

Enantioselective synthesis of α,α -fluoro- β -lactams using amino alcohol ligands

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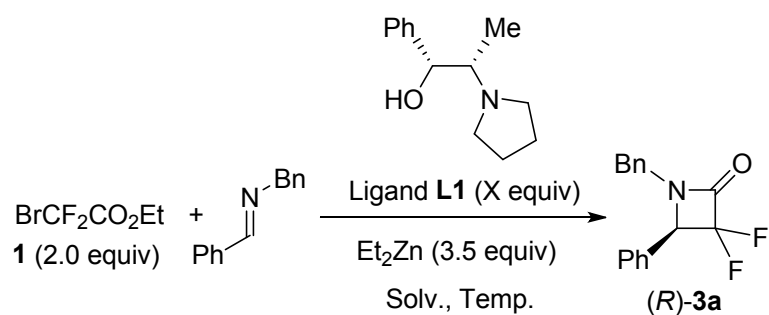
SUPPORTING INFORMATION

List of contents

Screening of reaction conditions	S2
Copies of ¹ H and ¹³ C NMR 3a-h	S3-11
Copies of HPLC chromatograms of the products	S12-15

Screening of reaction condition

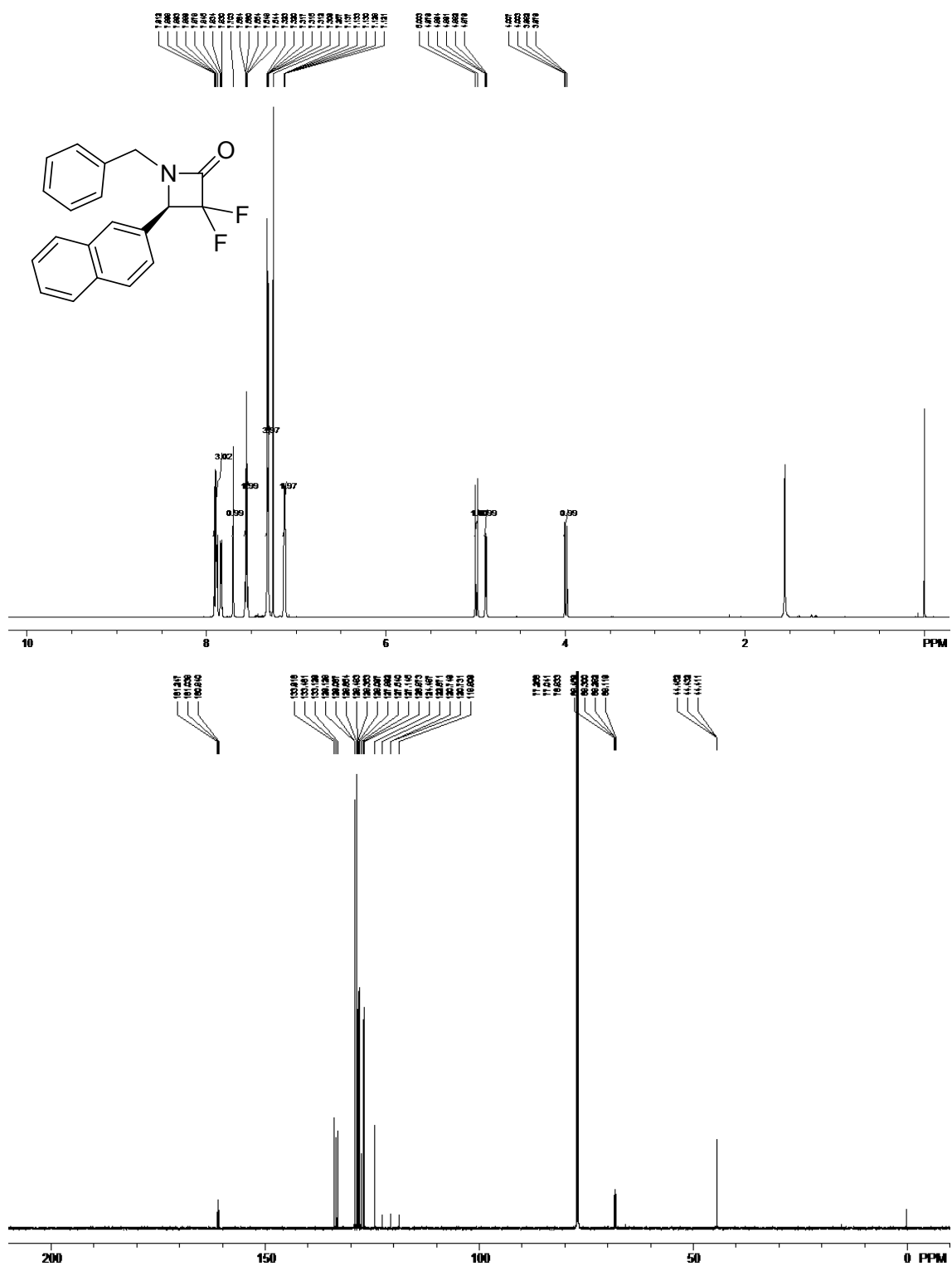
Enantioselective imino-Reformatsky reaction of **1**



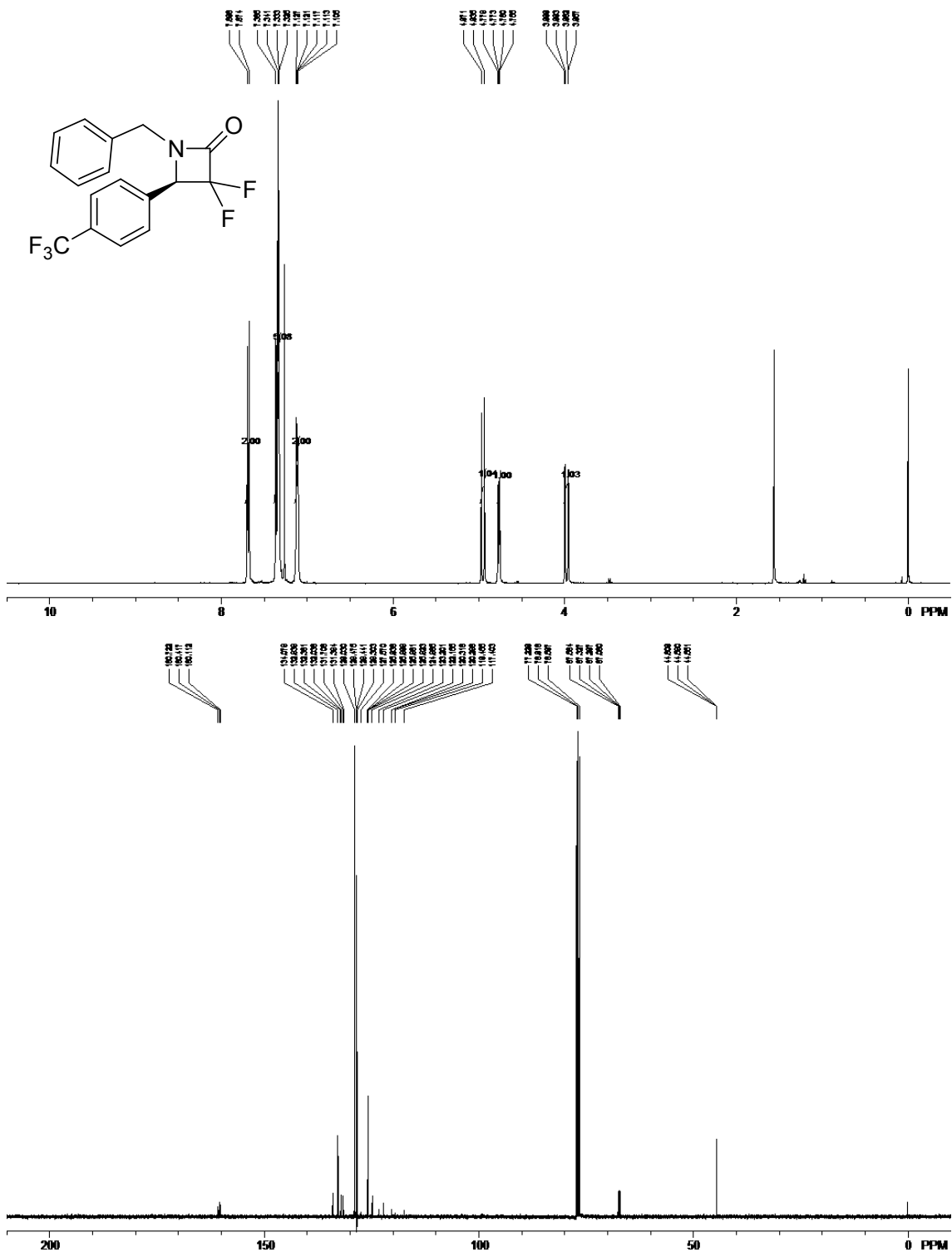
Entry	Ligand (equiv)	Solv.	Temp. (°C)	Yield of 3a (%) ^a	Ee of 3a (%)
1	1	CH ₂ Cl ₂	r.t.	72	91
2	1	CH ₂ Cl ₂	0	67	91
3	1	CH ₂ Cl ₂	-40	62	>99
4	0.75	CH ₂ Cl ₂	0	63	96
5	0.1	CH ₂ Cl ₂	0	38	5
6	0.75	DCE	0	30	97
7	0.75	BTF	0	19	19
8	none	CH ₂ Cl ₂	0	62	0

a: Isolated yields.

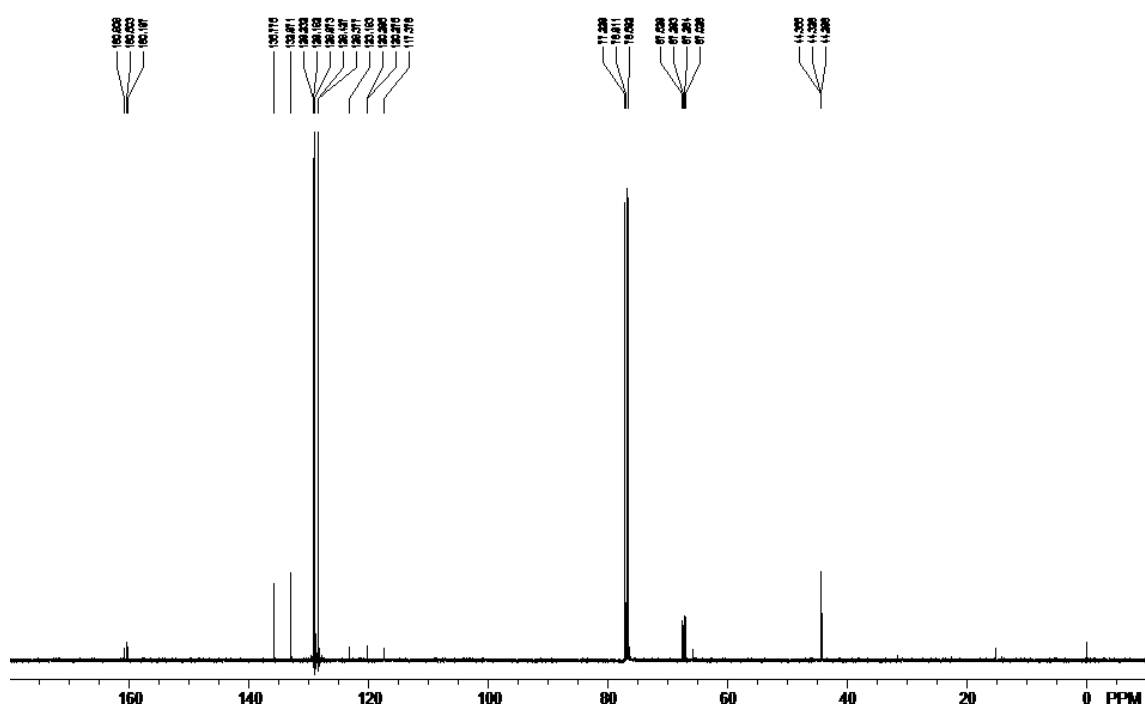
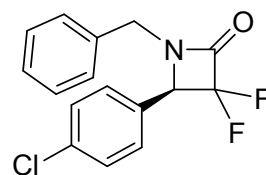
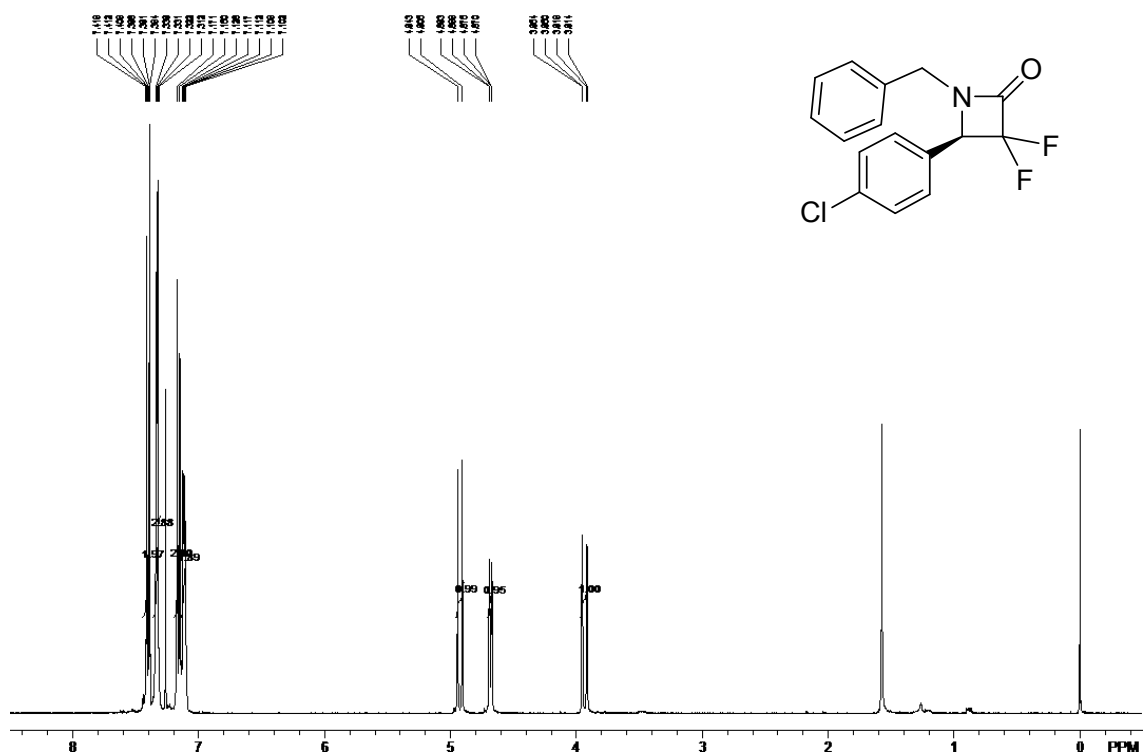
(*R*)-1-Benzyl-3,3-difluoro-4-(naphthalen-2-yl)azetidin-2-one **3b**



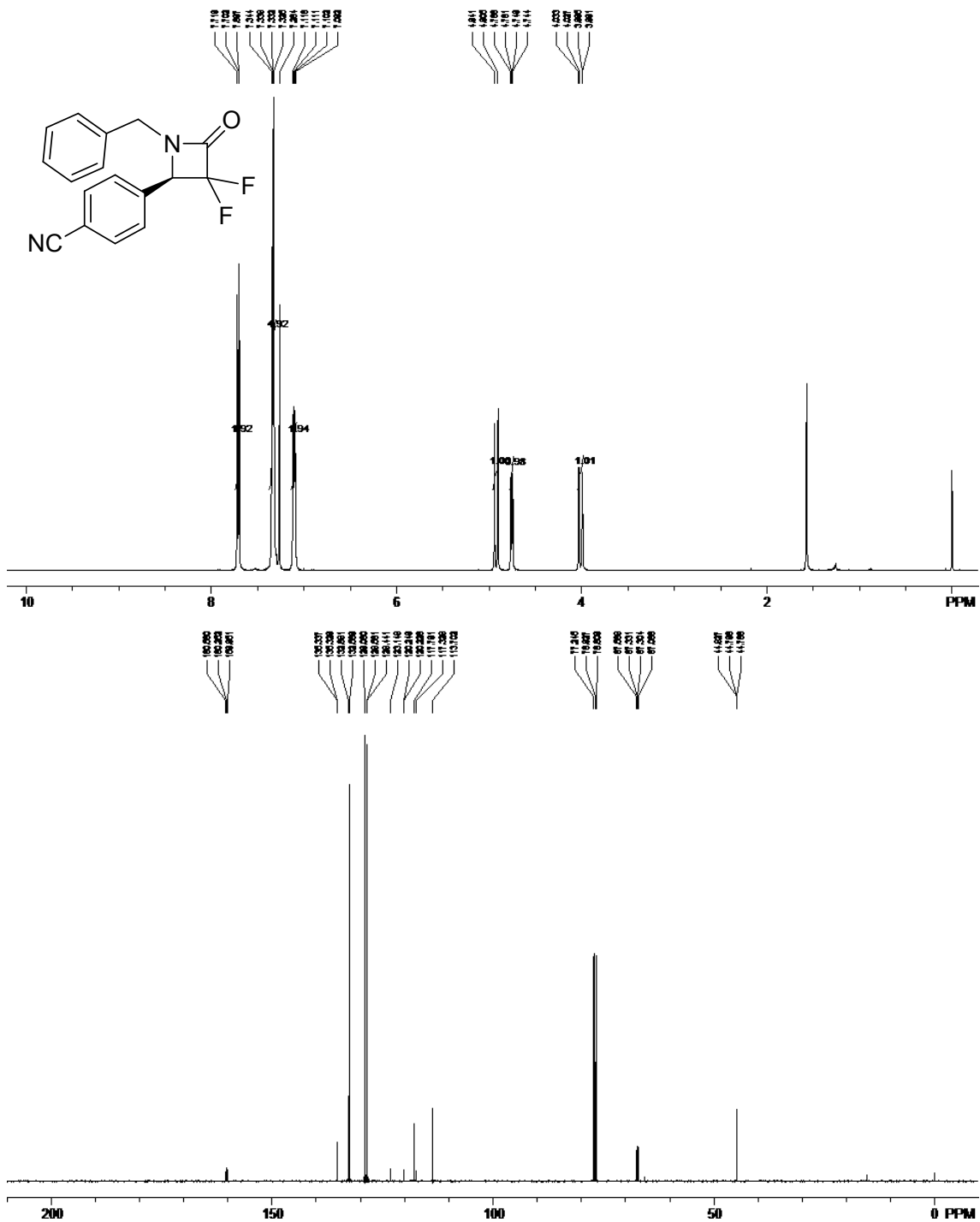
(R)-1-Benzyl-3,3-difluoro-4-[4-(trifluoromethyl)phenyl]azetidin-2-one **3c**



(*R*)-1-Benzyl-4-(4-chlorophenyl)-3,3-difluoroazetidin-2-one **3d**



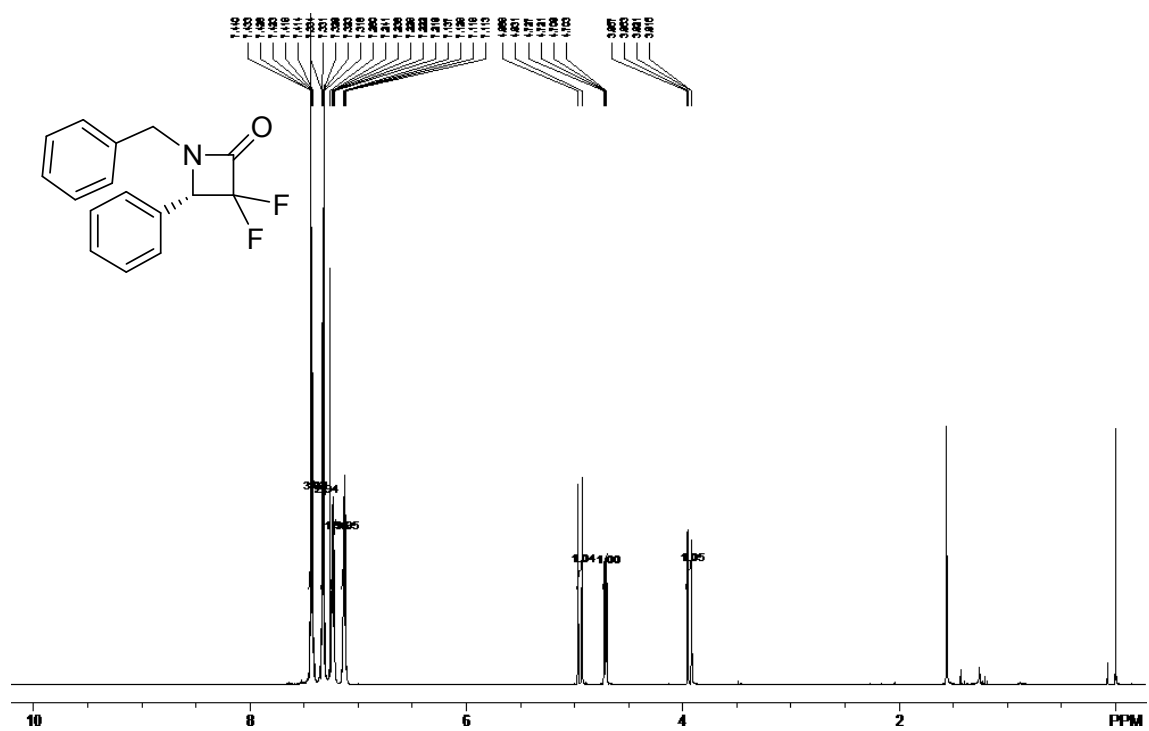
(R)-4-(1-Benzyl-3,3-difluoro-4-oxoazetidin-2-yl)benzonitrile **3f**



(R)-1-Benzyl-3,3-difluoro-4-(p-tolyl)azetidin-2-one **3g**



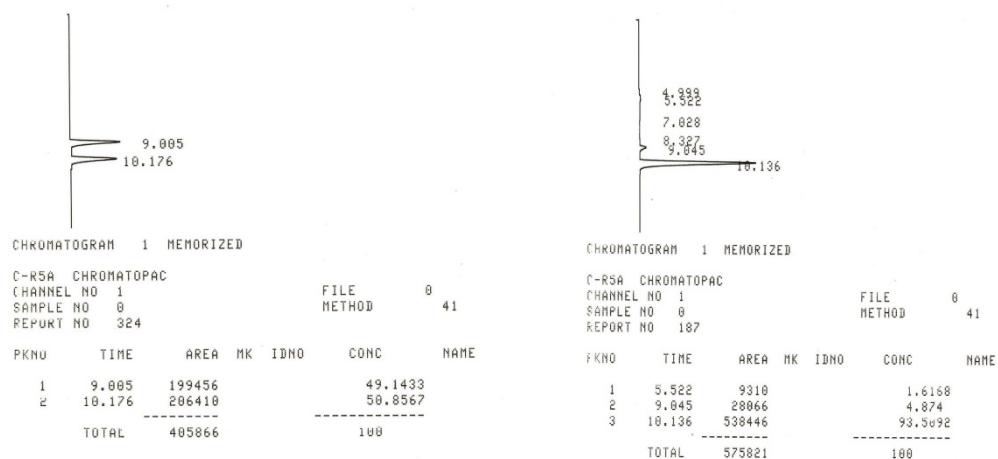
(S)-1-Benzyl-3,3-difluoro-4-phenylazetidin-2-one **3a**



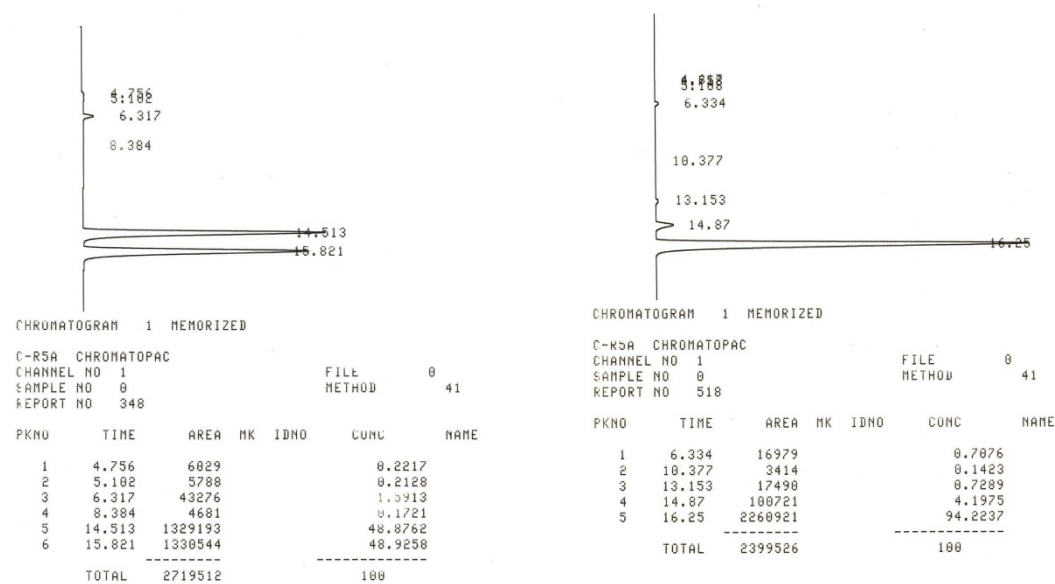
Copies of HPLC chromatgrams of the products

The chromatgrams showed racemate charts in left column and chiral charts in right column.

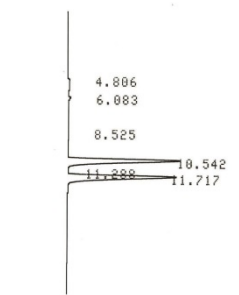
(*R*)-1-Benzyl-3,3-difluoro-4-phenylazetidin-2-one **3a**



(*R*)-1-Benzyl-3,3-difluoro-4-(naphthalen-2-yl)azetidin-2-one **3b**



(R)-1-Benzyl-3,3-difluoro-4-[4-(trifluoromethyl)phenyl]azetidin-2-one 3c

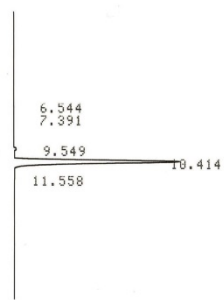


CHROMATOGRAM 1 MEMORIZED

C-RSA CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 425

FILE METHOD 0 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	4.806	3883			0.3632	
2	6.083	9763			0.9132	
3	8.525	5752			0.538	
4	10.542	525625			49.1656	
5	11.717	524068			49.02	
TOTAL		1069091			100	



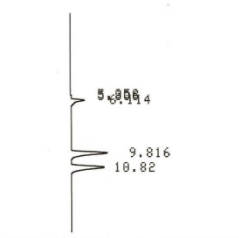
CHROMATOGRAM 1 MEMORIZED

C-RSA CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 434

FILE METHOD 0 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	6.544	2324			0.3223	
2	9.549	12514			1.7354	
3	10.414	703243			97.5201	
4	11.558	3045			0.4222	
TOTAL		721126			100	

(R)-1-Benzyl-4-(4-chlorophenyl)-3,3-difluoroazetidin-2-one 3d

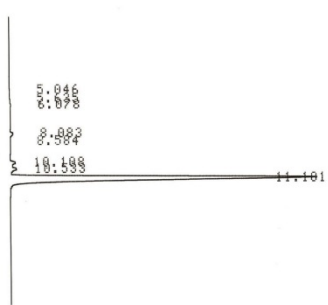


CHROMATOGRAM 1 MEMORIZED

C-RSA CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 491

FILE METHOD 0 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	6.114	42871			12.6078	
2	9.816	149792			44.0522	
3	10.82	147371			43.34	
TOTAL		340033			100	



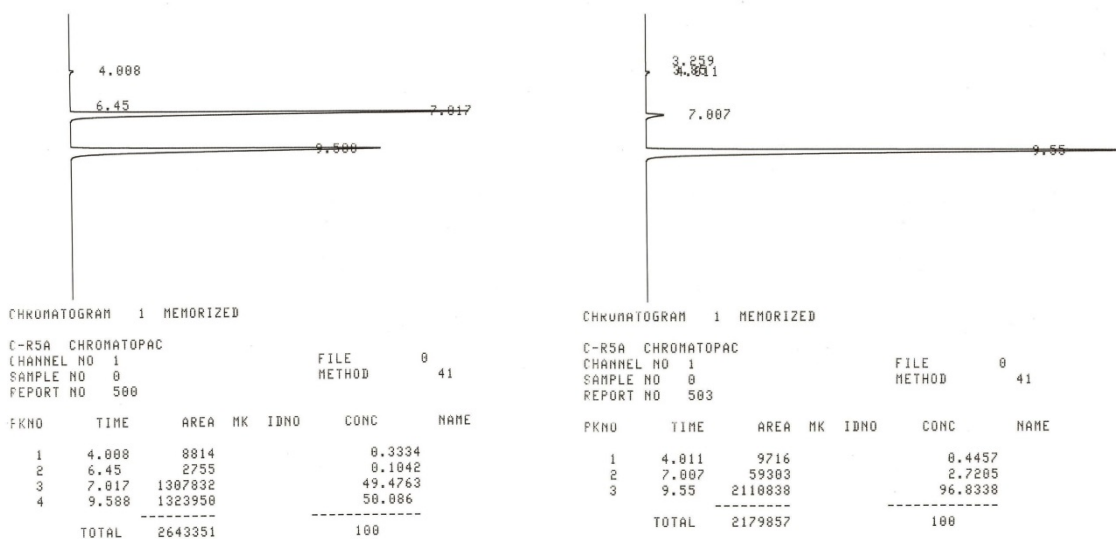
CHROMATOGRAM 1 MEMORIZED

C-RSA CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 170

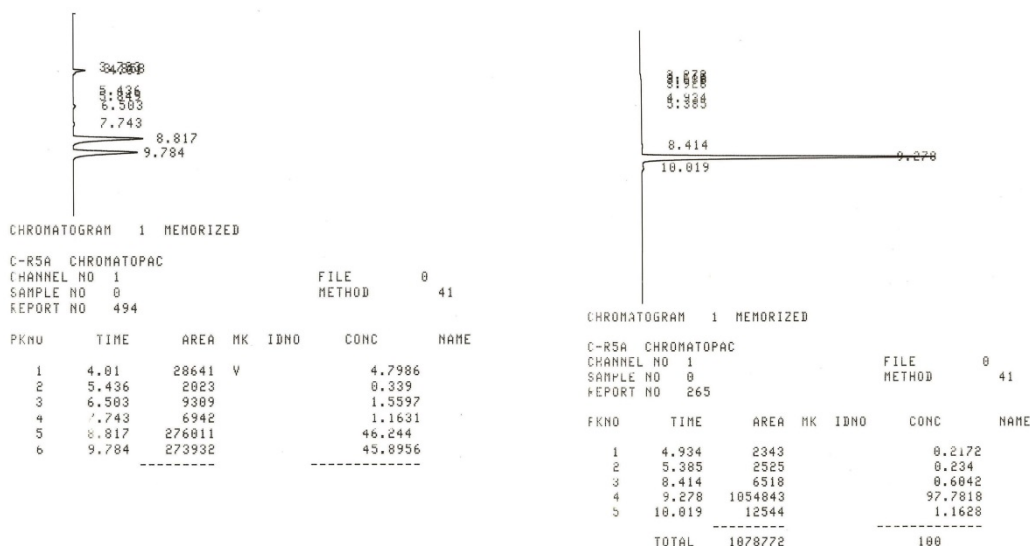
FILE METHOD 0 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	5.046	2210			0.1469	
2	6.078	3643			0.2422	
3	8.083	14989			0.9966	
4	8.584	3062			0.2036	
5	10.108	24992			1.6616	
6	10.533	29994			1.9942	
7	11.181	1425183			94.7549	
TOTAL		1504072			100	

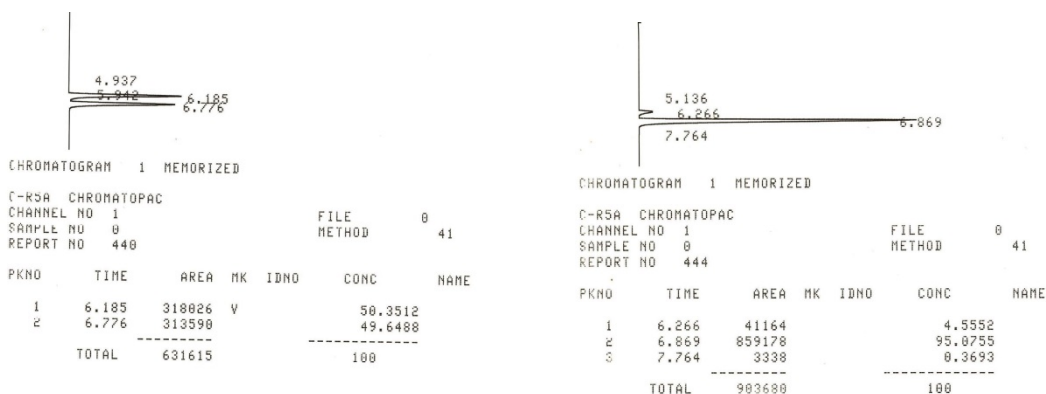
(R)-1-Benzyl-3,3-difluoro-4-(4-methoxycarbonylphenyl)azetidin-2-one 3e



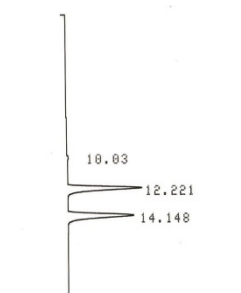
(R)-4-(1-Benzyl-3,3-difluoro-4-oxoazetidin-2-yl)benzotrile 3f



(R)-1-Benzyl-3,3-difluoro-4-(p-tolyl)azetidin-2-one 3g



(R)-1-Benzyl-3,3-difluoro-4-(4-methoxyphenyl)azetid-2-one 3h

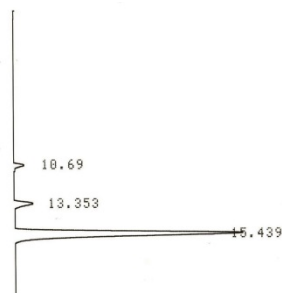


CHROMATOGRAM 1 MEMORIZED

C-R5A CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 362

FILE 0
METHOD 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	10.03	6604			0.9038	
2	12.221	362179			49.5653	
3	14.148	361928			49.531	
TOTAL		738711			100	



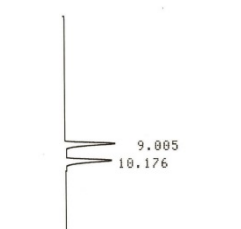
CHROMATOGRAM 1 MEMORIZED

C-R5A CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 2

FILE 0
METHOD 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	10.69	45436			2.893	
2	13.353	104475			6.652	
3	15.439	1420657			90.455	
TOTAL		1570568			100	

(S)-1-Benzyl-3,3-difluoro-4-phenylazetid-2-one 3a

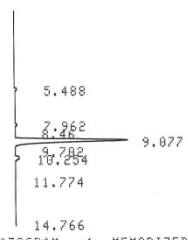


CHROMATOGRAM 1 MEMORIZED

C-R5A CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 324

FILE 0
METHOD 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	9.005	199456			49.1433	
2	10.176	206410			50.8567	
TOTAL		405866			100	



CHROMATOGRAM 1 MEMORIZED

C-R5A CHROMATOPAC
CHANNEL NO 1
SAMPLE NO 0
REPORT NO 292

FILE 0
METHOD 41

PKNO	TIME	AREA	MK	IDNO	CONC	NAME
1	5.488	9596			2.0006	
2	7.962	10408			2.1697	
3	8.46	3895			0.6451	
4	9.077	423062			88.1971	
5	9.702	2711			0.5652	
6	10.254	24328			5.0718	
7	11.774	3144			0.6554	
8	14.766	3334			0.6951	
TOTAL		479678			100	