Electronic Supplementary Information

New Enantiopure NHCs Derived From Camphor

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General Experimental

All reactions were conducted under an atmosphere of dry nitrogen. Glassware was dried in an oven or flame-dried under vacuum prior to use. THF and diethyl ether were distilled from sodium benzophenone ketyl. Toluene was distilled from sodium. CH_2Cl_2 and acetonitrile were distilled from calcium hydride. Reactions were monitored by TLC with Merck Silica gel 60 F_{254} plates or with neutral Aluminiumoxid 60 F_{254} plates. Flash column chromatography was performed on Silica gel 60 (70 – 230 mesh ASTM) or active neutral Aluminiumoxid 90 (70 - 230 mesh ASTM) from Merck. Diamine **3**[1] and ketene **9**[2] and dimethyl ketene[3] were prepared according to literature procedures. Aldehydes were distilled or sublimed. All other chemicals, which preparation is not described below, were bought from Aldrich, Fluka, Merck or Lancaster. Melting points were taken on a Dr. Tottoli apparatus from Büchi and are uncorrected. Infrared spectra were recorded on a Vector 22 FT-IR from Bruker. The absorption of solids was measured by potassium bromide pellets, the absorption of liquids by using a thin layer between sodium chloride plates. ^{1}H-NMR spectra were taken on an AMX 400 (400 MHz) or an AC 250 P (200 MHz) from Bruker in $CDCl_3$ unless otherwise stated. ^{13}C-NMR spectra were taken on an AMX 400 (100 MHz) or on an AC 250 P (50 MHz) from Bruker in $CDCl_3$ unless otherwise stated. HSQC spectra were taken on an AMX 400 from Bruker. Mass spectra were recorded on MS 5889 B from Hewlett Packard. The samples were injected *via* direct injection (DCP). Electron spray mass spectrometry was performed directly on a MS LC/MSD 1100 MSD from Hewlett Packard. High resolution mass spectra were recorded on Bruker Daltonik Tesla-Fourier Transform-Ion Cyclotron Resonance Massspectrometer mit Electrospray-Ionisierung by Dr. Dräger at the Institute of Organic Chemistry, University of Hannover. Elemental analysis were carried out on a "Elementar Analyzer", model 1106 from Carlo Erba Instrumentazione at the Institute of Pharmaceutical Chemistry of the Technical University of Braunschweig and are reported as the average of

two runs. Optical rotations were measured using a 1 dm path length (c is given as g/100 mL) on a Perkin-Elmer 243 B polarimeter in the reported solvent. Melting points were taken on a Dr. Tottoli apparatus from BÜCHI and are uncorrected. HPLC analysis was carried out using a Daicel CHIRALPACK AD-H column with a Waters 510 Pump system and a Waters 410 Differential Refractometer.

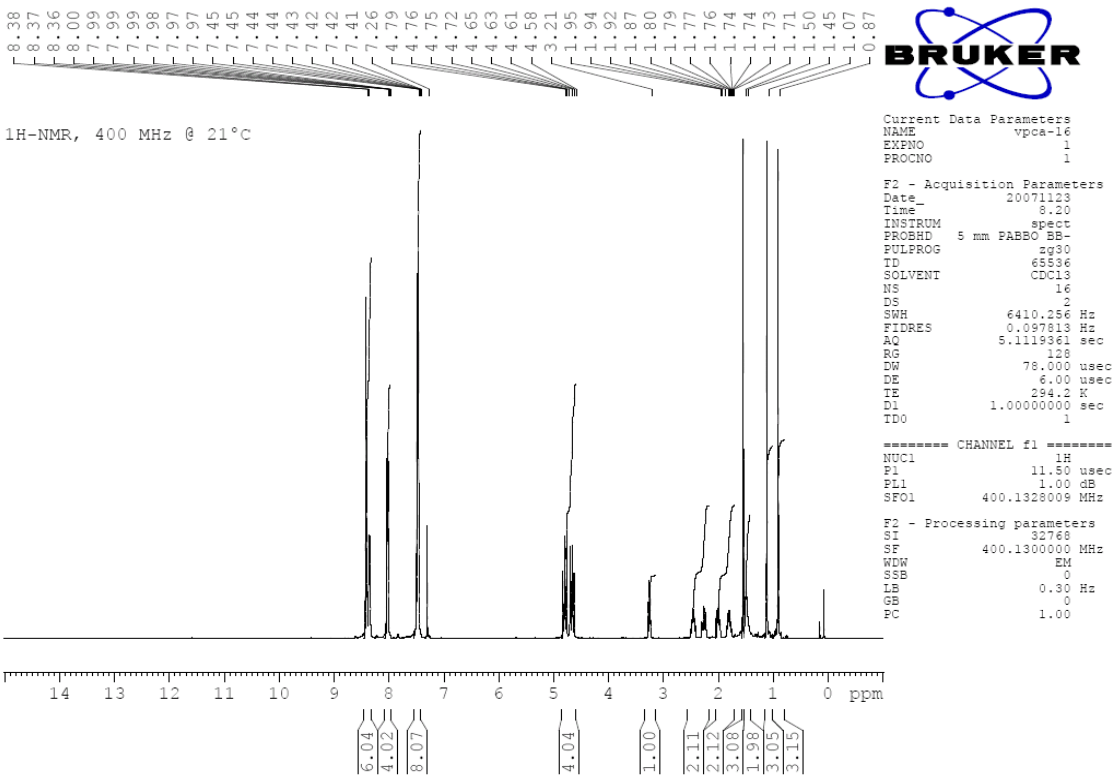
***N*,*N*-Dibenzyl-1,2,2-trimethylcyclopentane-1,3-diamine (4a)**

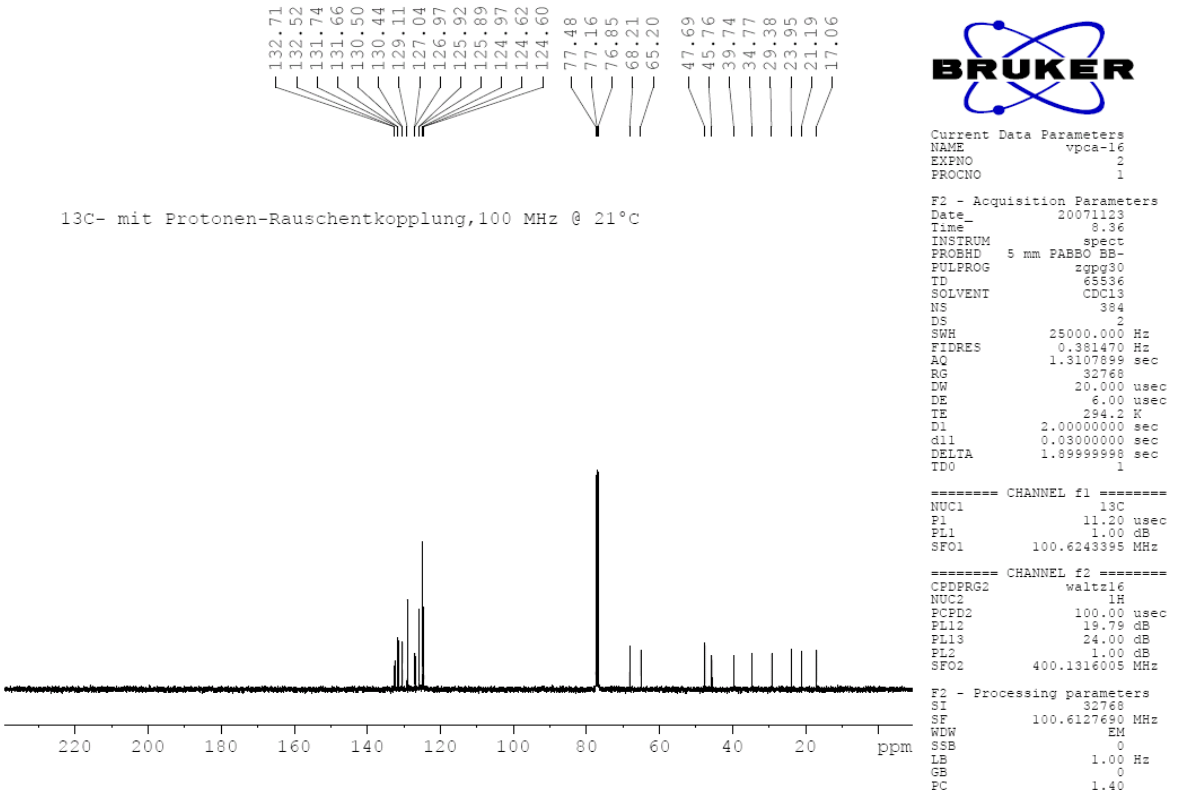
Diamine (**3**) (11.67 g, 82 mmol) and benzaldehyde (25 mL, 246 mmol, 3 eq.) were refluxed overnight in dry toluene (150 mL) in presence of a catalytic amount of camphorsulfonic acid on a Dean Stark. After evaporation, the brown oil obtained was directly reduced in the next step. The imine (82 mmol) was stirred in dry methanol (100 mL) under a stream of nitrogen and $NaBH_4$ (11.4 g, 300 mmol, 3.6 eq.) was carefully added. After 5 h at rt water was carefully added and methanol was evaporated. Ethyl acetate was added and the organic layer was washed with 2 N HCl (3 x 100 mL). The aqueous layer was then basified with NaOH and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was removed to give a yellow oil (18.2 g, 56 mmol, 69 % over two steps). Spectral data were consistent with literature values.[3]

***N*,*N*- Bis(anthracen-9-ylmethyl)-1,2,2-trimethylcyclopentane-1,3-diamine (4b)**

Diamine (**3**) (5.68 g, 40 mmol.) and anthracene-9-carbaldehyde (20.6 g, 100 mmol, 2.5 eq.) were refluxed overnight in dry toluene (25 mL) in presence of a catalytic amount of *p*-toluenesulfonic acid on a Dean Stark. After evaporation, the yellow solid Schiff's base obtained was directly reduced in the next step. $NaBH_4$ (15.2 g, 400 mmol, 10 eq.) was dissolved in anhydrous methanol (50 mL) and then added in small portion to a suspension of crude Schiff´s base (40 mmol) in $CHCl_3$ / methanol (150 mL, 2:1 v/v) at 50 °C under nitrogen over 3 h and the resulting solution was allowed to react at rt overnight. The solvent was removed under reduced pressure and the residue was treated with excess water. Then it was extracted with CH_2Cl_2 and the solvent was evaporated under vacuum.The crude product **4b** was purified by FCC (10% EtOAc/CH_2Cl_2) to give a yellow solid (12.5 g, 40 mmol, 60 % over two steps). $[\alpha]_D^{22}$ = +4.6 (c = 0.5, $CHCl_3$); mp 171 °C; MS (ESI, 0 V), *m/z* 523 (M + 1, 100 %); IR (KBr) 3307, 3285, 3057, 1807, 1682, 1497, 1337, 1227, 1179, 1157,731, 631 cm^{-1}. ^{1}H-NMR (400 MHz) δ = 8.43-8.36 (m, 6 H, H-Ar), 8.04-7.93 (m, 4 H, H-Ar), 7.47-7.41 (m, 8 H, H-Ar), 4.79-4.61 (m, 4 H, 2 NC*H*$_2$Ar), 3.21 (t, *J* = 8 Hz,1 H, NC*H*(C)CH$_2$), 2.38-2.21 (m, 2 H, NCH(C)C*H*$_2$), 2.07-1.71 (m, 2 H, NCH(C)C*H*$_2$), 1.50 (s, 3 H, C*H*$_3$), 1.45 (brs, 2

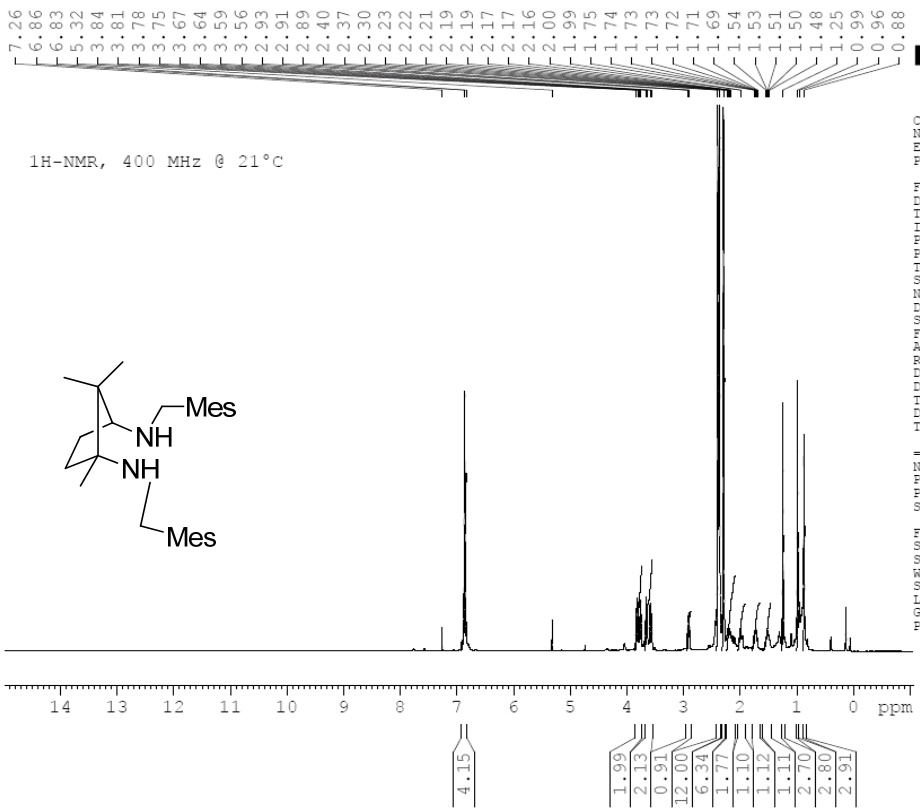
H, 2 NH), 1.05 (s, 3 H, C(CH_3)(CH_3)), 0.87 (s, 3 H, C(CH_3)(CH_3)); ^{13}C-NMR (100 MHz) δ = 132.71 (C-Ar), 132.52 (C-Ar), 131.74 (C-Ar), 131.50 (C-Ar), 129.11 (C-Ar), 127.04 (C-Ar), 125.92 (C-Ar), 124.97 (C-Ar), 124.62 (C-Ar), 124.60 (C-Ar), 68.21 (N*C*(CH_3)(C)CH_2), 65.20 (N*C*H(C)CH_2), 47.69 (CH(C)N*C*H_2Ar), 45.76 (C(CH_3)(C)N*C*H_2Ar), 39.74 (*C*(CH_3)$_2$), 34.77 (NC(CH_3)(C)*C*H_2), 29.38 (NCH(C)*C*H_2), 23.95 (NC(*C*H_3)(C)CH_2), 21.19 (C(*C*H_3)(CH_3)), 17.06 (*C*H_3); HRMS: Anal. calculated for $C_{38}H_{39}N_2^+$: 523.3113, found: 523.3113.





_N_,_N_-Bis(2′,4′,6′-trimethylbenzyl)-1,2,2-trimethylcyclopentane-1,3-diamine (4c)

2,4,6-Trimethylbenzylchloride (0.67 g, 4 mmol, 2 eq.) in dry acetonitrile (20 mL) was added to the stirred solution of diamine (**3**) (0.284 g, 2 mmol) and triethylamine (0.55 ml, 4 mmol, 2 eq.) were added at rt. The resulting mixture was heated at reflux for 20 h. Triethylamine hydrochloride was filtered off and the solvent was removed under vacuum. Excess 2,4,6-trimethylbenzylchloride was separated from the product by FCC on silica gel with CH_2Cl_2 as eluent and the product was eluted with 10% EtOAc/CH_2Cl_2. Evaporation of the solvent gave the title compound **4c** as an oil (0.54 g, 2 mmol, 67 %). $[\alpha]_D^{22}$ = +4.2 (c = 0.5, $CHCl_3$); MS (ESI, 0 V), *m/z* 407 (M+1, 100 %); IR (KBr) 3290, 2960,1724, 1614, 1580, 1447, 1372, 850, 716 cm^{-1}. ^{1}H-NMR (400 MHz) δ = 6.86 (d, J = 12 Hz, 4 H, H-Ar), 3.84-3.56 (m, 4 H, 2 NCH_2Ar), 2.91 (t, J = 8 Hz, 1 H, NCH(C)CH_2), 2.37 (d, J = 12.0 Hz, 12 H, 2(CH_3)$_2$-Ar), 2.23 (s, 6 H, 2(CH_3)-Ar), 2.19-1.47 (m, 4 H, NCH(C)CH_2), 1.25 (s, 3 H, CH_3), 0.96 (s, 3 H, C(CH_3)(CH_3)), 0.88 (s, 3 H, C(CH_3)(CH_3)); ^{13}C-NMR (100 MHz) δ = 137.13 (C-Ar), 136.26 (C-Ar), 136.11 (C-Ar), 134.76 (C-Ar), 134.51 (C-Ar), 128.92 (C-Ar), 68.04 (NC(CH_3)(C)CH_2), 64.31 (NCH(C)CH_2), 47.46 (CH(C)NCH$_2$Ar), 40.91 (C(CH_3)(C)NCH$_2$Ar), 34.12 (C(CH_3)$_2$), 28.87 (NC(CH_3)(C)CH$_2$), 23.87(CH_3-Ar), 20.98 (NCH(C)CH$_2$), 20.60 (NC(CH$_3$)(C)CH_2), 19.54 ((CH_3)$_2$-Ar), 19.53 (C(CH$_3$)(CH_3)), 16.77 (CH$_3$).

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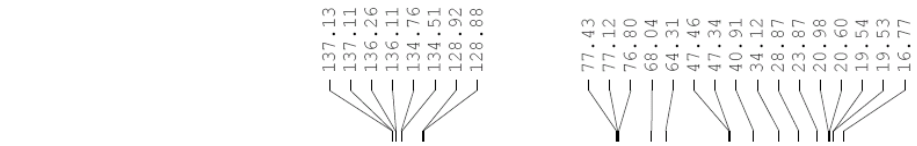

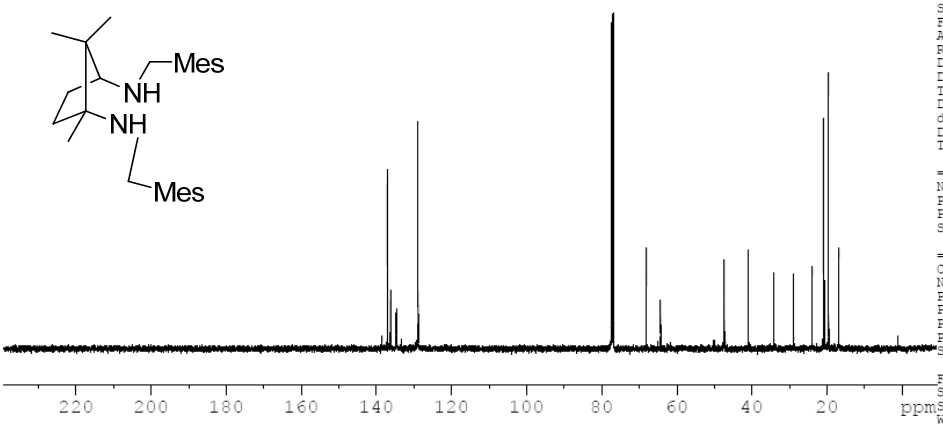


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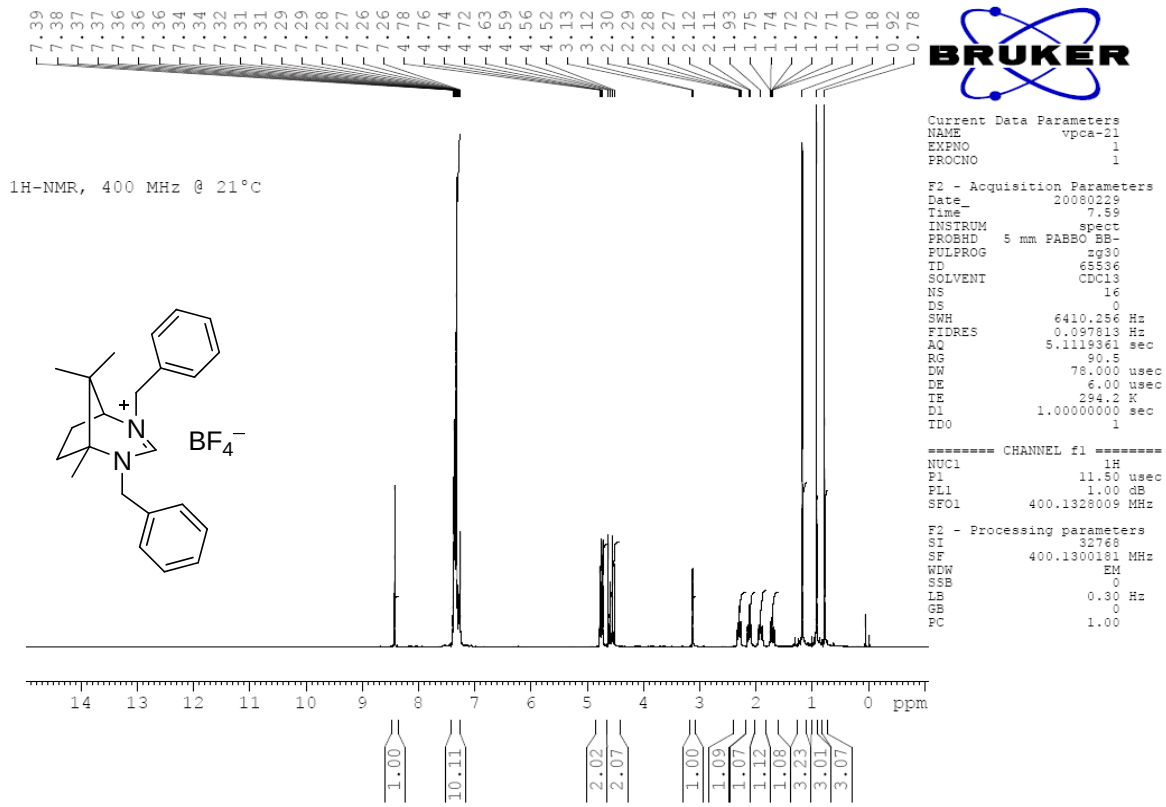
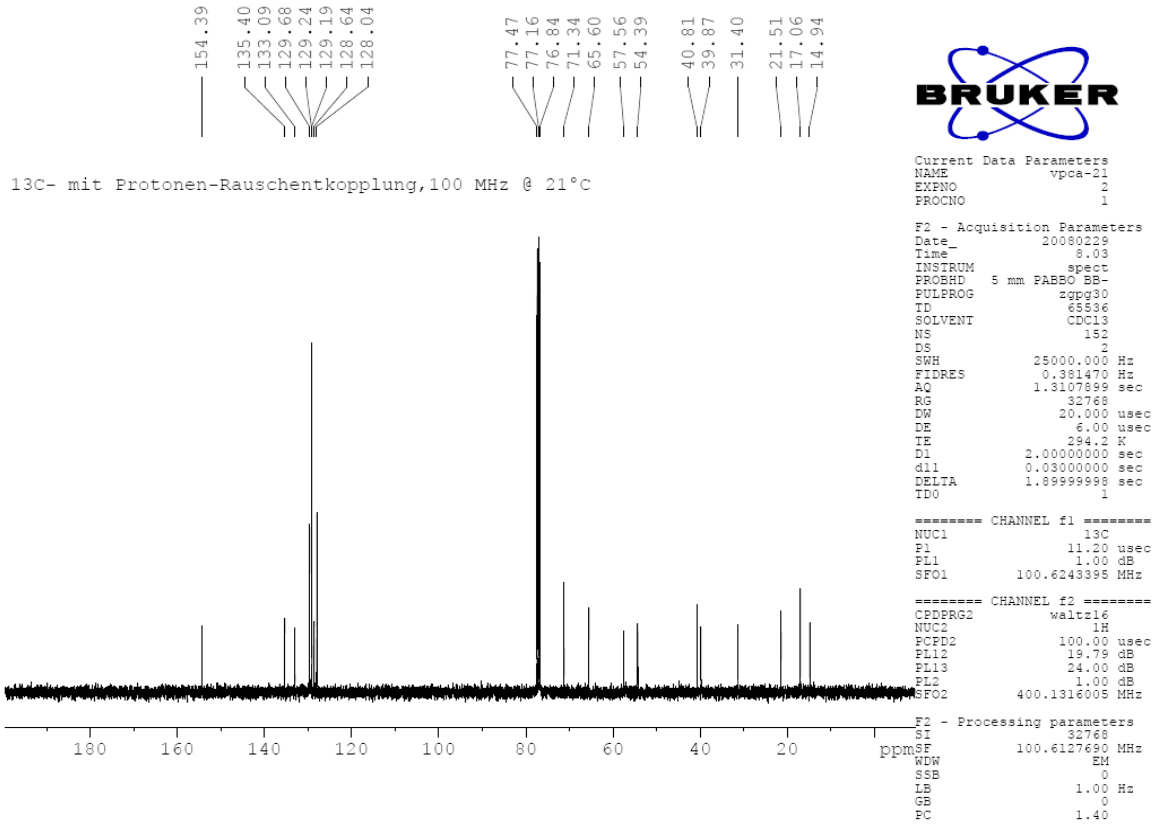
2,4-Dibenzyl-5,8,8-trimethyl-4-aza-2-azonia-bicyclo[3.2.1]oct-2-ene tetrafluoroborate (5a)

N,*N*-Dibenzyl-1,2,2-trimethylcyclopentane-1,3-diamine (**4a**) (1.02 g, 3.16 mmol), triethyl orthoformate (0.53 mL, 3.16 mmol, 1 eq.) and ammonium tetrafluoroborate (331 mg, 3.16 mmol, 1eq.) were heated for 2 h at 120 °C in a closed vessel. Recrystallization in dry ethanol gave white needles (698 mg, 1.67 mmol, 53 %). $[\alpha]_D^{22}$ = +39.0 (c = 0.94, $CHCl_3$); mp 167 °C; IR (KBr) 2986, 1662, 1453, 1402, 1067, 706 cm^{-1}. MS (ESI, 0 V), *m/z* 333 (M+, 100 %); ^{1}H-NMR (400 MHz) δ = 8.47 (s, 1 H, NC*H*N), 7.38-7.31 (m, 10 H, H-Ar), 4.82-4.42 (m, 4 H, 2 NCH_2Ar), 3.12 (d, *J* = 4.6 Hz, 1 H, NC*H*(C)CH_2), 2.34-1.67 (m, 4 H, NCH(C)CH_2), 1.22 (s, 3 H, CH_3), 0.92 (s, 3 H, C(CH_3)(CH_3)), 0.78 (s, 3 H, C(CH_3)(CH_3)); ^{13}C-NMR (100 MHz) δ = 154.39 (*C*HN_2), 135.40 (C-Ar), 133.09 (C-Ar), 129.68 (C-Ar), 129.24 (C-Ar), 128.64 (C-Ar), 128.04 (C-Ar), 71.34 (N*C*(CH_3)(C)CH_2), 65.60 (N*C*H(C)CH_2), 57.56 (CH(C)N*C*H_2Ar), 54.39 (C(CH_3)(C)N*C*H_2Ar), 40.81 (*C*(CH_3)$_2$), 39.87 (NC(CH_3)(C)*C*H_2), 31.40 (NCH(C)*C*H_2), 21.51 (NC(*C*H_3)(C)CH_2), 17.06 (C(*C*H_3)(CH_3)), 14.94 (*C*H_3); Anal. calculated for $C_{23}H_{29}N_2BF_4$: C, 65.73; H, 6.95; N, 6.67, found: C, 65.64; H, 7.01; N, 6.68.

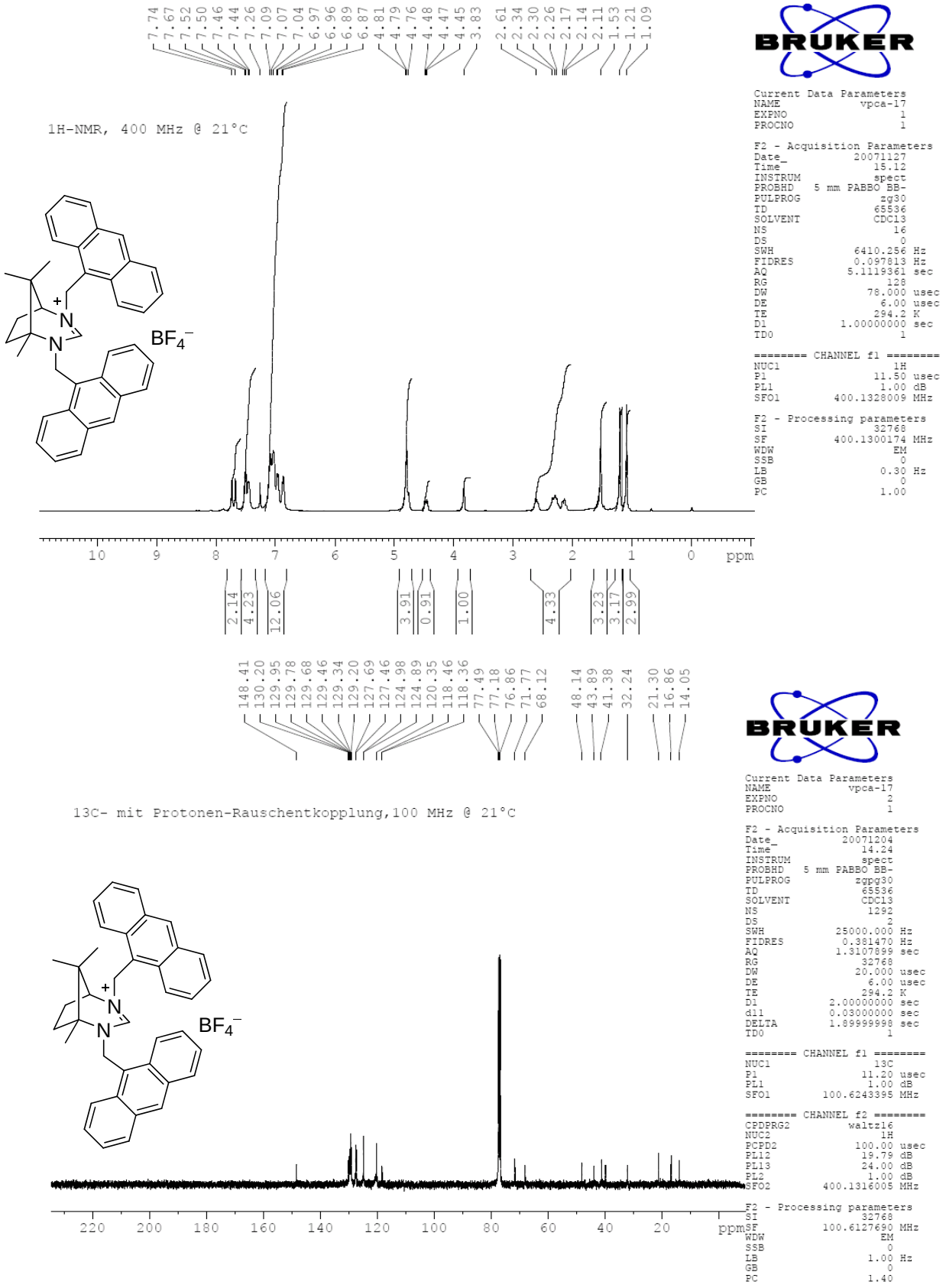




2,4-Bis(anthracen-9-ylmethyl)-5,8,8-trimethyl-4-aza-2-azonia-bicyclo[3.2.1]oct-2-ene tetrafluoroborate (5b)

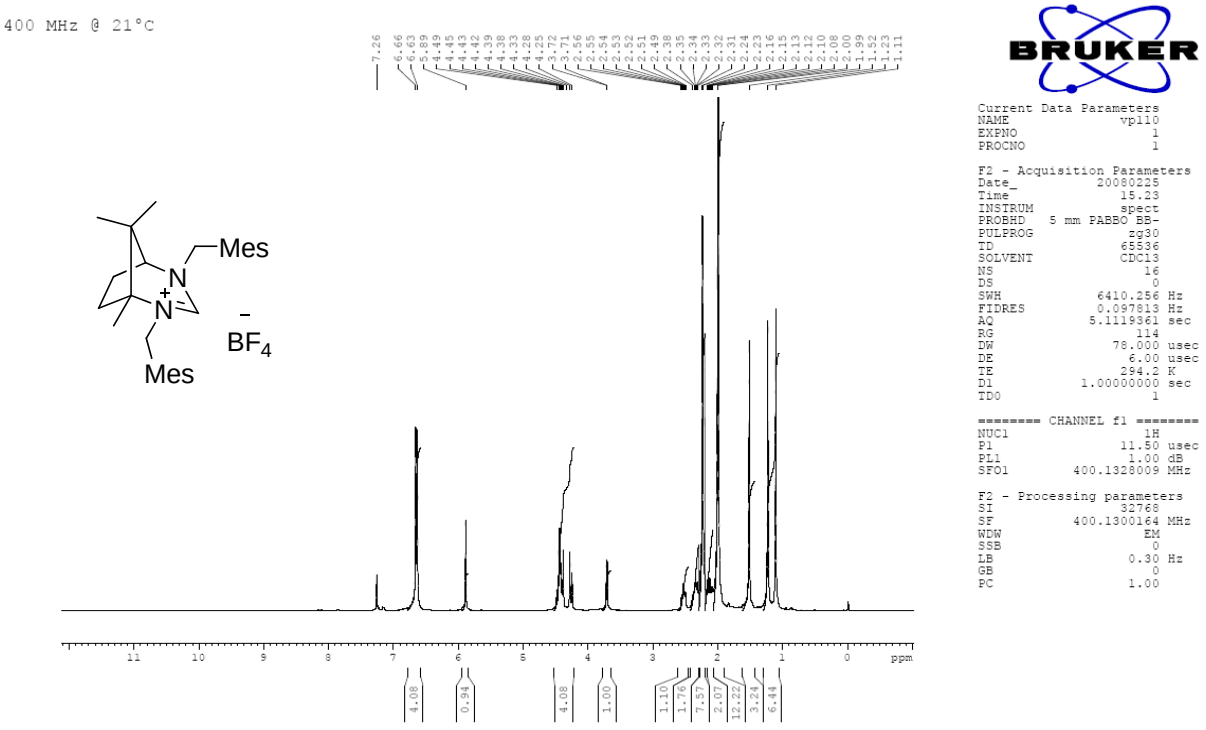
N,*N*-Bis(anthracen-9-ylmethyl)-1,2,2-trimethylcyclopentane-1,3-diamine (**4b**) (0.52 g, 1 mmol), triethylorthoformate (0.2 mL, 1.2 mmol, 1.2 eq.) and ammonium tetrafluoroborate (104 mg, 1 mmol, 1 eq.) were heated in dry toluene (10 mL) for 5 h at 100 °C in a closed vessel. The product was filtered and then washed twice with diethyl ether and hexane to give a yellow solid (0.43g, 1 mmol, 70 %). $[\alpha]_D^{22}$ = +38.0 (c = 0.5, $CHCl_3$); mp 197-198 °C; IR (KBR) 3156, 3056, 2985, 1815, 1672, 1297, 1194, 1160,729, 668, 634 cm^{-1}. MS (ESI, 0 V), *m/z* 533 (M+, 100 %); ^{1}H-NMR (400 MHz) δ = 7.74-7.44 (m, 6 H, H-Ar), 7.09-6.87 (m, 12 H, H-Ar), 4.81-4.76 (m, 3 H, NCH_2Ar), 4.79 (s, 1 H, NC*H*N, assigned by HSQC), 4.47 (d, *J* = 8 Hz, 1 H, NCH_2Ar), 3.83 (s, 1 H, NC*H*(C)CH_2), 2.61-2.11 (m, 4 H, NCH(C)CH_2), 1.53 (s, 3 H, CH_3), 1.21 (s, 3 H, C(CH_3)(CH_3)), 1.09 (s, 3 H, C(CH_3)(CH_3)); ^{13}C-NMR (100 MHz) δ = 148.41 (*C*HN_2), 130.20 (C-Ar), 1290.95 (C-Ar), 129.78 (C-Ar), 129.68 (C-Ar), 129.46 (C-Ar), 129.34 (C-Ar), 129.20 (C-Ar), 127.69 (C-Ar), 127.46 (C-Ar), 124.98 (C-Ar), 124.89 (C-Ar), 120.35 (C-Ar), 118.46 (C-Ar), 118.36 (C-Ar), 71.77 (N*C*(CH_3)(C)CH_2), 68.12 (N*C*H(C)CH_2), 48.14 (CH(C)N*C*H_2Ar), 43.89 (C(CH_3)(C)N*C*H_2Ar), 41.38 (*C*(CH_3)$_2$), 39.95 (NC(CH_3)(C)*C*H_2), 32.24 (NCH(C)*C*H_2), 21.30 (NC(*C*H_3)(C)CH_2), 16.86 (C(*C*H_3)(CH_3)),

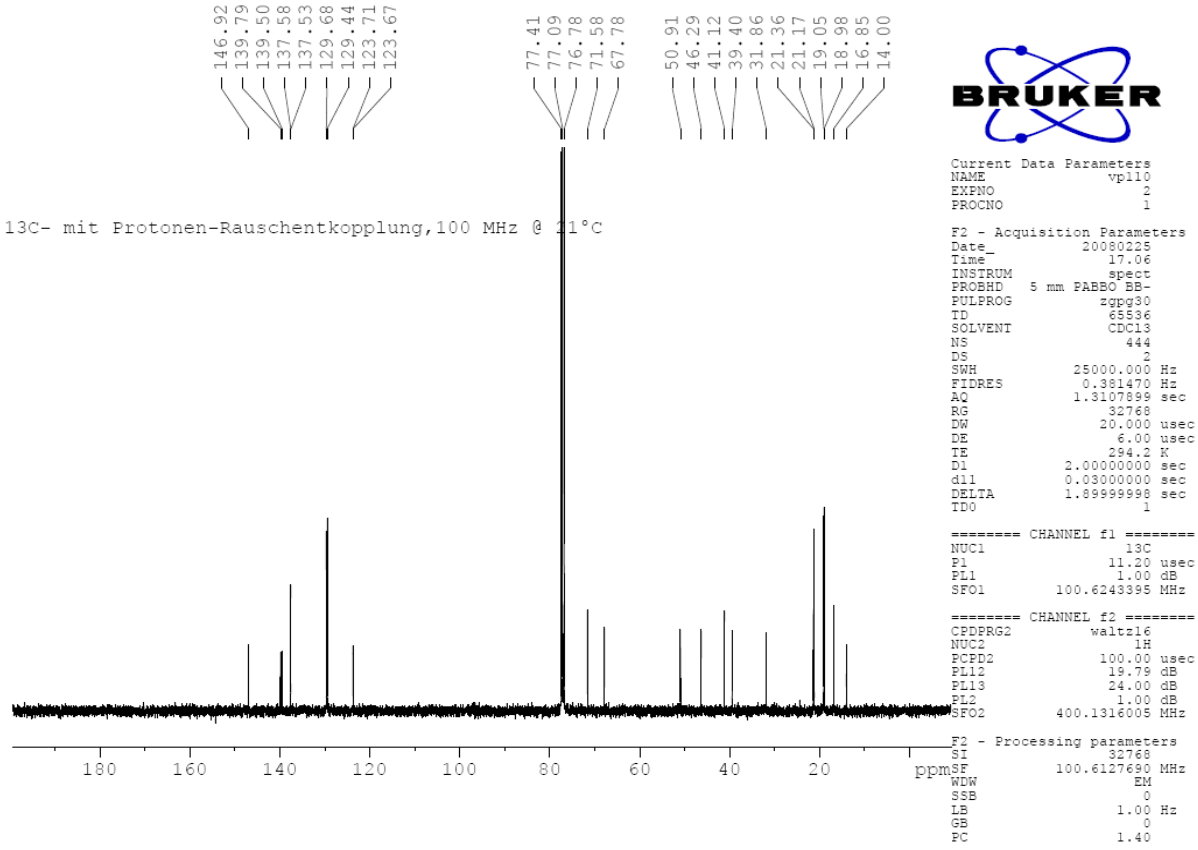
14.05 (CH_3); Anal. calculated for $C_{39}H_{37}N_2BF_4$: C, 75.49; H, 6.01; N, 4.51, found: C, 75.02; H, 6.48; N, 4.39. HRMS: Anal. calculated for $C_{39}H_{37}N_2^+$: 533.2957, found: 533.2938.



2,4-Bis(2′,4′,6′-trimethylbenzyl)-5,8,8-trimethyl-4-aza-2-azonia-bicyclo[3.2.1]oct-2-ene tetrafluoroborate (5c)

N,*N*-Bis(2′,4′,6′-trimethylbenzyl)-1,2,2-trimethylcyclopentane-1,3-diamine (**4c**) (0.41 g, 1 mmol), triethylorthoformate (0.2 mL, 1.2 mmol, 1.2 eq.) and ammonium tetrafluoroborate (104 mg, 1 mmol, 1eq.) were heated in dry toluene (5 mL) for 5 h at 100 °C in a closed vessel. The product was filtered and then washed twice with diethyl ether and hexane to give a white solid (317 mg, 1 mmol, 63%). $[\alpha]_D^{22}$ = +35 (c = 0.5, $CHCl_3$); mp 188-189 °C; IR (KBR) 3078, 2981, 1673, 1614, 1583, 1196, 955, 897, 722 cm^{-1}. MS (ESI, 0 V), *m/z* 417 (M+, 100 %); ^{1}H-NMR (400 MHz) δ = 6.66 (d, *J*= 12 Hz, 4 H, H-Ar), 5.89 (s, 1 H, NC*H*N, assigned by HSQC), 4.49-4.25 (m, 4 H, 2 NCH_2Ar), 3.72 (d, *J* = 4.0 Hz, 1 H, NC*H*(C)CH_2), 2.56-2.31 (m, 2 H, NCH(C)CH_2), 2.24 (d, *J*= 12 Hz, 6 H, 2 (CH_3)-Ar), 2.16-2.08 (m, 2 H, NCH(C)CH_2), 2.00 (d, *J*= 4 Hz, 12 H, 2(CH_3)$_2$-Ar), 1.52 (s, 3 H, CH_3), 1.23 (s, 3 H, C(CH_3)(CH_3)), 1.11 (s, 3 H, C(CH_3)(CH_3)); ^{13}C-NMR (100 MHz) δ = 146.92 (*C*HN_2), 139.79 (C-Ar), 139.50 (C-Ar), 137.58 (C-Ar), 129.68 (C-Ar), 129.44 (C-Ar), 123.71 (C-Ar), 71.58 (NC(CH_3)(C)CH_2), 67.78 (N*C*H(C)CH_2), 50.91 (CH(C)N*C*H_2Ar), 46.29 (C(CH_3)(C)N*C*H_2Ar), 41.12 (*C*(CH_3)$_2$), 39.40 (NC(CH_3)(C)*C*H_2), 31.86 (NCH(C)*C*H_2), 21.36 (CH_3-Ar), 19.05 (NC(*C*H_3)(C)CH_2), 18.98 ((CH_3)$_2$-Ar), 16.85 (C(*C*H_3)(CH_3)), 14.00 (*C*H_3). HRMS: Anal. calculated for $C_{29}H_{41}N_2^+$: 417.3270, found: 417.3262.





2-Methyl-4-(2′,4′,6′-trimethylbenzyl)-1,8,8-trimethyl-2,4-diaza-bicyclo[3.2.1]oct-2-ene iodide (7)

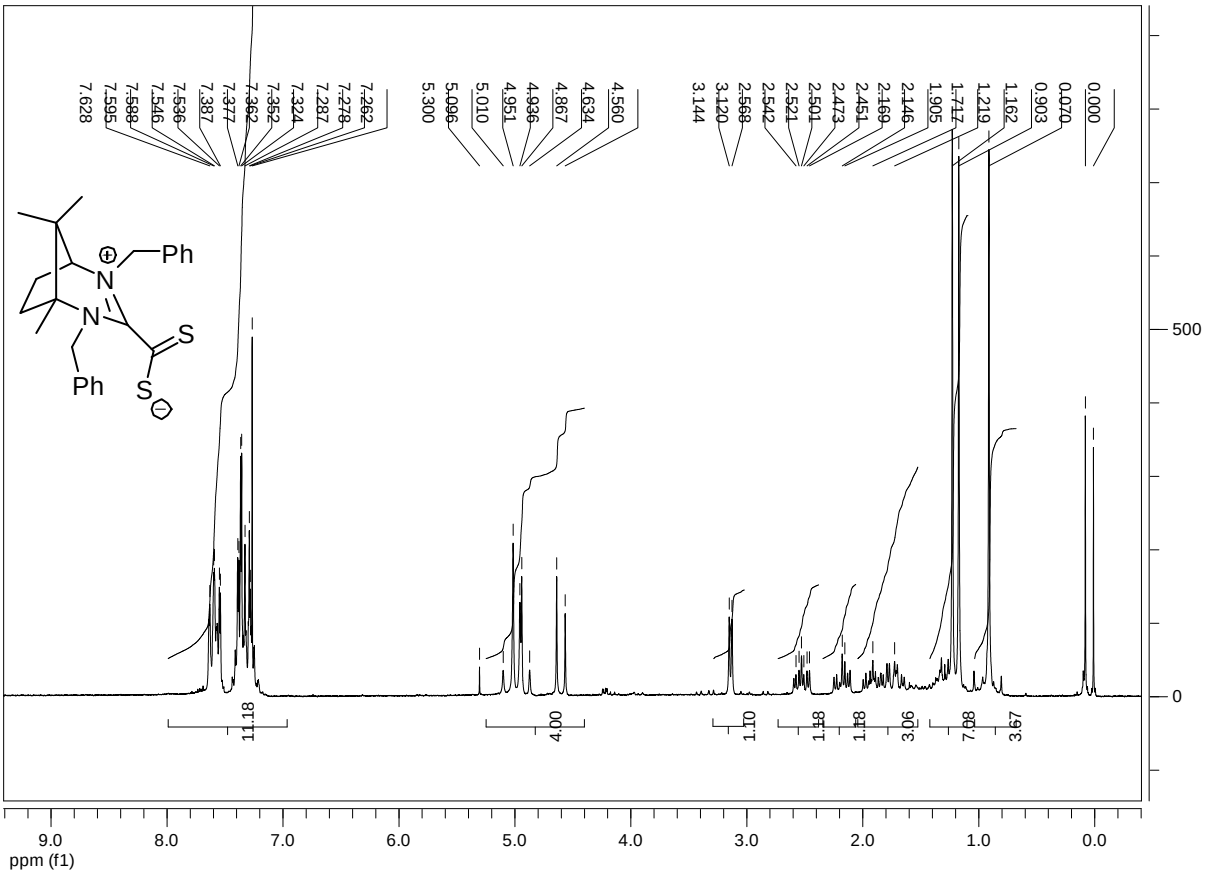
To a stirred solution of diamine (**3**) (0.56 g, 4 mmol) in dry CH_3CN (20 mL) was added 2,4,6-trimethylbenzylchloride (0.67 g, 4 mmol, 1 eq.) and triethylamine (0.6 mL, 4 mmol) at rt. The resulting mixture was refluxed overnight. The mixture was cooled to rt and water was then added and the impure product was extracted into CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and the solvent was removed to give a brown oil (0.76 g, 4 mmol, 69 %). The brown oil obtained was directly used in the next step.

A mixture of the diamine (0.55 g, 2 mmol), triethylorthoformate (0.8 mL, 5 mmol, 2.5 equiv) and acetic acid (0.3 mL, 5 mmol, 2.5 equiv) in CH_3CN (10 mL) was refluxed for 2 h under nitrogen. The resulting mixture was then allowed to cool to rt before being concentrated to dryness, taken up in 40% aqueous KOH (10 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were then dried with KOH pellets, filtrated, and concentrated to dryness. The residue was washed with diethyl ether and impurities were filtered off, the solvent was evaporated under reduced pressure to give a brown oil (**7**, 0.40 g, 2 mmol, 71%). The brown oil obtained was directly used in the next step.

The compound **7** (0.284 g, 1 mmol) and CH_3I (0.6 mL, 10 mmol, 10 eq.) in CH_3CN (8 mL) were refluxed for 5 h. After cooling to room temperature, the solvent was removed under reduced pressure to obtain the product **7** which was washed with diethyl ether to give a solid compound (0.33 g, 1 mmol, 78%). $[\alpha]_D^{22}$ = +16.0 (c = 0.60, $CHCl_3$); mp 101-102 °C; MS (ESI, 0 V), *m/z* 299 (M+, 100 %); ^{1}H-NMR (200 MHz) δ = 8.94 (s, 1 H, NC*H*N), 6.80 (d, *J*= 12 Hz, 2 H, H-Ar), 4.79-4.55 (m, 2 H, NC*H*$_2$Ar), 3.89-3.80 (m, 1 H, NC*H*(C)CH$_2$), 2.56-2.01 (m, 4 H, NCH(C)C*H*$_2$), 2.40 (s, 3 H, 2 (CH$_3$)-Ar), 2.00 (s, 6 H, 2 (CH$_3$)$_2$-Ar), 1.21 (s, 3 H, CH$_3$), 1.01 (s, 3 H, C(CH$_3$)(C*H*$_3$)), 0.83 (s, 3 H, C(C*H*$_3$)(CH$_3$)); ^{13}C-NMR (50 MHz) δ = 153.30 (*C*HN$_2$), 139.23 (C-Ar), 138.17 (C-Ar), 129.99 (C-Ar), 129.77 (C-Ar), 125.40 (C-Ar), 70.12 (N*C*(CH$_3$)(C)CH$_2$), 64.25 (N*C*H(C)CH$_2$), 50.64 (CH(C)N*C*H$_2$Ar), 41.09 ((CH$_3$)N), 38.60 (C(CH$_3$)(C)N*C*H$_2$Ar), 37.60 (*C*(CH$_3$)$_2$), 30.71 (NC(CH$_3$)(C)*C*H$_2$), 21.92 (NCH(C)*C*H$_2$), 21.10 (CH$_3$-Ar), 20.57 ((CH$_3$)$_2$-Ar), 16.95 (C(*C*H$_3$)(CH$_3$)), 14.39 (*C*H$_3$). HRMS: Anal. Calculated for $C_{20}H_{31}N_2^+$: 299.2487, found: 299.2486.

2,4-Dibenzyl-5,8,8-trimethyl-4-aza-2-azonia-bicyclo[3.2.1]oct-2-en-2-ium-3-carbodithioate (8):

Dry toluene (4 mL), and KHMDS (1.5 eq.) were added and stirred for 30 min. CS_2 (0.95 mL, 15.8 mmol, 5 eq.) was added and the mixture became reddish. Water was added, the aqueous layer was extracted 3 times with CH_2Cl_2 and the combined organic layers were dried (Na_2SO_4). The solvent was removed. The obtained product was columned with CH_2Cl_2 to give a red solid (481 mg, 1.16 mmol, 37 %). $[\alpha]_D^{22}$ = –91.4 (c = 0.98, $CHCl_3$); mp 185 °C; MS (EI), *m/z* 407 (M+, 50%), 331 (21), 316 (100), 109 (29), 91 (90); IR (KBr) 2967, 1556, 1452, 1346, 1261, 1054, 704 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.62-7.65 (m, 4 H, H-Ar), 7.41-7.25 (m, 6 H, H-Ar), 5.06-4.58 (m, 4 H, 2 NC*H*$_2$Ar), 3.13 (d, *J* = 5 Hz, 1 H, NC*H*(C)CH$_2$), 2.52 (m, 1 H, NC(CH$_3$)(C)C*H*$_2$), 2.17 (m, 1 H, NC(CH$_3$)(C)C*H*$_2$), 1.90 (m, 1 H, NCH(C)C*H*$_2$), 1.72 (m, 1 H, NCH(C)C*H*$_2$), 1.22 (s, 3 H, (C(C*H*$_3$)(CH$_3$)), 1.16 (s, 3 H, (C(CH$_3$)(C*H*$_3$)), 0.90 (s, 3 H, C*H*$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 232.53 (*C*S$_2$), 164.57 (*C*N$_2$), 137.24 (C-Ar), 133.90 (C-Ar), 129.61 (C-Ar), 128.74 (C-Ar), 128.68 (C-Ar), 128.43 (C-Ar), 127.60 (C-Ar), 127.51 (C-Ar), 72.28 (N*C*(CH$_3$)(C)CH$_2$), 65.04 (N*C*H(C)CH$_2$), 55.77 (CH(C)N*C*H$_2$Ar), 52.70 (C(CH$_3$)(C)N*C*H$_2$Ar), 41.70 (*C*(CH$_3$)$_2$), 38.60 (NC(CH$_3$)(C)*C*H$_2$), 30.03 (NCH(C)*C*H$_2$), 22.21 (NC(*C*H$_3$)(C)CH$_2$), 17.24 (C(*C*H$_3$)(CH$_3$)), 16.46 (C(CH$_3$)(*C*H$_3$)); Anal. calculated for $C_{24}H_{28}N_2S_2$: C, 70.54; H, 6.91; N, 6.86, found: C, 70.17; H, 6.78; N, 6.58.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4.936
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4.634
4.560
3.144
3.120
2.569
2.542
2.521
2.501
2.473
2.451
2.169
2.146
1.905
1.717
1.219
1.162
0.903
0.070
0.000
Ph
N
N
S
Ph
S
11.18
4.00
1.10
1.18
1.84
3.06
7.88
3.67
500
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7.0
6.0
5.0
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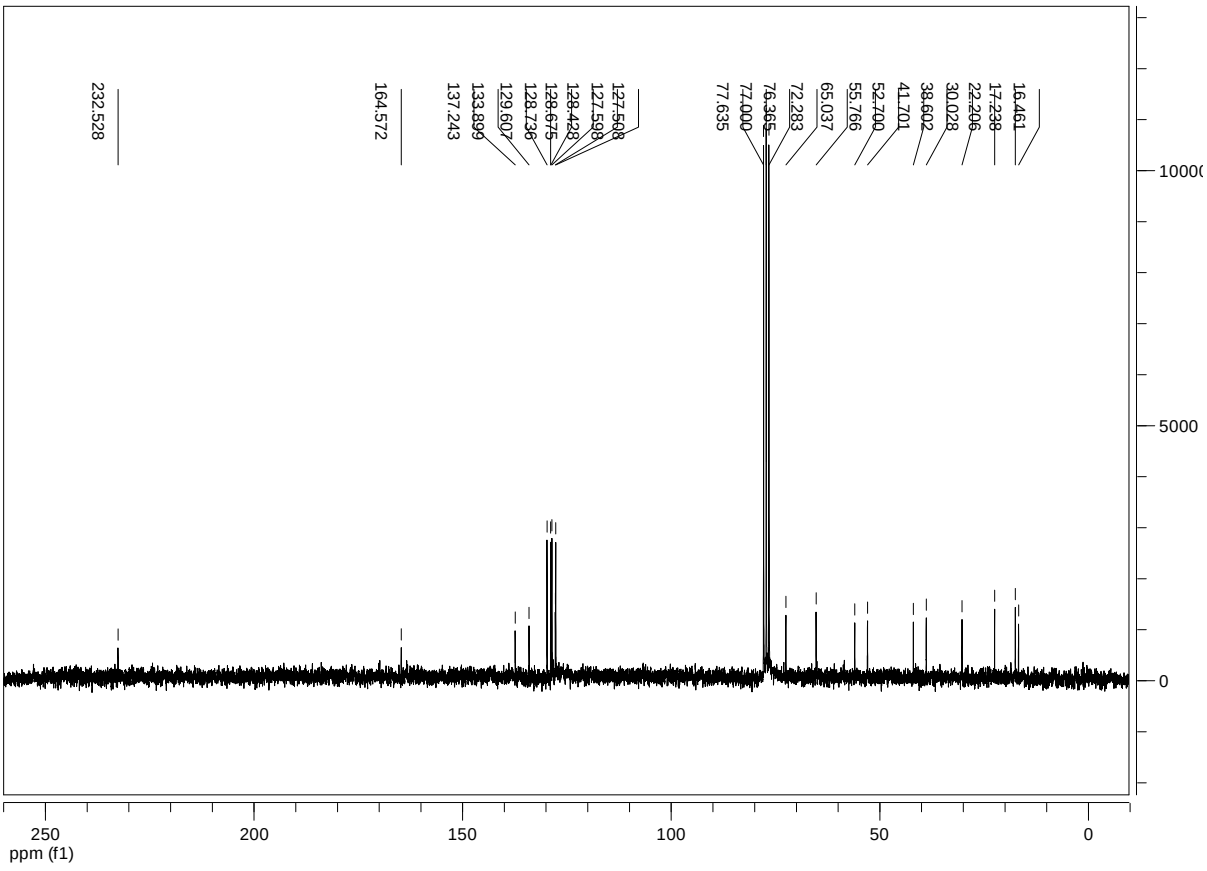
3.0
2.0
1.0
0.0
ppm (f1)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133.899
129.607
128.736
128.675
128.428
127.598
127.508
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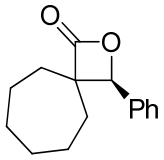
72.283
65.037
55.766
52.700
41.701
38.602
30.028
22.206
17.238
16.461
10000
5000
0
250
200
150
100
50
0
ppm (f1)

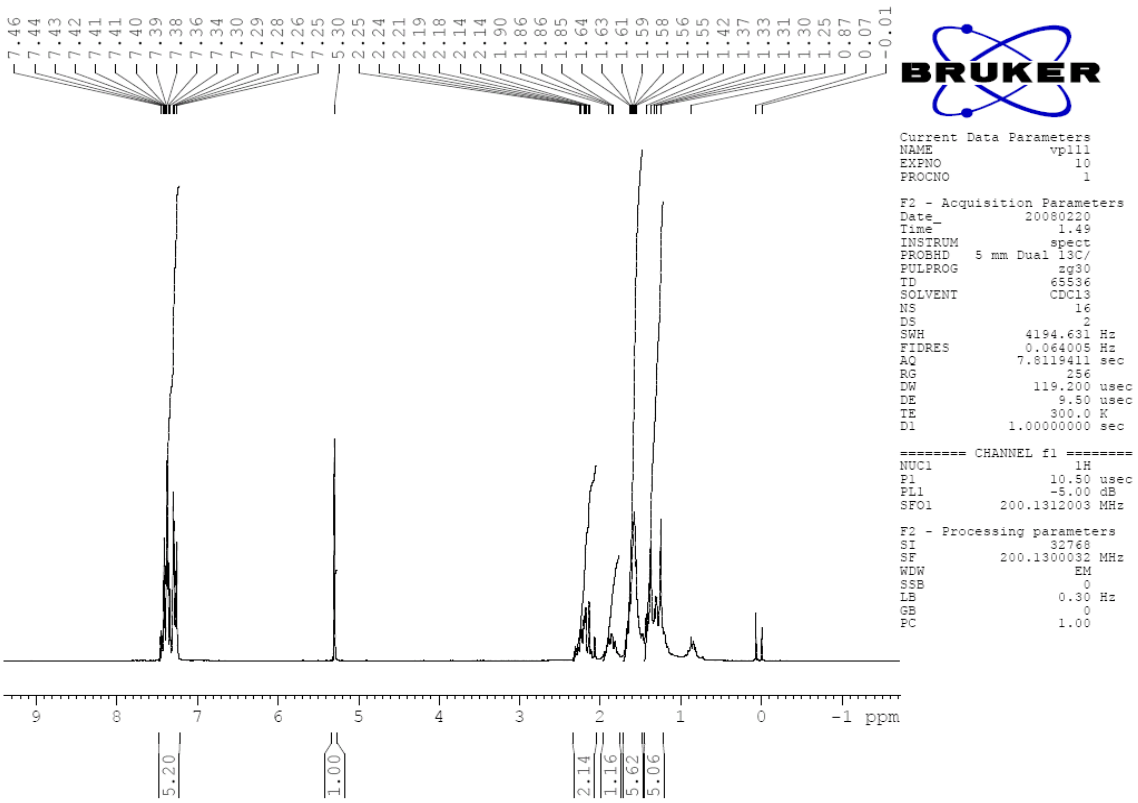
General procedure for the carbene catalyzed reaction of ketenes with aldehydes

Salt **5b** (38 mg, 0.06 mmol, 10 mol%) was placed into a dry Schlenk flask and dry toluene (2 mL) was added. The suspension was cooled to −60 °C and KHMDS (48 μL, 0.024 mmol, 8 mol%) was slowly added. The mixture was stirred for 1.5 h at −60 °C or 30 min at rt, then benzaldehyde **10** (30 μL, 0.03 mm0l) and hexamethyleneketene **9** (93 mg, 0.0075 mmol) were added. The reaction mixture was stirred for 10 min (for differences in reaction times and temperatures see Table 1 and Table 2) and the solvent was removed under reduced pressure giving the crude product, which was purified by FCC (diethyl ether/hexane, 2/98) giving the corresponding lactone **11**.

3,3- Spirocycloheptyl-4-phenyl-oxetan-2-one (13) (Table 2, Entry 1)



Yield 76%, 92% *ee*; $[\alpha]_D^{22}$ = +20.0 (c = 0.5, CH_2Cl_2); mp 55-56 °C; ^{1}H-NMR (400 MHz) δ = 7.46-7.25 (m, 5 H, H-Ar), 5.30 (s, 1 H), 2.25-2.14 (m, 2 H), 1.90-1.85 (m, 2 H), 1.64-1.55 (m, 4 H), 1.42-1.25 (m, 4 H); ^{13}C-NMR (100 MHz) δ = 175.48, 135.49, 128.71, 125.85, 84.18, 63.96, 35.42, 30.41, 29.82, 29.12, 29.09, 23.79, 22.86. Spectral data were consistent with literature values.[4] Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 1% *i*PrOH/hexane: (*R*) t_1 = 11.1 min, (*S*) t_2 = 16.3 min.


7.46 7.44 7.43 7.42 7.41 7.41 7.40 7.39 7.38 7.36 7.34 7.30 7.29 7.28 7.26 7.25 5.30 2.25 2.24 2.21 2.19 2.18 2.14 2.14 1.90 1.86 1.86 1.85 1.64 1.63 1.61 1.59 1.58 1.56 1.55 1.42 1.37 1.33 1.31 1.30 1.25 0.87 0.07 -0.01
BRUKER
Current Data Parameters
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PROCNO 1
F2 - Acquisition Parameters
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PULPROG zg30
TD 65536
SOLVENT CDCl3
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DS 2
SWH 4194.631 Hz
FIDRES 0.0640005 Hz
AQ 7.8119411 sec
RG 256
DW 119.200 usec
DE 9.50 usec
TE 300.0 K
D1 1.00000000 sec
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PL1 -5.00 dB
SFO1 200.1312003 MHz
F2 - Processing parameters
SI 32768
SF 200.1300032 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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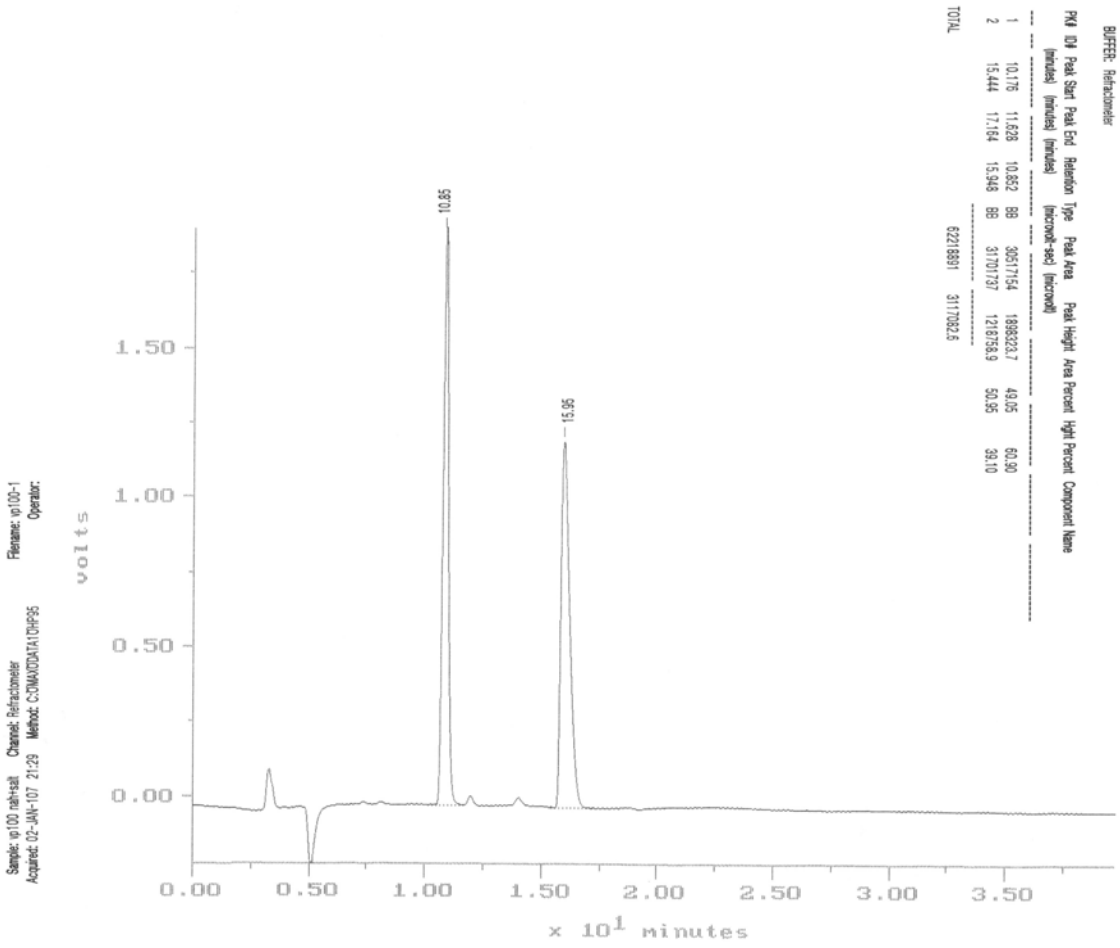
5.20 1.00 2.14 1.16 5.62 5.06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0.00 0.50 1.00 1.50 2.00 2.50 3.00 3.50
x 10^1 minutes
BUFFER: Refractometer
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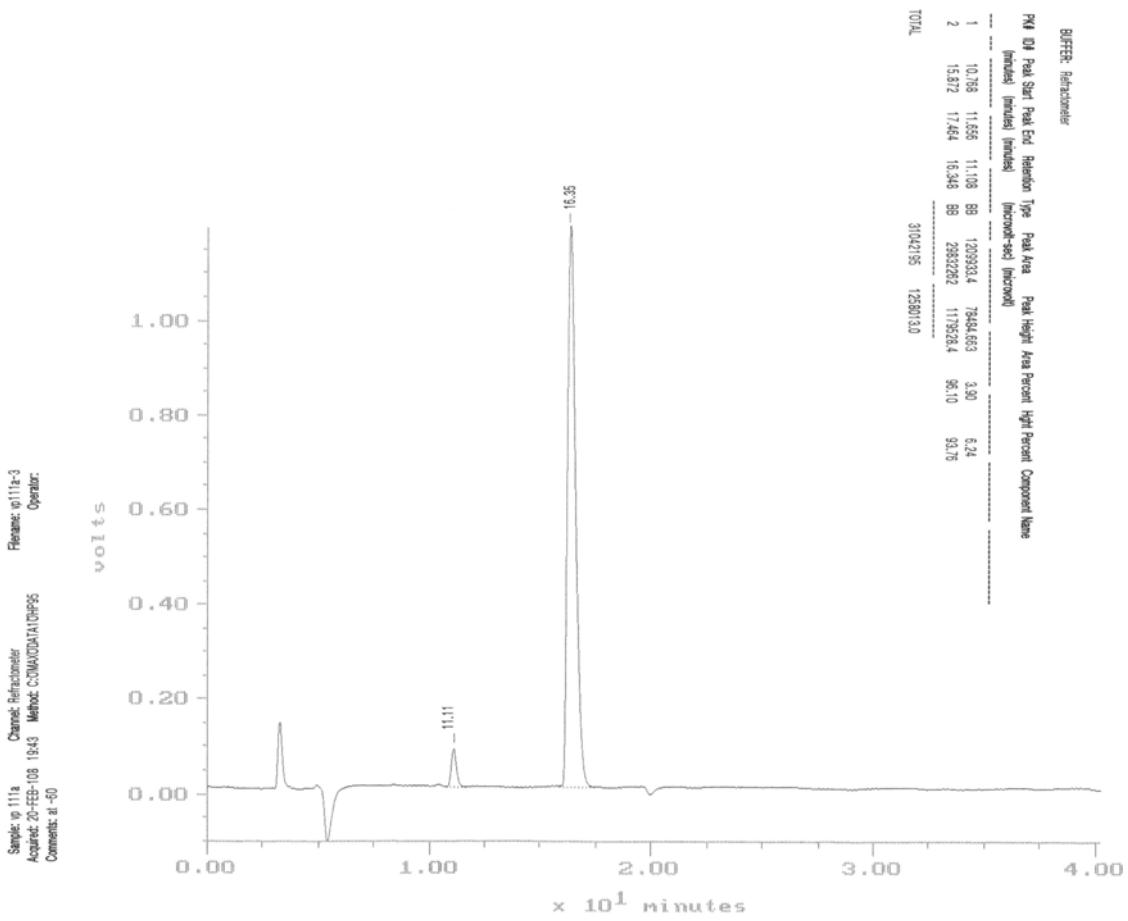
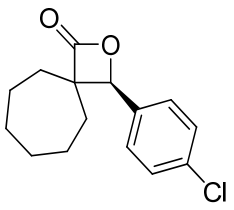
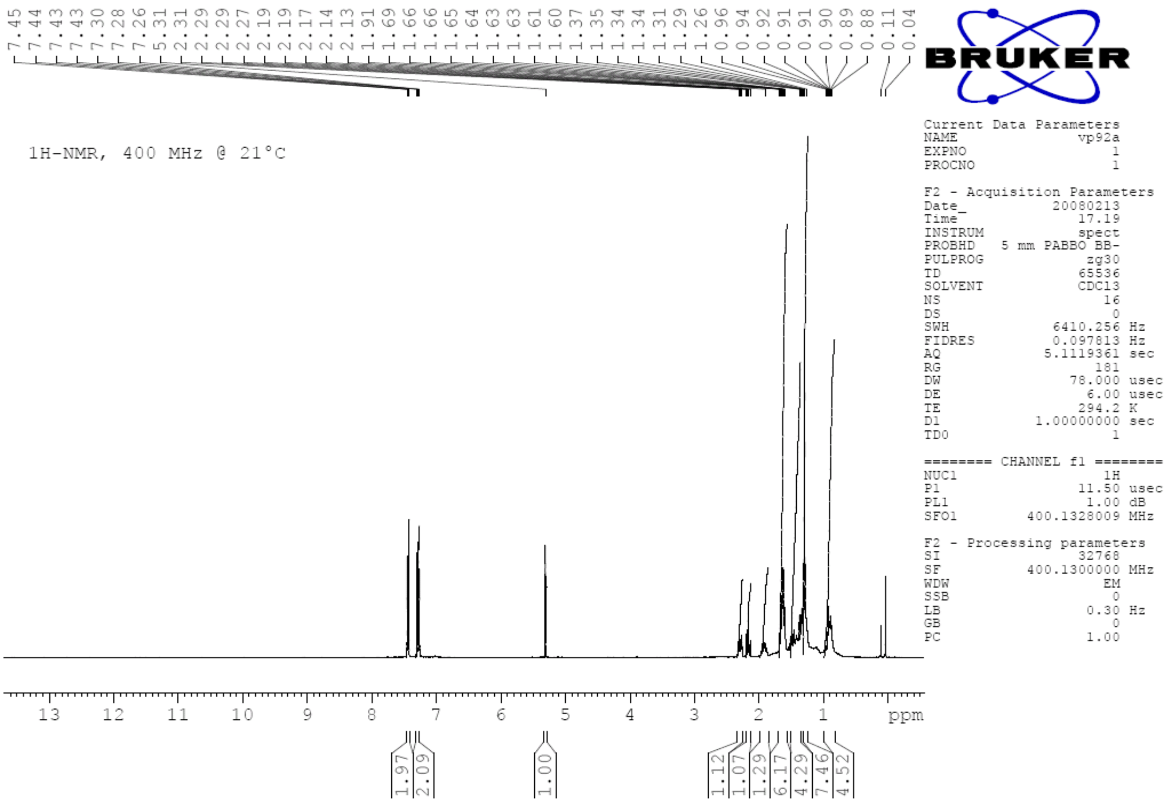
TOTAL 62219891 3117082.5



3,3- Spirocycloheptyl-4-(4-chlorophenyl)-oxetan-2-one (Table 2, Entry 5)



Oil, Yield 80%, 81% *ee*; $[\alpha]_D^{22}$ = +7.2 (c = 0.50, CH_2Cl_2); IR (NaCl) 1827, 1460, 1092, 940 cm^{-1}; ^{1}H-NMR (400 MHz) δ = 7.45 (d, *J*= 8.0 Hz, 2 H, Ar-H), 7.30 (d, *J*= 8.0 Hz, 2 H-Ar), 5.31 (s, 1 H), 2.31-2.27 (m, 1 H), 2.19-2.13 (m, 1 H), 1.90-1.85 (m, 1 H), 1.69-1.60 (m, 4 H), 1.37-1.26 (m, 5 H); ^{13}C-NMR (100 MHz) δ = 174.96, 134.44, 133.95, 128.93, 127.145, 83.40, 64.10, 35.22, 30.25, 29.74, 29.03, 28.98, 23.66, 22.74. Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 1% *i*PrOH/hexane: (*R*) t_1 = 11.8 min, (*S*) t_2 = 16.0 min.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BRUKER
Current Data Parameters
NAME vp92a
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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Time 17.19
INSTRUM spect
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PULPROG zg30
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SOLVENT CDCl3
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SWH 6410.256 Hz
FIDRES 0.097813 Hz
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RG 181
DW 78.000 usec
DE 6.00 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.50 usec
PL1 1.00 dB
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
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GB 0
PC 1.00
ppm
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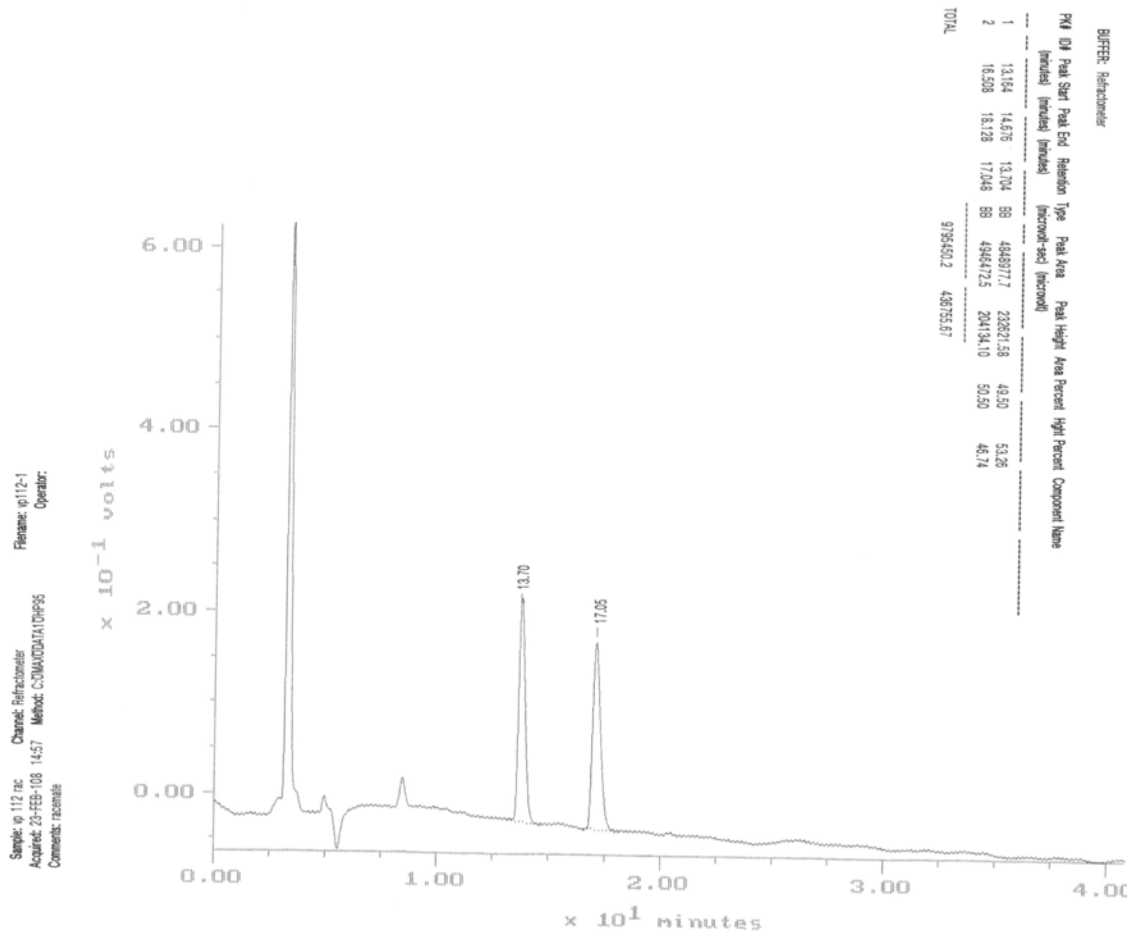
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2 16.508 18.128 17.048 BB 4946472.5 204134.10 50.50 46.74
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17.05
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Acquired: 23-FEB-108 14:57
Comments: racemate
Channel: Refractometer
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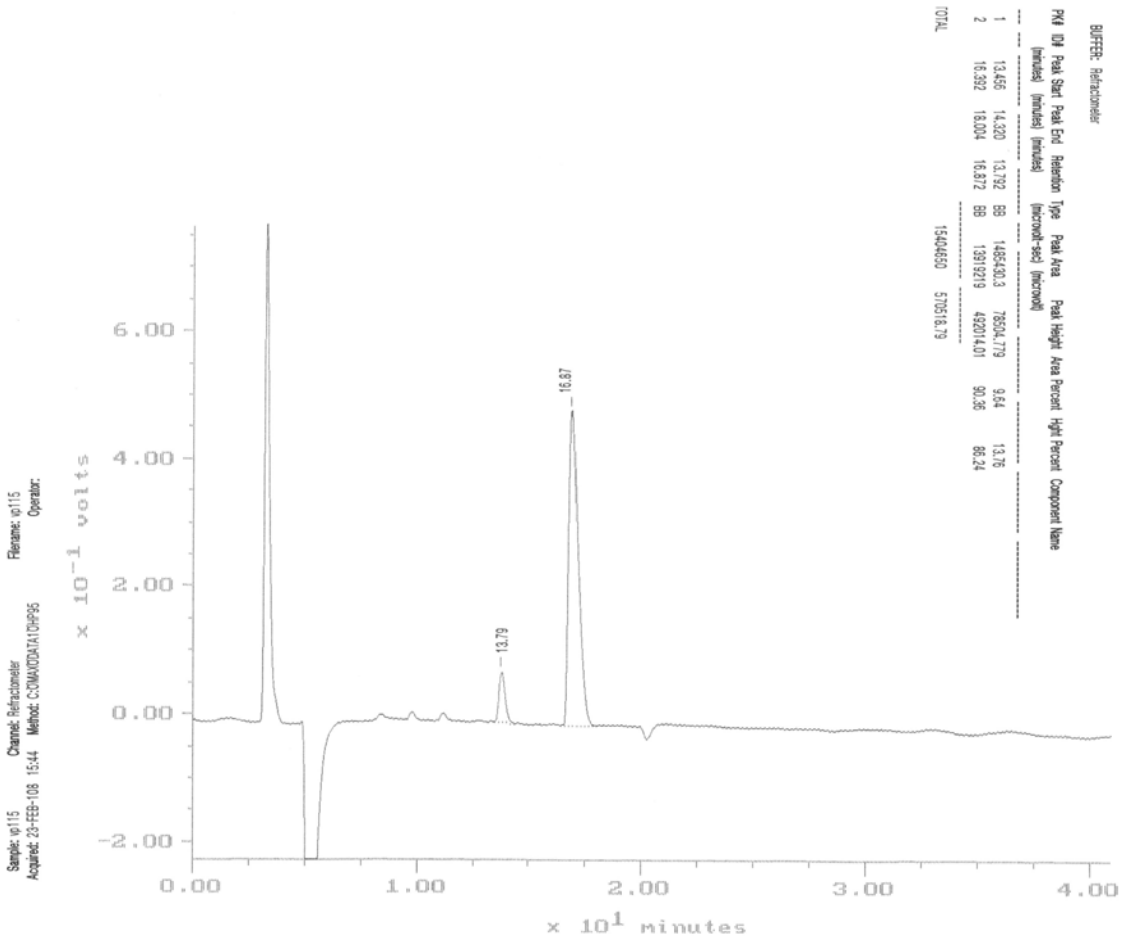
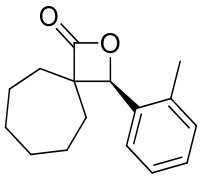
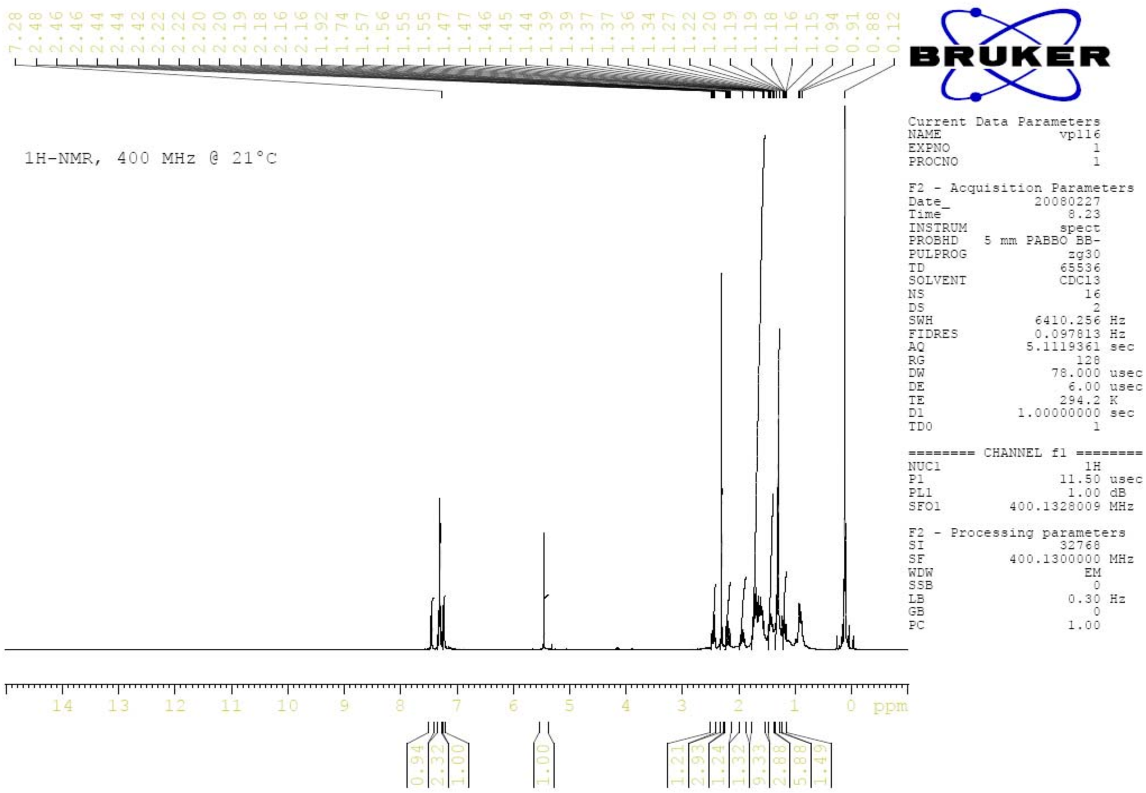
Operator:

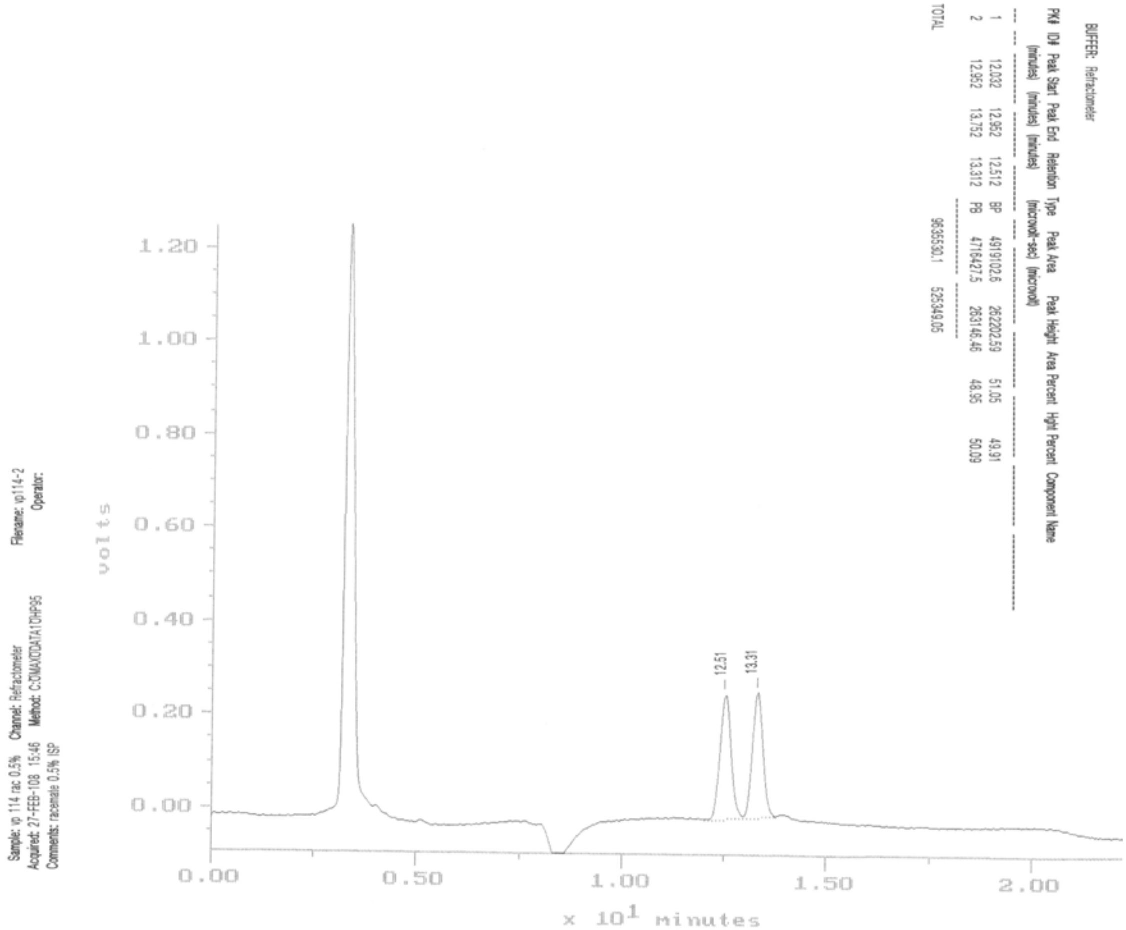


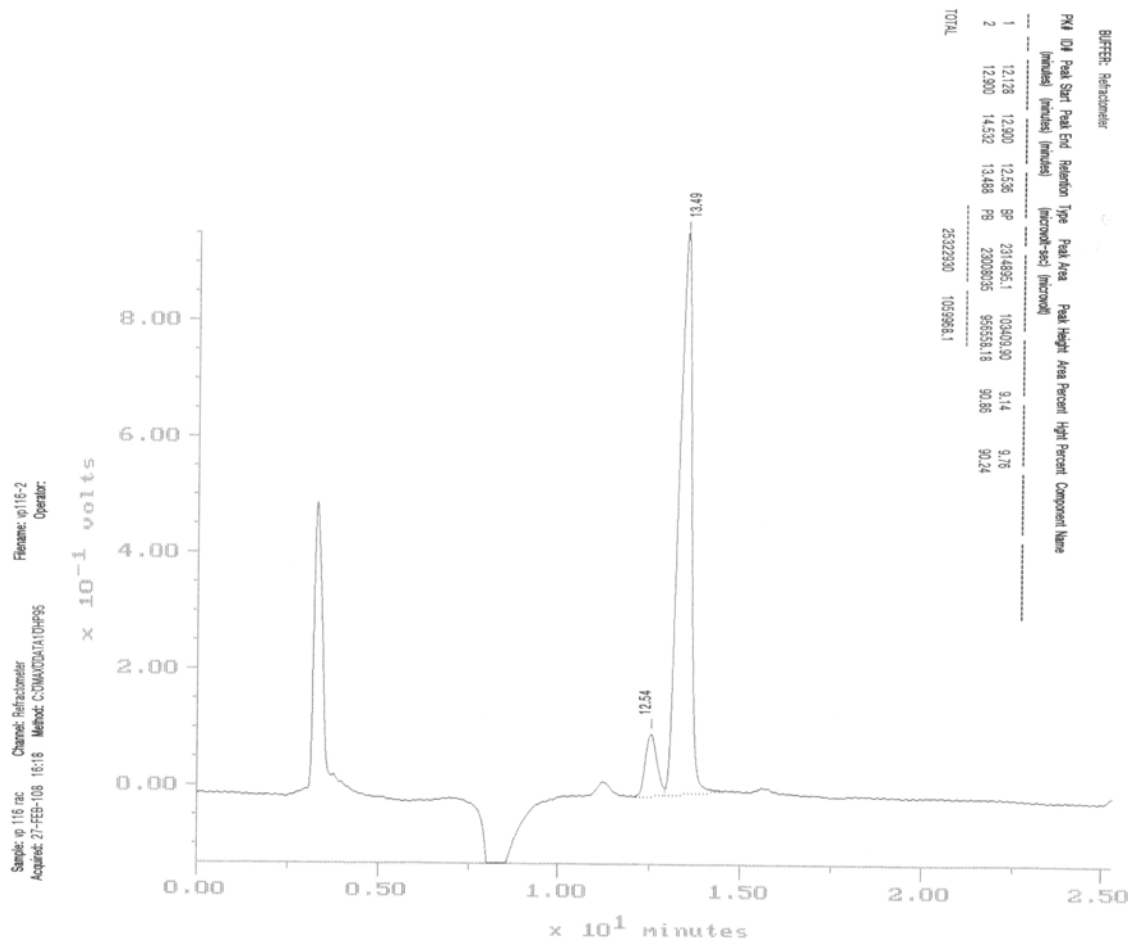
3,3- Spirocycloheptyl-4-(2-methylphenyl)-oxetan-2-one (Table 2, Entry 4)



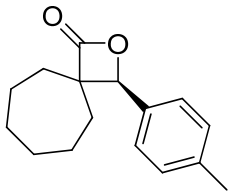
Oil, Yield 73%, 80% *ee*; $[\alpha]_D^{22}$ = +8.6 (c = 1.0, CH_2Cl_2); IR (NaCl) 1827, 1458, 1460, 1102, 937 cm^{-1}; ^{1}H-NMR (400 MHz) δ = 7.49-7.47 (m, 1 H, Ar-H), 7.35-7.27 (m, 2H, Ar-H), 7.19 (d, *J*= 8.0 Hz, 2H-Ar), 5.40 (s, 1 H), 2.48-2.42 (m, 1 H), 2.30 (s, 3 H), 2.22-2.16 (m, 1 H), 1.94-1.90 (m, 1 H), 1.76-1.74 (m, 1 H), 1.57-1.44 (m, 9 H); ^{13}C-NMR (100 MHz) δ = 174.21, 133.06, 132.89, 128.93, 129.21, 127.14, 125.29, 124.44, 81.66, 62.70, 34.85, 30.92, 28.95, 28.65, 28.36, 22.67, 21.95, 18.36. Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 0.5% *i*PrOH/hexane: (*R*) t_1 = 12.5 min, (*S*) t_2 = 13.5 min.


1H-NMR, 400 MHz @ 21°C

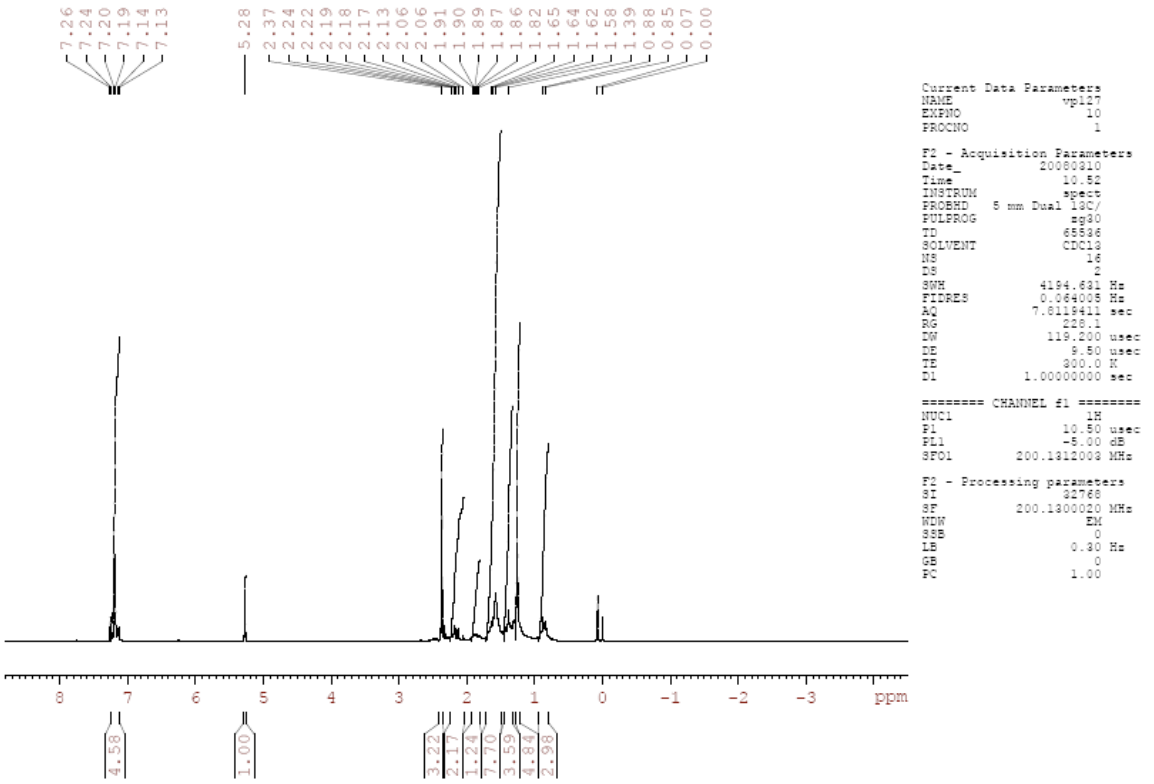




3,3- Spirocycloheptyl-4-(4-methylphenyl)-oxetan-2-one (Table 2, Entry 3)



Oil, Yield 82%, 91% *ee*; $[\alpha]_D^{22}$ = +9.6 (c = 1.0, CH_2Cl_2); IR (NaCl) 1823, 1459, 1260, 1106, 938 cm^{-1}; ^{1}H-NMR (200 MHz) δ = 7.18-7.05 (m, 4 H, Ar-H), 5.20 (s, 1 H), 2.30 (s, 3 H), 2.25-2.05 (m, 2 H), 1.90—1.70 (m, 1 H), 1.94-1.90 (m, 1 H), 1.57-1.50 (m, 4 H), 1.25-1.22 (m, 5 H); ^{13}C-NMR (50 MHz) δ = 175.69, 138.46, 132.46, 129.40, 125.85, 84.32, 63.79, 35.40, 30.30, 29.84, 29.15, 23.83, 22.93, 21.35. Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 1% *i*PrOH/hexane: (*R*) t_1 = 10.4 min, (*S*) t_2 = 14.1 min.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2.06
1.91
1.90
1.89
1.87
1.86
1.82
1.65
1.64
1.62
1.58
1.39
0.88
0.85
0.07
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8
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6
5
4
3
2
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-1
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ppm
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DW 119.200 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
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PL1 -5.00 dB
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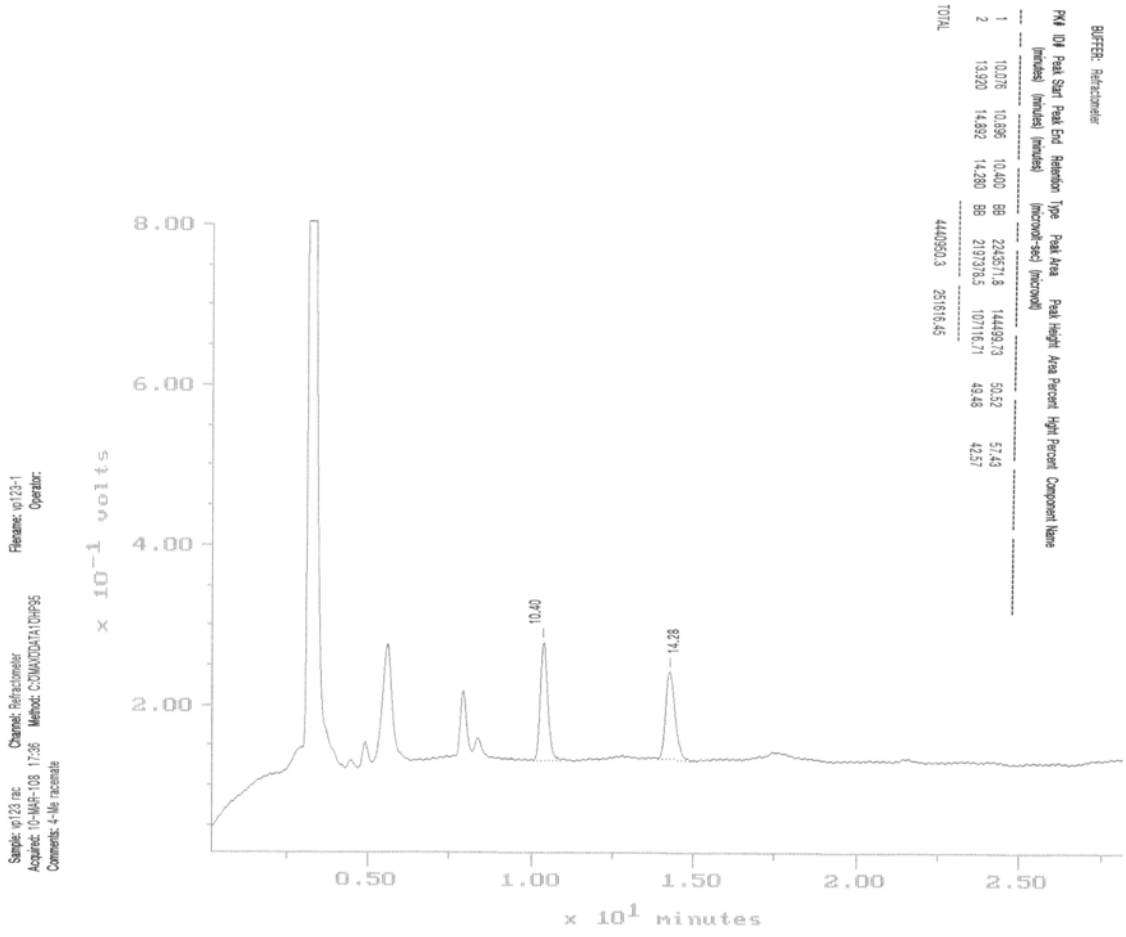
LB 0.30 Hz
GB 0
PC 1.00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1.00
1.50
2.00
2.50
x 10¹ minutes
BUFFER: Refractometer
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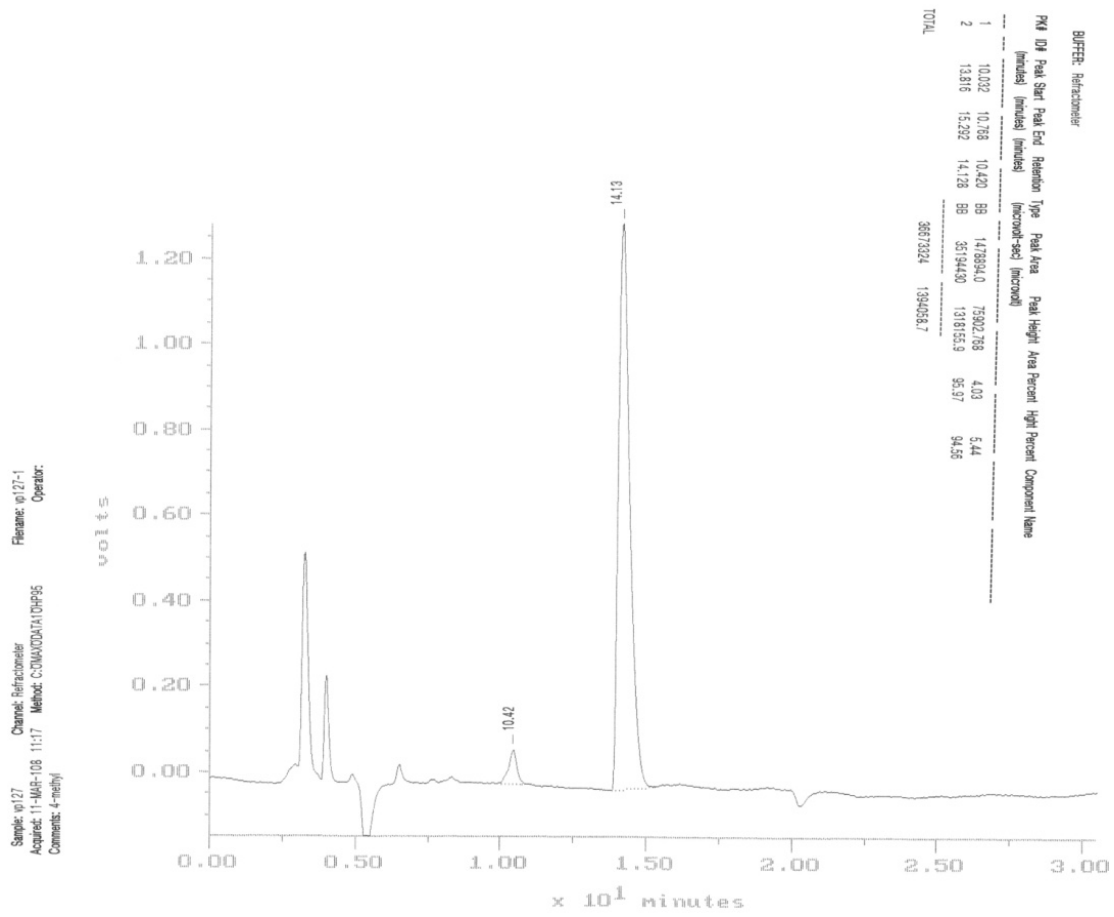
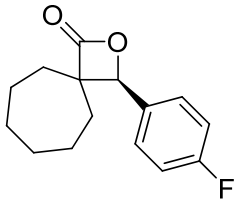
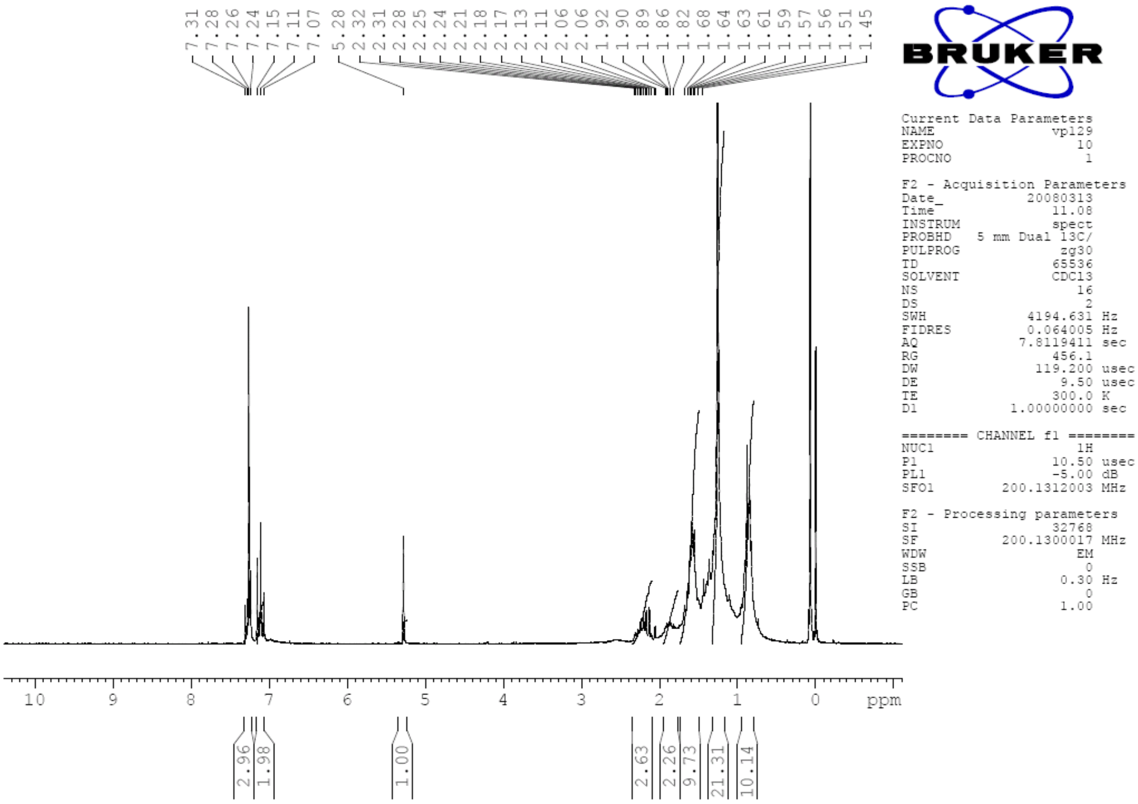
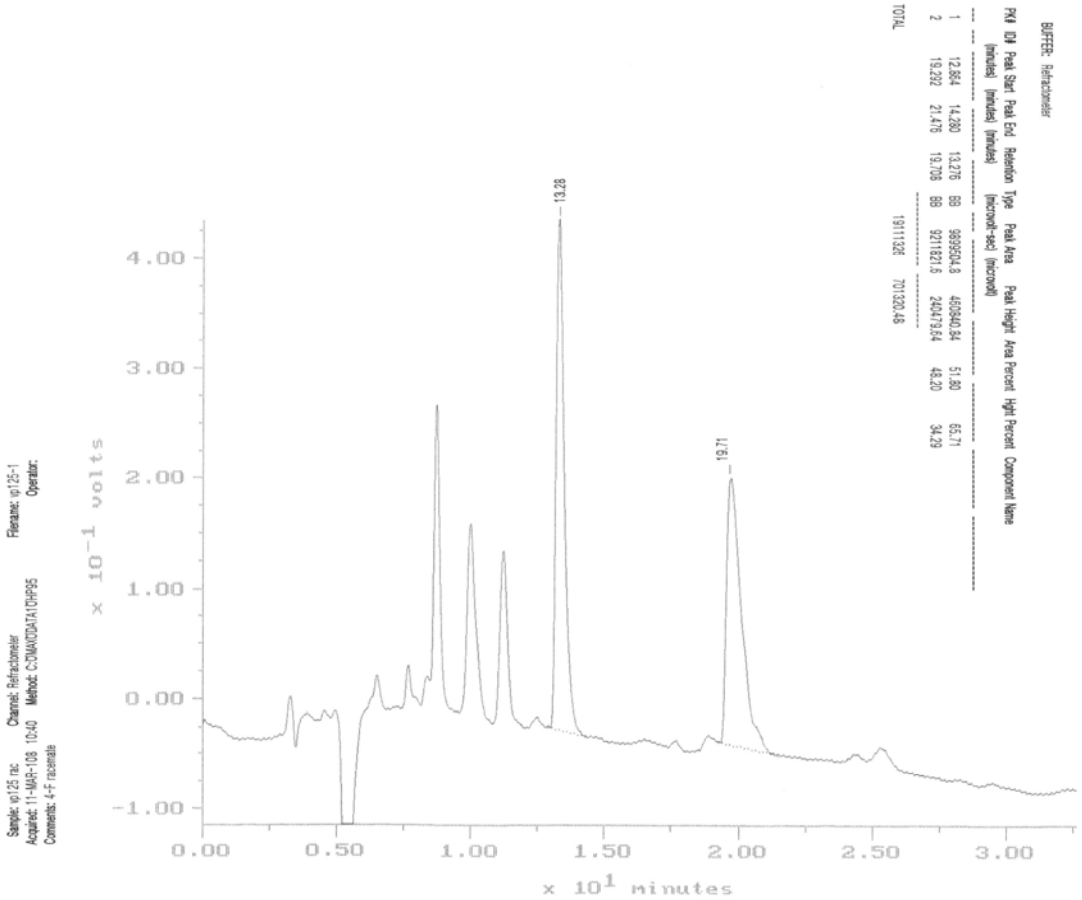


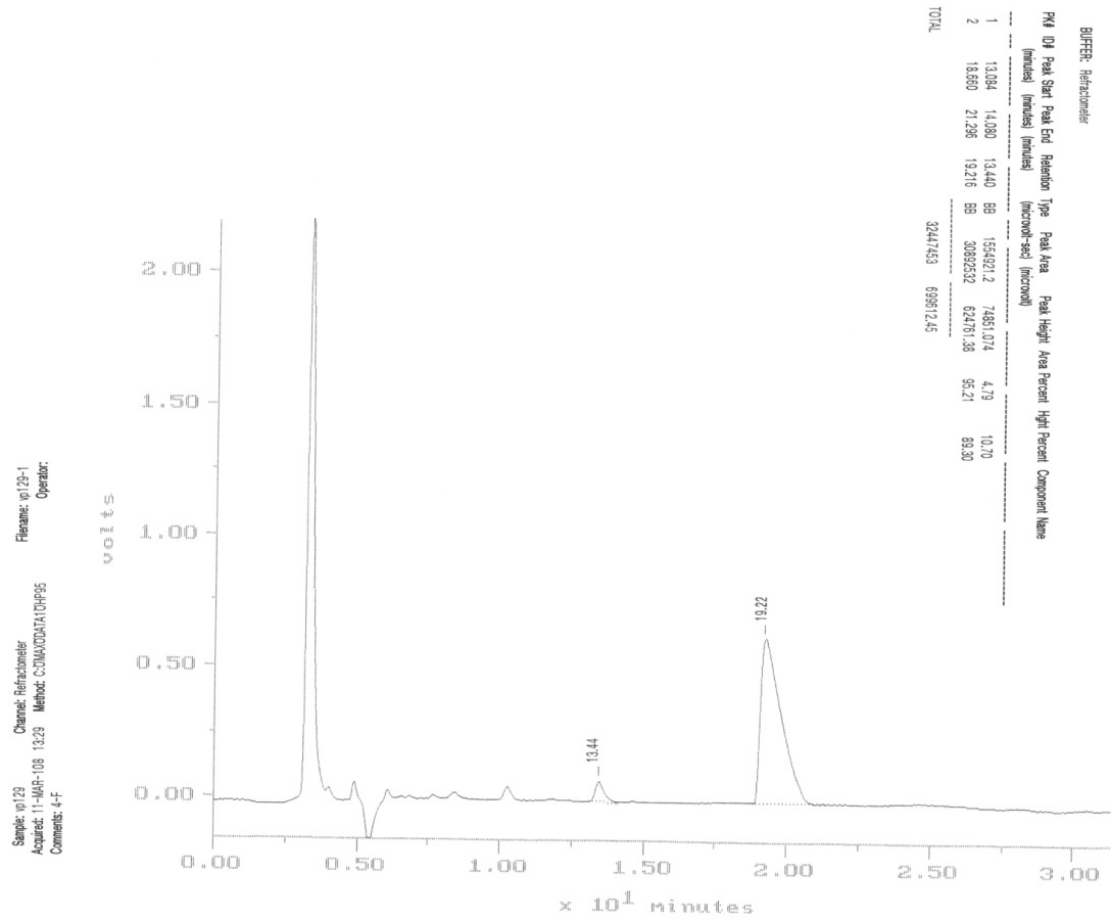
3,3- Spirocycloheptyl-4-(4-fluorolphenyl)-oxetan-2-one (Table 2, Entry 2)



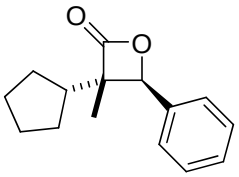
Oil, Yield 72%, 91% *ee*, $[\alpha]_D^{22}$ = +8.0 (c = 1.0, CH_2Cl_2); IR (NaCl) 1826, 1512, 1459, 1261, 1109, 939 cm^{-1}. ^{1}H-NMR (200 MHz) δ = 7.31-7.24 (m, 2 H, Ar-H), 7.15-7.07 (m, 2 H, Ar-H), 5.28 (s, 1 H), 2.30 (s, 3 H), 2.32-2.06 (m, 2 H), 1.92-1.82 (m, 2 H), 1.68-1.63 (m, 4 H), 1.45-1.25 (m, 4 H); ^{13}C-NMR (50 MHz), δ = 174.59, 162.22 (d, J = 245 Hz), 131.13, 127.05 (d, J = 8 Hz), 115.23 (d, J = 22 Hz), 83.01, 63.45, 34.76, 29.72, 29.57, 28.51, 27.82, 23.19, 22.25. Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 1% *i*PrOH/hexane: (*R*) t_1 = 13.4 min, (*S*) t_2 = 19.2 min.


7.31 7.28 7.26 7.24 7.15 7.11 7.07 5.28 2.32 2.31 2.28 2.25 2.24 2.21 2.18 2.17 2.13 2.11 2.06 2.06 1.92 1.90 1.89 1.86 1.82 1.68 1.64 1.63 1.61 1.59 1.57 1.56 1.51 1.45
BRUKER
Current Data Parameters
NAME vp129
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080313
Time 11.08
INSTRUM spect
PROBHD 5 mm Dual 13C/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 4194.631 Hz
FIDRES 0.064005 Hz
AQ 7.8119411 sec
RG 456.1
DW 119.200 usec
DE 9.50 usec
TE 300.0 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 10.50 usec
PL1 -5.00 dB
SFO1 200.1312003 MHz
F2 - Processing parameters
SI 32768
SF 200.1300017 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10 9 8 7 6 5 4 3 2 1 0 ppm
2.96 1.98 1.00 2.63 2.26 9.73 21.31 10.14


BUFFER: Refractometer
PKN ID# Peak Start (minutes) Peak End (minutes) Retention (minutes) Type Peak Area (microvolt-sec) Peak Height (microvolt) Area Percent Hght Percent Component Name
1 12.864 14.260 13.276 BB 9899504.8 460840.84 51.80 65.71
2 19.292 21.476 19.708 BB 9211821.6 240479.64 48.20 34.29
TOTAL 19111326 701320.48
13.28
19.71
4.00 3.00 2.00 1.00 0.00 -1.00
x 10^-1 volts
0.00 0.50 1.00 1.50 2.00 2.50 3.00
x 10^1 minutes
Sample: vp125 rac Channel: Refractometer Filename: vp125-1
Acquired: 11-MAR-108 10:40 Method: C:\TMAX\DATA1\DHP95 Operator:
Comments: 4-F racemate

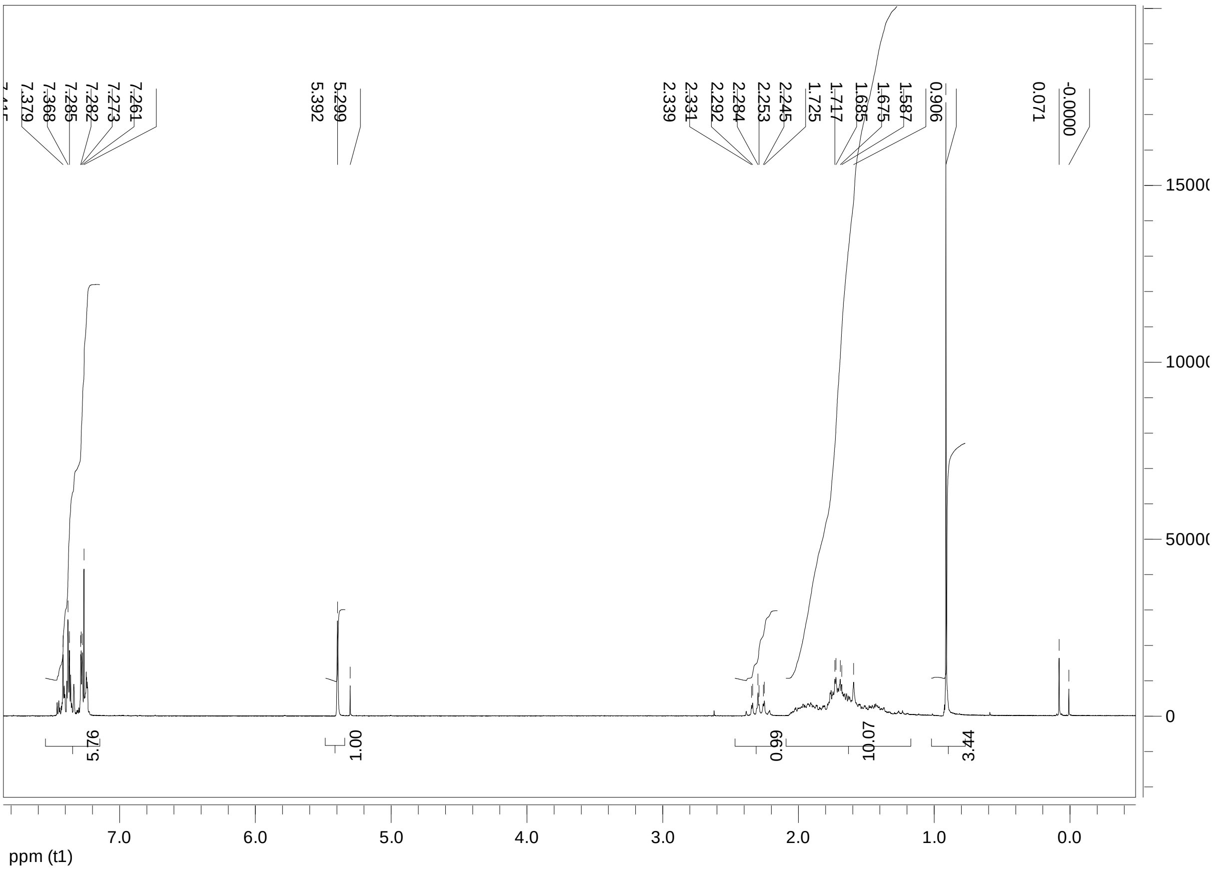


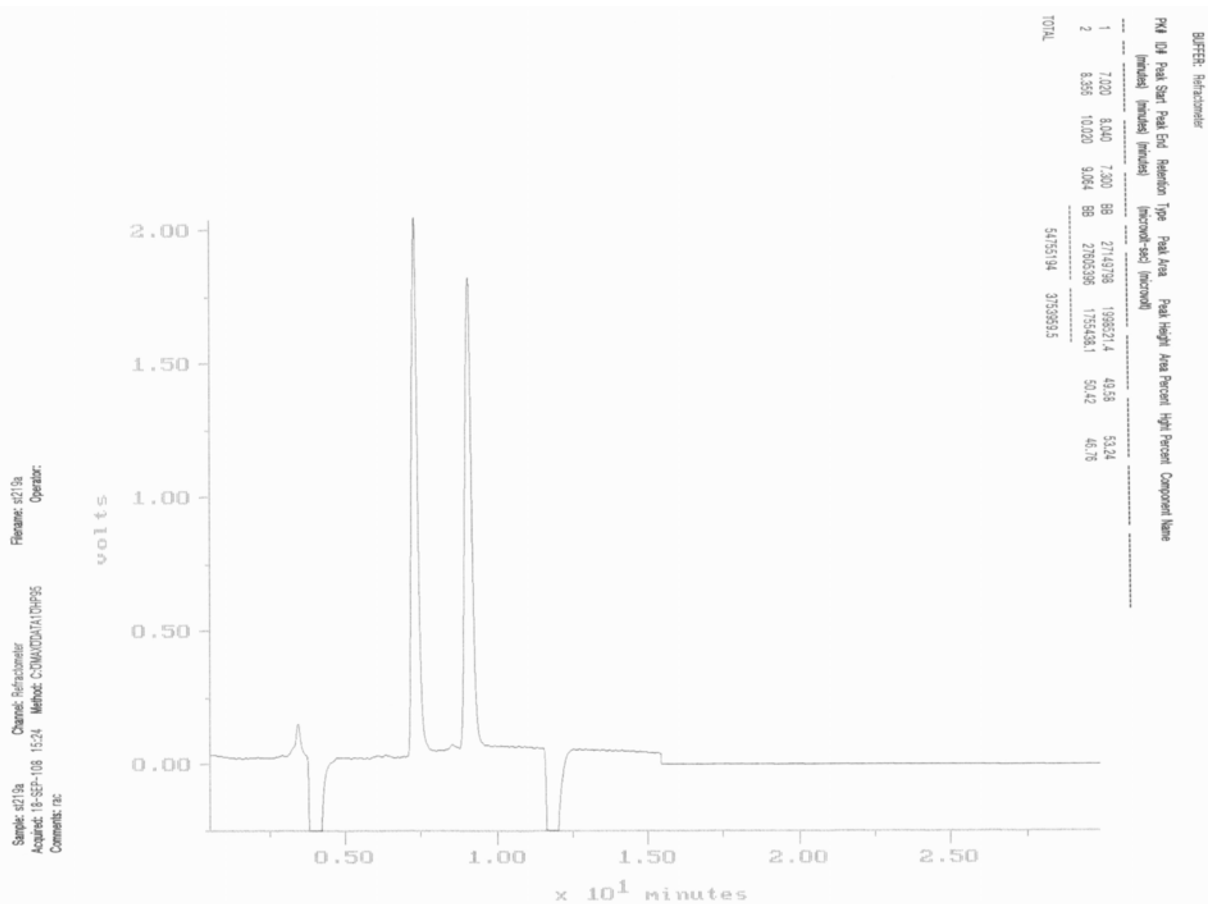
3-cyclopentyl-3-methyl-4-phenyloxetan-2-one (Table 2, Entry 6)

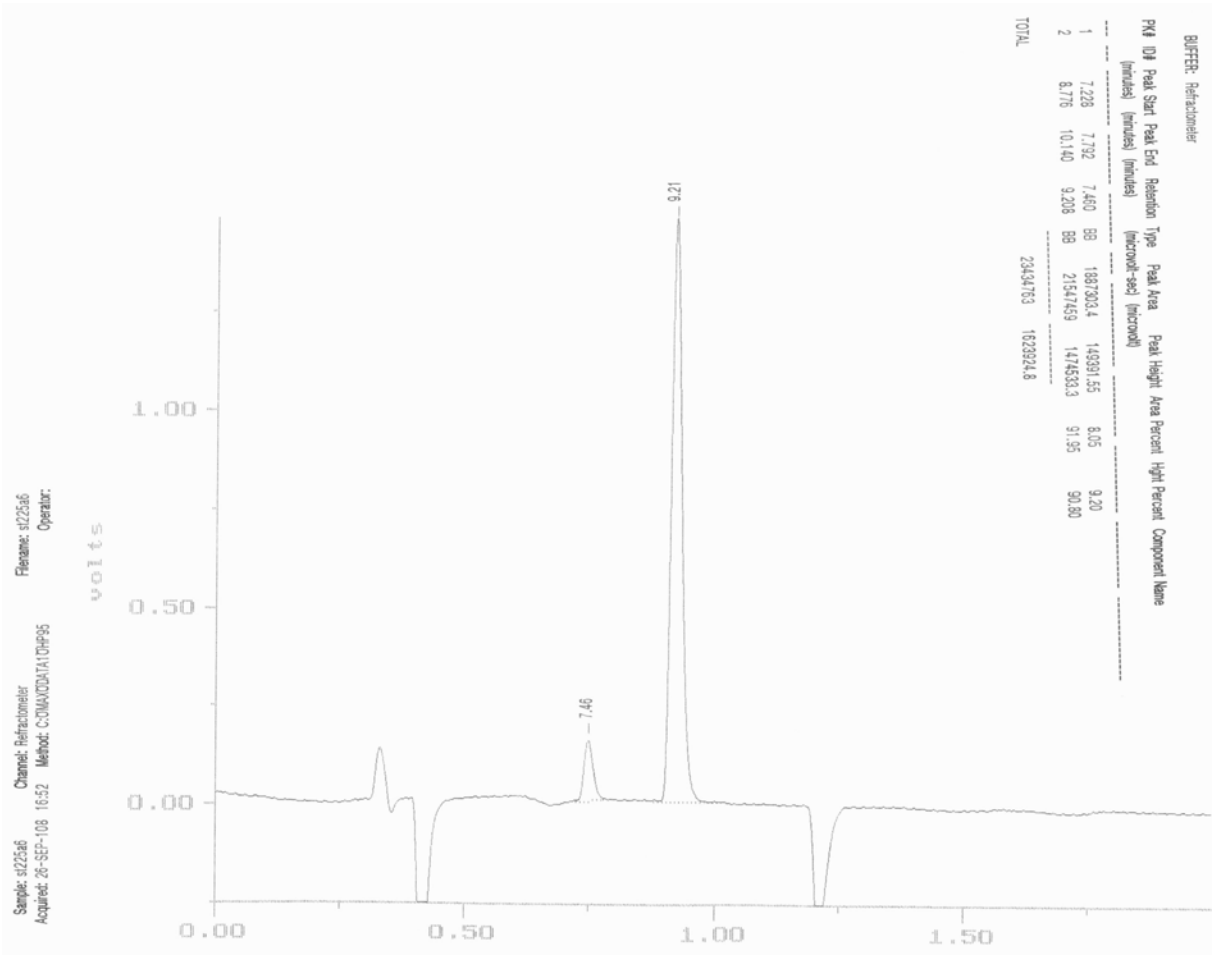


Oil, Yield 99%, *trans*:*cis* 1:2

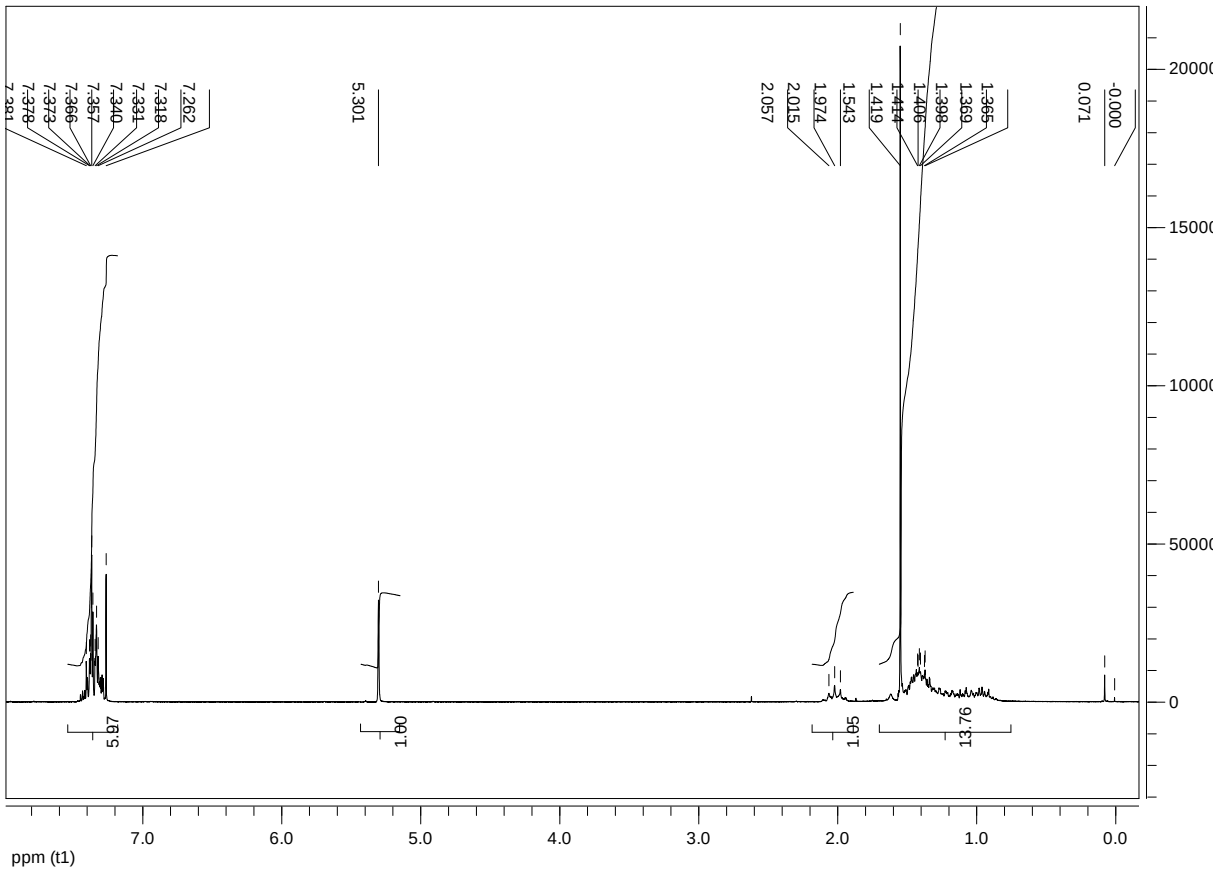
trans: 82% *ee*, Spectral data were consistent with literature values.[4] Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 1% *i*PrOH/hexane: (*R*) t_1 = 7.4 min, (*S*) t_2 = 9.2 min.

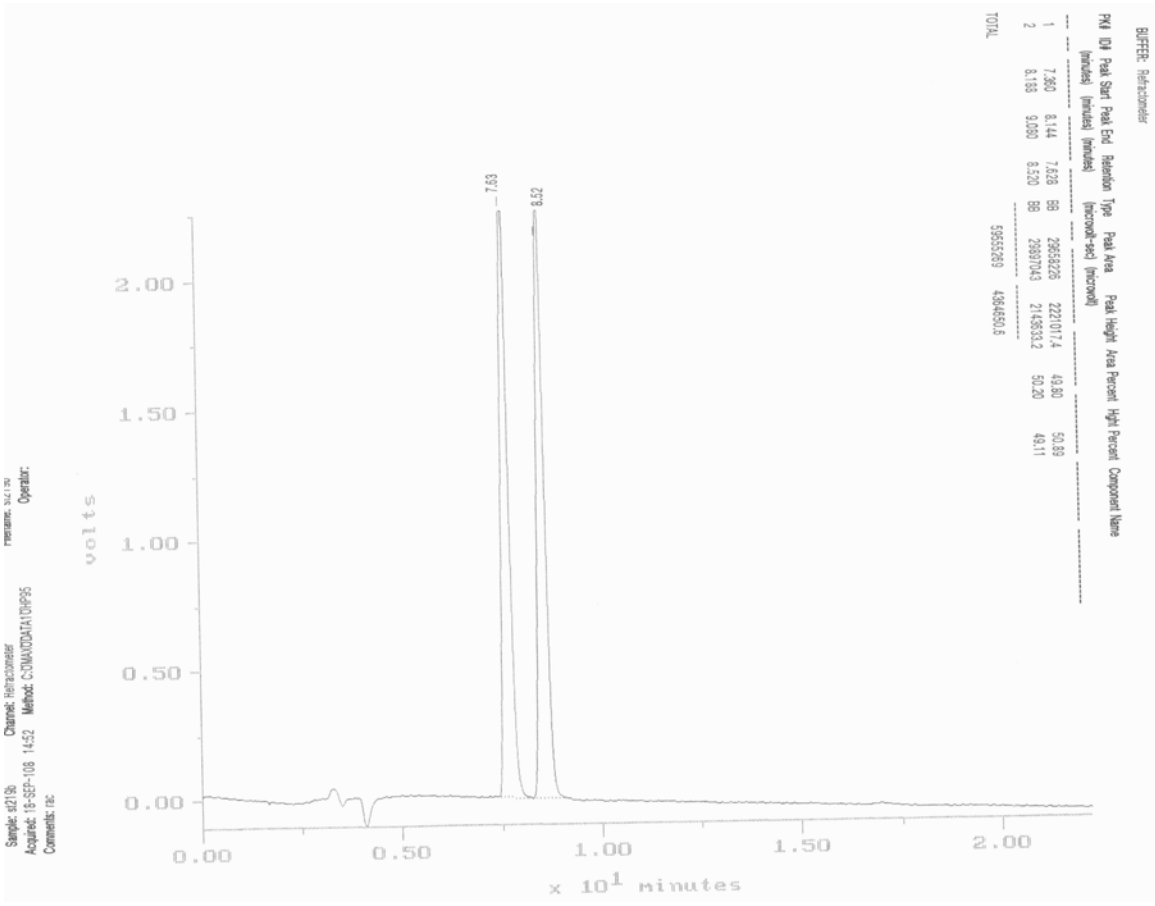

7.379 7.368 7.285 7.282 7.273 7.261
5.392 5.299
2.339 2.331 2.292 2.284 2.253 2.245 1.725 1.717 1.685 1.675 1.587 0.906
0.071 -0.0000
5.76 1.00 0.99 10.07 3.44
ppm (t1)

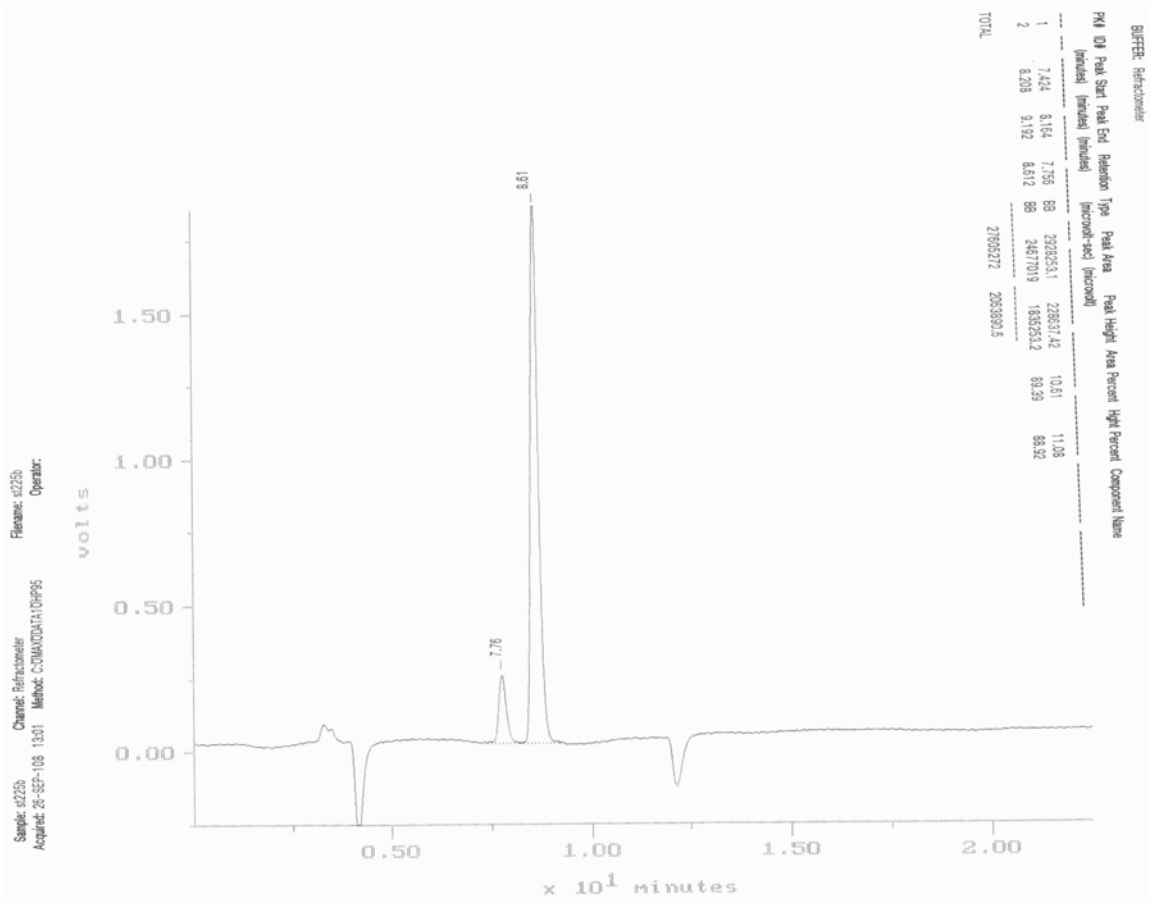

BUFFER: Refractometer
Sample: st219a
Acquired: 18-SEP-108 15:24
Comments: rac
Channel: Refractometer
Method: C:\T3MAX\DATA1\DHP95
Filename: st219a
Operator:
volts
x 10¹ minutes



cis: 79% *ee*, Spectral data were consistent with literature values.[4] Enantiomeric ratio was determined by HPLC (AD-H, 1.0 mL / min; 1% *i*PrOH/hexane: (*R*) t_1 = 7.6 min, (*S*) t_2 = 8.5 min.


7.391
7.378
7.373
7.366
7.357
7.340
7.331
7.318
7.262
5.301
2.057
2.015
1.974
1.543
1.419
1.414
1.406
1.398
1.369
1.365
0.071
-0.000
5.07
1.00
1.05
13.76
ppm (t1)


volts
minutes
x 10^1



References

1 D. Jaramillo, D. P. Buck, J. G. Collins, R. R. Fenton, F. H. Stootman, N. J. Wheate, J. R. Aldrich-Wright, *Eur. J. Inorg. Chem.*, 2006, 839.

2 B. L. Hodous, G. C. Fu, *J. Am. Chem. Soc.*, 2002, **124**, 1578.

3 K. He, Z. Zhou, L. Wang, K. Li, G. Zhao, Q. Zhou, C. Tang, *Tetrahedron*, 2004, **60**, 10505.

4 J. E. Wilson, G. C. Fu, *Angew. Chem. Int. Ed.*, 2004, **43**, 6358.