Structural and mechanistic studies of the base-induced Sommelet–Hauser rearrangement of *N*-α-branched benzylic azetidine-2-carboxylic acid-derived ammonium salts

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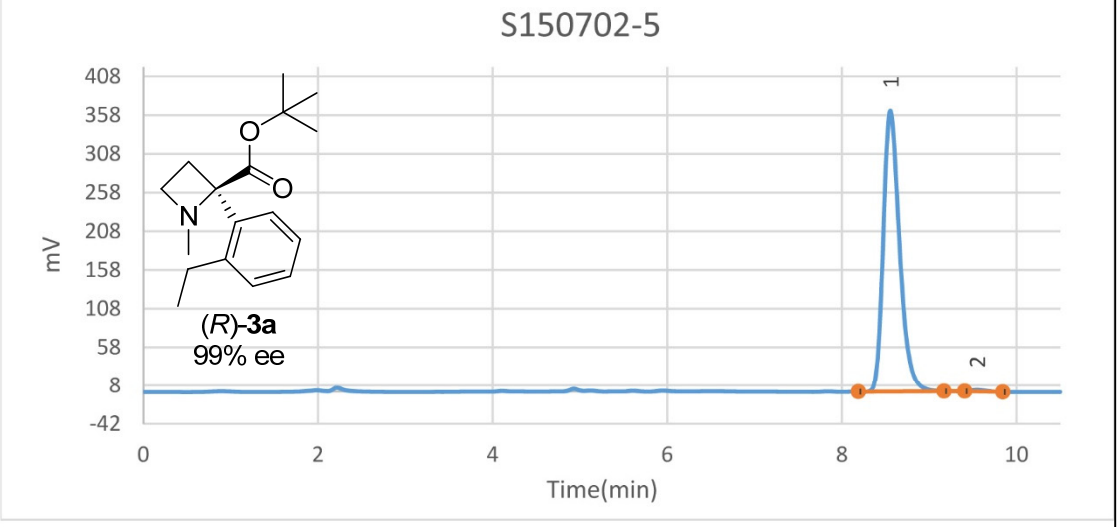
Electronic Supplementary Information

Contents:

1. HPLC chromatogram of 3a and 4a for determination of ee

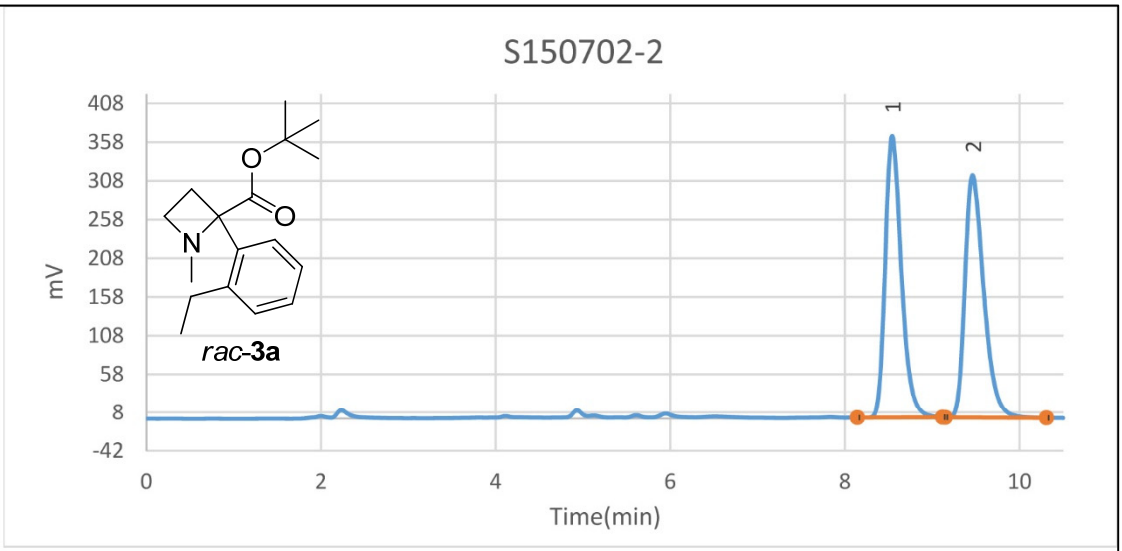
The ee were determined by HPLC analysis using chiral column in comparison with the racemic compounds.

(*R*)-**3a** (99% ee): Daicel Chiralcel OD-RH column (15 cm), H_2O/MeCN = 30/70 as the eluent, flow rate = 0.50 mL/min, t_R = 8.6 min for (*R*)-**3a** (99.5%) and 9.6 min for (*S*)-**3a** (0.5%).



OD-RH (15 cm), H_2O/MeCN = 30/70, 0.5 mL/min

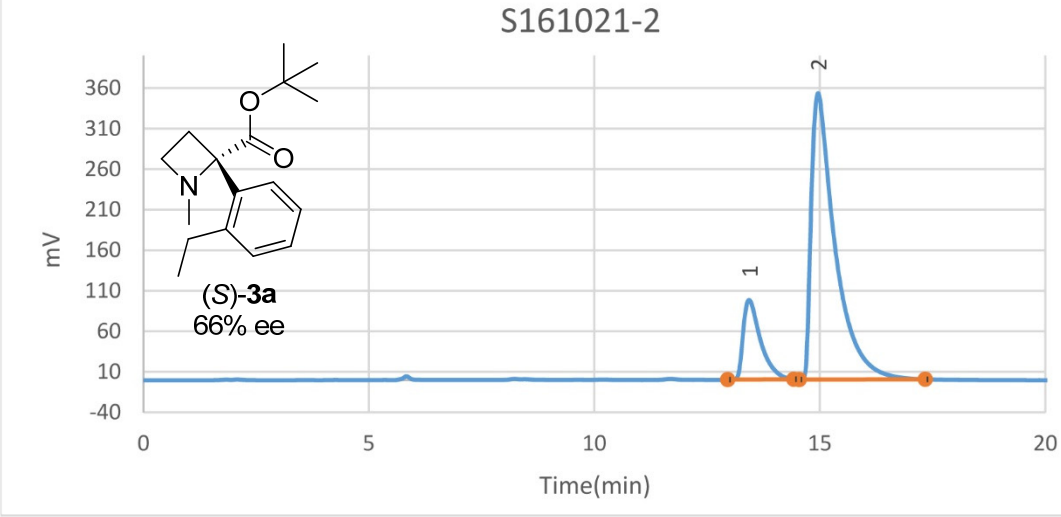
No.	Rt	Area	Area(%)
1	8.55	4731442	99.5058
2	9.55	23498	0.4942
		4754940	100



OD-RH (15 cm), H_2O/MeCN = 30/70, 0.5 mL/min

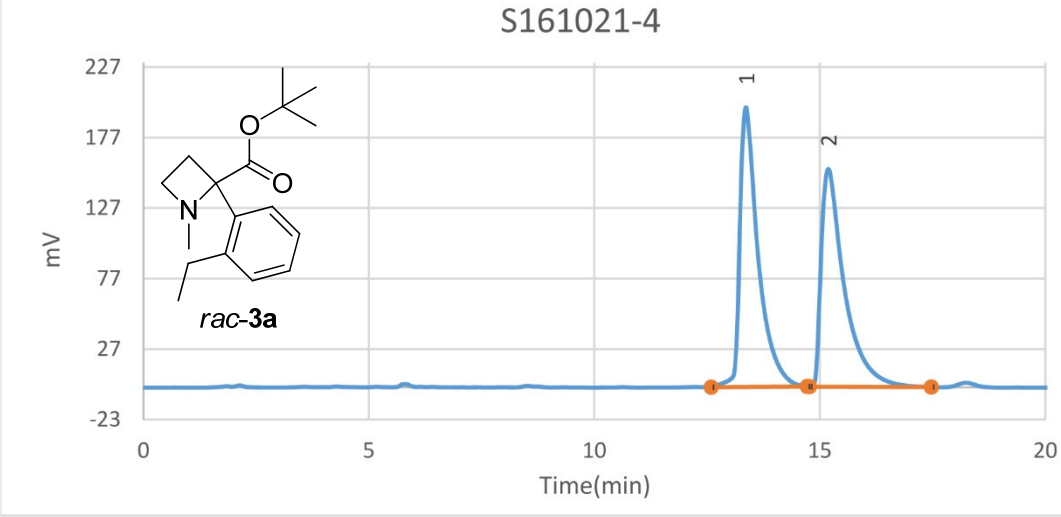
No.	Rt	Area	Area(%)
1	8.54	4708704	49.8966
2	9.46	4728218	50.1034
		9436923	100

(*S*)-**3a** (66% ee): Daicel Chiralcel OD-RH column (15 cm), H_2O/MeCN = 40/60 as the eluent, flow rate = 0.50 mL/min, t_R = 13.4 min for (*R*)-**3a** (16.9%) and 15.0 min for (*S*)-**3a** (83.1%).



OD-RH (15 cm), H_2O/MeCN = 40/60, 0.5 mL/min

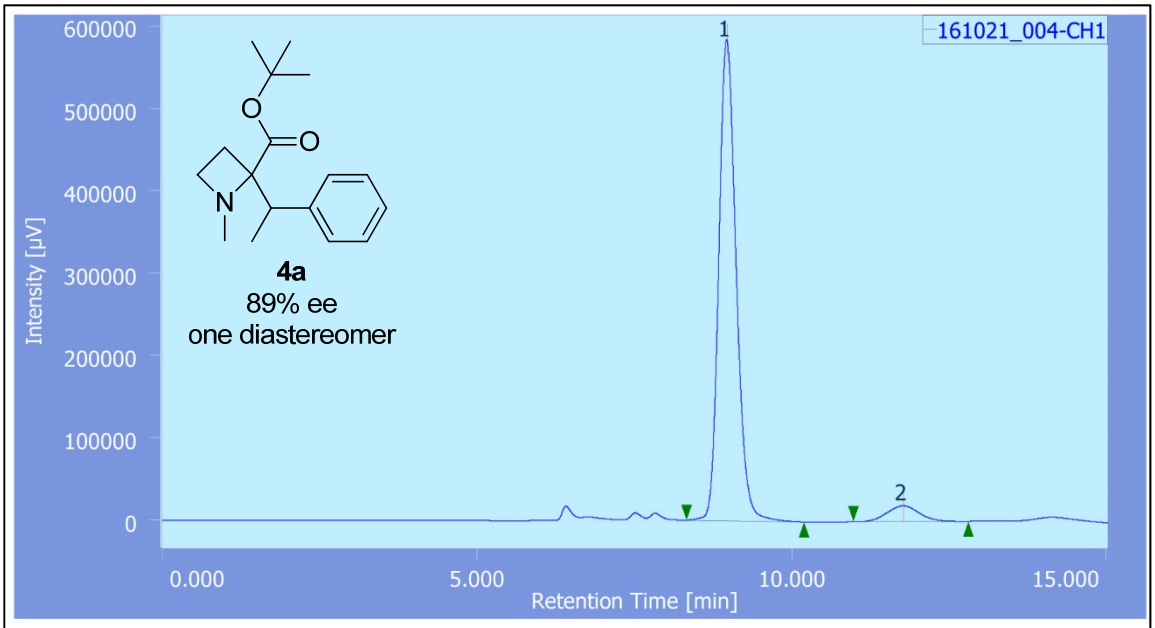
No.	Rt	Area	Area(%)
1	13.43	2624976	16.8835
2	14.96	12922576	83.1165
		15547552	100



OD-RH (15 cm), H_2O/MeCN = 40/60, 0.5 mL/min

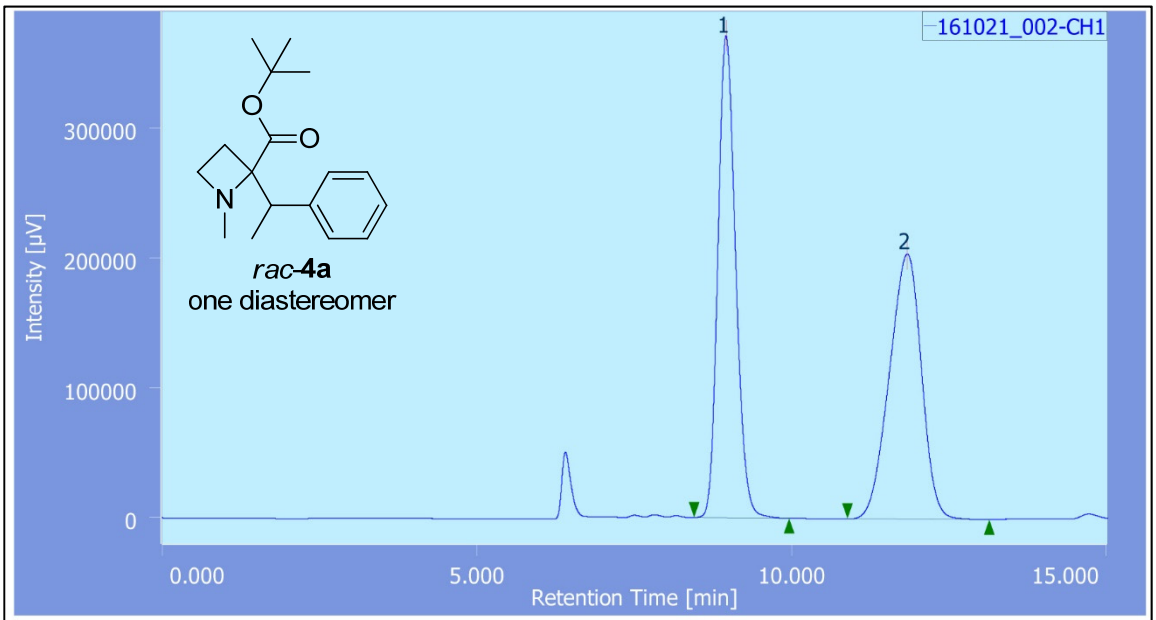
No.	Rt	Area	Area(%)
1	13.36	5607185	50.5339
2	15.19	5488694	49.4661
		11095879	100

4a (89% ee): Daicel Chiralcel OJ-H column (25 cm), *n*-hexane/2-PrOH = 95/5 as the eluent, flow rate = 0.50 mL/min, t_R = 9.0 min (94.3%) and 11.8 min (5.7%).



column	OJ-H, 0.5mL/min
date	2016/10/21 17:47:37
solvent	Hexane-isopropanol(95-5)

#	tR [min]	area [μV·sec]	area%
1	8.962	11164209	94.297
2	11.760	675256	5.703

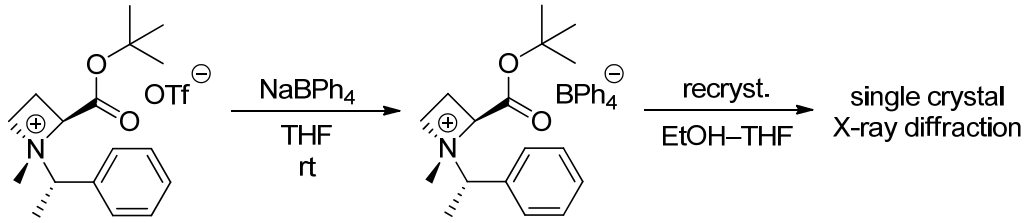


column	OJ-H, 0.5mL/min
date	2016/10/21 16:58:42
solvent	Hexane-isopropanol(95-5)

#	tR [min]	area [μV·sec]	area%
1	8.953	7240656	50.045
2	11.830	7227654	49.955

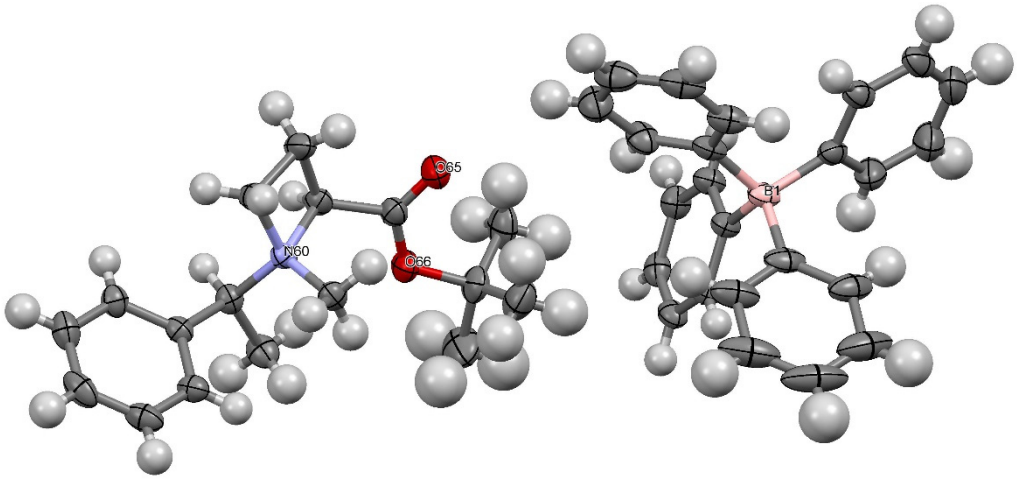
2. Preparation and crystal data of (1*S*,2*S*,1'*S*)-2a-BPh_4 and (1*R**,2*R**,1'*S**)-2e-BPh_4

(1*S*,2*S*,1´*S*)-2-(*tert*-Butoxycarbonyl)-1-methyl-1-(1´-phenylethyl)azetidin-1-ium tetraphenylborate [(1*S*,2*S*,1´*S*)-2a-BPh_4]



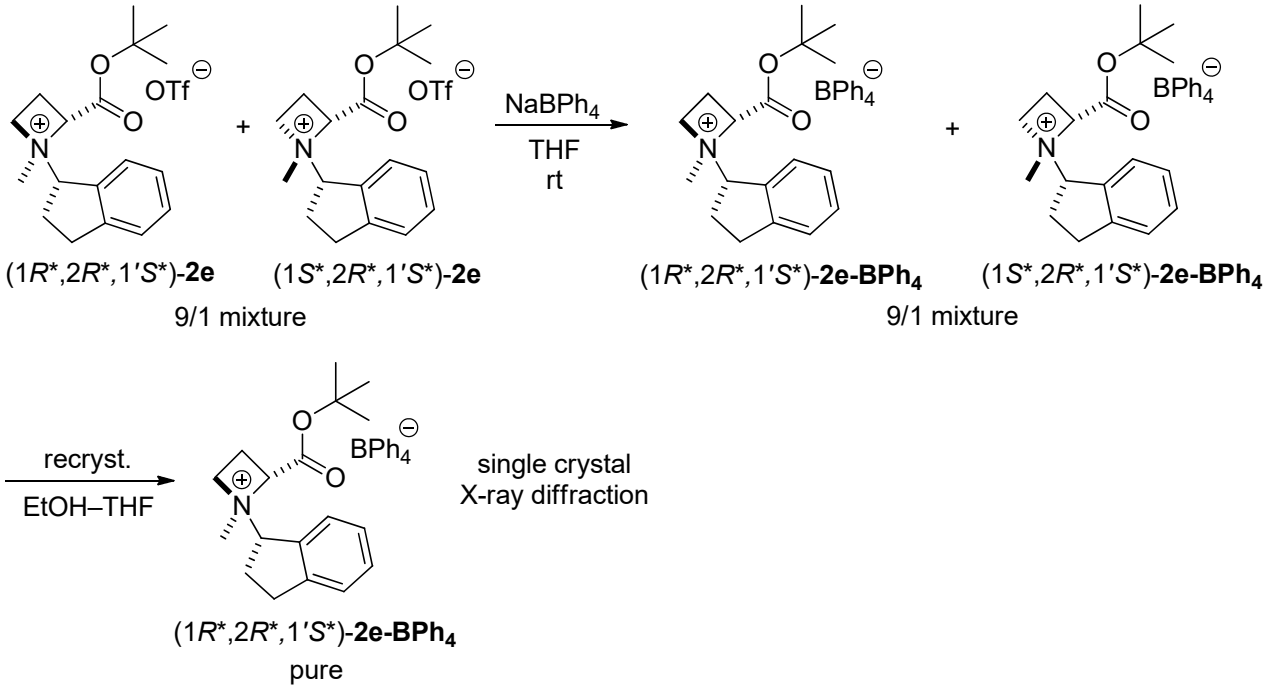
(1*S*,2*S*,1'*S*)-**2a** (1*S*,2*S*,1'*S*)-**2a-BPh_4**

A mixture of (1*S*,2*S*,1´*S*)-**2a** (193 mg, 0.454 mmol) and sodium tetraphenylborate (233 mg, 0.681 mmol) in THF (4.5 mL) was stirred for 2 days at room temperature. The resulting mixture was concentrated and the residue was crystallized from EtOH–THF to obtain (1*S*,2*S*,1´*S*)-**2a-BPh_4** (221 mg, 82% yield) as colourless crystals. Recrystallization from EtOH–THF gave a single crystal suitable for X-ray crystallographic analysis. CCDC-1553028 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the CCDC. Colourless crystals; mp 181–182 °C; $[\alpha]^{26}_{589}$ –24.5 (*c* 1.0 in acetone); IR (KBr) ν_{max}/cm^{-1} 3034, 3004, 2981, 1735, 1579, 1477, 1458, 1424, 1395, 1370, 1355, 1250, 1147, 1065, 1032, 1011, 866, 836, 773, 747, 737, 707; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.67-7.61 (2H, m, Ph), 7.59-7.49 (3H, m, Ph), 7.38-7.30 (8H, m, Ph), 6.93 (8H, dd, *J* = 8.0, 7.2 Hz, Ph), 6.79 (4H, tt, *J* = 7.2, 1.2 Hz, Ph), 5.49 (1H, dd, *J* = 9.8, 9.8 Hz, 2-H), 5.03 (1H, q, *J* = 6.8 Hz, 1´-H), 4.70 (1H, ddd, *J* = 10.0, 9.8, 9.8 Hz, 4-H), 3.52 (1H, dddd, *J* = 10.0, 9.8, 3.4, 0.8 Hz, 4-H), 3.18 (3H, s, NCH_3), 3.01 (1H, dddd, *J* = 12.2, 10.0, 10.0, 9.8 Hz, 3-H), 2.63-2.48 (1H, m, 3-H), 1.86 (3H, d, *J* = 6.8 Hz, 1´-CH_3), 1.58 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, acetone-d_6) δ 165.0 (q, *J* = 49 Hz), 164.6, 137.1 (q, *J* = 2 Hz), 132.8, 131.7, 131.3, 130.3, 126.1 (q, *J* = 3 Hz), 122.4, 86.2, 74.6, 72.5, 62.0, 41.1, 28.0, 18.4, 14.6; HRMS (ESI): calcd. for $C_{17}H_{26}NO_2$ $[M–BPh_4]^+$ 276.1958, found 276.2951.



Empirical Formula	$C_{41}H_{46}BNO_2$
Formula Weight	595.60
Crystal System	orthorhombic
Lattice Parameters	a = 13.4025(10) Å
	b = 15.8388(12) Å
	c = 16.5989(13) Å
	V = 3523.6(5) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	4
Temperature	293 K
No. of Reflections Measured	Total: 36211
	Unique: 8075 (R_{int} = 0.0360)
Residuals: R_1 ($I > 2.00\sigma(I)$)	0.0442
Residuals: wR_2 (All reflections)	0.1085
Goodness of Fit Indicator	1.014
Flack parameter (Parsons' quotients = 1927)	0.2(4)

(1*R,2*R**,1′*S**)-2-(*tert*-Butoxycarbonyl)-1-(2′,3′-dihydro-1′*H*-inden-1′-yl)-1-methylazetidin-1-ium tetraphenylborate [(1*R**,2*R**,1′*S**)-2e-BPh$_4$]**



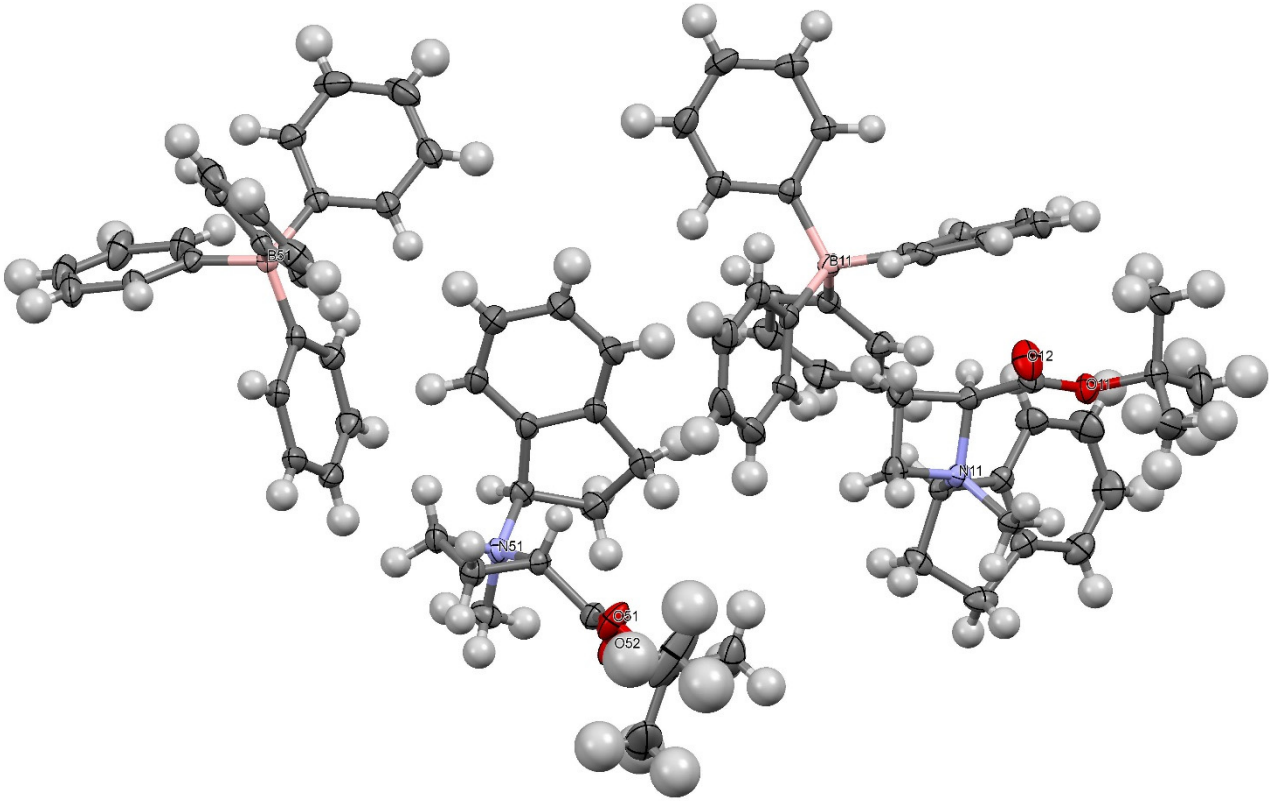
(1*R**,2*R**,1′*S**)-**2e** (1*S**,2*R**,1′*S**)-**2e**
9/1 mixture

(1*R**,2*R**,1′*S**)-**2e-BPh$_4$** (1*S**,2*R**,1′*S**)-**2e-BPh$_4$**
9/1 mixture

(1*R**,2*R**,1′*S**)-**2e-BPh$_4$**
pure

A 9/1 mixture of (1*R**,2*R**,1′*S**)-**2e** and (1*S**,2*R**,1′*S**)-**2e** (127 mg, 0.290 mmol) and sodium tetraphenylborate (0.12 g, 0.35 mmol) in THF (2.9 mL) was stirred for 24 h at room temperature. The resulting mixture was concentrated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 50/1 to 10/1 as the eluent) to obtain a 9/1 mixture of (1*R**,2*R**,1′*S**)-**2e-BPh$_4$** and (1*S**,2*R**,1′*S**)-**2e-BPh$_4$** (146 mg, 83% yield) as a white solid. Recrystallization from EtOH–THF of the

mixture afforded pure (1*R**,2*R**,1′*S**)-**2e-BPh$_4$** (105 mg, 60% yield) as colourless crystals. The 2nd recrystallization from EtOH–THF gave a single crystal suitable for X-ray crystallographic analysis. CCDC-1553029 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the CCDC. Colourless crystals; mp 146–147 °C; IR (KBr) ν_{max}/cm^{-1} 3052, 2996, 2980, 1738, 1579, 1478, 1462, 1426, 1394, 1370, 1352, 1254, 1233, 1149, 1031, 1000, 896, 842, 753, 734, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.38 (8H, m, ArH), 7.39 (1H, ddd, *J* = 7.4, 7.4, 1.2 Hz, ArH), 7.26 (1H, d, *J* = 7.4 Hz, ArH), 7.20 (1H, dd, *J* = 7.4, 7.4 Hz, ArH), 7.02 (9H, dd, *J* = 7.4, 7.4 Hz, ArH), 6.91 (4H, tt, *J* = 7.4, 1.2 Hz, ArH), 4.06 (1H, dd, *J* = 9.6, 9.6 Hz, 2-H), 3.86 (1H, d, *J* = 8.4 Hz, 1′-H), 2.78 (1H, ddd, *J* = 10.2, 10.0, 9.6 Hz, 4-H), 2.71 (1H, ddd, *J* = 17.4, 9.0, 8.8 Hz, 3′-H), 2.62 (1H, ddd, *J* = 17.4, 8.8, 8.4 Hz, 3′-H), 2.39 (1H, ddd, *J* = 10.2, 10.0, 4.0 Hz, 4-H), 2.04 (1H, dddd, *J* = 12.5, 10.0, 10.0, 9.6 Hz, 3-H), 1.90 (1H, dddd, *J* = 16.0, 9.0, 8.8, 8.4 Hz, 2′-H), 1.77 (3H, s, NCH_3), 1.61 (1H, dddd, *J* = 12.5, 9.6, 9.6, 4.0 Hz, 3-H), 1.47-1.31 (1H, m, 2′-H), 1.37 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (q, *J* = 49 Hz), 162.6, 146.4, 136.0, 132.3, 131.3, 127.1, 127.0, 125.82 (q, *J* = 2 Hz), 125.76, 122.1, 85.8, 79.5, 70.4, 61.6, 39.6, 30.4, 27.7, 26.2, 17.6; HRMS (ESI): calcd. for $C_{18}H_{26}NO_2$ $[M–BPh_4]^+$ 288.1958, found 288.1953.

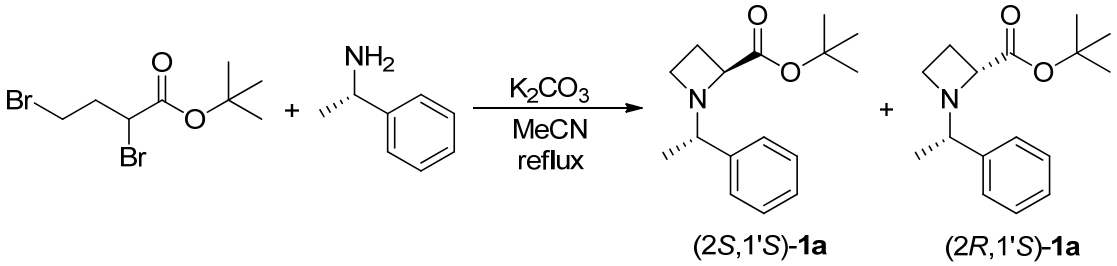


(1:1 mixture of conformational isomers)

Empirical Formula	$C_{84}H_{92}B_2N_2O_4$
Formula Weight	1215.21
Crystal System	triclinic
Lattice Parameters	a = 10.1389(13) Å
	b = 10.2830(13) Å
	c = 19.617(3) Å
	α = 79.125(6)°
	β = 89.681(6)°
	g = 62.353(4)°
	V = 1771.3(4) $Å^3$
Space Group	P1 (#1)
Z value	1
Temperature	293 K
No. of Reflections Measured	Total: 18195
	Unique: 15384 (R_{int} = 0.0233)
Residuals: R_1 ($I > 2.00\sigma(I)$)	0.0552
Residuals: wR_2 (All reflections)	0.1265
Goodness of Fit Indicator	1.063
Flack parameter (Parsons' quotients = 4314)	-0.1(8)

3. Preparation of substrates

***tert*-Butyl 1-((*S*)-1′-phenylethyl)azetidine-2-carboxylate [(2*S*,1′*S*)-1a and (2*R*,1′*S*)-1a]**



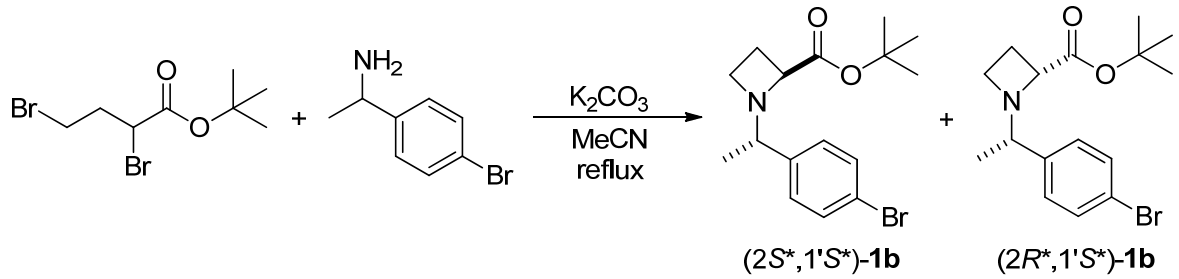
A mixture of (*S*)-1-phenylethylamine (400 μL, 3.10 mmol), *tert*-butyl 2,4-dibromobutanoate (937 mg, 3.10 mmol), and K_2CO_3 (1.29 g, 9.3 mmol) in MeCN (16 mL) was refluxed for 6 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel [*n*-hexane/EtOAc = 7/1 to 4/1 as the eluent, R_f: (2*S*,1′*S*) > (2*R*,1′*S*)] to obtain (2*S*,1′*S*)-**1a** (261 mg, 32% yield) as a colourless oil and (2*R*,1′*S*)-**1a** (270 mg, 33% yield) as a colourless oil. The stereochemistry of each diastereomers were clarified in our previous work.[1] (2*S*,1′*S*)-**1a**: $[\alpha]^{22}_{589}$ –111.1 (*c* 1.0 in EtOH); IR (film) ν_{max}/cm^{-1} 3061, 3025, 3003, 2973, 2930, 2869, 2837, 2779, 1742, 1718, 1493, 1478, 1453, 1391, 1366, 1319, 1284, 1232, 1213, 1152, 1101, 1071, 1042, 1031, 975, 945, 847, 763, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (4H, m, Ph), 7.22 (1H, dddd, *J* = 7.4, 6.6, 1.6, 1.6 Hz, Ph), 3.62 (1H, dd, *J* = 8.6, 8.2 Hz, 2-H), 3.43 (1H, q, *J* = 6.6 Hz, 1′-H), 3.08 (1H, dddd, *J* = 8.4, 7.0, 2.8, 0.8 Hz, 4-H), 2.73 (1H, ddd, *J* = 8.9, 8.2, 7.0 Hz, 4-H), 2.21 (1H, dddd, *J* = 10.6, 8.9, 8.6, 8.4 Hz, 3-H), 2.12 (1H, dddd, *J* = 10.6, 8.2, 8.2, 2.8 Hz, 3-H), 1.48 (9H, s, *t*Bu), 1.23 (3H, d, *J* = 6.6 Hz, 1′-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 142.9, 128.2, 127.4, 127.0, 80.6, 67.3, 64.8, 49.5, 28.0, 21.2, 20.7; HRMS (ESI): calcd. for $C_{16}H_{24}NO_2$ $[M+H]^+$ 262.1802, found 262.1794. (2*R*,1′*S*)-**1a**: $[\alpha]^{22}_{589}$ +56.8 (*c* 1.0 in EtOH); IR (film) ν_{max}/cm^{-1} 3062, 3026, 3003, 2973, 2930, 2870, 2827, 2784, 1735, 1493, 1477, 1453, 1391, 1366, 1302, 1276, 1233, 1208, 1153, 1114, 1081, 1057, 1030, 1012, 975, 947, 846, 762, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (2H, m, Ph), 7.26 (2H, dddd, *J* = 7.2, 7.2, 1.6, 1.6 Hz, Ph), 7.20 (1H, tt, *J* = 7.2, 1.6 Hz, Ph), 3.54 (1H, dddd, *J* = 8.2, 6.6, 2.6, 0.6 Hz, 4-H), 3.50 (1H, dd, *J* = 8.2, 8.2 Hz, 2-H), 3.36 (1H, q, *J* = 6.6 Hz, 1′-H), 2.96 (1H, ddd, *J* = 9.2, 8.2, 6.6 Hz, 4-H), 2.22 (1H, dddd, *J* = 10.5, 9.2, 8.2, 8.2 Hz, 3-H), 2.11 (1H, dddd, *J* = 10.5, 8.2, 8.2, 2.6 Hz, 3-H), 1.26 (3H, d, *J* = 6.6 Hz, 1′-CH_3), 1.17 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 142.2, 128.2, 128.1, 127.3, 80.1, 68.0, 65.4, 50.7, 27.7, 20.8, 20.0; HRMS (ESI): calcd. for $C_{16}H_{24}NO_2$ $[M+H]^+$ 262.1802, found 262.1792.

(*rac*)-*tert*-Butyl 1-(1′-phenylethyl)azetidine-2-carboxylate [(2*S,1′*S**)-1a and (2*R**,1′*S**)-1a]**

Prepared by the same procedure with (2*S*,1′*S*)-**1a** and (2*R*,1′*S*)-**1a** using (*rac*)-1-phenylethylamine instead of (*S*)-1-phenylethylamine. (2*S**,1′*S**)-**1a**: 31% yield; colourless oil. (2*R**,1′*S**)-**1a**: 28% yield; colourless oil.

[1] E. Tayama, K. Watanabe and Y. Matano, *Eur. J. Org. Chem.*, 2016, 3631.

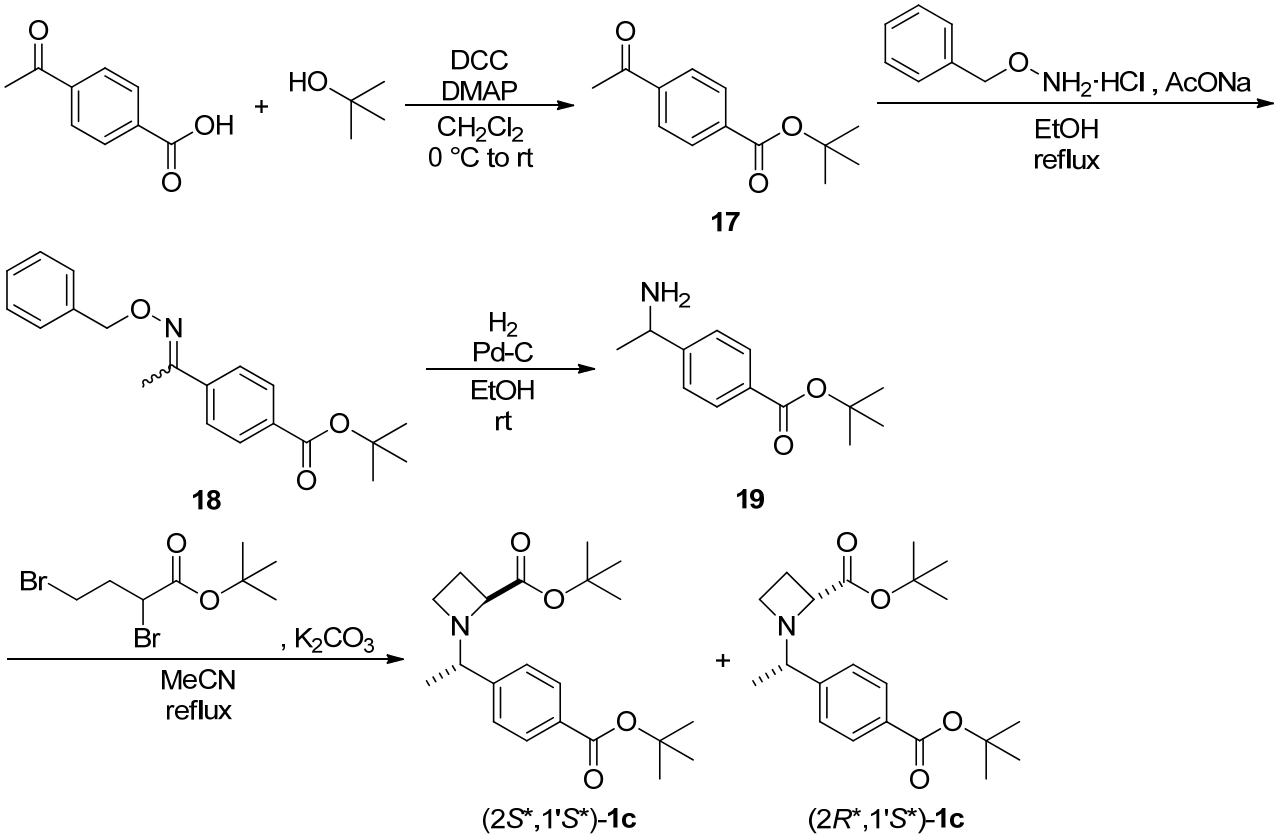
***tert*-Butyl 1-(1′-(4′′-bromophenyl)ethyl)azetidine-2-carboxylate [(2*S**,1′*S**)-1b and (2*R**,1′*S**)-1b]**



(2*S**,1′*S**)-**1b** (2*R**,1′*S**)-**1b**

A mixture of 1-(4-bromophenyl)ethylamine (170 μL, 1.18 mmol), *tert*-butyl 2,4-dibromobutanoate (362 mg, 1.20 mmol), and K_2CO_3 (835 mg, 6.0 mmol) in MeCN (6 mL) was refluxed for 6 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel [*n*-hexane/EtOAc = 15/1 to 3/1 as the eluent, R_f: (2*S**,1′*S**) > (2*R**,1′*S**)] to obtain (2*S**,1′*S**)-**1b** (109 mg, 27% yield) as a colourless oil and (2*R**,1′*S**)-**1b** (117 mg, 29% yield) as a colourless oil. The relative stereochemistry of each diastereomers were assigned by analogy with **1a**. (2*S**,1′*S**)-**1b**: IR (film) ν_{max}/cm^{-1} 2972, 2930, 2836, 1741, 1589, 1482, 1453, 1392, 1367, 1320, 1288, 1234, 1213, 1154, 1097, 1070, 1043, 1010, 976, 945, 826, 780, 746, 716; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (2H, ddd, *J* = 8.4, 2.0, 2.0 Hz, ArH), 7.23 (2H, ddd, *J* = 8.4, 2.0, 2.0 Hz, ArH), 3.63 (1H, dd, *J* = 8.4, 8.4 Hz, 2-H), 3.39 (1H, q, *J* = 6.8 Hz, 1′-H), 3.11-3.04 (1H, m, 4-H), 2.69 (1H, ddd, *J* = 8.4, 8.4, 7.2 Hz, 4-H), 2.21 (1H, dddd, *J* = 10.6, 8.8, 8.4, 8.4 Hz, 3-H), 2.13 (1H, dddd, *J* = 10.6, 8.4, 8.4, 2.8 Hz, 3-H), 1.48 (9H, s, *t*Bu), 1.19 (3H, d, *J* = 6.8 Hz, 1′-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 142.0, 131.3, 129.1, 120.6, 80.6, 66.7, 64.6, 49.7, 27.9, 21.2, 20.7; HRMS (ESI): calcd. for $C_{16}H_{23}BrNO_2$ $[M+H]^+$ 340.0907, found 340.0896. (2*R**,1′*S**)-**1b**: IR (film) ν_{max}/cm^{-1} 2972, 2930, 2870, 2830, 1737, 1591, 1486, 1454, 1406, 1391, 1366, 1340, 1297, 1233, 1208, 1153, 1115, 1100, 1071, 1010, 977, 947, 830, 762, 740, 715; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (2H, d, *J* = 8.4 Hz, ArH), 7.21 (2H, d, *J* = 8.4 Hz, ArH), 3.52 (1H, ddd, *J* = 8.8, 6.8, 2.6 Hz, 4-H), 3.46 (1H, dd, *J* = 8.4, 8.4 Hz, 2-H), 3.32 (1H, q, *J* = 6.6 Hz, 1′-H), 2.95 (1H, ddd, *J* = 8.8, 8.4, 6.8 Hz, 4-H), 2.22 (1H, dddd, *J* = 10.6, 8.8, 8.8, 8.4 Hz, 3-H), 2.10 (1H, dddd, *J* = 10.6, 8.4, 8.4, 2.6 Hz, 3-H), 1.22 (3H, d, *J* = 6.6 Hz, 1′-CH_3), 1.19 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 141.2, 131.1, 129.8, 121.0, 80.2, 67.3, 65.3, 50.5, 27.5, 20.6, 19.8; HRMS (ESI): calcd. for $C_{16}H_{23}BrNO_2$ $[M+H]^+$ 340.0907, found 340.0900.

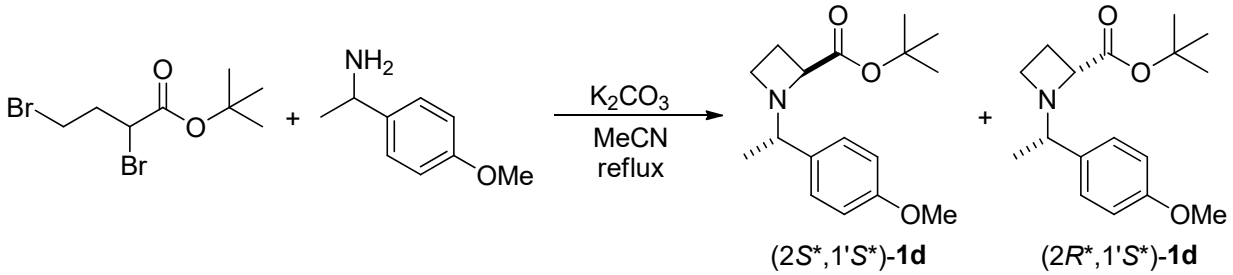
***tert*-Butyl 1-(1′-(4′′-(*tert*-butoxycarbonyl)phenyl)ethyl)azetidine-2-carboxylate [(2*S**,1′*S**)-1c and (2*R**,1′*S**)-1c]**



A solution of DCC (1.03 g, 5.0 mmol) in CH_2Cl_2 (10 mL) was added to a solution of 4-acetylbenzoic acid (0.82 g, 5.0 mmol), DMAP (0.18 g, 1.5 mmol), and *t*-BuOH (1.43 mL, 15 mmol) in CH_2Cl_2 (15 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and for 5 h at room temperature. The resulting mixture was filtered and the filtrate was concentrated. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 9/1 to 6/1 as the eluent) to obtain *tert*-butyl 4-acetylbenzoate (**17**) (522 mg, 47% yield) as colourless crystals. A mixture of **17** (514 mg, 2.33 mmol), *O*-benzylhydroxylamine hydrochloride (409 mg, 2.56 mmol), and AcONa (210 mg, 2.56 mmol) in EtOH (4.7 mL) was refluxed for 15 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 15/1 to 10/1 as the eluent) to obtain *tert*-butyl 4-(1-((benzyloxy)imino)ethyl)benzoate (**18**) (760 mg, quant.) as colourless crystals. ^{1}H NMR analysis of **18** showed a 9/1 mixture of geometric isomers. A mixture of **18** (760 mg, 2.34 mmol) and Pd-C (loading: 10 wt.%, 49 mg) in EtOH (12 mL) was stirred for 15 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH = 9/1 to 5/1 as the eluent) to give *tert*-butyl 4-(1-aminoethyl)benzoate (**19**) (489 mg, 94% yield) as a colourless oil. A mixture of **19** (482 mg, 2.18 mmol), *tert*-butyl 2,4-dibromobutanoate (658 mg, 2.18 mmol), and K_2CO_3 (0.90 g, 6.5 mmol) in MeCN (11 mL) was refluxed for 15 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel [*n*-hexane/EtOAc = 7/1 to 3/1 as the eluent, R_f: (2*S**,1′*S**) > (2*R**,1′*S**)] to obtain (2*S**,1′*S**)-**1c** (234 mg, 30% yield) as colourless crystals and (2*R**,1′*S**)-**1c** (244 mg, 31% yield) as a colourless oil. The relative stereochemistry of each diastereomers

were assigned by analogy with **1a**. (2*S**,1′*S**)-**1c**: mp 54–57 °C; IR (KBr) ν_{max}/cm^{-1} 2975, 2933, 2860, 1738, 1709, 1609, 1476, 1457, 1417, 1392, 1368, 1295, 1257, 1229, 1211, 1164, 1115, 1103, 1044, 1018, 973, 949, 852, 775, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (2H, d, J = 8.4 Hz, ArH), 7.40 (2H, d, J = 8.4 Hz, ArH), 3.65 (1H, dd, J = 8.2, 8.2 Hz, 2-H), 3.48 (1H, q, J = 6.6 Hz, 1′-H), 3.10 (1H, ddd, J = 7.8, 7.3, 1.8 Hz, 4-H), 2.70 (1H, ddd, J = 8.0, 8.0, 7.8 Hz, 4-H), 2.30-2.08 (2H, m, 3-H), 1.59 (9H, s, *t*Bu), 1.49 (9H, s, *t*Bu), 1.21 (3H, d, J = 6.6 Hz, 1′-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 165.7, 147.9, 130.9, 129.5, 127.2, 80.8, 80.6, 67.1, 64.7, 49.7, 28.2, 28.0, 21.3, 20.8; HRMS (ESI): calcd. for $C_{21}H_{32}NO_4$ $[M+H]^+$ 362.2326, found 362.2310. (2*R**,1′*S**)-**1c**: IR (film) ν_{max}/cm^{-1} 2975, 2931, 2871, 2832, 1735, 1709, 1610, 1577, 1477, 1456, 1416, 1391, 1367, 1346, 1294, 1255, 1208, 1166, 1116, 1057, 1018, 978, 947, 917, 849, 775, 733, 708; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (2H, ddd, J = 8.4, 1.8, 1.8 Hz, ArH), 7.37 (2H, ddd, J = 8.4, 1.8, 1.8 Hz, ArH), 3.58-3.51 (1H, m, 4-H), 3.50 (1H, dd, J = 8.4, 8.0 Hz, 2-H), 3.43 (1H, q, J = 6.4 Hz, 1′-H), 2.98 (1H, ddd, J = 8.6, 8.6, 7.0 Hz, 4-H), 2.23 (1H, dddd, J = 10.2, 8.8, 8.6, 8.4 Hz, 3-H), 2.12 (1H, dddd, J = 10.2, 8.6, 8.0, 2.6 Hz, 3-H), 1.57 (9H, s, *t*Bu), 1.25 (3H, d, J = 6.4 Hz, 1′-CH_3), 1.17 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 165.7, 147.1, 131.1, 129.4, 127.9, 80.7, 80.3, 67.6, 65.3, 50.6, 28.2, 27.6, 20.9, 19.9; HRMS (ESI): calcd. for $C_{21}H_{32}NO_4$ $[M+H]^+$ 362.2326, found 362.2315.

***tert*-Butyl 1-(1′-(4′′-methoxyphenyl)ethyl)azetidine-2-carboxylate [(2*S**,1′*S**)-1d and (2*R**,1′*S**)-1d]**



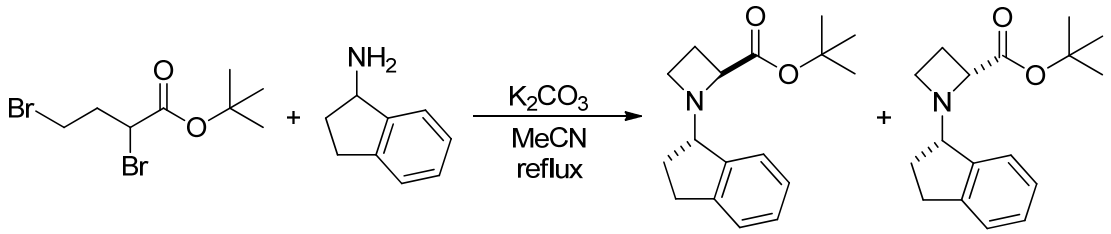
(2*S**,1'*S**)-**1d** (2*R**,1'*S**)-**1d**

A mixture of 1-(4-methoxyphenyl)ethylamine (1.01 g, 6.68 mmol), *tert*-butyl 2,4-dibromobutanoate (2.02 g, 6.69 mmol), and K_2CO_3 (2.76 g, 20 mmol) in MeCN (33 mL) was refluxed for 6 h. The resulting mixture was cooled to room temperature followed by filtered. Evaporation of the volatiles and purification of the residue by chromatography on silica gel [*n*-hexane/EtOAc = 6/1 to 2/1 as the eluent, R_f: (2*S**,1′*S**) > (2*R**,1′*S**)] gave (2*S**,1′*S**)-**1d** (415 mg, 21% yield) as colourless crystals and (2*R**,1′*S**)-**1d** (486 mg) as a colourless oil with small amounts of impurities. Re-purification of (2*R**,1′*S**)-**1d** by chromatography on aminopropyl-modified silica gel (Chromatorex NH–DM1020[2]) (*n*-hexane/EtOAc = 20/1 to 10/1 as the eluent) gave pure (2*R**,1′*S**)-**1d** (446 mg, 23% yield) as a colourless oil. The relative stereochemistry of each diastereomers were assigned by analogy with **1a**. (2*S**,1′*S**)-**1d**: mp 65–68 °C; IR (KBr) ν_{max}/cm^{-1} 2979, 2932, 2863, 2836, 2798, 1749, 1610, 1583, 1511, 1456, 1391, 1367, 1317, 1289, 1249, 1231, 1210, 1158, 1101, 1030, 976, 941, 848, 824, 759, 734; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, J = 8.8 Hz, ArH), 6.84 (2H, d, J = 8.8 Hz, ArH), 3.77 (3H, s, OCH_3), 3.59 (1H, dd, J = 8.4, 8.4 Hz, 2-H), 3.37 (1H, q, J = 6.4 Hz, 1′-H), 3.05 (1H, ddd, J = 8.8, 7.0, 2.4 Hz, 4-H), 2.71 (1H, ddd, J = 8.4, 8.4, 7.0 Hz, 4-H), 2.19 (1H, dddd, J = 10.4, 8.8, 8.4, 8.4 Hz, 3-H), 2.10 (1H, dddd, J = 10.4, 8.4, 8.4, 2.4 Hz, 3-H), 1.48 (9H, s, *t*Bu), 1.20 (3H, d, J = 6.4 Hz, 1′-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 158.5, 134.8, 128.3, 113.4, 80.3, 66.4, 64.6, 55.0, 49.2, 27.9, 21.1, 20.5; HRMS (ESI): calcd. for $C_{17}H_{26}NO_3$ $[M+H]^+$ 292.1907, found 292.1900. (2*R**,1′*S**)-**1d**: IR (film)

[2] Commercially available from Fuji Silysia Chemical Ltd., Japan.

ν_{max}/cm^{-1} 2969, 2931, 2869, 2834, 1737, 1612, 1585, 1512, 1456, 1390, 1366, 1297, 1245, 1208, 1153, 1105, 1058, 1036, 977, 946, 834, 764, 734; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (2H, d, J = 8.6 Hz, ArH), 6.81 (2H, d, J = 8.6 Hz, ArH), 3.77 (3H, s, OCH_3), 3.52 (1H, ddd, J = 8.6, 6.4, 2.4 Hz, 4-H), 3.47 (1H, dd, J = 8.4, 8.4 Hz, 2-H), 3.30 (1H, q, J = 6.6 Hz, 1′-H), 2.93 (1H, ddd, J = 8.6, 8.2, 6.4 Hz, 4-H), 2.20 (1H, dddd, J = 10.2, 8.6, 8.6, 8.4 Hz, 3-H), 2.09 (1H, dddd, J = 10.2, 8.4, 8.2, 2.4 Hz, 3-H), 1.24 (3H, d, J = 6.6 Hz, 1′-CH_3), 1.19 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 158.8, 134.2, 129.1, 113.5, 80.0, 67.3, 65.2, 55.2. 50.6, 27.7, 20.7, 19.9; HRMS (ESI): calcd. for $C_{17}H_{26}NO_3$ $[M+H]^+$ 292.1907, found 292.1903.

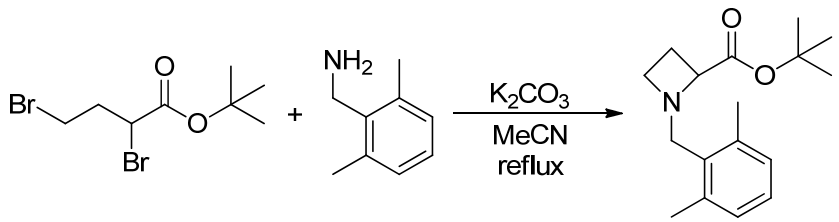
***tert*-Butyl 1-(2′,3′-dihydro-1′*H*-inden-1′-yl)azetidine-2-carboxylate [(2*S**,1′*S**)-1e and (2*R**,1′*S**)-1e]**



(2*S**,1'*S**)-**1e** (2*R**,1'*S**)-**1e**

A mixture of 2,3-dihydro-1*H*-inden-1-amine (128 μL, 1.00 mmol), *tert*-butyl 2,4-dibromobutanoate (302 mg, 1.00 mmol), and K_2CO_3 (0.41 g, 3.0 mmol) in MeCN (5 mL) was refluxed for 15 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 4/1 to 2/1 as the eluent, R_f: (2*S**,1′*S**) > (2*R**,1′*S**)] to obtain (2*S**,1′*S**)-**1e** (68.4 mg, 25% yield) as a yellow oil and (2*R**,1′*S**)-**1e** (57.6 mg, 21% yield) as a yellow oil. The relative stereochemistry of each diastereomers were assigned by analogy with **1a**. (2*S**,1′*S**)-**1e**: IR (film) ν_{max}/cm^{-1} 3069, 3003, 2973, 2934, 2846, 1739, 1477, 1458, 1391, 1366, 1323, 1298, 1237, 1212, 1154, 1097, 1061, 1043, 1024, 994, 942, 847, 753, 738; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (1H, d, J = 7.6 Hz, ArH), 7.25 (1H, d, J = 7.6 Hz, ArH), 7.20 (1H, ddd, J = 7.6, 7.6, 1.0 Hz, ArH), 7.12 (1H, ddd, J = 7.6, 7.6, 1.0 Hz, ArH), 3.94 (1H, dd, J = 6.6, 2.6 Hz, 1′-H), 3.78 (1H, dd, J = 8.4, 8.2 Hz, 2-H), 3.32-3.26 (1H, m, 4-H), 3.12 (1H, ddd, J = 15.8, 8.4, 8.4 Hz, 3′-H), 3.07 (1H, ddd, J = 9.0, 8.6, 6.8 Hz, 4-H), 2.77 (1H, ddd, J = 15.8, 8.2, 3.4 Hz, 3′-H), 2.27 (1H, dddd, J = 10.6, 8.6, 8.6, 8.4 Hz, 3-H), 2.18 (1H, dddd, J = 10.6, 8.4, 8.2, 2.6 Hz, 3-H), 2.14-1.98 (2H, m, 2′-H), 1.47 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 144.8, 142.4, 127.7, 125.7, 125.0, 124.8, 80.8, 70.5, 64.0, 49.1, 30.8, 29.9, 28.0, 21.4; HRMS (ESI): calcd. for $C_{17}H_{24}NO_2$ $[M+H]^+$ 274.1802, found 274.1796. (2*R**,1′*S**)-**1e**: IR (film) ν_{max}/cm^{-1} 3068, 2972, 2932, 2852, 1735, 1477, 1458, 1391, 1366, 1334, 1316, 1294, 1232, 1208, 1154, 1097, 1055, 1018, 990, 947, 845, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (1H, d, J = 7.2 Hz, ArH), 7.23 (1H, dd, J = 7.4, 1.0 Hz, ArH), 7.20 (1H, ddd, J = 7.4, 7.2, 1.0 Hz, ArH), 7.15-7.09 (1H, m, ArH), 4.06 (1H, t, J = 5.0 Hz, 1′-H), 3.79 (1H, ddd, J = 8.2, 8.2, 0.6 Hz, 2-H), 3.35 (1H, dddd, J = 8.2, 6.5, 3.1, 0.6 Hz, 4-H), 3.080 (1H, ddd, J = 8.6, 8.2, 6.8 Hz, 4-H), 3.079 (1H, ddd, J = 16.0, 8.0, 8.0 Hz, 3′-H), 2.77 (1H, ddd, J = 16.0, 6.5, 6.5 Hz, 3′-H), 2.29-2.14 (2H, m, 3-H), 2.06 (2H, ddd, J = 8.0, 6.5, 5.0 Hz, 2′-H), 1.34 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 144.7, 142.2, 127.6, 125.8, 125.1, 124.7, 80.4, 68.9, 62.8, 48.2, 30.7, 28.6, 27.9, 21.5; HRMS (ESI): calcd. for $C_{17}H_{24}NO_2$ $[M+H]^+$ 274.1802, found 274.1791.

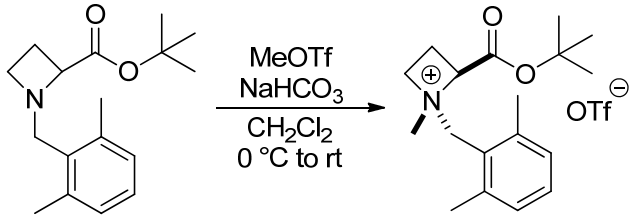
***tert*-Butyl 1-(2,6-dimethylbenzyl)azetidine-2-carboxylate (20)**



20

A mixture of 2,6-dimethylbenzylamine (268 mg, 1.98 mmol), *tert*-butyl 2,4-dibromobutanoate (600 mg, 1.99 mmol), and K_2CO_3 (1.39 g, 10 mmol) in MeCN (10 mL) was refluxed for 6 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 20/1 to 10/1 as the eluent) to obtain **20** (353 mg, 65% yield) as a colourless oil. IR (film) ν_{max}/cm^{-1} 3065, 3004, 2974, 2930, 2844, 1735, 1588, 1470, 1390, 1366, 1296, 1236, 1158, 1094, 1067, 1040, 1018, 976, 940, 847, 769; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07-6.95 (3H, m, Ar), 3.83 (1H, d, J = 12.4 Hz, CH_2Ar), 3.65 (1H, dd, J = 9.2, 8.0 Hz, 2-H), 3.63 (1H, d, J = 12.4 Hz, CH_2Ar), 3.17 (1H, ddd, J = 8.4, 6.4, 2.4 Hz, 4-H), 2.95 (1H, ddd, J = 9.2, 7.8, 6.4 Hz, 4-H), 2.44 (6H, s, $ArCH_3$), 2.27 (1H, dddd, J = 10.0, 9.2, 9.2, 8.4 Hz, 3-H), 2.10 (1H, dddd, J = 10.0, 8.0, 7.8, 2.4 Hz, 3-H), 1.39 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 137.8, 134.1, 128.1, 126.9, 80.6, 65.9, 55.4, 50.9, 27.9, 21.4, 20.4; HRMS (ESI): calcd. for $C_{17}H_{26}NO_2$ $[M+H]^+$ 276.1958, found 276.1953.

(1*S,2*S**)-2-(*tert*-Butoxycarbonyl)-1-(2,6-dimethylbenzyl)-1-methylazetidin-1-ium trifluoromethanesulfonate [(1*S**,2*S**)-7]**



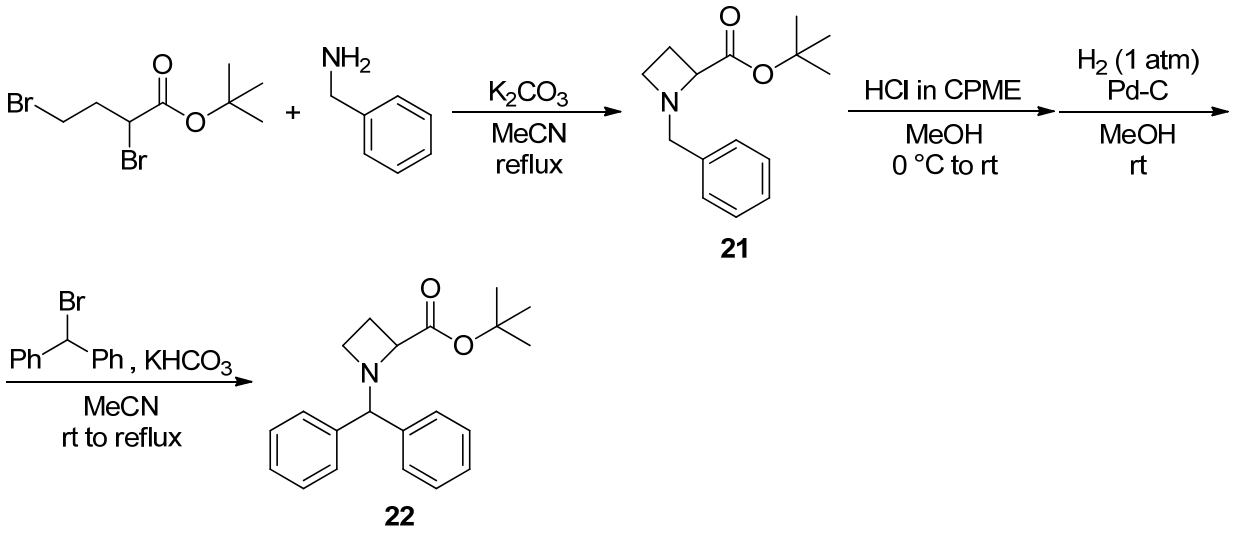
20 (1*S**,2*S**)-**7**

A mixture of **20** (353 mg, 1.28 mmol) and $NaHCO_3$ (0.30 g, 3.6 mmol) in CH_2Cl_2 (6 mL) was treated with MeOTf (160 μL, 1.41 mmol) at 0 °C and stirred for 1 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and purified by chromatography on silica gel (CH_2Cl_2/MeOH = 50/1 to 20/1 as the eluent) to obtain (1*S**,2*S**)-**7** (500 mg, 89% yield) as a colourless gum. The relative stereochemistry was determined by analogy with **1a** and analogous derivatives reported previously.[3] IR (film) ν_{max}/cm^{-1} 2982, 1737, 1594, 1467, 1396, 1371, 1329, 1261, 1224, 1153, 1055, 1030, 978, 912, 888, 835, 783, 755, 730; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (1H, t, J = 7.8 Hz, ArH), 7.15 (2H, d, J = 7.8 Hz, ArH), 5.34 (1H, dd, J = 9.6, 9.6 Hz, 2-H), 4.88 (1H, d, J = 14.4 Hz, CH_2Ar), 4.71 (1H, d, J = 14.4 Hz, CH_2Ar), 4.60 (1H, ddd, J = 10.0, 10.0, 9.2 Hz, 4-H), 4.00 (1H, ddd, J = 9.6, 9.2, 2.0 Hz, 4-H), 3.13 (3H, s, NCH_3), 3.00 (1H, dddd, J = 10.8, 10.0, 9.6, 9.6 Hz, 3-H), 2.64-2.51 (1H, m, 3-H), 2.43 (6H, s, $ArCH_3$), 1.51 (9H, s, *t*Bu); ^{13}C

[3] (a) F. Couty, O. David, F. Durrat, G. Evano, S. Lakhdar, J. Marrot and M. Vargas-Sanchez, *Eur. J. Org. Chem.*, 2006, 3479; (b) F. Couty, F. Durrat, G. Evano and D. Prim, *Tetrahedron Lett.*, 2004, **45**, 7525; see also, ref 1.

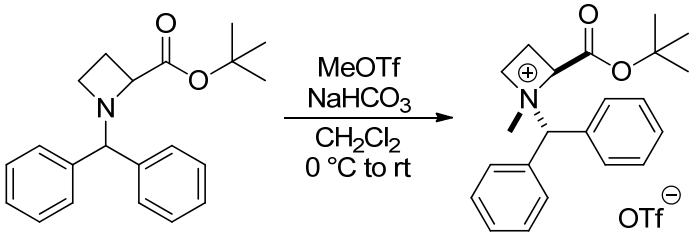
NMR (100 MHz, $CDCl_3$) δ 163.3, 139.4, 130.2, 129.3, 124.8, 120.3 (q, J = 319 Hz), 85.8, 69.1, 62.0, 61.3, 44.0, 27.3, 20.4, 19.2; HRMS (ESI): calcd. for $C_{18}H_{28}NO_2$ $[M–OTf]^+$ 290.2115, found 290.2106.

***tert*-Butyl 1-benzhydrylazetidine-2-carboxylate (22)**



A mixture of benzylamine (546 μL, 5.00 mmol), *tert*-butyl 2,4-dibromobutanoate (1.51 g, 5.00 mmol), and K_2CO_3 (2.07 g, 15 mmol) in MeCN (25 mL) was refluxed for 12 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 6/1 to 4/1 as the eluent) to obtain *tert*-butyl 1-benzylazetidine-2-carboxylate (**21**) (651 mg, 53% yield) as a colourless oil. A solution of **21** (646 mg, 2.61 mmol) in MeOH (13 mL) was treated with ca. 4 M hydrogen chloride in cyclopentyl methyl ether (CPME) (0.78 mL, 3.1 mmol) at 0 °C. After stirring for 30 min at room temperature, the solution was evaporated. A mixture of the residue and palladium on activated carbon (loading: 10 wt.%, 0.14 g) in MeOH (13 mL) was stirred at room temperature for 2 days under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated. A mixture of the residual oil, α-bromodiphenylmethane (645 mg, 2.61 mmol), and potassium hydrogen carbonate (1.30 g, 13.0 mmol) in MeCN (13 mL) was stirred for 1 h at room temperature and refluxed for 7 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 20/1 to 10/1 as the eluent) to obtain **22** (623 mg, 74% yield) as colourless crystals. Mp 91–92 °C; IR (KBr) ν_{max}/cm^{-1} 3066, 3002, 2984, 2960, 2933, 2876, 2843, 2813, 1738, 1599, 1491, 1453, 1392, 1364, 1345, 1309, 1290, 1224, 1209, 1159, 1152, 1094, 1078, 1053, 1029, 950, 845, 780, 744, 706; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.44 (2H, m, Ph), 7.43-7.38 (2H, m, Ph), 7.30-7.24 (2H, m, Ph), 7.24-7.17 (3H, m, Ph), 7.14 (1H, tt, J = 7.2, 1.2 Hz, Ph), 4.48 (1H, s, C*H*Ph_2), 3.66 (1H, dd, J = 8.4, 8.4 Hz, 2-H), 3.41 (1H, dddd, J = 8.1, 7.2, 3.4, 0.8 Hz, 4-H), 2.87 (1H, ddd, J = 8.5, 8.5, 7.2 Hz, 4-H), 2.29-2.13 (2H, m, 3-H), 1.20 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 141.7, 141.4, 128.4, 128.3, 128.2, 127.5, 127.2, 127.0, 80.1, 77.3, 65.3, 51.3, 27.7, 21.0; HRMS (ESI): calcd. for $C_{21}H_{26}NO_2$ $[M+H]^+$ 324.1958, found 324.1955.

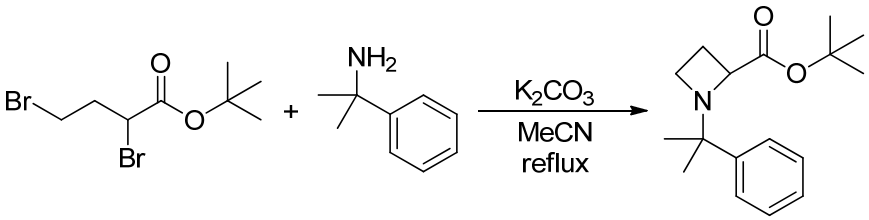
(1*S,2*S**)-1-Benzhydryl-2-(*tert*-butoxycarbonyl)-1-methylazetidin-1-ium trifluoromethanesulfonate [(1*S**,2*S**)-11]**



22 (1*S**,2*S**)-**11**

A mixture of **22** (381 mg, 1.18 mmol) and $NaHCO_3$ (0.29 g, 3.5 mmol) in CH_2Cl_2 (6 mL) was treated with MeOTf (256 μL, 2.26 mmol) at 0 °C and stirred for 1 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain (1*S**,2*S**)-**11** (528 mg, 92% yield) as a white amorphous. The relative stereochemistry was determined by analogy with **1a** and analogous derivatives reported previously.[3] IR (KBr) ν_{max}/cm^{-1} 3064, 2982, 2935, 1733, 1499, 1456, 1396, 1372, 1259, 1224, 1153, 1030, 1000, 933, 909, 890, 835, 793, 776, 754, 721; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.70 (4H, m, Ph), 7.52-7.42 (6H, m, Ph), 6.08 (1H, s, C*H*Ph$_2$), 5.47 (1H, dd, *J* = 9.8, 9.4 Hz, 2-H), 5.02 (1H, ddd, *J* = 9.8, 9.8, 9.4 Hz, 4-H), 3.89 (1H, ddd, *J* = 9.8, 9.8, 3.4 Hz, 4-H), 3.34 (3H, s, NCH_3), 2.95 (1H, dddd, *J* = 12.0, 9.8, 9.8, 9.8 Hz, 3-H), 2.65 (1H, dddd, *J* = 12.0, 9.4, 9.4, 3.4 Hz, 3-H), 1.35 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 131.4, 131.0, 130.8, 130.5, 130.4, 129.8, 129.7, 120.8 (q, *J* = 319 Hz), 85.7, 80.7, 69.8, 62.0, 43.6, 27.6, 18.8; HRMS (ESI): calcd. for $C_{22}H_{28}NO_2$ [M–OTf]$^+$ 338.2115, found 338.2111.

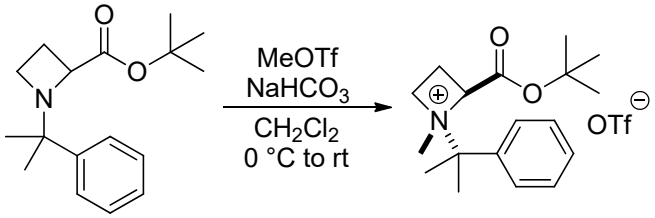
***tert*-Butyl 1-(2′-phenylpropan-2′-yl)azetidine-2-carboxylate (23)**



23

A mixture of cumylamine (0.72 mL, 5.0 mmol), *tert*-butyl 2,4-dibromobutanoate (1.51 g, 5.00 mmol), and K_2CO_3 (2.07 g, 15 mmol) in MeCN (25 mL) was refluxed for 15 h. The resulting mixture was cooled to room temperature followed by filtered. The filtrate was evaporated and the residue was purified by chromatography on silica gel (*n*-hexane/EtOAc = 8/1 to 6/1 as the eluent) to obtain **23** (471 mg, 34% yield) as a colourless oil. IR (film) ν_{max}/cm^{-1} 3058, 2974, 2930, 2865, 1741, 1717, 1600, 1493, 1477, 1446, 1391, 1381, 1366, 1296, 1255, 1233, 1207, 1152, 1110, 1072, 1052, 1030, 1002, 944, 919, 899, 846, 766, 700; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (2H, ddd, *J* = 7.8, 1.6, 1.6 Hz, Ph), 7.33 (2H, dddd, *J* = 7.8, 7.2, 1.6, 1.6 Hz, Ph), 7.23 (1H, tt, *J* = 7.2, 1.6 Hz, Ph), 3.76 (1H, dd, *J* = 8.4, 8.4 Hz, 2-H), 3.04 (1H, ddd, *J* = 8.4, 6.4, 2.6 Hz, 4-H), 2.96 (1H, ddd, *J* = 8.4, 8.4, 6.4 Hz, 4-H), 2.14 (1H, dddd, *J* = 10.2, 8.4, 8.4, 8.4 Hz, 3-H), 1.92 (1H, dddd, *J* = 10.2, 8.4, 8.4, 2.6 Hz, 3-H), 1.41 (9H, s, *t*Bu), 1.39 (3H, s, 2′-CH_3), 1.33 (3H, s, 2′-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 144.3, 127.9, 126.8, 126.5, 80.2, 59.3, 57.8, 43.8, 27.9, 25.7, 22.3, 20.2; HRMS (ESI): calcd. for $C_{17}H_{26}NO_2$ [M+H]$^+$ 276.1958, found 276.1957.

(1*R,2*S**)-2-(*tert*-Butoxycarbonyl)-1-methyl-1-(2′-phenylpropan-2′-yl)azetidin-1-ium trifluoromethanesulfonate [(1*R**,2*S**)-14]**

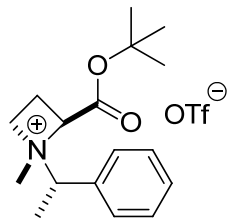


23 (1*R**,2*S**)-**14**

A mixture of **23** (432 mg, 1.57 mmol) and $NaHCO_3$ (0.40 g, 4.8 mmol) in CH_2Cl_2 (8 mL) was treated with MeOTf (355 μL, 3.14 mmol) at 0 °C and stirred for 1 h at room temperature. The resulting mixture was evaporated to ca. 1/2 to 1/3 volume and purified by chromatography on silica gel (CH_2Cl_2/MeOH = 20/1 to 10/1 as the eluent) to obtain (1*R**,2*S**)-**14** (630 mg, 91% yield) as a colourless gum. The relative stereochemistry was determined by analogy with **1a** and analogous derivatives reported previously.[3] IR (film) ν_{max}/cm^{-1} 3065, 2984, 2938, 1735, 1634, 1503, 1471, 1452, 1424, 1397, 1372, 1263, 1225, 1155, 1102, 1083, 1050, 1031, 1001, 977, 918, 878, 837, 773, 755, 734, 705; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.61 (2H, m, Ph), 7.57-7.47 (3H, m, Ph), 5.25 (1H, dd, J = 9.6, 9.4 Hz, 2-H), 4.76 (1H, ddd, J = 10.0, 9.6, 9.6 Hz, 4-H), 3.74 (1H, ddd, J = 10.0, 10.0, 3.6 Hz, 4-H), 3.16 (3H, s, NCH_3), 2.90 (1H, dddd, J = 12.4, 10.0, 9.6, 9.6 Hz, 3-H), 2.45 (1H, dddd, J = 12.4, 9.6, 9.4, 3.6 Hz, 3-H), 2.04 (3H, s, 2′-CH_3), 1.93 (3H, s, 2′-CH_3), 1.51 (9H, s, *t*Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 135.0, 130.5, 129.5, 128.3, 120.7 (q, J = 319 Hz), 86.1, 73.2, 67.3, 58.1, 42.5, 27.7, 23.8, 22.5, 17.5; HRMS (ESI): calcd. for $C_{18}H_{28}NO_2$ $[M–OTf]^+$ 290.2115, found 290.2111.

4. Copies of NMR spectra of substrates and rearrangement products (2–4, 7, 9–14, 16)

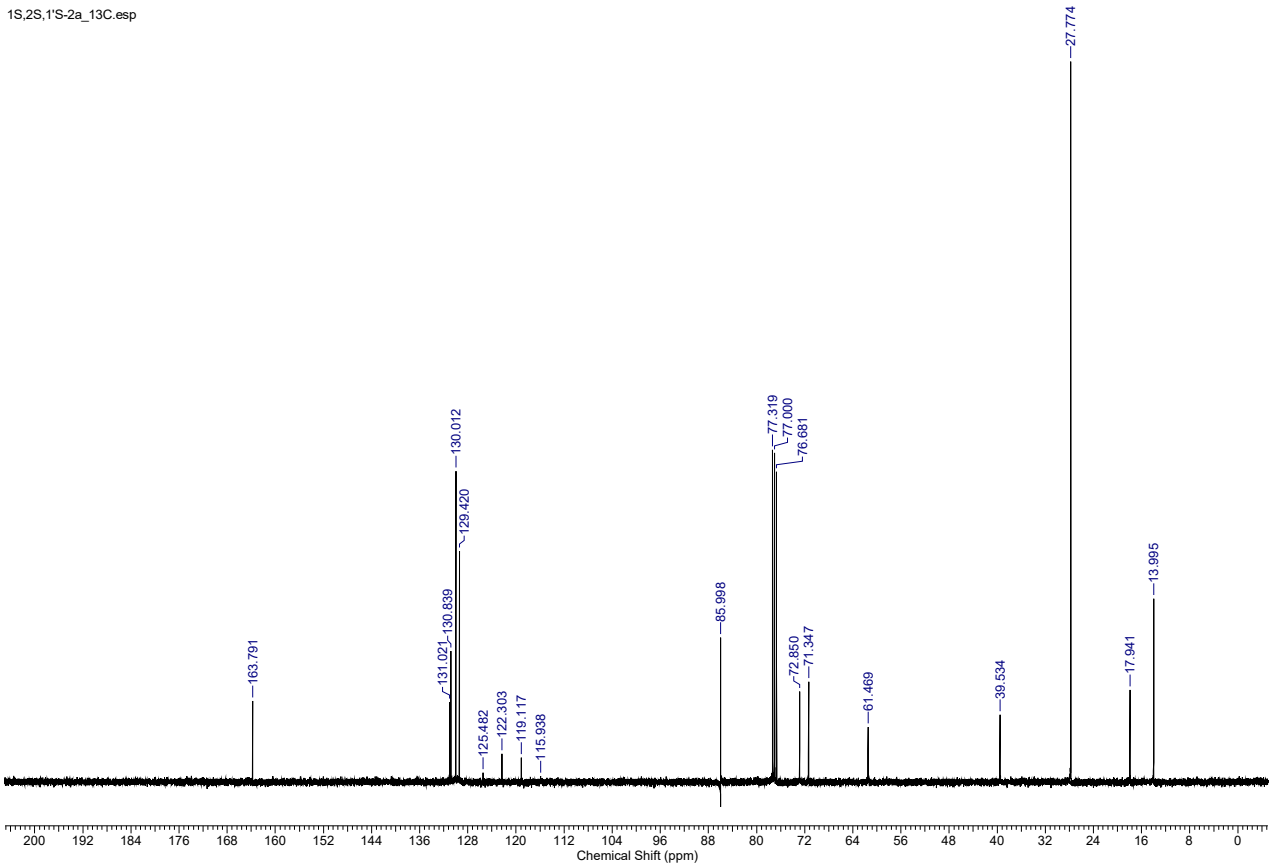
1S,2S,1'S-2a_1H.esp



(1*S**,2*S**,1'*S**)-**2a**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S,1'S-2a_13C.esp



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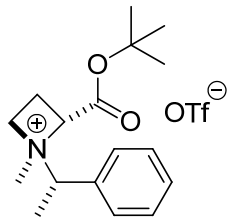
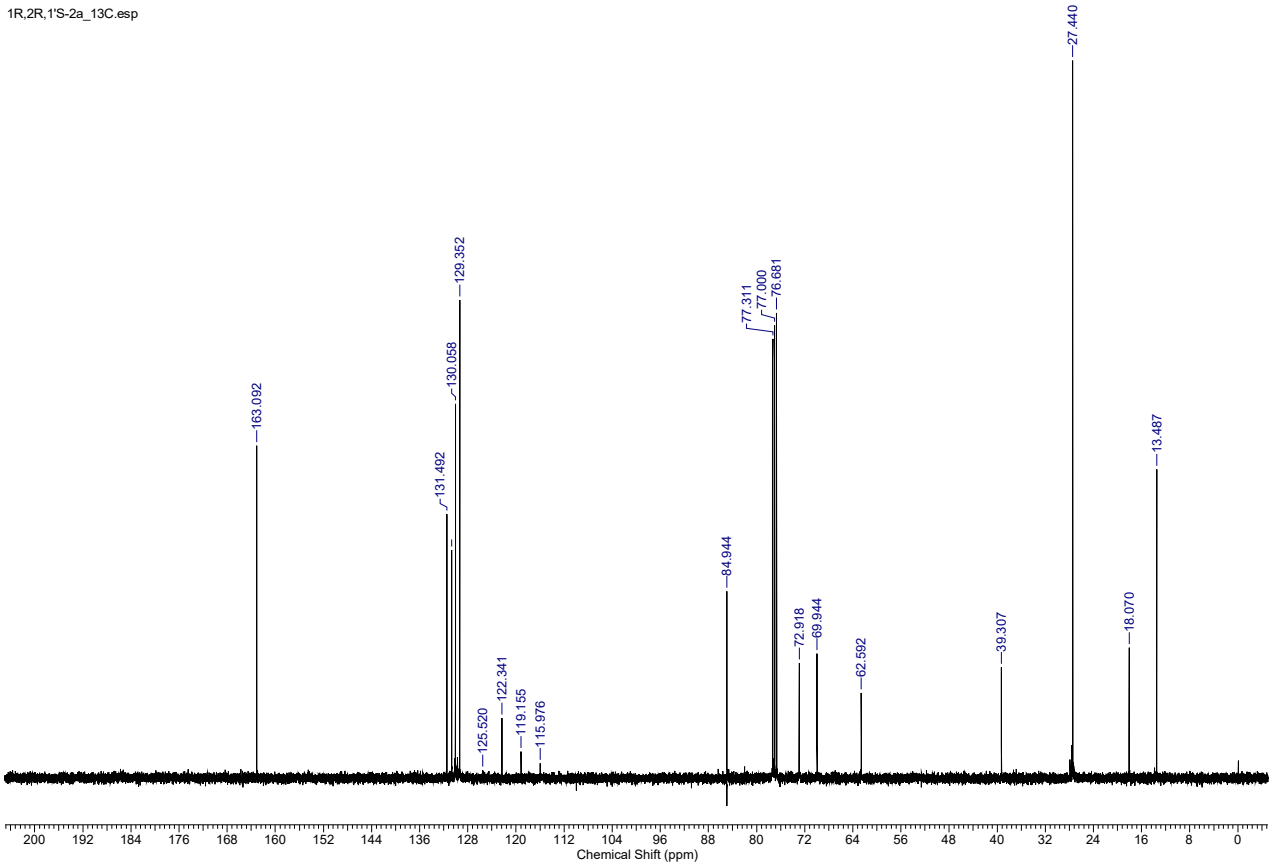


(1*R**,2*R**,1'*S**)-**2a**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1R,2R,1'S-2a_13C.esp



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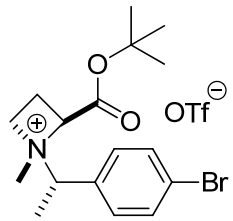
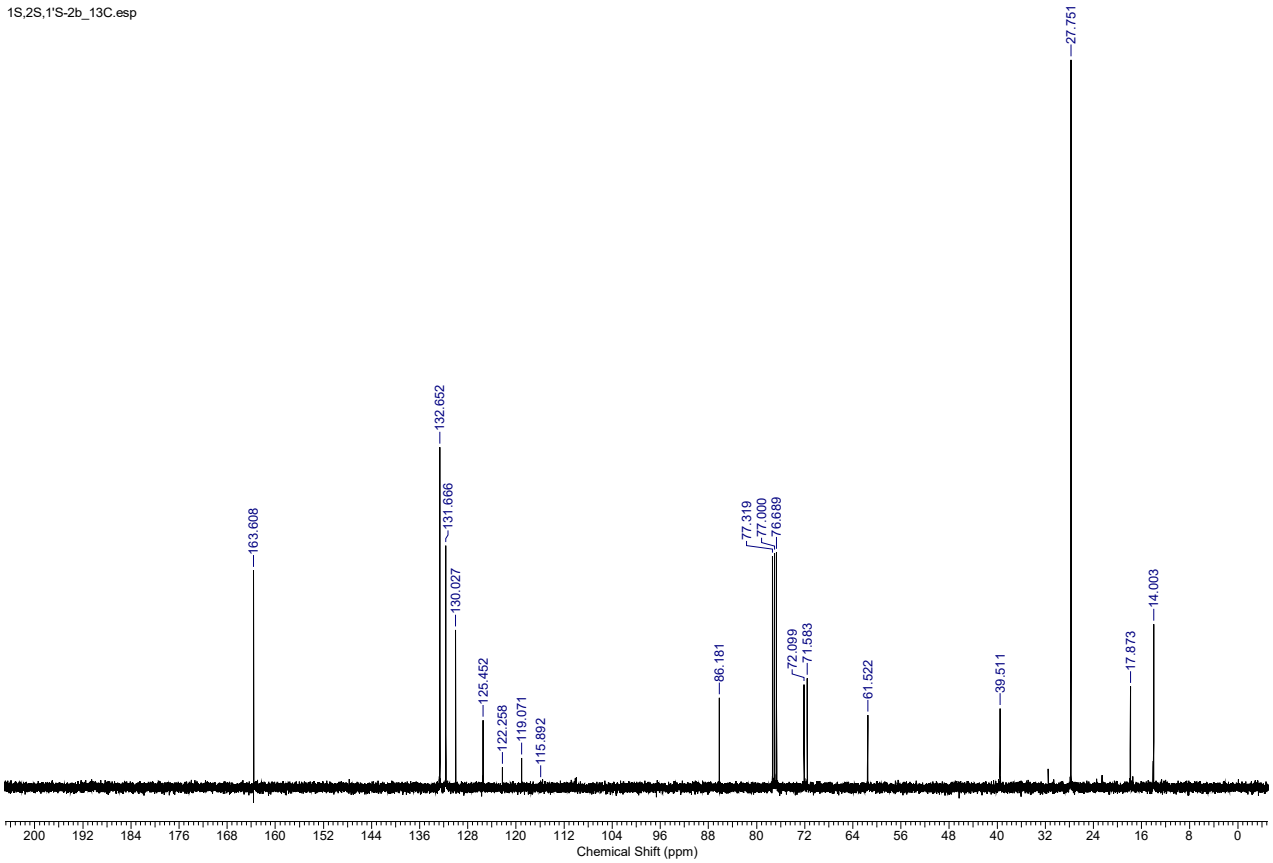


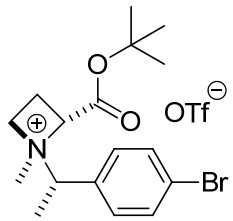
(1*S**,2*S**,1'*S**)-**2b**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S,1'S-2b_13C.esp



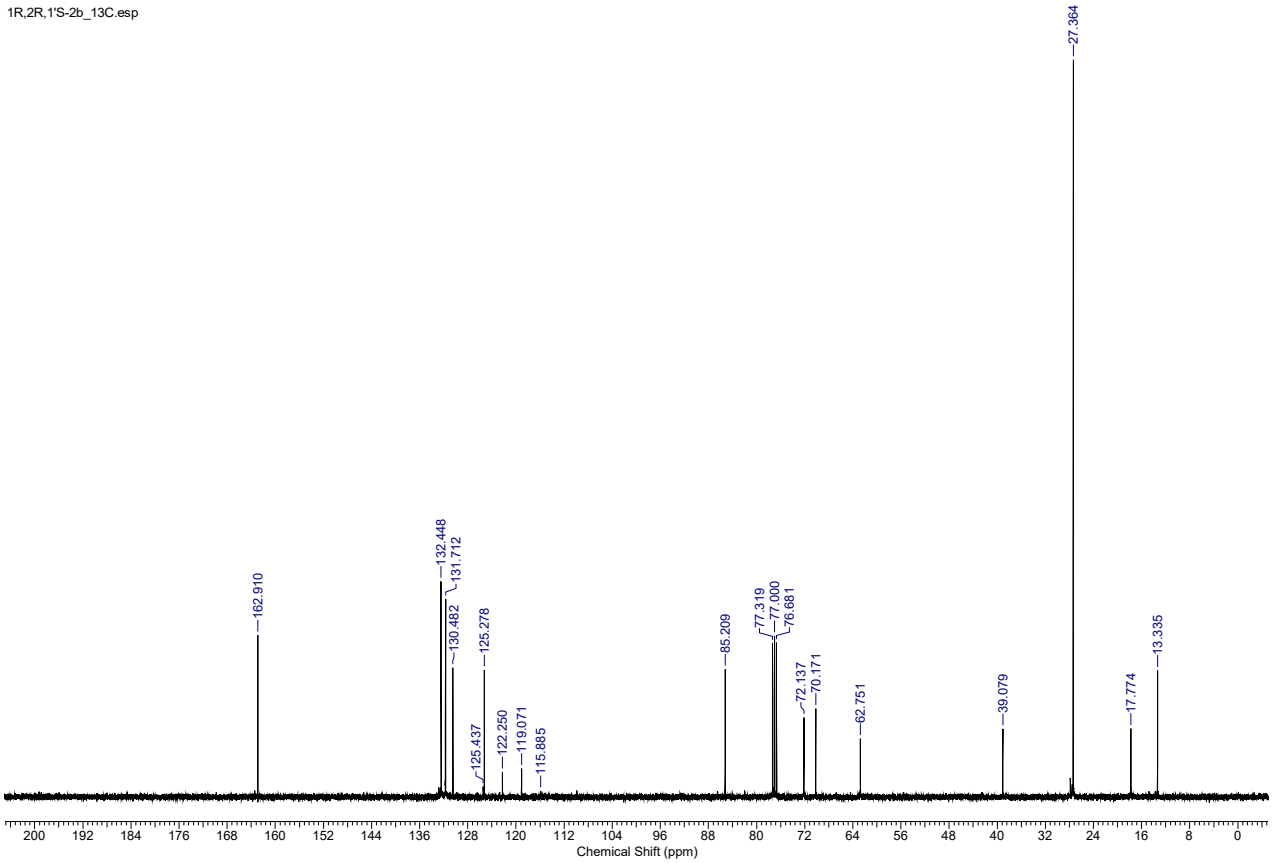
1R,2R,1'S-2b_1H.esp



(1*R**,2*R**,1'*S**)-**2b**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1R,2R,1'S-2b_13C.esp



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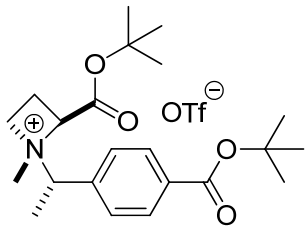
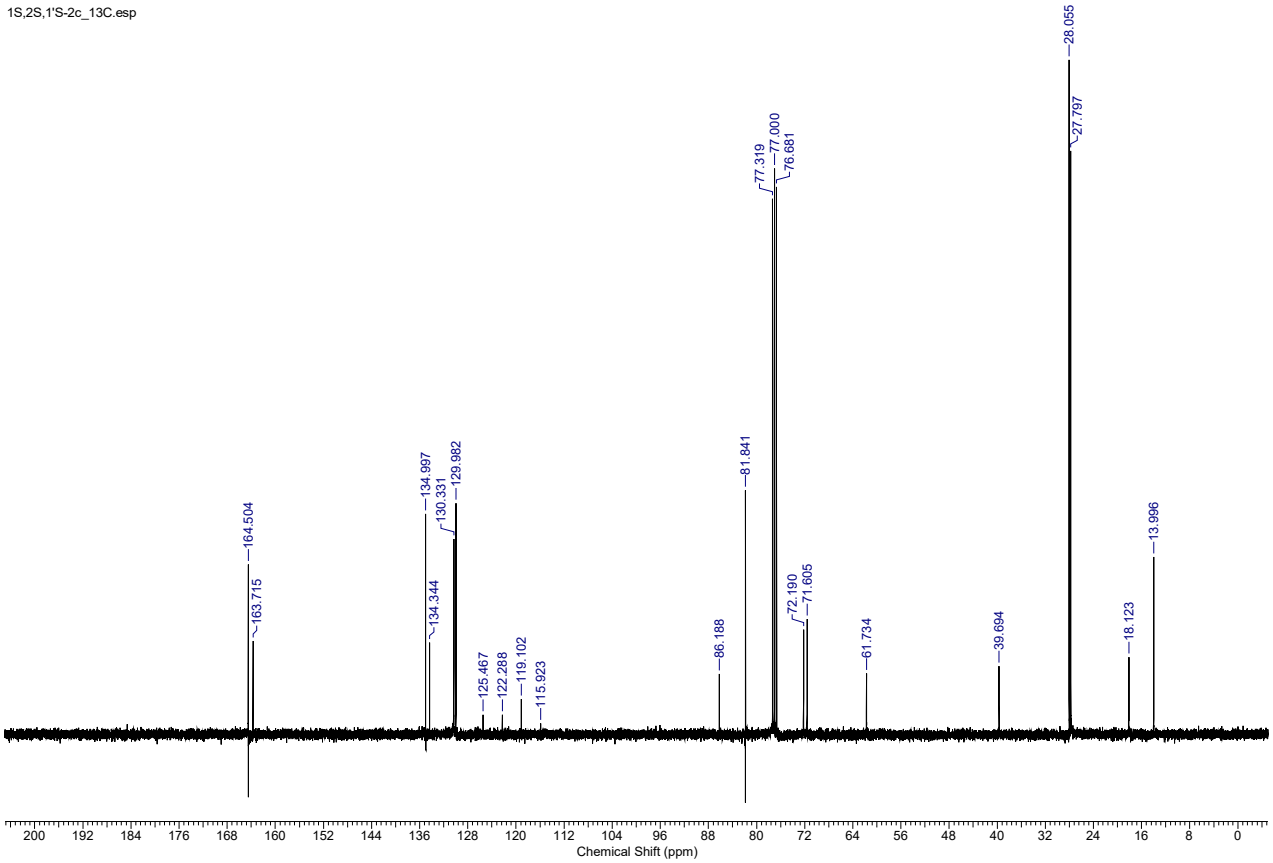


(1*S**,2*S**,1'*S**)-**2c**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S,1'S-2c_13C.esp



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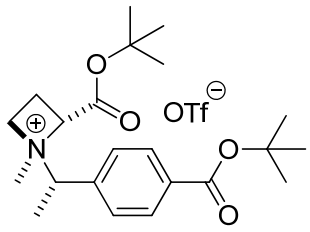
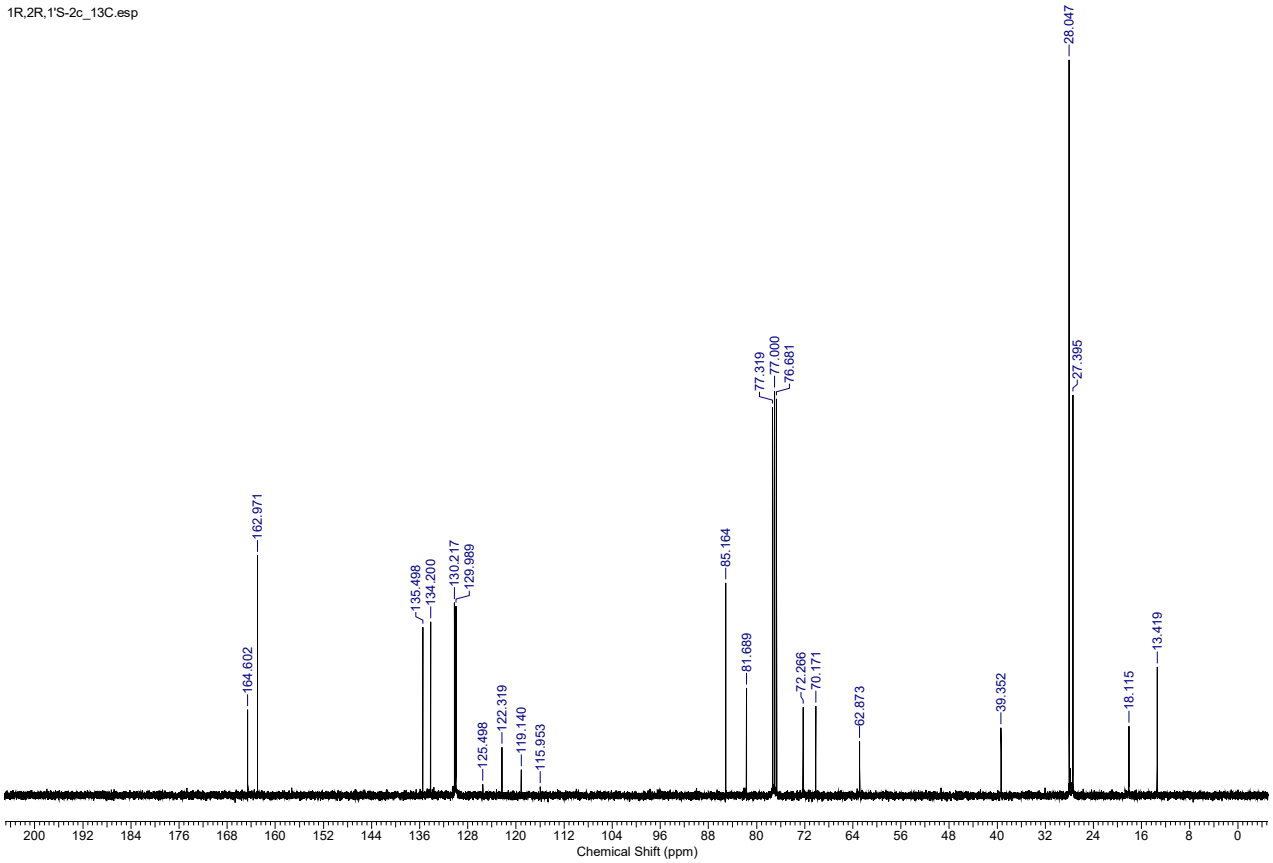


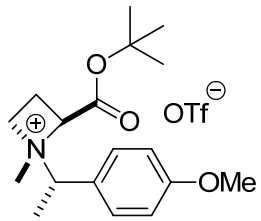
(1*R**,2*R**,1'*S**)-**2c**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1R,2R,1'S-2c_13C.esp



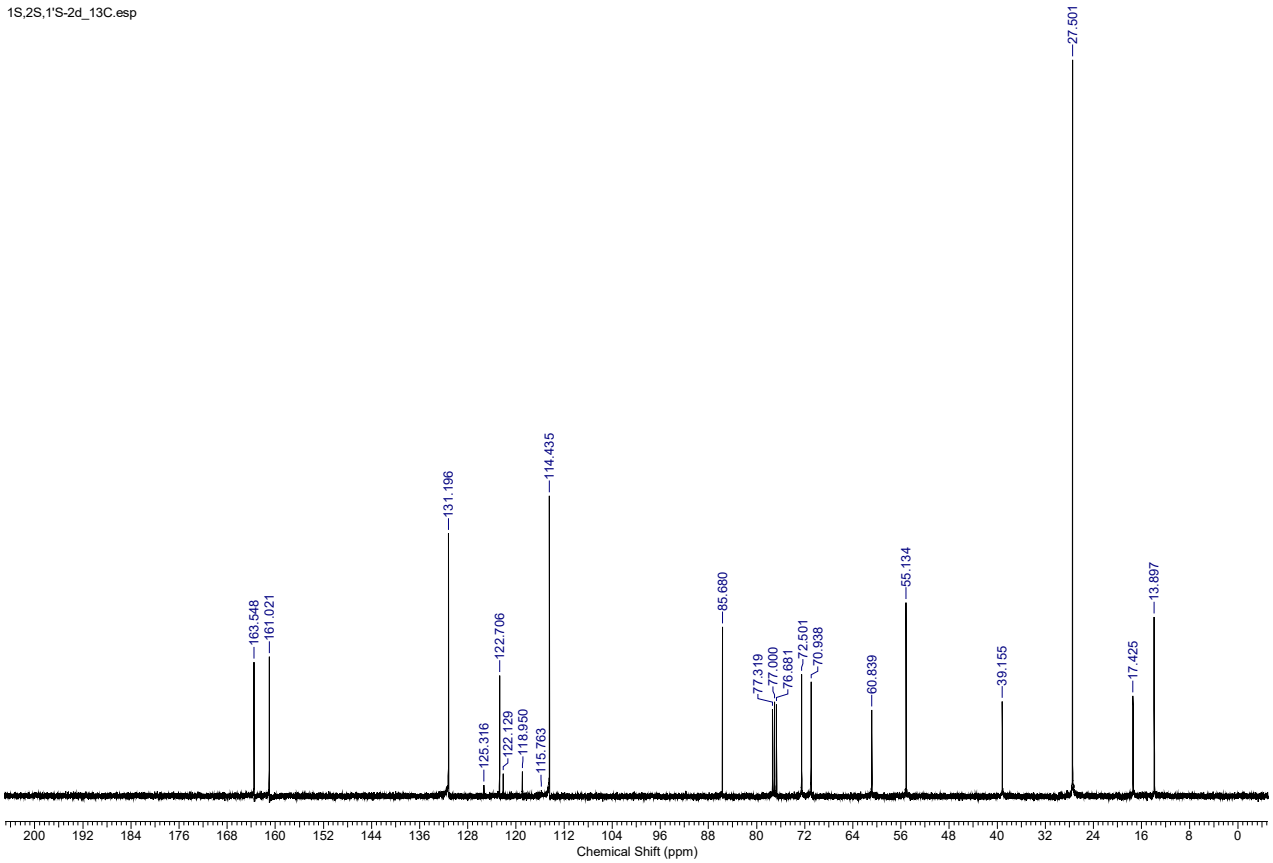
1S,2S,1'S-2d_1H.esp



(1*S**,2*S**,1'*S**)-**2d**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S,1'S-2d_13C.esp



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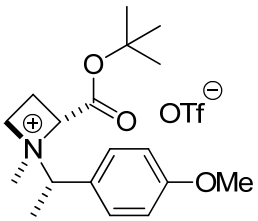
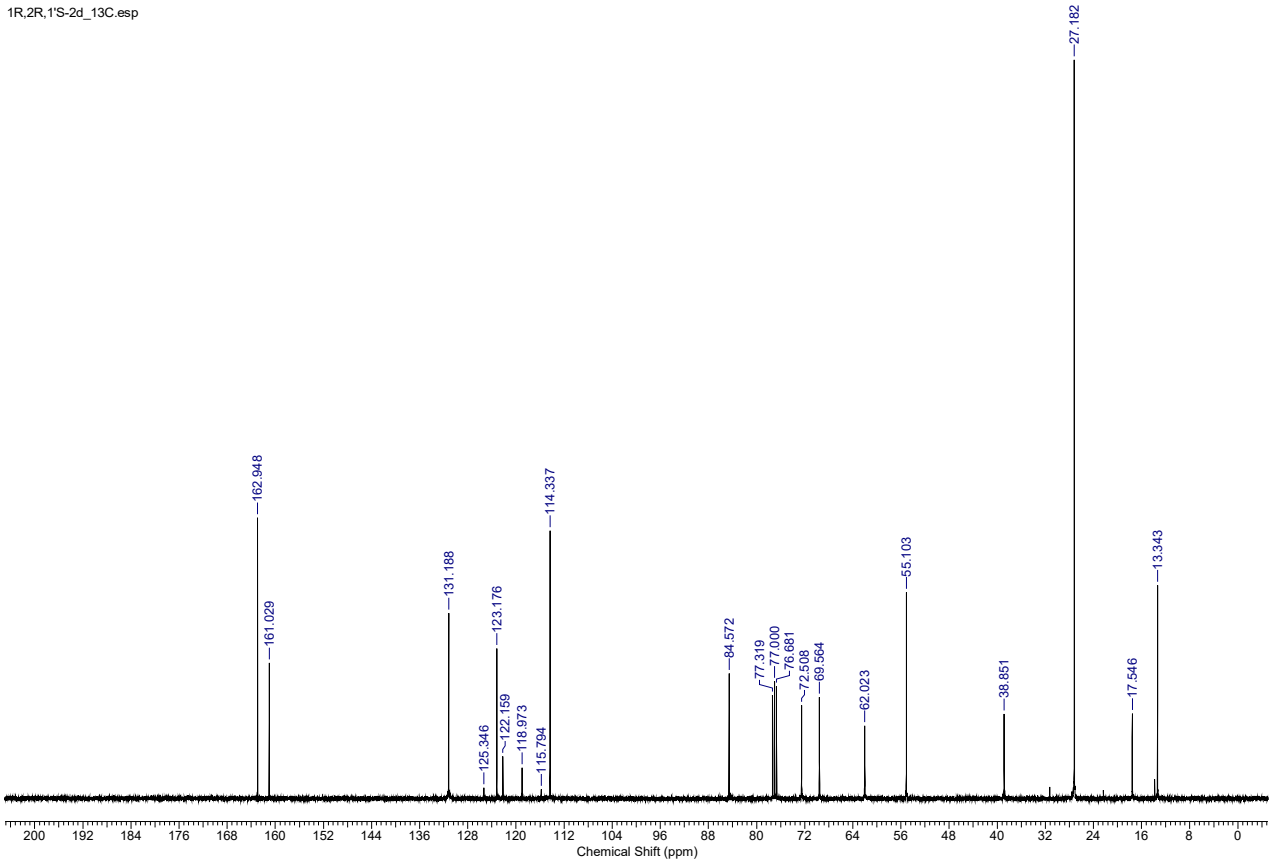


(1*R**,2*R**,1'*S**)-**2d**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1R,2R,1'S-2d_13C.esp



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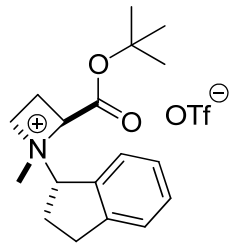
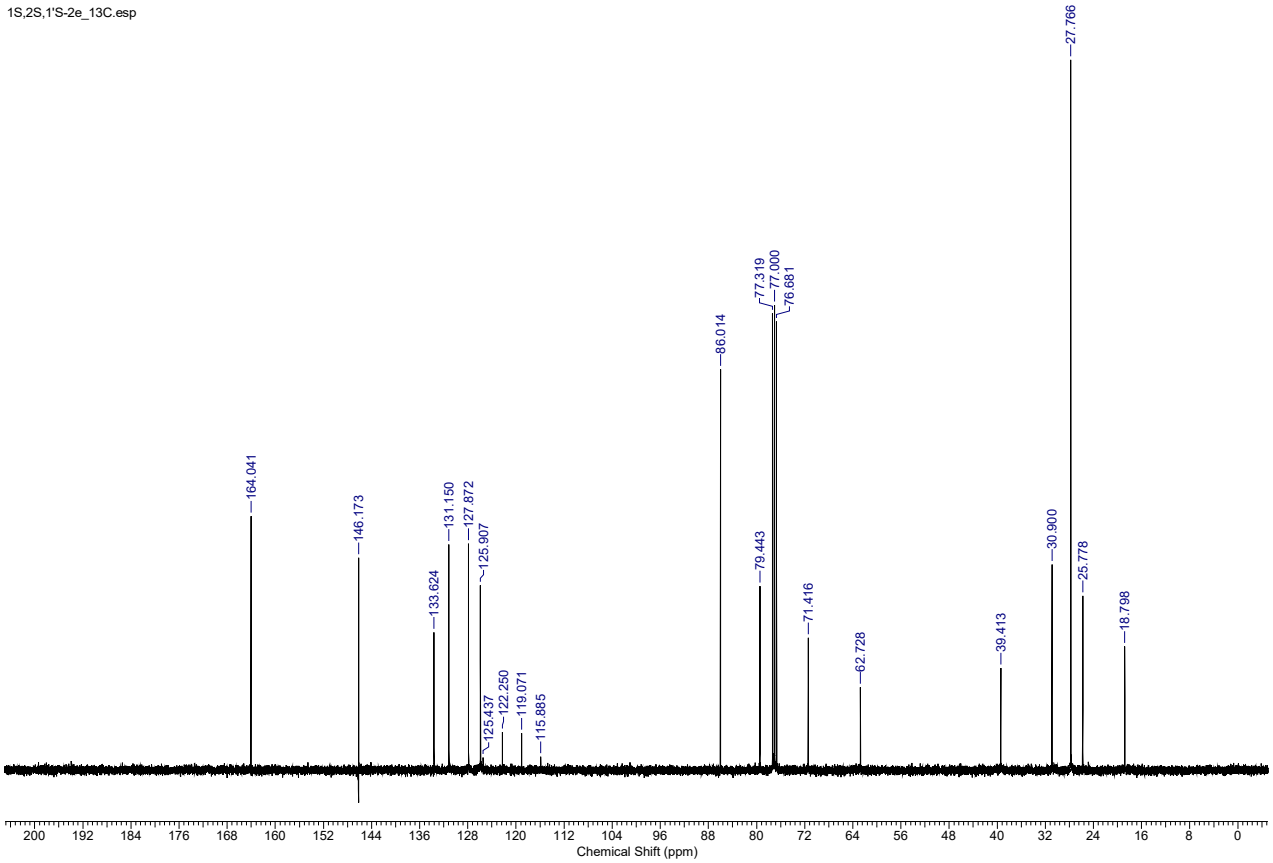


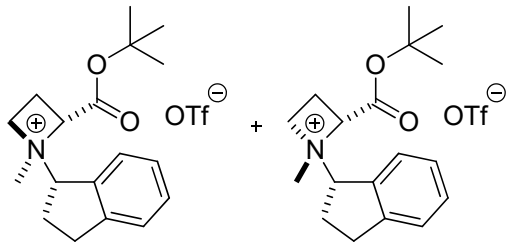
(1*S**,2*S**,1'*S**)-**2e**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S,1'S-2e_13C.esp



1R,2R,1'S-2e_1H.esp

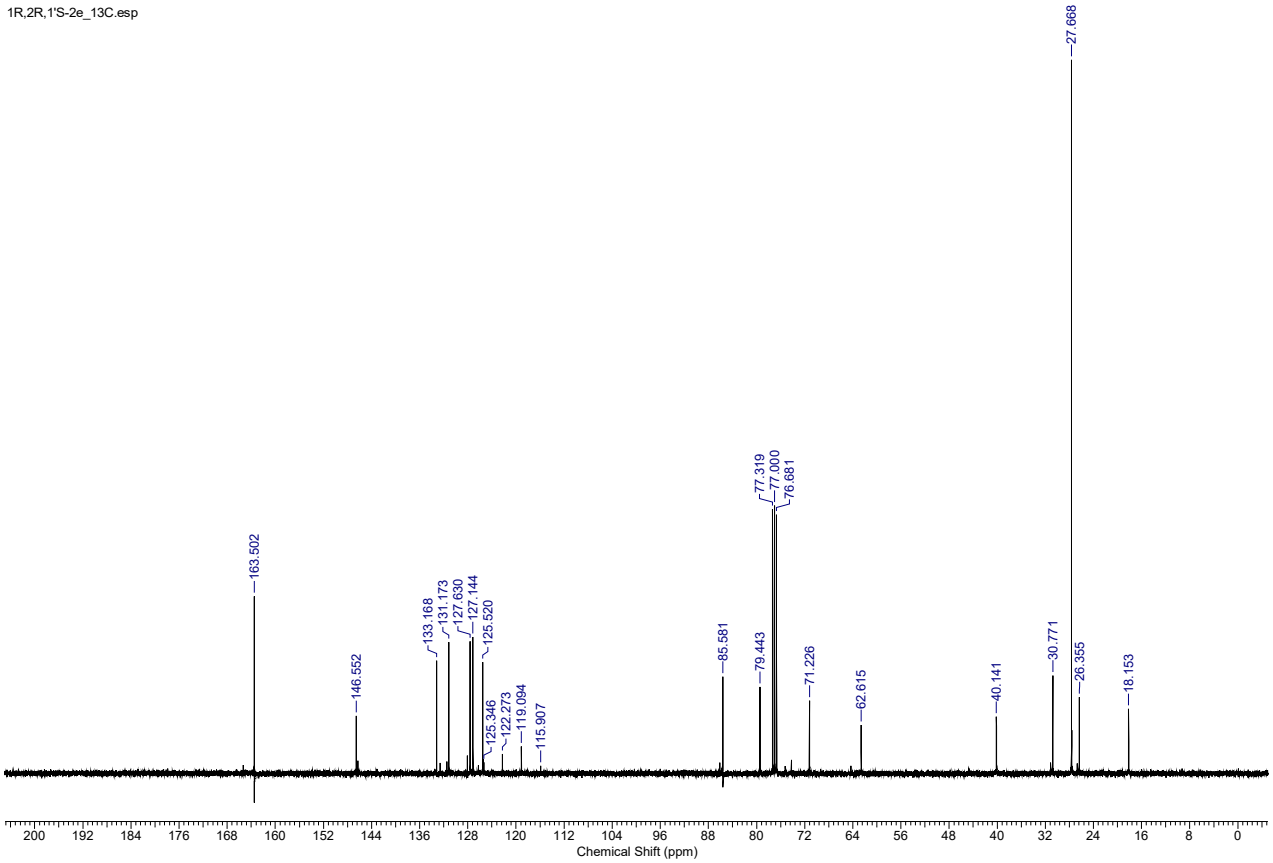


(1*R**,2*R**,1'*S**)-**2e** (1*S**,2*R**,1'*S**)-**2e**

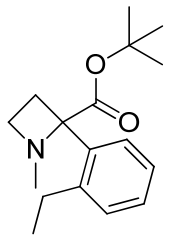
9/1 mixture

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1R,2R,1'S-2e_13C.esp



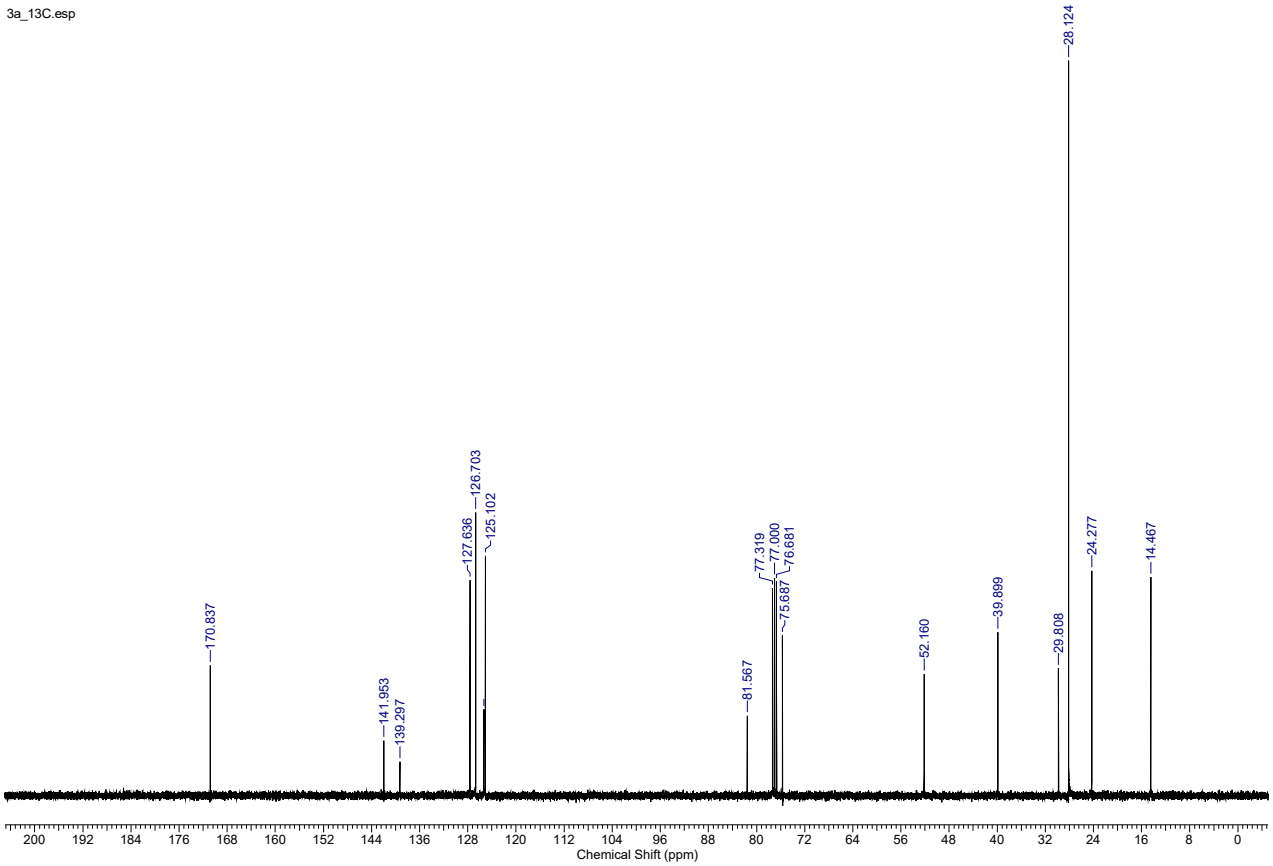
3a_1H.esp



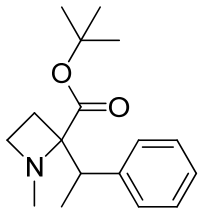
3a

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

3a_13C.esp



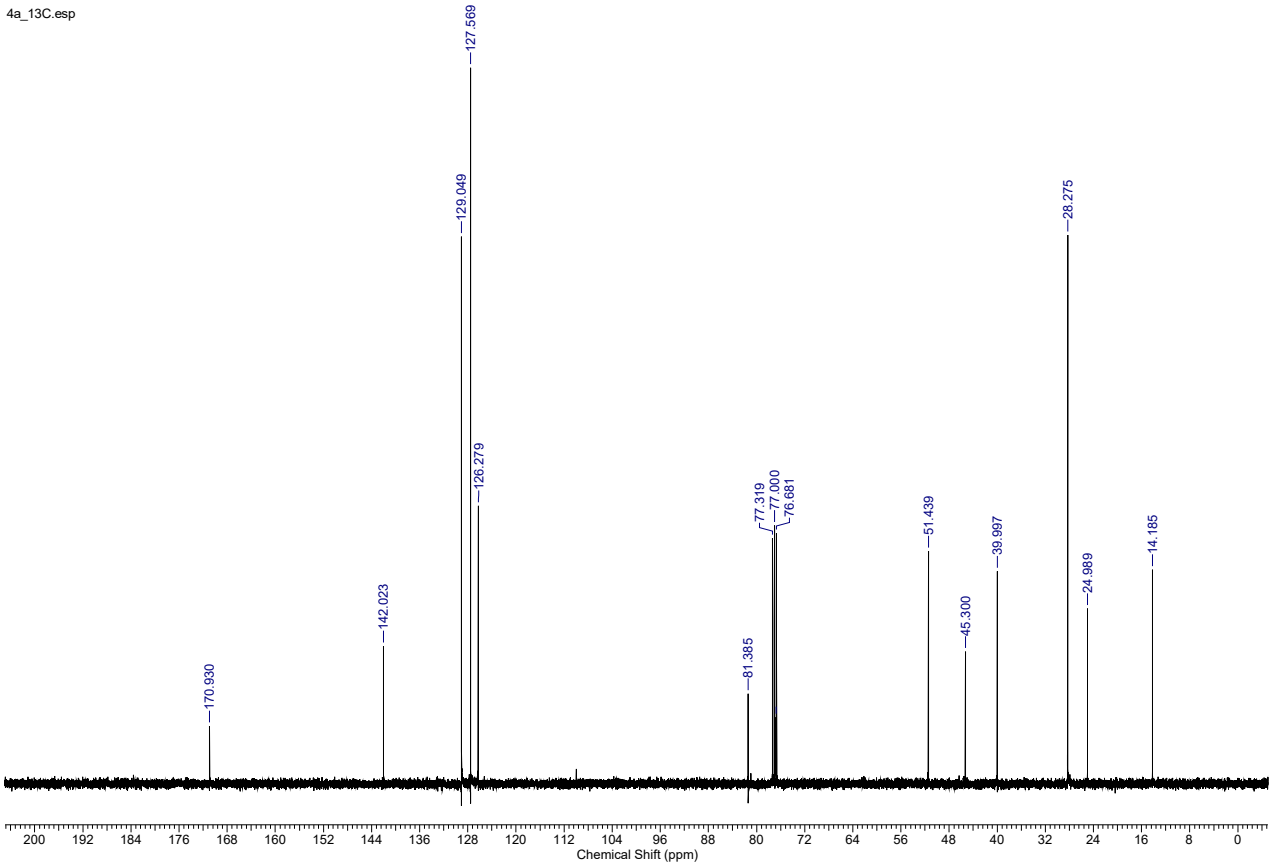
4a_1H.esp



4a

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

4a_13C.esp



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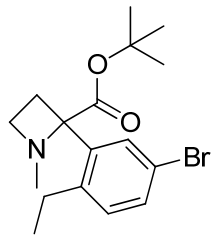
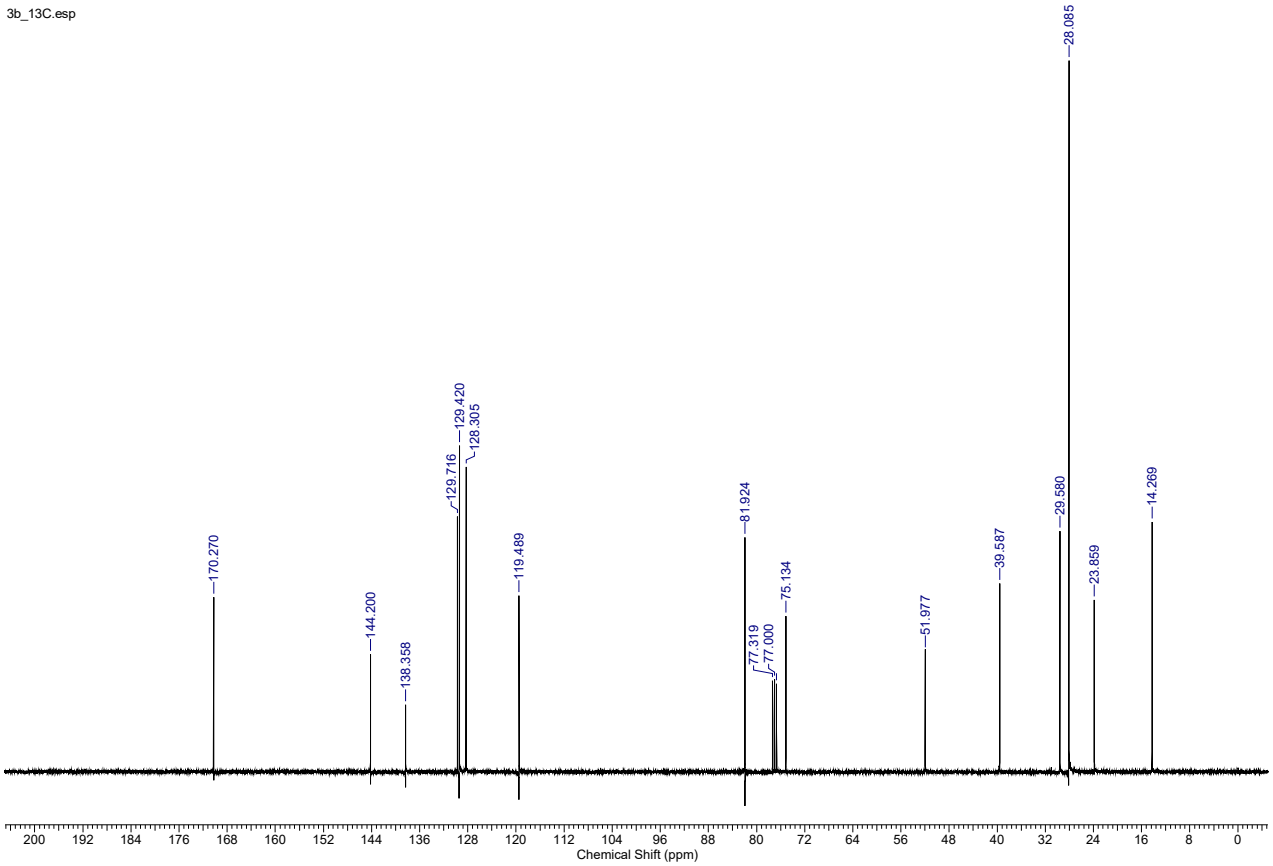


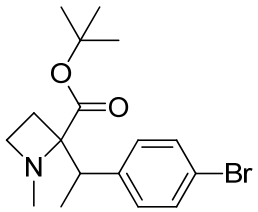
3b

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

3b_13C.esp



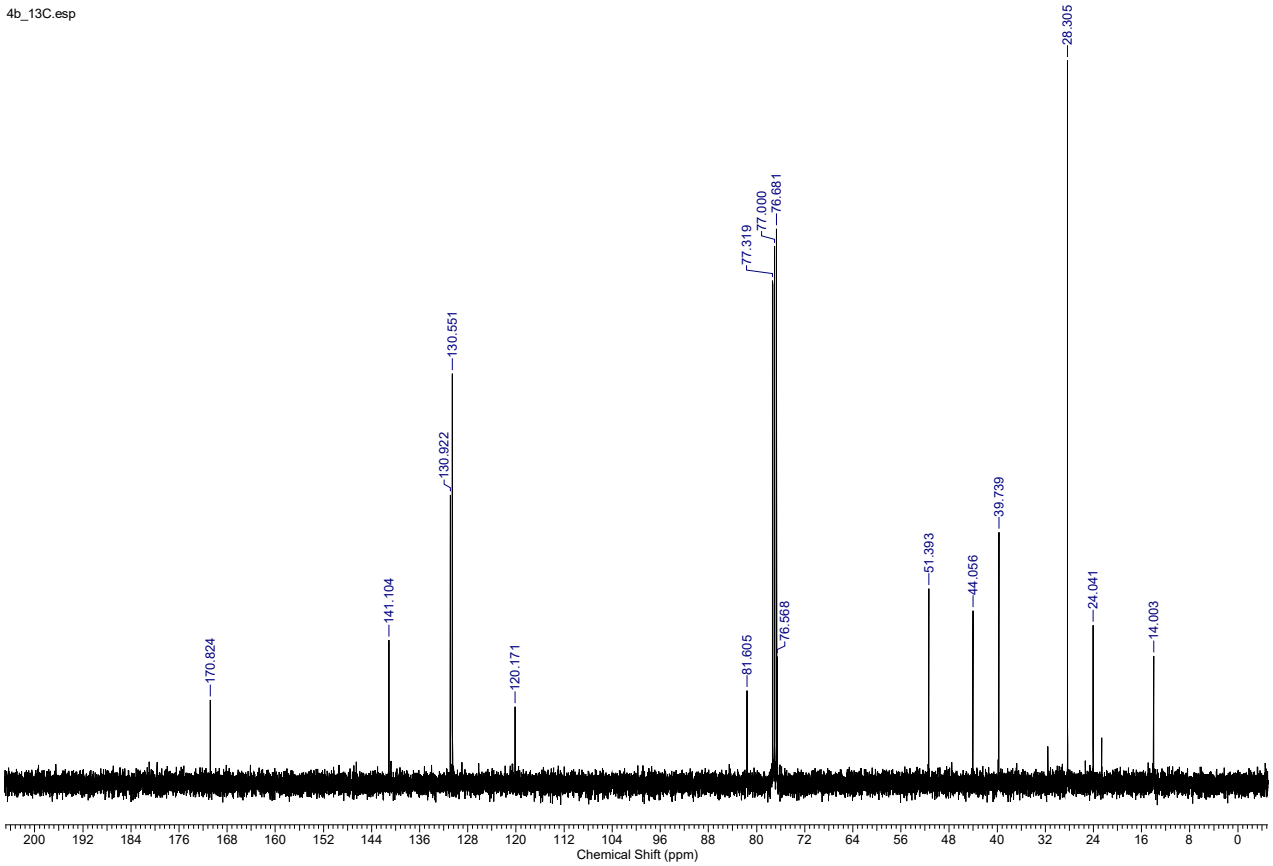
4b_1H.esp



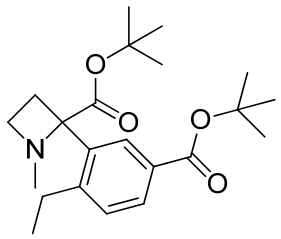
4b

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

4b_13C.esp



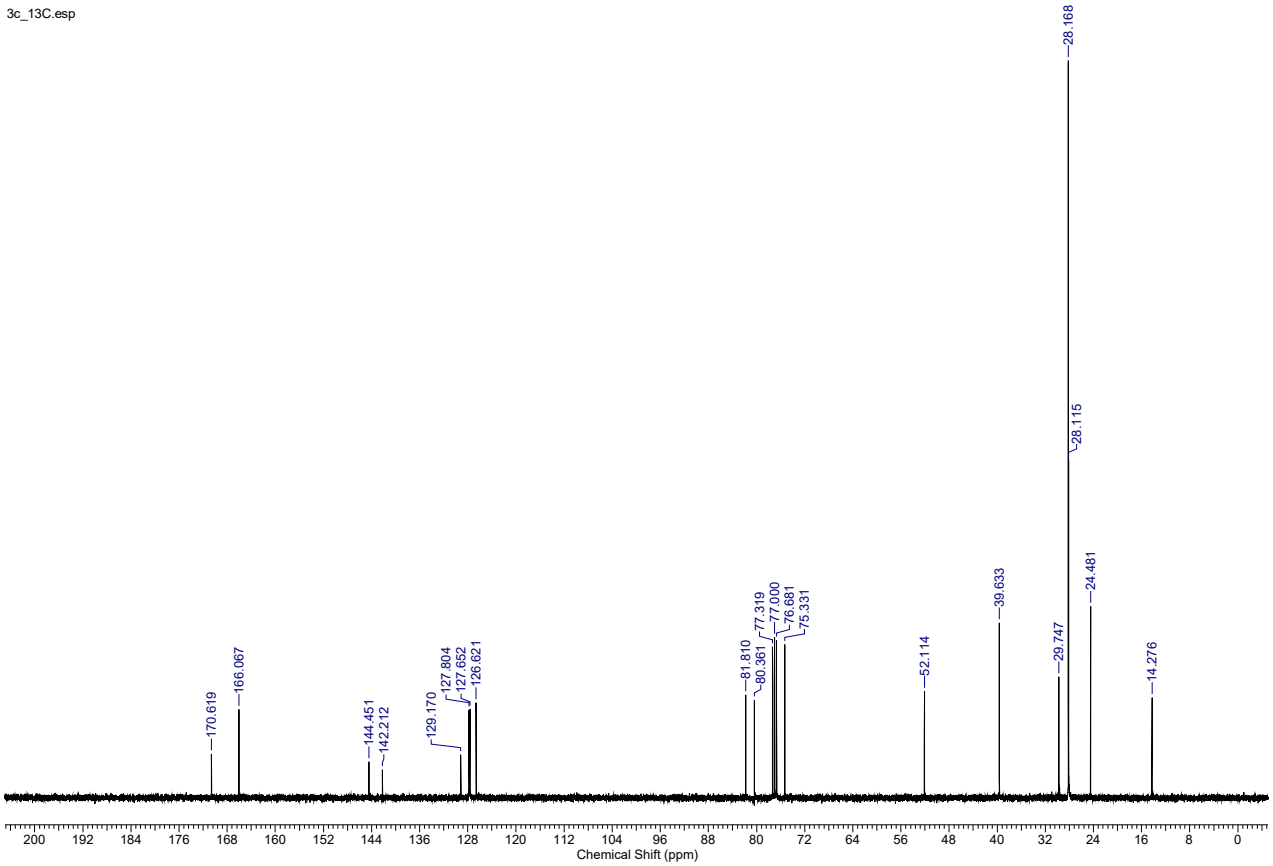
3c_1H.esp



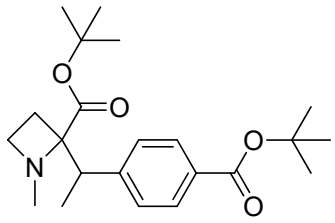
3c

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

3c_13C.esp



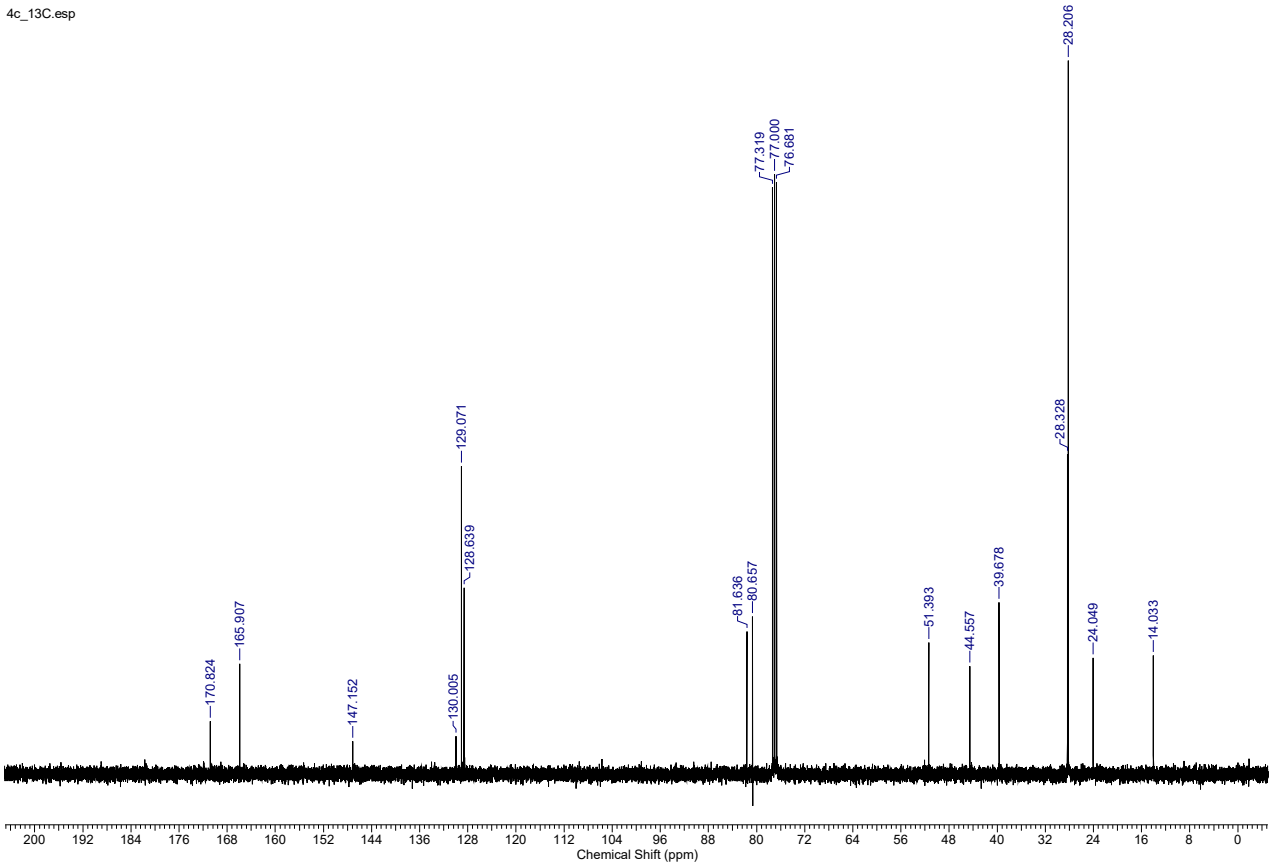
4c_1H.esp



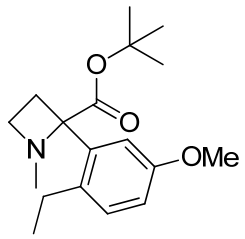
4c

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

4c_13C.esp



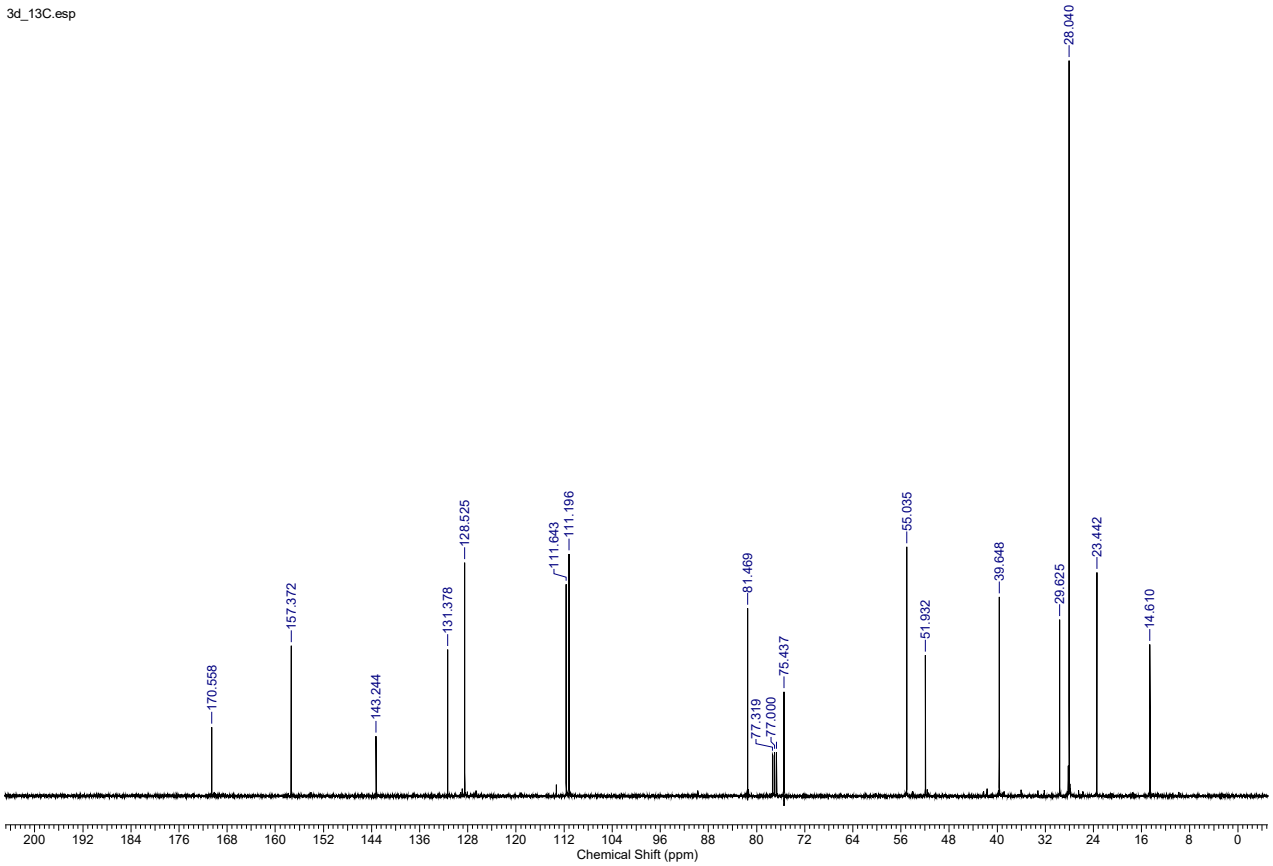
3d_1H.esp



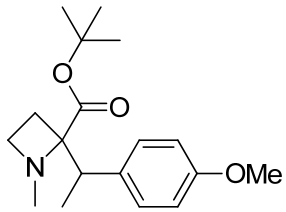
3d

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

3d_13C.esp



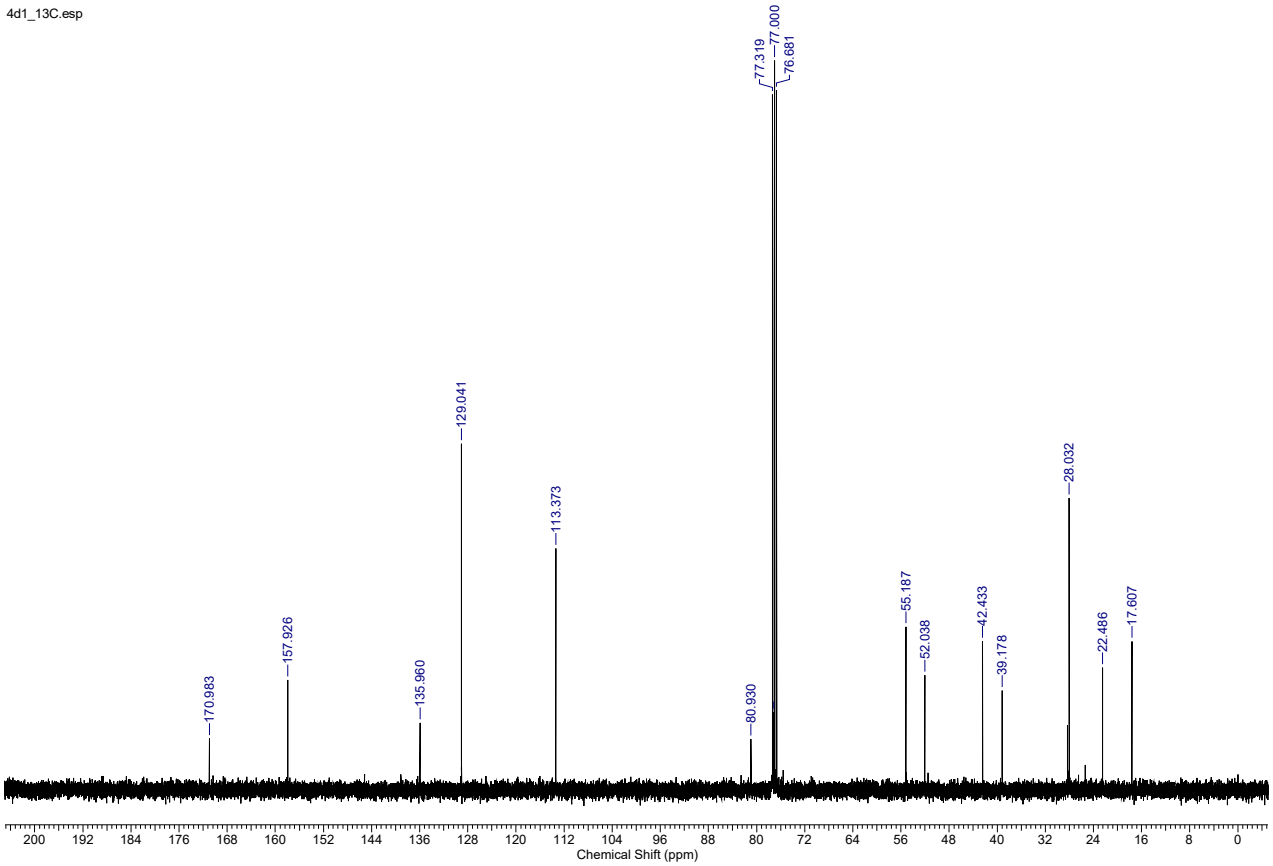
4d1_1H.esp



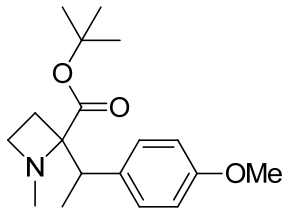
4d1

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

4d1_13C.esp



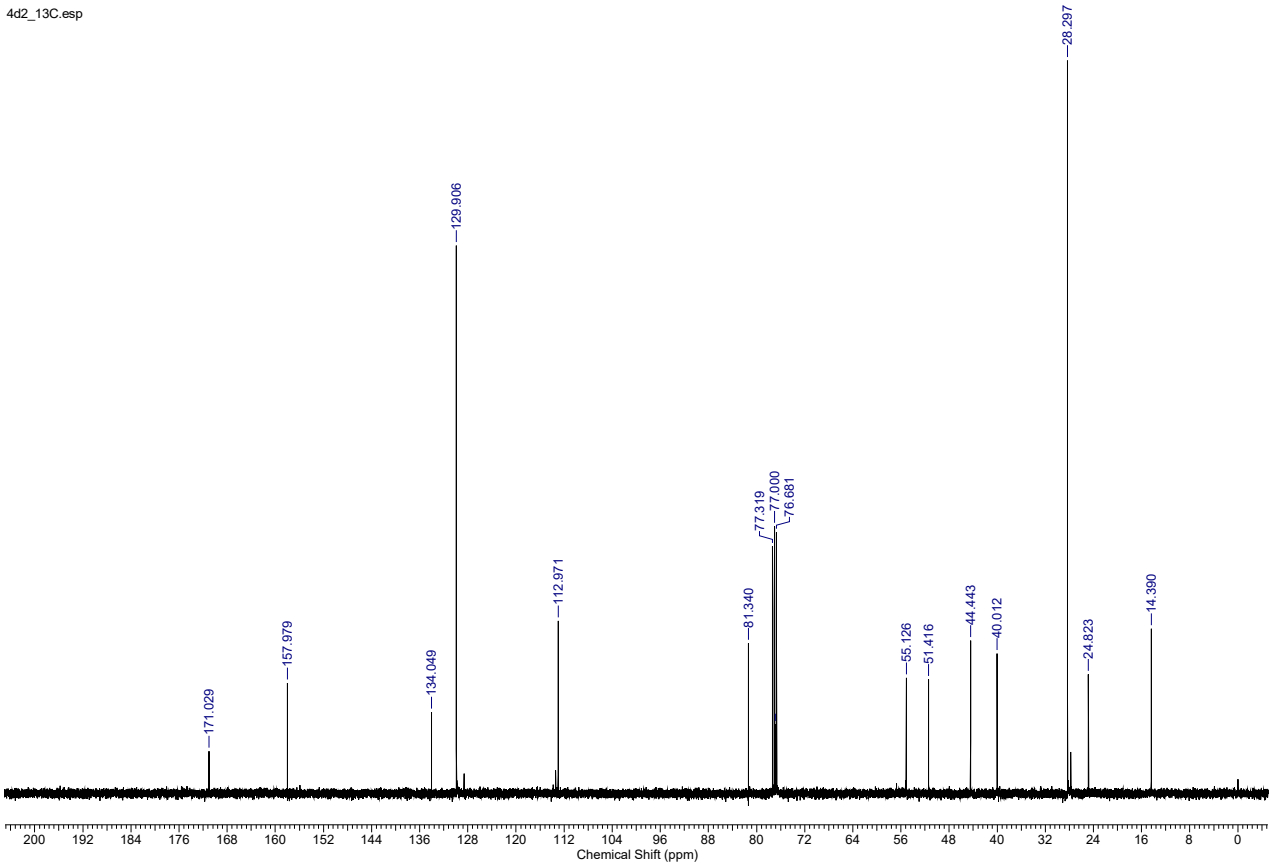
4d2_1H.esp



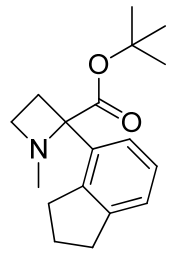
4d2

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

4d2_13C.esp



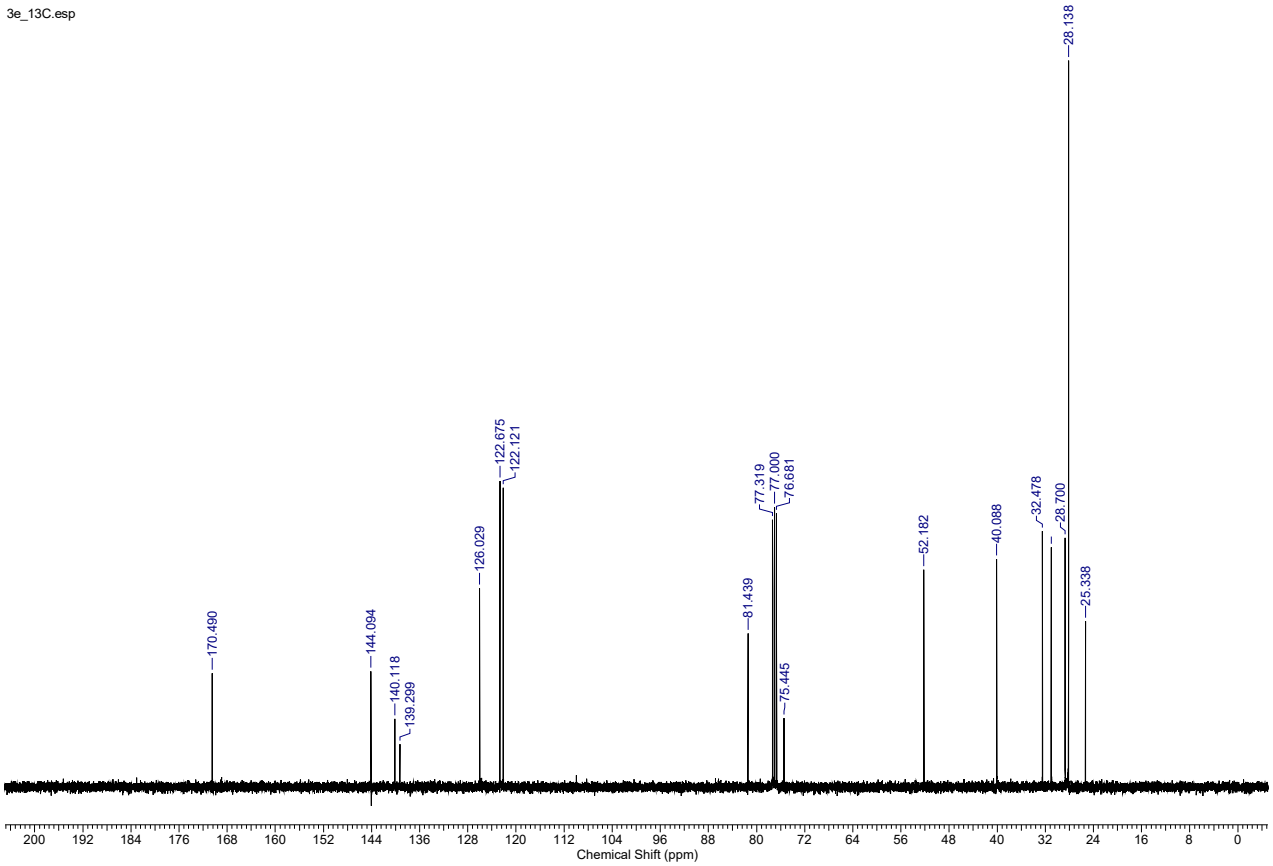
3e_1H.esp



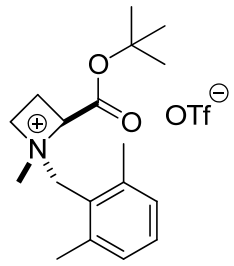
3e

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

3e_13C.esp



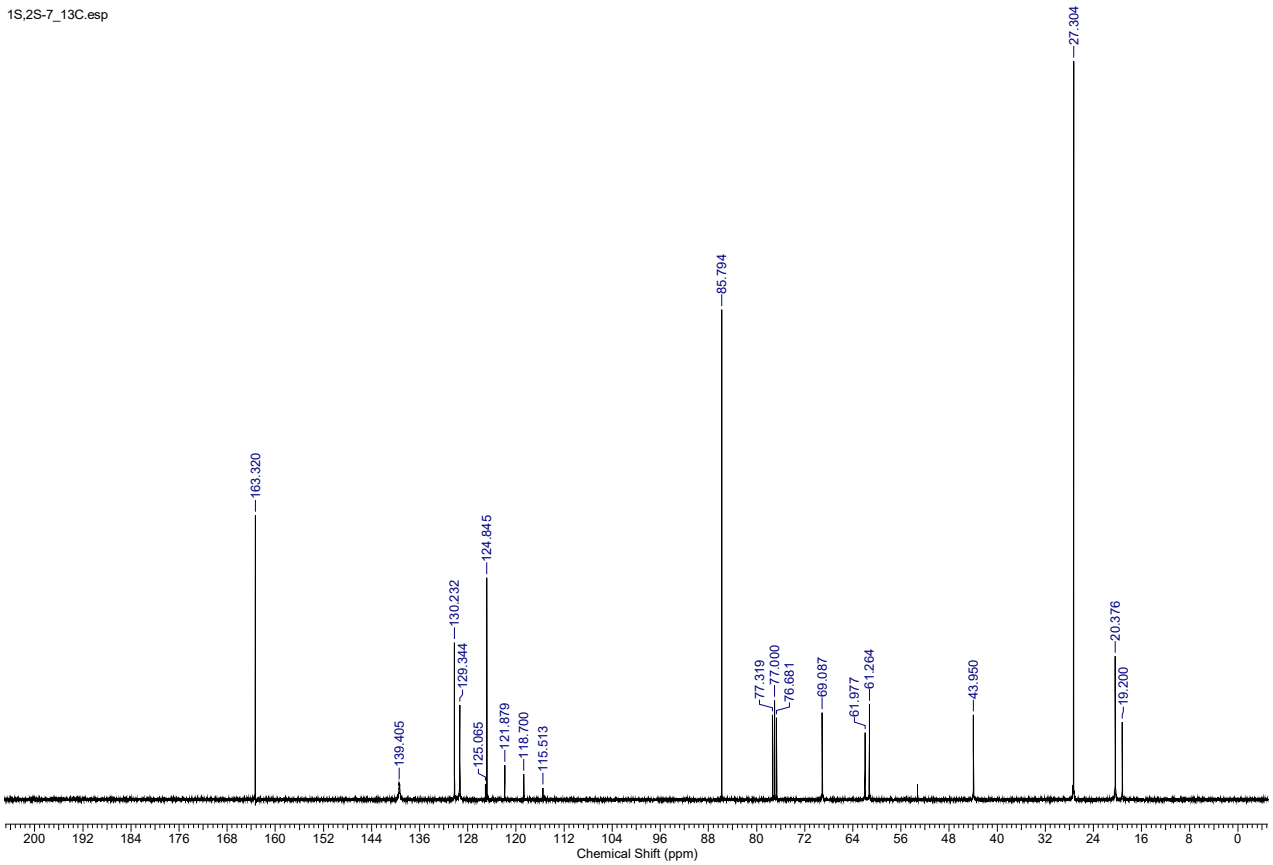
1S,2S-7_1H.esp



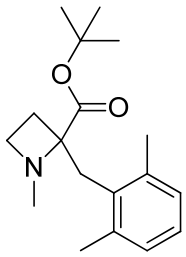
(1*S**,2*S**)-**7**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S-7_13C.esp



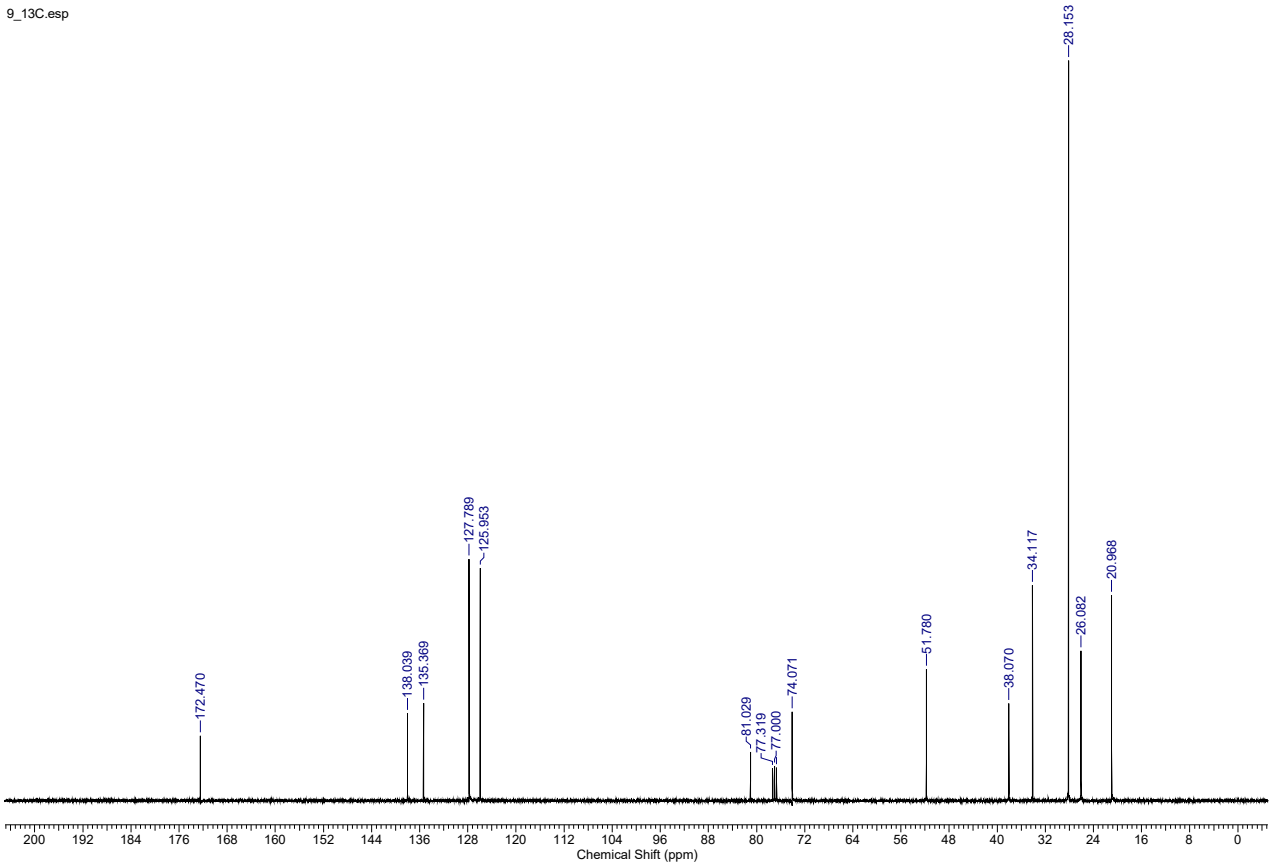
9_1H.esp



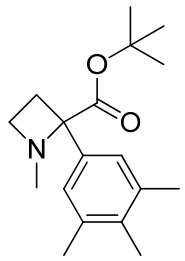
9

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

9_13C.esp



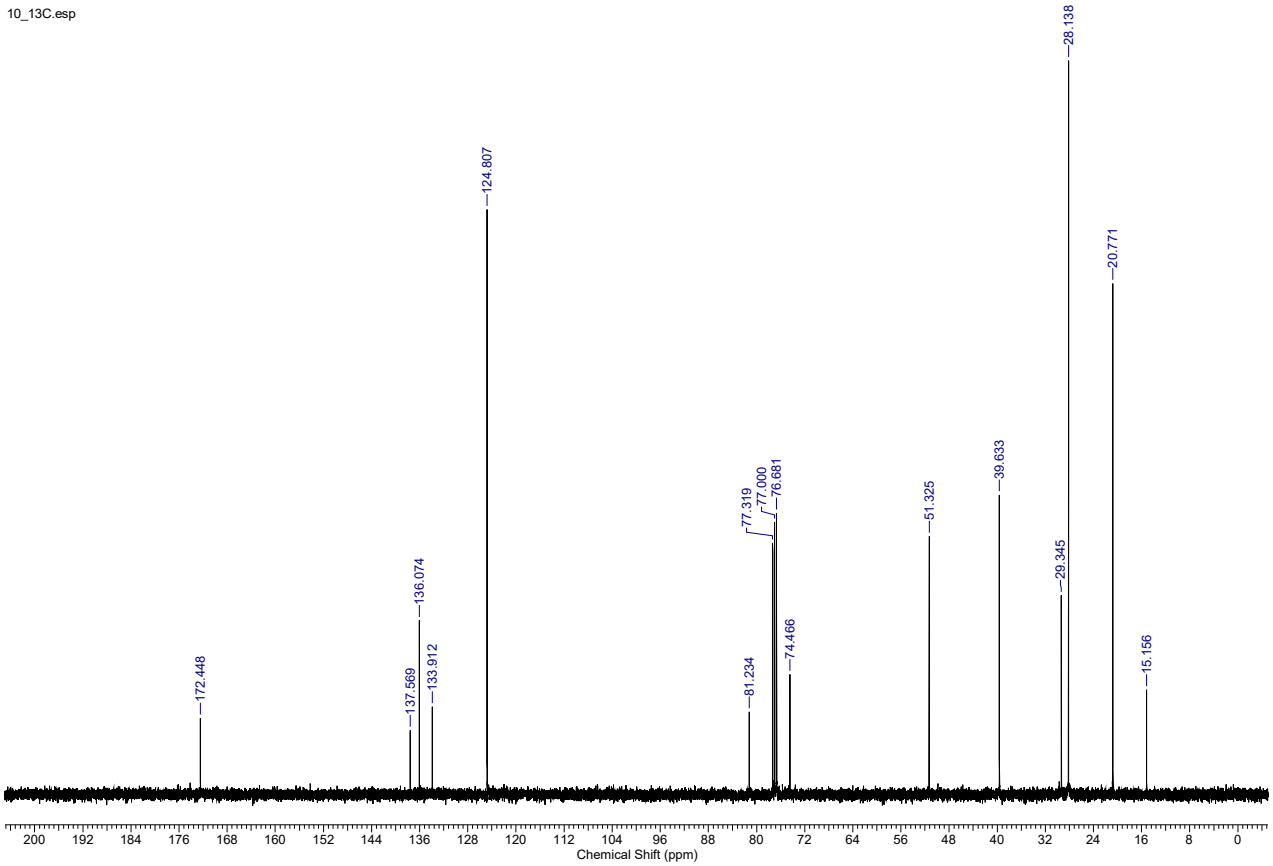
10_1H.esp



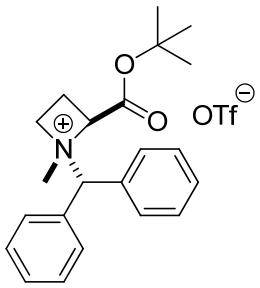
10

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

10_13C.esp



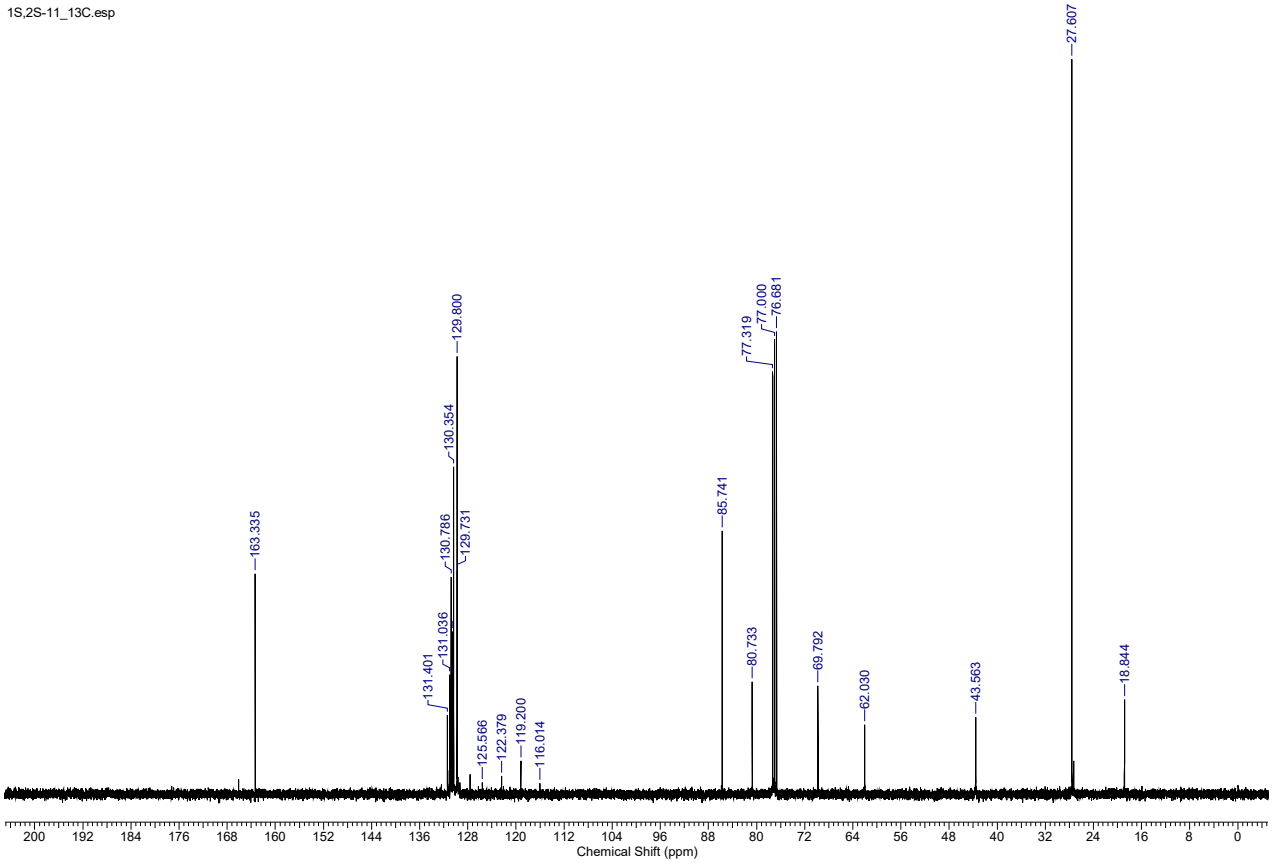
1S,2S-11_1H.esp



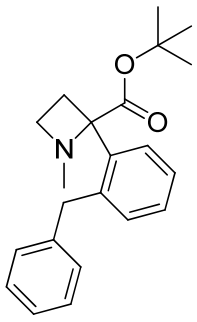
(1*S**,2*S**)-**11**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1S,2S-11_13C.esp



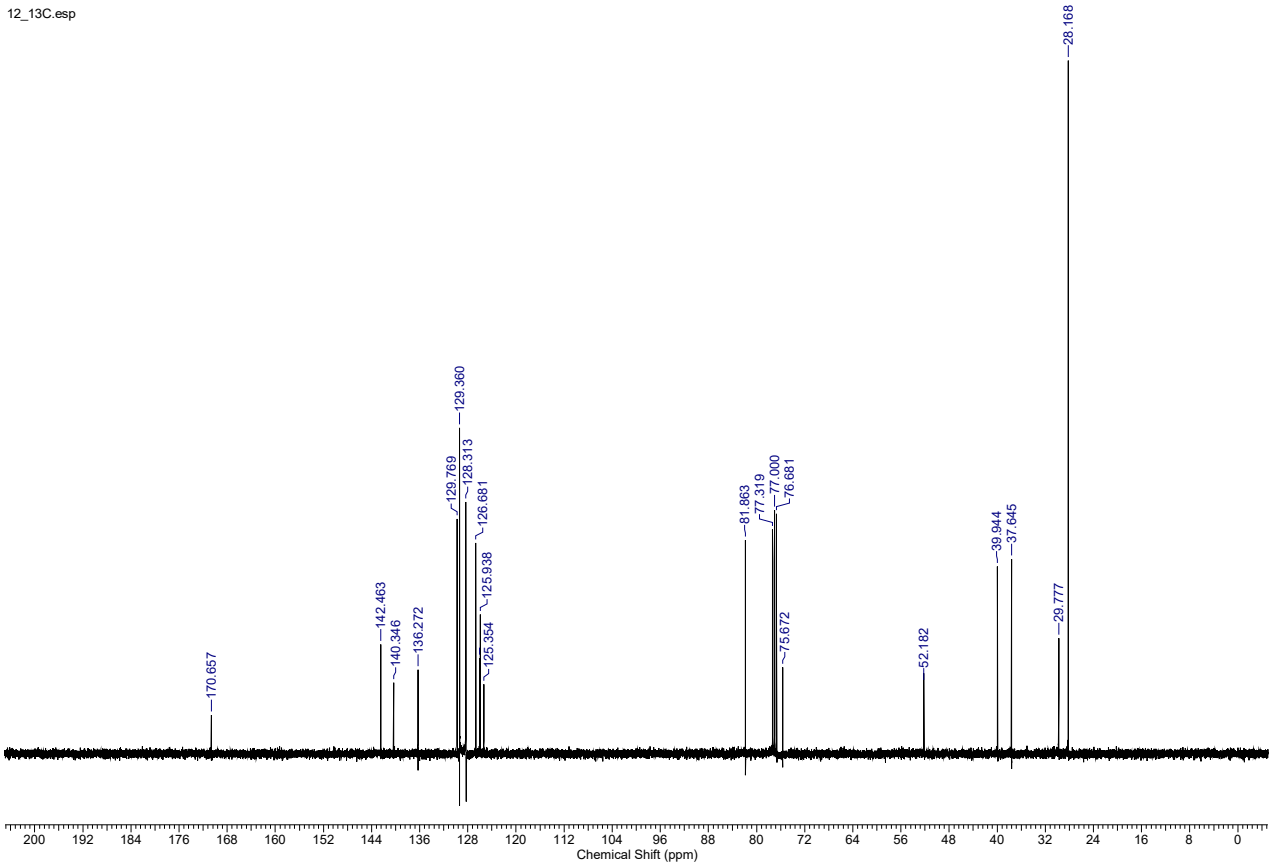
12_1H.esp



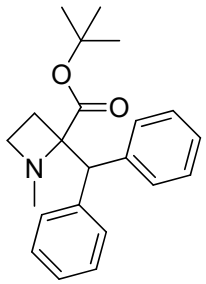
12

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

12_13C.esp



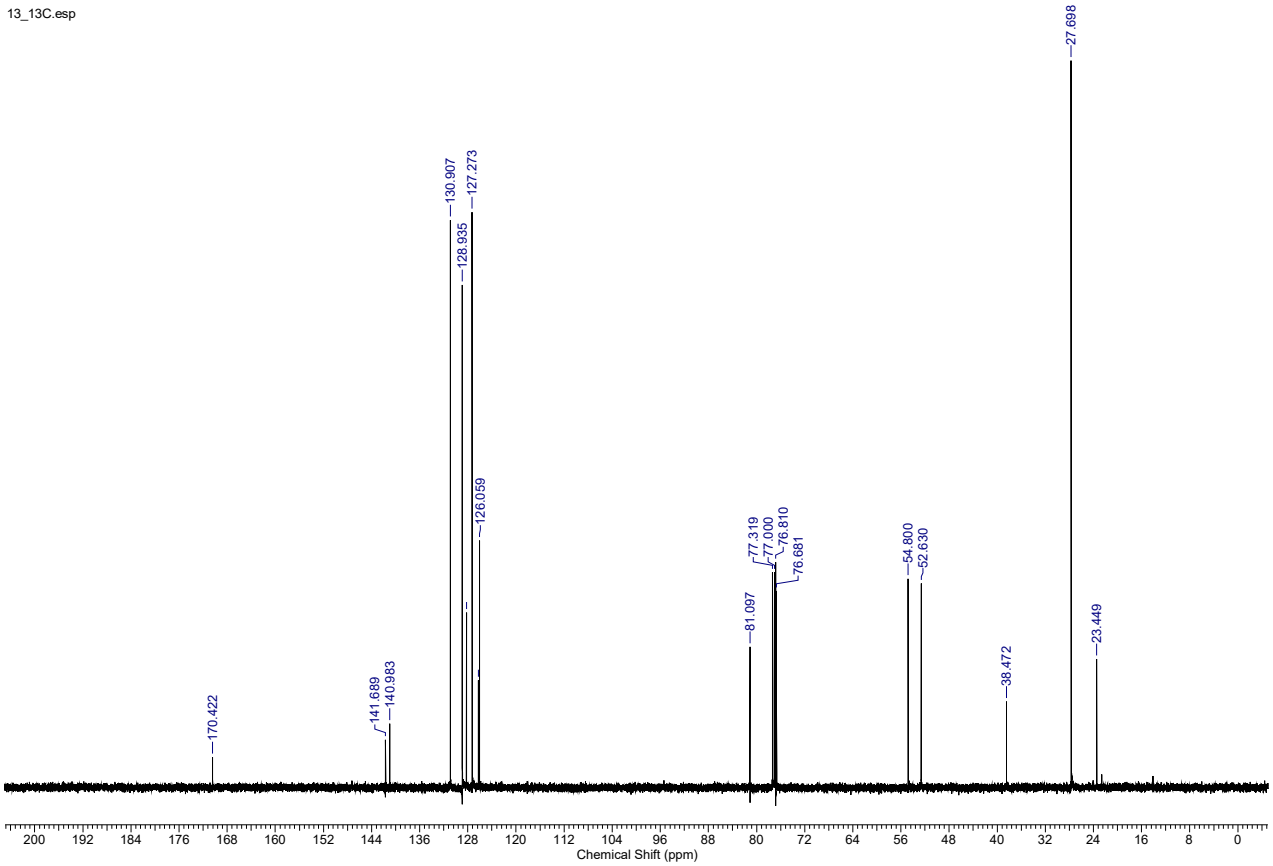
13_1H.esp



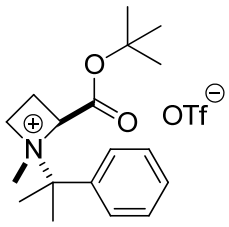
13

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

13_13C.esp



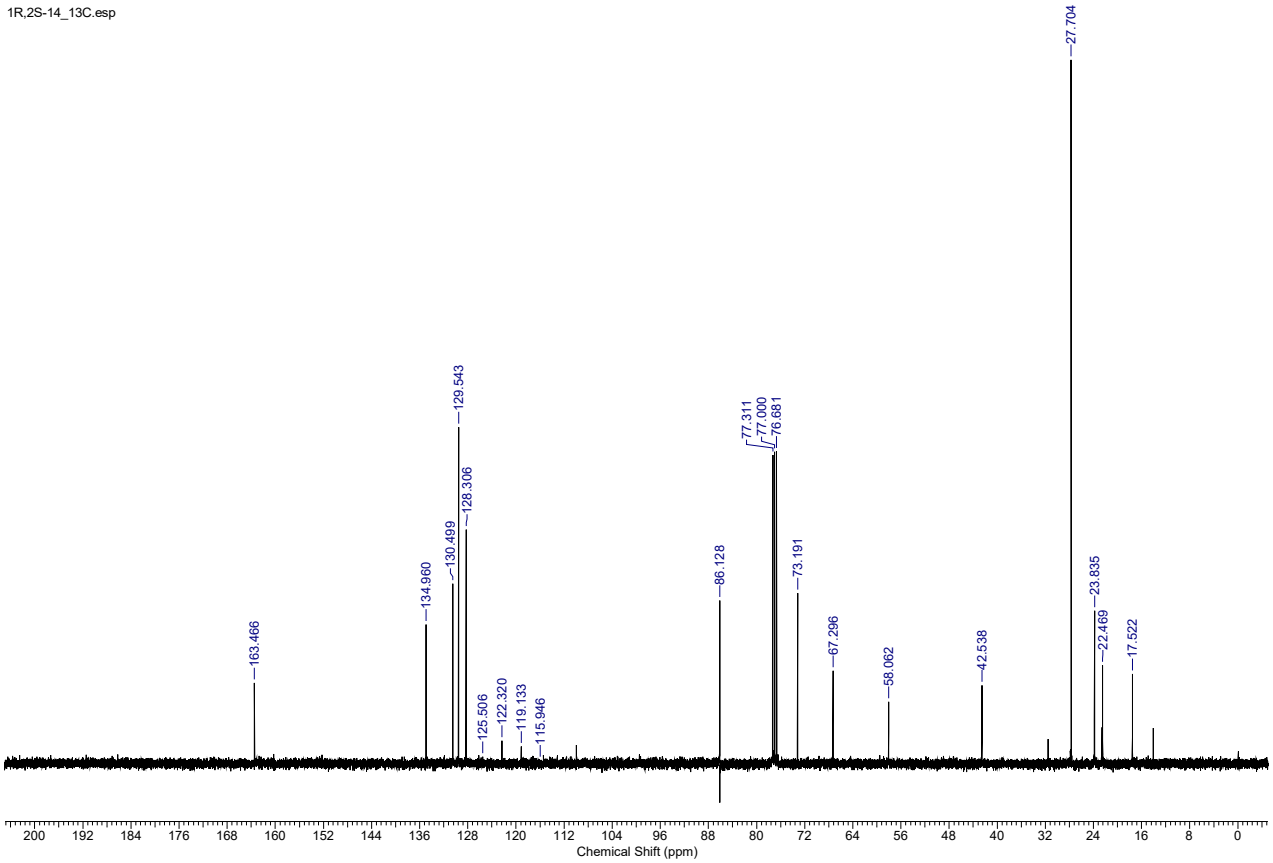
1R,2S-14_1H.esp



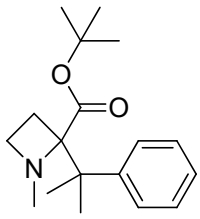
(1*R**,2*S**)-**14**

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

1R,2S-14_13C.esp



16_1H.esp



16

^{1}H: $CDCl_3$, ^{13}C: $CDCl_3$

16_13C.esp