KHMDS in toluene (0.04 mL, 0.0174 mmol, 4.5 mol% or 0.08 mL, 0.0347 mmol, 9 mol%) was added to a suspension of triazolium salt **1** (5.3 mg, 0.0193 mmol, 5 mol% or 10.5 mg, 0.0386 mmol, 10 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed the imine (0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred at room temperature before concentration.



**(±)-3,3,4-Triphenyl-1-tosylazetidin-2-one (±)-5.** The β-lactam **(±)-5** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 20:80 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-5** (162.6 mg, 93% yield) as a white solid (mp = 184-185°C). IR (KBr disk) $\nu$ 3063, 3037, 2928, 1776 (C=O), 1597, 1495, 1452, 1447, 1383, 1370, 1262, 1210, 1188, 1172, 1141, 1090, 1070, 1028; $^1$H NMR $\delta$ 2.32 (3H, s), 5.70 (1H, s), 6.77-6.94 (7H, m), 6.98 (2H, t, $J$ = 7.6), 7.05 (1H, t, $J$ = 7.2), 7.11-7.27 (5H, m), 7.31 (2H, d, $J$ = 7.2), 7.65 (2H, d, $J$ = 8.0); $^{13}$C NMR δ 21.8 ($CH_3$), 69.3 (CH), 72.9 (C), 127.0 (2 CH), 127.3 (CH), 127.7 (2 CH), 127.9 (3 CH), 128.0 (2 CH), 128.1 (2 CH), 128.4 (2 CH), 128.5 (CH), 129.0 (2 CH), 129.9 (2 CH), 134.0 (C), 135.4 (C), 135.9 (C), 139.0 (C), 145.4 (C), 166.9 (C); CIMS ($NH_3$) m/z 471 (M + $NH_4^+$, 4), 257 (67), 256 ($Ph_2C$=$CH^+$-Ph, 29), 212 ($Ph_2C$=C=O + $NH_4^+$, 27), 106 (O=C-N-$SO_2$, 100), 91 ($C_6H_5^+$-$CH_3$, 77); HRMS (CI, $NH_3$) [M + $NH_4^+$] $C_{28}H_{27}N_2O_3S$ requires 471.1737, found, 471.1738; Anal. Calcd. for $C_{28}H_{23}NO_3S$: C 74.15, H 5.11, N 3.09%, Found: C 73.84, H 4.97, N 3.12%.

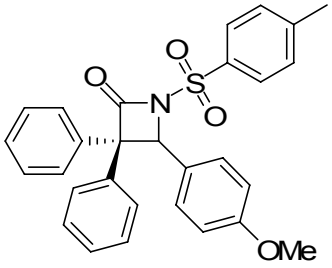


**(±)-3,3-Diphenyl-4-(2-naphthyl)-1-tosylazetidin-2-one (±)-8.** The β-lactam **(±)-8** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(2-naphthylidene)-4-methylbenzenesulfonamide (119.3 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 20:80 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-8** (177.9 mg, 92% yield) as a white solid (mp = 182-183°C). IR (KBr disk) $\nu$ 3054, 1792 (C=O), 1595, 1496, 1449, 1374, 1361, 1167, 1128, 1121, 1088; $^1$H NMR $\delta$ 2.39 (3H, s), 5.94 (1H, s), 6.81 (1H, dd, *J* = 8.4, 1.2), 6.83-7.03 (5H, m), 7.18 (2H, d, *J* = 8.0), 7.22-7.39 (4H, m), 7.39-7.51 (5H, m), 7.56 (1H, s), 7.63 (1H, dd, *J* = 5.6, 3.2), 7.69 (3H, d, *J* = 8.0); $^{13}$C NMR δ 27.7 ($CH_3$), 69.7 (CH), 72.8 (C), 124.8 (CH), 126.3 (CH), 126.5 (CH), 127.0 (2 CH), 127.3 (CH), 127.7 (4 CH), 128.0 (4 CH), 128.1 (CH), 128.2 (2 CH), 129.0 (2 CH), 129.8 (2 CH), 131.5 (C), 132.7 (C), 133.1 (C), 135.5 (C), 135.7 (C), 139.2 (C), 145.4 (C), 166.8 (C); CIMS m/z 504 (M + $H^+$, 18), 308 (M - $Ph_2C$=C=O, 13), 307 (100), 306 (40), 198 (O=C-N=$SO_2$-tol, 38), 194 ($Ph_2C$=C=O, 18), 155 ($SO_2$-tol, 16), 141 ($C_{11}H_9$, 5); HRMS (CI) [M + $H^+$] $C_{32}H_{26}NO_3S$ requires 504.1633, found, 504.1631.

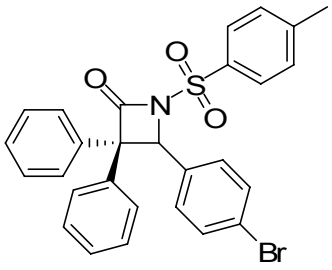


**(±)-3,3-Diphenyl-4-(2-furanyl)-1-tosylazetidin-2-one (±)-9.** The β-lactam **(±)-9** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(2-furfurylidene)-4-methylbenzenesulfonamide (96.1 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 20:80 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-9** (146.0 mg, 85% yield) as a white solid (mp = 160°C). IR (KBr disk) $\nu$ 3129, 3090, 3069, 1792 (C=O), 1596, 1496, 1450, 1364, 1257, 1170, 1138, 1089; $^1$H NMR $\delta$ 2.34 (3H, s), 5.69

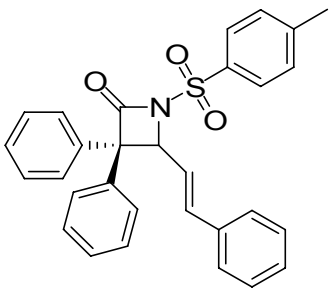
(1H, s), 6.02-6.14 (2H, m), 6.84-6.95 (1H, m), 7.96-7.09 (5H, m), 7.14-7.28 (5H, m), 7.29-7.32 (2H, m), 7.65 (2H, d, $J$ = 8.4); $^{13}$C NMR δ 21.7 ($CH_3$), 62.8 (CH), 72.1 (C), 110.5 (CH), 111.4 (CH), 126.8 (2 CH), 127.1 (2 CH), 127.4 (CH), 127.6 (2 CH), 128.0 (CH), 128.2 (2 CH), 129.0 (2 CH), 129.8 (2 CH), 135.4 (C), 136.2 (C), 138.7 (C), 143.1 (C), 145.3 (C), 147.2 (C), 166.0 (C); CIMS m/z 444 (M + $H^+$, 4), 288 (M – $SO_2$-tol, 6), 247 ($MH^+$ – O=C=N=$SO_2$tol, 18), 205 (100), 198 (O=C-N-$SO_2$-tol, 38), 194 ($Ph_2C$=C=O, 5); HRMS (CI) [M + $H^+$] $C_{26}H_{22}NO_4S$ requires 444.1270, found, 444.1265.




**(±)-3,3-Diphenyl-4-(4-methoxyphenyl)-1-tosylazetidin-2-one (±)-10.** The β-lactam **(±)-10** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(4-methoxybenzylidene)-4-methylbenzenesulfonamide (111.6 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 24 hours at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 20:80 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-10** (109.2 mg, 59% yield) as a white solid (mp = 183-184°C). IR (KBr disk) $\nu$ 3161, 2931, 2834, 1773 (C=O), 1595, 1515, 1496, 1447, 1368, 1248, 1173, 1138, 1089; $^1$H NMR $\delta$ 2.42 (3H, s), 3.73 (3H, s), 5.72 (1H, s), 6.59 (2H, d, $J$ = 8.4), 6.84 (2H, d, $J$ = 8.8), 6.89-6.98 (2H, m), 6.98-7.09 (3H, m), 7.18-7.43 (7H, m), 7.72 (2H, d, $J$ = 8.4); $^{13}$C NMR δ 21.7 ($CH_3$), 55.2 ($CH_3$), 69.3 (CH), 72.6 (C), 113.5 (2 CH), 125.9 (C), 126.9 (2 CH), 127.2 (CH), 127.7 (2 CH), 127.8 (CH), 128.0 (2 CH), 128.2 (2 CH), 128.9 (2 CH), 129.3 (2 CH), 129.8 (2 CH), 135.6 (C), 135.9 (C), 139.3 (C), 145.3 (C), 159.7 (C), 166.9 (C); CIMS m/z 484 (M + $H^+$, 3), 287 ($MH^+$ – O=C=N-$SO_2$tol, 43), 286 (28), 198 (O=C=N-$SO_2$-tol, 93), 172 (100), 155 ($SO_2$tol, 93), 135 (MeO-$C_6H_4$-CN, 39); HRMS (CI) [M + $H^+$] $C_{29}H_{26}NO_4S$ requires 484.1583, found, 484.1565.



**(±)-4-(4-Bromophenyl)-3,3-diphenyl-1-tosylazetidin-2-one (±)-11.** The β-lactam **(±)-11** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(4-bromobenzylidene)-4-methylbenzenesulfonamide (130.4 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 20:80 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-11** (181.8 mg, 89% yield) as a white solid (mp = 214-215°C). IR (KBr disk) $\nu$ 3161, 2931, 2834, 1773 (C=O), 1595, 1494, 1447, 1367, 1170, 1141, 1089; $^1$H NMR $\delta$ 2.43 (3H, s), 5.70 (1H, s), 6.82 (2H, d, *J* = 8.4), 6.87-6.94 (2H, m), 6.98-7.10 (3H, m), 7.20 (2H, d, *J* = 8.4), 7.23-7.38 (7H, m), 7.73 (2H, d, *J* = 8.4); $^{13}$C NMR δ 21.8 ($CH_3$), 68.5 (CH), 73.0 (C), 122.7 (C), 127.0 (2 CH), 127.6 (CH), 127.7 (2 CH), 127.9 (2 CH), 128.0 (CH), 128.4 (2 CH), 129.0 (2 CH), 129.5 (2 CH), 129.9 (2 CH), 131.2 (2 CH), 133.3 (C), 135.2 (C), 135.5 (C), 138.7 (C), 145.6 (C), 166.6 (C); CIMS m/z 534 ($MH^+$ ($^{81}$Br), 87), 532 ($MH^+$ ($^{79}$Br), 83), 378 (M ($^{81}$Br) – 2 * $C_6H_5$), 376 (M ($^{79}$Br) – 2 * $C_6H_5$), 337 (M ($^{81}$Br) – $Ph_2C$=C=O, 33), 336 (M ($^{81}$Br) – O=C=N-$SO_2$tol, 42), 335 (M ($^{79}$Br) – $Ph_2C$=C=O, 36), 334 (M ($^{79}$Br) – O=C=N-$SO_2$tol, 35), 256 (28), 226 (22), 198 (O=C=N-$SO_2$-tol, 29), 194 ($Ph_2C$=C=O, 100); HRMS (CI) [M ($^{79}$Br) + $H^+$] $C_{28}H_{27}{}^{79}BrN_2O_3S$ requires 532.0582, found, 532.0471; [M ($^{81}$Br) + $H^+$] $C_{28}H_{27}{}^{81}BrN_2O_3S$ requires 534.0562, found, 534.0457; Anal. Calcd. for $C_{28}H_{22}BrNO_3S$: C 63.16, H 4.16, N 2.63%, Found: C 63.38, H 4.08, N 2.55%.

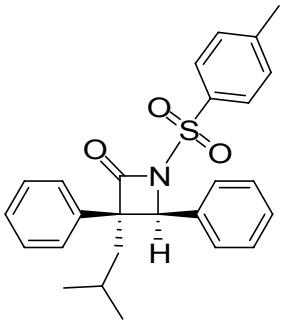


**(±)-3,3-Diphenyl-4-(2-phenylvinyl)-1-tosylazetidin-2-one (±)-12.** The β-lactam **(±)-12** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(3-phenyl-allylidene)-4-methylbenzenesulfonamide (110.0 mg, 0.386 mmol, 1.0 equiv)

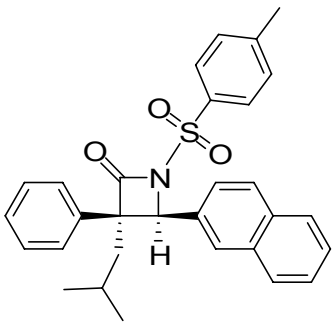
and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 20:80 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-12** (174.2 mg, 94% yield) as a white solid (mp = 164-165°C). IR (KBr disk) $\nu$ 3061, 3028, 2360, 1771 (C=O), 1596, 1494, 1448, 1365, 1171, 1147, 1089; $^1$H NMR $\delta$ 2.42 (3H, s), 5.34 (1H, d, *J* = 9.6), 5.43 (1H, dd, *J* = 15.2, 9.6), 6.87 (1H, d, *J* = 15.6), 7.04-7.20 (2H, m), 7.20-7.48 (15H, m), 7.86 (2H, d, *J* = 8.0); $^{13}$C NMR δ 21.7 ($CH_3$), 68.6 (CH), 71.0 (C), 123.7 (CH), 126.88 (2 CH), 126.93 (2 CH), 127.7 (2 CH), 127.9 (CH), 127.95 (2 CH), 128.0 (CH), 128.6 (3 CH), 128.7 (2 CH), 129.0 (2 CH), 130.0 (2 CH), 135.5 (C), 136.0 (C), 136.1 (C), 136.6 (C), 138.7 (C), 145.3 (C), 166.1 (C); CIMS m/z 480 ($M + H^+$, 4), 349 (3), 307 (8), 282 (18), 198 (O=C=N-$SO_2$-tol, 100), 172 (13), 155 ($SO_2$tol, 37); Anal. Calcd. for $C_{30}H_{25}NO_3S$: C 75.13, H 5.25, N 2.92%, Found: C 75.05, H 5.09, N 2.87%.

## VI. General procedure for the synthesis of β-lactams 14 to 18 (Figure 5).

A 0.45 M solution of KHMDS in toluene (0.08 mL, 0.0347 mmol, 9 mol%) was added to a suspension of triazolium salt **1** (10.5 mg, 0.0386 mmol, 10 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of isobutylphenylketene **13** (87.3 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed the imine (0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred at room temperature before concentration. The initial diastereoselectivity was measured by $^1$H NMR on the crude product and can be improved (after purification by column chromatography) by trituration of the product in $Et_2O$ and filtration. This procedure allowed the characterisation of the major *syn* diastereoisomer.

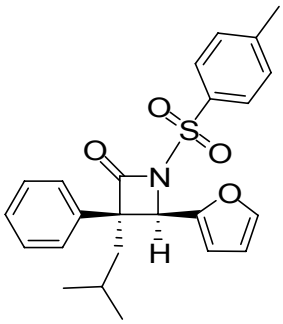


***syn*-3,4-diphenyl-3-isobutyl-1-tosylazetidin-2-one (±)-14.**[3] The β-lactam **(±)-14** was obtained using isobutylphenylketene **13** (87.3 mg, 0.501 mmol, 1.3 equiv) and *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature (dr = 68:32 *syn*:*anti*) and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-14** (148.7 mg, 89% yield). Trituration in $Et_2O$ gave a white solid (mp = 156-158°C, dr = 89:11 *syn*:*anti*). IR (KBr disk) $\nu$ 3064, 3034, 2958, 2927, 2868, 2360, 1770 (C=O), 1597, 1496, 1447, 1364, 1241, 1188, 1170, 1145, 1090; $^1$H NMR *syn*: $\delta$ 0.69 (3H, d, *J* = 6.8), 0.87 (3H, d, *J* = 6.4), 1.48-1.61 (1H, m), 1.92 (1H, dd, *J* = 14.6, 6.0), 2.04 (1H, dd, *J* = 14.0, 6.4), 2.43 (3H, s), 5.00 (1H, s), 6.77 (2H, d, *J* = 7.6), 6.85-6.92 (2H, m), 6.95-7.05 (5H, m), 7.10 (1H, t, *J* = 7.4), 7.15-7.30 (2H, m), 7.71 (2H, d, *J* = 8.4); *anti* (visible peaks): δ 0.37 (3H, d, *J* = 6.4), 2.43 (3H, s), 5.05 (1H, s), 7.80 (2H, d, *J* = 8.4); $^{13}$C NMR *syn*: δ 21.7 ($CH_3$), 23.7 ($CH_3$), 23.8 ($CH_3$), 24.9 (CH), 47.5 ($CH_2$), 69.3 (C), 69.8 (CH), 127.0 (CH), 127.4 (2 CH), 127.6 (2 CH), 127.9 (2 CH), 127.95 (2 CH), 128.0 (2 CH), 128.4 (CH), 129.7 (2 CH), 134.2 (C), 134.9 (C), 135.7 (C), 145.2 (C), 168.1 (C); *anti* (visible peaks): δ 23.0, 24.0, 24.5, 42.1, 69.9, 126.1, 127.4, 127.8, 128.6, 128.8, 128.9, 129.8, 168.5.



***syn*-3-Isobutyl-4-(2-naphthyl)-3-phenyl-1-tosylazetidin-2-one (±)-15.** The β-lactam **(±)-15** was obtained using isobutylphenylketene **13** (87.3 mg, 0.501 mmol, 1.3 equiv) and *N*-(2-naphthylidene)-4-methylbenzenesulfonamide (119.3 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature (dr = 63:37 *syn*:*anti*) and the residue

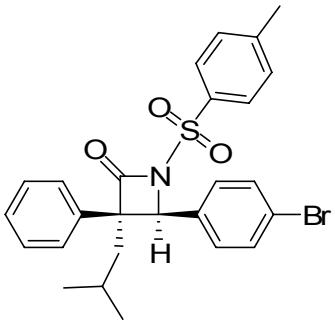
was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-15** (165.8 mg, 89% yield). Trituration in $Et_2O$ gave a white solid (mp = 146-148°C, dr = 90:10 *syn*:*anti*). IR (KBr disk) $\nu$ 3060, 2956, 2927, 2870, 2358, 1784 (C=O), 1597, 1496, 1467, 1448, 1368, 1187, 1172, 1088; $^1$H NMR *syn*: $\delta$ 0.72 (3H, d, *J* = 6.8), 0.91 (3H, d, *J* = 6.8), 1.51-1.65 (1H, m), 2.00 (1H, dd, *J* = 14.4, 6.0), 2.11 (1H, dd, *J* = 14.0, 6.4), 2.38 (3H, s), 5.18 (1H, s), 6.62 (1H, dd, *J* = 8.4, 1.2), 6.88-7.00 (5H, m),7.16 (2H, d, *J* = 8.0), 7.32 (1H, d, *J* = 8.8), 7.38-7.48 (3H, m), 7.60 (1H, dd, *J* = 6.0, 3.2), 7.60-7.69 (3H, m); *anti* (visible peaks): δ 0.33 (3H, d, *J* = 6.4), 2.45 (3H, s), 5.21 (1H, s); $^{13}$C NMR *syn*: δ 21.7 ($CH_3$), 23.7 ($CH_3$), 23.8 ($CH_3$), 24.9 (CH), 47.8 ($CH_2$), 69.2 (C), 70.0 (CH), 124.9 (CH), 126.2 (CH), 126.4 (CH), 127.0 (CH), 127.4 (2 CH), 127.5 (CH), 127.6 (2 CH), 127.9 (CH), 128.0 (2 CH), 128.2 (CH), 129.7 (2 CH), 131.7 (C), 132.6 (C), 133.1 (C), 134.8 (C), 135.6 (C), 145.1 (C), 168.0 (C); CIMS m/z 484 ($M + H^+$, 100), 287 ($MH^+$ - O=C=N-$SO_2$tol, 37), 198 (O=C=N-$SO_2$-tol, 40), 174 (Ph(*i*Bu)C=C=O, 75), 154 ($SO_2$tol, 29); HRMS ($ESI^+$) [$M + Na^+$] $C_{30}H_{29}NNaO_3S$ requires 506.1766, found, 506.1768.




**s*yn*-4-(2-furanyl)-3-isobutyl-3-phenyl-1-tosylazetidin-2-one (±)-16.**[3]

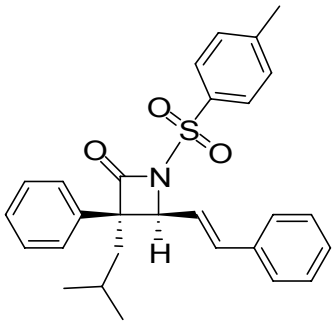
The β-lactam **(±)-16** was obtained using isobutylphenylketene **13** (87.3 mg, 0.501 mmol, 1.3 equiv) and *N*-(2-furfurylidene)-4-methylbenzenesulfonamide (96.1 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour at room temperature (dr = 81:19 *syn*:*anti*) and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-16** (141.2 mg, 86% yield). Trituration in $Et_2O$ gave a white solid (mp = 130-132°C, dr = 86:14 *syn*:*anti*). IR (KBr disk) $\nu$ 3066, 2958, 2872, 2360, 1767 (C=O), 1597, 1497, 1468, 1449, 1367, 1242, 1187, 1170, 1089; $^1$H NMR *syn*: $\delta$ 0.74 (3H, d, *J* = 6.8), 0.87 (3H, d, *J* = 6.8), 1.43-1.61 (1H, m), 1.95 (1H, dd, *J* = 14.0, 5.6), 2.01 (1H, dd, *J* = 14.4, 7.2), 2.41 (3H, s), 5.10 (1H, s), 6.11 (2H, d, *J* = 0.8), 6.88 (1H, s), 6.96-7.06 (2H, m), 7.07-7.17 (3H, t, *J* = 3.2), 7.21-7.23 (2H, m), 7.69 (2H, d, *J* = 8.4); *anti* (visible

peaks): δ 0.44 (3H, d, *J* = 6.4), 0.68 (3H, d, *J* = 6.4), 1.18-1.32 (1H, m), 1.73 (1H, dd, *J* = 14.4, 7.6), 2.43 (3H, s), 5.15 (1H, s), 6.39-6.51 (2H, m), 7.72 (2H, d, *J* = 8.4); $^{13}$C NMR *syn*: δ 21.7 ($CH_3$), 23.5 ($CH_3$), 23.8 ($CH_3$), 24.9 (CH), 47.6 ($CH_2$), 62.5 (CH), 68.4 (C), 110.4 (CH), 111.4 (CH), 126.5 (2 CH), 127.1 (CH), 127.5 (2 CH), 128.0 (2 CH), 129.7 (2 CH), 135.4 (C), 135.5 (C), 142.9 (CH), 145.0 (C), 147.3 (C), 167.3 (C); *anti* (visible peaks): 23.1, 24.5, 42.1, 62.7, 110.8, 111.2, 126.3, 126.4, 127.6, 127.7, 128.9, 129.8, 143.3.



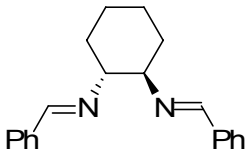

**s*yn*-4-(4-Bromophenyl)-3-isobutyl-3-phenyl-1-tosylazetidin-2-one (±)-17.** The β-lactam **(±)-17** was obtained using isobutylphenylketene **13** (87.3 mg, 0.501 mmol, 1.3 equiv) and *N*-(4-bromobenzylidene)-4-methylbenzenesulfonamide (130.4 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 16 hours (dr = 57:43 *syn*:*anti*) at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-17** (186.4 mg, 94% yield). Trituration in $Et_2O$ gave a white solid (mp = 184-186°C, dr = 82:18 *syn*:*anti*). IR (KBr disk) $\nu$ 3027, 2960, 2924, 2869, 2360, 1784 (C=O), 1596, 1487, 1468, 1448, 1407, 1362, 1231, 1168, 1139, 1087; $^1$H NMR *syn*: $\delta$ 0.67 (3H, d, *J* = 6.4), 0.87 (3H, d, *J* = 6.8), 1.47-1.61 (1H, m), 1.90 (1H, dd, *J* = 14.4, 6.0), 2.03 (1H, dd, *J* = 14.4, 6.4), 2.44 (3H, s), 4.93 (1H, s), 6.65 (2H, d, *J* = 8.4), 6.83-6.92 (2H, m), 7.01-7.09 (3H, m), 7.13 (2H, d, *J* = 8.4), 7.28 (2H, d, *J* = 8.0), 7.71 (2H, d, *J* = 8.4); *anti* (visible peaks): δ 0.41 (3H, d, *J* = 6.4), 0.71 (3H, d, *J* = 6.4), 4.96 (1H, s), 6.71 (2H, d, *J* = 8.4), 7.55 (2H, d, *J* = 8.4), 7.80 (2H, d, *J* = 8.0); $^{13}$C NMR *syn*: δ 21.8 ($CH_3$), 23.7 ($CH_3$), 23.8 ($CH_3$), 24.9 (CH), 47.4 ($CH_2$), 69.0 (CH), 69.4 (C), 122.5 (C), 127.3 (CH), 127.4 (2 CH), 127.6 (2 CH), 128.2 (2 CH), 129.6 (2 CH), 129.9 (2 CH), 131.1 (2 CH), 133.4 (C), 134.5 (C), 135.5 (C), 145.5 (C), 167.7 (C); *anti* (visible peaks): 22.9, 24.0, 24.6, 42.1, 69.3, 126.0, 127.8, 129.0, 129.4, 129.9, 131.9, 168.2; CIMS m/z 514 ($MH^+$ ($^{81}$Br), 28), 512 ($MH^+$ ($^{79}$Br), 32), 358 (M ($^{81}$Br) – $SO_2$tol, 6), 356 (M ($^{79}$Br) – $SO_2$tol, 6), 316 (M ($^{81}$Br) – O=C=N-$SO_2$tol, 4), 314 (M ($^{79}$Br) – $Ph_2C$=C=O, 4), 198 (O=C=N-$SO_2$-tol, 20), 174

(Ph(*i*Bu)C=C=O, 100), 155 ($SO_2$tol, 15); HRMS (CI) [M ($^{79}$Br) + $H^+$] $C_{26}H_{27}{}^{79}BrNO_3S$ requires 512.0895, found, 512.0908; [M ($^{81}$Br) + $H^+$] $C_{26}H_{27}{}^{81}BrNO_3S$ requires 514.0875, found, 514.0872.

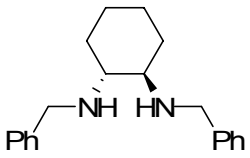


**s*yn*-3-Isobutyl-3-phenyl-4-(2-phenylvinyl)-1-tosylazetidin-2-one (±)-18.**[3] The β-lactam **(±)-18** was obtained using isobutylphenylketene **13** (87.3 mg, 0.501 mmol, 1.3 equiv) and *N*-(3-phenyl-allylidene)-4-methylbenzenesulfonamide (110.0 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 3 hours (dr = 76:24 *syn*:*anti*) at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(±)-18** (128.4 mg, 72% yield). Trituration in $Et_2O$ gave a white solid (mp = 130-132°C, dr = 94:6 *syn*:*anti*). IR (KBr disk) $\nu$ 3085, 3060, 3028, 2956, 2928, 2871, 2360, 1775 (C=O), 1597, 1496, 1449, 1367, 1187, 1174, 1152, 1135, 1087; $^1$H NMR *syn*: $\delta$ 0.73 (3H, d, *J* = 6.4), 0.88 (3H, d, *J* = 6.8), 1.52-1.64 (1H, m), 1.91 (1H, dd, *J* = 14.0, 5.6), 1.99 (1H, dd, *J* = 14.0, 6.8), 2.38 (3H, s), 4.62 (1H, d, *J* = 9.6), 5.21 (1H, dd, J = 15.6, 9.6), 6.70 (1H, d, *J* = 16.0), 7.07 (2H, dd, *J* = 7.6, 3.6), 7.18-7.32 (10H, m), 7.79 (2H, d, *J* = 8.4); *anti* (visible peaks): δ 0.60 (3H, d, *J* = 6.8), 0.80 (3H, d, *J* = 6.4), 2.42 (3H, s), 6.16 (1H, dd, *J* = 16.0, 8.8), 6.80 (2H, d, *J* = 16.0); $^{13}$C NMR *syn*: δ 21.7 ($CH_3$), 23.6 ($CH_3$), 23.8 ($CH_3$), 24.7 (CH), 47.2 ($CH_2$), 67.4 (C), 68.8 (CH), 124.2 (CH), 126.8 (2 CH), 127.4 (2 CH), 127.5 (CH), 127.6 (3 CH), 128.5 (2 CH), 128.6 (2 CH), 129.9 (2 CH), 135.0 (C), 135.6 (C), 136.1 (C), 136.3 (C), 145.1 (C), 167.4 (C); *anti* (visible peaks): 122.4, 126.0, 126.9, 128.8, 128.9.

## VII. Preparation of a $C_2$-symmetric imidazolinium salt 19



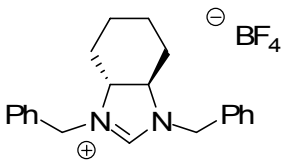
**(1*R*,2*R*)-Bis(benzylidene)cyclohexyl-1,2-diamine**. A mixture of (1*R*,2*R*)-*trans*-cyclohexane-1,2-diammonium (*S*)-tartrate[5] (1.00 g, 3.77 mmol), $K_2CO_3$ (1.05 g, 7.58 mmol) and $H_2O$ (5 mL) were stirred until complete dissolution occurred, to which was then added EtOH (20 mL). The mixture was heated at reflux (80 ºC) and a solution of benzaldehyde (0.77 mL, 7.58 mmol) in EtOH (8 mL) was added over 30 minutes. The mixture was heated at reflux for a further 2 hours, then when the solution had cooled to ambient temperature. Water (5 mL) was added and the mixture cooled to 0 ºC for 3 hours. The mixture was concentrated *in vacuo* to afford the crude diimine. The residue was redissolved in $CH_2Cl_2$ (15 mL), washed with water (2 × 10 mL) and brine (10 mL), dried ($Na_2SO_4$), filtered and concentrated *in vacuo* to give the title compound (1.05 g, 96%) as a pale cream solid (mp = 133-135°C). $^1$H NMR: $\delta$ 1.45–1.57 (2H, m), 1.63–1.89 (6H, m), 3.36–3.41 (2H, m), 3.35–3.42 (2H, m), 7.28–7.36 (6H, m), 7.61 (4H, dd, $J$ = 7.6, 2.1), 8.20 (2H, s); $[\alpha]^{20}_D$ -261.4 (*c* 0.05, $CH_3OH$), lit. -263.0 (*c* 0.19, $CH_3OH$). Data are in accordance with the literature.[6,7].



**(1*R*,2*R*)-Dibenzylcyclohexyl-1,2-diamine**. To a solution of (1*R*,2*R*)-bis(benzylidene)cyclohexyl-1,2-diimine (1.05 g, 3.62 mmol) in MeOH (8 mL) was added $NaBH_4$ (287 mg, 7.59 mmol) portionwise over 30 minutes. The solution was heated at reflux for 15 minutes then cooled to ambient temperature. Water (8 mL) was added and the mixture extracted with $CH_2Cl_2$ (3 × 10 mL). The organics were combined, washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrate *in vacuo* to give the title compound (1.00 g, 94%) as a colourless oil. $^1$H NMR: $\delta$: 1.45–1.57 (2H, m), (1.63–1.89 (6H, m), (1.78 (2H, br s), 3.36–3.41 (2H, m), 3.58 (2H, q, $J$ = 13.2), 3.82 (2H, q, $J$ = 13.2), 7.10–7.31 (10H, m); $[\alpha]^{20}_D$ -69.2

[5] J. F. Larrow, E. N. Jacobsen, Y. Gao, Y. Hong, X. Nie, and C. M. Zepp, *J. Org. Chem.,* **1994**, *59*, 1939.
[6] S. E. Denmark, H. Stadler, R. L. Dorow, and J.-H. Kim, *J. Org. Chem.,* **1991,** *56***,** 5063.
[7] P. Krasik, and H. Alper, *Tetrahedron,* **1994**, *50*, 4347.

(*c* 0.05, $CHCl_3$), lit. -68.0 (*c* 1.3, $CHCl_3$)[8] Spectroscopic data are in accordance with the literature.[9]

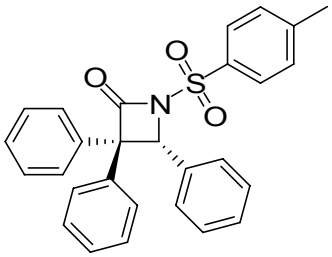



**(3a*R*,7a*R*)-1,3-Dibenzyl-3a,4,5,6,7,7a-hexahydro-1*H*-benzo[*d*]imidazolium tetrafluoroborate 19**. A mixture of (1*R*,2*R*)-dibenzylcyclohexyl-1,2-diamine (500 mg, 1.70 mmol), triethyl orthoformate (0.70 mL, 4.25 mmol), MeOH (5 mL) and ammonium tetrafluoroborate (180 mg, 1.72 mmol) were heated at 110 ºC for 5 hours. Hexane (15 mL) was added to the mixture to precipitate the product as a colourless solid. Recrystallisation from $CH_2Cl_2$ afforded **19** (550 mg, 82%) as a colourless solid (mp = 150-152°C). $[\alpha]^{20}_D$ -66.8 (*c* 0.05, MeOH); IR (KBr disk): 3108 (=C-H), 3072 (=C-H), 1611 (conj cyclic C=N), 1586 (conj cyclic C=N), 1062 (C-N stretch) and 1059 (C-N stretch); $^1$H NMR ($CD_3OD$) $\delta$ : 1.28–1.03 (4H, m), 1.66–1.64 (2H, m), 1.98–1.95 (2H, m), 3.31–3.18 (2H, m), 4.63 (4H, dd, *J* = 15.1, 6.9), 7.33–7.24 (10H, m), 8.57 (1H, s); $^{13}$C NMR ($CD_3OD$) δ : 24.5 (2 $CH_2$), 28.5 (2 $CH_2$), 51.5 (2 $CH_2$), 69.0 (2 CH), 129.4 (2 CH), 129.7 (CH), 130.1 (2 CH), 134.8 (C), 161.9 (CH); HRMS ($ESI^+$) [$M^+$] $C_{21}H_{25}N_2^+$ requires 305.2012, found 305.2019.

## VIII. General procedure for the enantioselective synthesis of β-lactams (*R*)-5, (*R*)-8, (*S*)-9 and (*R*)-11 (Figure 6).

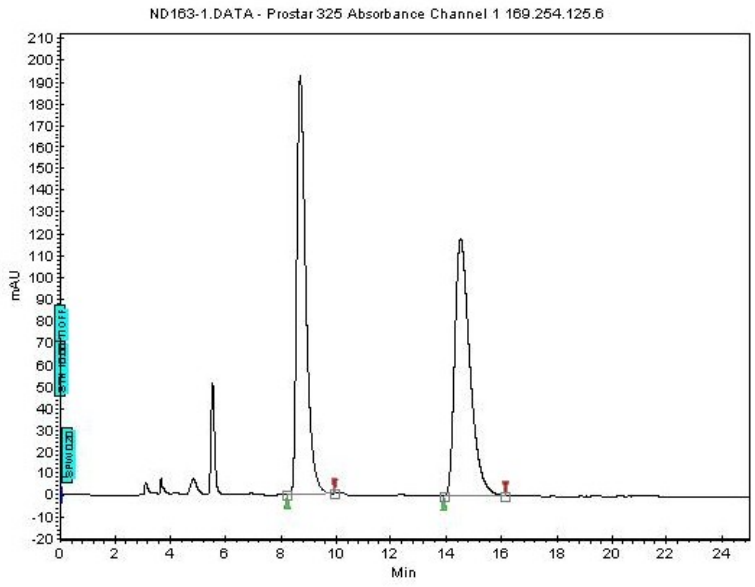
A 0.45 M solution of KHMDS in toluene (0.08 mL, 0.0347 mmol, 9 mol%) was added to a suspension of chiral imidazolinium salt **19** (15.2 mg, 0.0386 mmol, 10 mol%) or chiral triazolium salt **20** (14.5 mg, 0.0386 mmol, 10 mol%) in $Et_2O$ (1.5 mL) under nitrogen atmosphere and the mixture was stirred for 30 minutes at room temperature. A solution of diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) in $Et_2O$ (1.5 mL) was added, followed by the imine (0.386 mmol, 1.0 equiv) as a solid, then the reaction mixture was stirred at room temperature before concentration.

[8] A. Alexakis, A.-S. Chauvin, R. Stouvenel, E. Vrancken, S. Mutti and P. Mangeney, *Tetrahedron: Asymmetry* **2001**, 8, 1171.
[9] I. D. G. Watson, and A. K. Yudin, *J. Org. Chem.* **2003**, *68*, 5160.



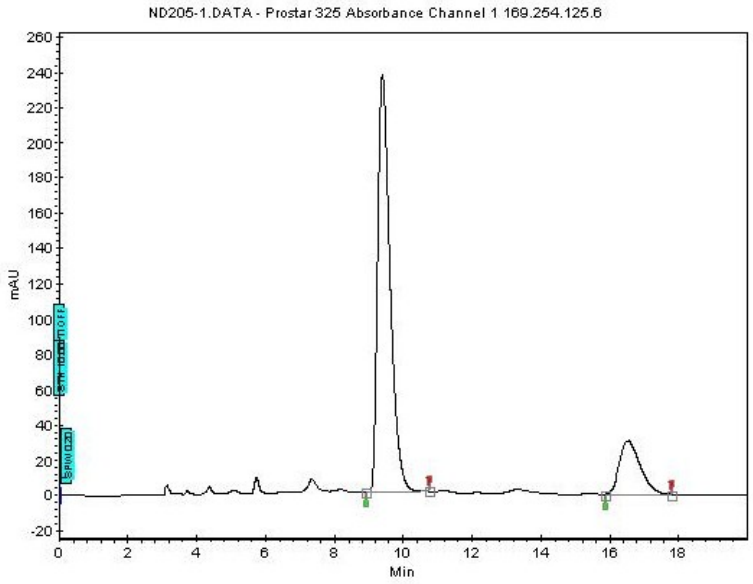
**(*R*)-3,3,4-Triphenyl-1-tosylazetidin-2-one (*R*)-5.** The β-lactam **(*R*)-5** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-benzylidene-4-methylbenzenesulfonamide **4** (100 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour (using the NHC from **19**) or 3 hours (using the NHC from **20**) at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(*R*)-5** as a yellowish solid (158.0 mg, 90% yield, from chiral imidazolinium salt **19** and 167.2 mg, 96% yield from chiral triazolium salt **20**). HPLC analysis: 64% ee (Daicel CHIRALCEL OD-H column, eluent: hexane/$^{i}$PrOH 90:10, flow: 1 mL/min, wavelengh: 254 nm, retention times: 9.4 min (major, *R*) and 16.5 min (minor, *S*)). $[\alpha]^{20}_{D}$ + 17.7 (*c* 1.00, $CHCl_3$, 64% ee). The initial e.e. can be improved by crystallisation ($CH_2Cl_2$/Hexane) and re-isolation of the β-lactam from the mother liquor, giving **(*R*)-5** as a further enantiomerically enriched product (mp = 152-154°C, 98% e.e.). $[\alpha]^{20}_{D}$ + 22.0 (*c* 0.63, $CHCl_3$, 98% ee).

HPLC trace **(±)-5**



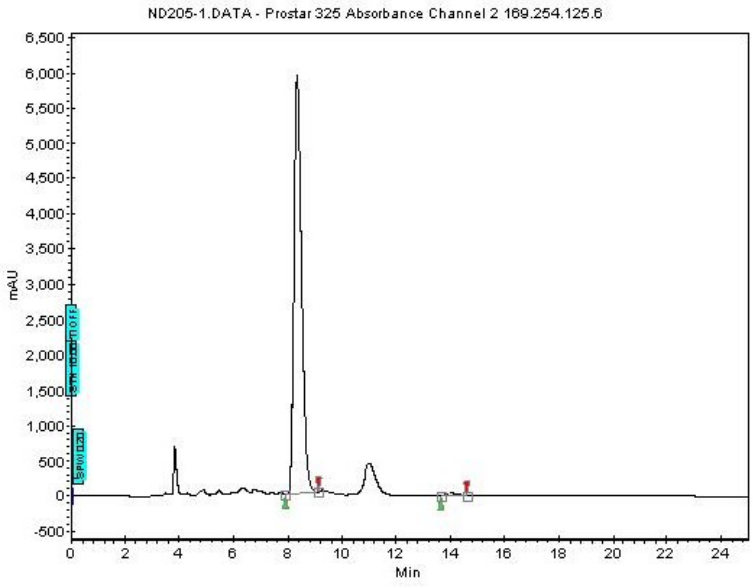

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.69 | 49.51 | 192.5 | 73.1 | 49.506 |
| 2 | UNKNOWN | 14.53 | 50.49 | 118.1 | 74.5 | 50.494 |
| | | | | | | |
| Total | | | 100.00 | 310.6 | 147.6 | 100.000 |

HPLC trace **(*R*)-5** (64% ee)

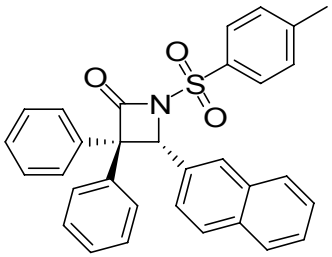



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 9.41 | 82.02 | 236.9 | 98.5 | 82.016 |
| 2 | UNKNOWN | 16.54 | 17.98 | 30.3 | 21.6 | 17.984 |
| | | | | | | |
| Total | | | 100.00 | 267.2 | 120.1 | 100.000 |

HPLC trace **(*R*)-5** (98% ee)



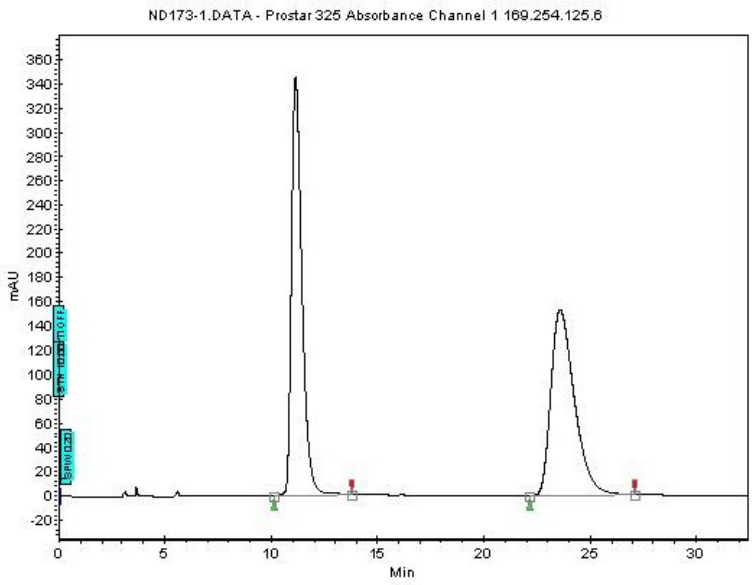

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.33 | 99.23 | 5925.9 | 1902.5 | 99.226 |
| 2 | UNKNOWN | 14.01 | 0.77 | 30.2 | 14.8 | 0.774 |
| | | | | | | |
| Total | | | 100.00 | 5956.1 | 1917.3 | 100.000 |



**(*R*)-3,3-Diphenyl-4-(2-naphthyl)-1-tosylazetidin-2-one (*R*)-8.**

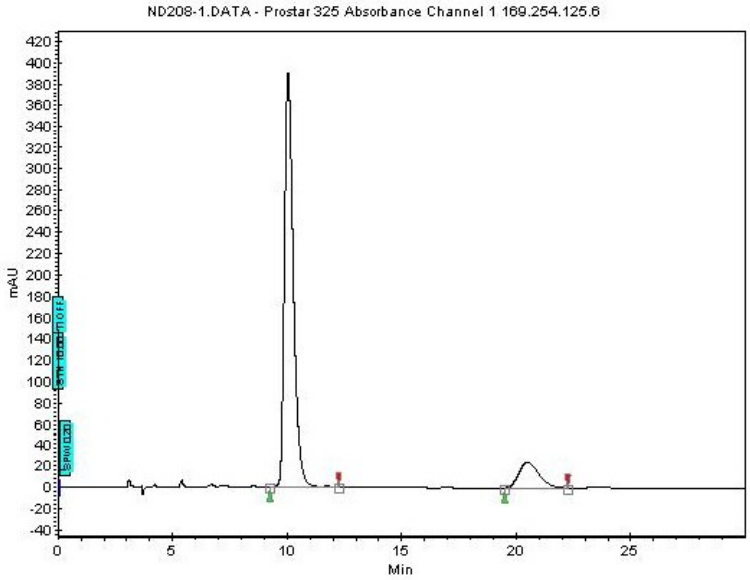
The β-lactam **(*R*)-8** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(2-naphthylidene)-4-methylbenzenesulfonamide (119.3 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour (using the NHC from **19**) or 3 hours (using the NHC from **20**) at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(*R*)-8** as a yellowish solid (184.1 mg, 95% yield, from chiral imidazolinium salt **19** and 178.5 mg, 92% yield from chiral triazolium salt **20**). HPLC analysis: 75% ee (Daicel CHIRALCEL OD-H column, eluent: hexane/$^{i}$PrOH 90:10, flow: 1 mL/min, wavelengh: 254 nm, retention times: 10.0 min (major, *R*) and 20.5 min (minor, *S*)). $[\alpha]^{20}_{D}$ − 5.0 (*c* 1.00, $CHCl_3$, 75% ee). The initial e.e. can be improved by crystallisation ($CH_2Cl_2$/Hexane) and re-isolation of the β-lactam from the mother liquor, giving **(*R*)-8** as a further enantiomerically enriched product (mp = 136-138°C, >99% e.e.). $[\alpha]^{20}_{D}$ - 5.9 (*c* 0.69, $CHCl_3$, >99% ee).

HPLC trace **(±)-8**



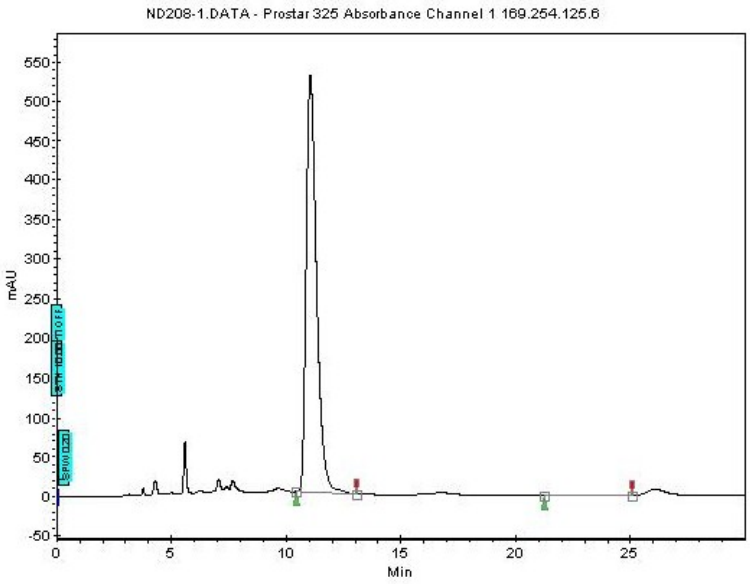

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 11.13 | 50.21 | 345.2 | 197.1 | 50.213 |
| 2 | UNKNOWN | 23.58 | 49.79 | 153.4 | 195.4 | 49.787 |
| | | | | | | |
| Total | | | 100.00 | 498.6 | 392.5 | 100.000 |

HPLC trace **(*R*)-8** (75% ee)

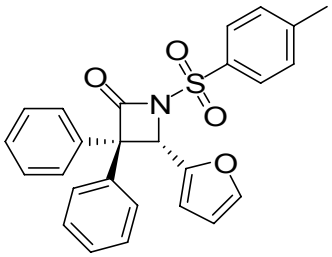



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 10.03 | 87.62 | 390.0 | 176.1 | 87.615 |
| 2 | UNKNOWN | 20.50 | 12.38 | 24.4 | 24.9 | 12.385 |
| | | | | | | |
| Total | | | 100.00 | 414.4 | 201.0 | 100.000 |

HPLC trace **(*R*)-8** (>99% ee)

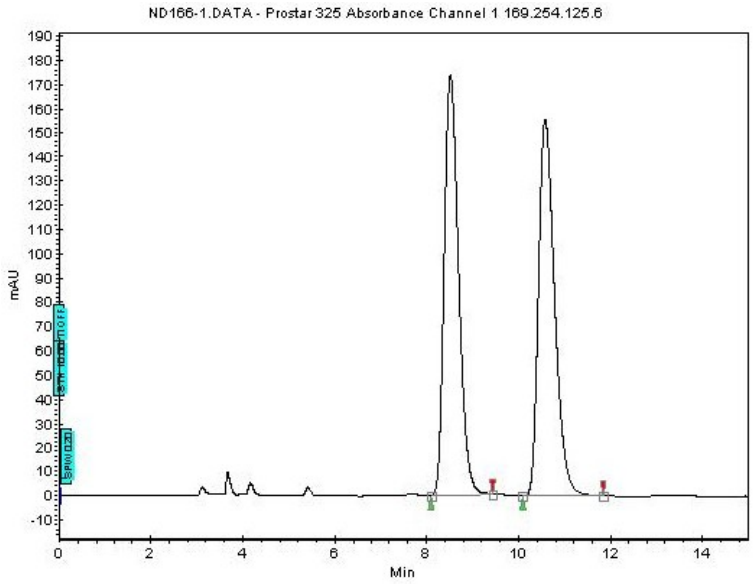



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 11.03 | 99.98 | 527.1 | 275.0 | 99.978 |
| 2 | UNKNOWN | 23.28 | 0.02 | 0.1 | 0.1 | 0.022 |
| | | | | | | |
| Total | | | 100.00 | 527.2 | 275.0 | 100.000 |



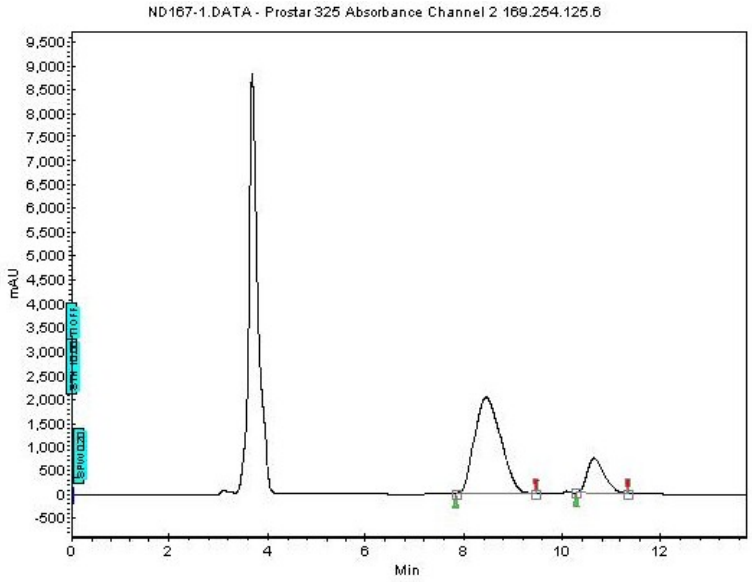
**(*S*)-3,3-Diphenyl-4-(2-furanyl)-1-tosylazetidin-2-one (*S*)-9.** The β-lactam **(*S*)-9** was obtained using diphenylketene **3** (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(2-furfurylidene)-4-methylbenzenesulfonamide (96.1 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 1 hour (using the NHC from **19**) or 3 hours (using the NHC from **20**) at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(*S*)-9** as a yellowish solid (146.0 mg, 85% yield, from chiral imidazolinium salt **19** and 158.8 mg, 93% yield from chiral triazolium salt **20**). HPLC analysis: 61% ee (Daicel CHIRALCEL OD-H column, eluent: hexane/$^{i}$PrOH 90:10, flow: 1 mL/min, wavelengh: 254 nm, retention times: 8.5 min (major, *S*) and 10.6 min (minor, *R*)). $[\alpha]^{20}_{D}$ + 32.6 (*c* 1.00, $CHCl_3$, 61% ee). The initial e.e. can be improved by crystallisation ($CH_2Cl_2$/Hexane) and re-isolation of the β-lactam from the mother liquor, giving **(*S*)-9** as a further enantiomerically enriched product (mp = 144-146°C, 92% e.e.). $[\alpha]^{20}_{D}$ + 45.7 (*c* 0.91, $CHCl_3$, 92% ee).

HPLC trace **(±)-9**



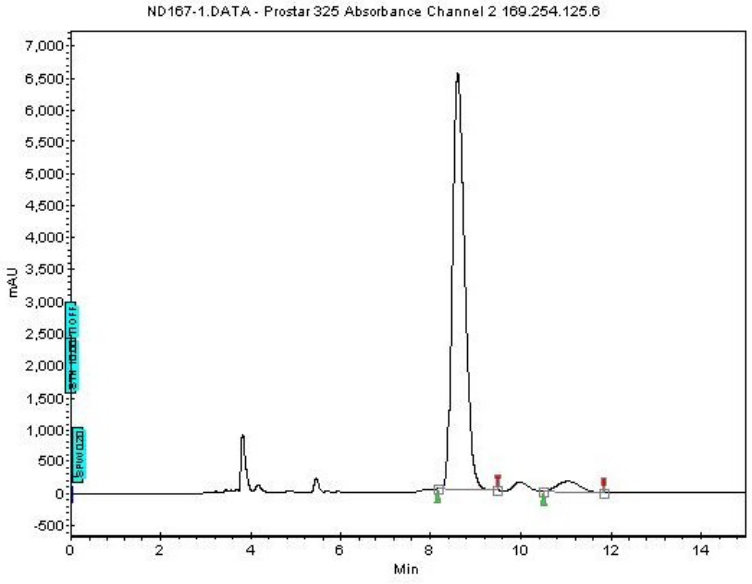

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.52 | 49.70 | 173.4 | 62.2 | 49.704 |
| 2 | UNKNOWN | 10.57 | 50.30 | 155.9 | 63.0 | 50.296 |
| | | | | | | |
| Total | | | 100.00 | 329.3 | 125.2 | 100.000 |

HPLC trace **(*S*)-9** (61% ee)

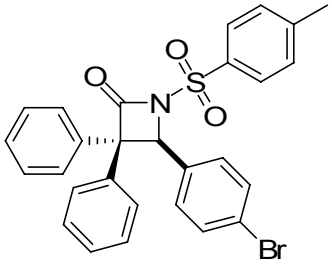



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.45 | 80.52 | 2032.1 | 1252.3 | 80.522 |
| 2 | UNKNOWN | 10.64 | 19.48 | 734.7 | 302.9 | 19.478 |
| | | | | | | |
| Total | | | 100.00 | 2766.8 | 1555.2 | 100.000 |

HPLC trace **(*S*)-9** (92% ee)

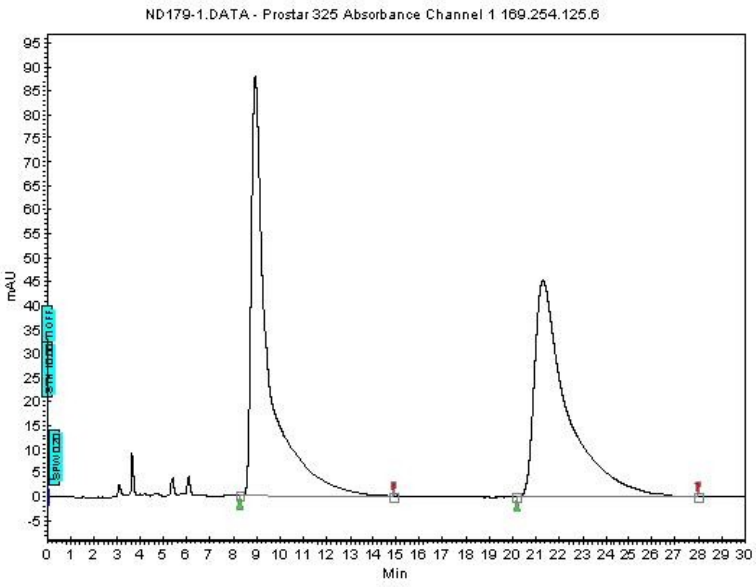



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.60 | 95.39 | 6505.8 | 2039.6 | 95.391 |
| 2 | UNKNOWN | 11.05 | 4.61 | 165.4 | 98.5 | 4.609 |
| | | | | | | |
| Total | | | 100.00 | 6671.1 | 2138.1 | 100.000 |



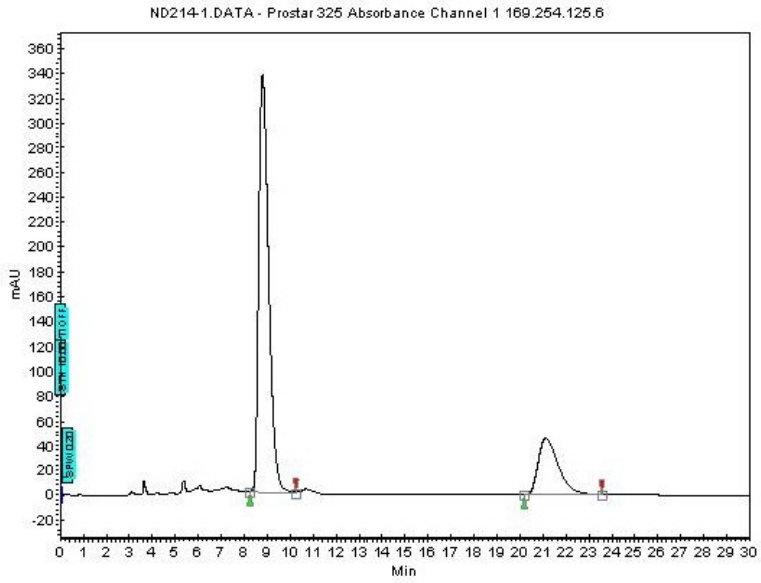
**(*R*)-3,3-diphenyl-4-(4-bromophenyl)-1-tosylazetidin-2-one (*R*)-11.** The β-lactam **(*R*)-11** was obtained using diphenylketene (97.4 mg, 0.501 mmol, 1.3 equiv) and *N*-(4-bromobenzylidene)-4-methylbenzenesulfonamide (130.4 mg, 0.386 mmol, 1.0 equiv) and following the above general procedure. The reaction mixture was concentrated after stirring for 2 hours (using the NHC from **19**) or 3 hours (using the NHC from **20**) at room temperature and the residue was purified by column chromatography (EtOAc/petroleum ether 10:90 then $CH_2Cl_2$/petroleum ether/EtOAc 50:45:5) to give β-lactam **(*R*)-11** as a yellowish solid (163.2 mg, 79% yield, from chiral imidazolinium salt **19** and 197.8 mg, 96% yield from chiral triazolium salt **20**). HPLC analysis: 57% ee (Daicel CHIRALCEL OD-H column, eluent: hexane/$^i$PrOH 90:10, flow: 1 mL/min, wavelengh: 254 nm, retention times: 8.8 min (major, *R*) and 21.1 min (minor, *S*)). $[\alpha]^{20}_D$ + 21. 8 (*c* 1.00, $CHCl_3$, 57% ee). The initial e.e. can be improved by crystallisation ($CH_2Cl_2$/Hexane) and re-isolation of the β-lactam from the mother liquor, giving **(*R*)-11** as a further enantiomerically enriched product (mp = 138-140°C, >99% e.e.). $[\alpha]^{20}_D$ + 25.2 (*c* 0.44, $CHCl_3$, >99% ee).

HPLC trace **(±)-11**



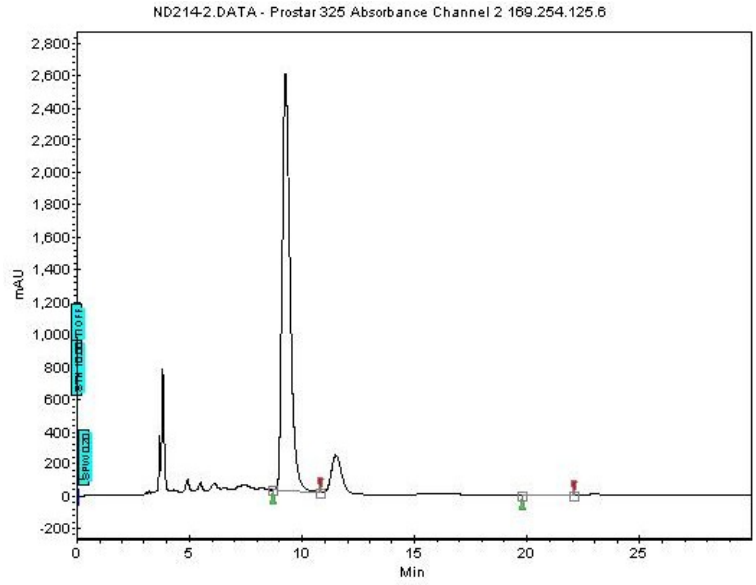

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.94 | 49.87 | 87.7 | 72.8 | 49.875 |
| 2 | UNKNOWN | 21.30 | 50.13 | 45.3 | 73.2 | 50.125 |
| | | | | | | |
| Total | | | 100.00 | 133.0 | 146.0 | 100.000 |

HPLC trace **(*R*)-11** (57% ee)



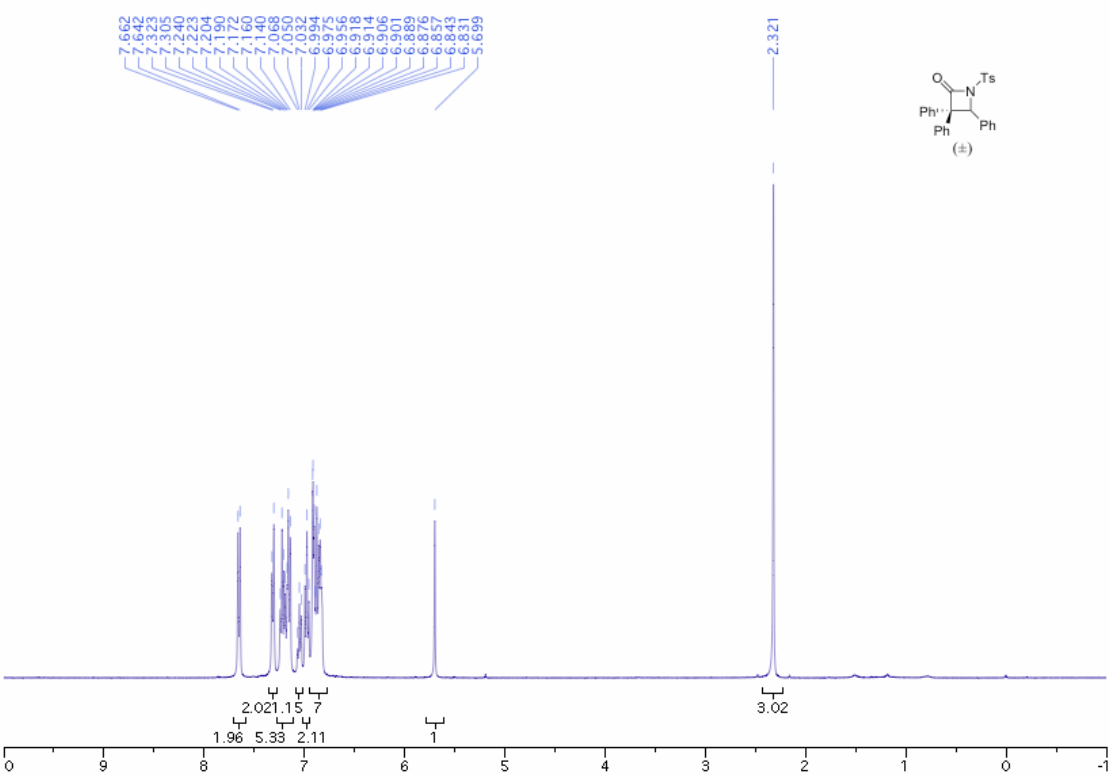

| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 8.79 | 78.34 | 336.1 | 167.4 | 78.341 |
| 2 | UNKNOWN | 21.12 | 21.66 | 45.6 | 46.3 | 21.659 |
| | | | | | | |
| Total | | | 100.00 | 381.7 | 213.7 | 100.000 |

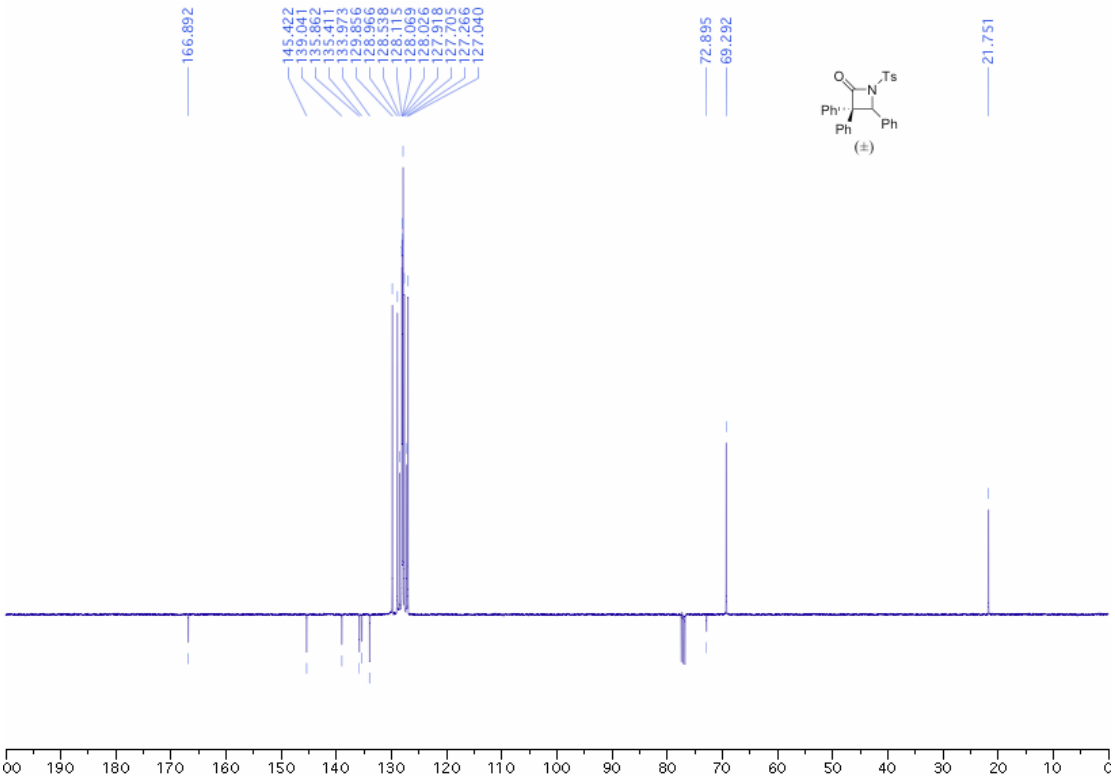
HPLC trace **(*R*)-11** (>99% ee)

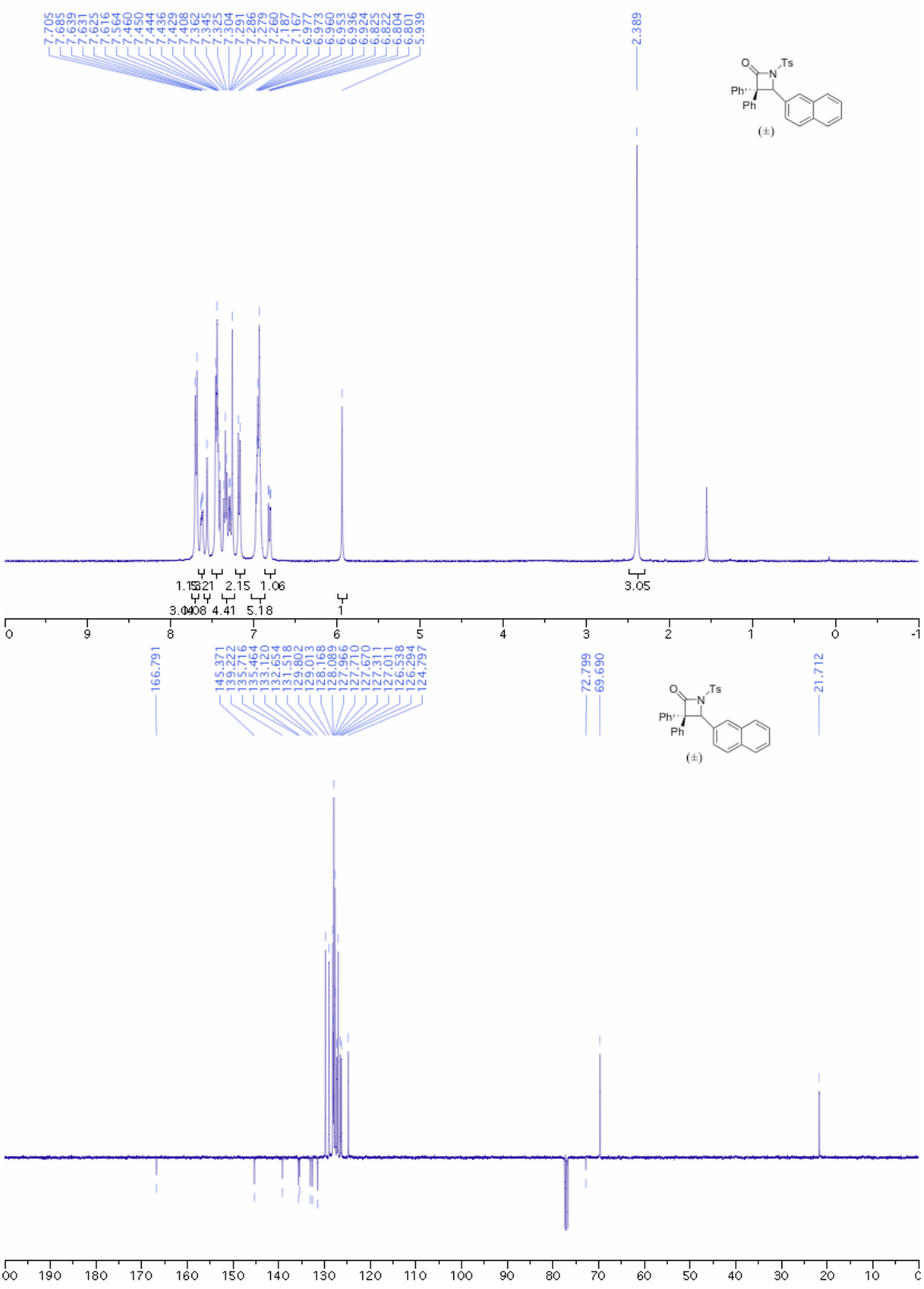



| Index | Name | Time [Min] | Quantity [% Area] | Height [mAU] | Area [mAU.Min] | Area % [%] |
|---|---|---|---|---|---|---|
| 1 | UNKNOWN | 9.27 | 99.98 | 2572.9 | 1040.8 | 99.981 |
| 2 | UNKNOWN | 21.20 | 0.02 | 0.4 | 0.2 | 0.019 |
| | | | | | | |
| Total | | | 100.00 | 2573.3 | 1041.0 | 100.000 |

## IX. Spectral Data

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7.616
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7.460
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7.429
7.408
7.362
7.345
7.304
7.291
7.286
7.279
7.260
7.187
7.167
6.977
6.973
6.960
6.953
6.936
6.924
6.825
6.822
6.804
6.801
5.939
2.389
Ts
N
O
Ph
Ph
(±)
1.15
3.21
2.15
1.06
3.04
4.08
4.41
5.18
1
3.05
166.791
145.371
139.222
135.716
135.464
133.120
132.654
131.868
131.802
129.013
128.168
128.089
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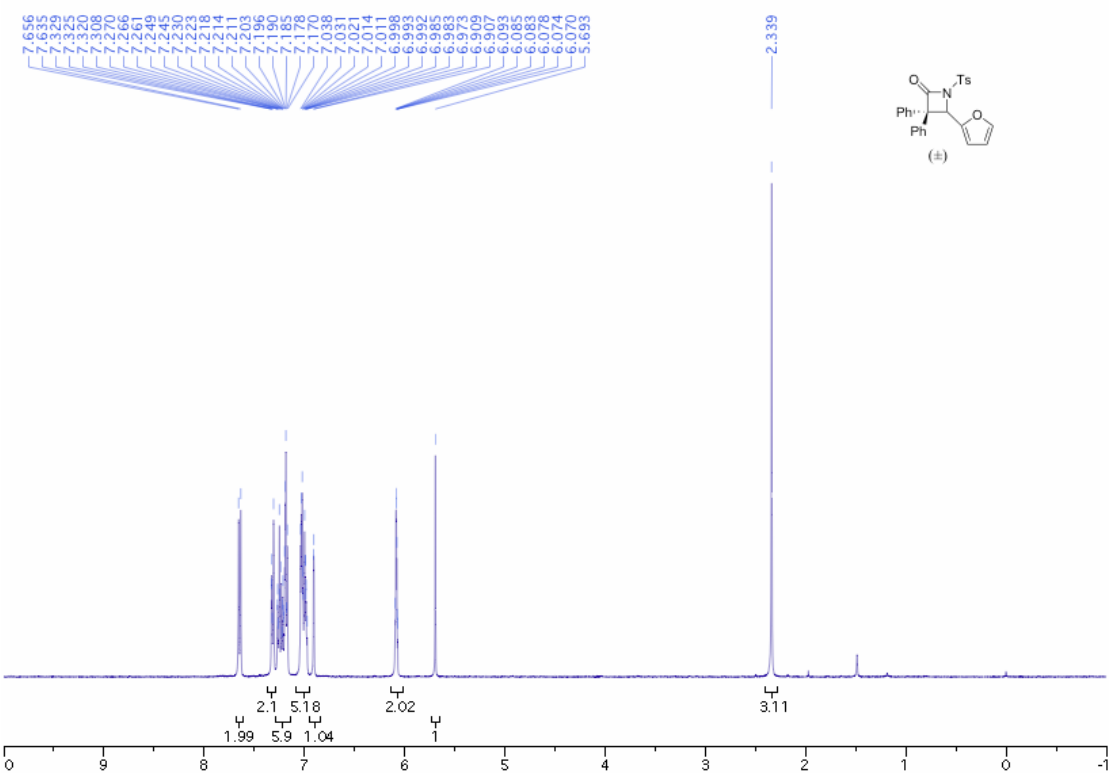
127.311
127.011
126.538
126.294
124.797
72.799
69.690
21.712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7.308
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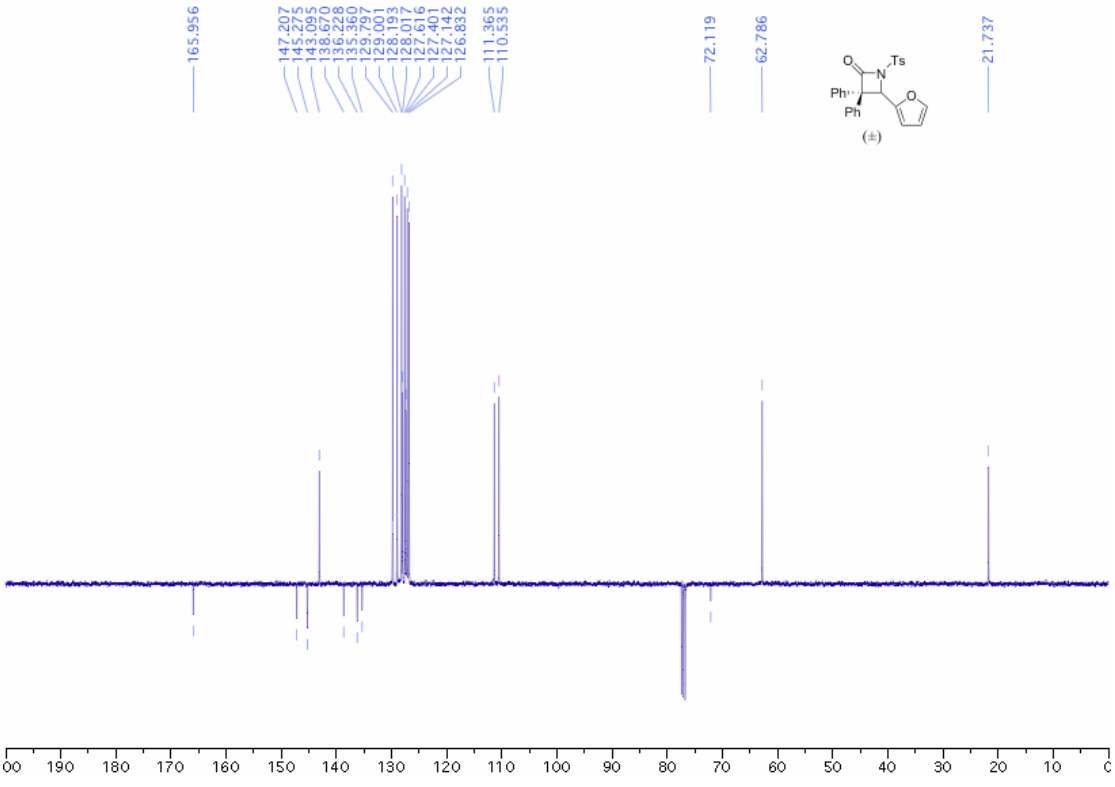
7.266
7.261
7.249
7.245
7.230
7.223
7.218
7.214
7.211
7.203
7.196
7.190
7.185
7.178
7.170
7.038
7.031
7.021
7.014
7.011
6.998
6.993
6.992
6.985
6.983
6.973
6.909
6.907
6.093
6.085
6.083
6.078
6.074
6.070
5.693
2.339
Ts
N
O
Ph
Ph
O
(±)
2.1
5.18
2.02
3.11
1.99
5.9
1.04
1
0
9
8
7
6
5
4
3
2
1
0
-1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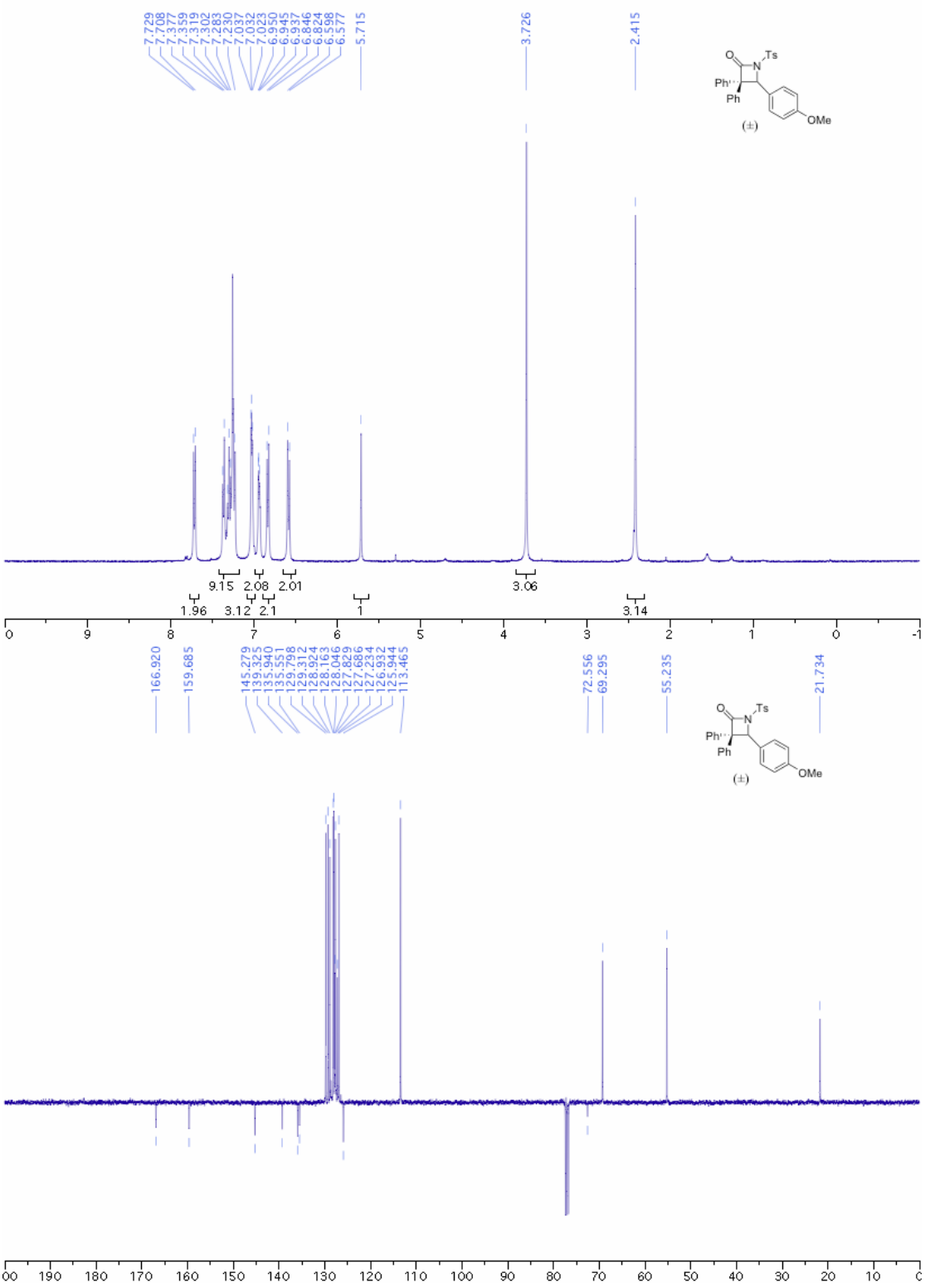
145.275
143.095
138.670
136.228
135.360
129.797
129.001
128.193
128.017
127.616
127.401
127.142
126.832
111.365
110.535
72.119
62.786
21.737
Ts
N
O
Ph
Ph
O
(±)
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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7.302
7.283
7.230
7.037
7.032
7.023
6.950
6.945
6.937
6.846
6.824
6.598
6.577
5.715
3.726
2.415
Ts
N
O
Ph
Ph
OMe
(±)
9.15
2.08
2.01
1.96
3.12
2.1
1
3.06
3.14
166.920
159.685
145.279
139.325
135.940
135.551
129.798
129.312
128.924
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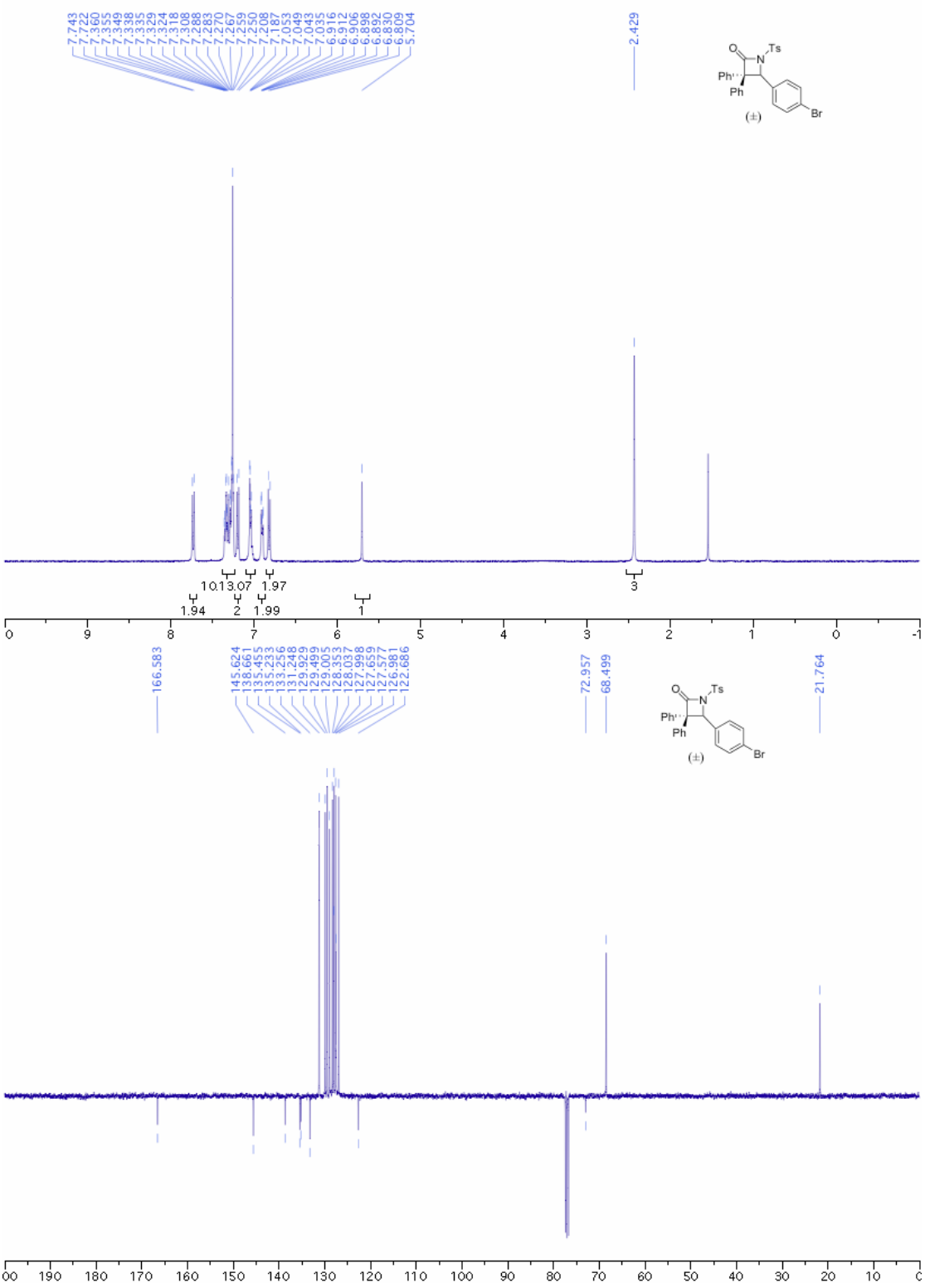
55.235
21.734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7.338
7.335
7.329
7.324
7.318
7.308
7.288
7.283
7.270
7.267
7.259
7.200
7.187
7.053
7.049
7.043
7.035
6.916
6.912
6.906
6.898
6.892
6.830
6.809
5.704
2.429
Ts
N
O
Ph
Ph
Br
(±)
10.13
3.07
1.97
1.94
2
1.99
1
3
0
9
8
7
6
5
4
3
2
1
0
-1
166.583
145.624
138.661
135.455
135.233
133.256
131.248
129.929
129.499
129.005
128.353
128.037
127.998
127.659
127.577
126.981
122.686
72.957
68.499
21.764
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180
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150
140
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120
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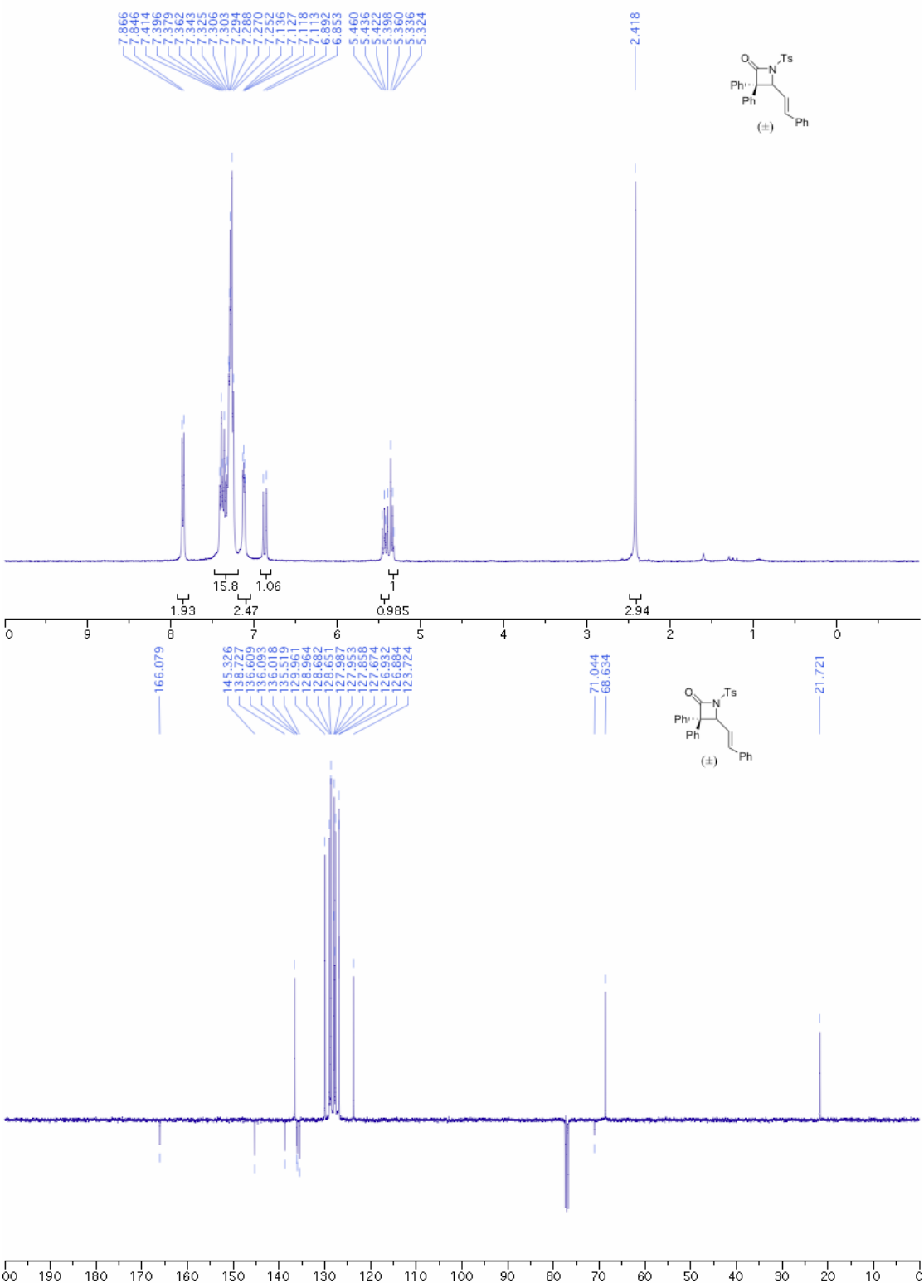
100
90
80
70
60
50
40
30
20
10
0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7.252
7.136
7.127
7.118
7.113
6.892
6.853
5.460
5.436
5.422
5.398
5.360
5.336
5.324
2.418
Ts
N
O
Ph
Ph
Ph
(±)
15.8
1.06
1
1.93
2.47
0.985
2.94
0
9
8
7
6
5
4
3
2
1
0
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136.609
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129.961
128.964
128.682
128.651
127.987
127.953
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127.674
126.932
126.884
123.724
71.044
68.634
21.721
Ts
N
O
Ph
Ph
Ph
(±)
00
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180
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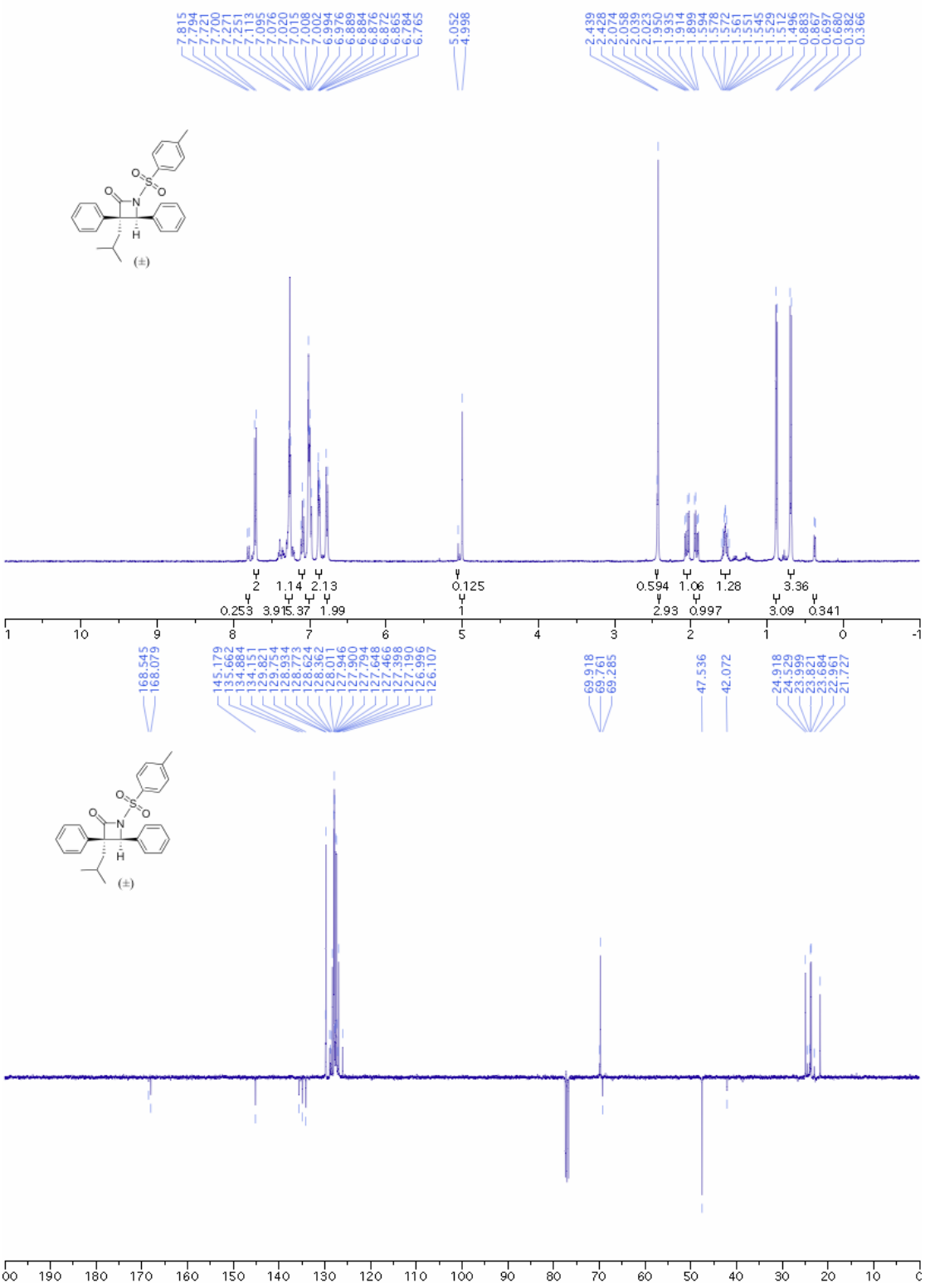
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0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7.271
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7.113
7.095
7.076
7.020
7.015
7.008
7.002
6.994
6.976
6.889
6.884
6.876
6.872
6.865
6.784
6.765
5.052
4.998
2.439
2.424
2.074
2.058
2.039
2.023
1.950
1.935
1.914
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1.578
1.572
1.561
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1.529
1.512
1.496
0.883
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0.697
0.680
0.382
0.366
(±)
2
1.14
2.13
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0.594
1.06
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3.91
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2.93
0.997
3.09
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127.946
127.900
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127.648
127.466
127.398
127.190
126.996
126.107
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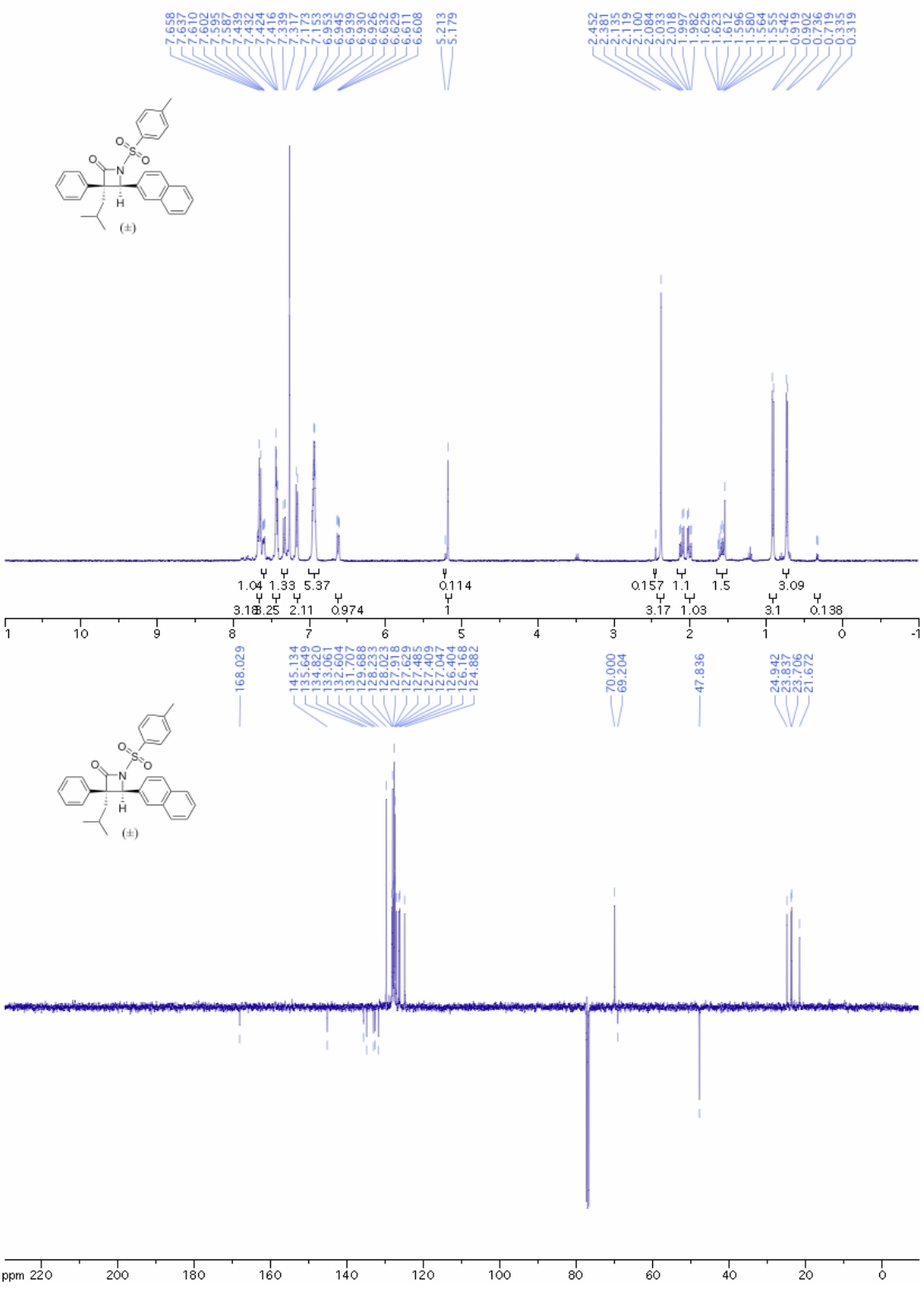
24.529
23.999
23.821
23.664
22.951
21.727
(±)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7.173
7.153
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6.926
6.632
6.629
6.611
6.608
5.213
5.179
2.452
2.381
2.135
2.119
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2.084
2.033
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1.629
1.623
1.612
1.596
1.580
1.564
1.555
1.542
0.919
0.902
0.736
0.719
0.335
0.319
(±)
1.04
1.33
5.37
0.114
0.157
1.1
1.5
3.09
3.18
8.25
2.11
0.974
1
3.17
1.03
3.1
0.138
168.029
145.134
135.649
134.820
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132.604
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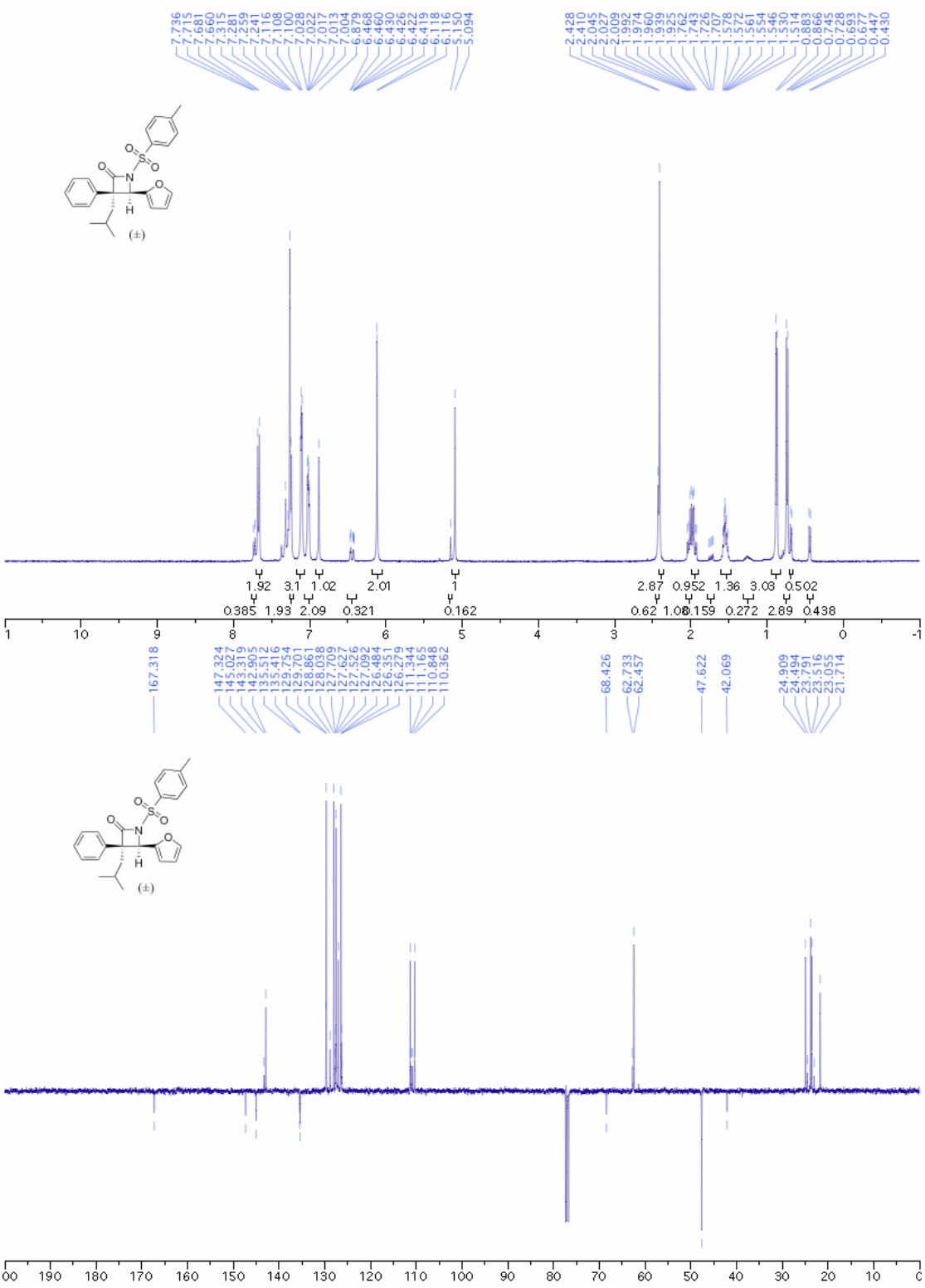
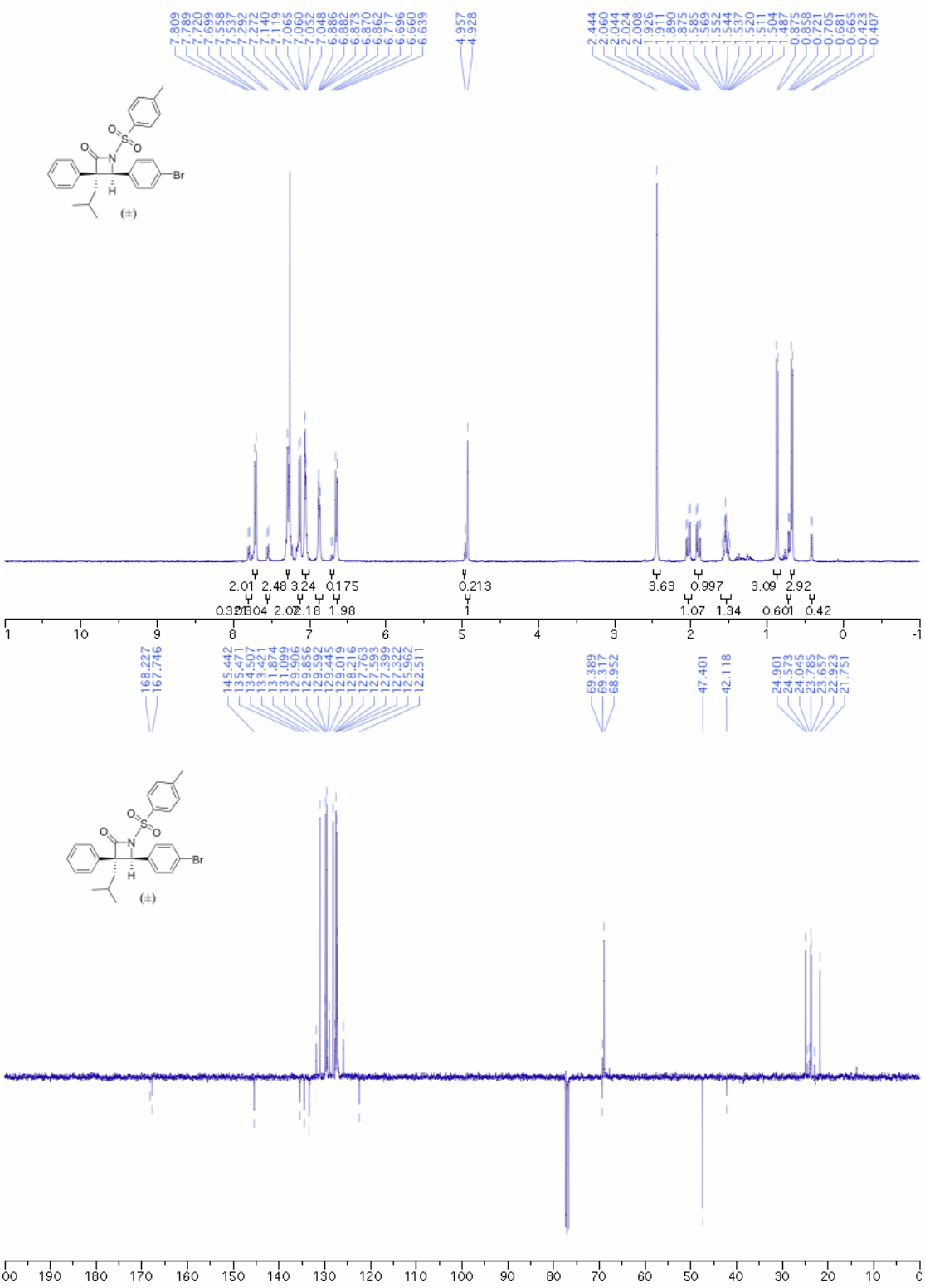
23.706
21.672
ppm

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6.717
6.696
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4.928
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2.060
2.044
2.024
2.008
1.926
1.911
1.890
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1.569
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1.544
1.537
1.520
1.511
1.504
1.487
0.875
0.858
0.721
0.705
0.681
0.665
0.423
0.407
O
S
O
N
O
Br
H
(±)
2.01 2.48 3.24 0.175
0.213
3.63 0.997
3.09 2.92
0.601 0.42
1.07 1.34
1 10 9 8 7 6 5 4 3 2 1 0 -1
168.227
167.746
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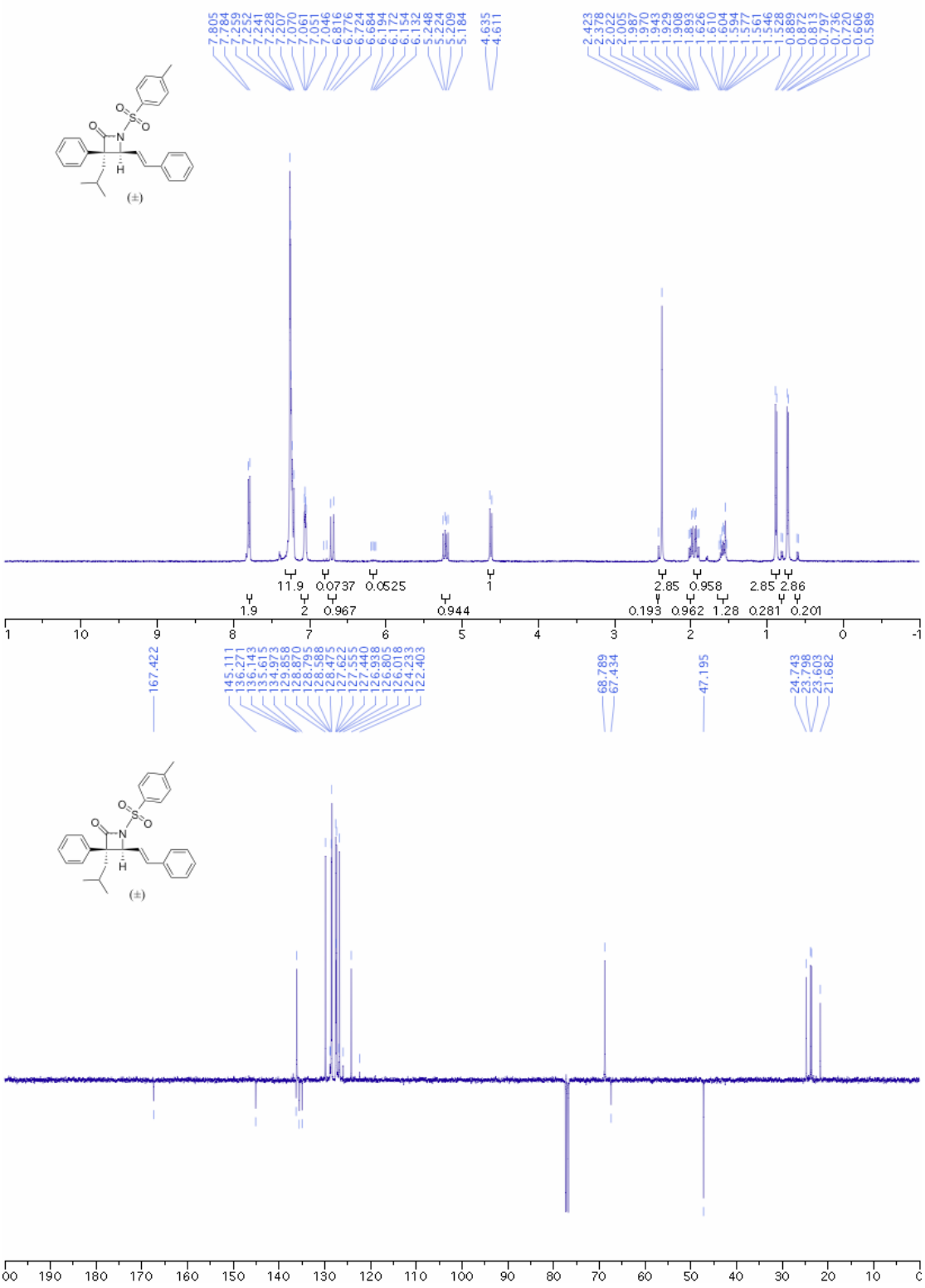
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0.797
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0.589
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1
2.85
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2.86
1.9
2
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136.143
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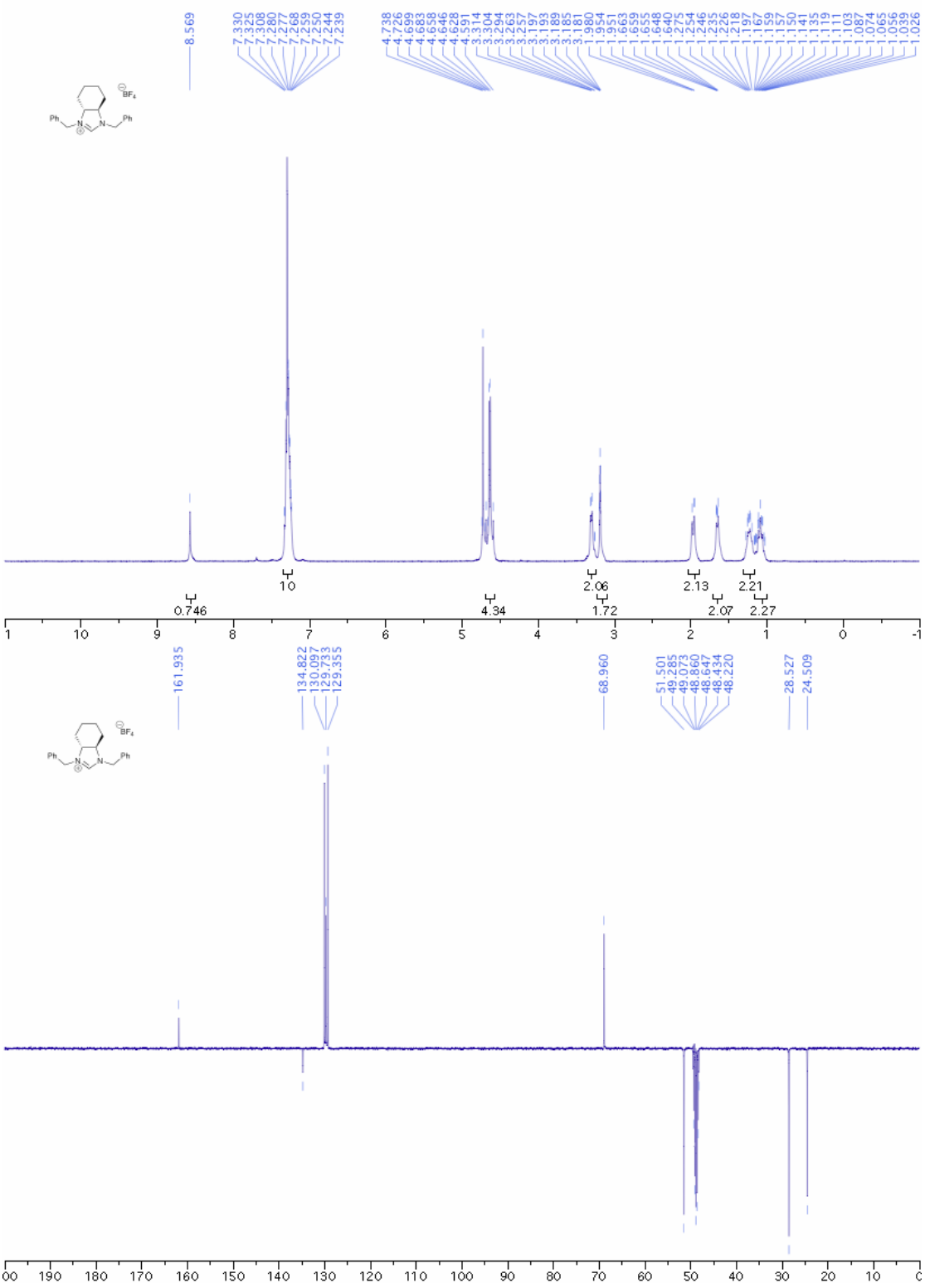
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1.135
1.119
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2.13
2.07
2.21
2.27
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48.434
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24.509