Concise Catalytic Asymmetric Synthesis of (*R*)-4-Amino Uhle's Ketone

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Supporting Information

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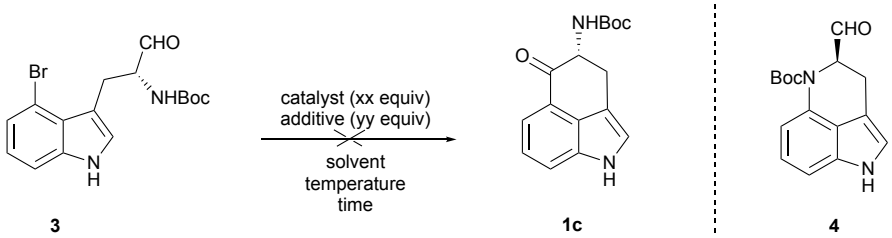
Table S1. Attempts toward the Synthesis of Uhle's Ketone 1c by Intramolecular Cross-electrophile Coupling [a]

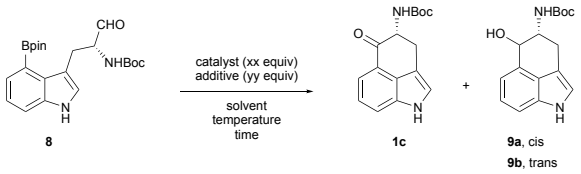


3 1c 4

entry	catalyst (equiv)	additive (equiv)	solvent	**3** recovered [b]	**4** yield[b]
1	$PdCl_2(PPh_3)_2$ (0.1)	Cs_2CO_3 (3)	toluene	0%	9%
2	$Pd(OAc)_2$ (0.05)	TBAB (1) pyrrolidine (2) MS 4A	DMF	10%	10%
3	$Pd(OAc)_2$ (0.05)	TBHP (5) Ag_2O (1.2)	H_2O	0%	0%
4[c]	Pd_2dba_3 (0.05)	Xantphos (0.10) NaO*t*-Bu (1.3)	dioxane	13%	0%

[a]Reaction conditions: **3** (0.1 mmol), heated at 110 °C for 20 h. [b]Yields were determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as internal standard. No formation of **1c** was observed. [c] *N*-*tert*-Butylhydrazones, obtained from **3** (0.19 mmol), *N*-*tert*-butyl hydrazine hydrochloride (0.21 mmol), DIPEA (0.21 mmol) in DCM (2 mL) a RT for 4 h, was used. TBAB = *tetra*-*n*-butylammonium bromide; TBHP = *tert*-butyl hydroperoxide; Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene; DIPEA = *N*,*N*-diisopropylethylamine.

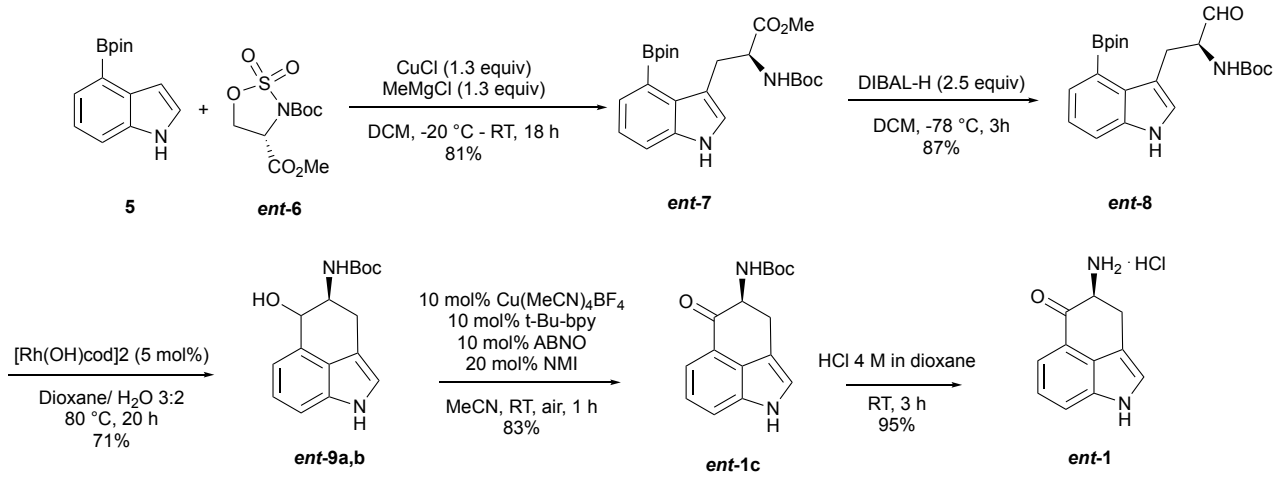
Table S2. Reaction Optimization for Intramolecular Cyclization of 8[a]



entry	catalyst (equiv)	additive (equiv)	solvent	**8** recovered[b]	**9a,b** yield [b]
1	$Rh_2(OAc)_4$ (0.03)	P(*t*-Bu)$_3$ (0.06) K_2CO_3 (1)	H_2O	92	0
2	$[RhCl(cod)]_2$	CsF (2)	dioxane/H_2O 10:1	0	22
3	$[Rh(OH)cod]_2$ (0.1)	CsF (3)	dioxane/acetone 4:1	0	29
4	[Rh(OH)cod]2 (0.1)	K_2CO_3(2) Cyclohexanone (5)	dioxane	0	33
5	[Rh(OH)cod]2 (0.1)	K_2CO_3(2) 3-pentanone (5)	dioxane	0	25
6[c]	$[Rh(OH)cod]_2$ (0.05)	-	dioxane	21	38
7[d]	$[Rh(OH)cod]_2$ (0.05)	-	dioxane	95	0
8[e]	$[Rh(OH)cod]_2$ (0.05)	-	xylene	0	10
9[d]	$[Rh(OH)cod]_2$ (0.05)	-	dioxane/H_2O 10:1	18	19
10[d]	$[Rh(OH)cod]_2$ (0.1)	-	THF/H_2O 7:1	0	47
11	$[Rh(OH)cod]_2$ (0.05)	-	H_2O/THF (15%v/v)	0	9
12	$Rh(OH)cod]_2$ (0.05)	dppe (0.01)	dioxane/H_2O 3:2	0	32
13	$Ni(cod)_2$ (0.1)	Ipr·HCl (0.1) CsF (3) clorobenzene (1.2)	toluene/dioxane 1:1	95	0
14[e]	$Ni(PPh_3)_4$ (0.05)	dcype (0.06) acetone (5)	DMSO	94	0
15	$[Ru(cymene)Cl_2]_2$ (0.025)	$(Cy)_3P·HBF_4$ (0.1) $K_3PO_4·3H_2O$ (2) 3,3-dimetil-2-butanone (2)	toluene/H_2O 10:1	0	0
16	$[Pd(allyl)Cl]_2$ (0.05)	Ipr·HCl (0.075) Cs_2CO_3 (2.5) 2-iodotoluene (2)	dioxane	0	10
17	$CoCl_2$ (0.05)	dppe (0.05)	THF/CH_3CN 1:1	95	0

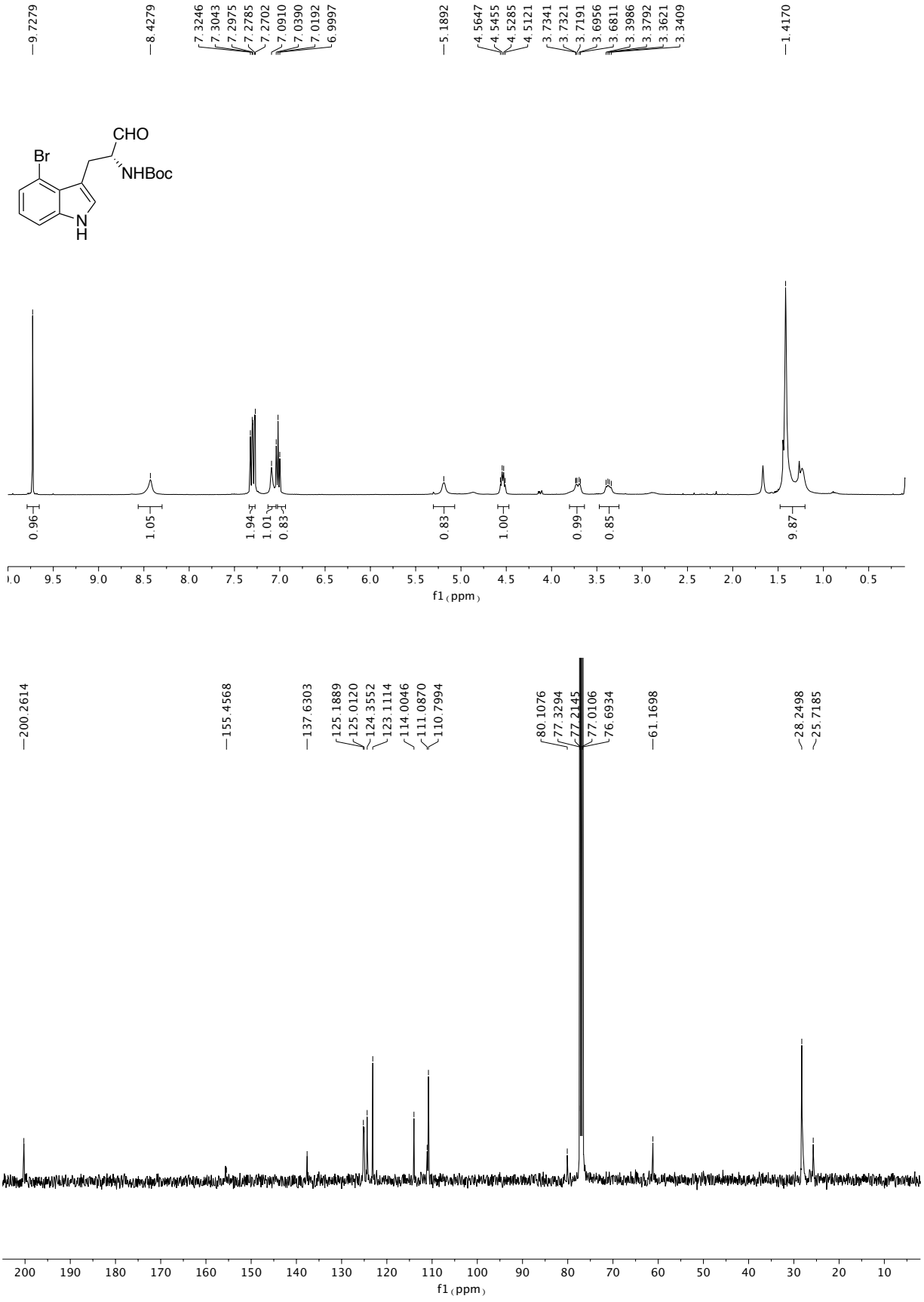
[a] Reaction conditions: **8** (0.1 mmol), heated at 80 °C for 20 h. [b]Yields were determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as internal standard. No formation of **1c** was observed. [c]Reaction performed at 50 °C. [d]Reaction performed at 30 °C. [e]Reaction performed at 120 °C. dcype = 1,2-bis(dicyclohexylphosphino)ethane; dppe = 1,2-bis(diphenylphosphino)ethane; Ipr·HCl = *N*,*N*′-(2,6-diisopropylphenyl)dihydroimidazolium chloride

Scheme S1. Synthesis of enantiomer of 4-amino-Uhle's ketone ***ent*-1**

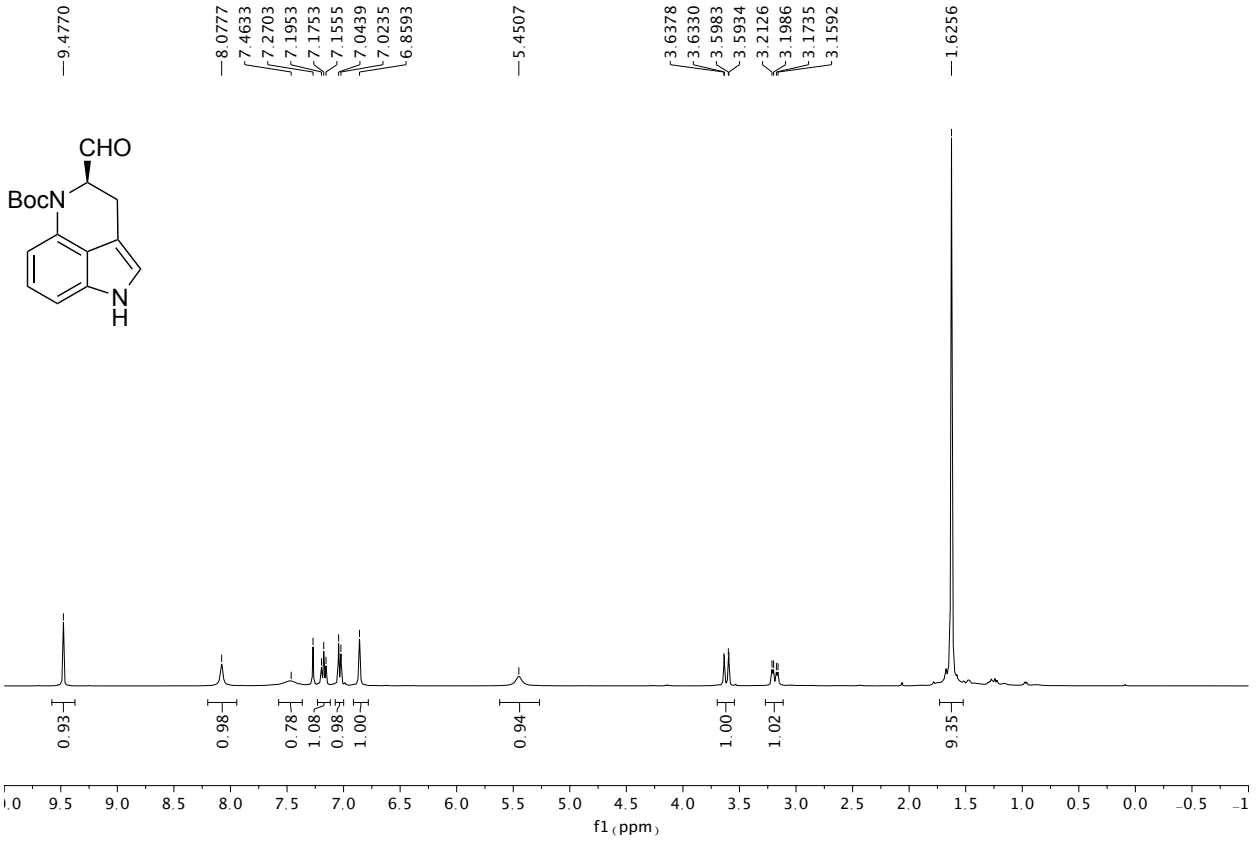


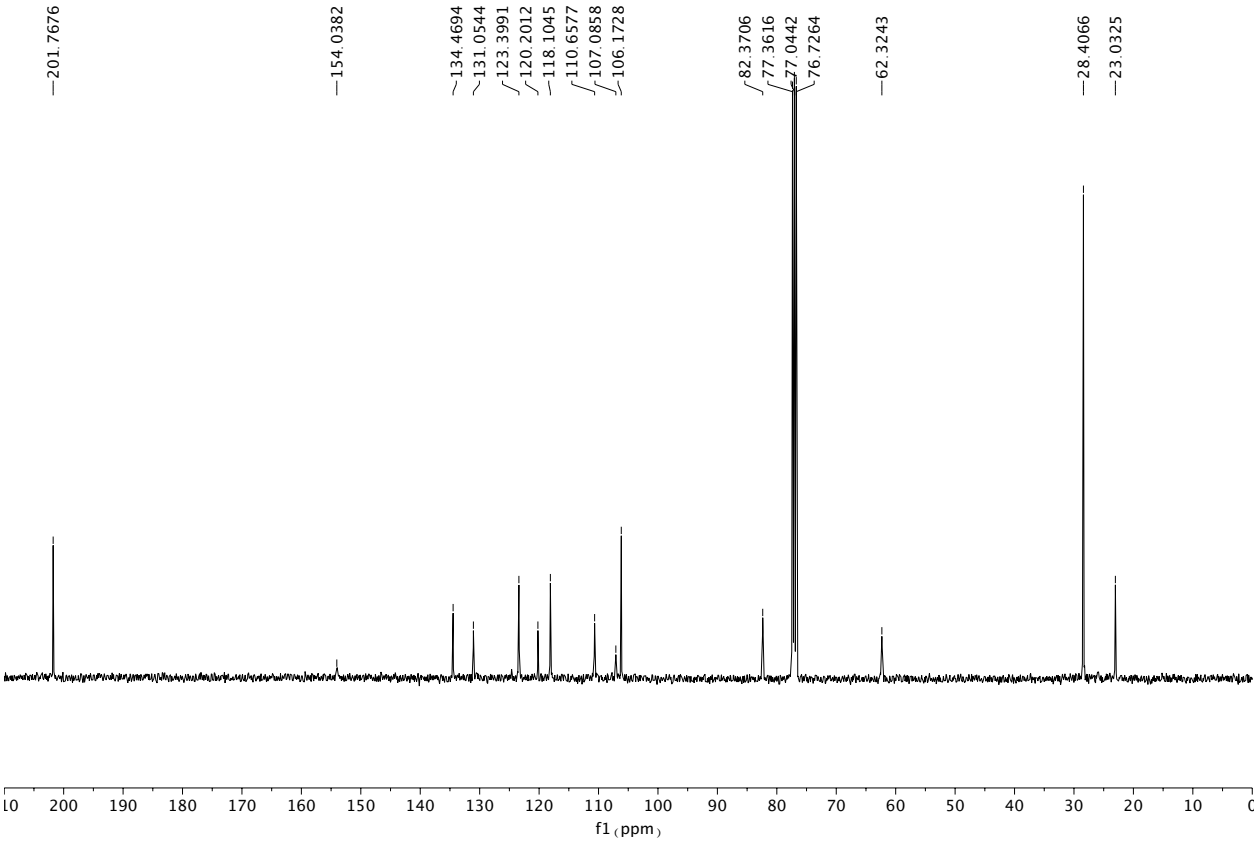
Copies of ^{1}H NMR and ^{13}C NMR spectra

***tert*-Butyl (*R*)-(1-(4-bromo-1*H*-indol-3-yl)-3-oxopropan-2-yl)carbamate (5)**

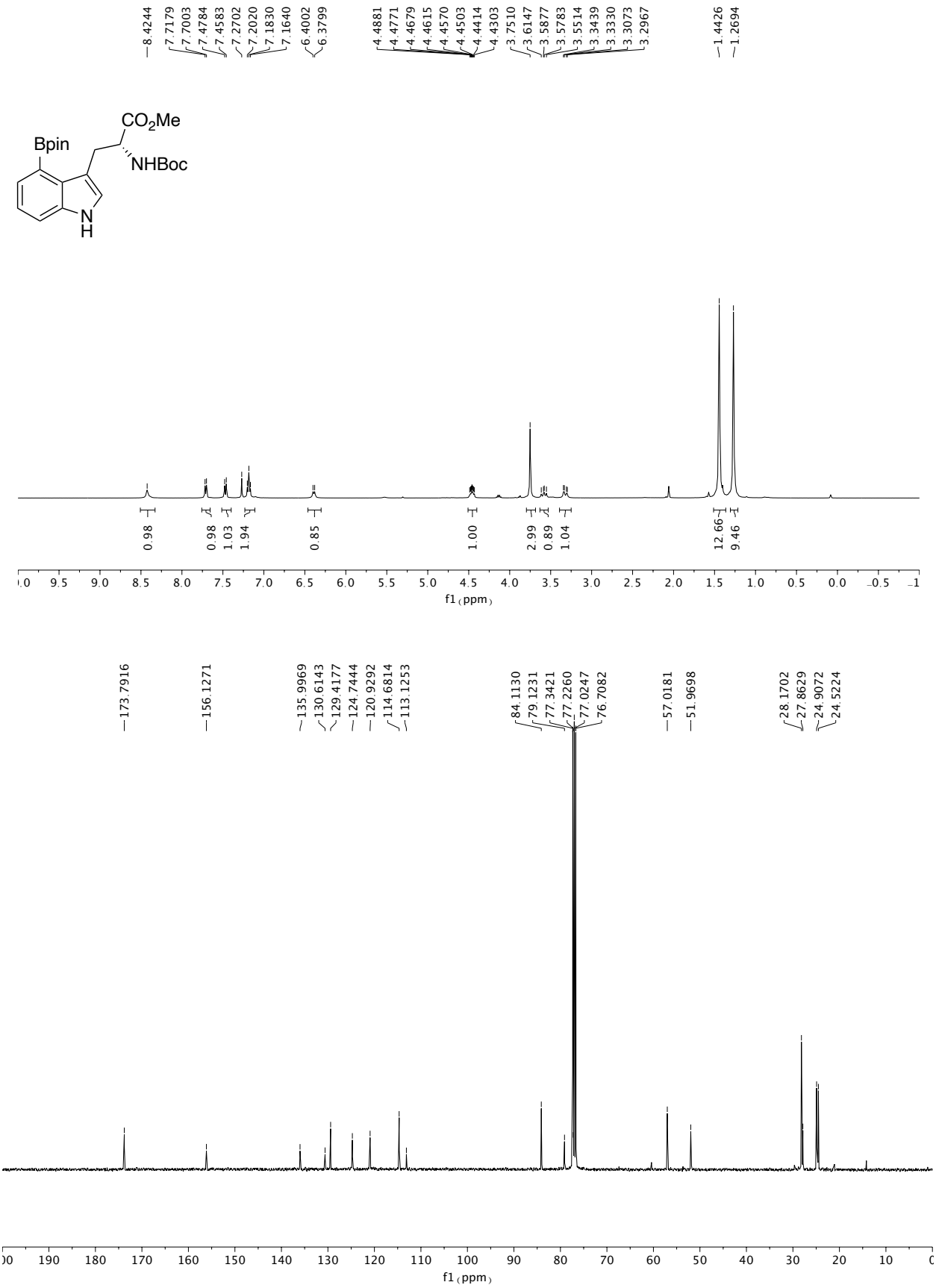


tert-Butyl 4-formyl-3,4-dihydropyrrolo[4,3,2-_de_]quinoline-5(1_H_)-carboxylate (4)

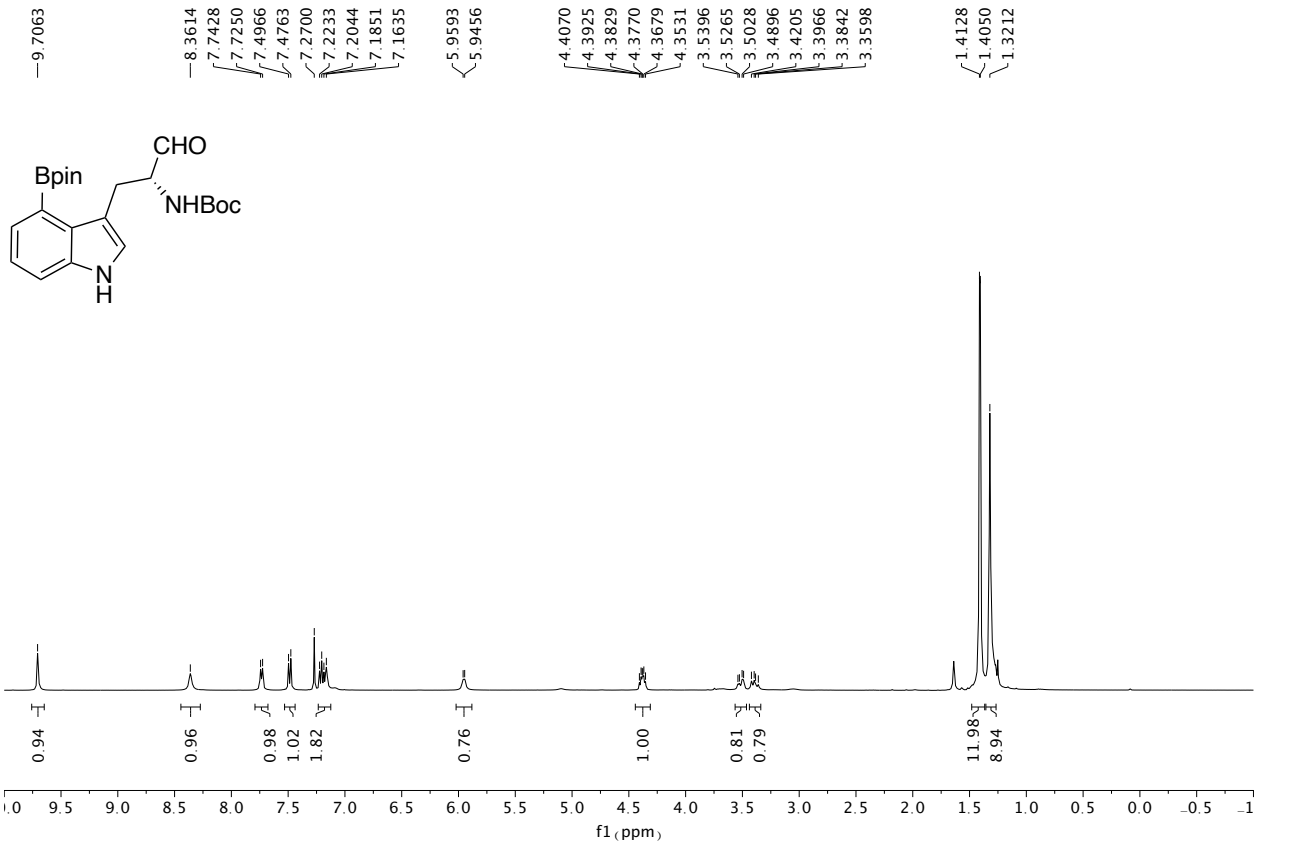


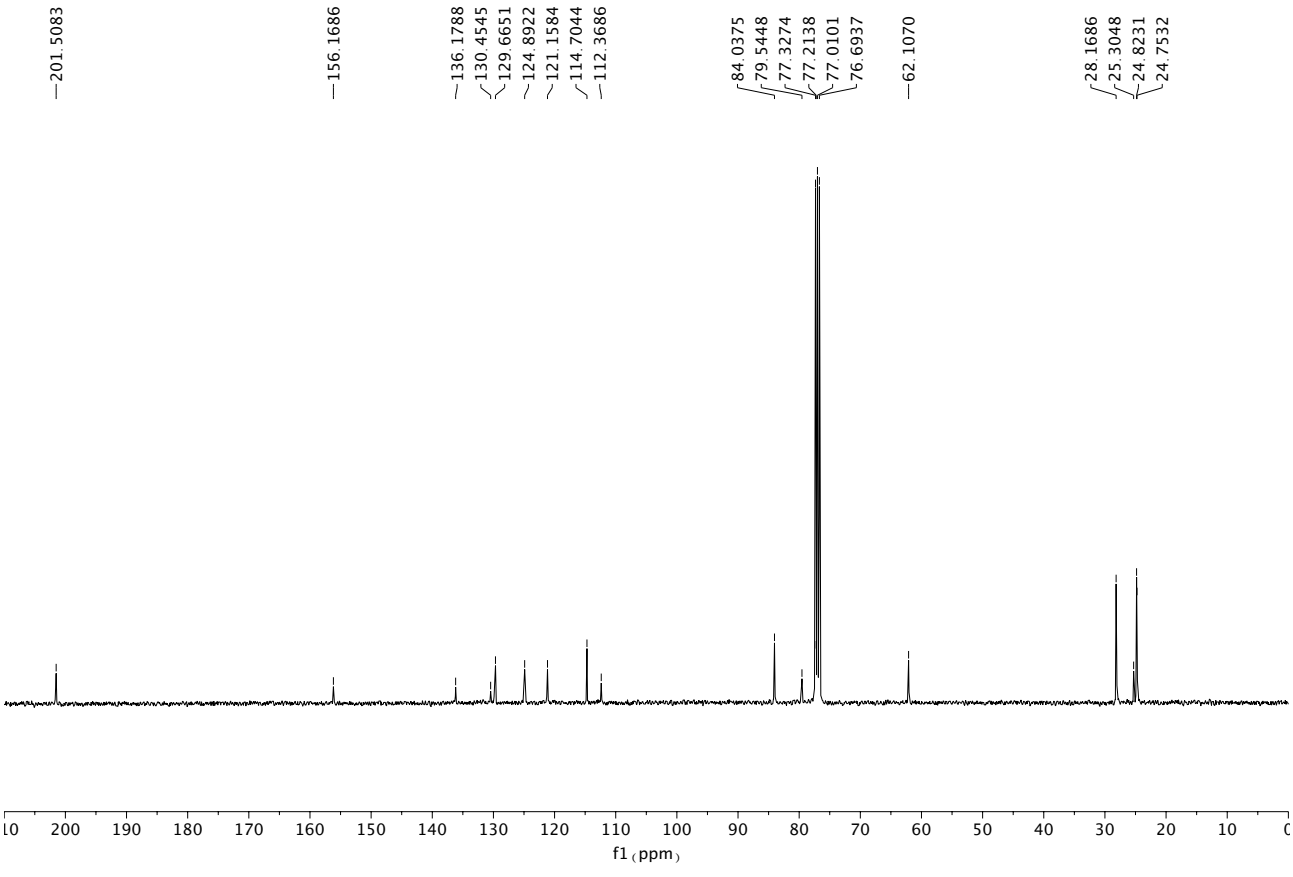


Methyl (*R*)-2-((tert-butoxycarbonyl)amino)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-3-yl)propanoate (7)

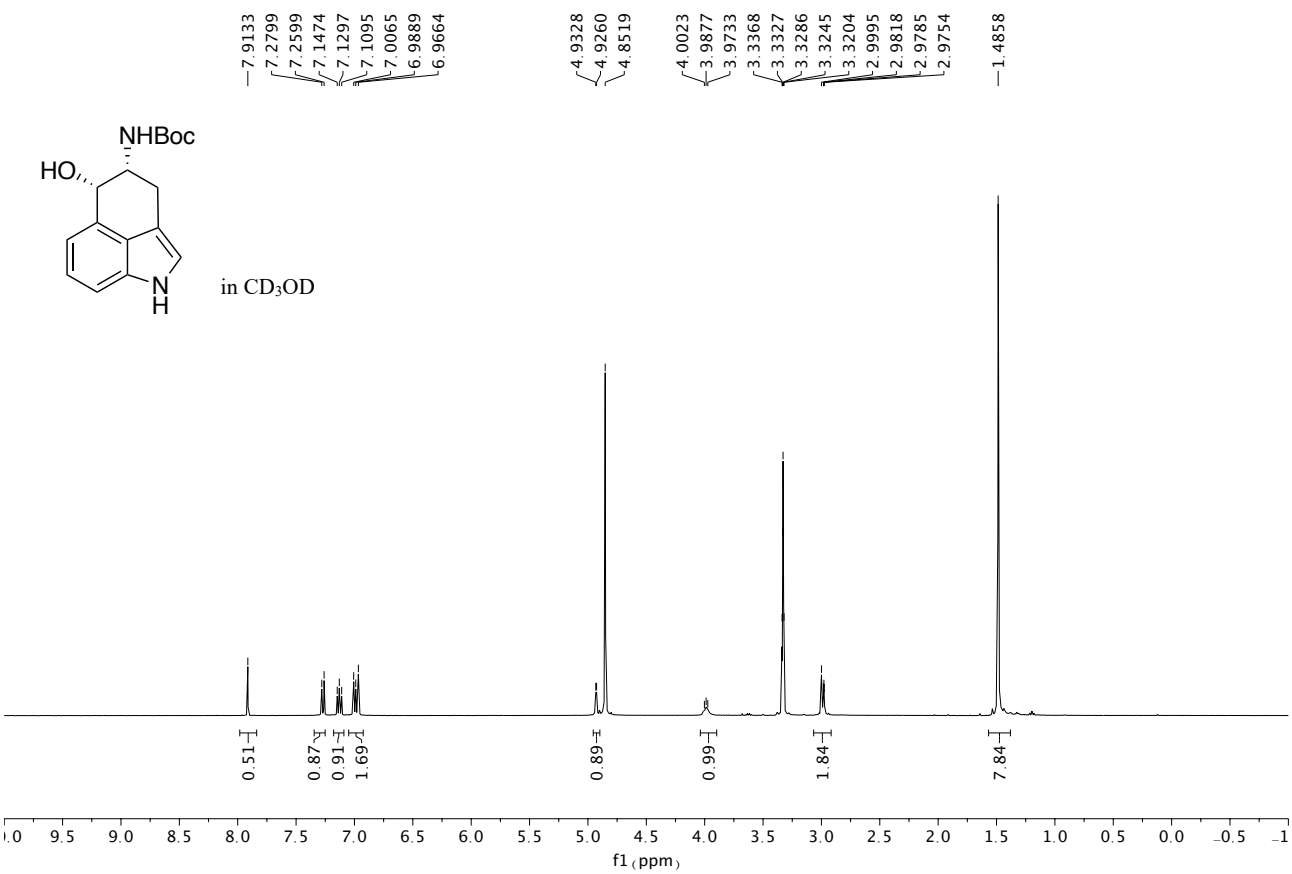


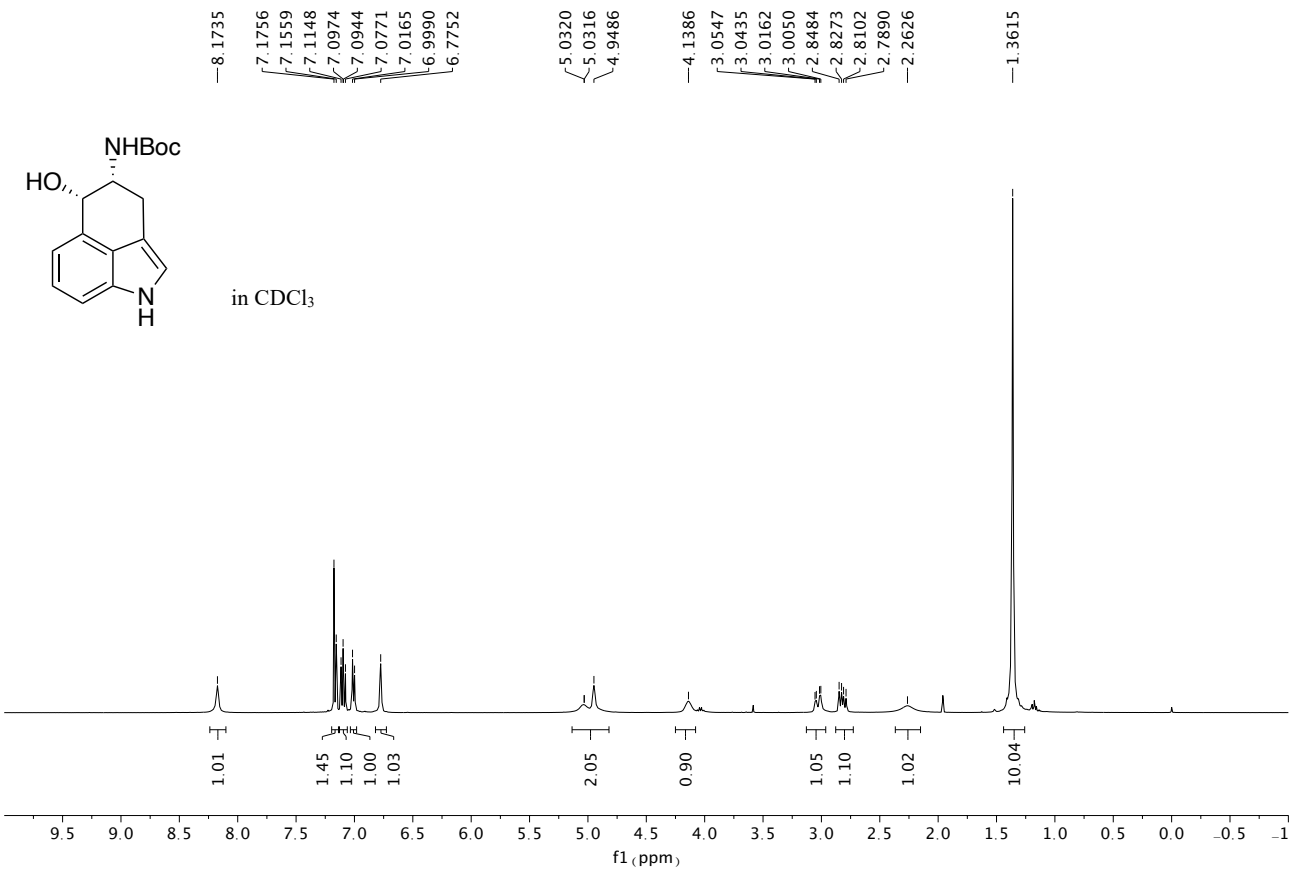
***tert*-Butyl (*R*)-(1-oxo-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indol-3-yl)propan-2-yl)carbamate (8)**

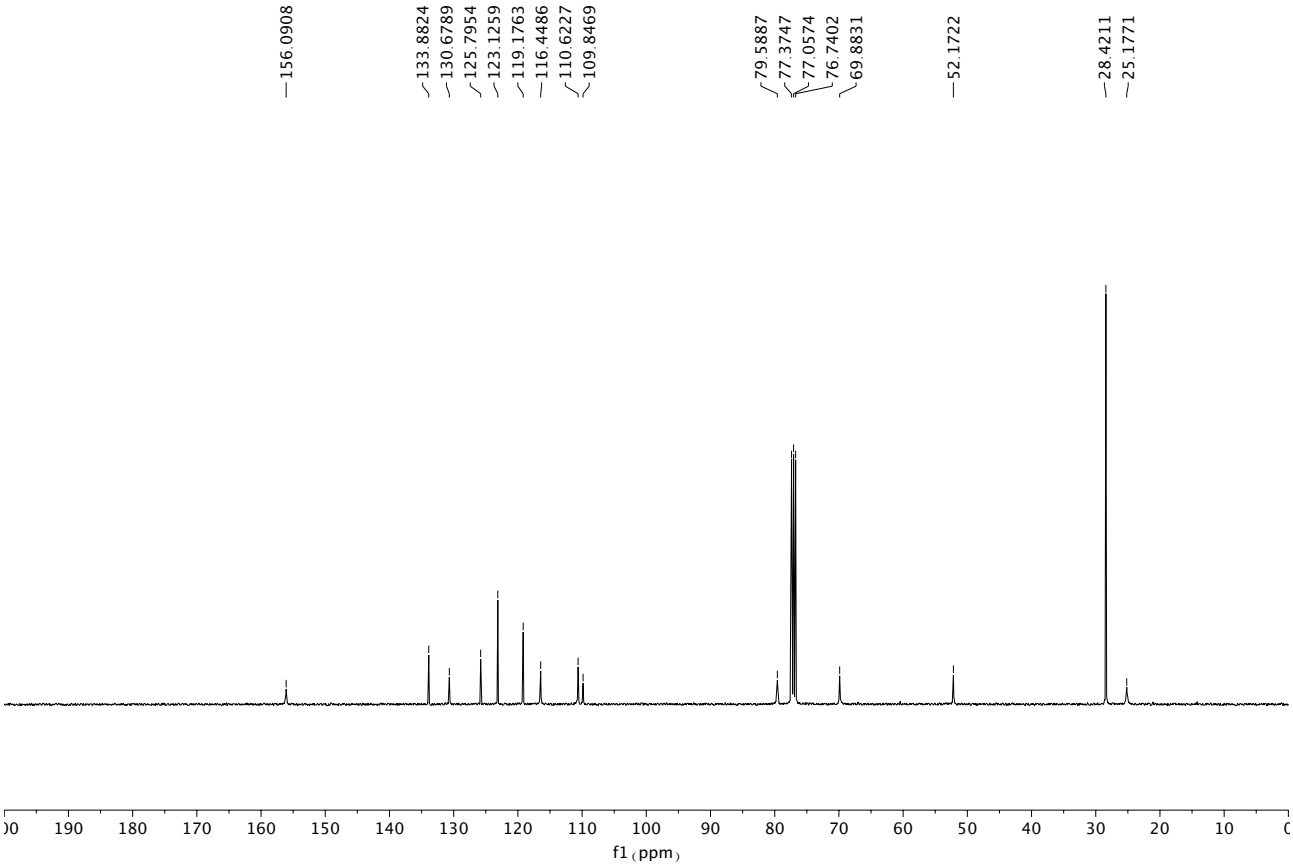




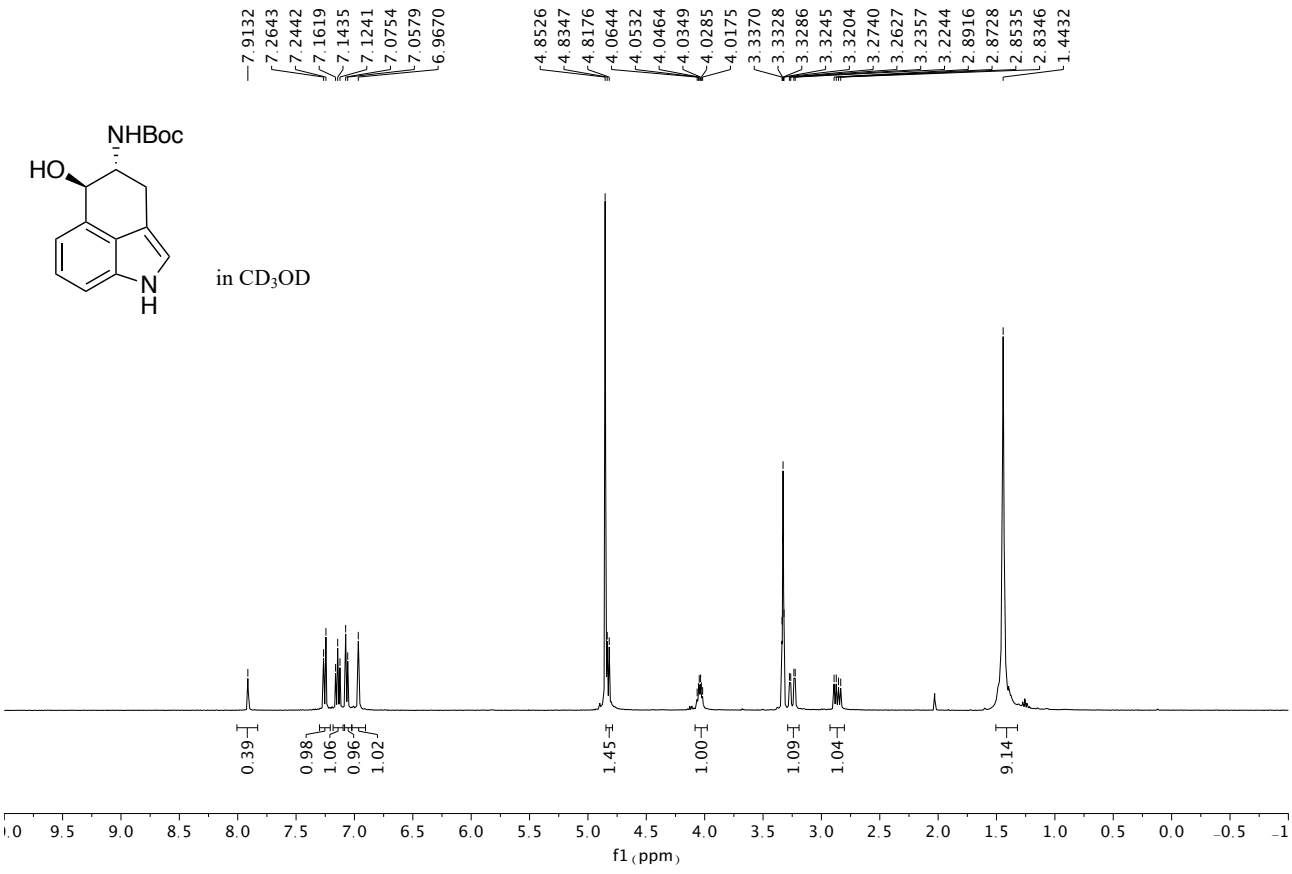
***tert*-Butyl ((4*R*,5*S*)-5-hydroxy-1,3,4,5-tetrahydrobenzo[*cd*]indol-4-yl)carbamate (9a)**

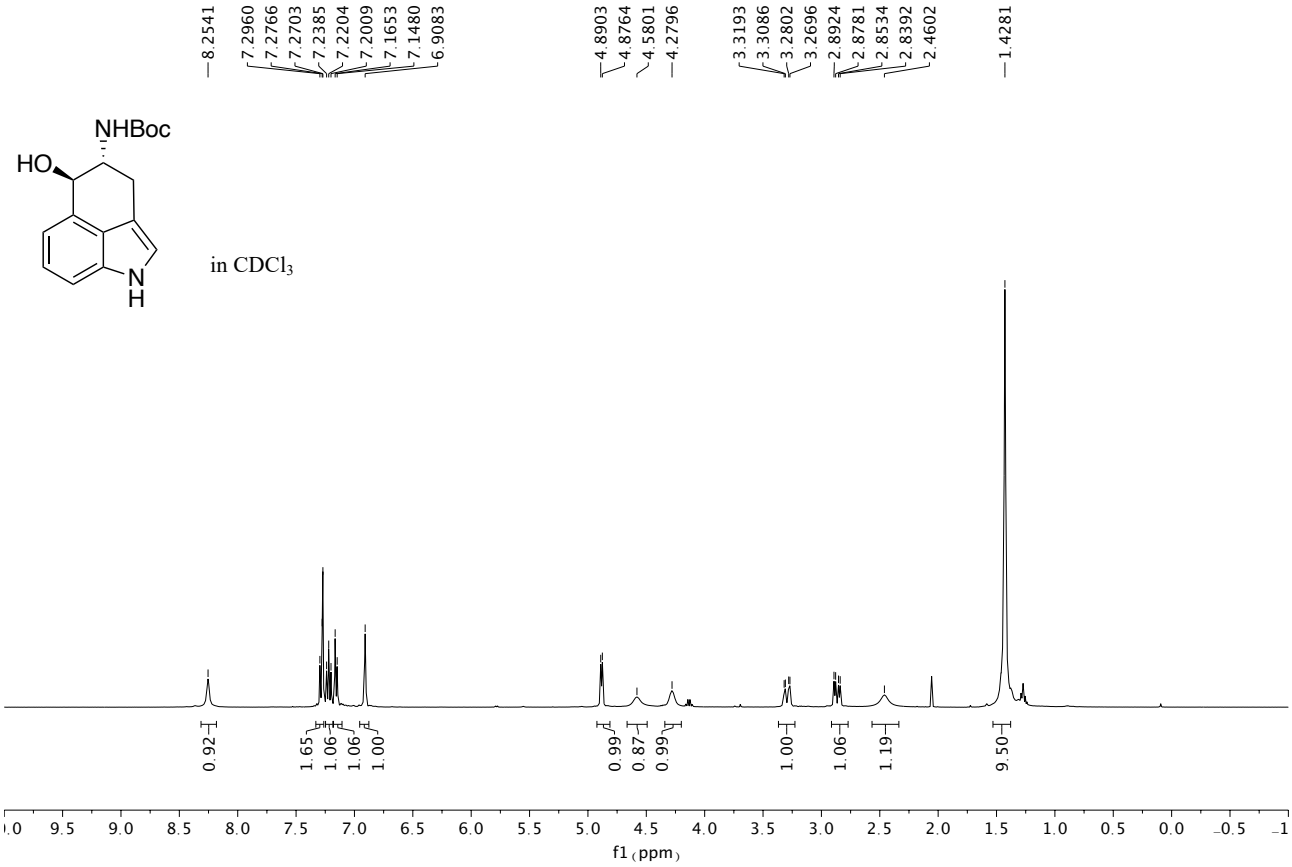






***tert*-Butyl ((4*R*,5*R*)-5-hydroxy-1,3,4,5-tetrahydrobenzo[*cd*]indol-4-yl)carbamate (9b)**

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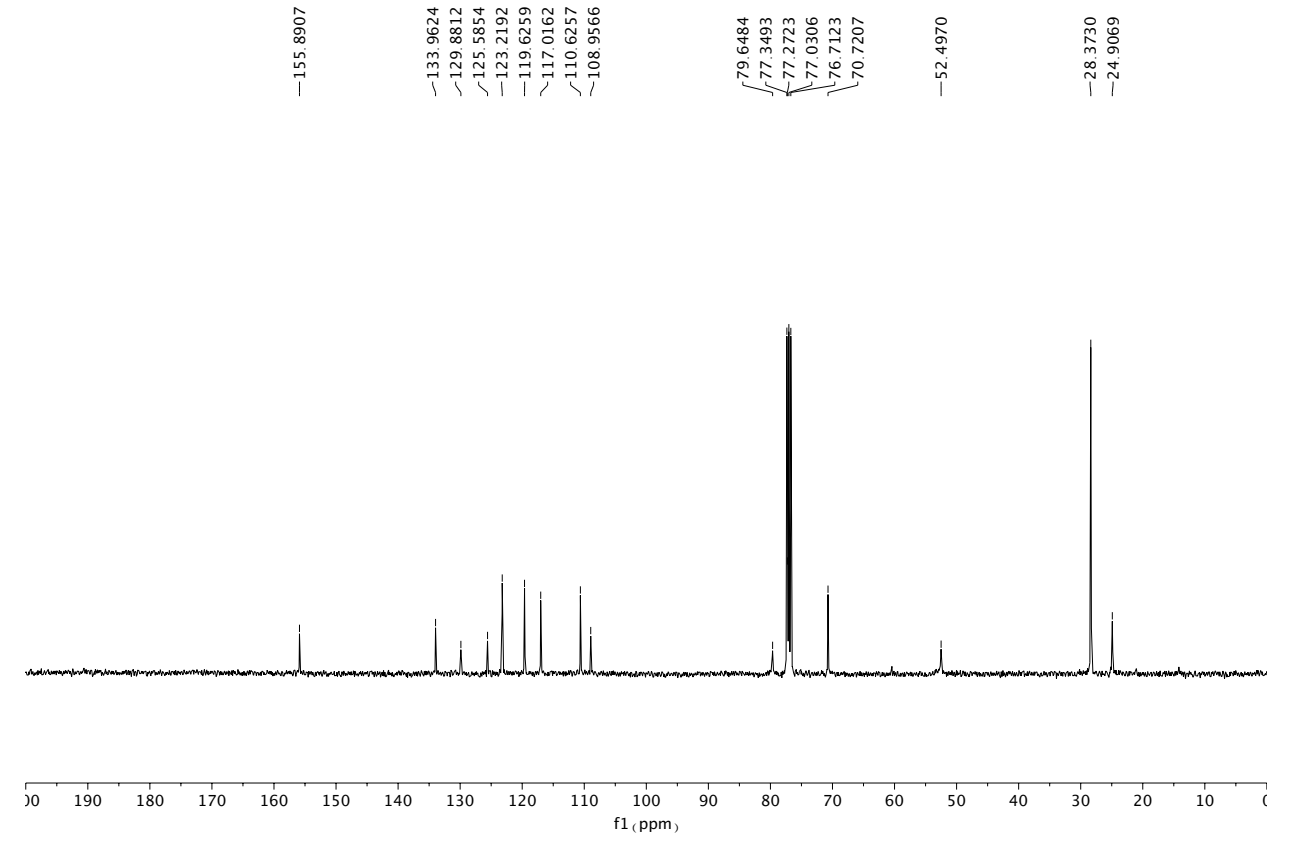
f1 (ppm)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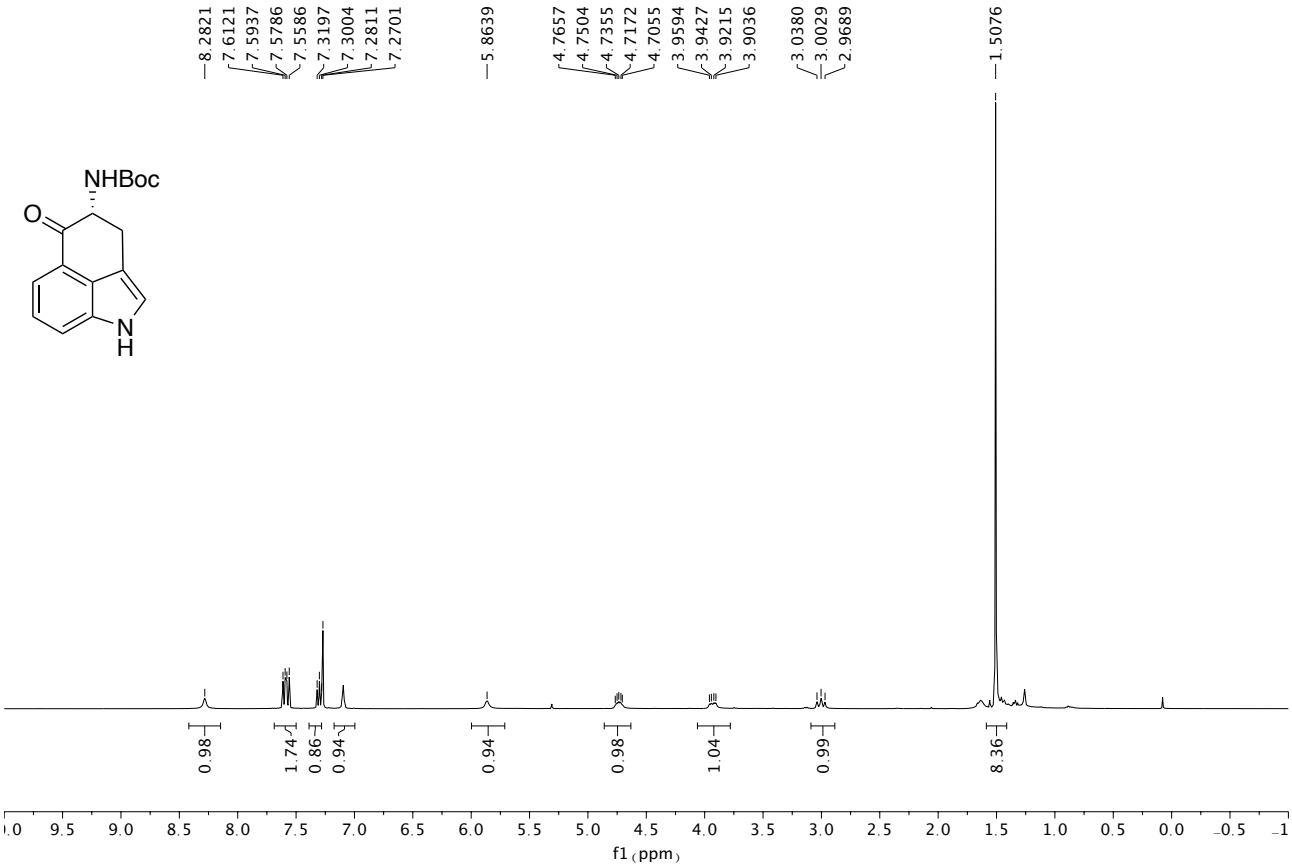
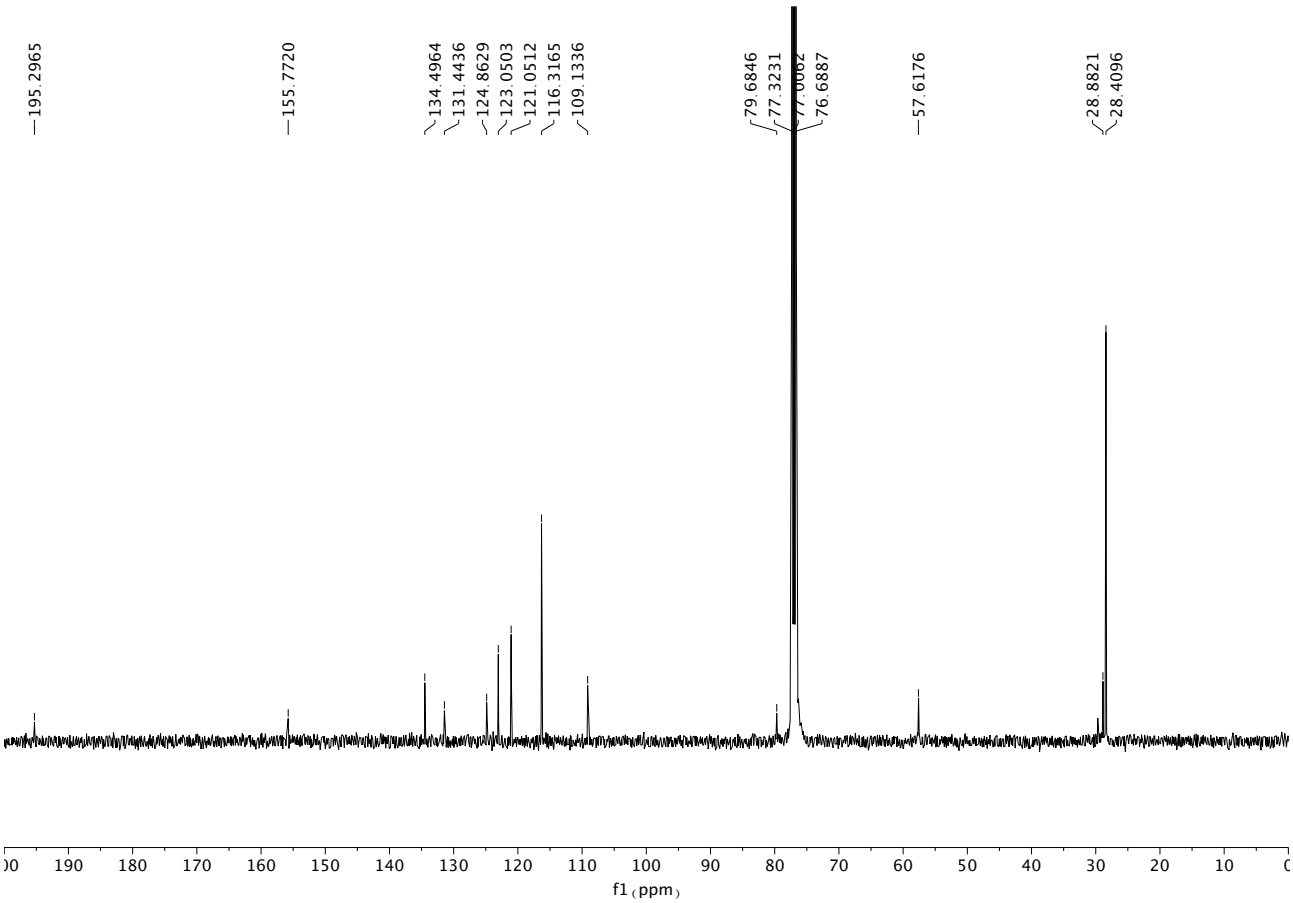
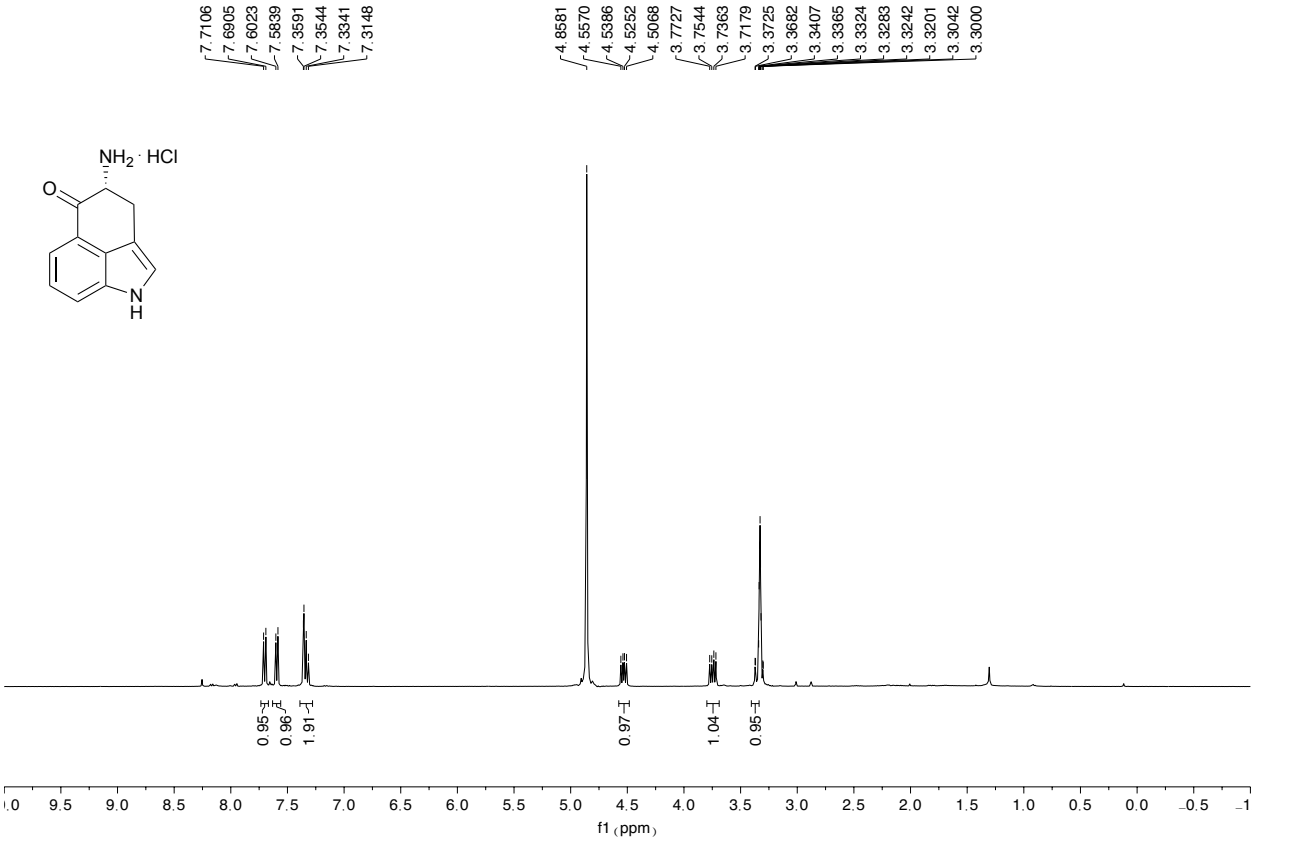
f1 (ppm)

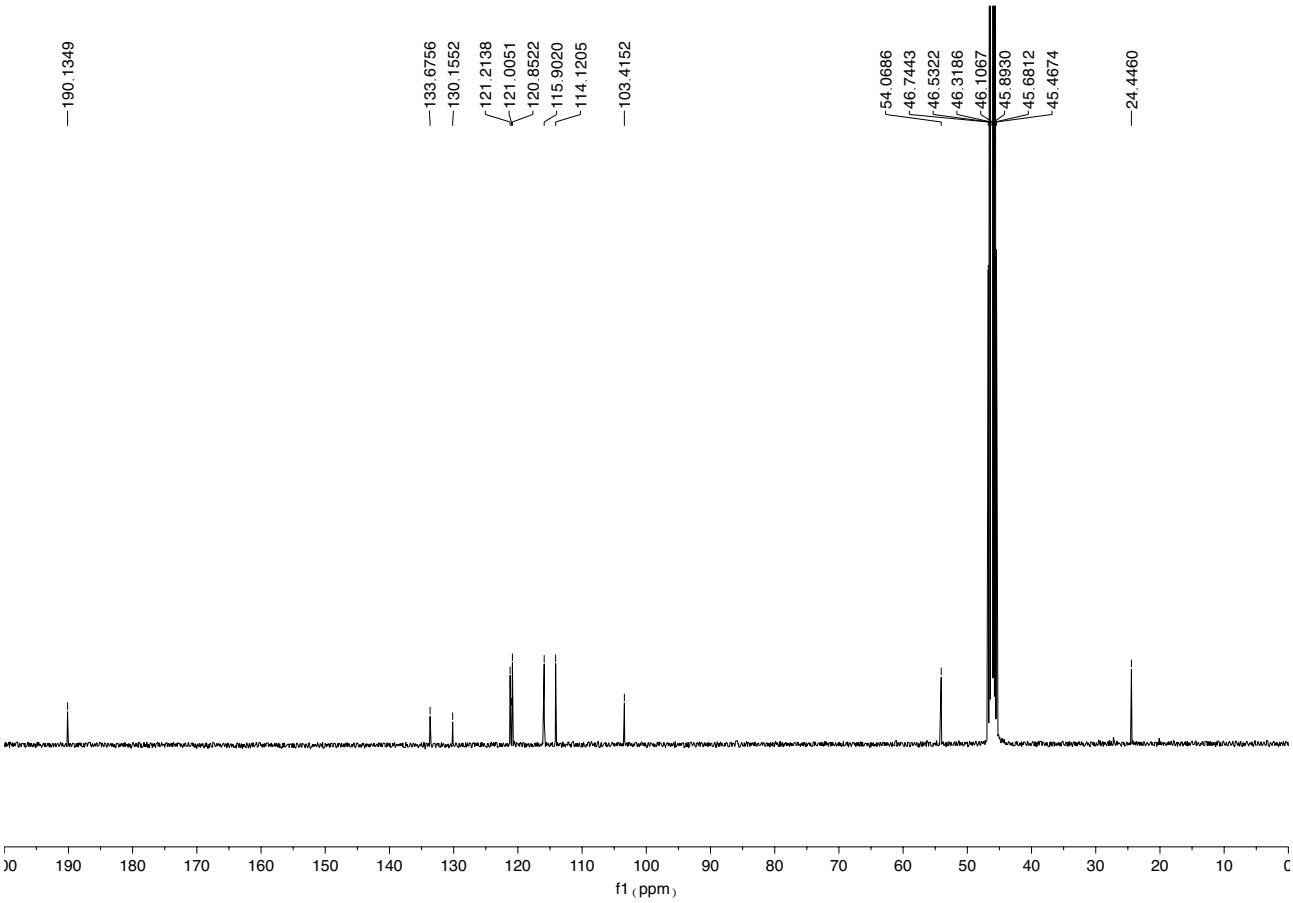
***tert*-Butyl (*R*)-(5-oxo-1,3,4,5-tetrahydrobenzo[*cd*]indol-4-yl)carbamate (1c)**





(*R*)-4-Amino-3,4-dihydrobenzo[*cd*]indol-5(1*H*)-one hydrochloride (-)-1

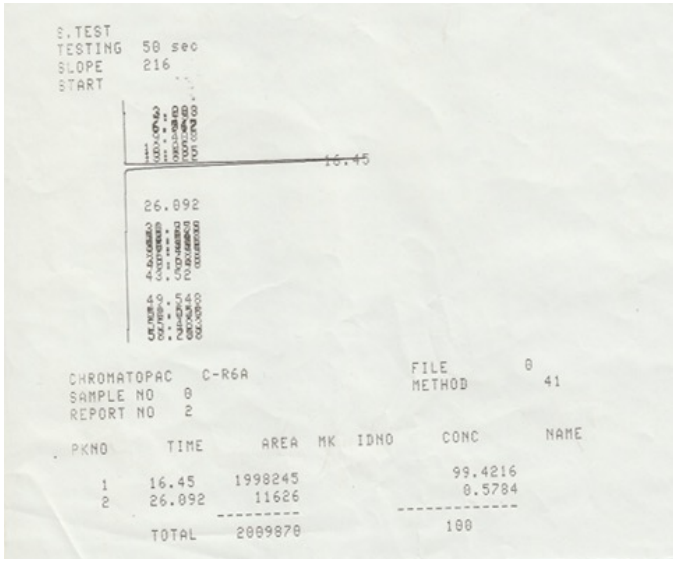




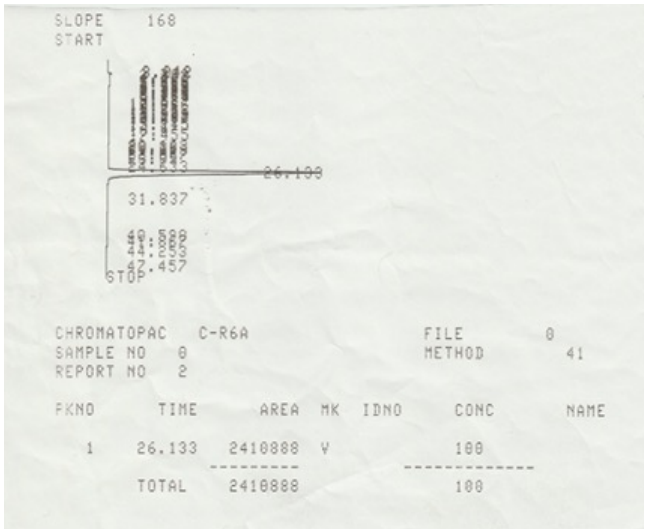
Copies of HPLC spectra

HPLC chromatogram (**(±)-1c**): racemic mixture

HPLC chromatogram of enantiomer **1c**



HPLC chromatogram of enantiomer ***ent*-1c**



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