Electronic Supplementary Information

Synthesis of dibenzylamino-1-methylcyclohexanol and dibenzylamino-1-trifluoromethylcyclohexanol isomers

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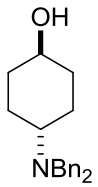
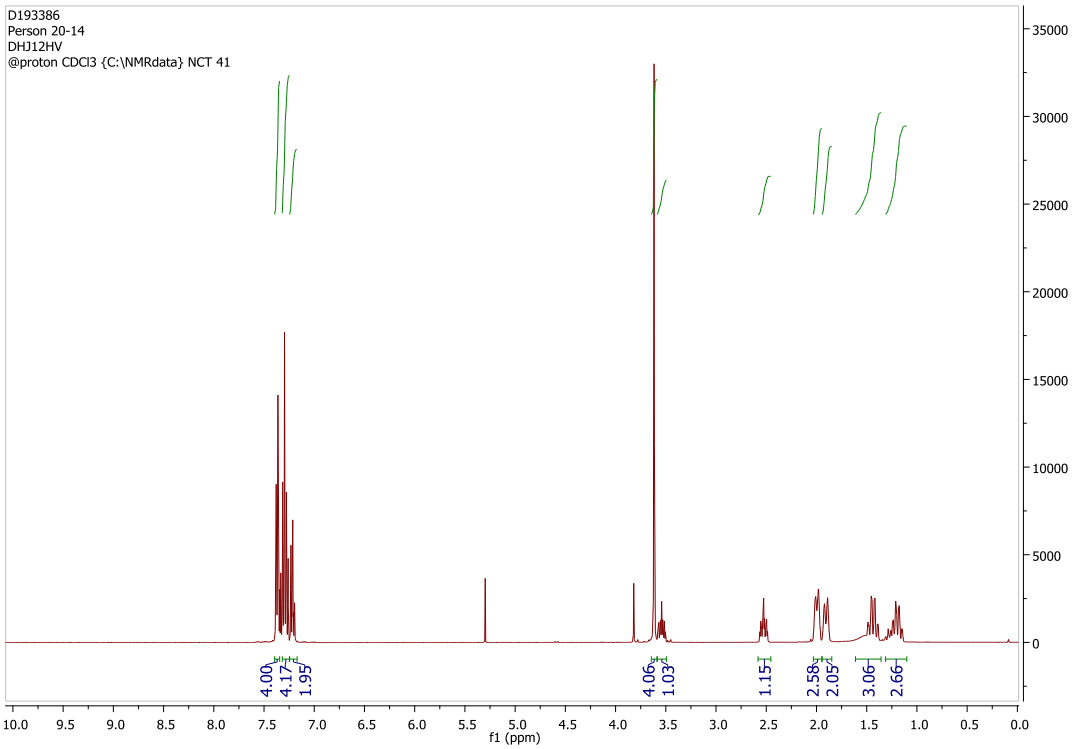
Crystal data and structure refinement

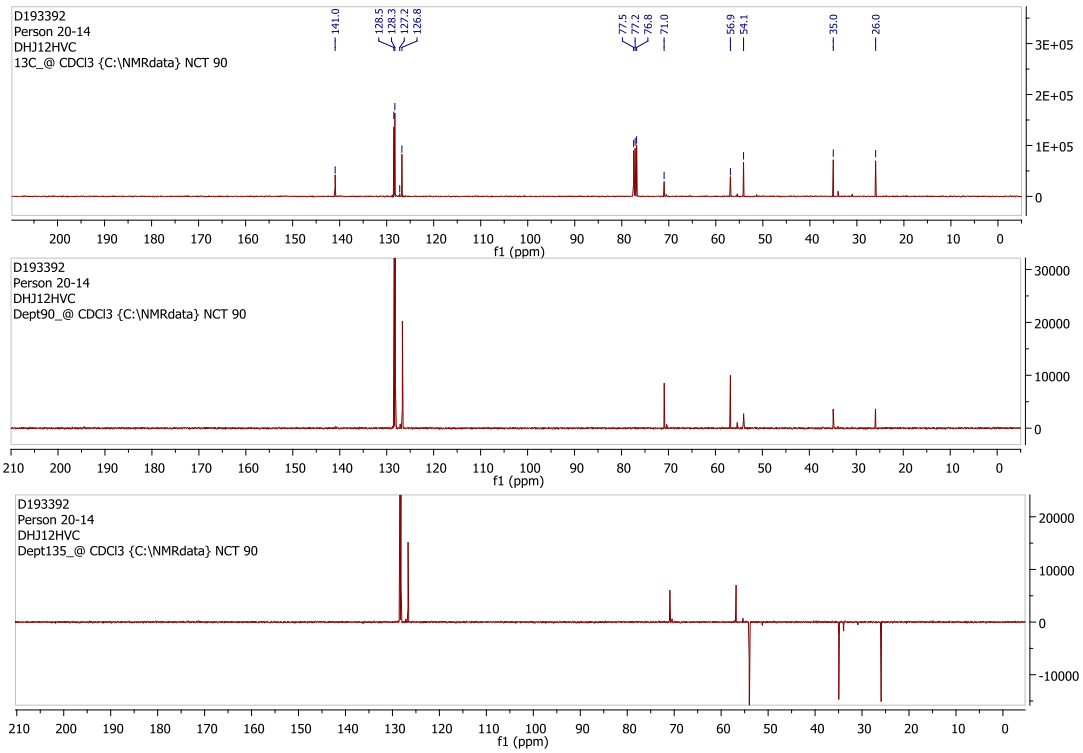
Trans-4-(dibenzylamino)cyclohexan-1-ol



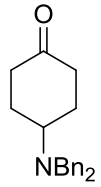
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



4-(Dibenzylamino)cyclohexan-1-one **24**



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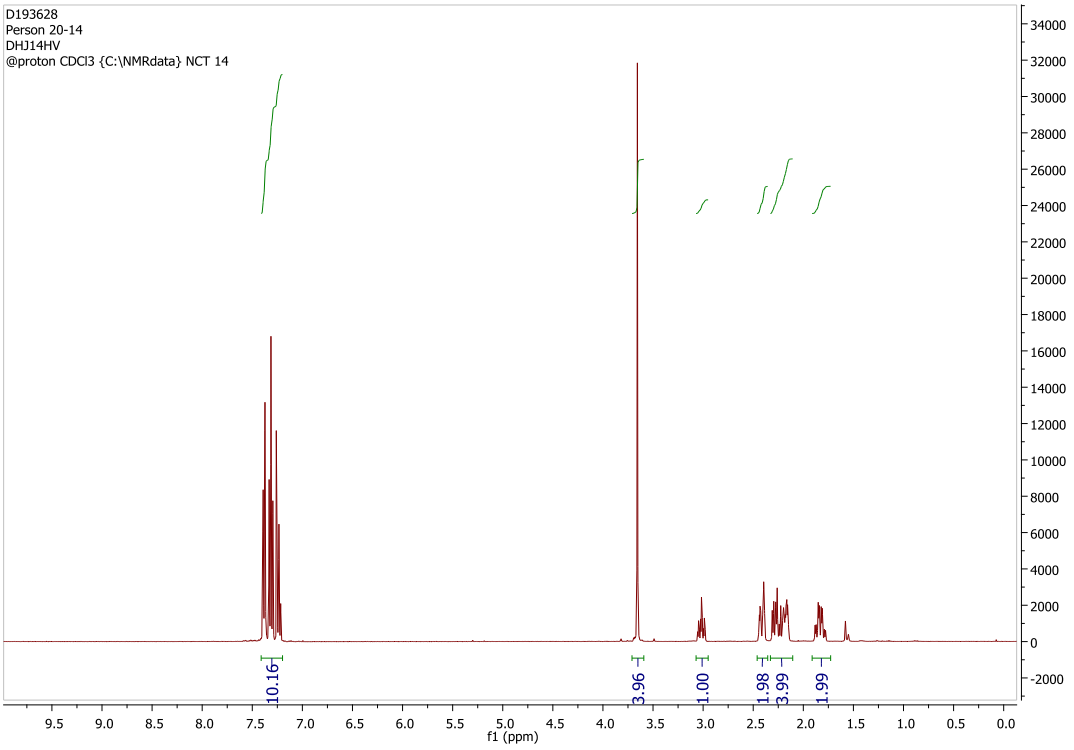

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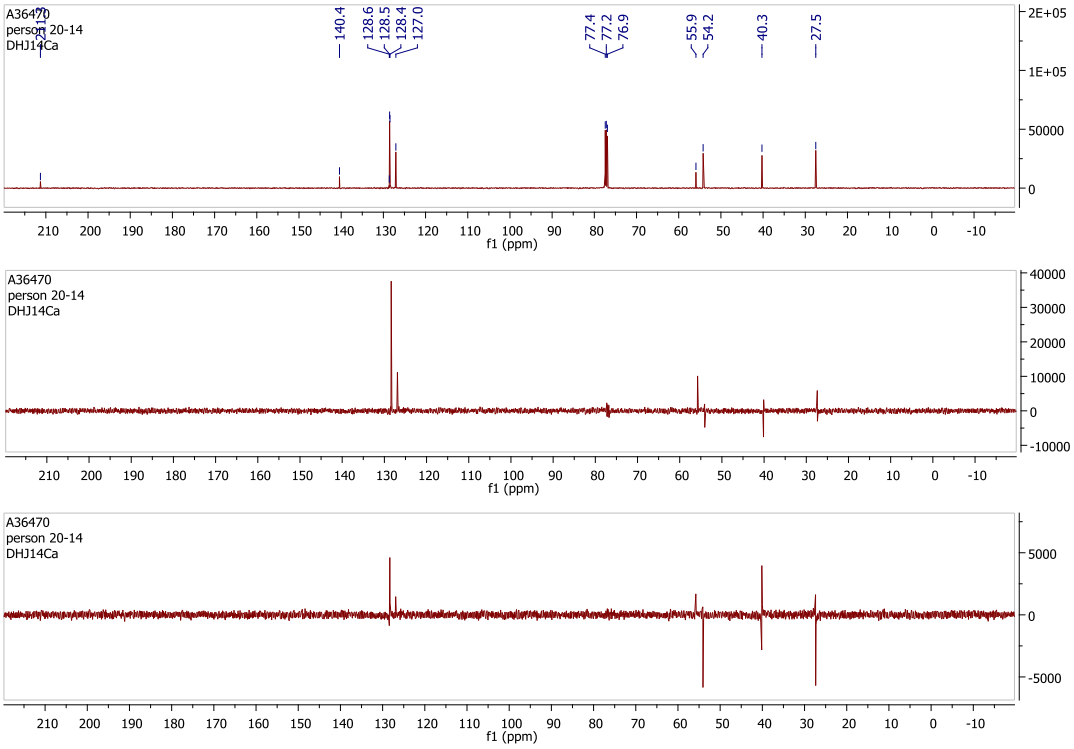

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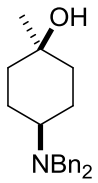

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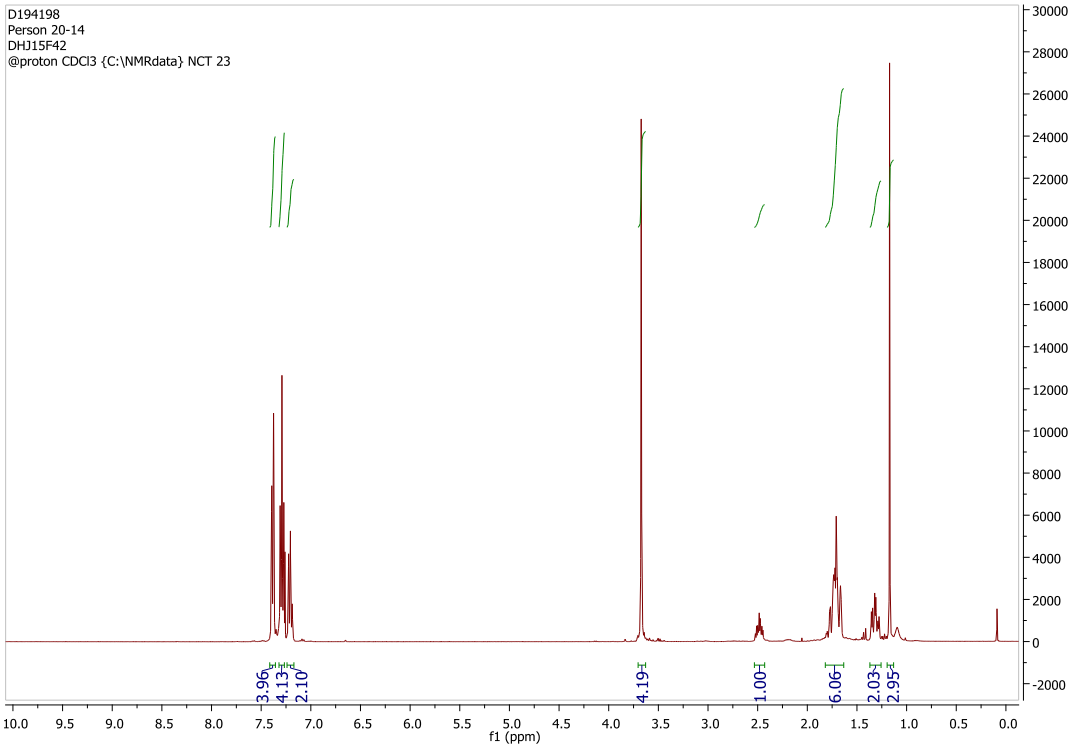
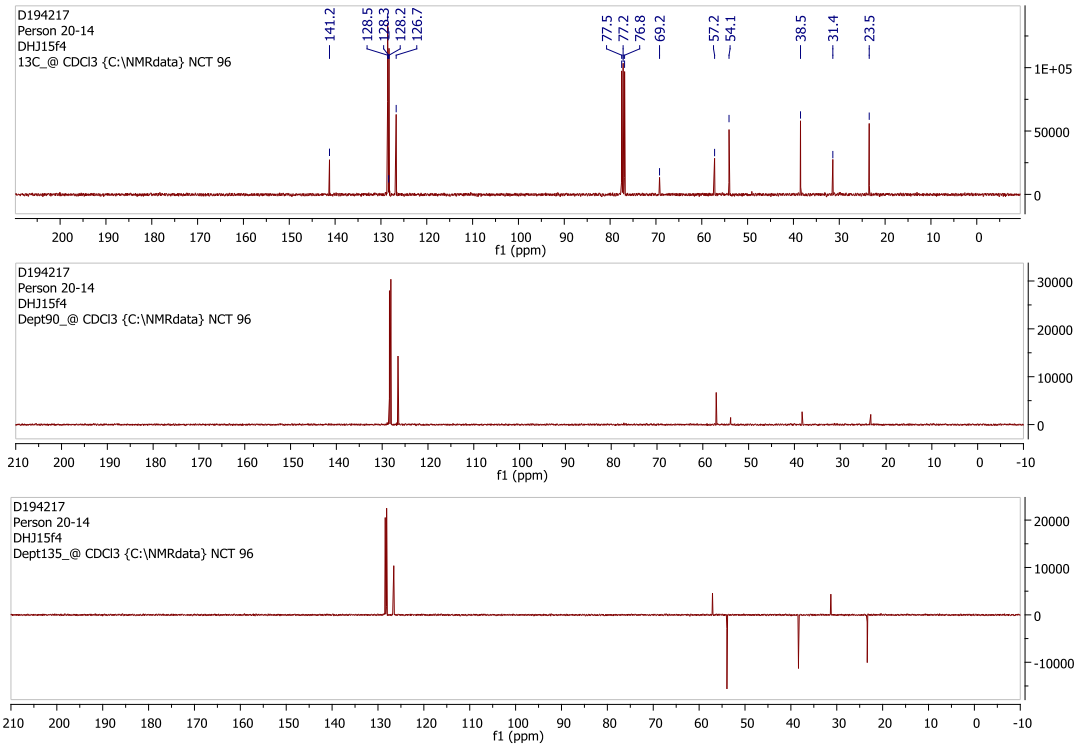
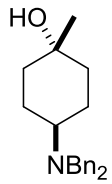
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



Trans-4-(dibenzylamino)-1-methylcyclohexan-1-ol **9**



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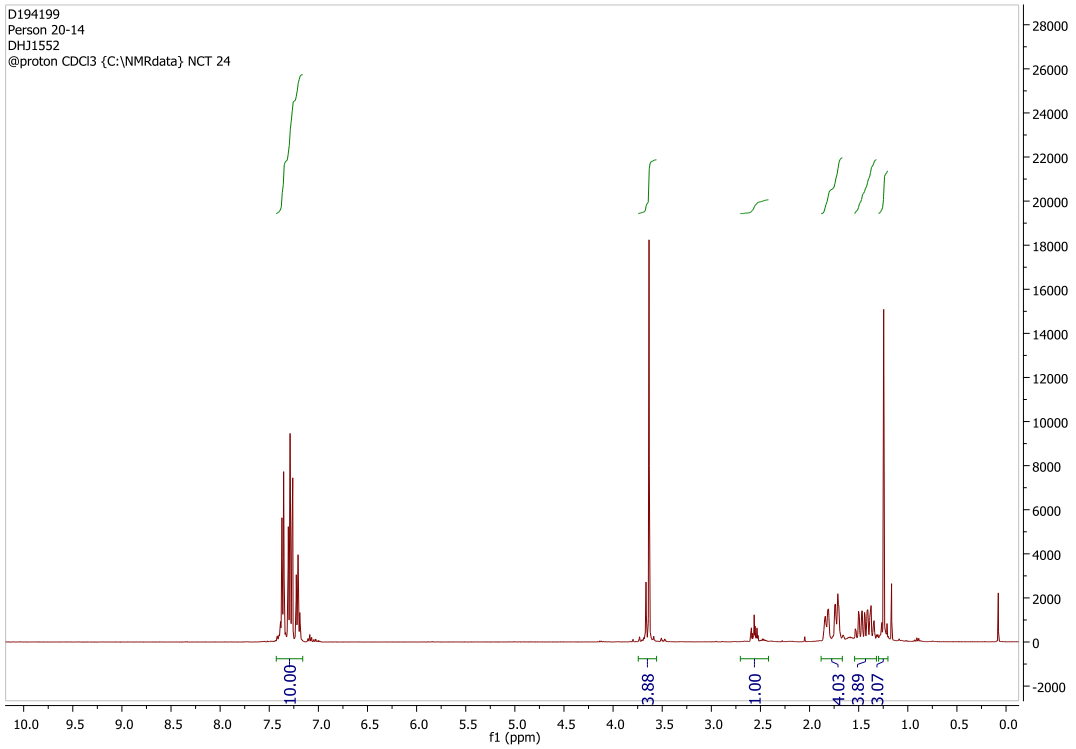

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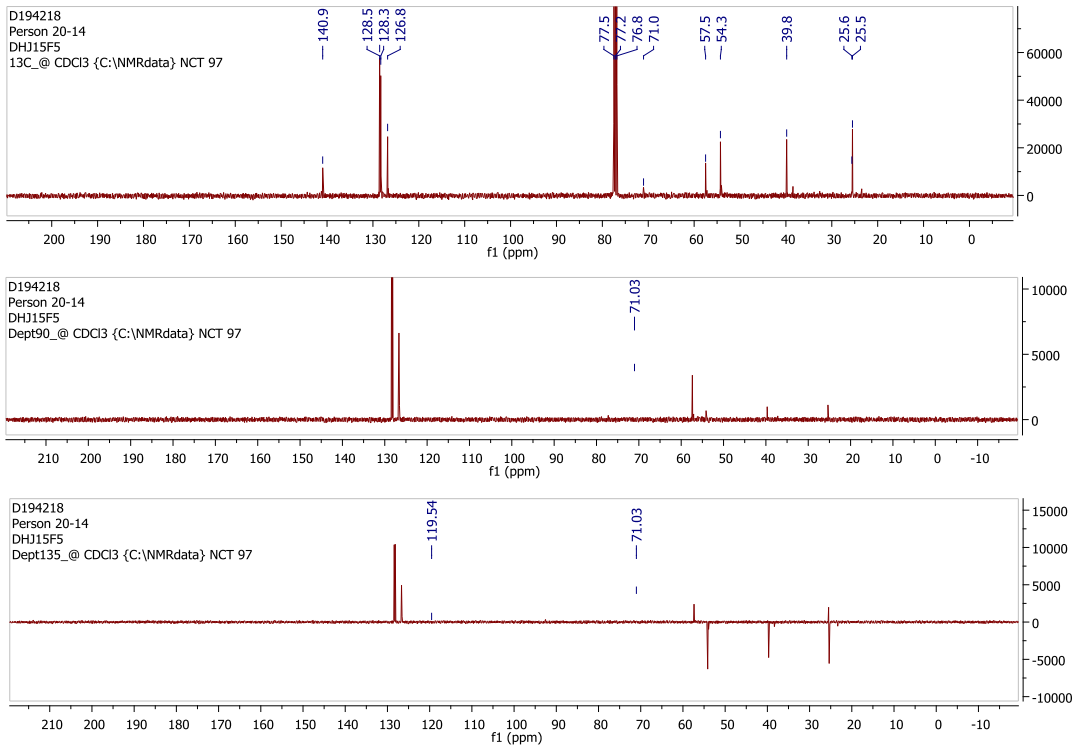
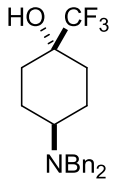


Trans-(dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **15**



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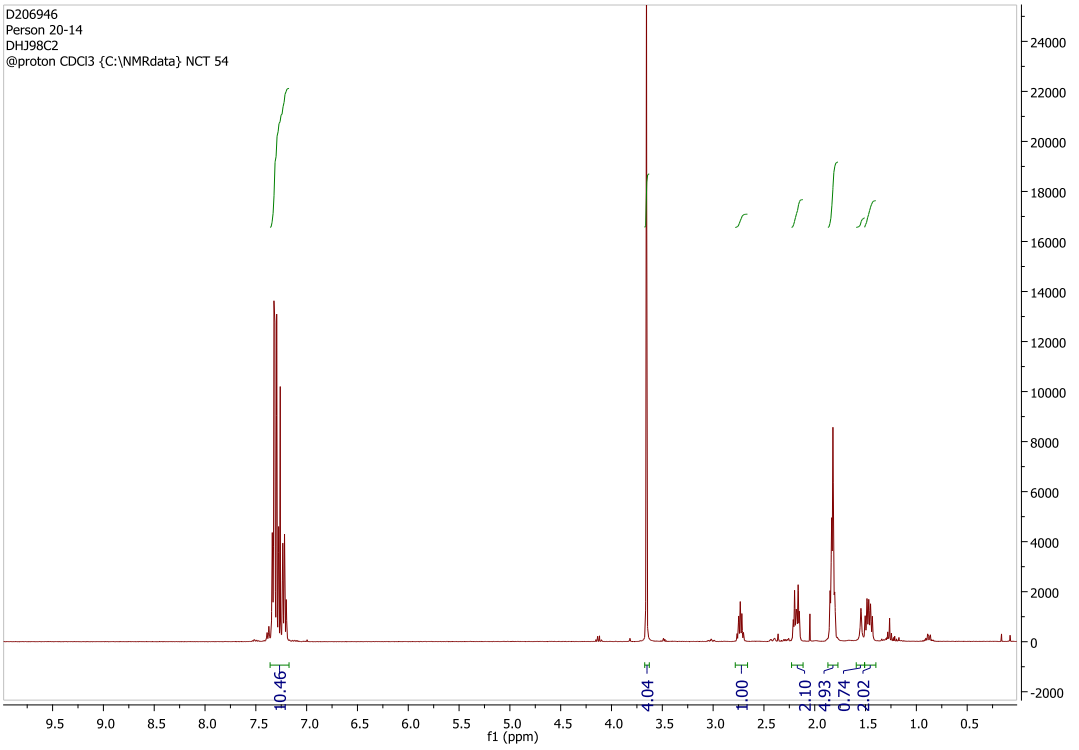
^{1}H NMR (400 MHz, $CDCl_3$)



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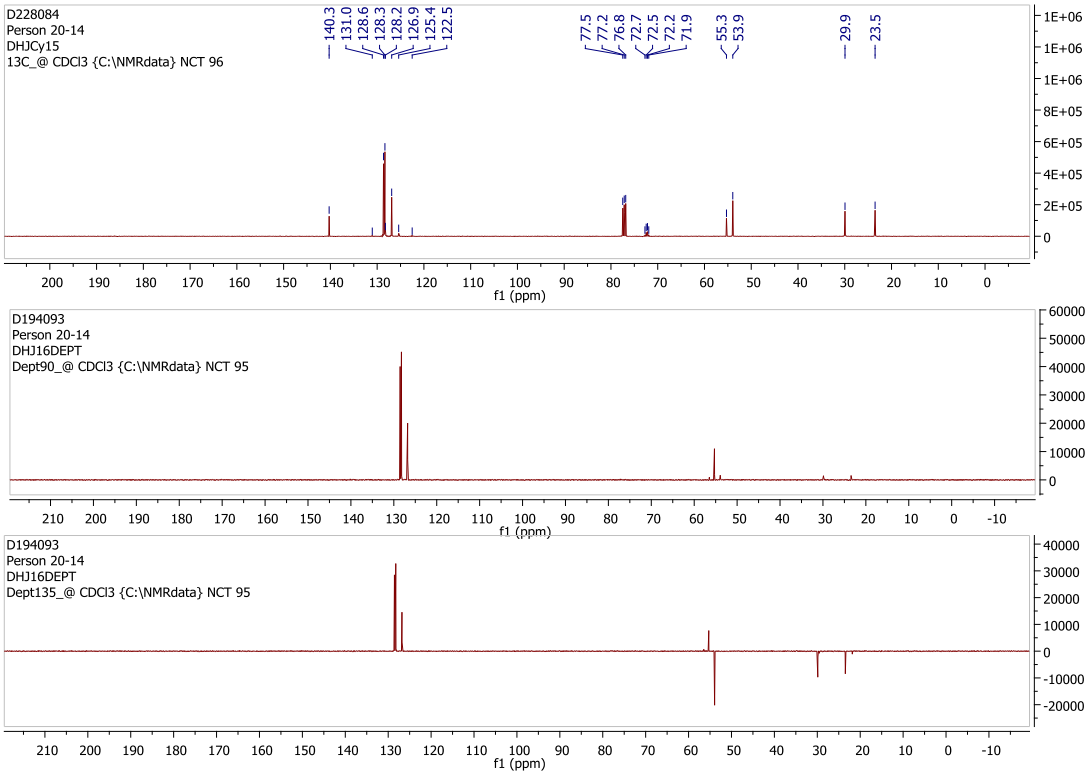
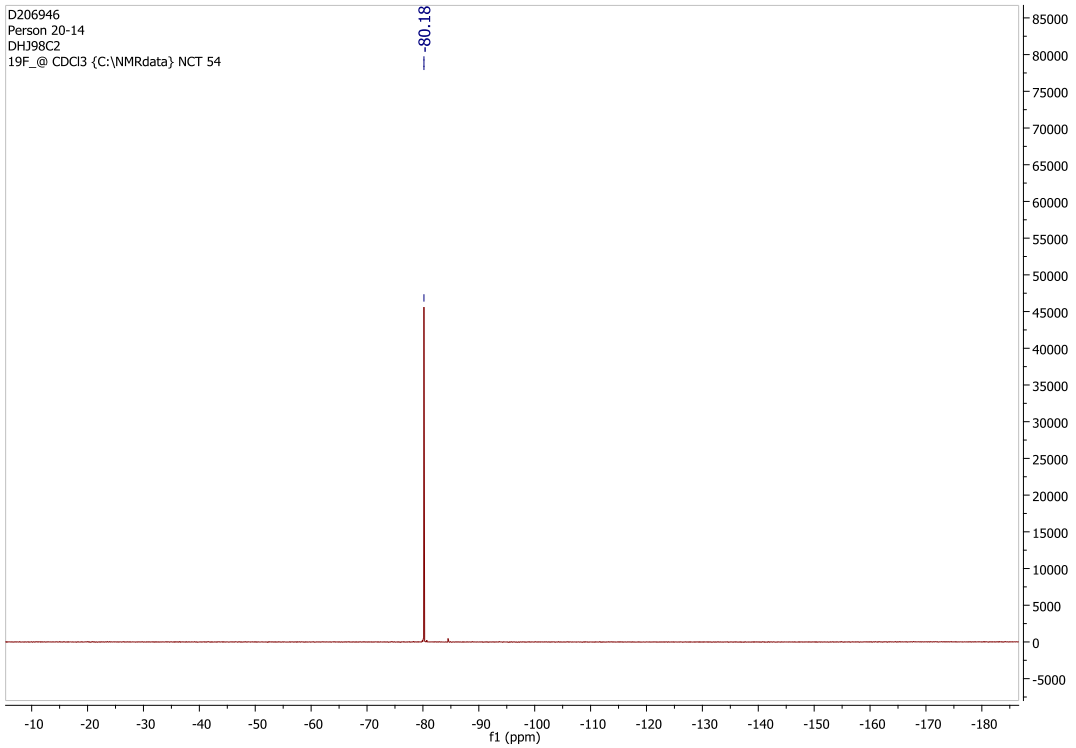
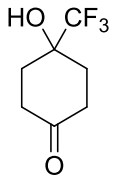


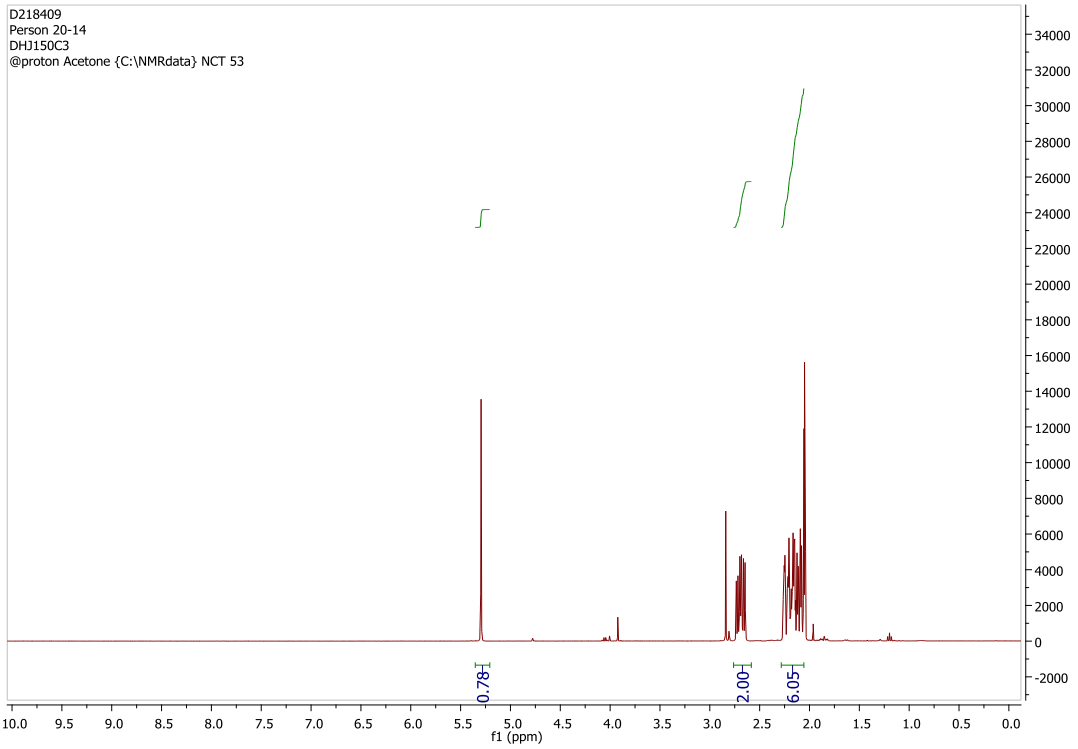
^{19}F NMR (376 MHz, $CDCl_3$)



4-Oxo-1-(trifluoromethyl)cyclohexan-1-ol



^{1}H NMR (400 MHz, $CDCl_3$)



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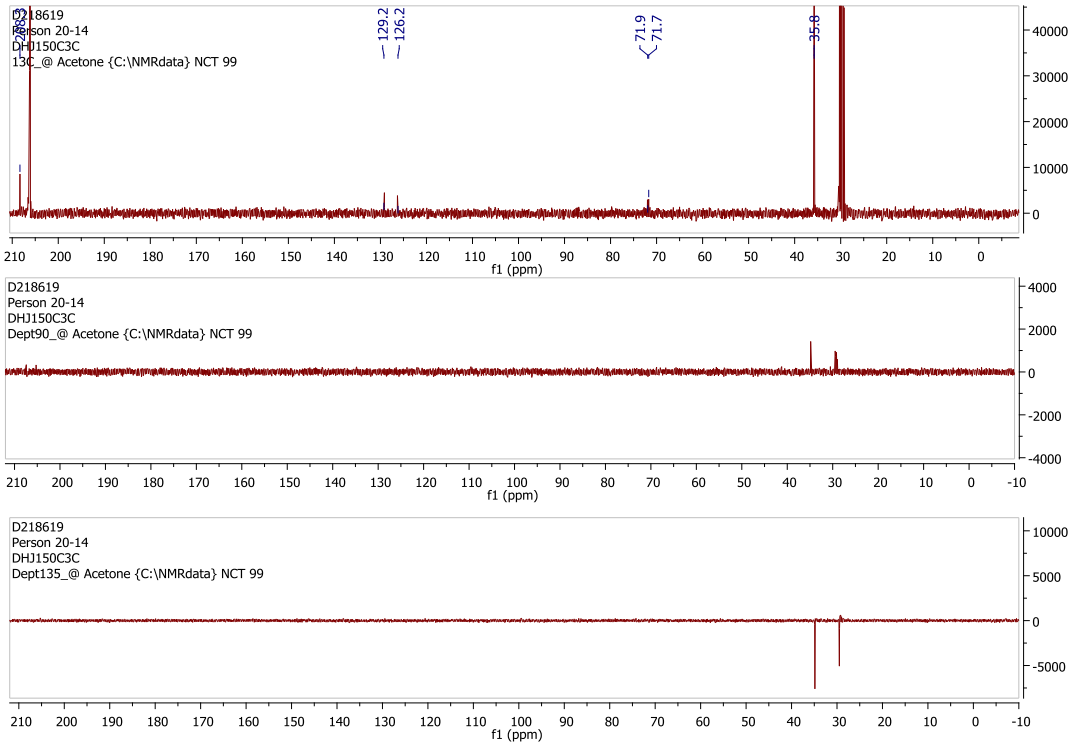
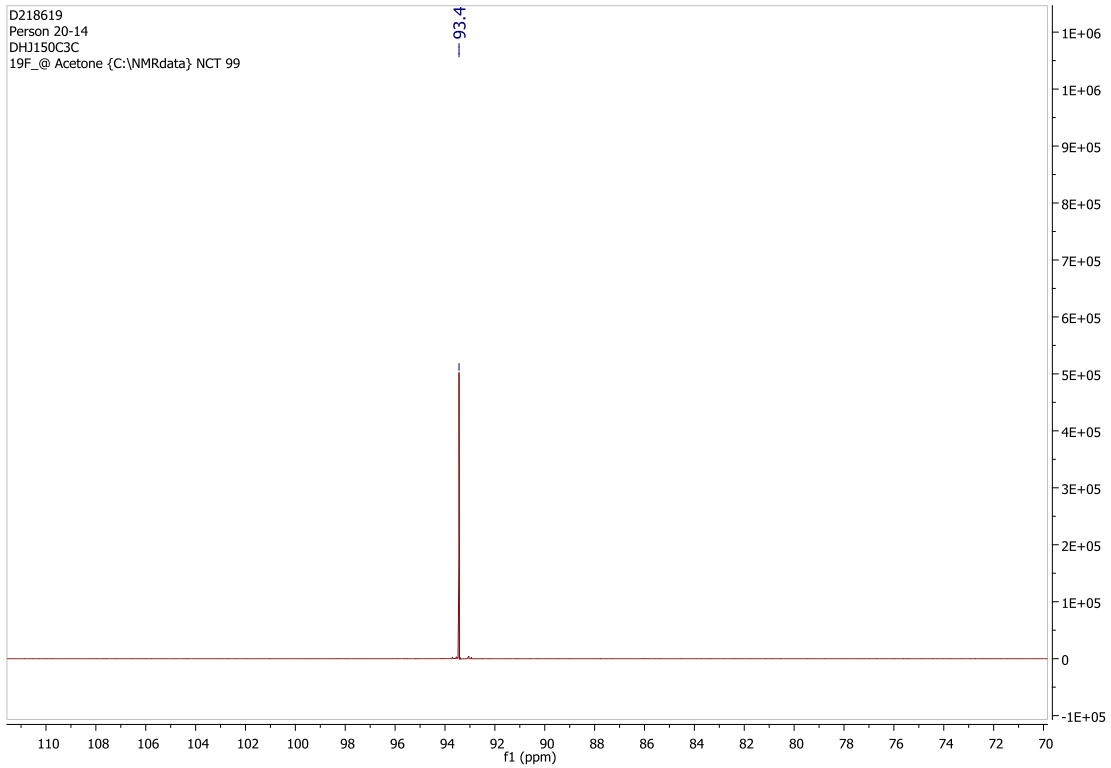
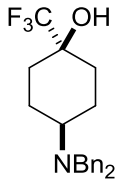


^{19}F NMR (376 MHz, $CDCl_3$)

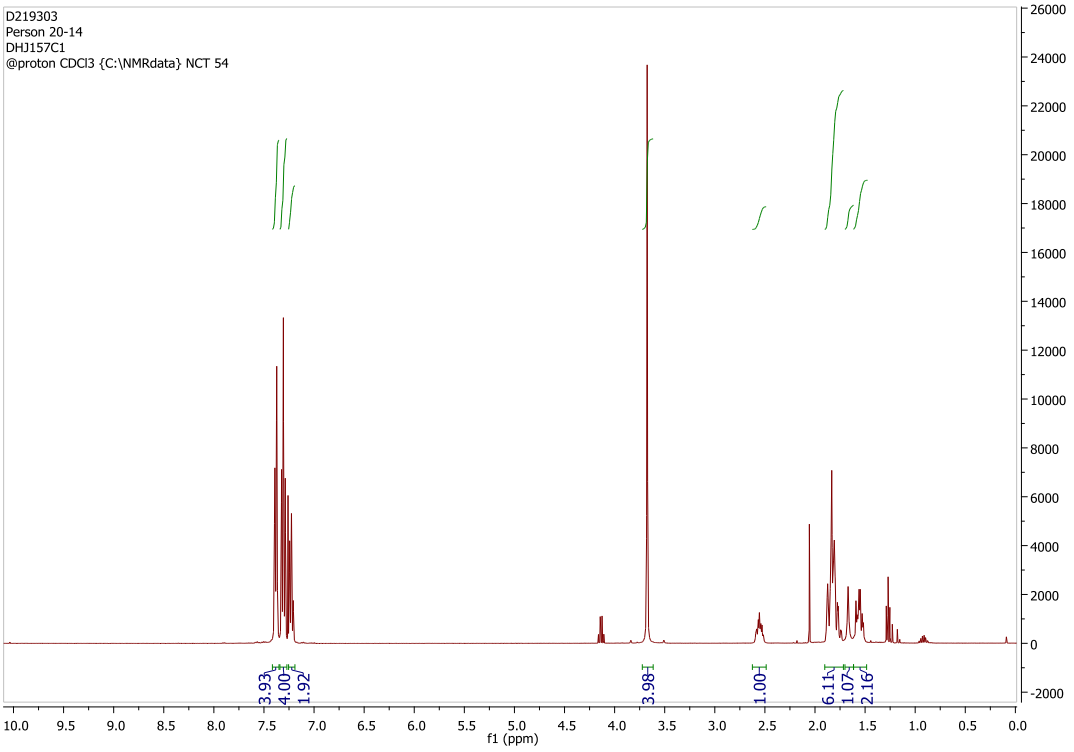


Cis-(4-dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **16**

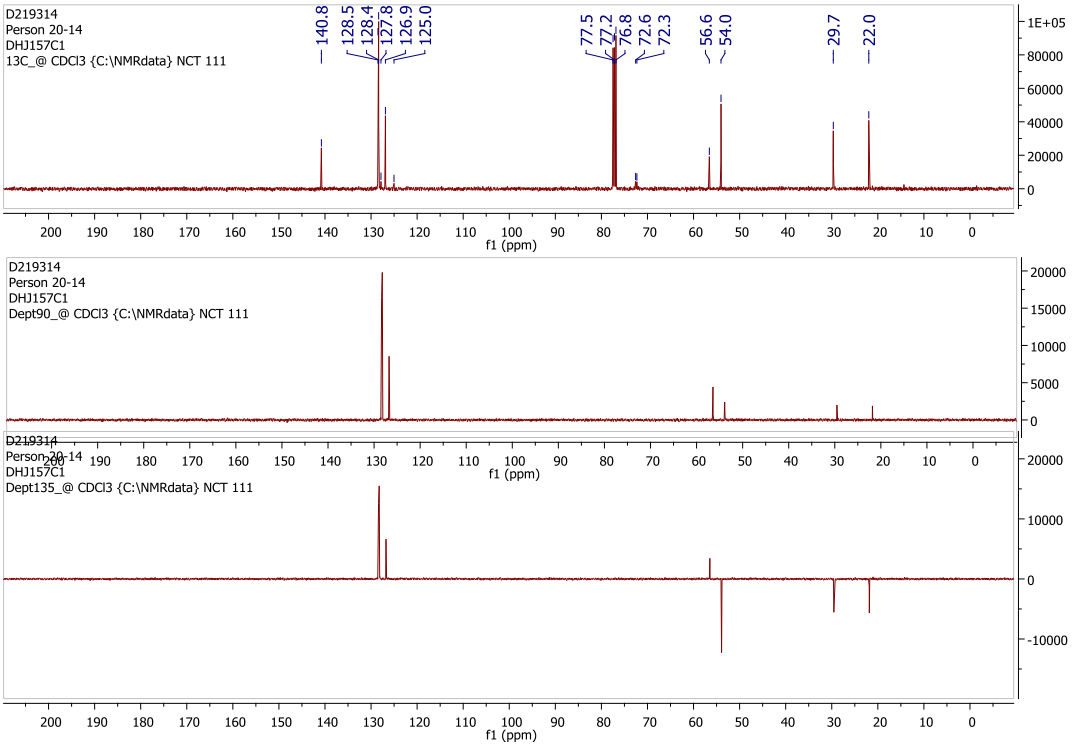


16

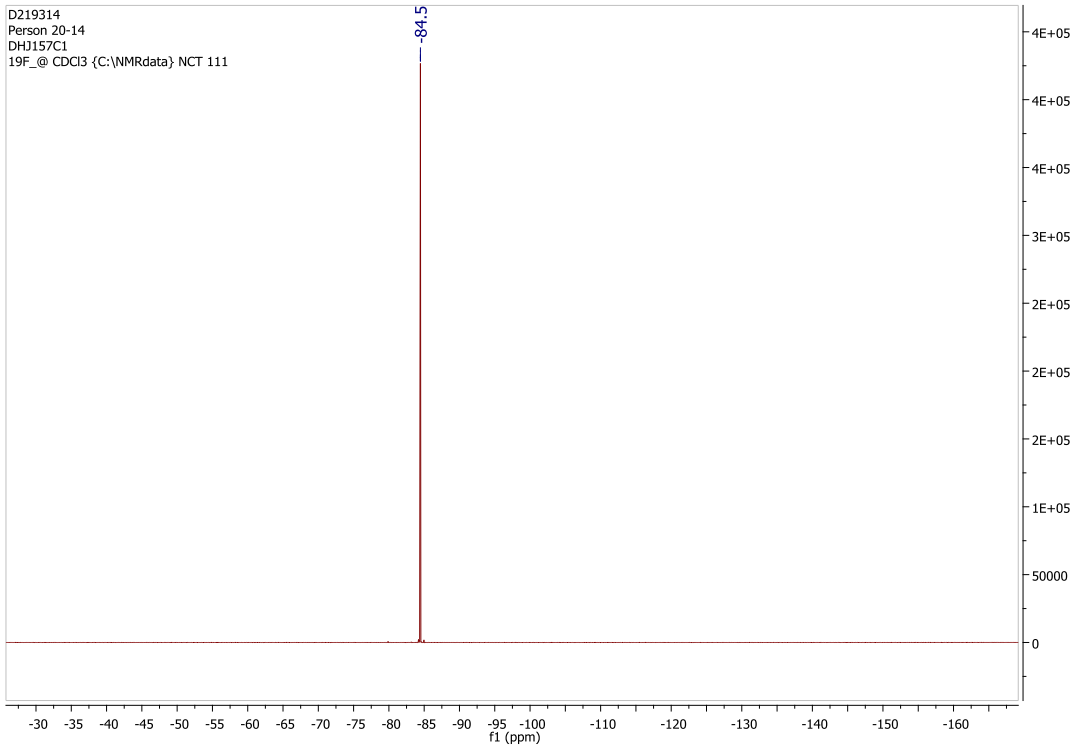
^{1}H NMR (400 MHz, $CDCl_3$)



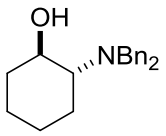
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)



Trans-2-(dibenzylamino)cyclohexan-1-ol



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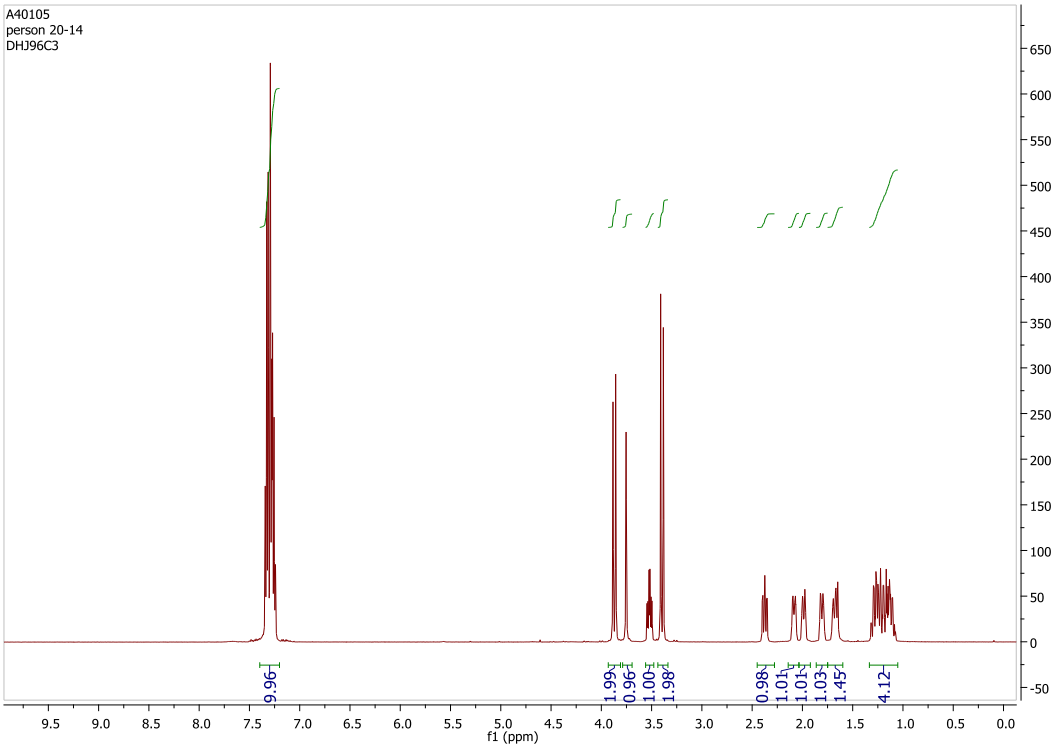
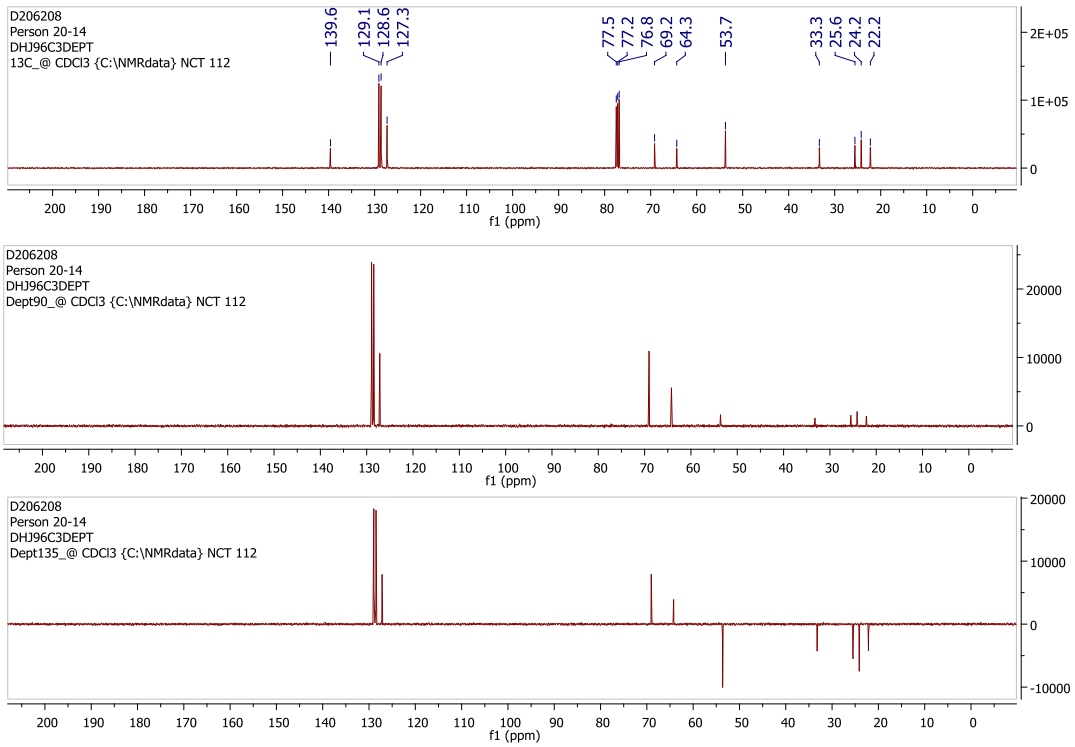
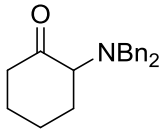


^{13}C NMR (101 MHz, $CDCl_3$)



2-(Dibenzylamino)cyclohexan-1-one **28**



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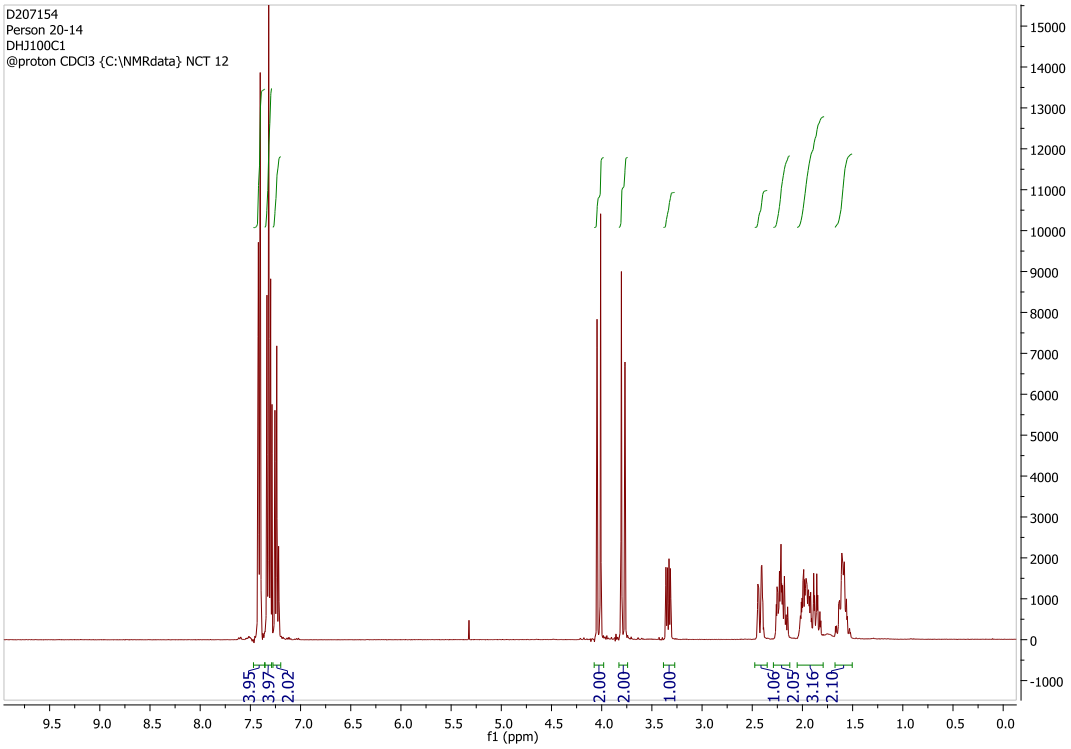
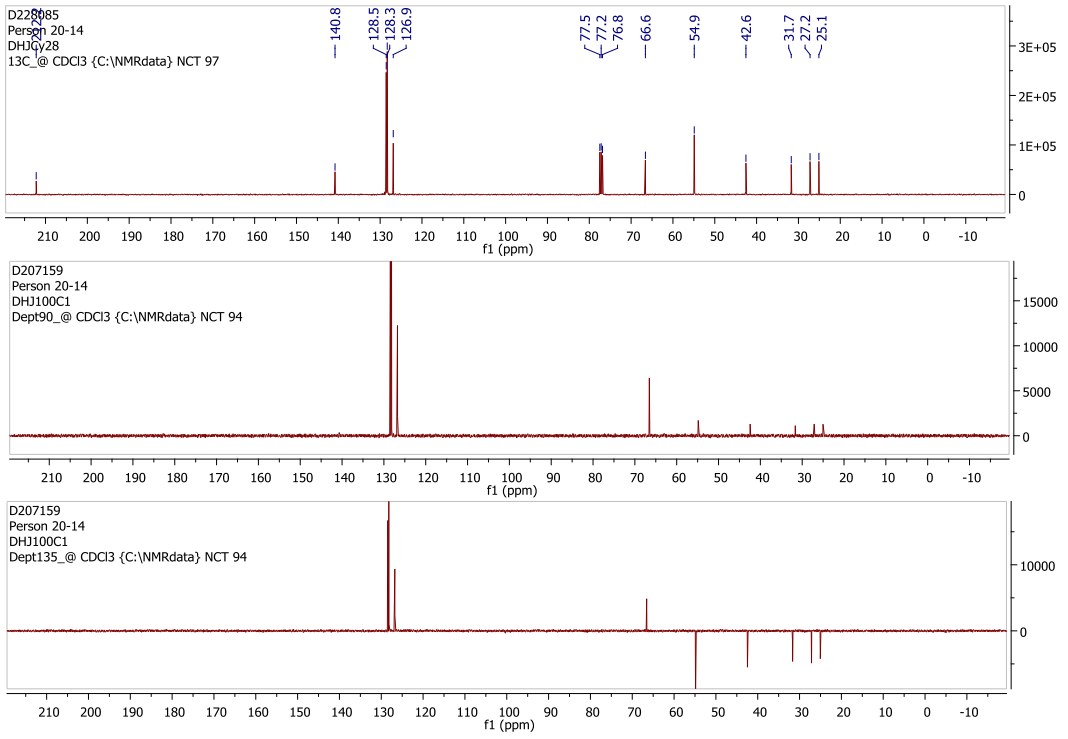
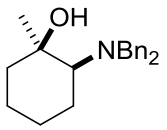
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

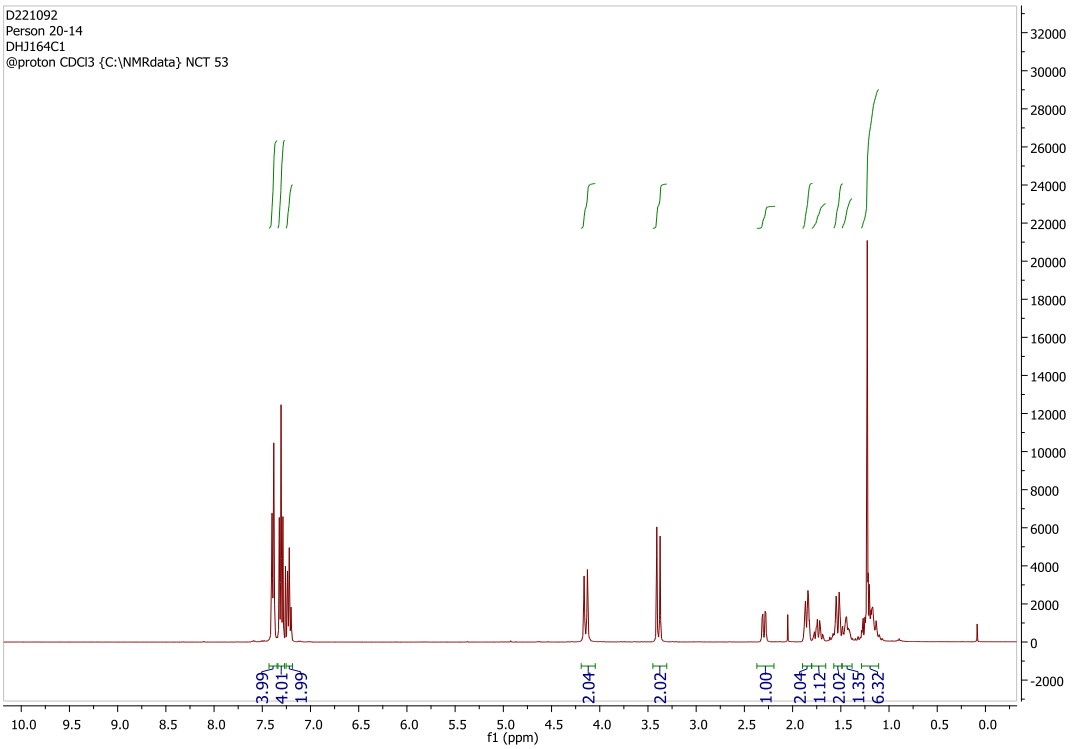


Cis-2-(dibenzylamino)-1-methylcyclohexan-1-ol **14**

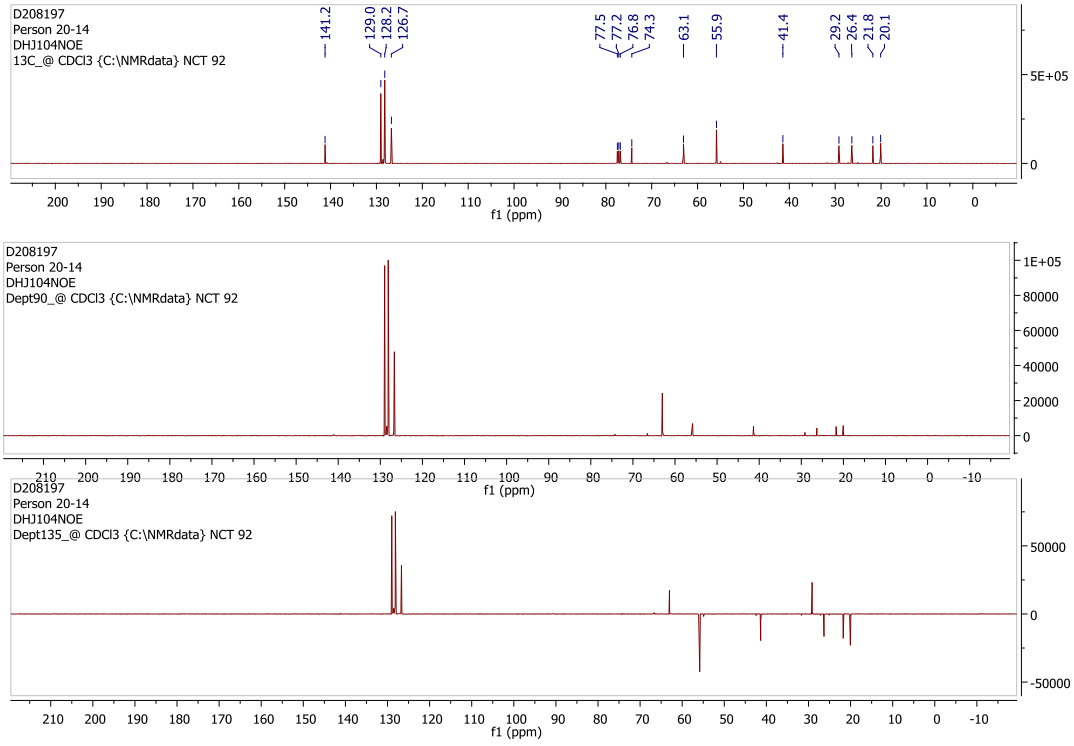


14

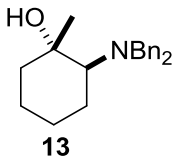
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



Trans-2-(dibenzylamino)-1-methylcyclohexan-1-ol **13**



13

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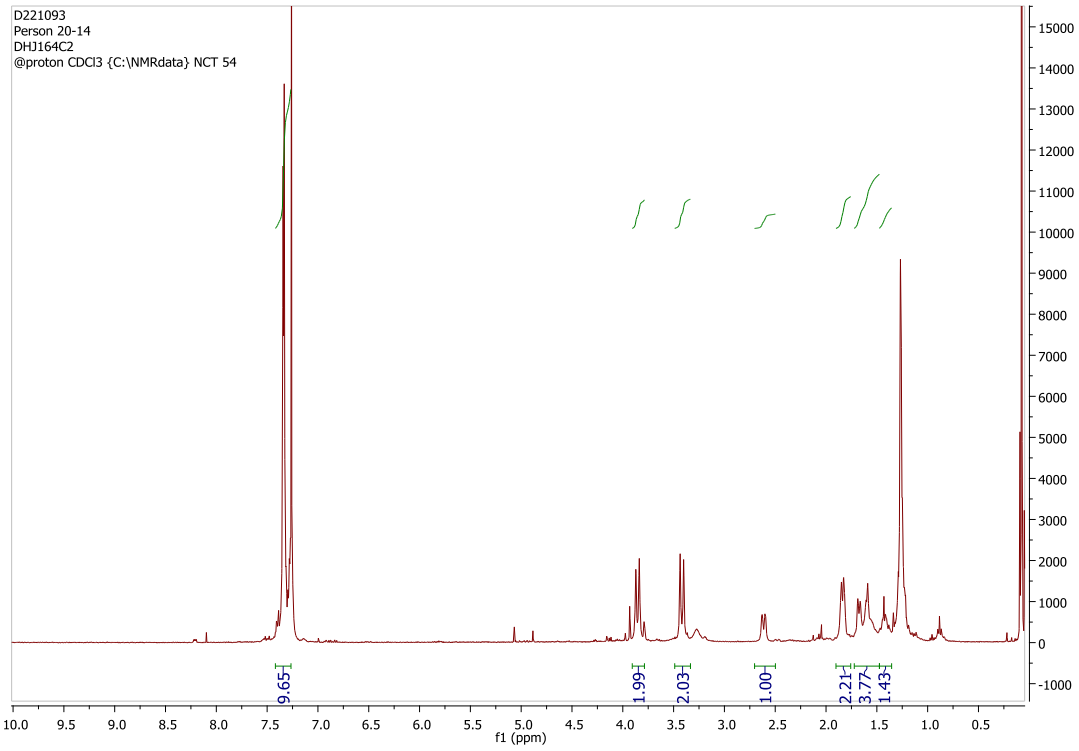

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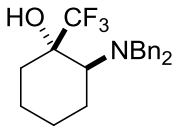

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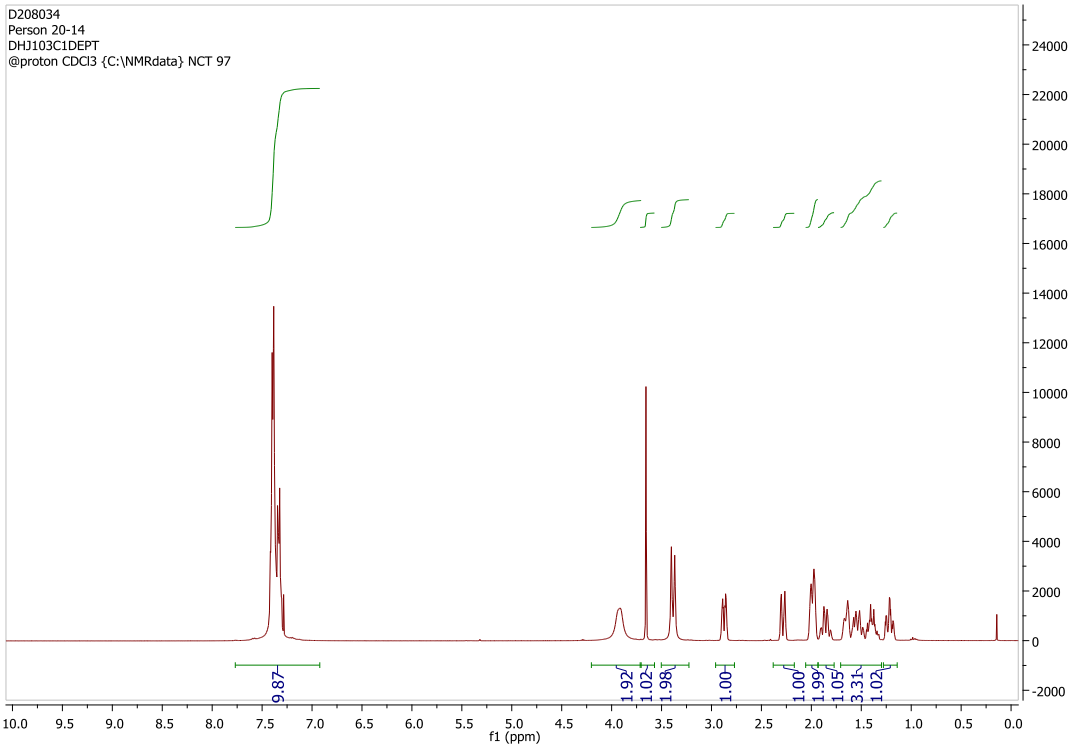

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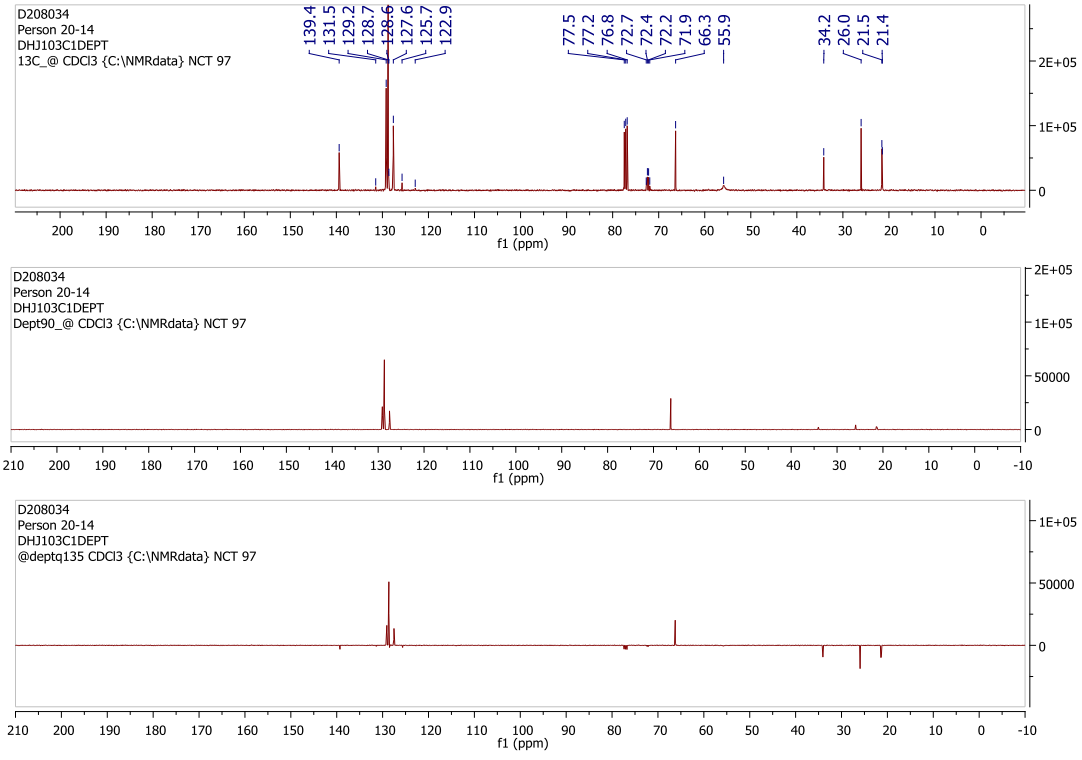
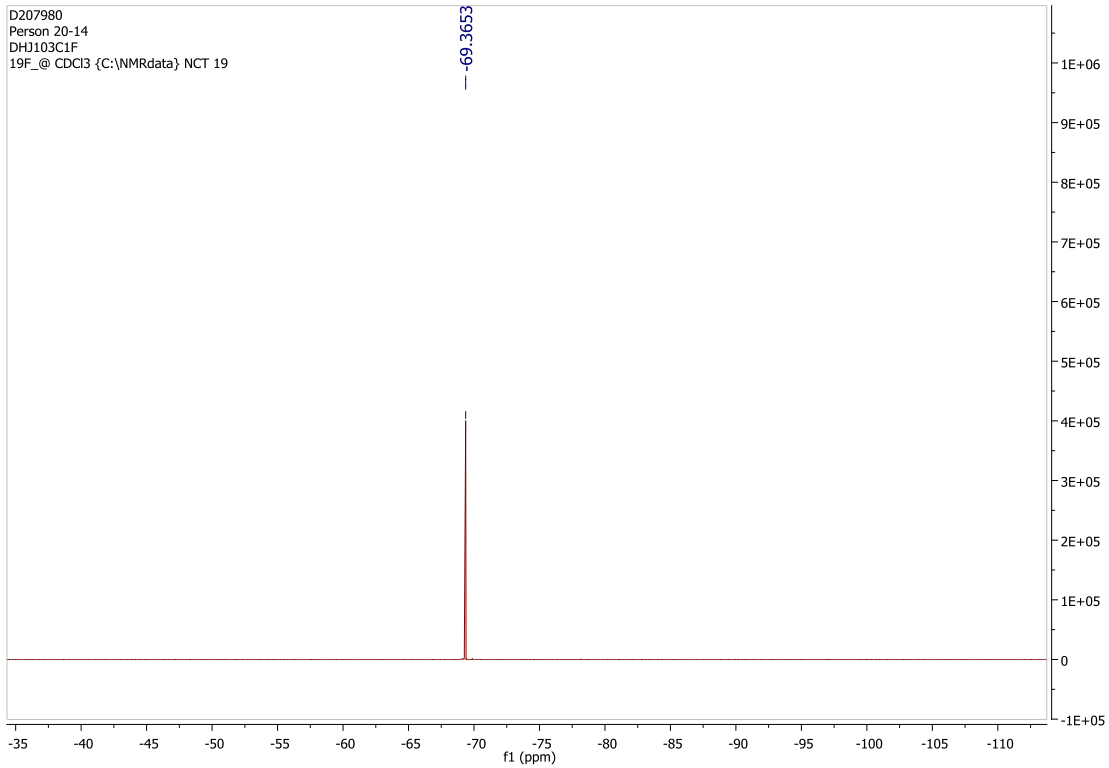
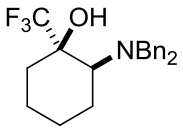


^{19}F NMR (376 MHz, $CDCl_3$)

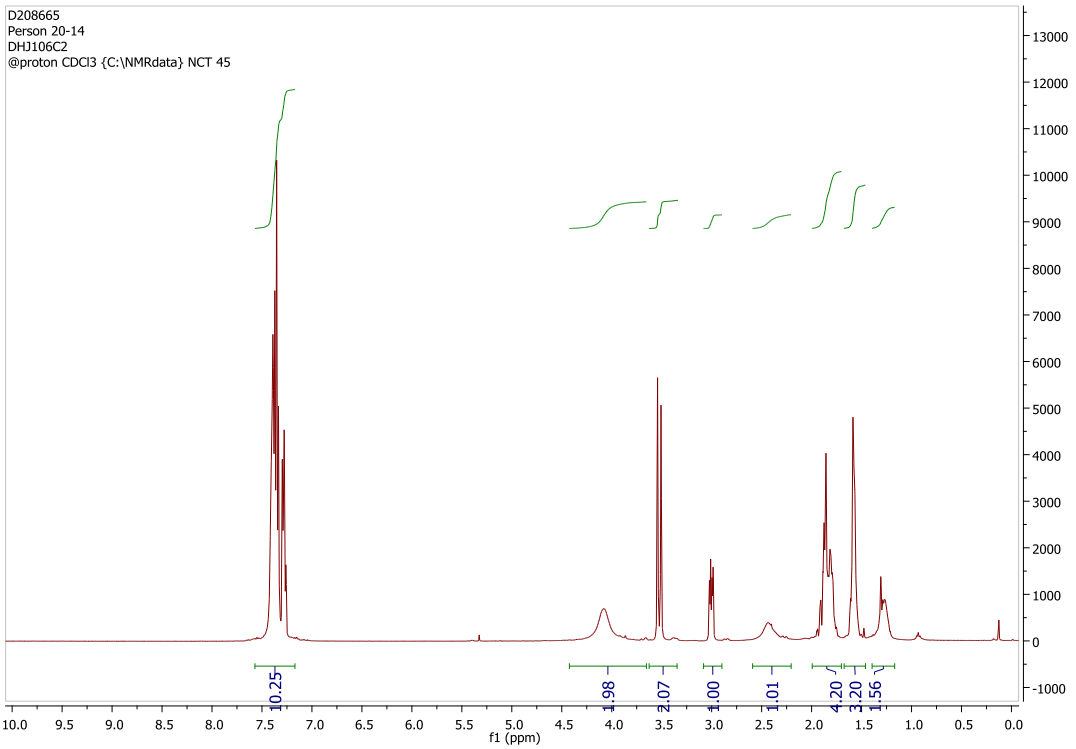


Cis-2-(dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **20**

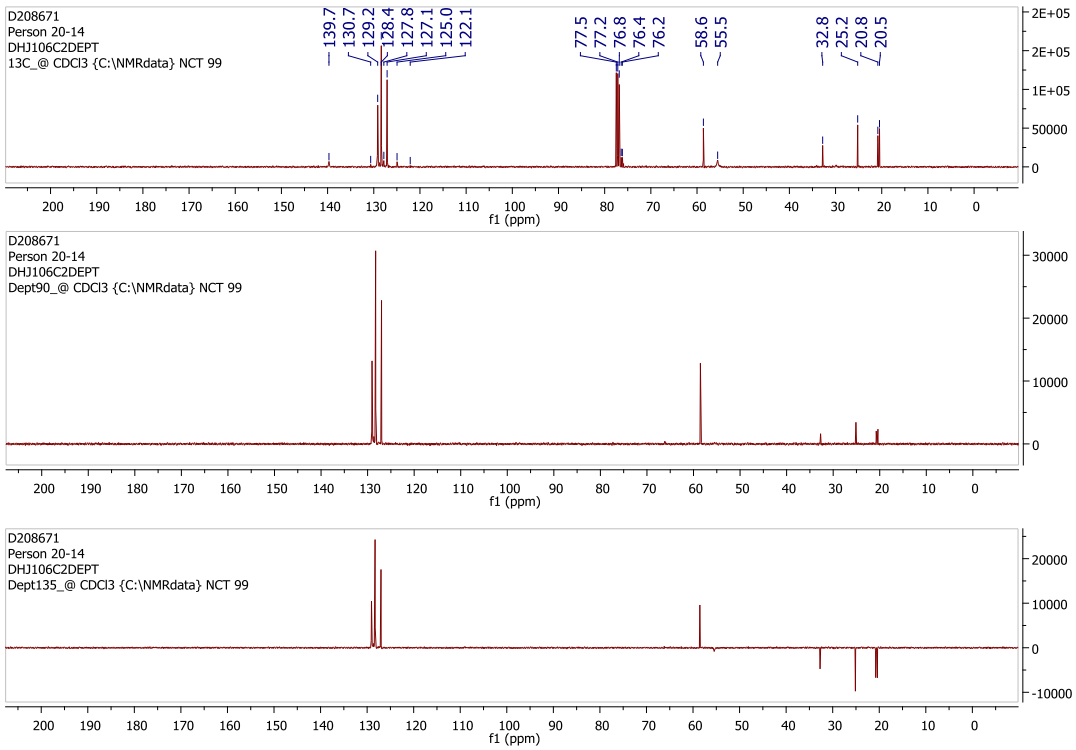


20

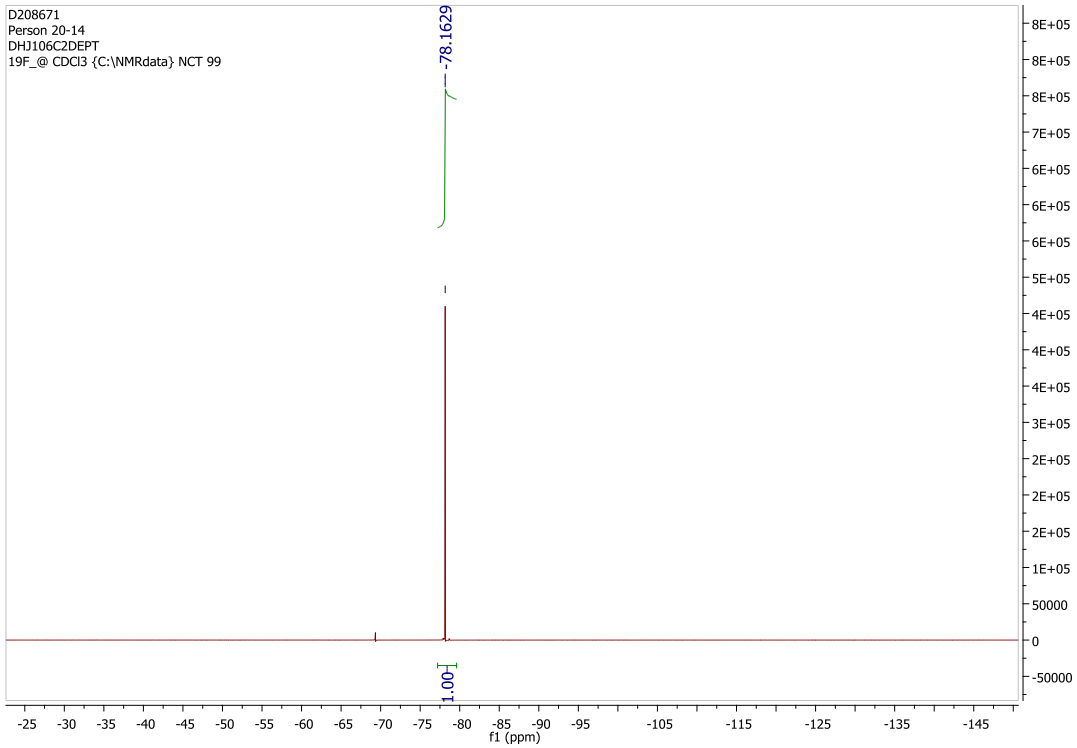
^{1}H NMR (400 MHz, $CDCl_3$)



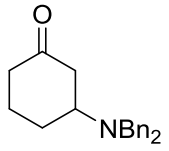
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)

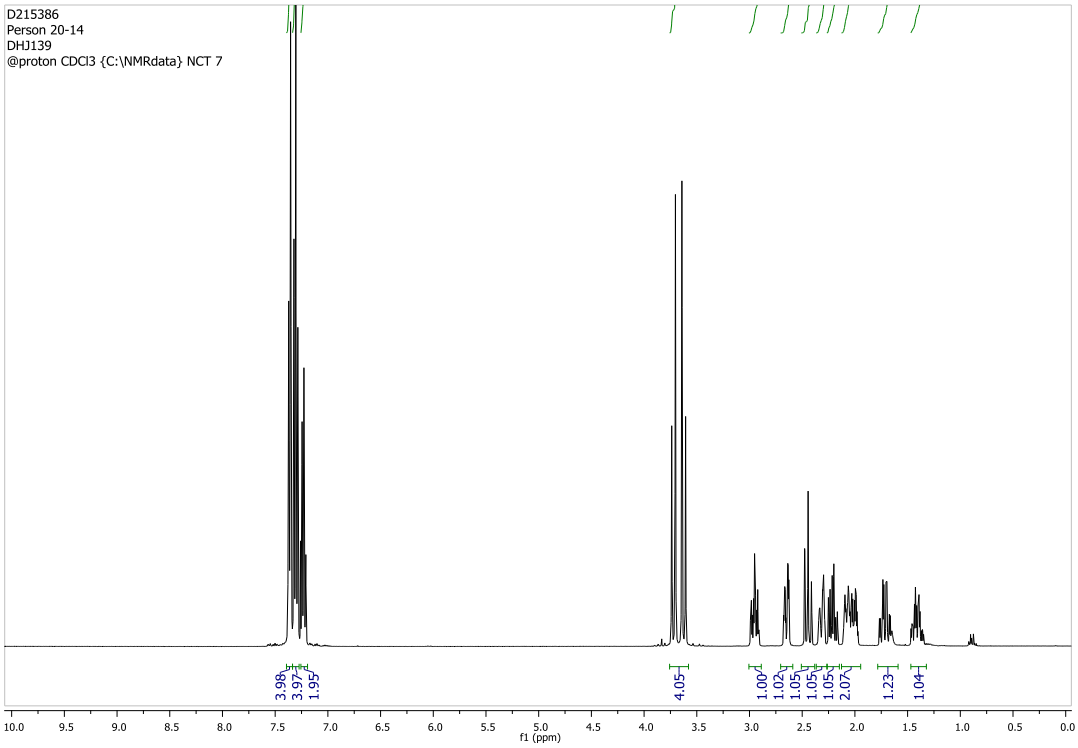


3-(Dibenzylamino)cyclohexan-1-one **30**

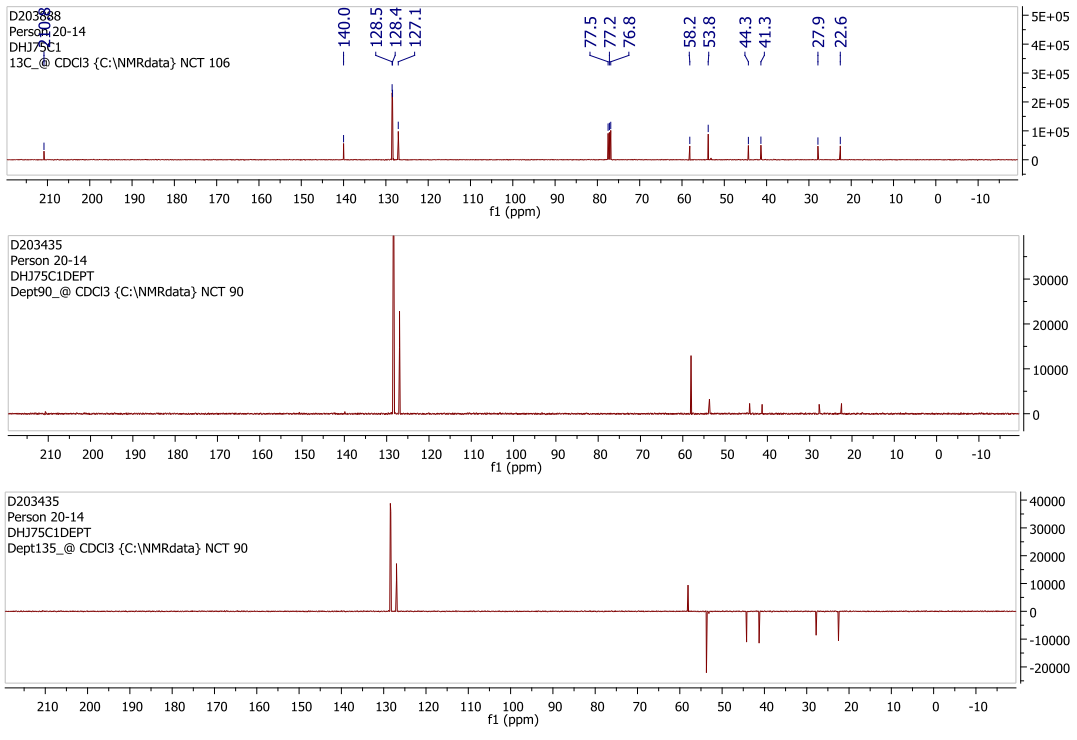


30

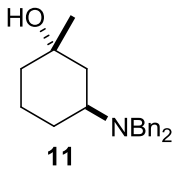
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

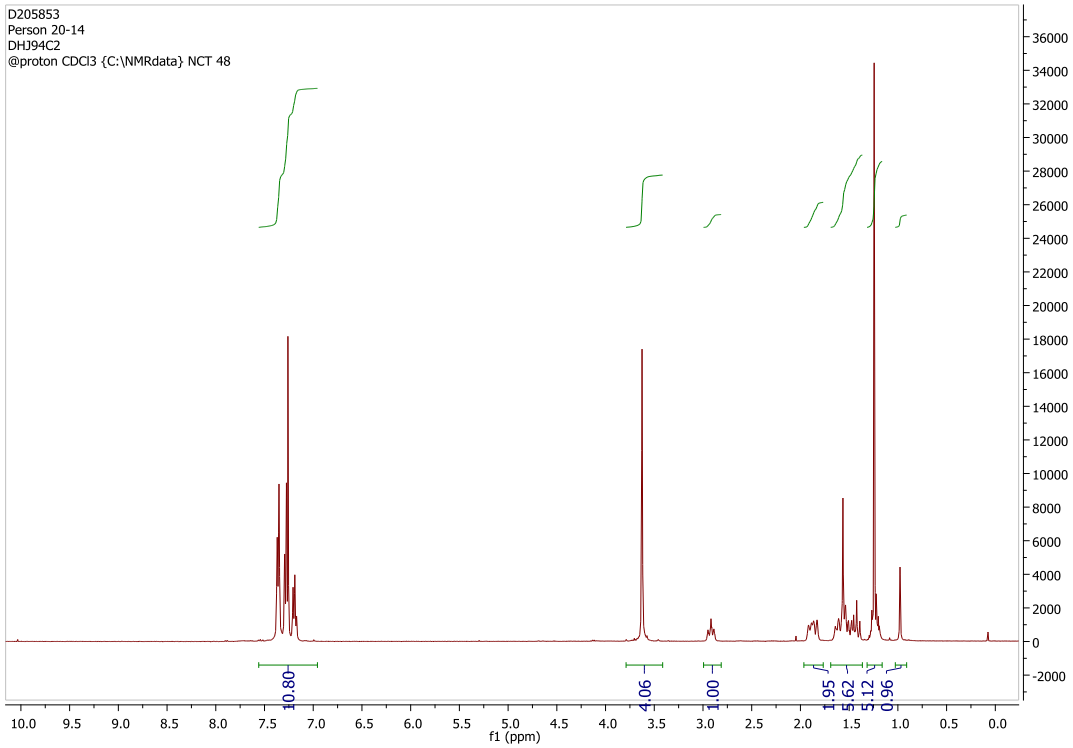


Trans-3-(dibenzylamino)-1-methylcyclohexan-1-ol **11**



11

^{1}H NMR (400 MHz, $CDCl_3$)



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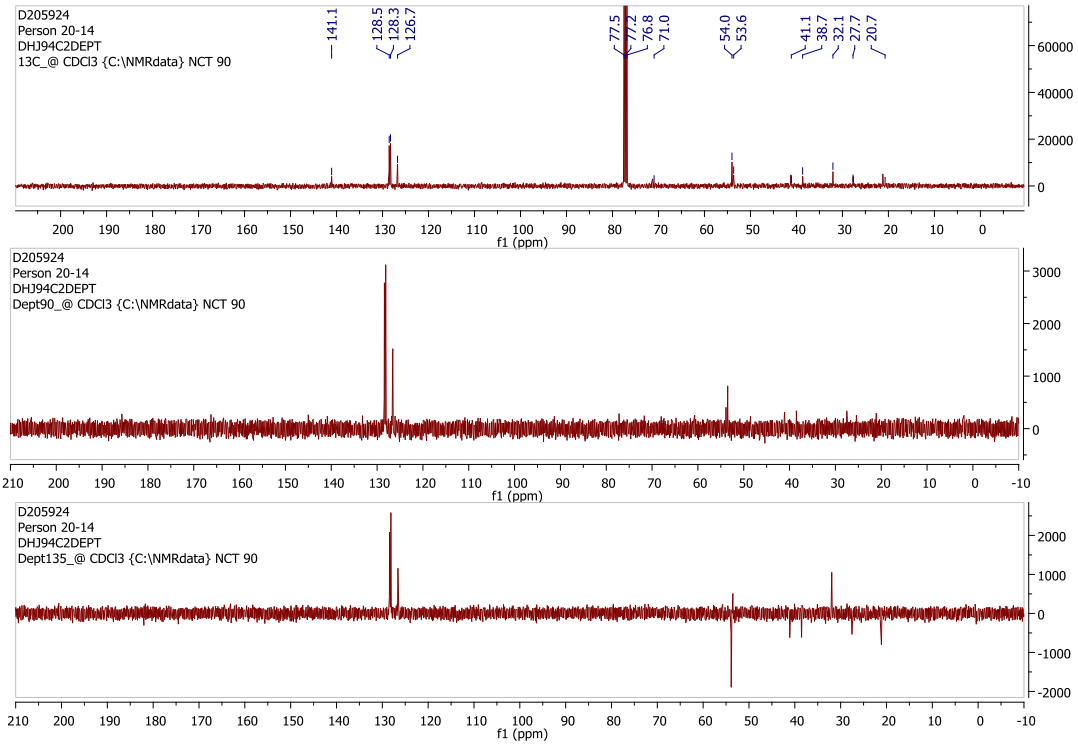
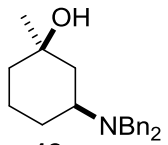


Cis-3-(dibenzylamino)-1-methylcyclohexan-1-ol **12**



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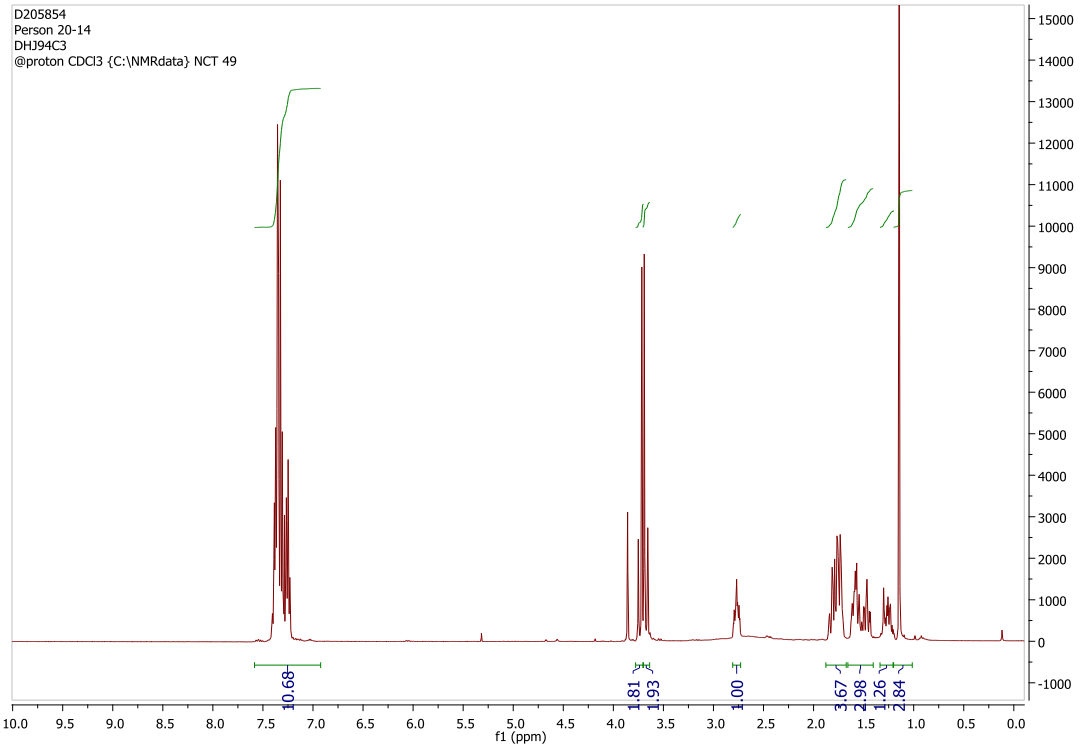
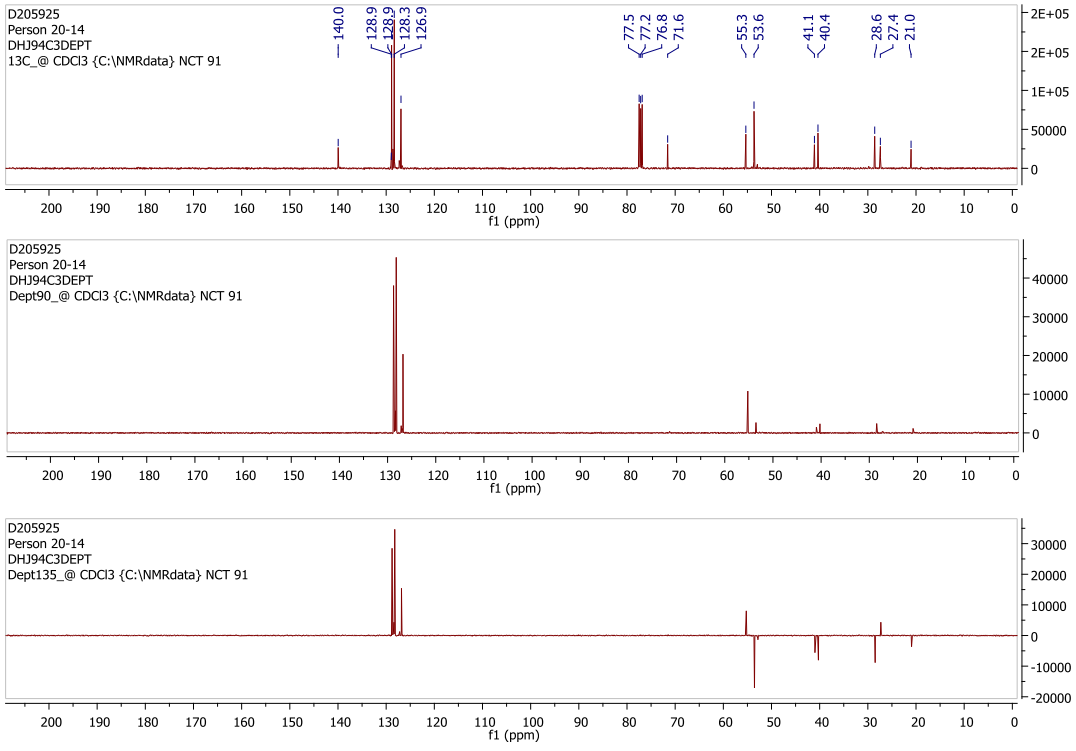
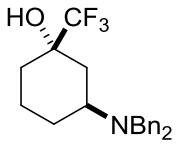
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

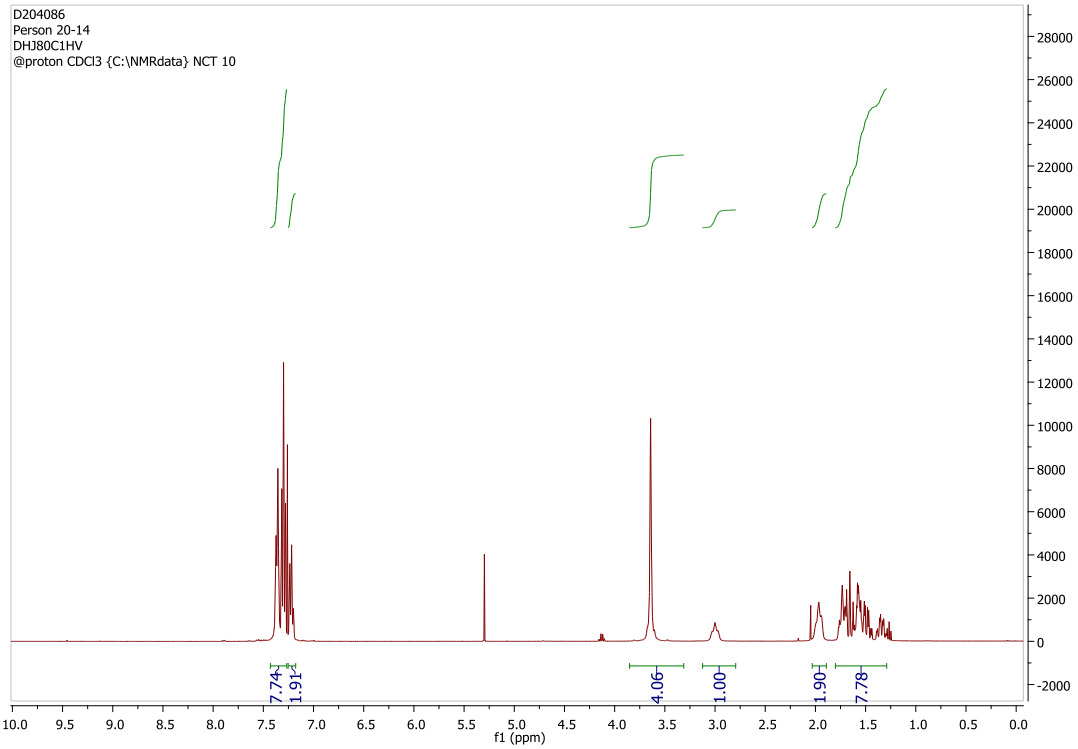


Trans-3-(dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **17**

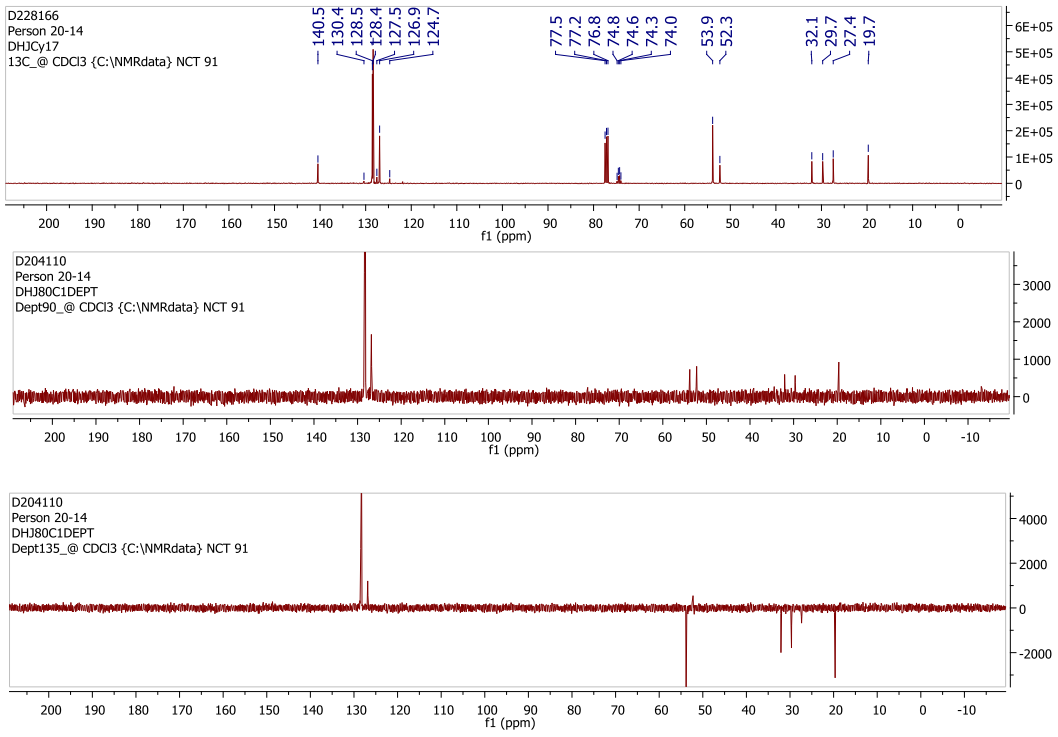


17

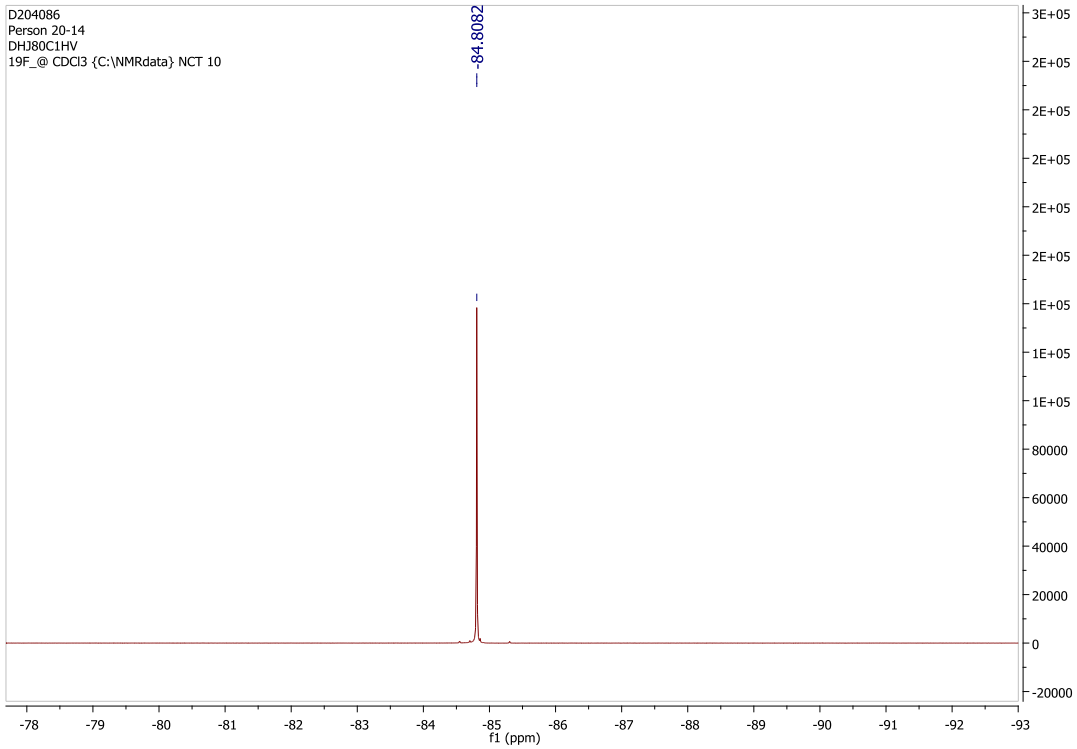
^{1}H NMR (400 MHz, $CDCl_3$)



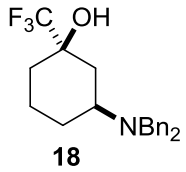
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)

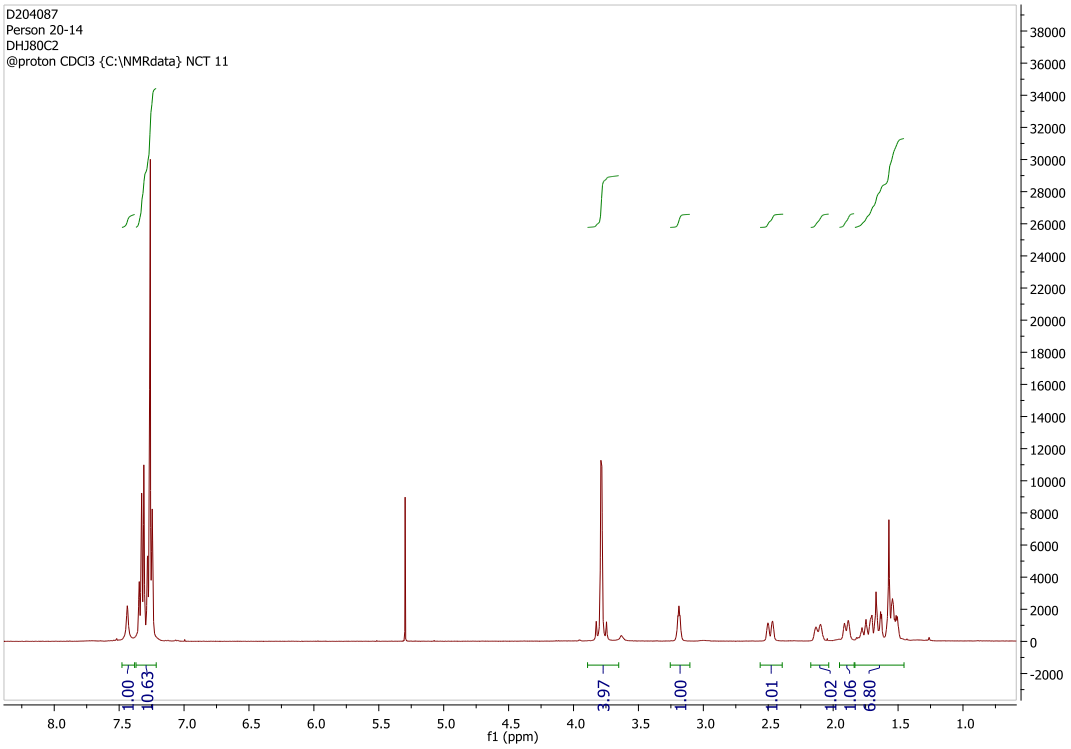


Cis-3-(dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **18**

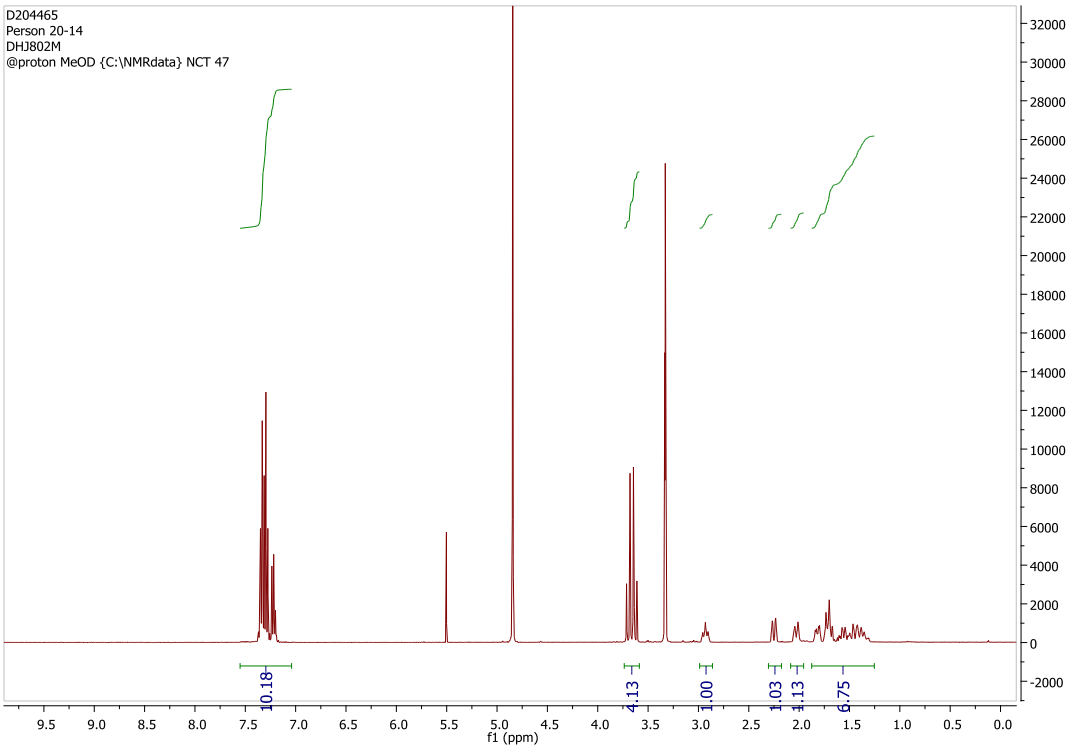


18

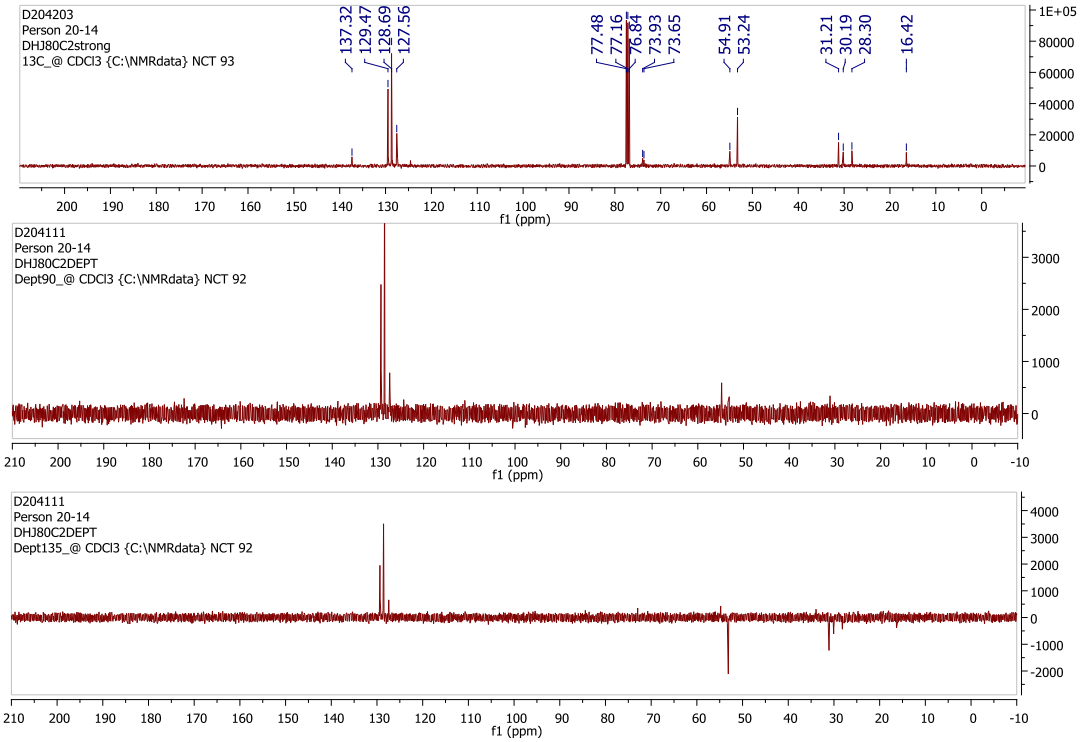
^{1}H NMR (400 MHz, $CDCl_3$)



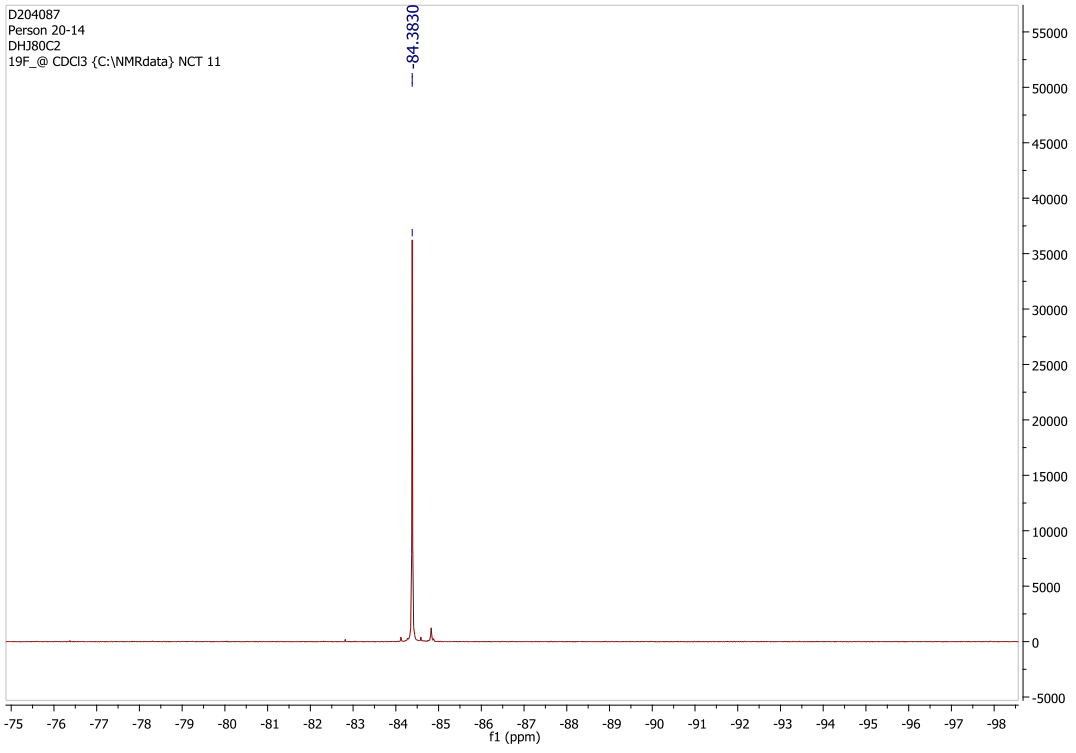
^{1}H NMR (400 MHz, MeOD)



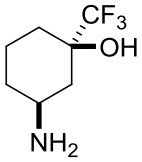
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)

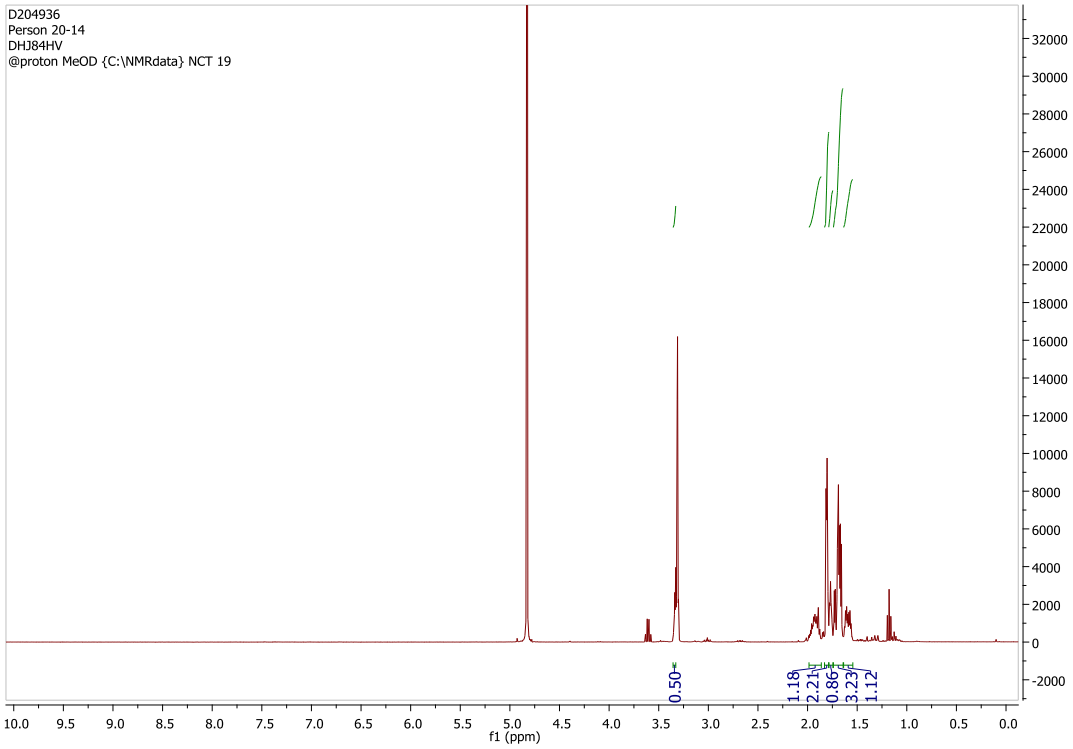


Cis-3-(amino)-1-trifluoromethylcyclohexan-1-ol **31**

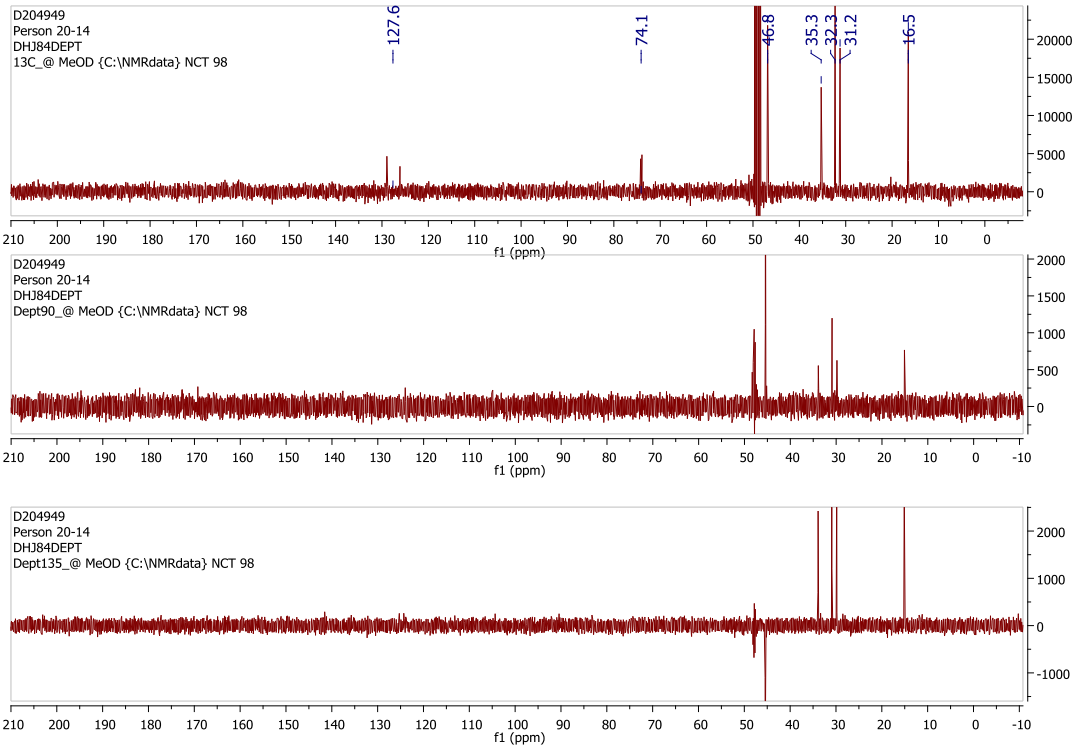


31

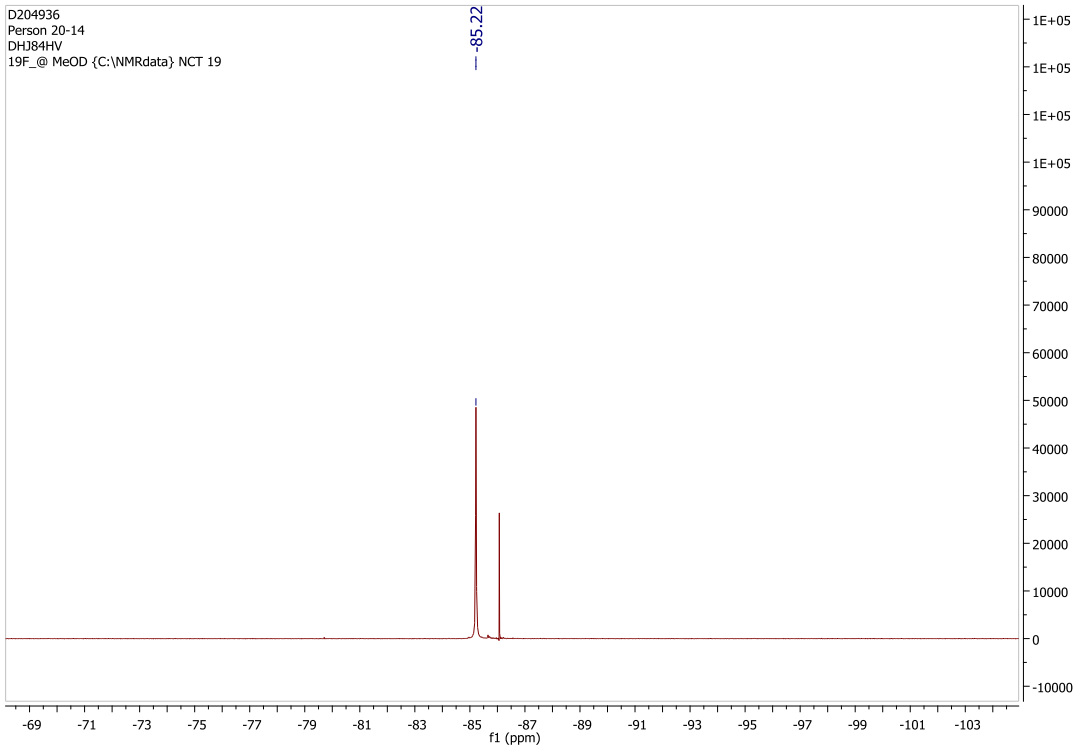
^{1}H NMR (400 MHz, MeOD)



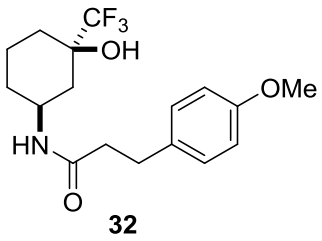
^{13}C NMR (101 MHz, MeOD)



^{19}F NMR (376 MHz, MeOD)

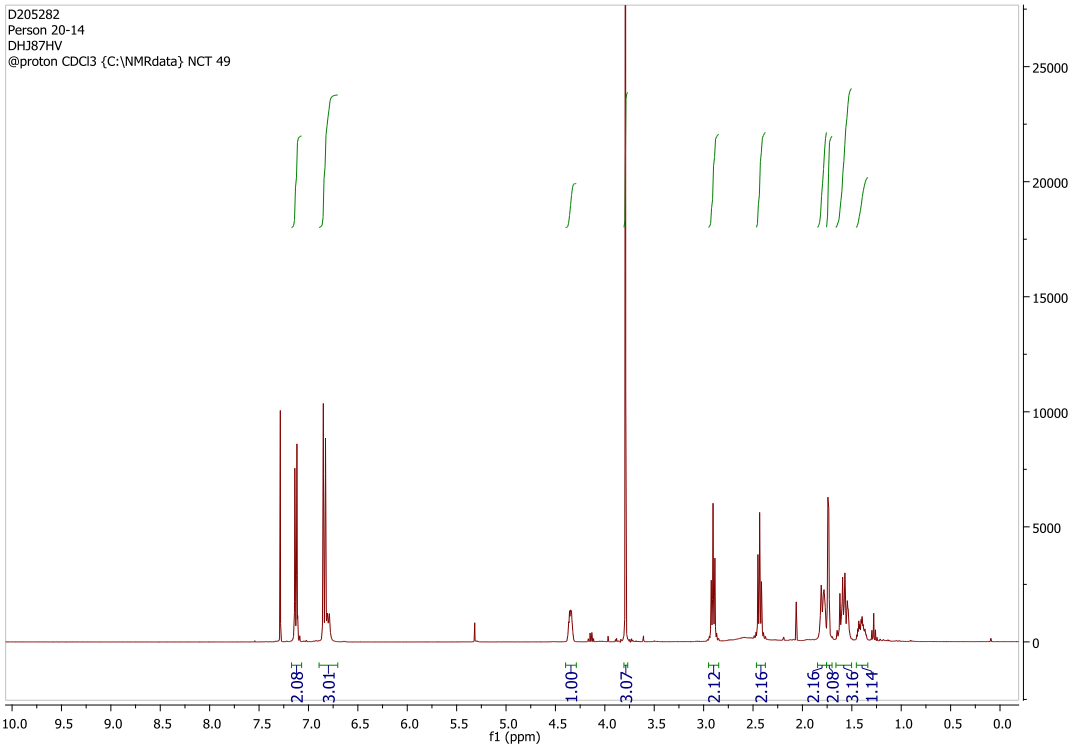


N-Cis-3-hydroxy-3-(trifluoromethyl)cyclohexyl)-3-(4-methoxyphenyl)propanamide **32**

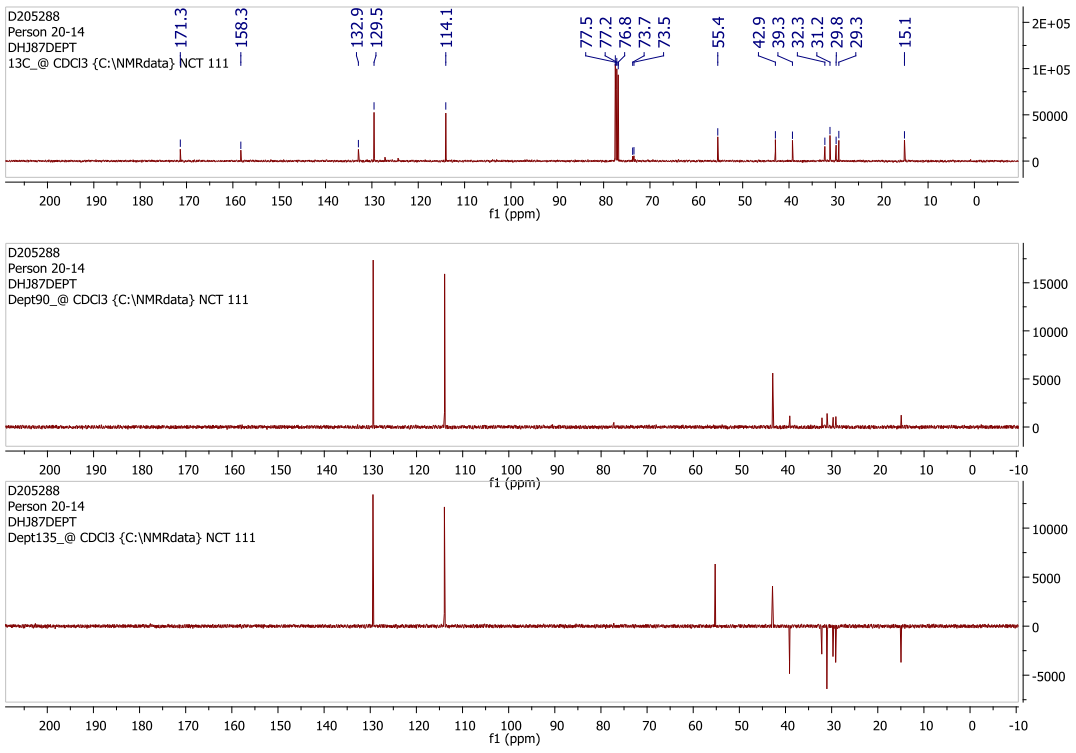


32

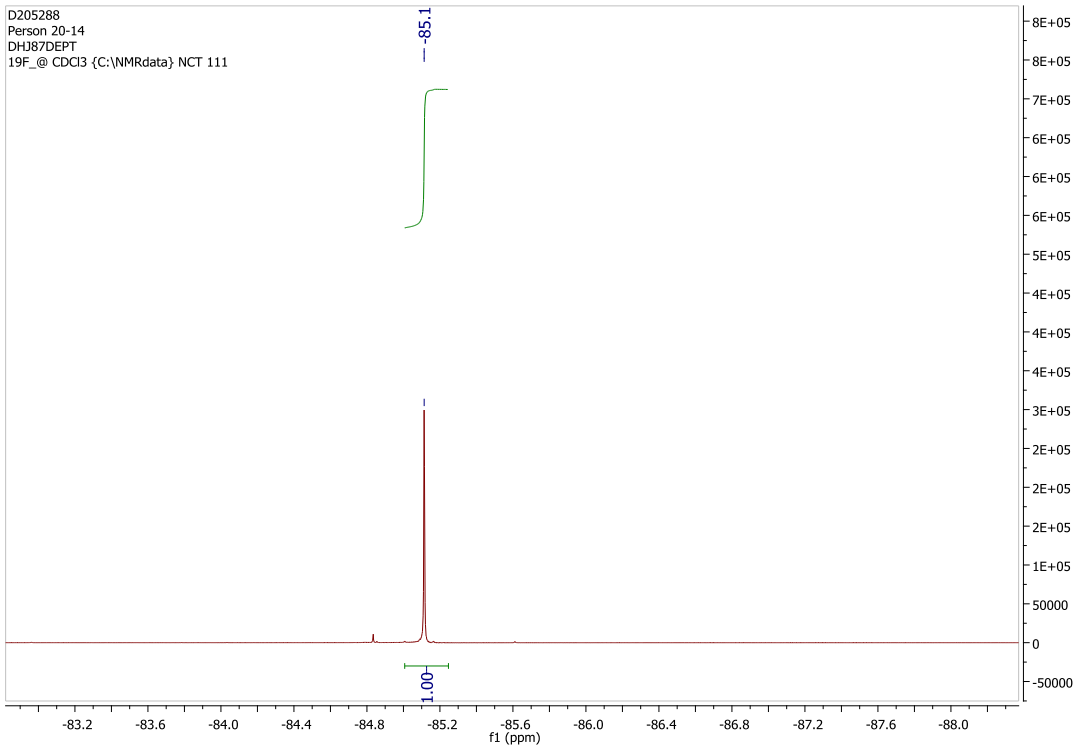
^{1}H NMR (400 MHz, $CDCl_3$)



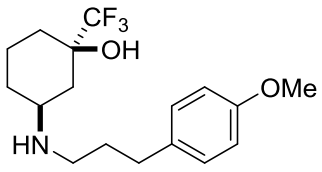
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)

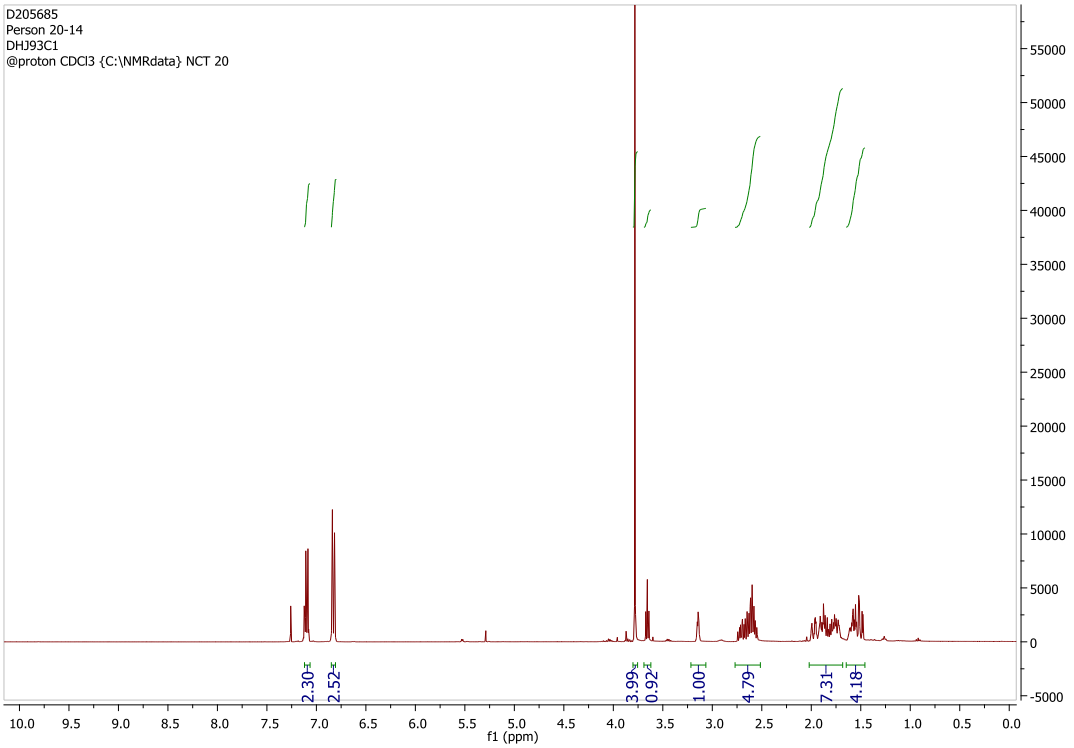


Cis-3-((3-(4-methoxyphenyl)propyl)amino)-1-(trifluoromethyl)cyclohexan-1-ol **33**

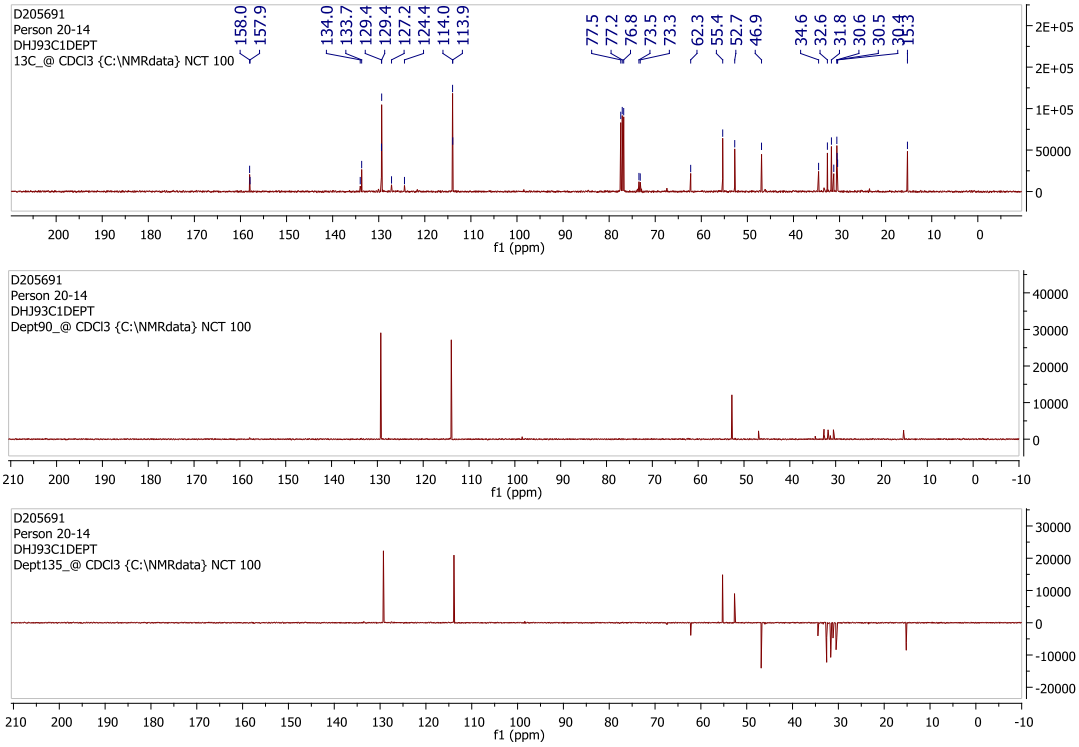


33

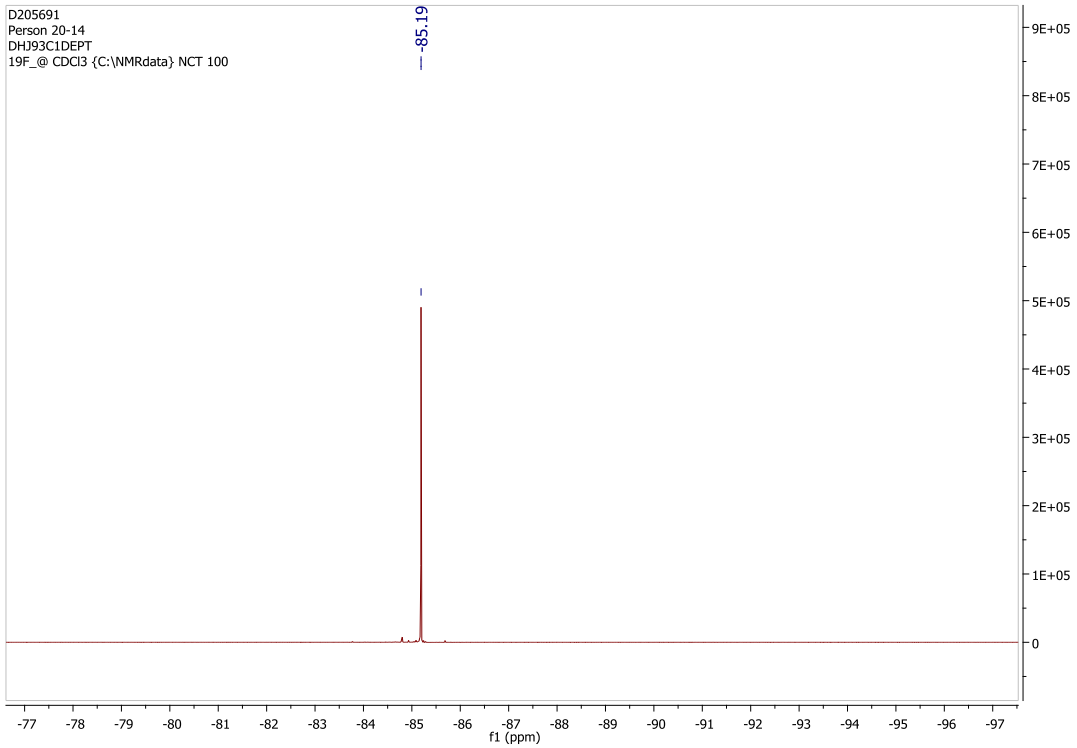
^{1}H NMR (400 MHz, $CDCl_3$)

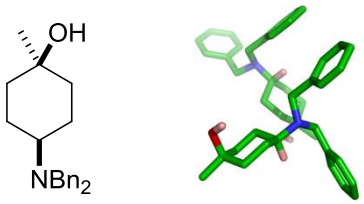


^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)

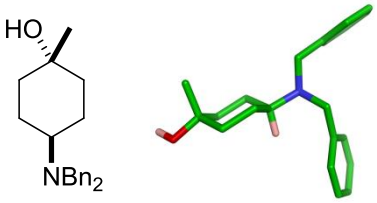




10

Table S1. Crystal data and structure refinement for *cis*-(4-dibenzylamino)-1-methylcyclohexan-1-ol **10**.

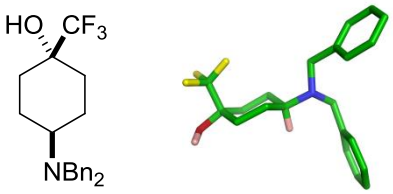
Identification code	CCDC 1064076	
Empirical formula	$C_{21}H_{27}NO$	
Formula weight	309.44	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Ccc2	
Unit cell dimensions	a = 23.0565(17) Å	α= 90°.
	b = 27.3947(17) Å	β= 90°.
	c = 11.6346(9) Å	γ = 90°.
Volume	7348.7(9) $Å^3$	
Z	16	
Density (calculated)	1.119 Mg/m^3	
Absorption coefficient	0.068 mm^{-1}	
F(000)	2688	
Crystal size	0.35 x 0.20 x 0.03 mm^3	
Theta range for data collection	2.97 to 27.00°.	
Index ranges	-29<=h<=28, -34<=k<=34, -14<=l<=14	
Reflections collected	24970	
Independent reflections	7436 [R(int) = 0.0598]	
Completeness to theta = 27.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.91453	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7436 / 5 / 429	
Goodness-of-fit on F^2	1.045	
Final R indices [I>2sigma(I)]	R1 = 0.0511, wR2 = 0.0847	
R indices (all data)	R1 = 0.0776, wR2 = 0.0942	
Absolute structure parameter	-1.3(12)	
Largest diff. peak and hole	0.152 and -0.168 e.$Å^{-3}$	



9

Table S2. Crystal data and structure refinement for *trans*-4-(dibenzylamino)-1-methylcyclohexan-1-ol **9**.

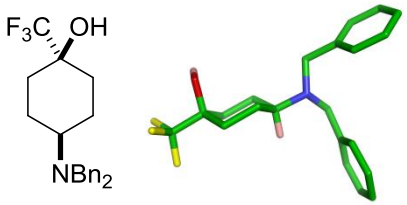
Identification code	CCDC 1064075	
Empirical formula	$C_{21}H_{27}NO$	
Formula weight	309.44	
Temperature	123(2) K	
Wavelength	1.54180 Å	
Crystal system	Trigonal	
Space group	P-3	
Unit cell dimensions	a = 18.6953(4) Å	α = 90°.
	b = 18.6953(4) Å	β = 90°.
	c = 9.2303(2) Å	γ = 120°.
Volume	2793.90(10) $Å^3$	
Z	6	
Density (calculated)	1.103 Mg/m^3	
Absorption coefficient	0.512 mm^{-1}	
F(000)	1008	
Crystal size	0.28 x 0.15 x 0.10 mm^3	
Theta range for data collection	4.73 to 73.12°.	
Index ranges	-17<=h<=23, -20<=k<=19, -11<=l<=6	
Reflections collected	6073	
Independent reflections	3634 [R(int) = 0.0219]	
Completeness to theta = 70.00°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.82144	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3634 / 0 / 213	
Goodness-of-fit on F^2	1.061	
Final R indices [I>2sigma(I)]	R1 = 0.0477, wR2 = 0.1266	
R indices (all data)	R1 = 0.0562, wR2 = 0.1352	
Largest diff. peak and hole	0.296 and -0.207 $e.Å^{-3}$	



15

Table S3. Crystal data and structure refinement *trans*-(dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **15**.

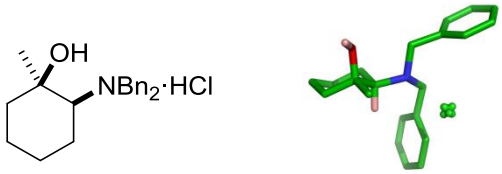
Identification code	CCDC 1064079	
Empirical formula	$C_{21}H_2F_3NO_{1.50}$	
Formula weight	372.42	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 16.8197(14) Å	α = 90°.
	b = 6.2849(5) Å	β = 93.240(7)°.
	c = 18.1930(14) Å	γ = 90°.
Volume	1920.1(3) $Å^3$	
Z	4	
Density (calculated)	1.288 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	788	
Crystal size	0.24 x 0.12 x 0.05 mm^3	
Theta range for data collection	3.21 to 27.00°.	
Index ranges	-21<=h<=21, -8<=k<=8, -23<=l<=23	
Reflections collected	20222	
Independent reflections	4183 [R(int) = 0.0440]	
Completeness to theta = 27.00°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.63335	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4183 / 4 / 256	
Goodness-of-fit on F^2	1.144	
Final R indices [I>2sigma(I)]	R1 = 0.0547, wR2 = 0.1108	
R indices (all data)	R1 = 0.0727, wR2 = 0.1176	
Largest diff. peak and hole	0.275 and -0.222 $e.Å^{-3}$	



16

Table S4. Crystal data and structure refinement for *cis*-(4-dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **16**.

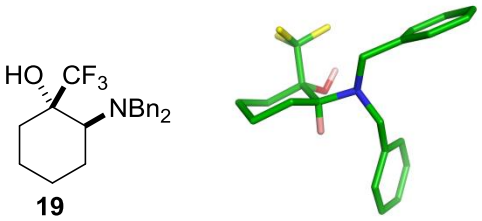
Identification code	CCDC 1064080	
Empirical formula	$C_{21}H_{24}F_3NO$	
Formula weight	363.41	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 17.8003(4) Å	α = 90°.
	b = 6.1791(2) Å	β = 101.206(2)°.
	c = 17.0864(3) Å	γ = 90°.
Volume	1843.50(8) $Å^3$	
Z	4	
Density (calculated)	1.309 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	768	
Crystal size	0.32 x 0.22 x 0.20 mm^3	
Theta range for data collection	3.50 to 29.56°.	
Index ranges	-23<=h<=24, -8<=k<=8, -22<=l<=22	
Reflections collected	16736	
Independent reflections	4716 [R(int) = 0.0266]	
Completeness to theta = 27.00°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.96542	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4716 / 0 / 239	
Goodness-of-fit on F^2	1.025	
Final R indices [I>2sigma(I)]	R1 = 0.0404, wR2 = 0.0932	
R indices (all data)	R1 = 0.0506, wR2 = 0.0999	
Extinction coefficient	0.0064(8)	
Largest diff. peak and hole	0.398 and -0.290 e.$Å^{-3}$	



14·HCl

Table S5. Crystal data and structure refinement for *cis*-2-(dibenzylamino)-1-methylcyclohexan-1-ol HCl salt **14**.

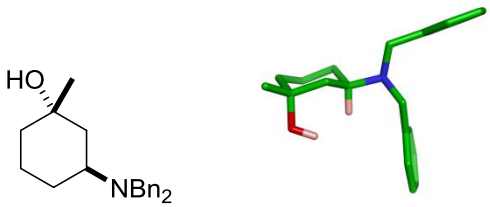
Identification code	CCDC 1064078	
Empirical formula	$C_{21}H_{28}ClNO$	
Formula weight	345.89	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$Pna2_1$	
Unit cell dimensions	a = 18.8610(10) Å	α = 90°.
	b = 7.1930(3) Å	β = 90°.
	c = 13.7442(6) Å	γ = 90°.
Volume	1864.64(15) $Å^3$	
Z	4	
Density (calculated)	1.232 Mg/m^3	
Absorption coefficient	0.212 mm^{-1}	
F(000)	744	
Crystal size	0.24 x 0.22 x 0.10 mm^3	
Theta range for data collection	3.20 to 30.02°.	
Index ranges	-25<=h<=24, -10<=k<=10, -18<=l<=18	
Reflections collected	26232	
Independent reflections	5038 [R(int) = 0.0323]	
Completeness to theta = 27.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.99094	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5038 / 1 / 226	
Goodness-of-fit on F^2	1.049	
Final R indices [I>2sigma(I)]	R1 = 0.0300, wR2 = 0.0691	
R indices (all data)	R1 = 0.0332, wR2 = 0.0711	
Absolute structure parameter	-0.03(4)	
Largest diff. peak and hole	0.262 and -0.180 e.$Å^{-3}$	



19

Table S6. Crystal data and structure refinement for *trans*-2-(dibenzylamino)-1-trifluoromethylcyclohexan-1-ol **19**.

Identification code	CCDC 1064081	
Empirical formula	$C_{21}H_{24}F_3NO$	
Formula weight	363.41	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.0335(3) Å	α = 95.431(3)°.
	b = 9.8976(3) Å	β = 101.143(3)°.
	c = 11.7319(3) Å	γ = 115.147(3)°.
Volume	912.99(5) $Å^3$	
Z	2	
Density (calculated)	1.322 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	384	
Crystal size	0.40 x 0.40 x 0.22 mm^3	
Theta range for data collection	3.21 to 30.46°.	
Index ranges	-12<=h<=11, -14<=k<=13, -16<=l<=16	
Reflections collected	16095	
Independent reflections	5061 [R(int) = 0.0168]	
Completeness to theta = 27.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.90539	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5061 / 0 / 240	
Goodness-of-fit on F^2	1.023	
Final R indices [I>2sigma(I)]	R1 = 0.0378, wR2 = 0.0956	
R indices (all data)	R1 = 0.0439, wR2 = 0.1005	
Extinction coefficient	0.034(3)	
Largest diff. peak and hole	0.379 and -0.239 $e.Å^{-3}$	



11

Table S7. Crystal data and structure refinement *trans*-3-(dibenzylamino)-1-methylcyclohexan-1-ol **11**.

Identification code	CCDC 1064077	
Empirical formula	$C_{23}H_{35}NO_3$	
Formula weight	373.52	
Temperature	123(2) K	
Wavelength	1.54180 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 17.524(2) Å	α = 90°.
	b = 6.4455(6) Å	β = 99.422(9)°.
	c = 19.9254(16) Å	γ = 90°.
Volume	2220.2(4) $Å^3$	
Z	4	
Density (calculated)	1.117 Mg/m^3	
Absorption coefficient	0.572 mm^{-1}	
F(000)	816	
Crystal size	0.25 x 0.04 x 0.04 mm^3	
Theta range for data collection	3.67 to 65.00°.	
Index ranges	-18<=h<=20, -4<=k<=7, -23<=l<=18	
Reflections collected	7857	
Independent reflections	3772 [R(int) = 0.0544]	
Completeness to theta = 65.00°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.35073	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3772 / 3 / 256	
Goodness-of-fit on F^2	1.039	
Final R indices [I>2sigma(I)]	R1 = 0.0759, wR2 = 0.1942	
R indices (all data)	R1 = 0.1198, wR2 = 0.2340	
Largest diff. peak and hole	0.235 and -0.205 e.$Å^{-3}$	

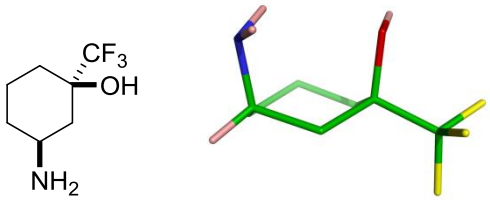


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Table S8. Crystal data and structure refinement for *cis*-3-(amino)-1-trifluoromethylcyclohexan-1-ol **31**.

Identification code	CCDC 1064082	
Empirical formula	$C_7H_{12}F_3NO$	
Formula weight	183.18	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2_1/c	
Unit cell dimensions	a = 8.3916(6) Å	α = 90°.
	b = 10.5116(5) Å	β = 101.449(6)°.
	c = 9.3538(6) Å	γ = 90°.
Volume	808.67(9) $Å^3$	
Z	4	
Density (calculated)	1.505 Mg/m^3	
Absorption coefficient	0.146 mm^{-1}	
F(000)	384	
Crystal size	0.32 x 0.25 x 0.08 mm^3	
Theta range for data collection	3.145 to 28.991°.	
Index ranges	-11<=h<=10, -14<=k<=14, -12<=l<=12	
Reflections collected	7340	
Independent reflections	2052 [R(int) = 0.0480]	
Completeness to theta = 27.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.57603	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2052 / 0 / 121	
Goodness-of-fit on F^2	1.051	
Final R indices [I>2sigma(I)]	R1 = 0.0436, wR2 = 0.0946	
R indices (all data)	R1 = 0.0678, wR2 = 0.1093	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.337 and -0.226 e.$Å^{-3}$	