Supplementary Data

Ugi Multicomponent Reactions of Optically Active Aldehydes and Chiral Aminoindanols: Diastereoselective Synthesis of Bisamides Relevant to SARS-CoV-2 Mpro Inhibitors

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General Methods:

General Methods: All reagents were purchased commercially and used without further purification unless specified. Unless otherwise stated, all reactions were carried out under an Argon atmosphere. Tetrahydrofuran was dried over sodium metal and distilled before use. Anhydrous dichloromethane was prepared by distillation over calcium hydride. Anhydrous methanol was prepared by drying over 3A molecular sieves. TLC analysis was carried out using 60 A, 250 µm thick F-254 glass-backed plates. Flash column chromatography was done using 230 400 mesh silica gel. 1H and 13C NMR spectra was obtained on either a Bruker AV-III-400-HD or NEO-500. Chemical shifts are reported in ppm, J-values in Hz, and all peaks are referenced to the residual deuterated solvent peak. NMR data is reported as: δ value (chemical shift, J-value (Hz), integration, where s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet). Optical rotations were obtained using an automatic digital polarimeter with a sodium lamp and are reported as follows: [α]λ T °C (c = 0.1(mg/mL), solvent). High-resolution mass spectrometry (HRMS) spectra were recorded under positive electron spray ionization (ESI+) at Agilent 6550 Q-TOF LC/MS instrument at the Purdue University Analytical Mass Spectrometry Facility.

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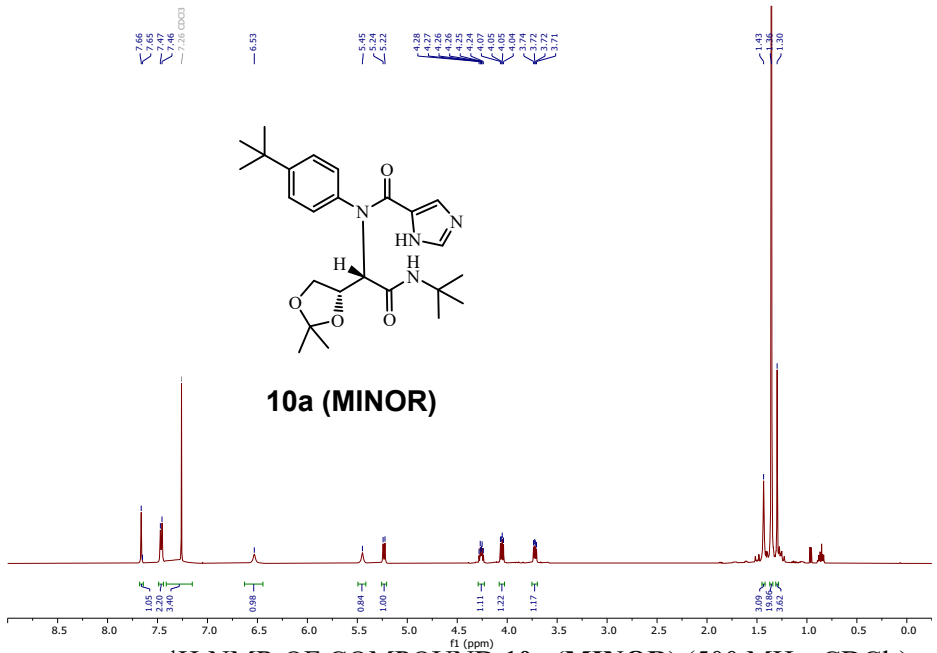
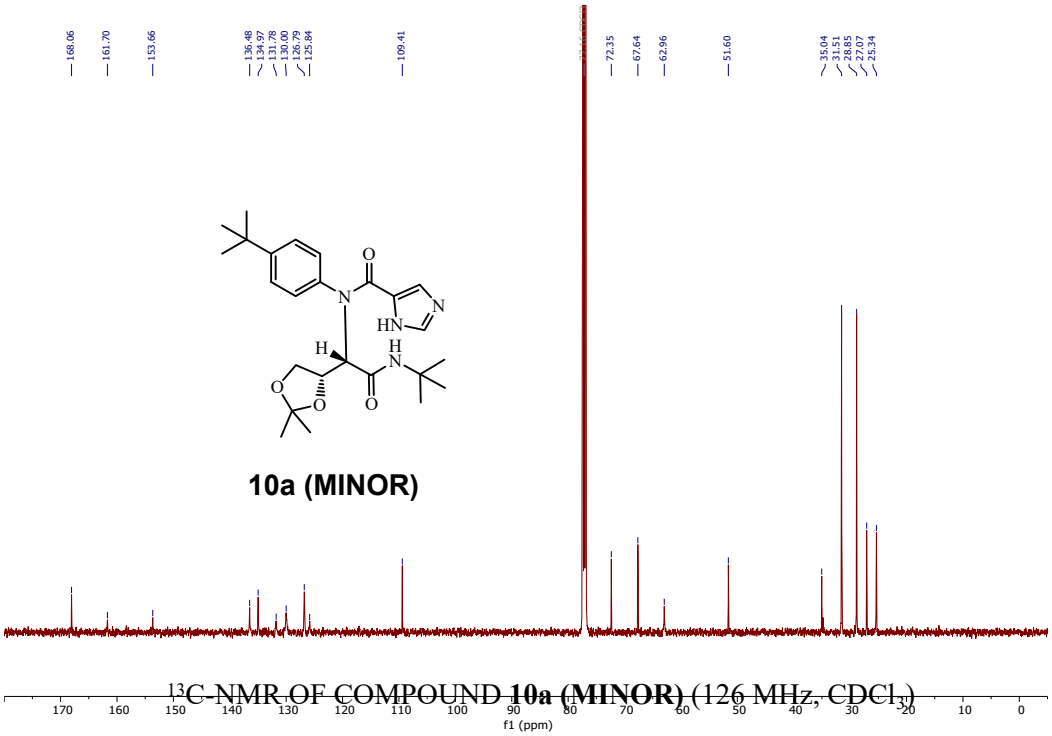
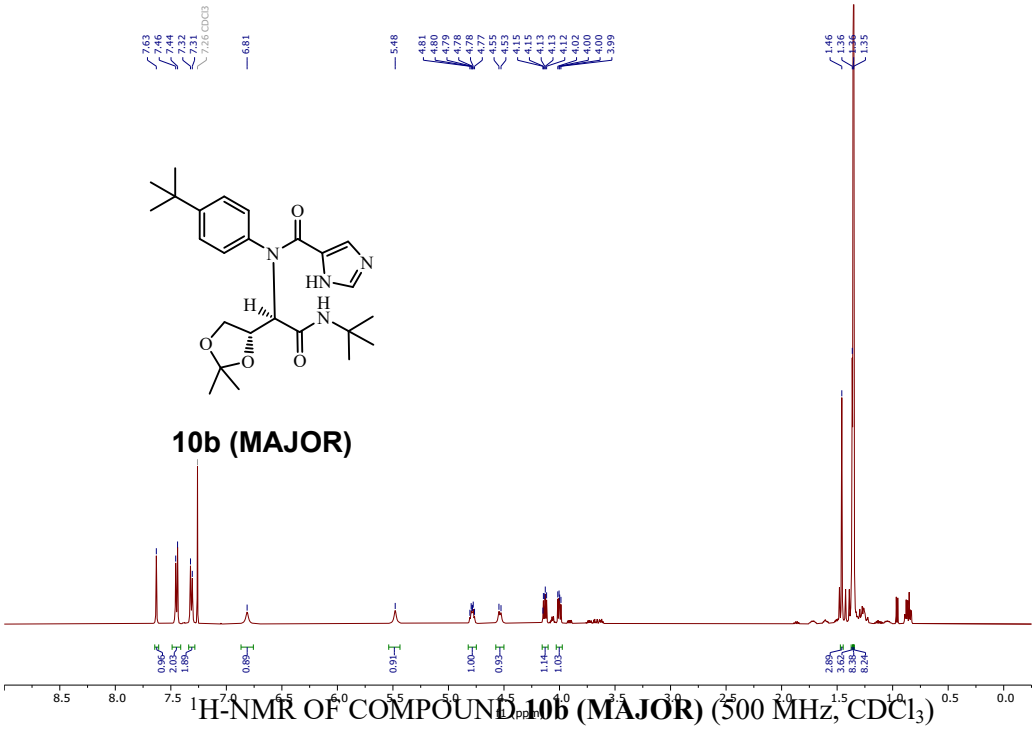
[1]H-NMR and [13]C-NMR of new compounds



^{1}H-NMR OF COMPOUND **10a (MINOR)** (500 MHz, $CDCl_3$)



^{13}C-NMR OF COMPOUND **10a (MINOR)** (126 MHz, $CDCl_3$)



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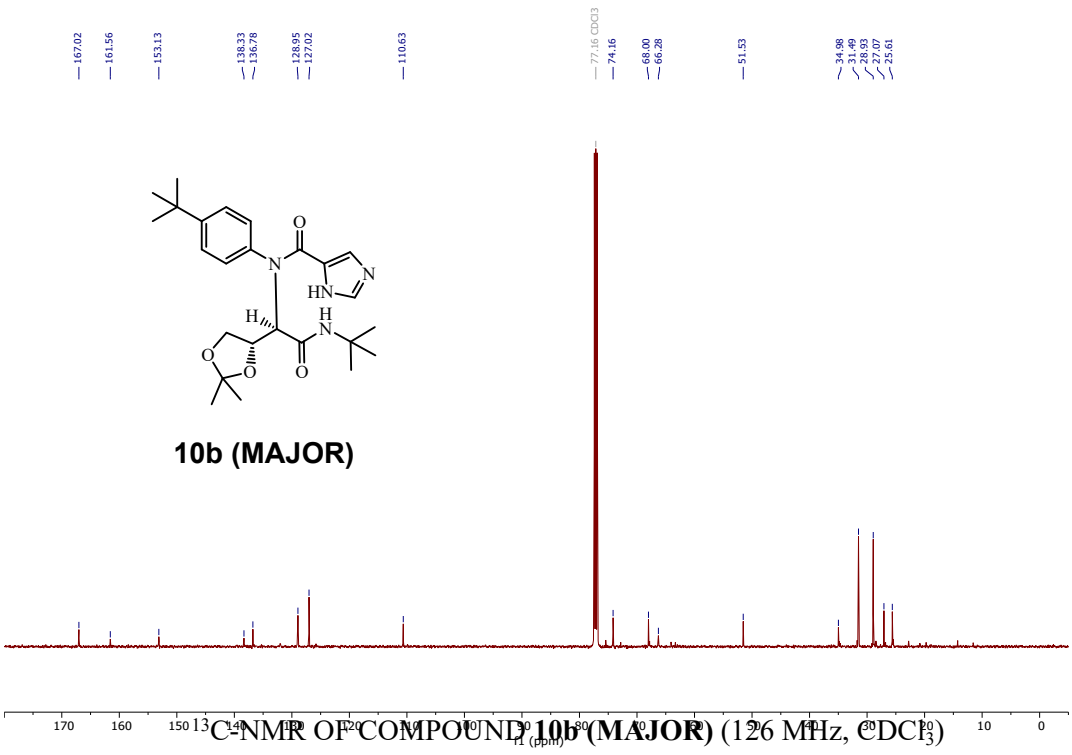

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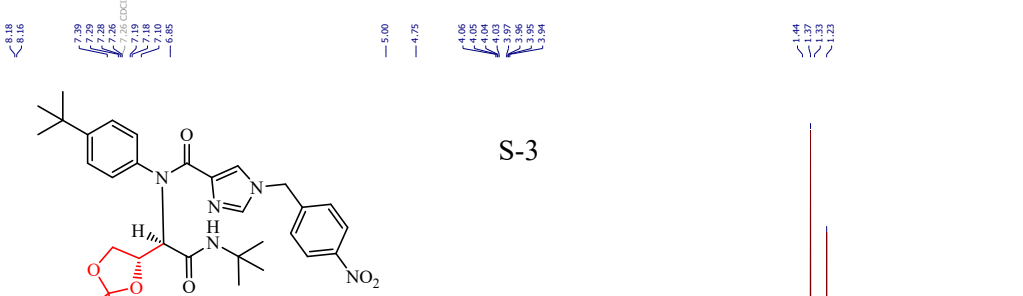

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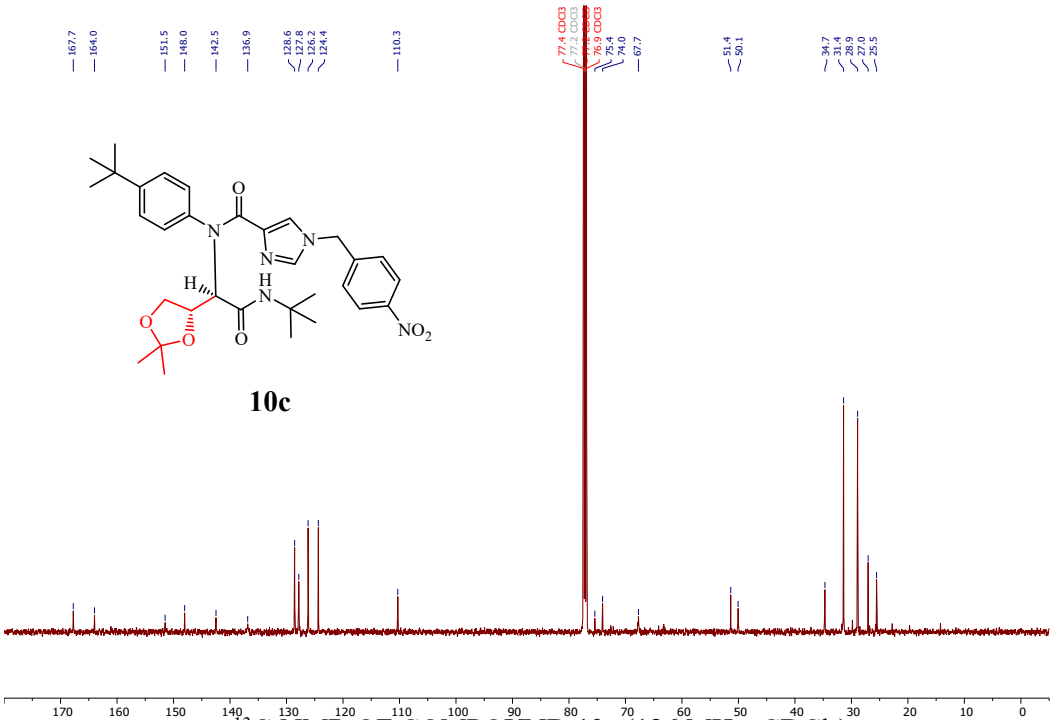
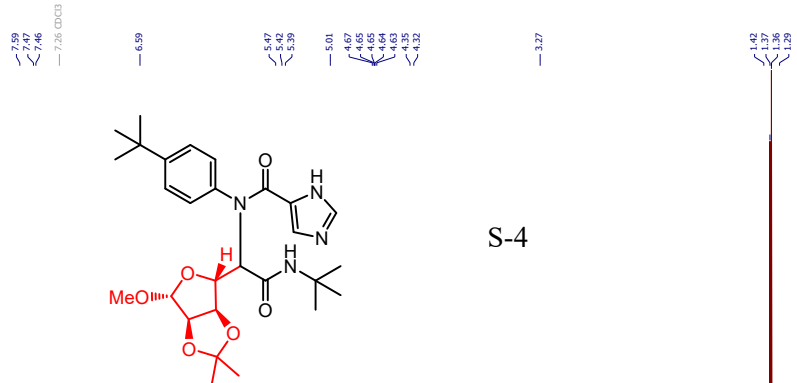


10c

^{13}C-NMR OF COMPOUND **10c** (126 MHz, $CDCl_3$)



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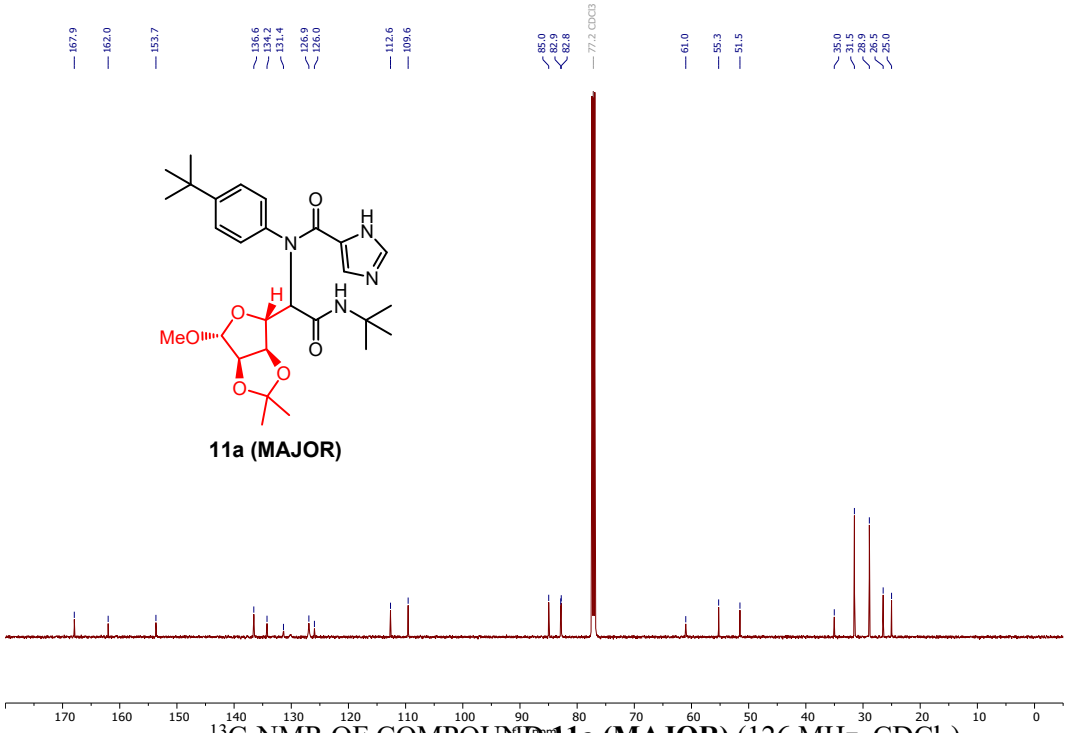

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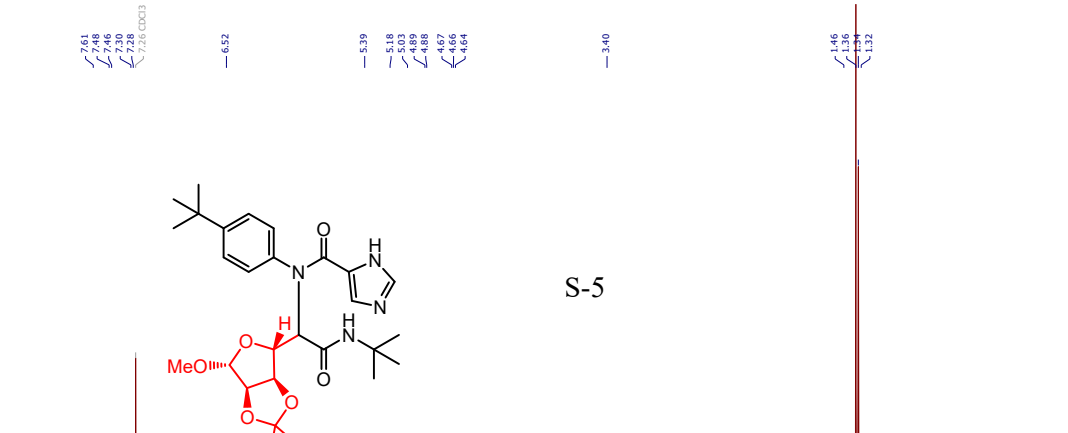

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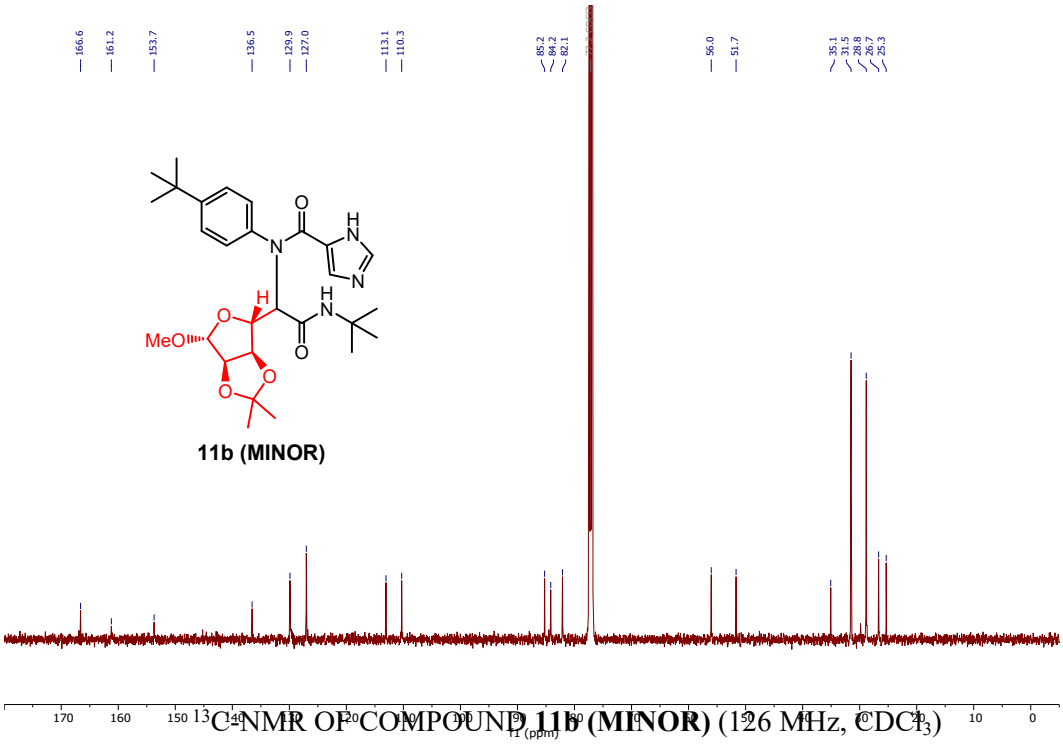

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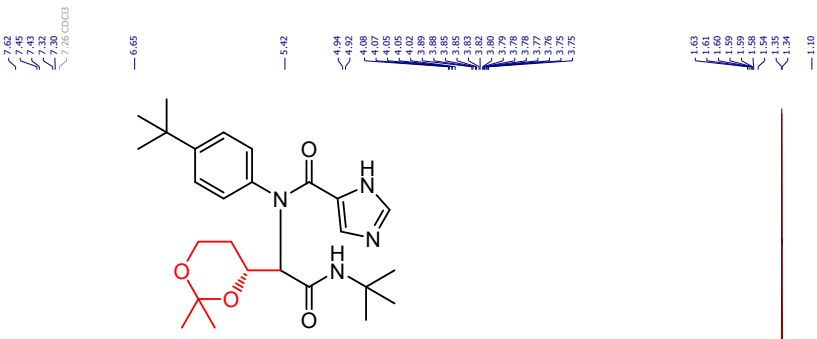

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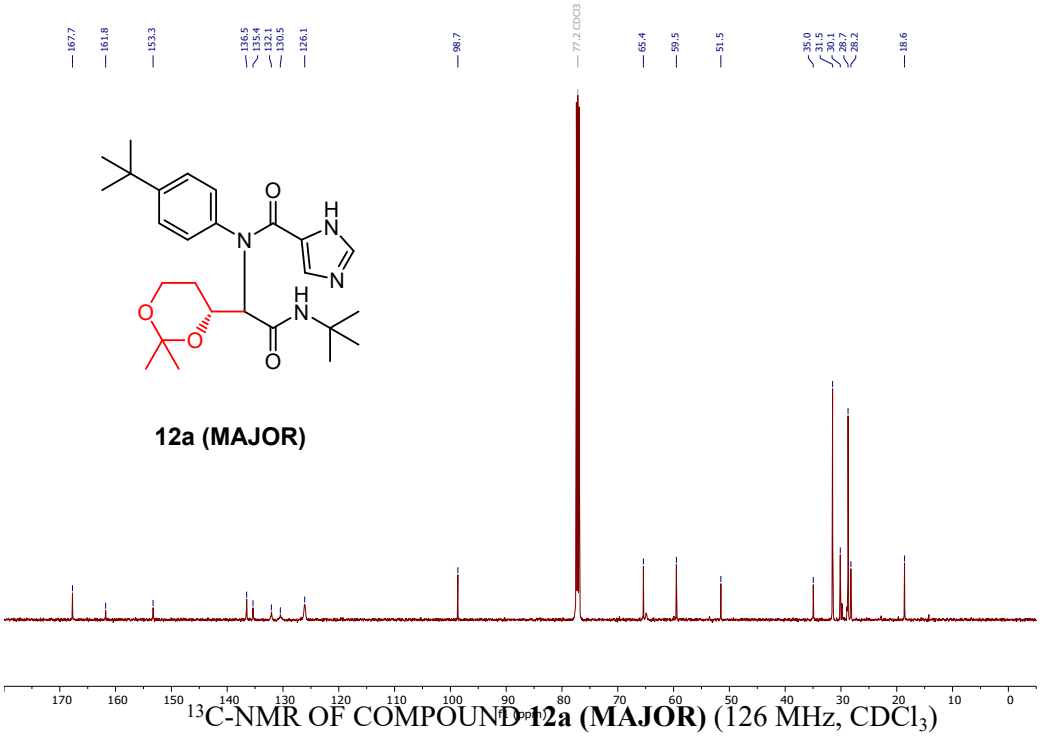

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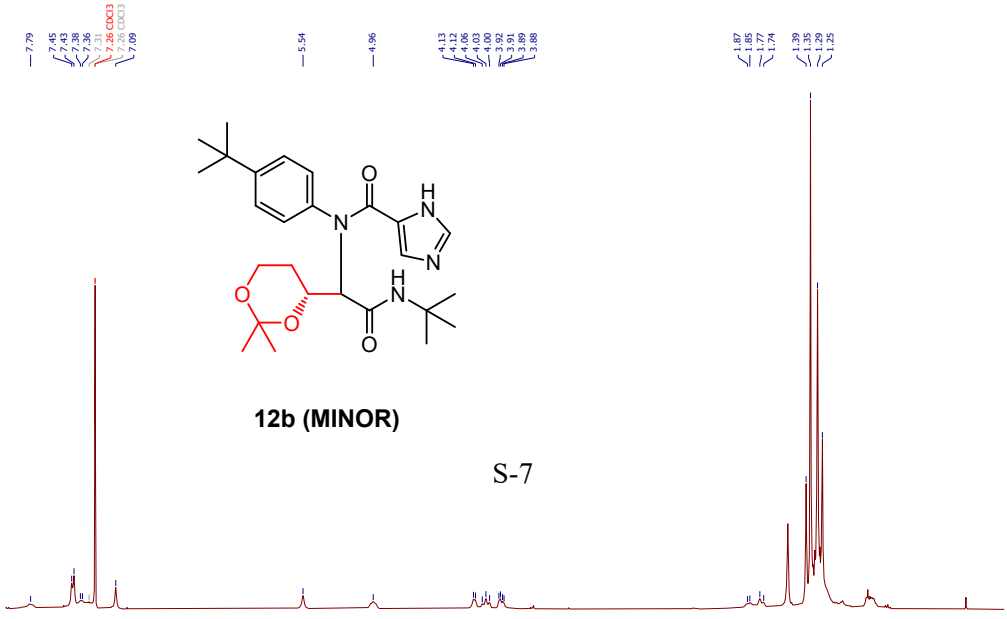

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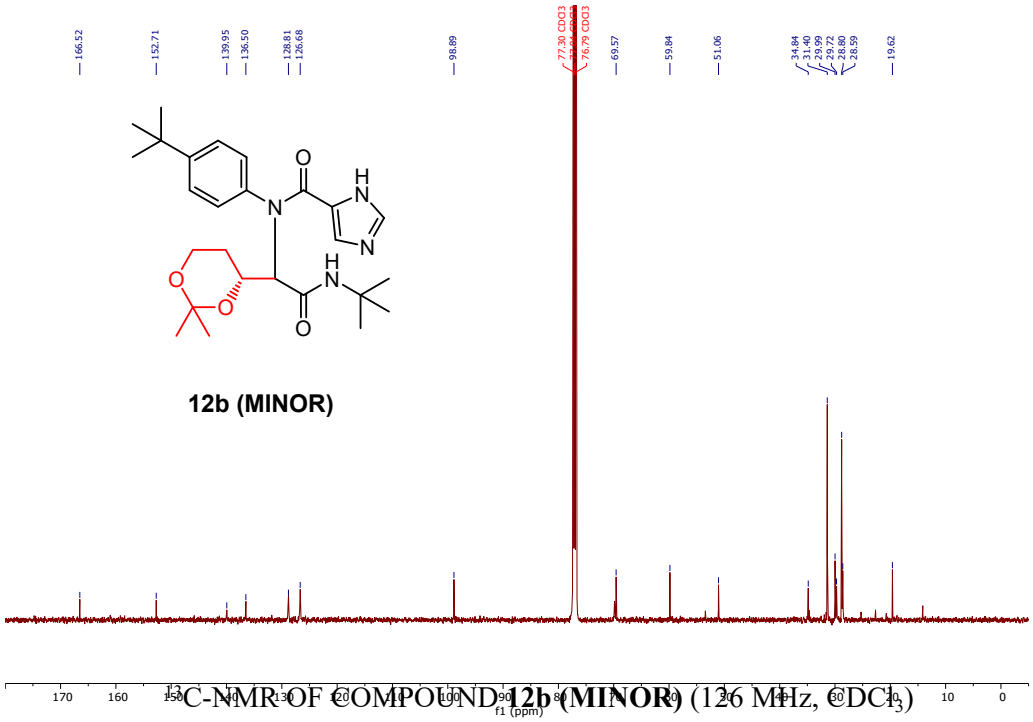

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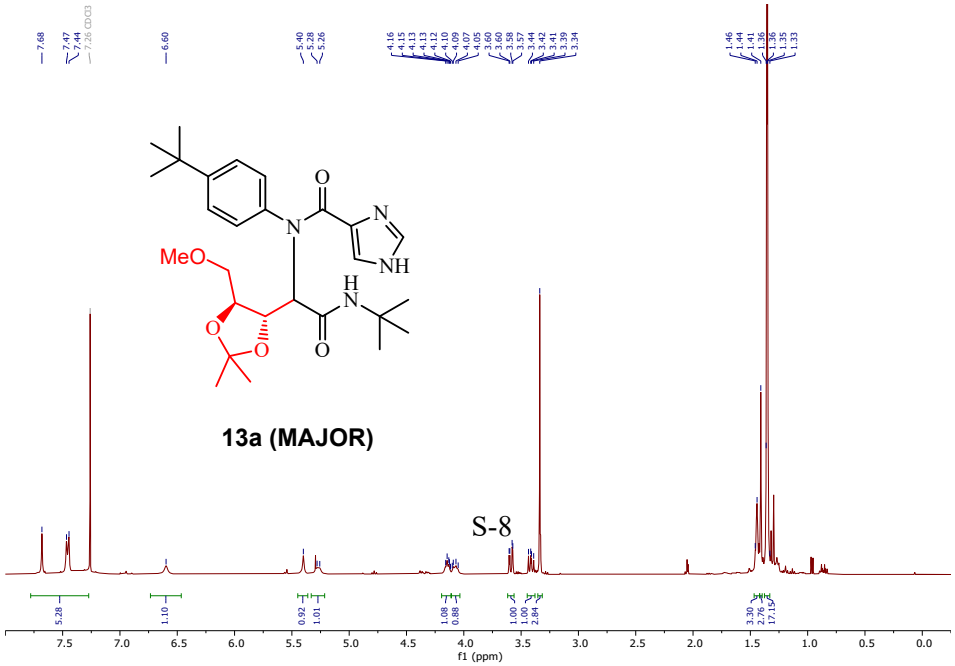

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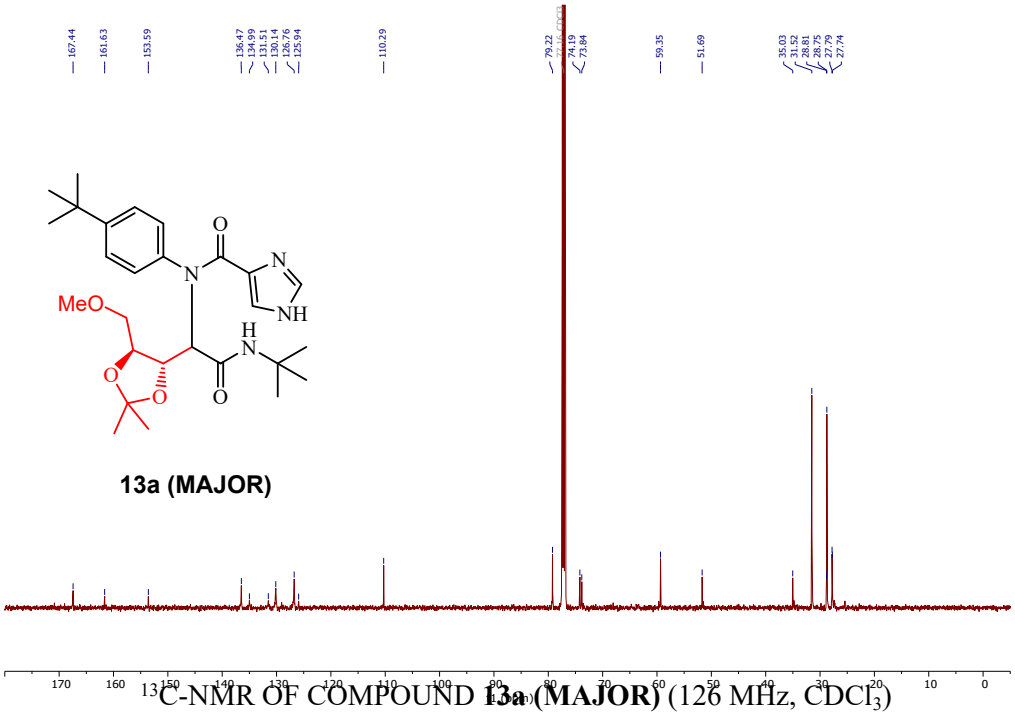

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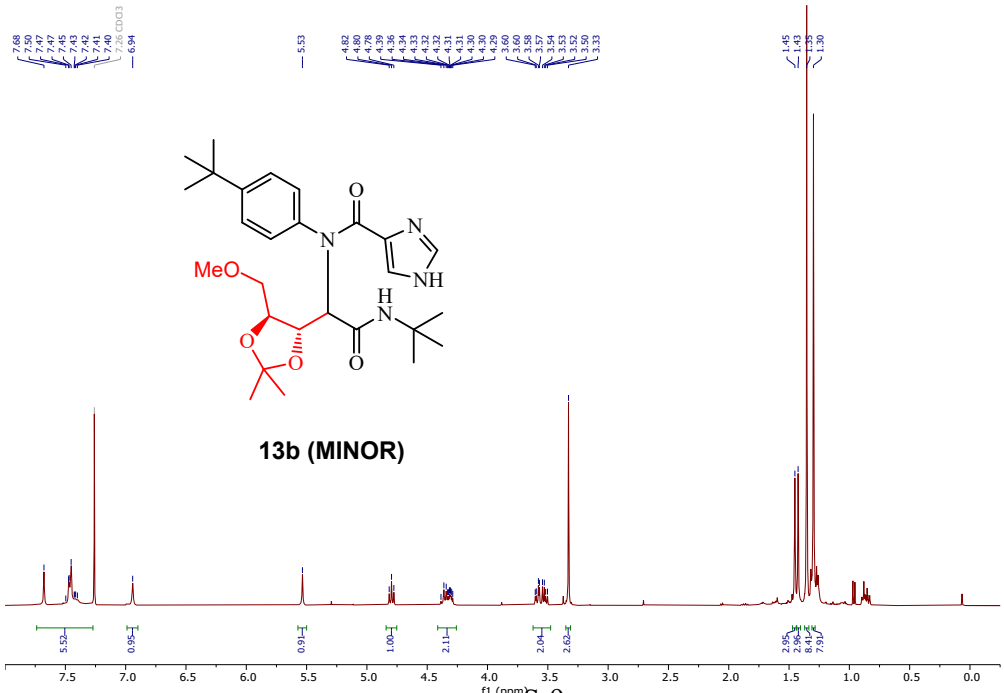

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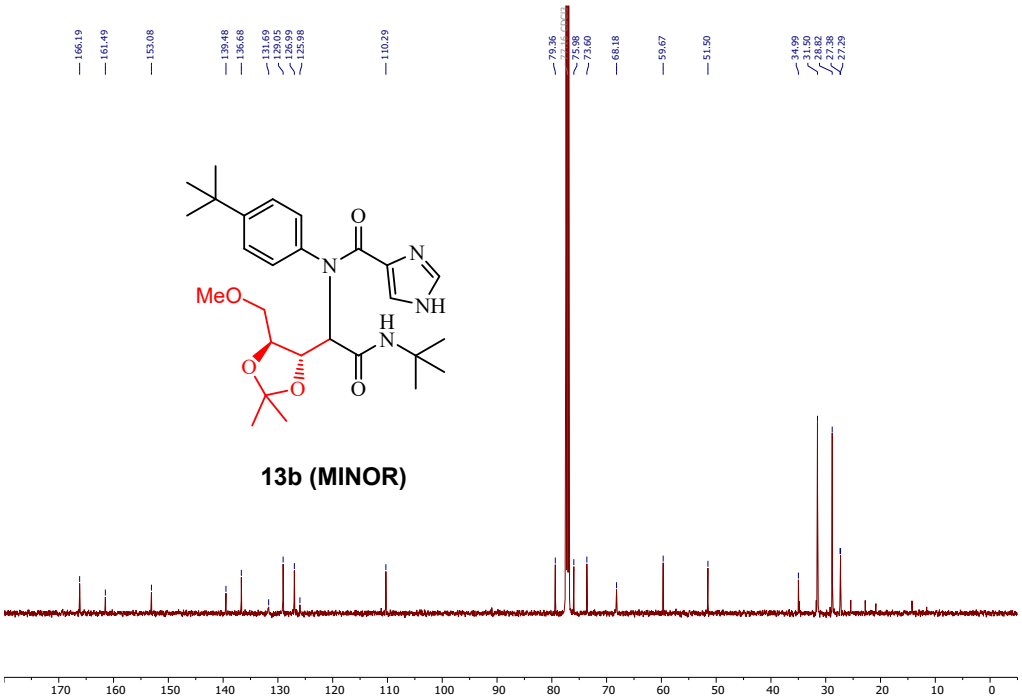

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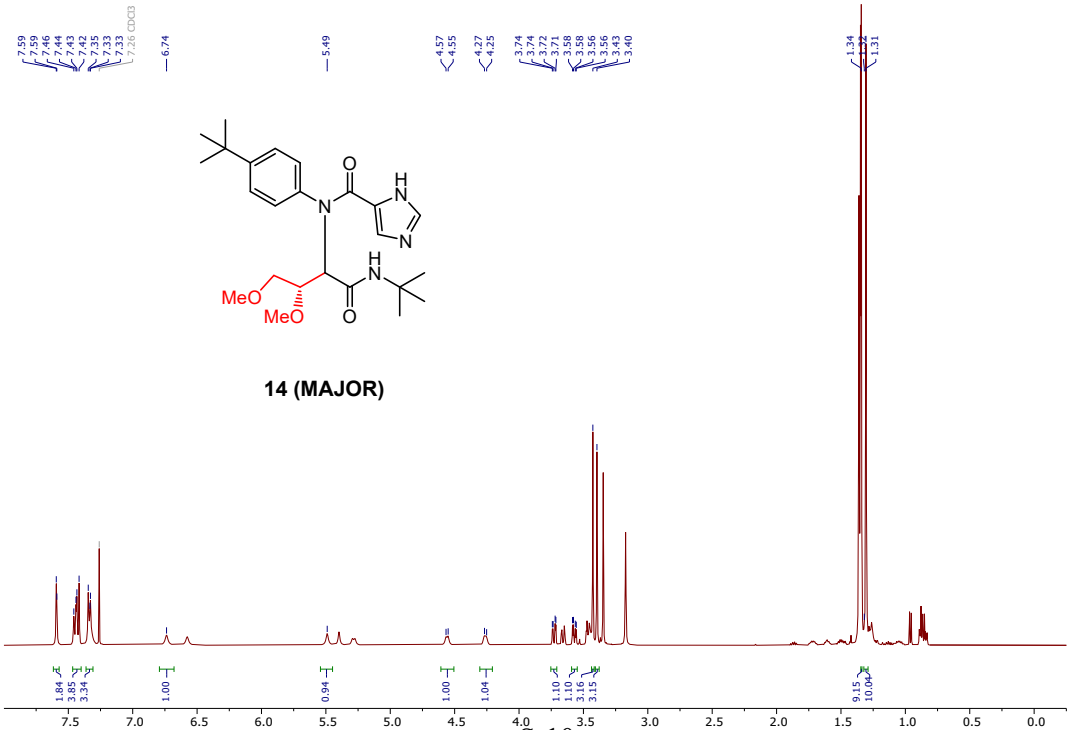

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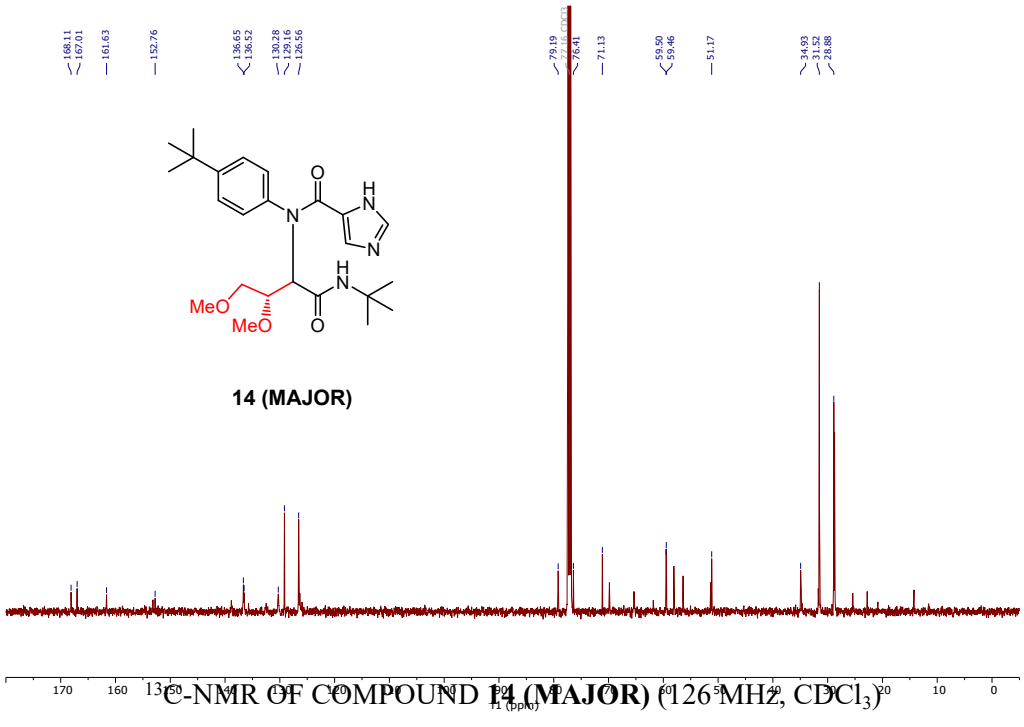

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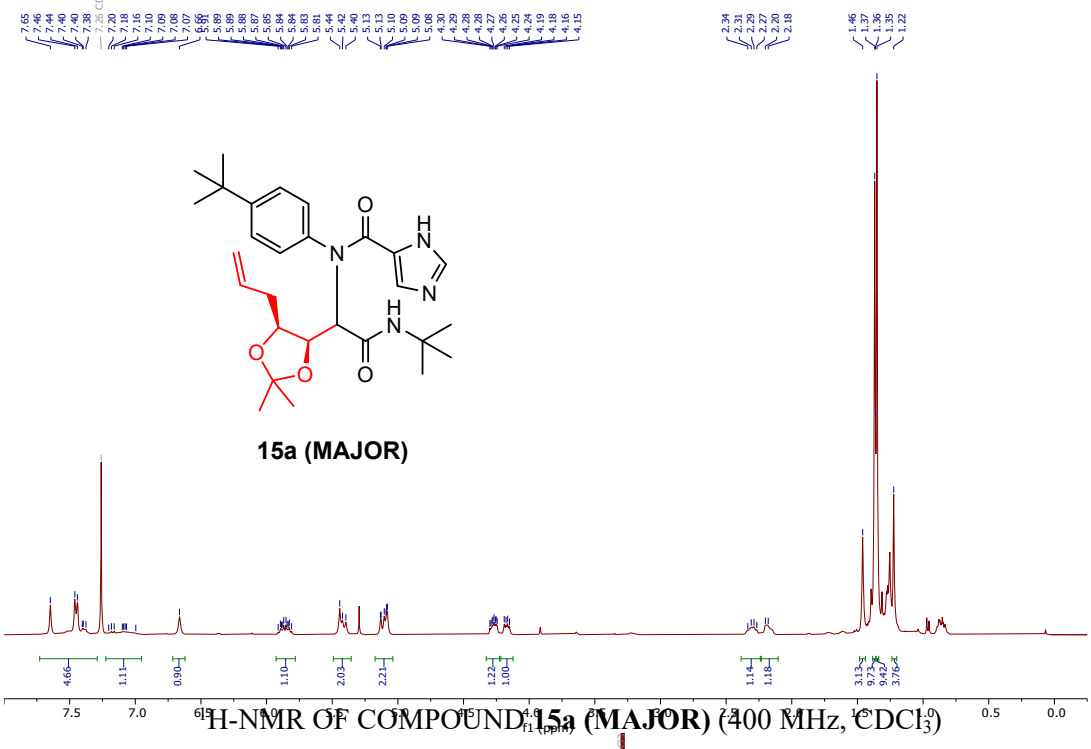

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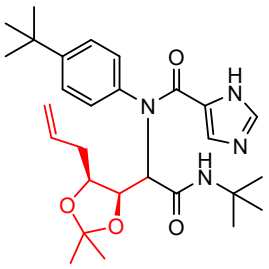
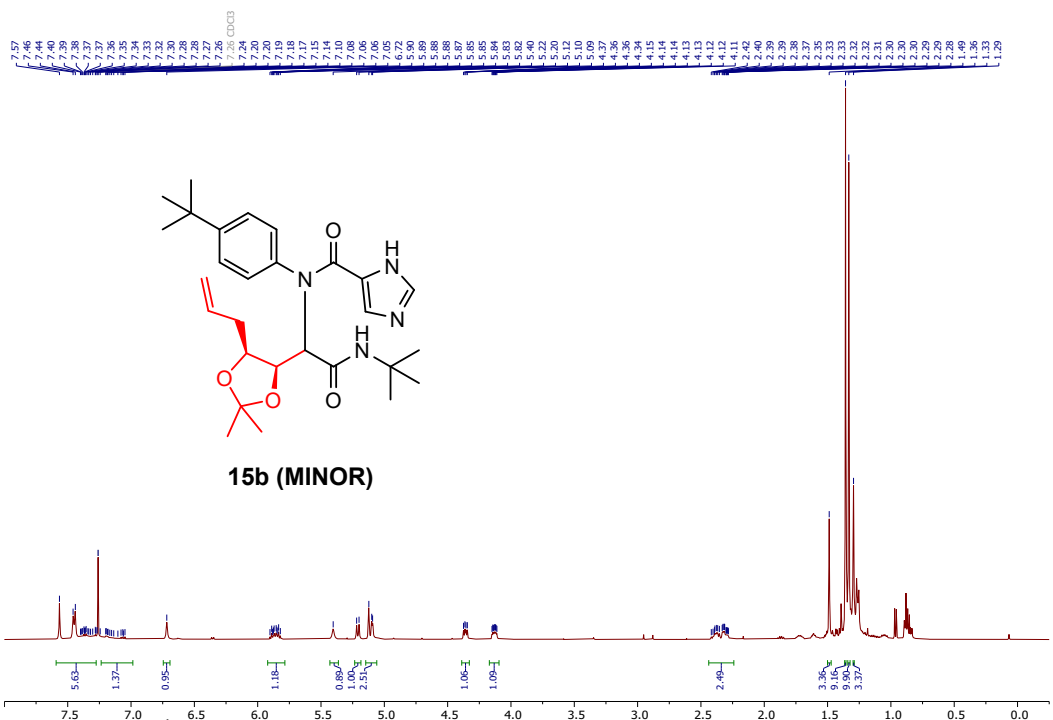


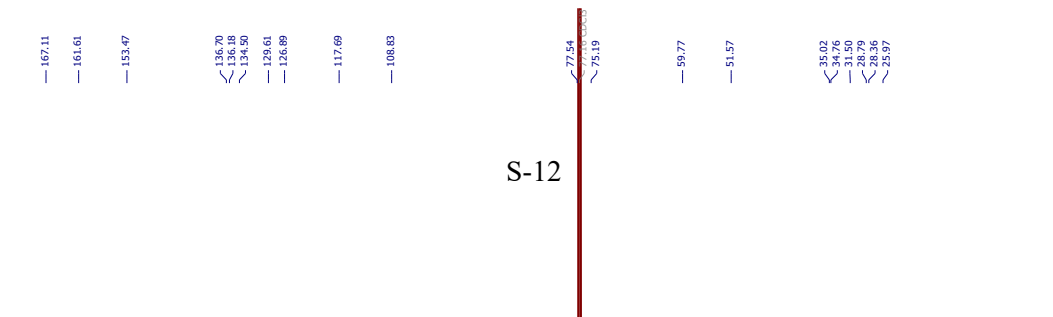
15a (MAJOR)

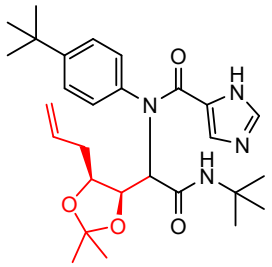
^{13}C-NMR OF COMPOUND **15a (MAJOR)** (126 MHz, $CDCl_3$)



15b (MINOR)

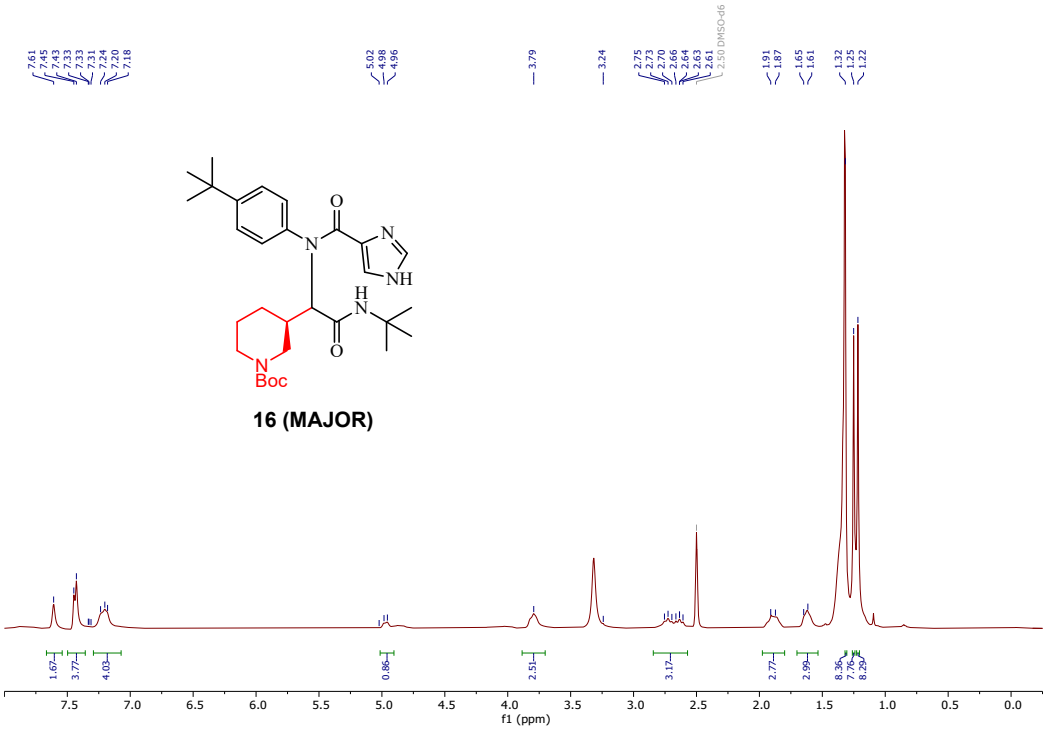
^{1}H-NMR OF COMPOUND **15b (MINOR)** (500 MHz, $CDCl_3$)





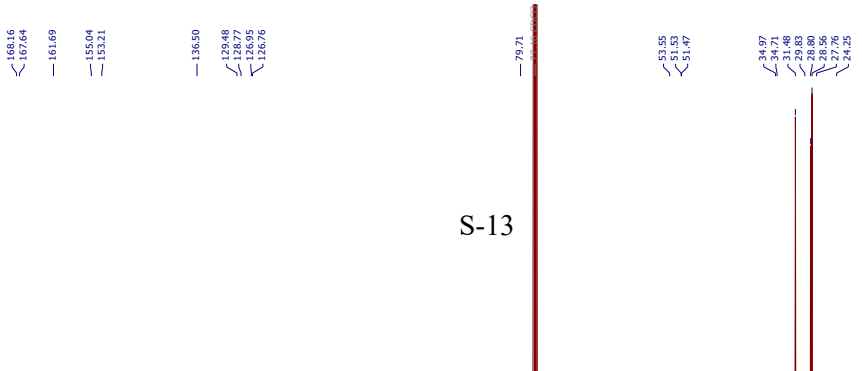
15b (MINOR)

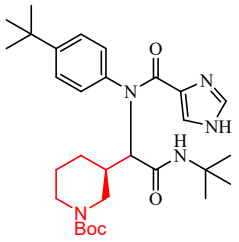
^{13}C-NMR OF COMPOUND **15b (MINOR)** (126 MHz, $CDCl_3$)



16 (MAJOR)

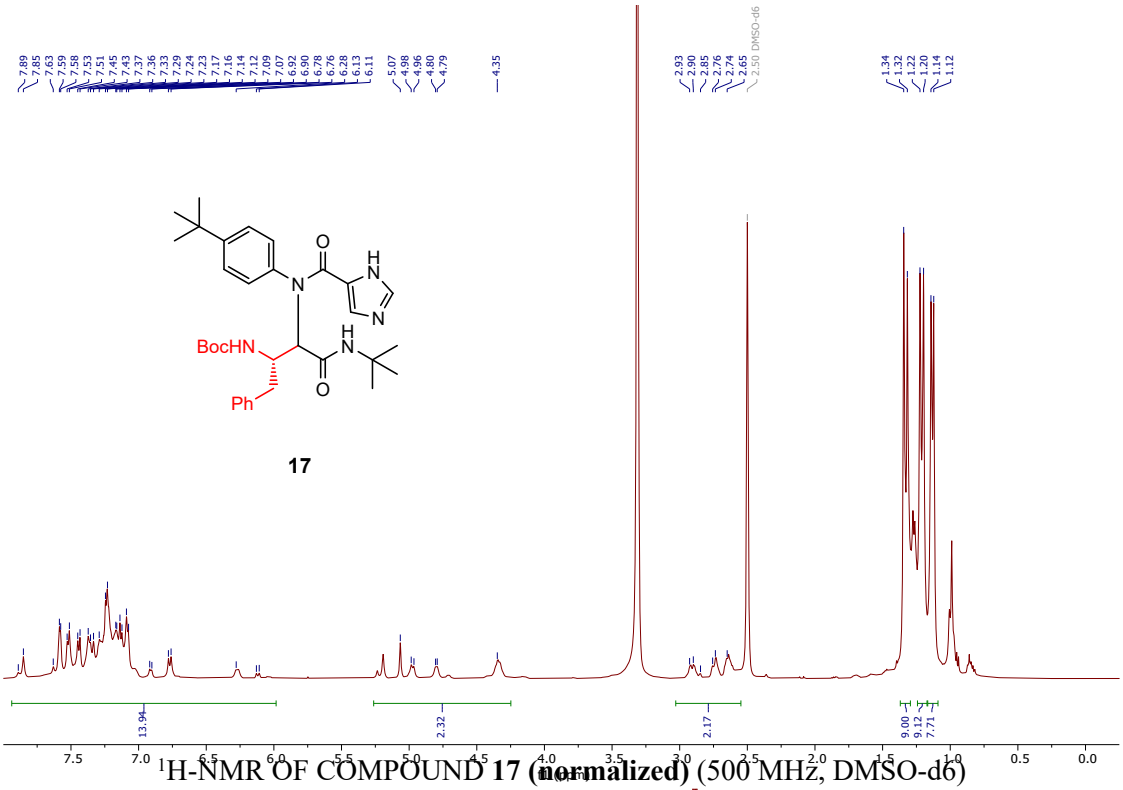
^{1}H-NMR OF COMPOUND **16 (MAJOR)** (400 MHz, $CDCl_3$)





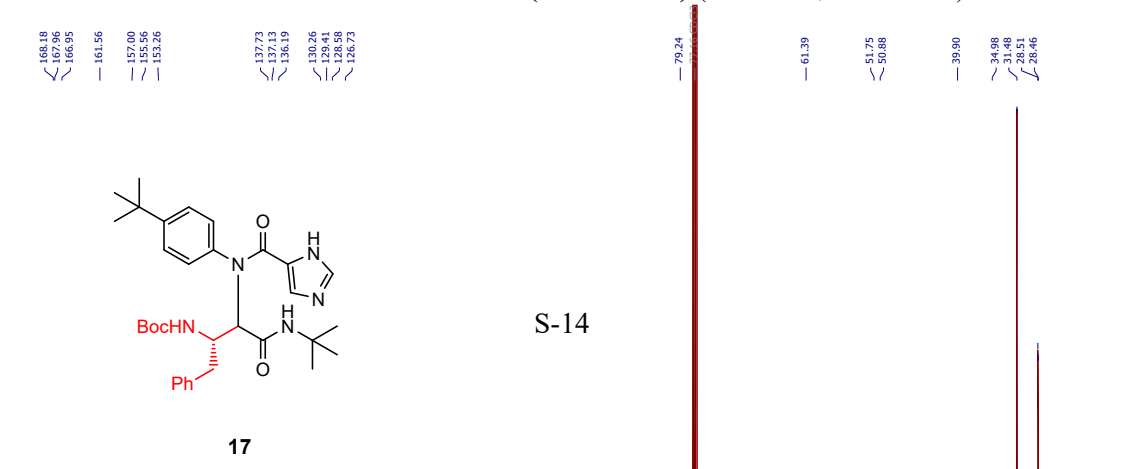
16 (MAJOR)

^{13}C-NMR OF COMPOUND **16 (MAJOR)** (126 MHz, $CDCl_3$)



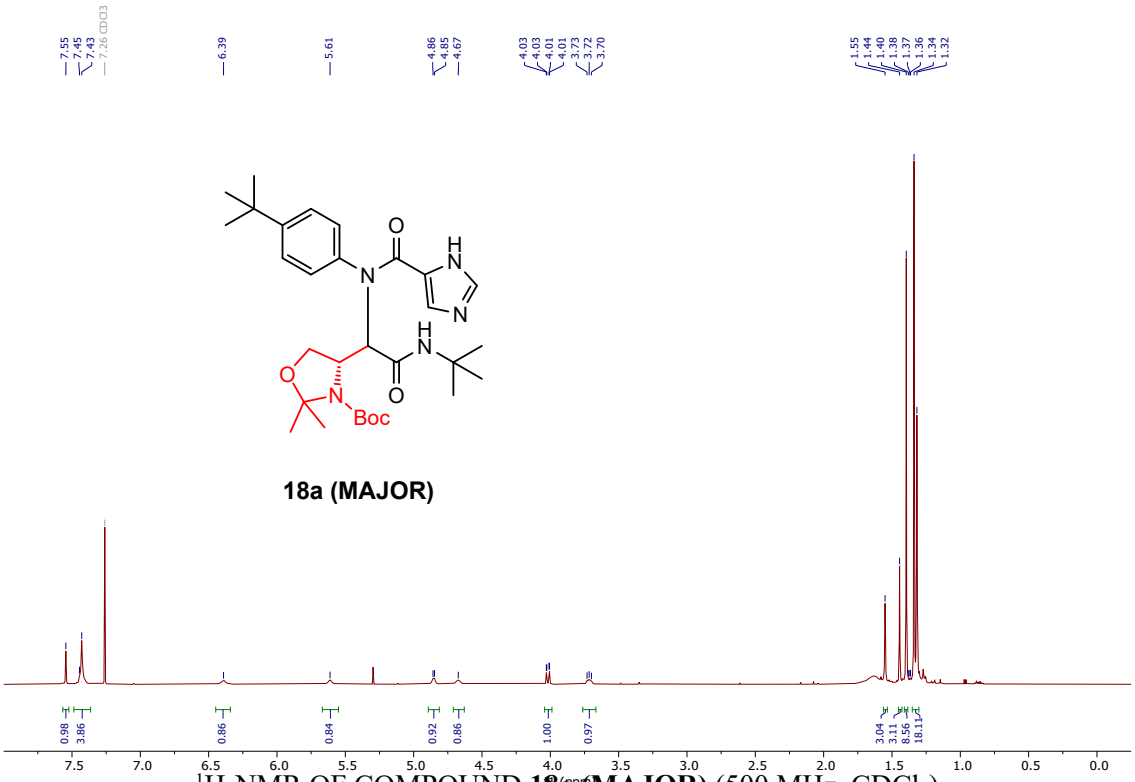
17

^{1}H-NMR OF COMPOUND **17 (normalized)** (500 MHz, DMSO-d6)



17

^{13}C-NMR OF COMPOUND **17** (126 MHz, DMSO-d6)



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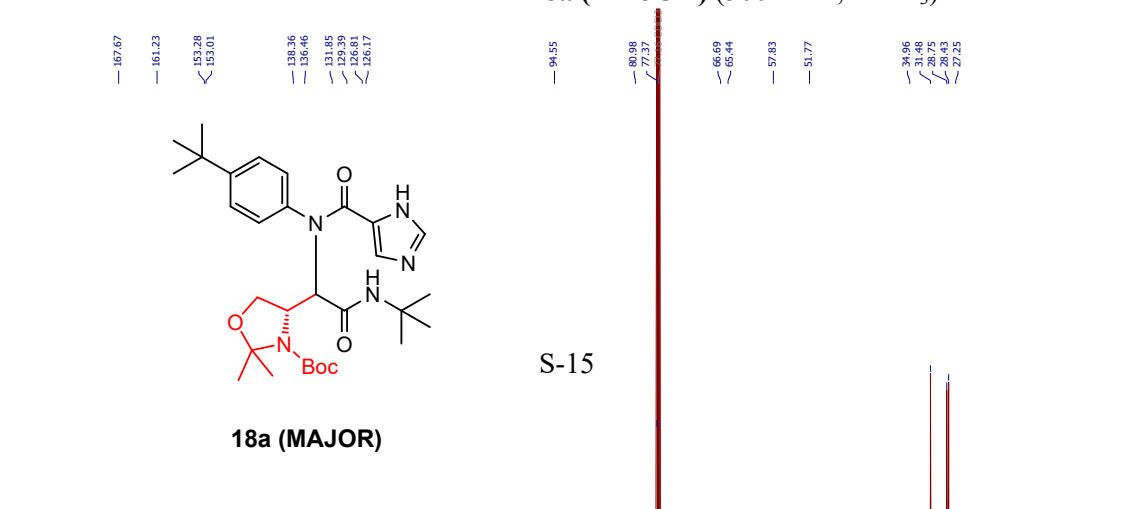

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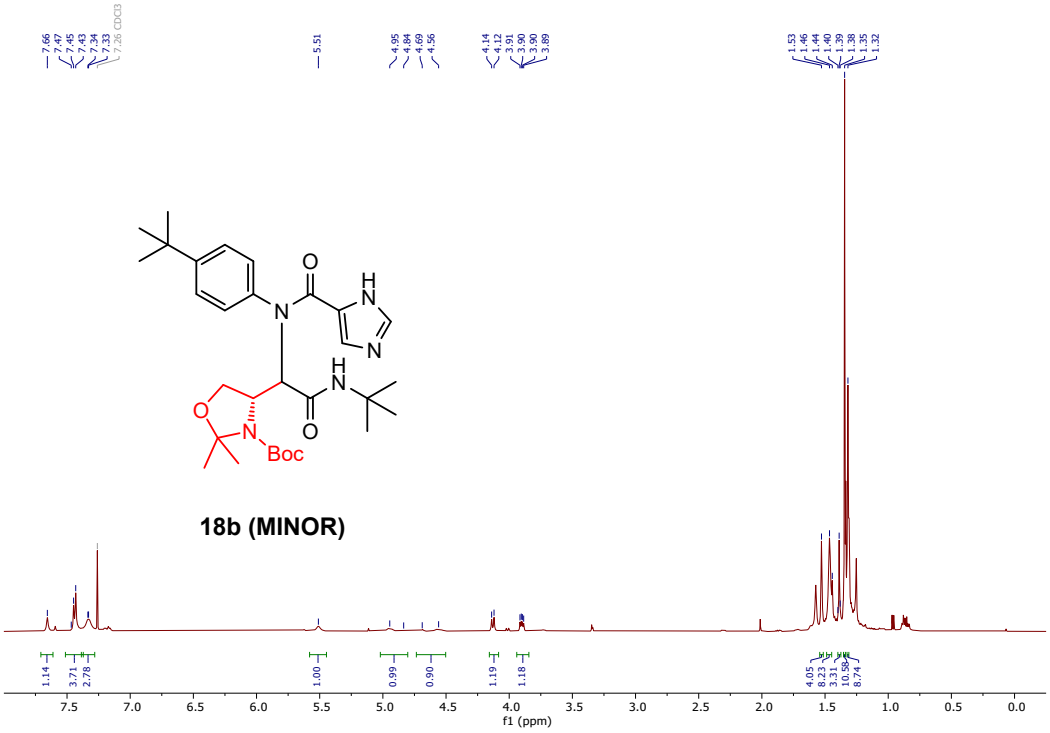

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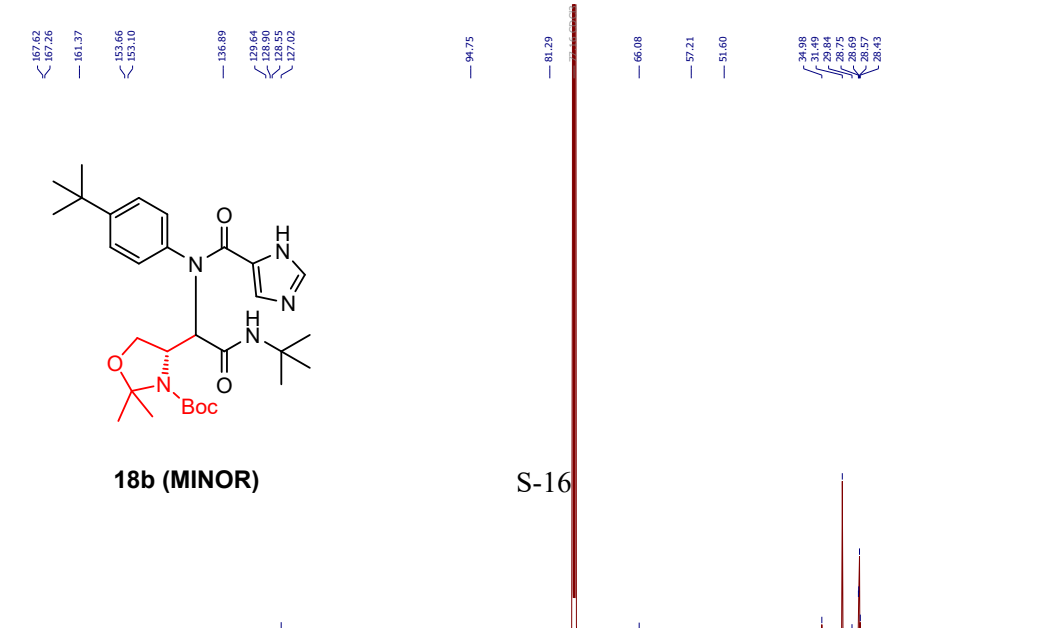

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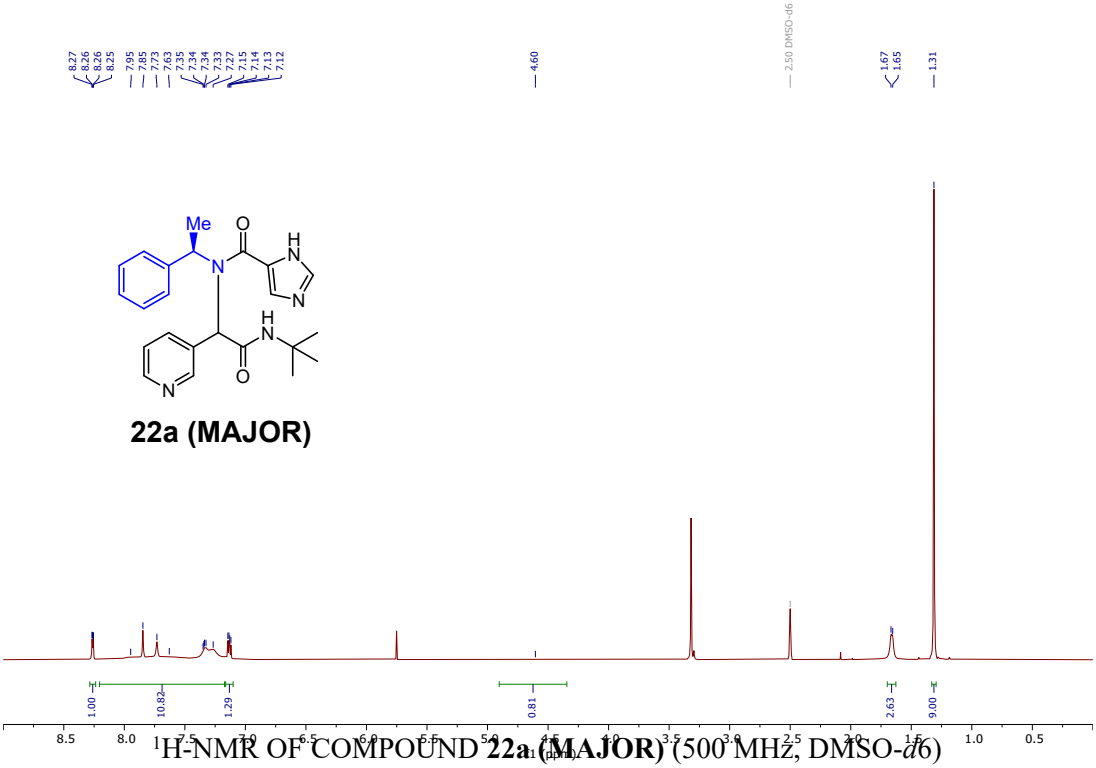

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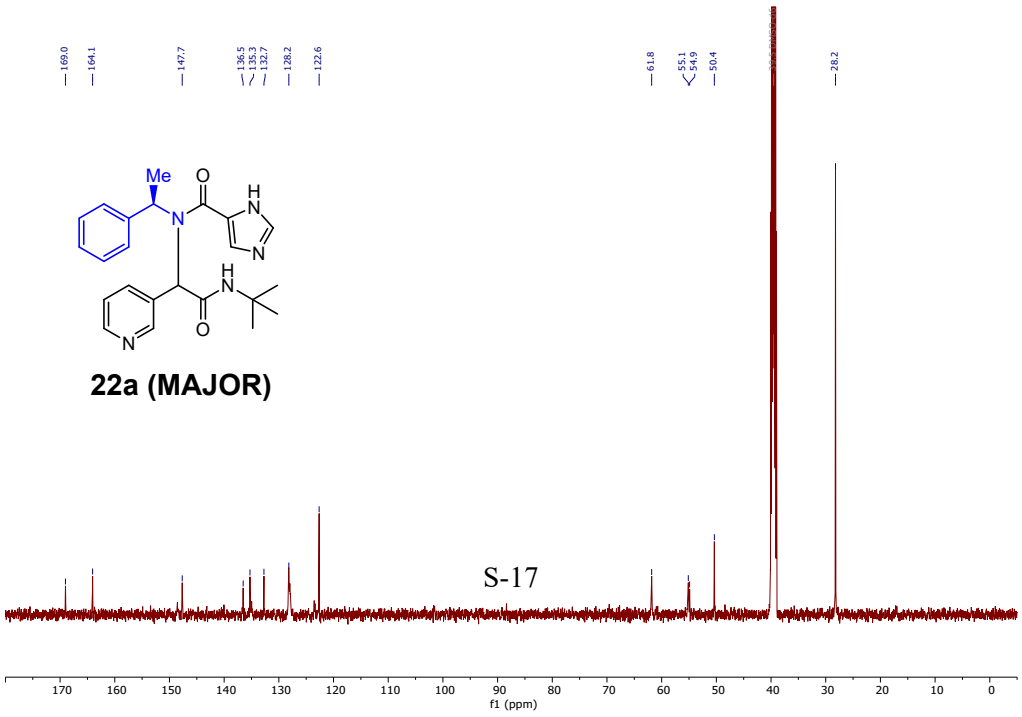
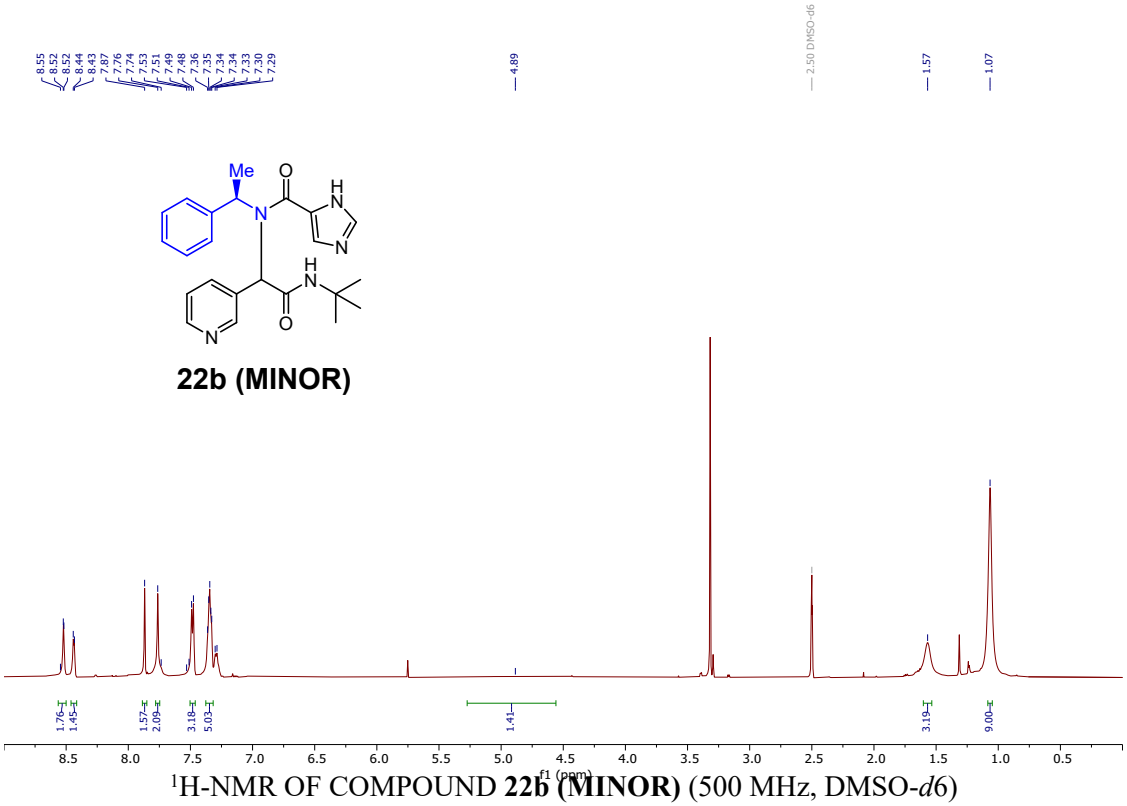


^{13}C-NMR OF COMPOUND **22a (MAJOR)** (126 MHz, DMSO-*d*6)



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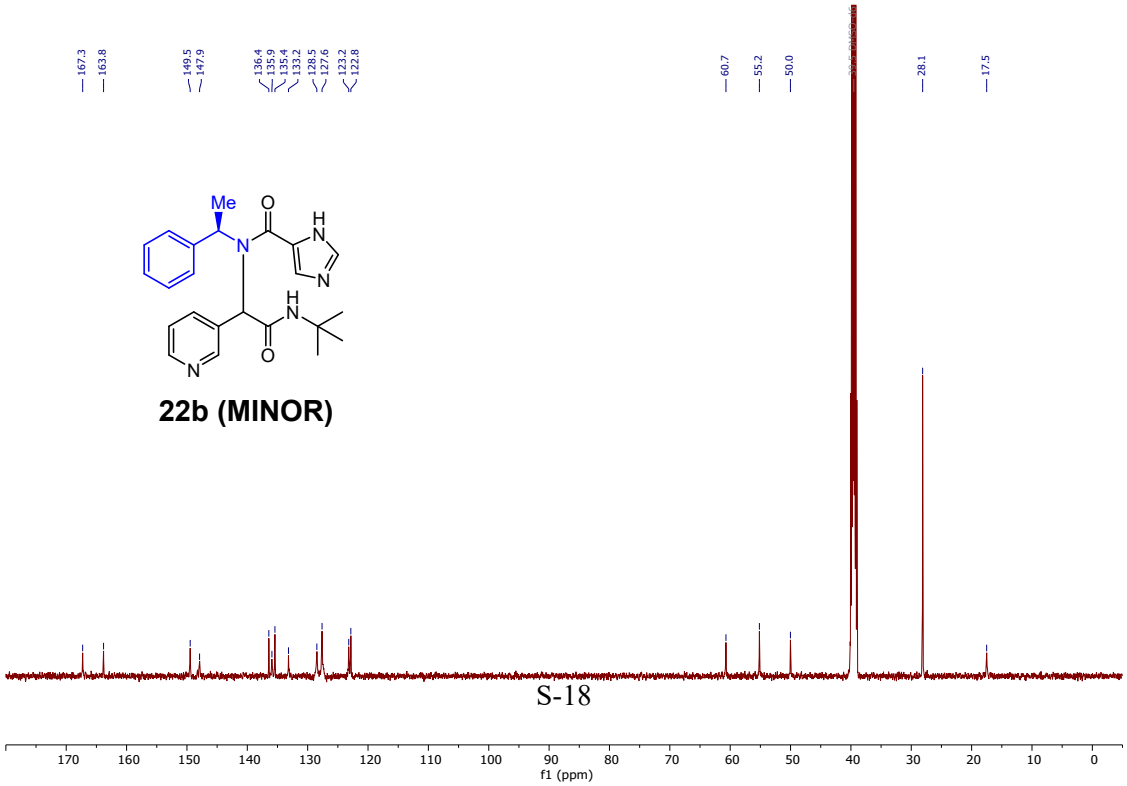
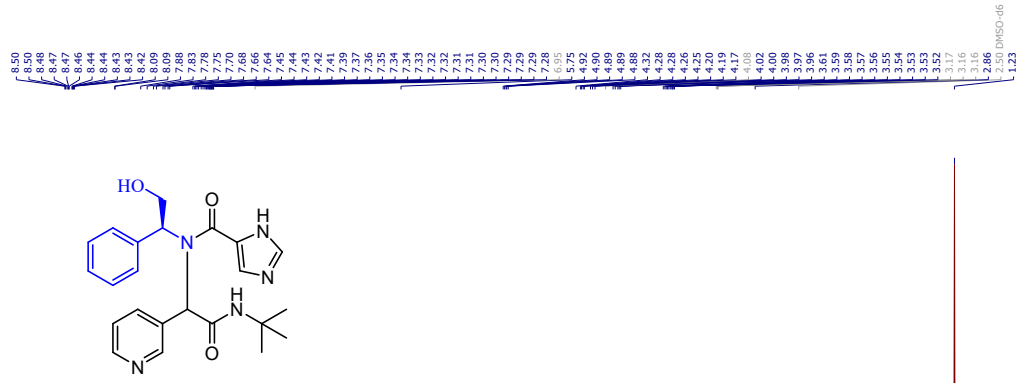
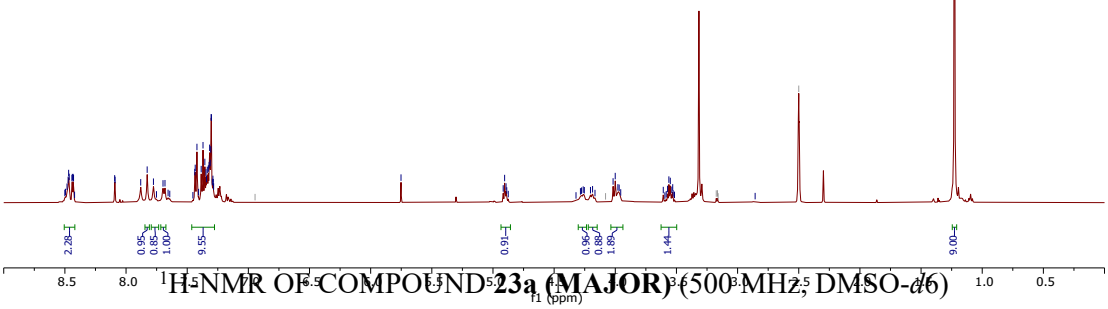


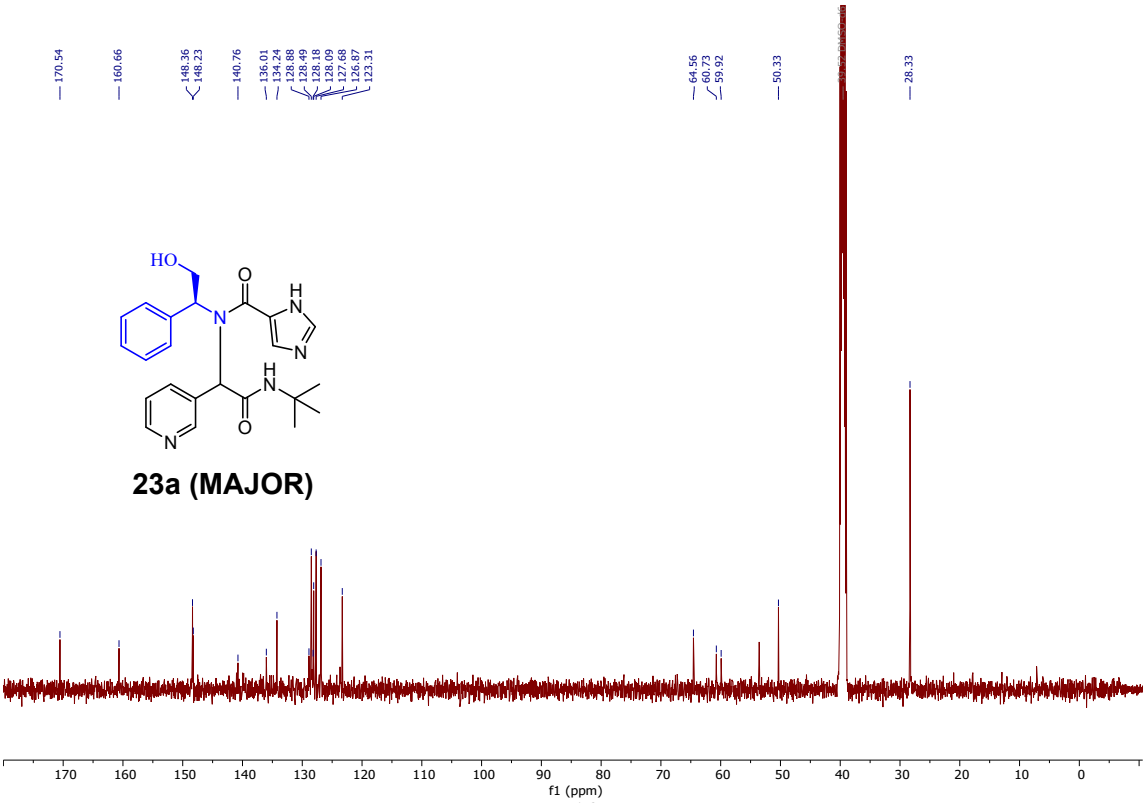
^{13}C-NMR OF COMPOUND **22b (MINOR)** (126 MHz, DMSO-*d6*)



23a (MAJOR)

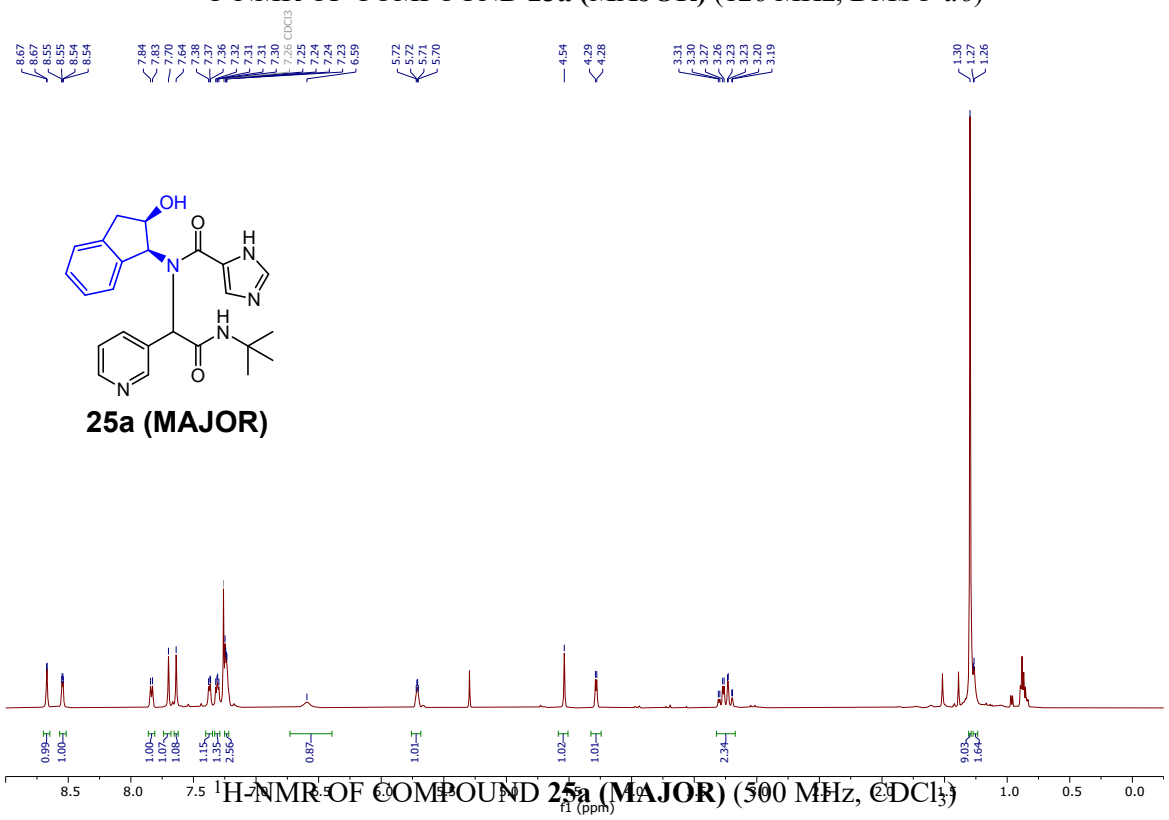


^{1}H-NMR OF COMPOUND **23a (MAJOR)** (500 MHz, DMSO-*d6*)



23a (MAJOR)

^{13}C-NMR OF COMPOUND **23a (MAJOR)** (126 MHz, DMSO-*d*6)



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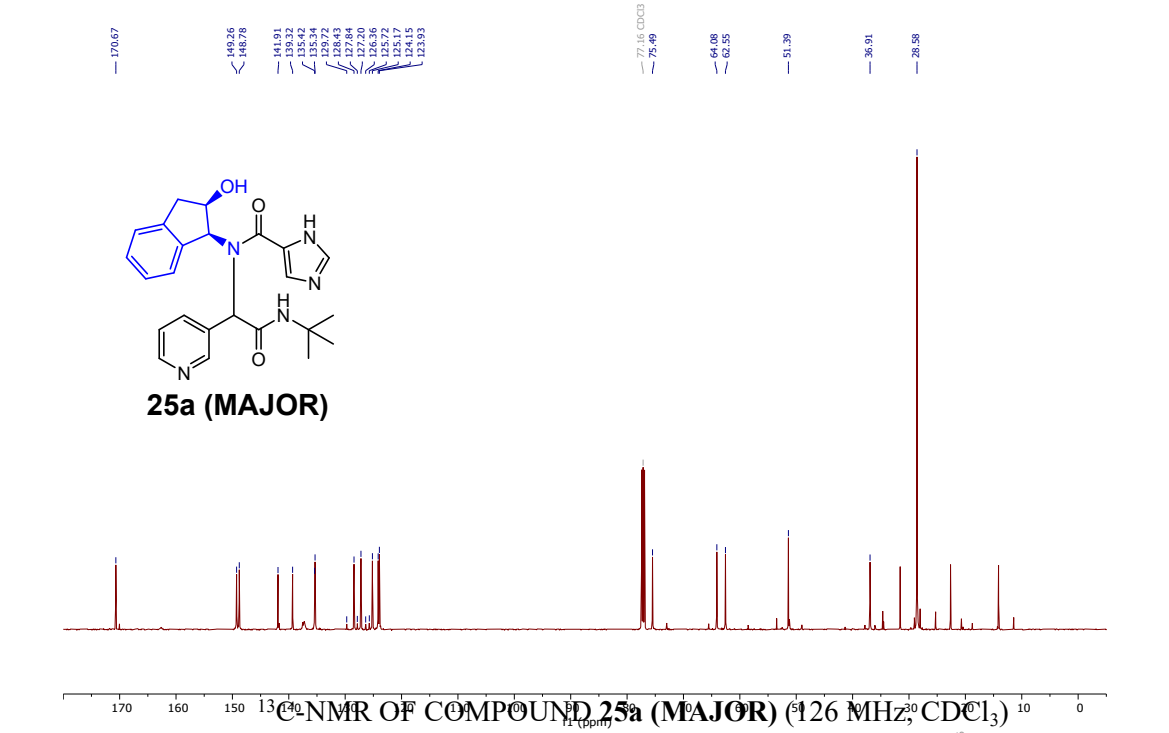

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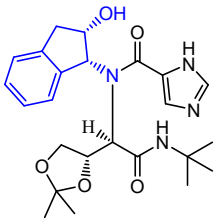
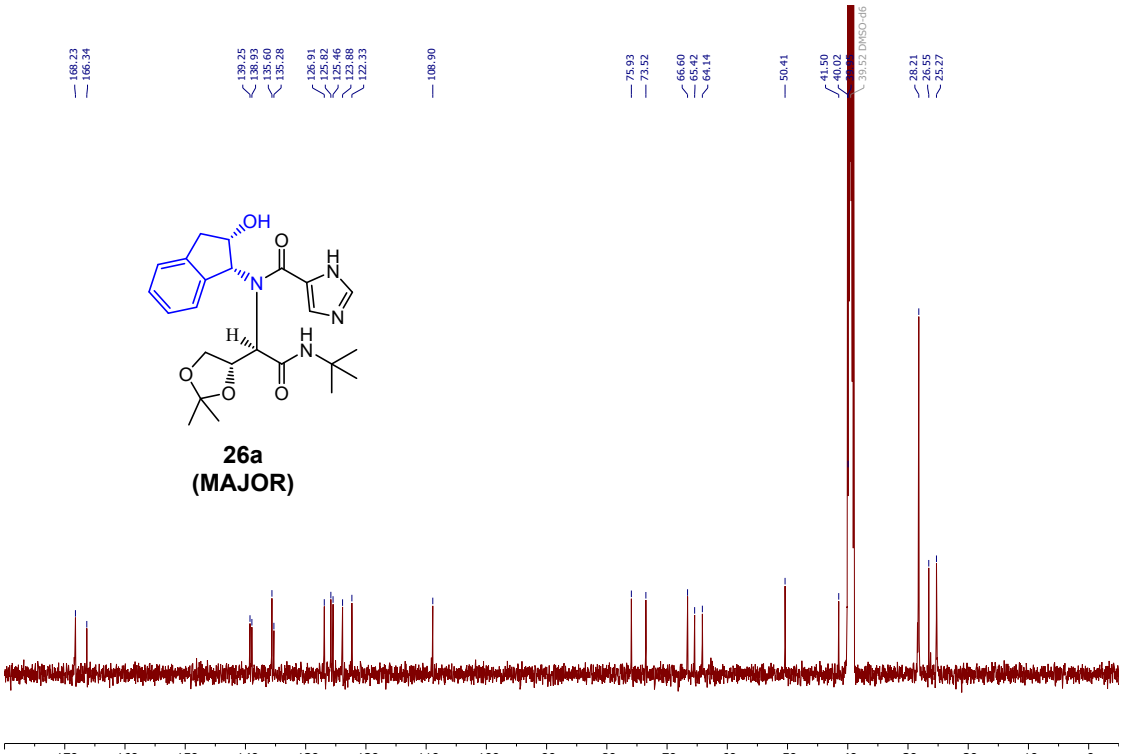


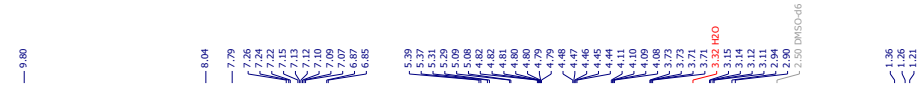
26a
(MAJOR)

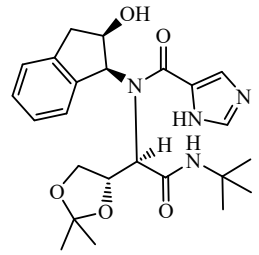
^{1}H-NMR OF COMPOUND **26a (MAJOR)** (500 MHz, DMSO-d_6)



26a
(MAJOR)

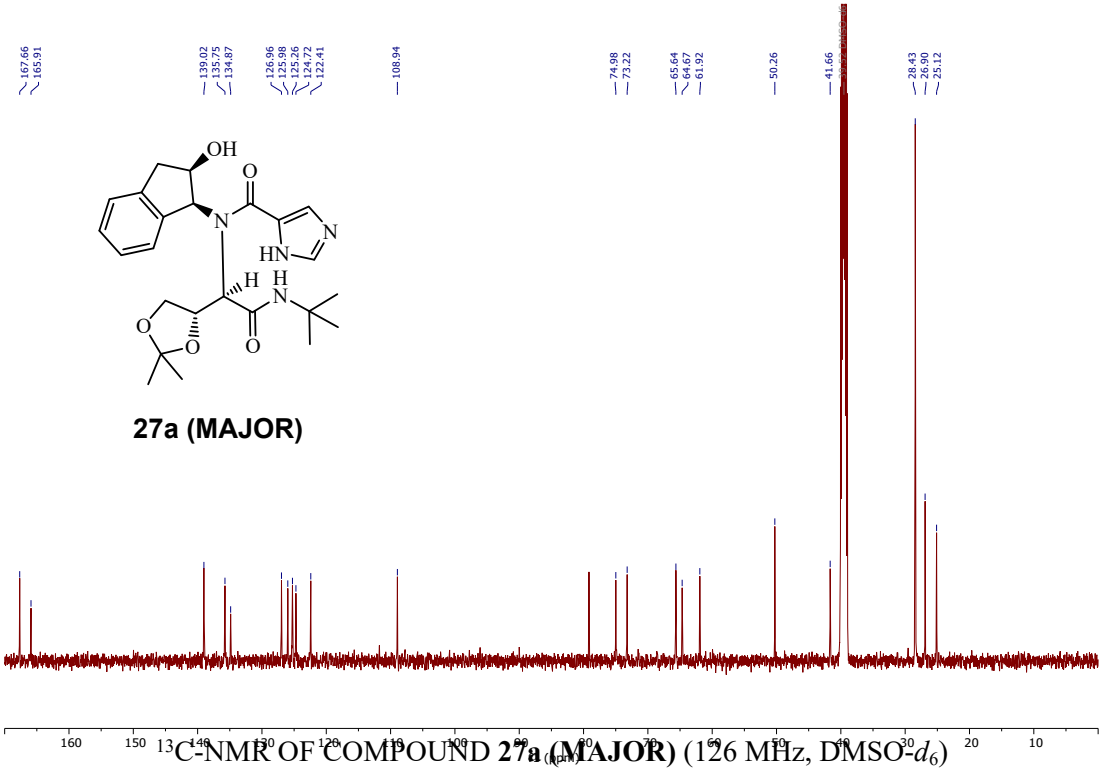
^{13}C-NMR OF COMPOUND **26a (MAJOR)** (126 MHz, DMSO-d_6)





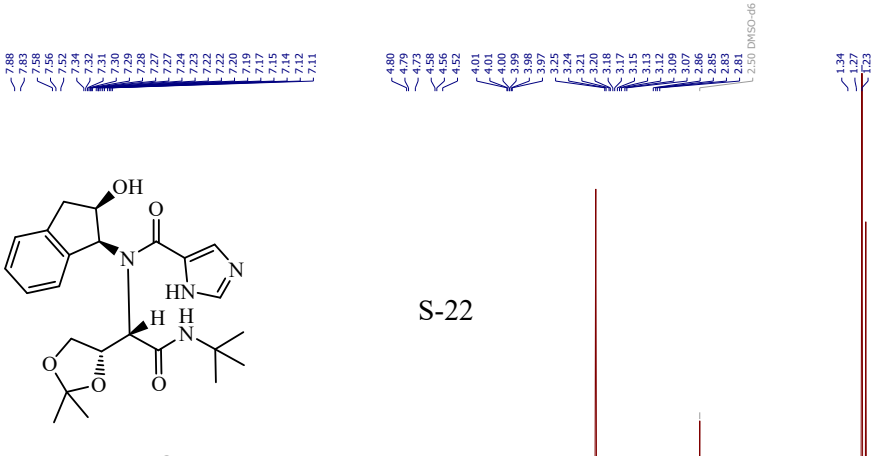
27a (MAJOR)

^{1}H-NMR OF COMPOUND **27a (MAJOR)** (500 MHz, DMSO-d_6)

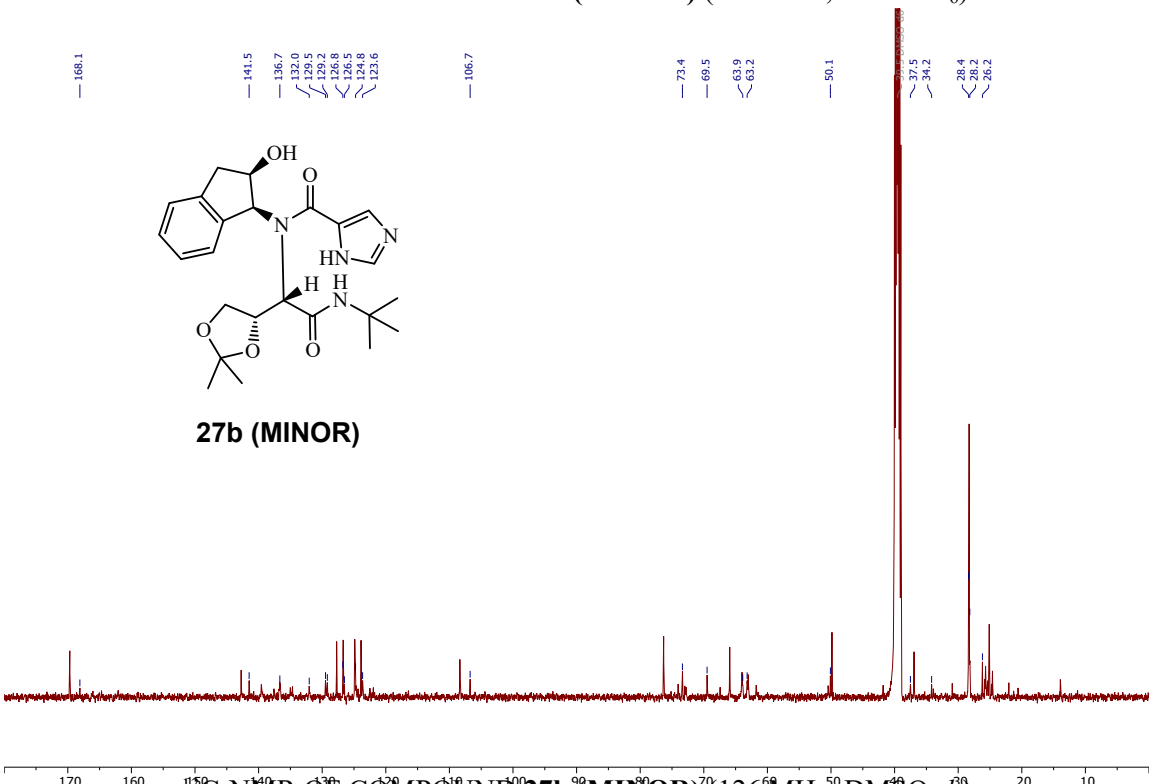


27a (MAJOR)

^{13}C-NMR OF COMPOUND **27a (MAJOR)** (126 MHz, DMSO-d_6)

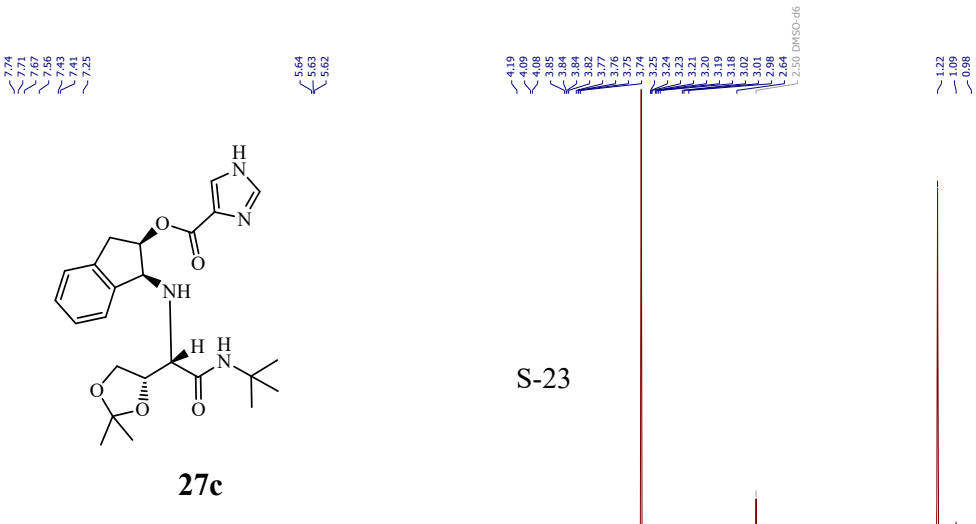


^{1}H-NMR OF COMPOUND **27b (MINOR)** (500 MHz, DMSO-d_6)



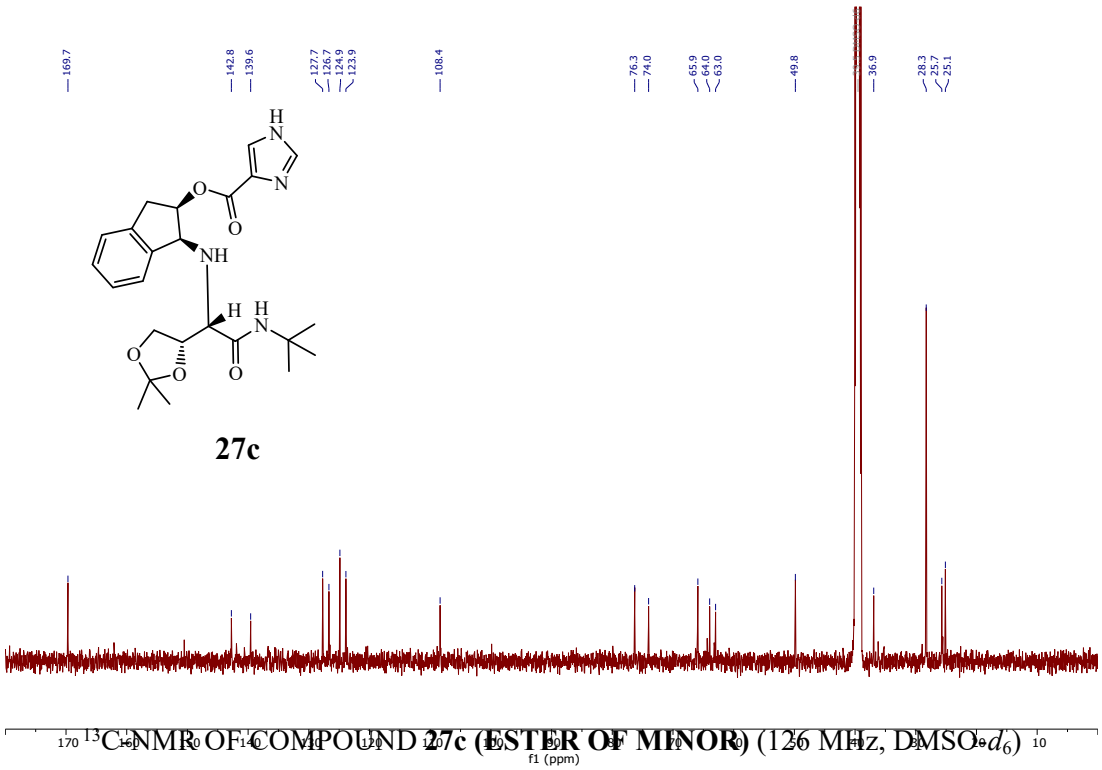
27b (MINOR)

^{13}C-NMR OF COMPOUND **27b (MINOR)** (126 MHz, DMSO-d_6)



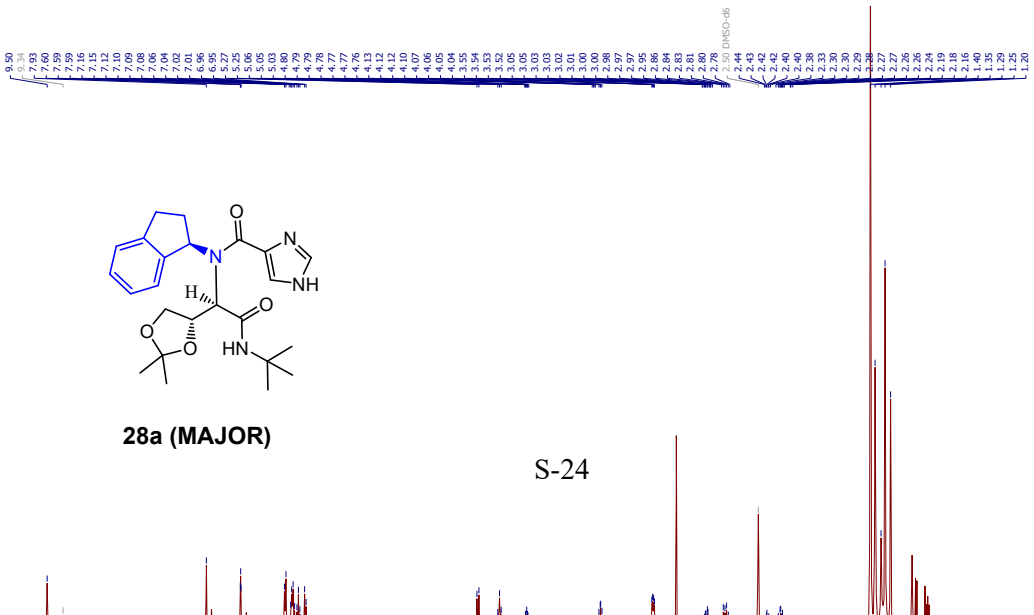
27c

^{1}H-NMR OF COMPOUND **27c (ESTER OF MINOR)** (500 MHz, DMSO-d_6)



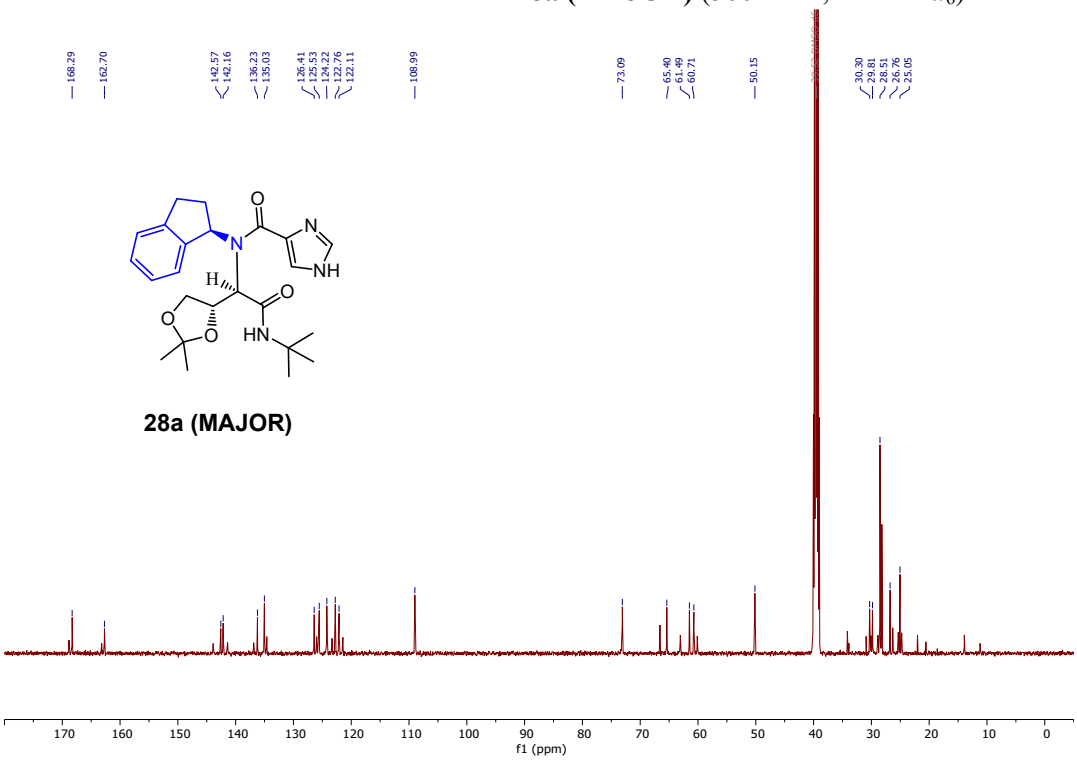
27c

^{13}C-NMR OF COMPOUND **27c (ESTER OF MINOR)** (126 MHz, DMSO-d_6)



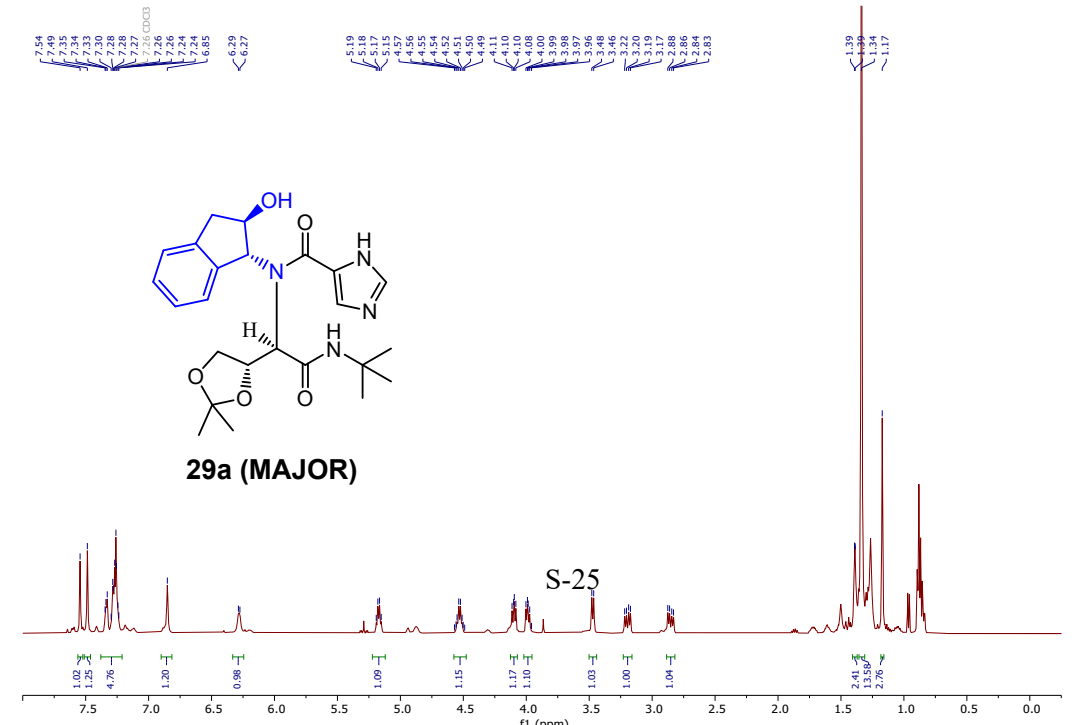
28a (MAJOR)

^{1}H-NMR OF COMPOUND **28a (MAJOR)** (500 MHz, DMSO-d_6)



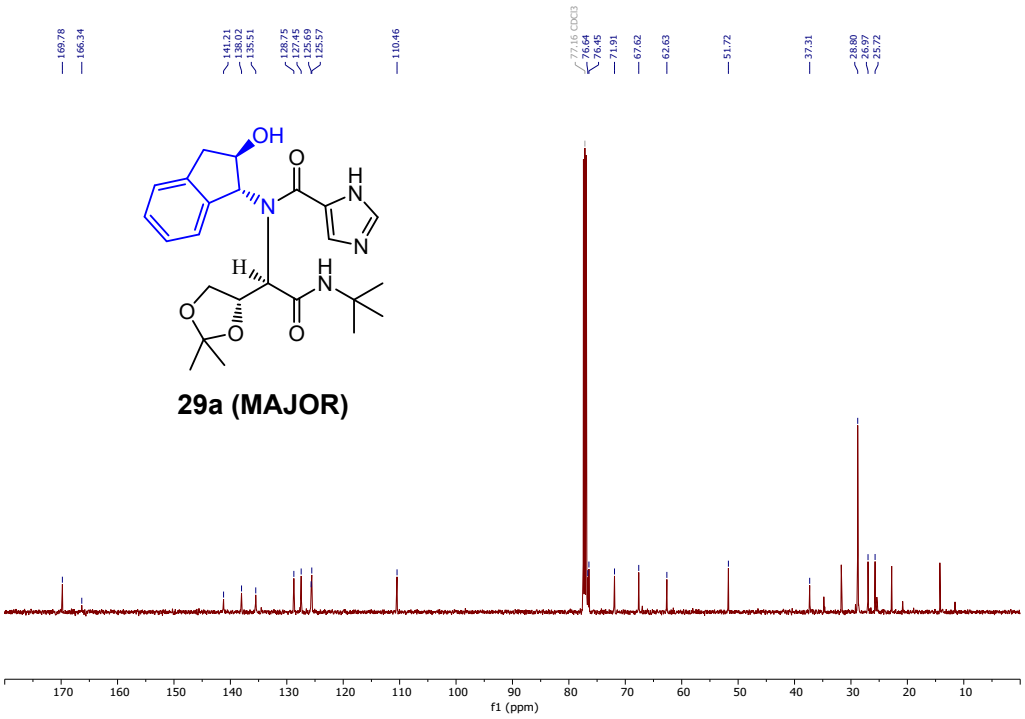
28a (MAJOR)

^{13}C-NMR OF COMPOUND **28 (MAJOR)** (126 MHz, DMSO-d_6)

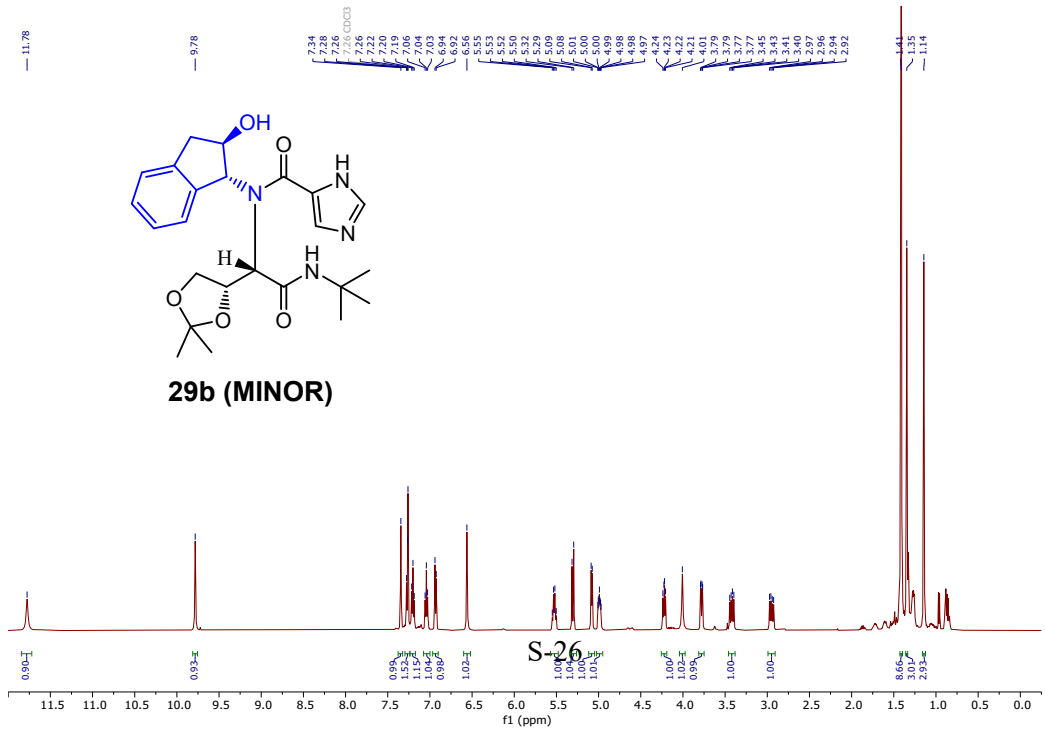


29a (MAJOR)

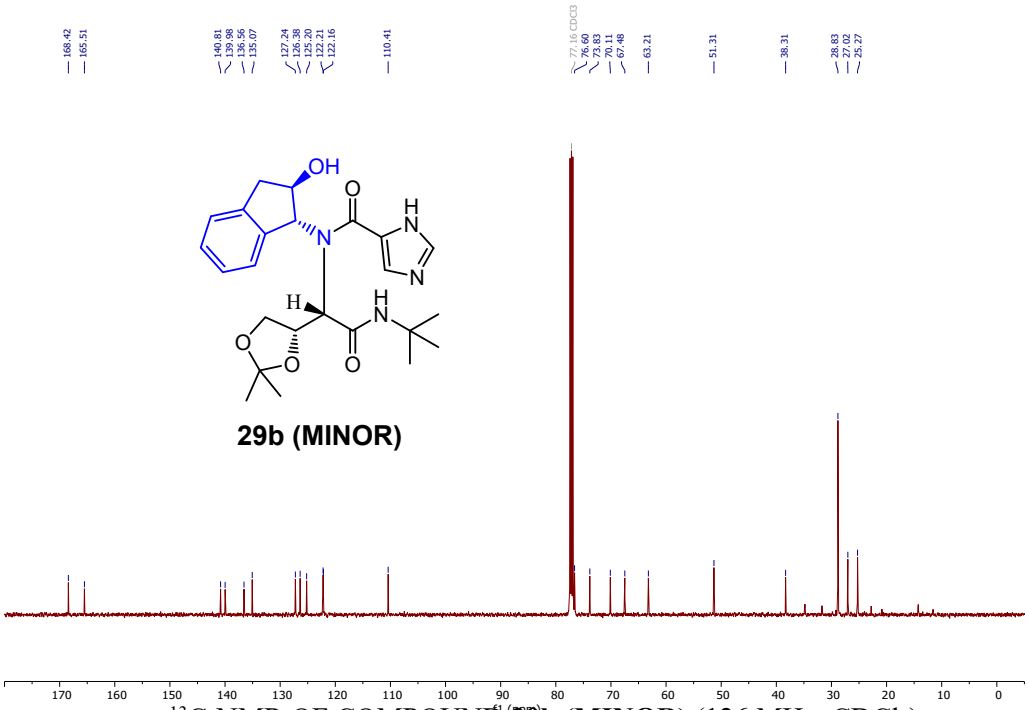
^{1}H-NMR OF COMPOUND **29a (MAJOR)** (500 MHz, $CDCl_3$)



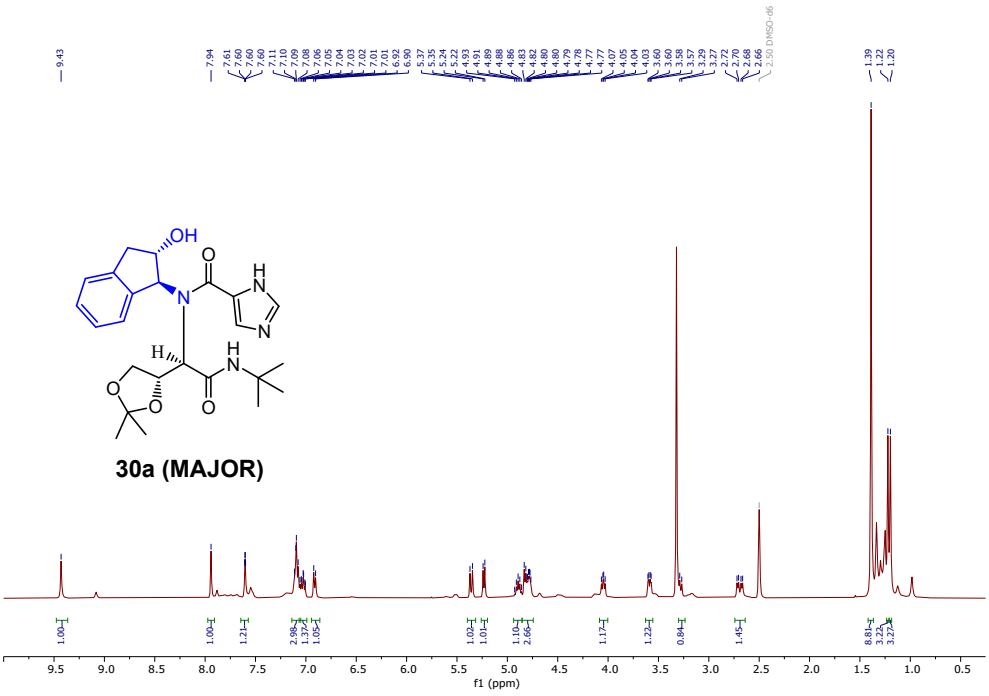
^{13}C-NMR OF COMPOUND **29a (MAJOR)** (126 MHz, $CDCl_3$)



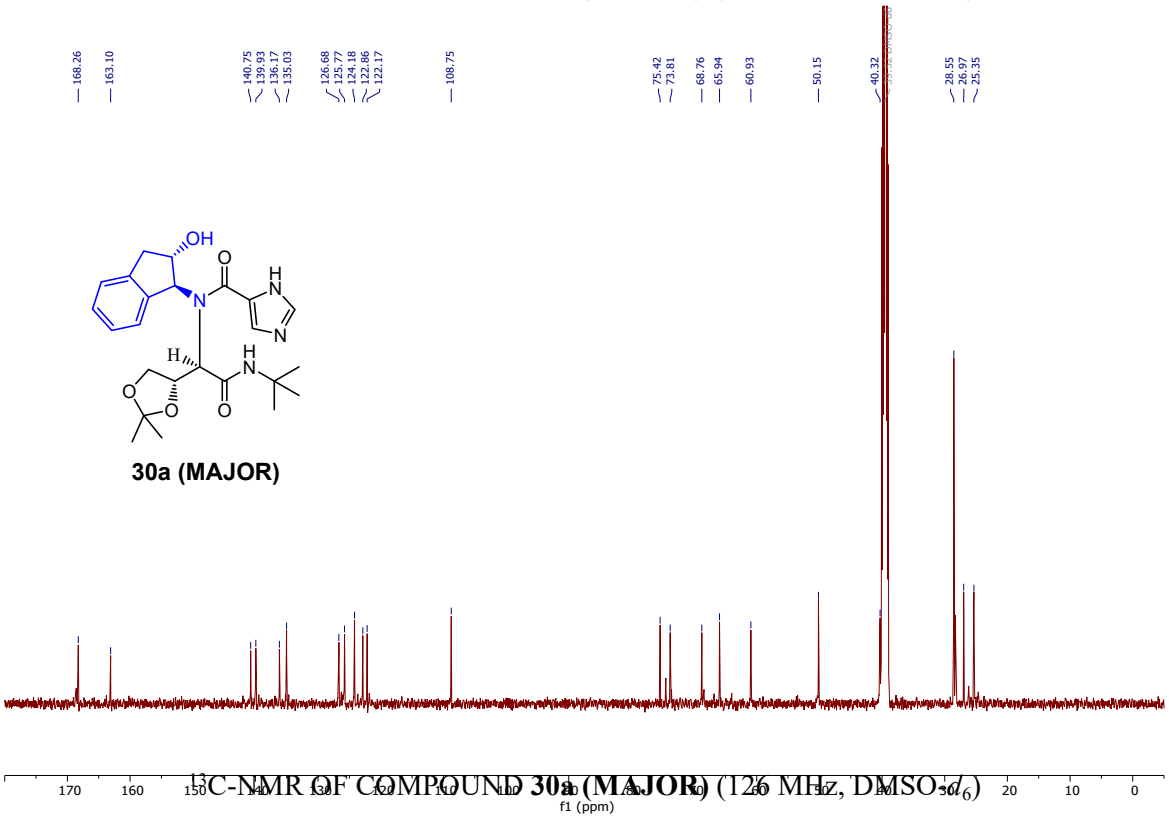
^{1}H-NMR OF COMPOUND **29b (MINOR)** (500 MHz, $CDCl_3$)



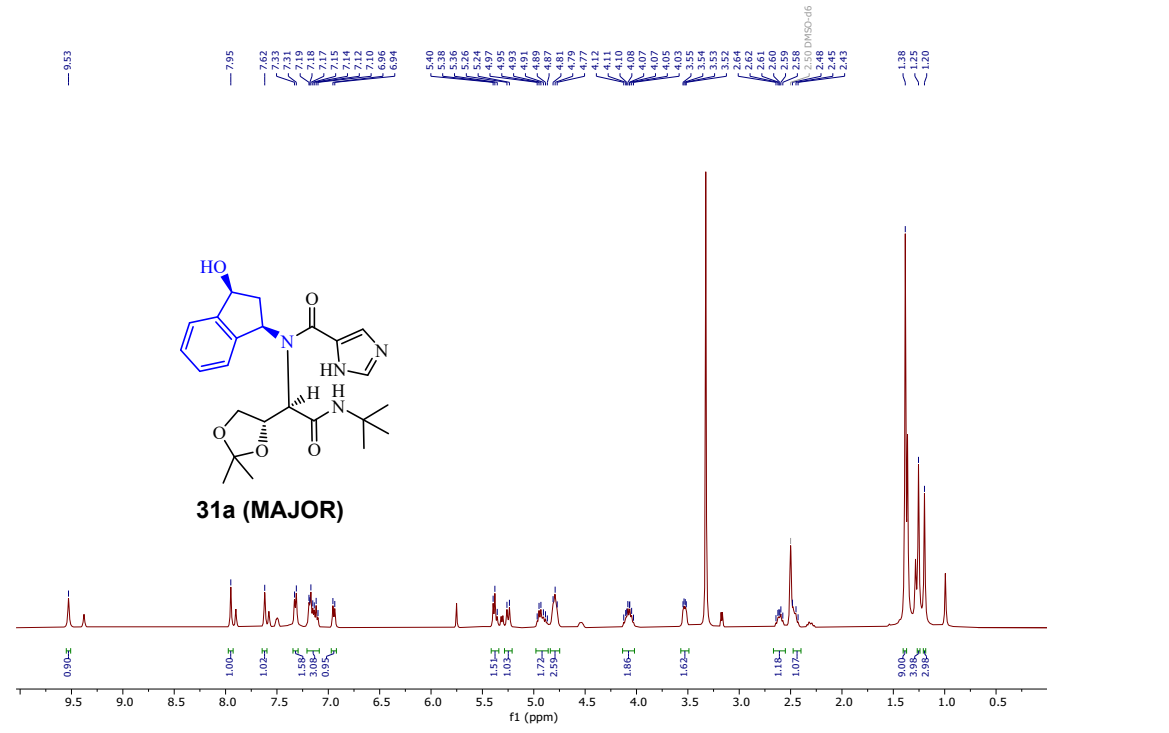
^{13}C-NMR OF COMPOUND **29b (MINOR)** (126 MHz, $CDCl_3$)



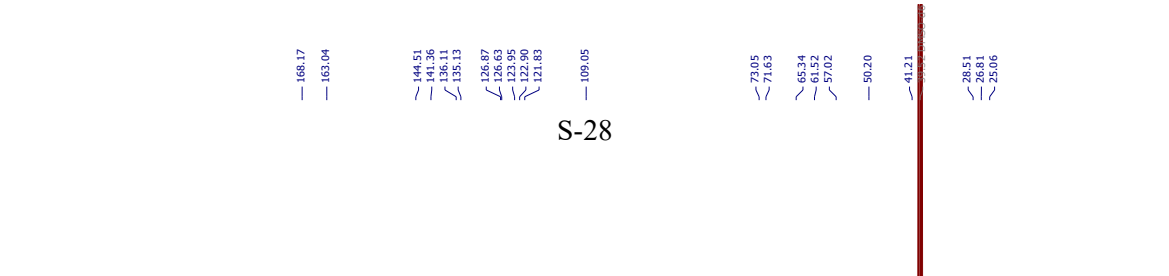
^{1}H-NMR OF COMPOUND **30a (MAJOR)** (400 MHz, DMSO-d_6)

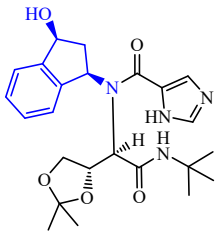


^{13}C-NMR OF COMPOUND **30a (MAJOR)** (126 MHz, DMSO-d_6)



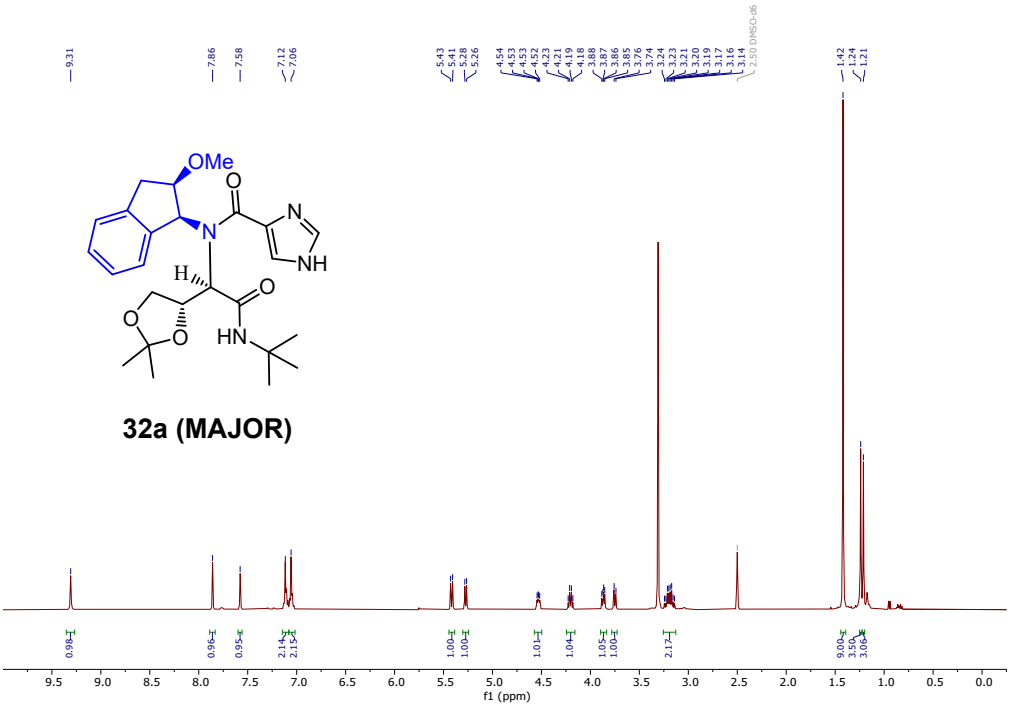
^{1}H-NMR OF COMPOUND **31a (MAJOR)** (500 MHz, DMSO-d_6)





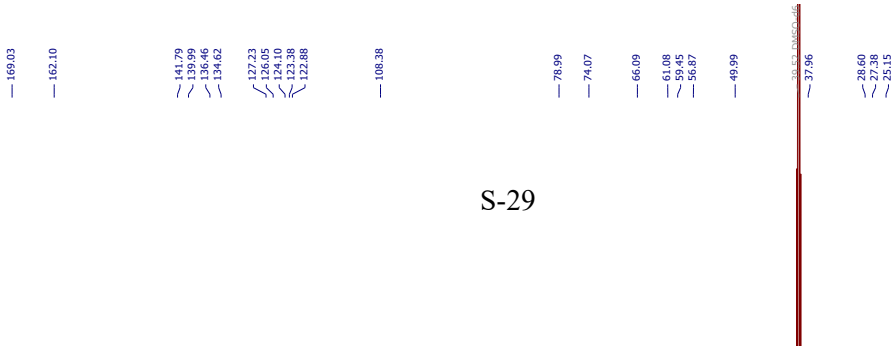
31a (MAJOR)

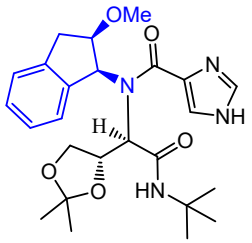
^{13}C-NMR OF COMPOUND **31a (MAJOR)** (126 MHz, DMSO-d_6)



32a (MAJOR)

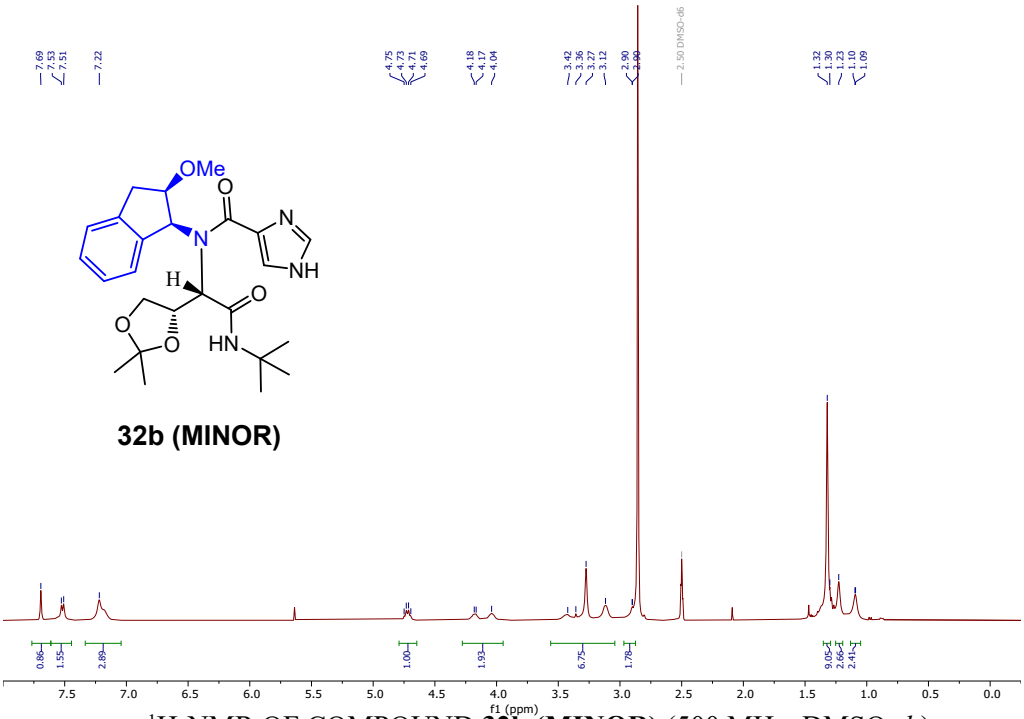
^{1}H-NMR OF COMPOUND **32a (MAJOR)** (500 MHz, DMSO-d_6)





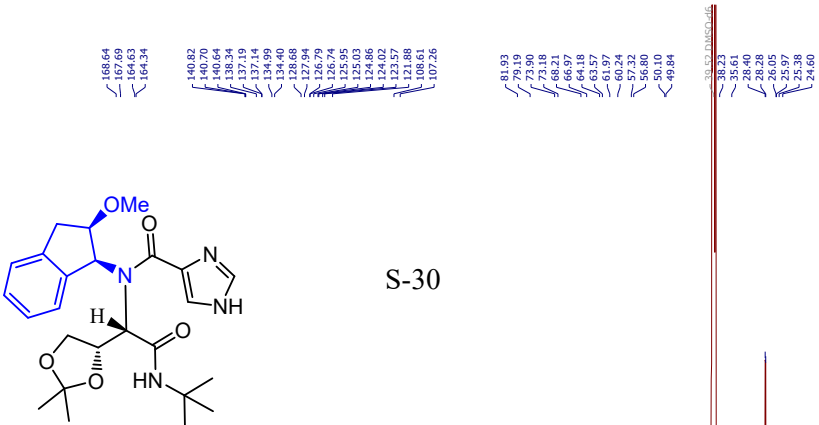
32a (MAJOR)

^{13}C-NMR OF COMPOUND **32a (MAJOR)** (126 MHz, DMSO-d_6)

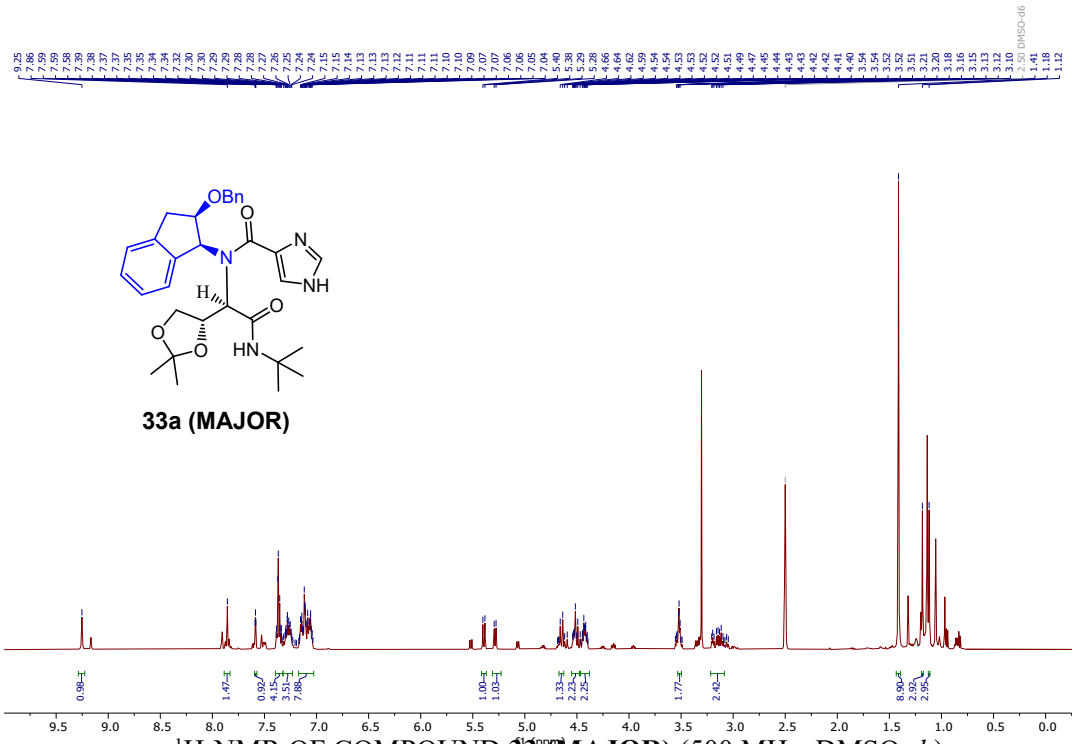


32b (MINOR)

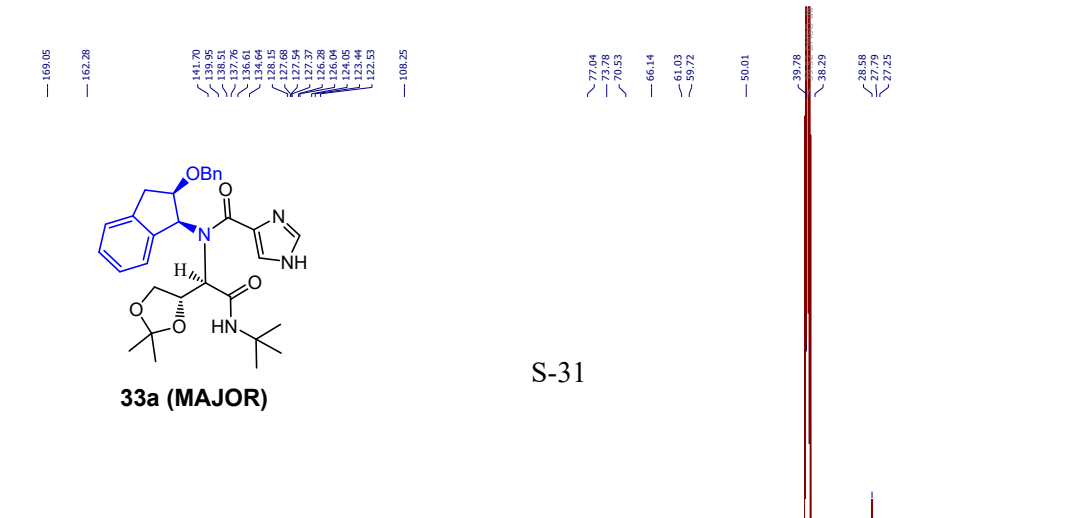
^{1}H-NMR OF COMPOUND **32b (MINOR)** (500 MHz, DMSO-d_6)



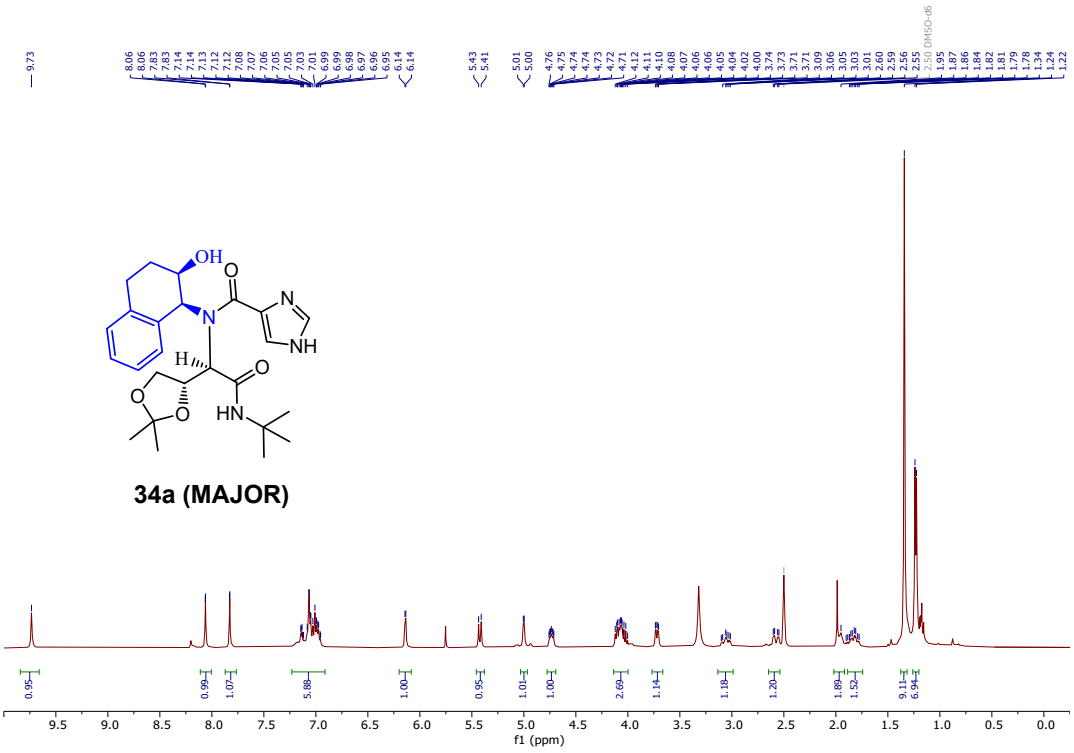
^{13}C-NMR OF COMPOUND **32b (MINOR)** (126 MHz, DMSO-d_6)



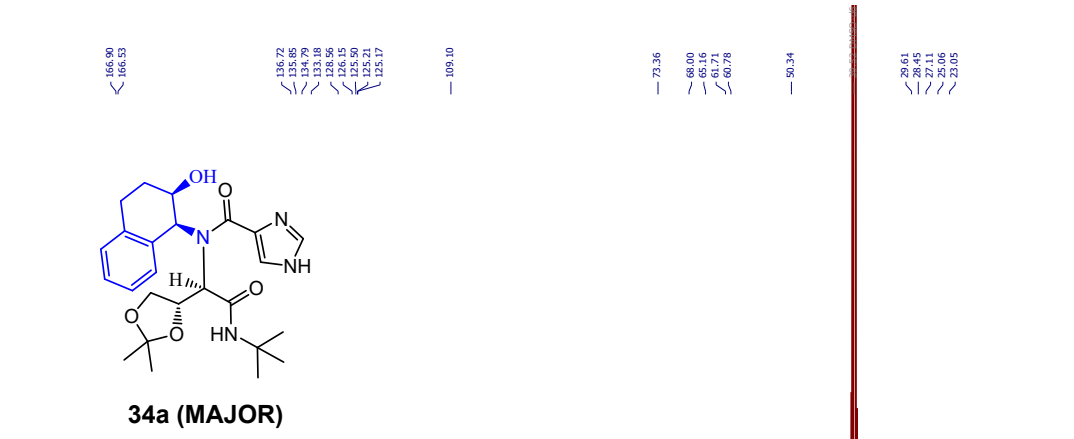
^{1}H-NMR OF COMPOUND **33a (MAJOR)** (500 MHz, DMSO-d_6)



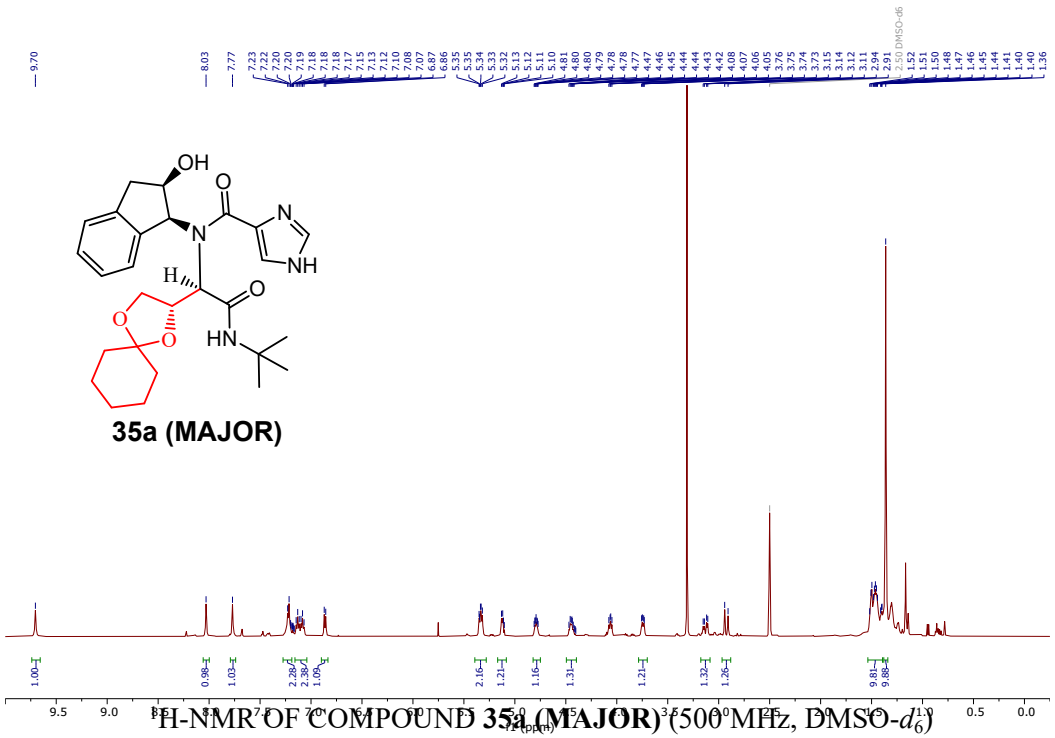
^{13}C-NMR OF COMPOUND **33a (MAJOR)** (126 MHz, DMSO-d_6)



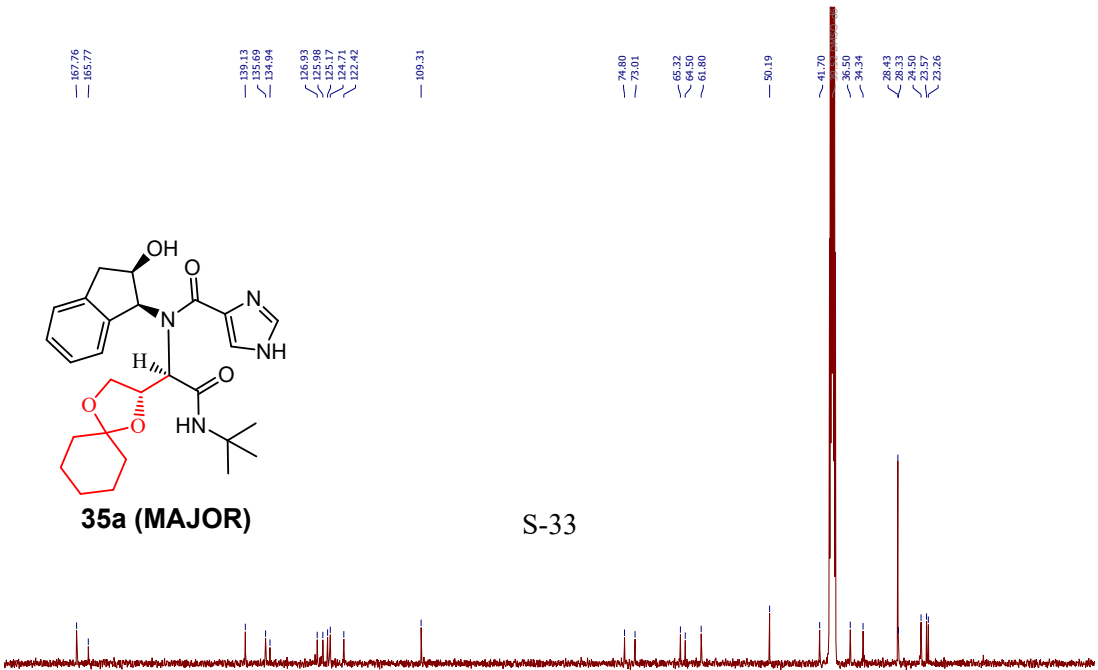
^{1}H-NMR OF COMPOUND **34a (MAJOR)** (500 MHz, DMSO-d_6)



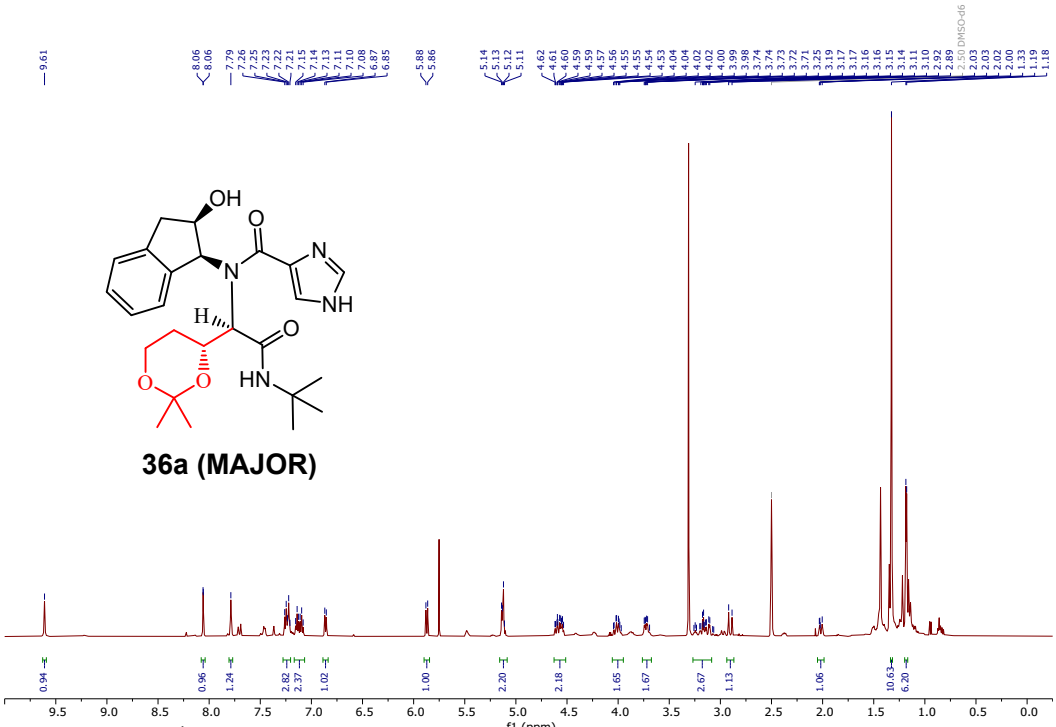
^{13}C-NMR OF COMPOUND **34a (MAJOR)** (126 MHz, DMSO-d_6)



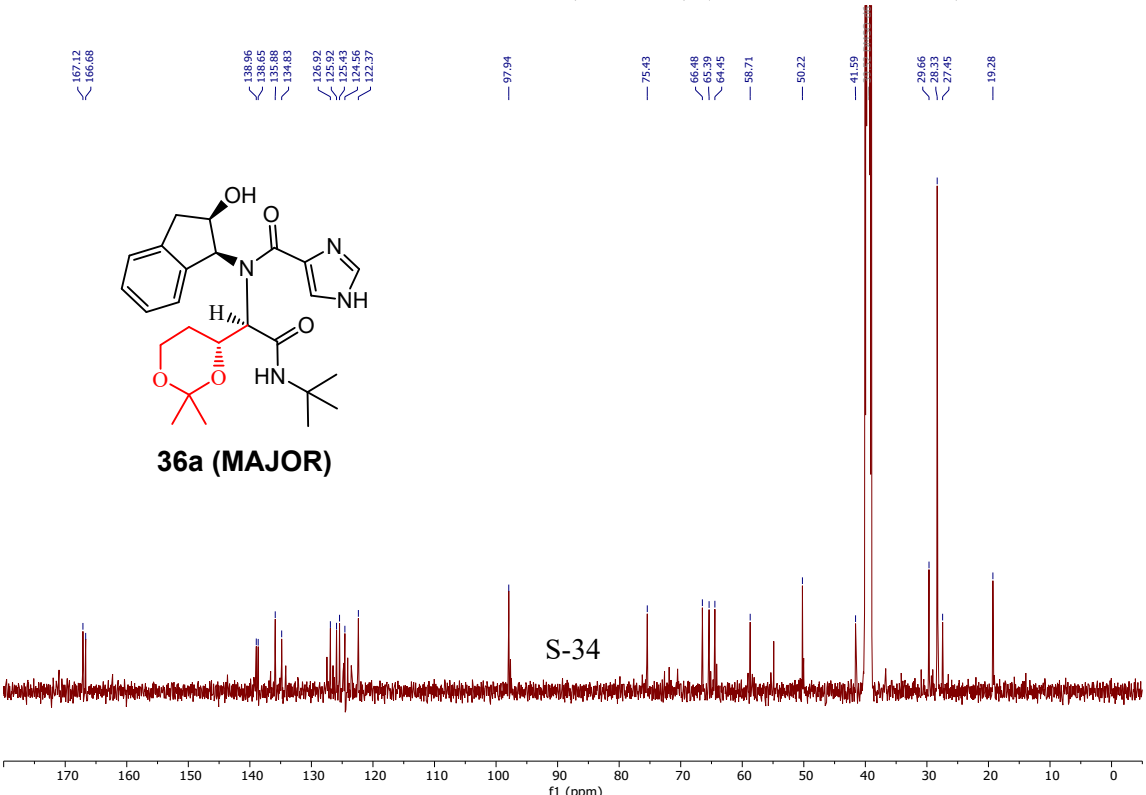
H-NMR OF COMPOUND **35a (MAJOR)** (500 MHz, DMSO-d_6)



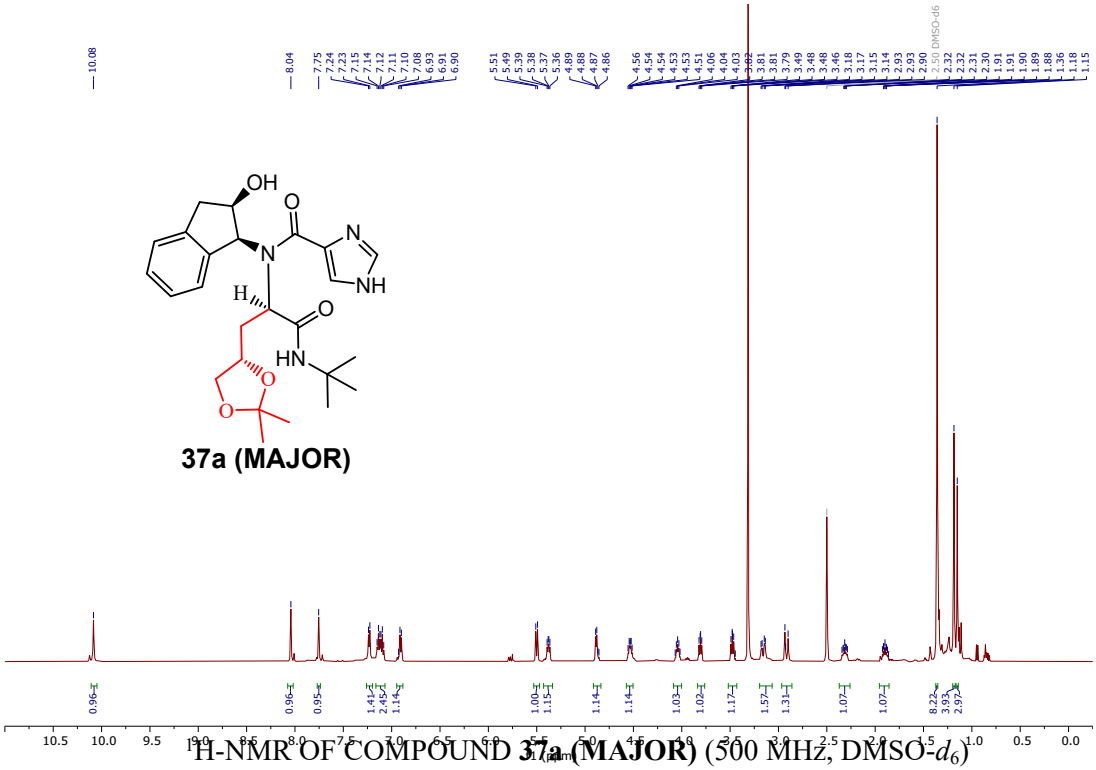
^{13}C-NMR OF COMPOUND **35a (MAJOR)** (126 MHz, DMSO-d_6)



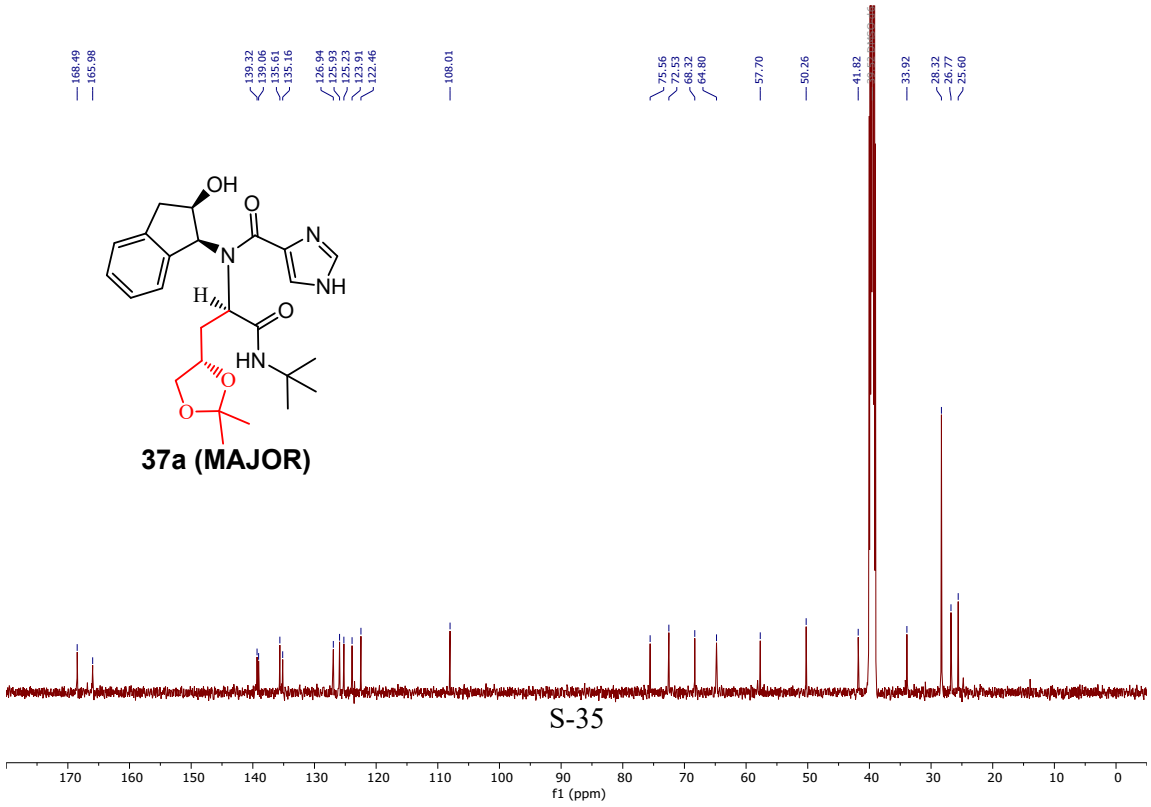
^{1}H-NMR OF COMPOUND **36a (MAJOR)** (500 MHz, DMSO-d_6)



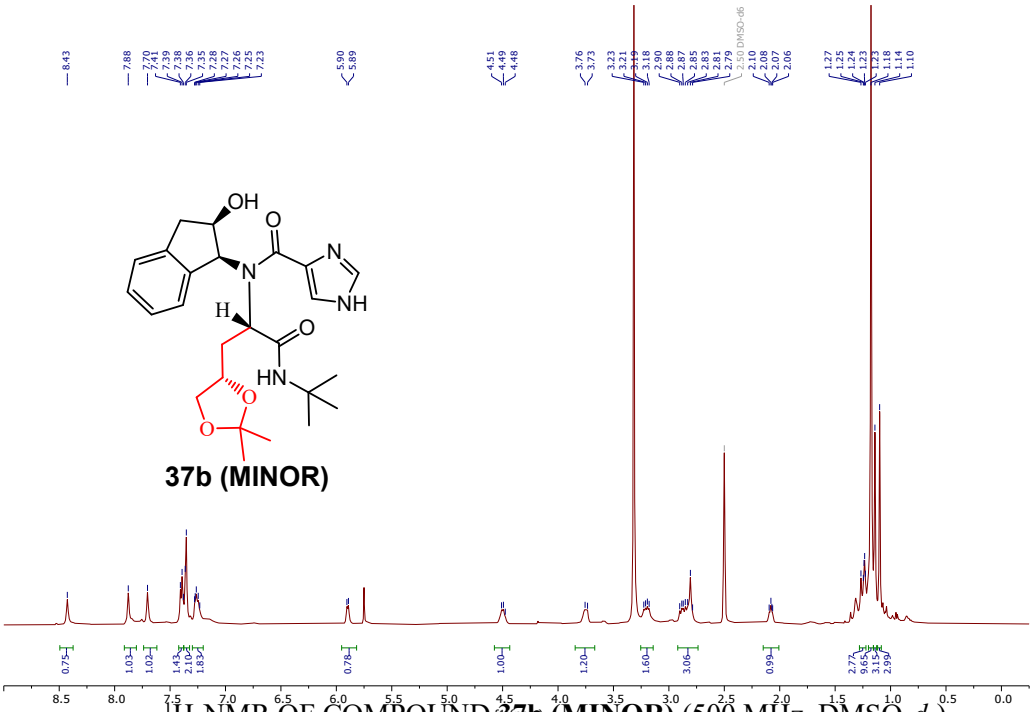
^{13}C-NMR OF COMPOUND **36a (MAJOR)** (126 MHz, DMSO-d_6)



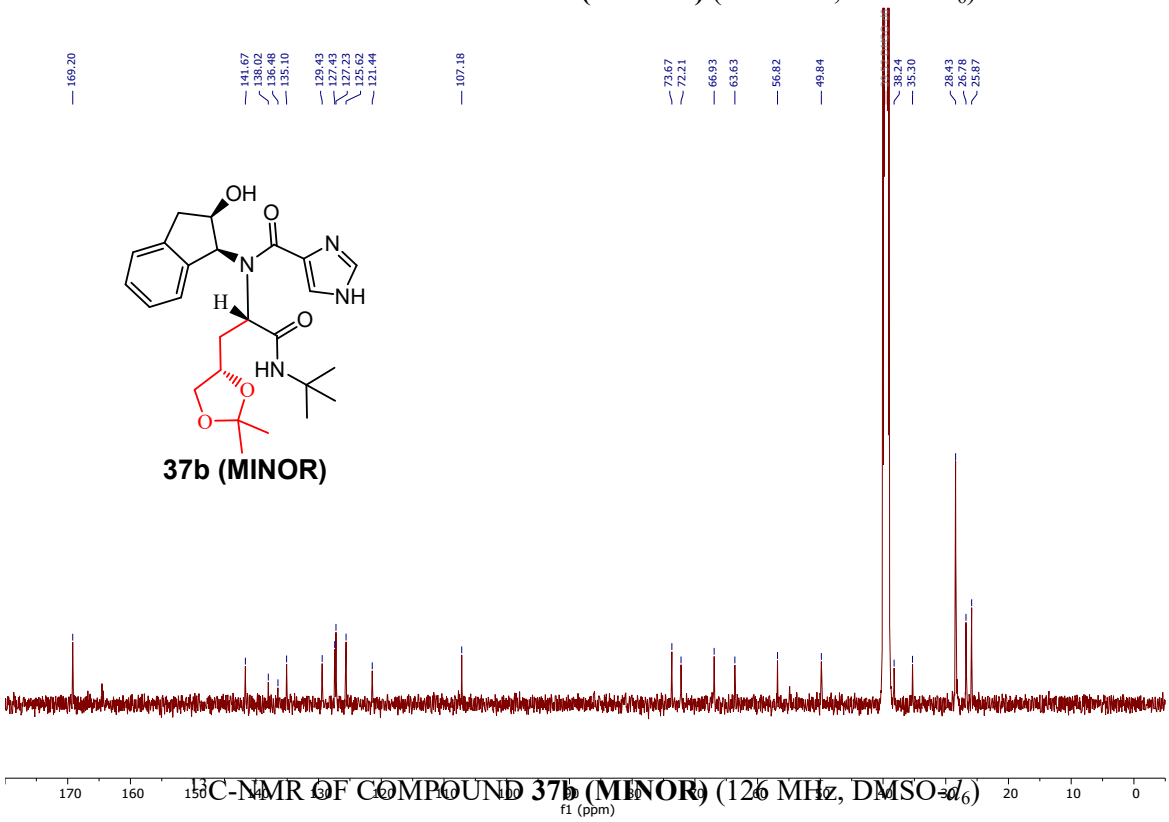
^{1}H-NMR OF COMPOUND **37a (MAJOR)** (500 MHz, DMSO-d_6)



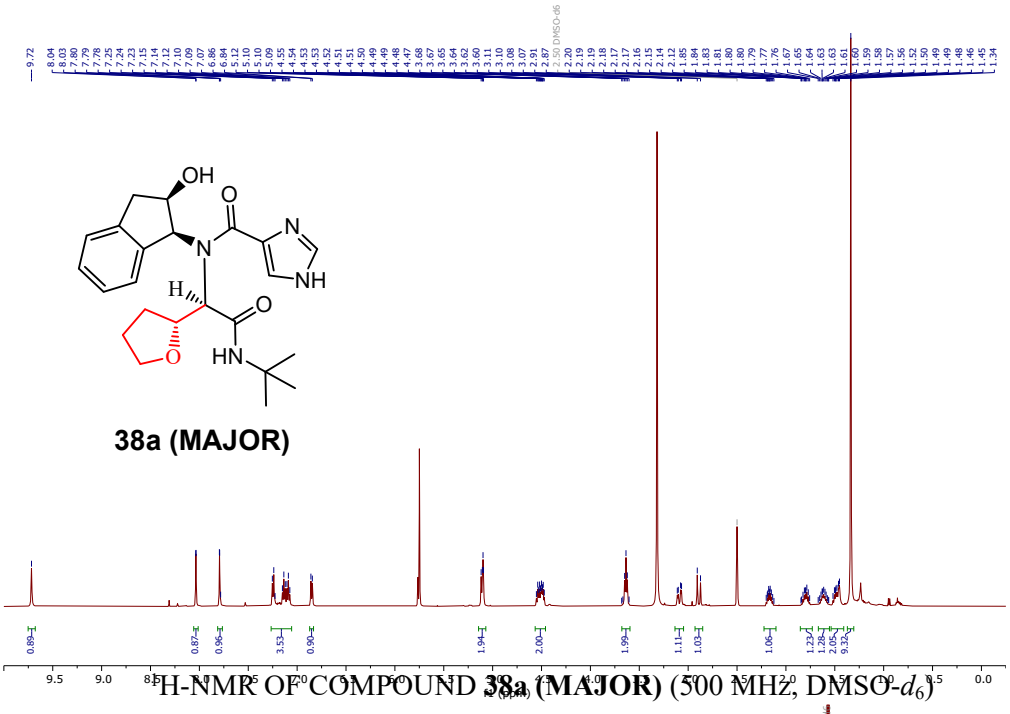
^{13}C-NMR OF COMPOUND **37a (MAJOR)** (126 MHz, DMSO-d_6)



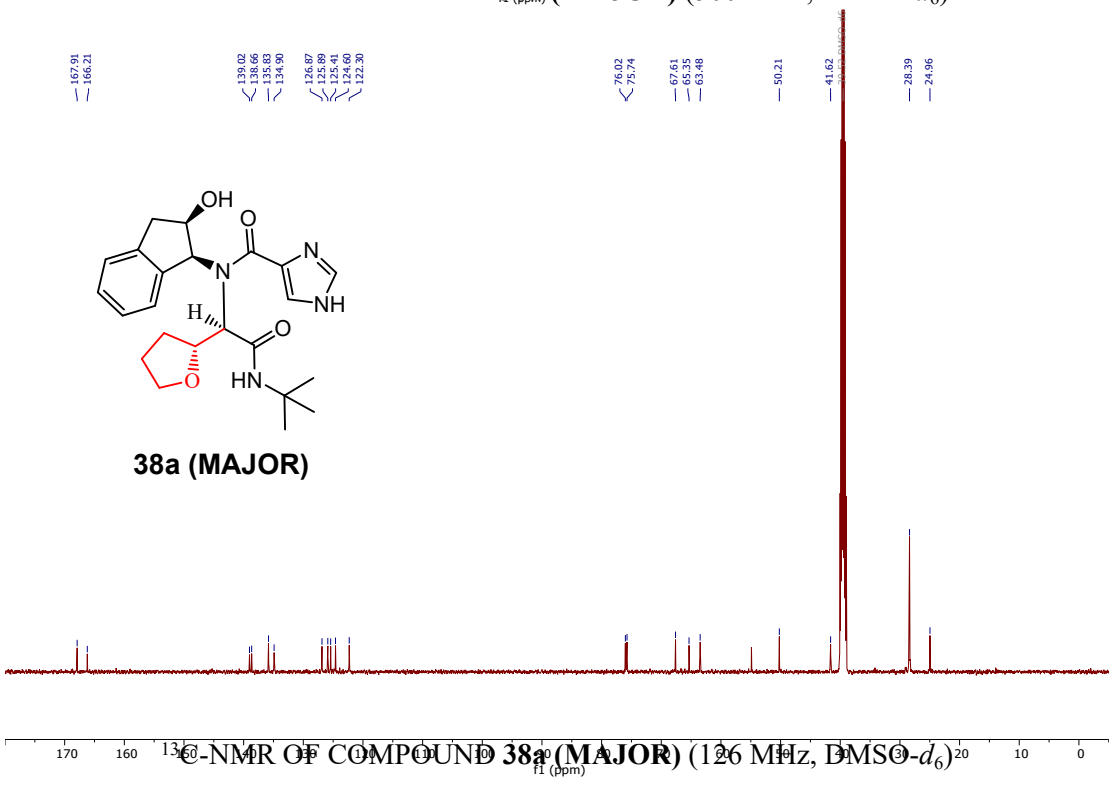
^{1}H-NMR OF COMPOUND **37b (MINOR)** (500 MHz, DMSO-d_6)



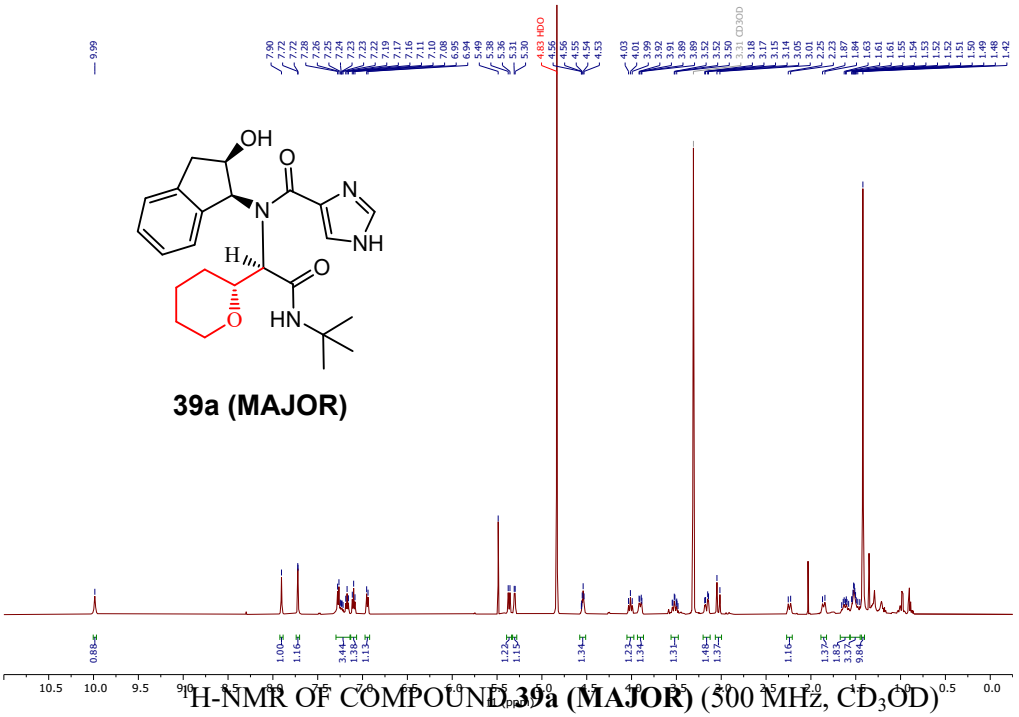
^{13}C-NMR OF COMPOUND **37b (MINOR)** (126 MHz, DMSO-d_6)



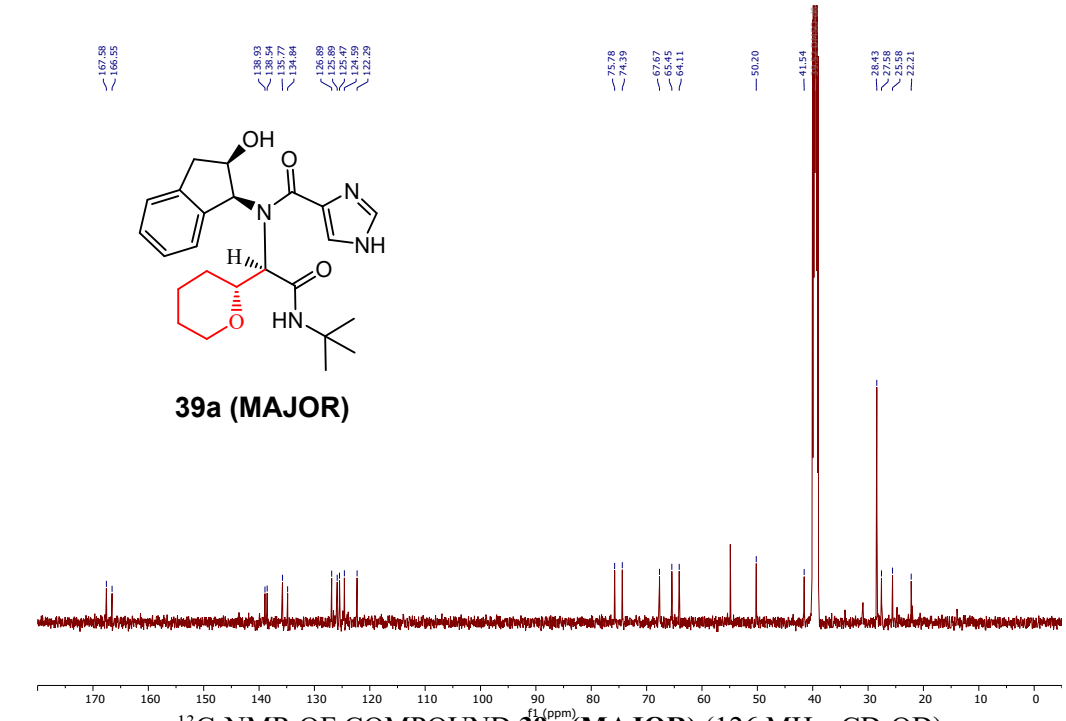
^{1}H-NMR OF COMPOUND **38a (MAJOR)** (500 MHz, DMSO-d_6)



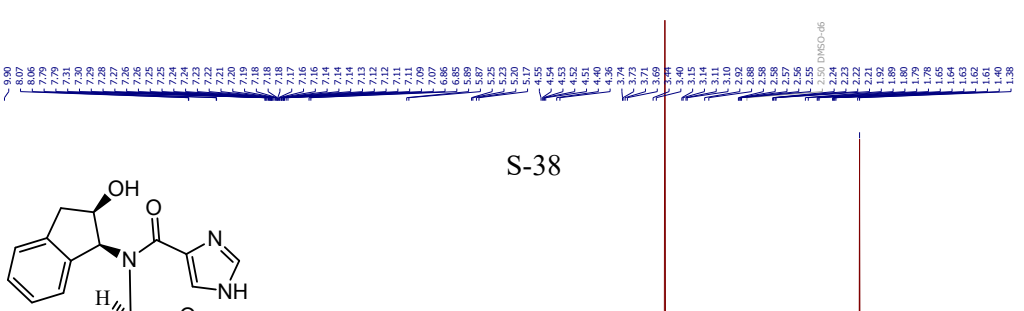
^{13}C-NMR OF COMPOUND **38a (MAJOR)** (126 MHz, DMSO-d_6)



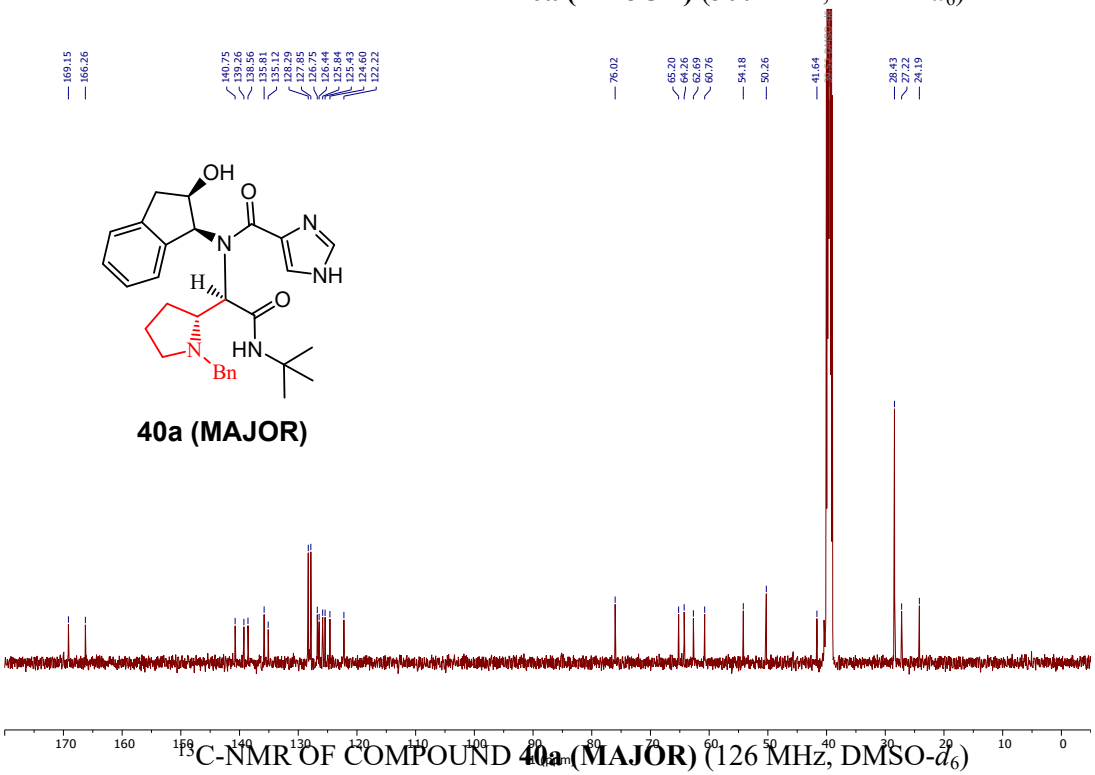
^{1}H-NMR OF COMPOUND **39a (MAJOR)** (500 MHz, CD_3OD)



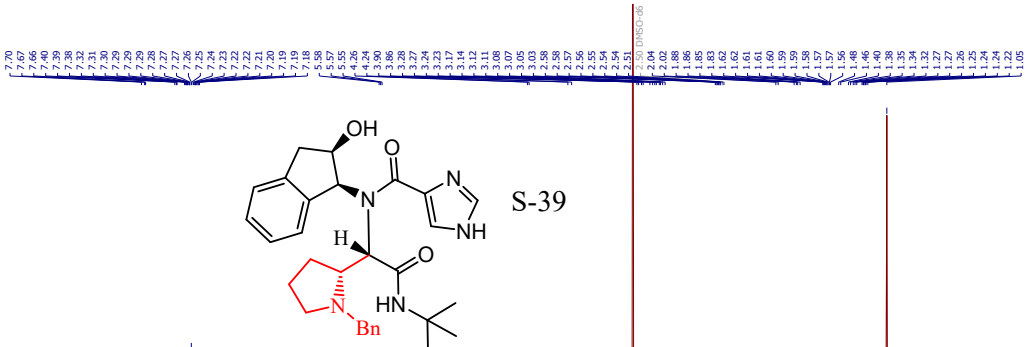
^{13}C-NMR OF COMPOUND **39a (MAJOR)** (126 MHz, CD_3OD)



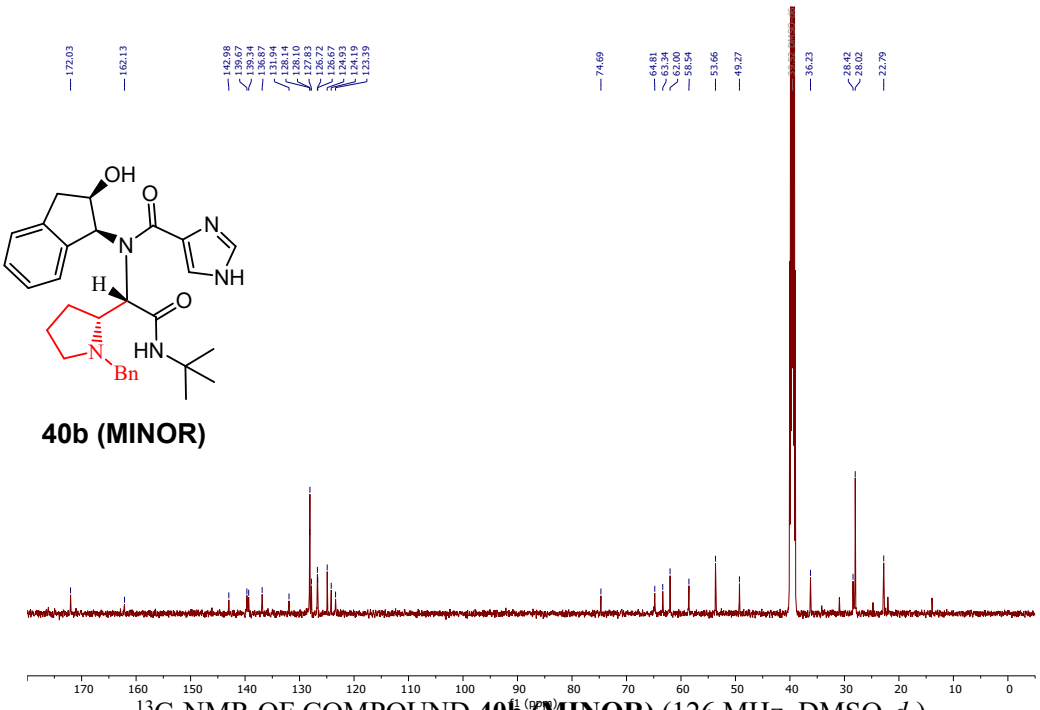
^{1}H-NMR OF COMPOUND **40a (MAJOR)** (500 MHz, DMSO-d_6)



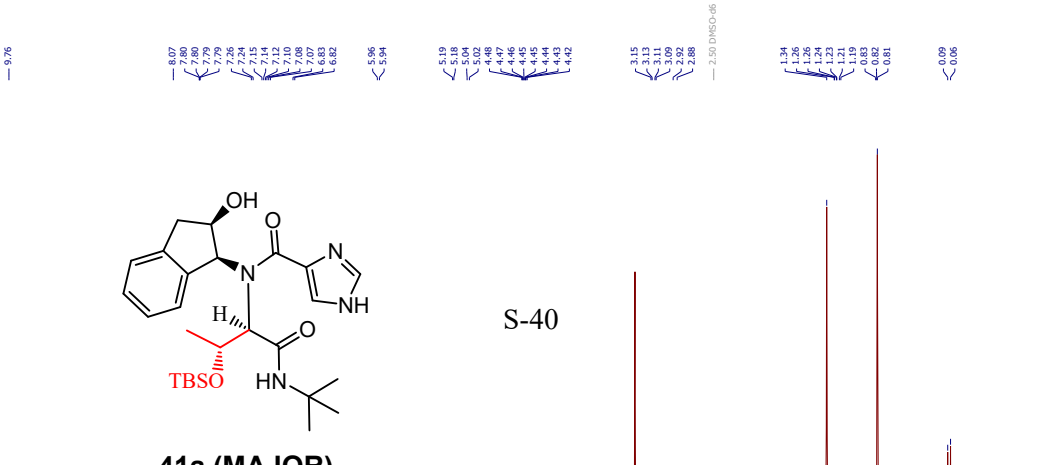
^{13}C-NMR OF COMPOUND **40a (MAJOR)** (126 MHz, DMSO-d_6)



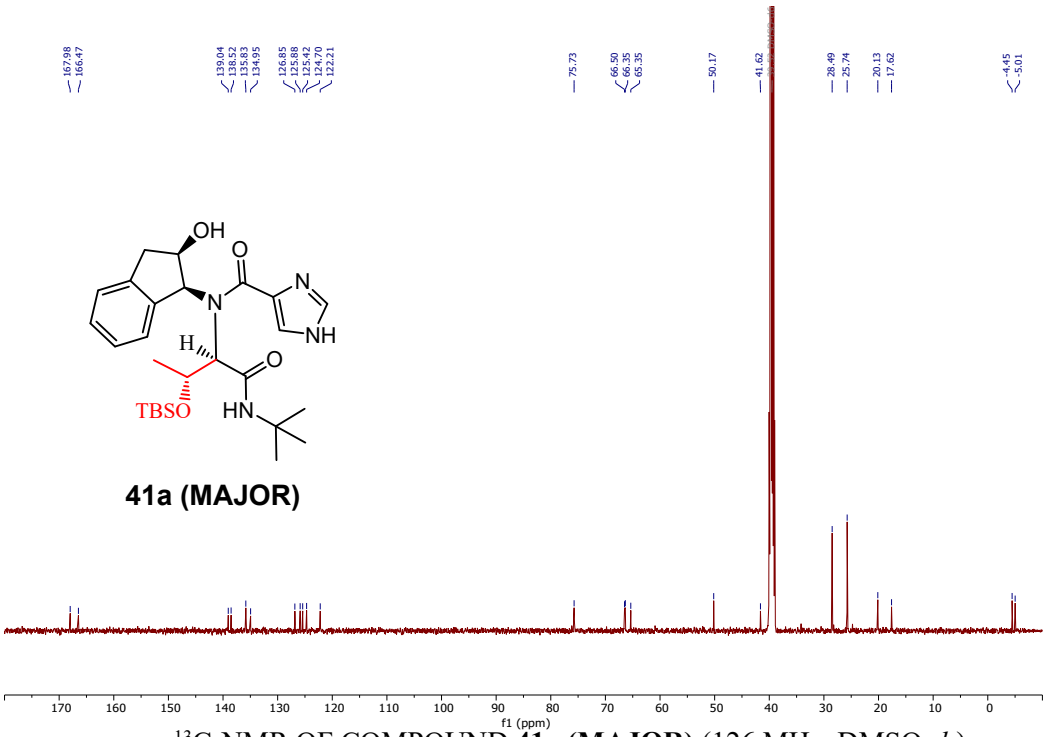
^{1}H-NMR OF COMPOUND **40b (MINOR)** (500 MHz, DMSO-d_6)



^{13}C-NMR OF COMPOUND **40b (MINOR)** (126 MHz, DMSO-d_6)



^{1}H-NMR OF COMPOUND **41a (MAJOR)** (500 MHz, DMSO-d_6)



^{13}C-NMR OF COMPOUND **41a (MAJOR)** (126 MHz, DMSO-d_6)

HPLC data

Unless otherwise stated, HPLC procedures are as follows: HPLC data is obtained via an Agilent 1260 Infinity II HPLC system utilizing a TOSOH Bioscience TSKgel CM-2SW column. Unless otherwise stated, solvent system used was a gradient solvent phase from 10% MeCN/H_2O to 90% MeCN/H_2O over 90 minutes at 0.500 ml/min. Sample was loaded at 1 mg/ml via a 5 µL injection, with the chromatogram being collected at λ = 254 nm. Fractions were collected based on absorbance at the λ = 254 nm range, and d.r.'s were calculated based on absolute areas of each peak that was identified to be a diastereomer based on the 254 nm range. Major and minor isomer peaks are labeled, along with ester peaks wherever detected. Peaks were verified via fraction collection of peaks and analysis by low resolution LC-MS to detect [M+H] and [M+Na] signals. For **22** and **23**, another method was used, where an isocratic phase of 20% MeCN/ H_2O

(w/ 0.1% TFA v/v) was used at 1.0 mL/min with a YMC-Pack ODS-A C18 column. For **40**, an isocratic phase of 10 % MeCN/ H_2O (w/ 0.1% TFA v/v) at 0.500 mL/min was used.

```
Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-15 14-27-07\001-P1-A1-AB-02-022.D
Sample Name: AB-02-022

    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   1
    Sample Operator : SYSTEM
    Acq. Instrument : GHOSH LC 1                     Location :   P1-A-01
    Injection Date  : 12/15/2023 2:28:07 PM               Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\Chem32\1\Data\UgiDias2samples 2023-12-15 14-27-07\UgiDiastereomers.M
    Last changed    : 12/15/2023 2:27:04 PM by SYSTEM
    Analysis Method : C:\Chem32\1\Data\UgiDias2samples 2023-12-15 14-27-07\UgiDiastereomers.M (
                      Sequence Method)
    Last changed    : 8/29/2024 12:09:28 PM by SYSTEM
    Method Info     : Amlan's Method
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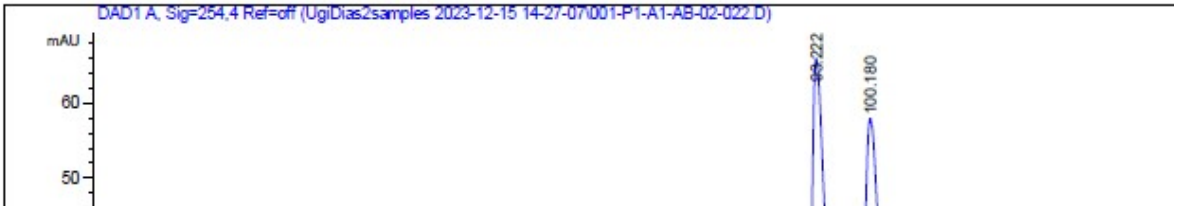

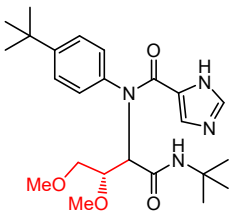

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Minor Isomer

Major Isomer

```
Data File C:\Chem32\1\Data\2021\AB-01-072 (1) 2023-11-10 10-20-12.D
Sample Name: AB-01-072

    ======================================================================
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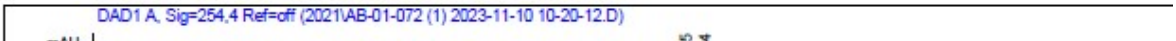
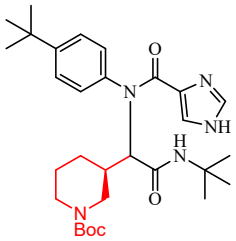
    Sample Operator : SYSTEM
    Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
    Injection Date  : 11/10/2023 10:21:07 AM             Inj :   1
                                                 Inj Volume : 5.000 µl
    Acq. Method     : C:\Chem32\1\Methods\def_LC.M
    Last changed    : 11/10/2023 10:19:57 AM by SYSTEM
                      (modified after loading)
    Analysis Method : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
    Last changed    : 8/30/2024 6:54:02 PM by SYSTEM
                      (modified after loading)
    Method Info     : Amlan's Method

    Sample Info     : TOSOH Bioscience, LLC 07167 TSKgel CM-2SW 4.6 mm ID 25 cm, 5 um, Colum #
                      N0006-81M
                      10% MeCN/H2O- 90% MeCN/H2O over 120 min
                      0.500 mL/min
                      215 nm
                      254 nm
                      5 uL inj
                      1 mg/mL
```



Major Isomer

Minor Isomer



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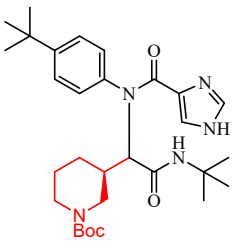
Data File C:\Chem32\1\Data\2021\AB-01-072 (1) 2023-11-10 10-20-12.D
Sample Name: AB-01-072

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.070	BB	0.0768	22.02206	4.22848	0.2767
2	6.665	BB	0.2495	105.13821	5.85512	1.3212
3	22.921	BB	0.3556	49.06979	2.07708	0.6166
4	96.255	BB	1.1875	3934.89307	50.25488	49.4474
5	99.304	BB	1.2073	3846.61353	47.37142	48.3380
Totals :				7957.73664	109.78696	

*** End of Report ***



16

Data File C:\Chem32\1\Data\2021\AB-01-163 (1) 2023-11-07 14-40-24.D
Sample Name: AB-01-163

```
    ======================================================================
    Acq. Operator   : SYSTEM
    Sample Operator : SYSTEM
    Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
    Injection Date  : 11/7/2023 2:41:18 PM             Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\Chem32\1\Methods\def_LC.M
    Last changed    : 11/7/2023 2:39:59 PM by SYSTEM
                      (modified after loading)
    Analysis Method : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
    Last changed    : 8/30/2024 6:54:02 PM by SYSTEM
                      (modified after loading)
    Method Info     : Amlan's Method

    Sample Info     : TOSOH Bioscience, LLC 07167 TSKgel CM-2SW 4.6 mm ID 25 cm, 5 um, Colum #
                      N0006-81M
                      10% MeCN/H2O- 90% MeCN/H2O over 90 min
                      0.500 mL/min
                      215 nm
                      254 nm
                      5 uL inj
                      1 mg/mL
```

Minor Isomer

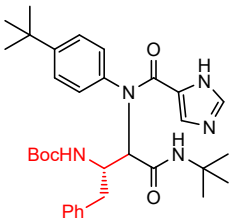
Major Isomer

Data File C:\Chem32\1\Data\2021\AB-01-163 (1) 2023-11-07 14-40-24.D
Sample Name: AB-01-163

Signal 1: DAD1 A, Sig=254,4 Ref=off

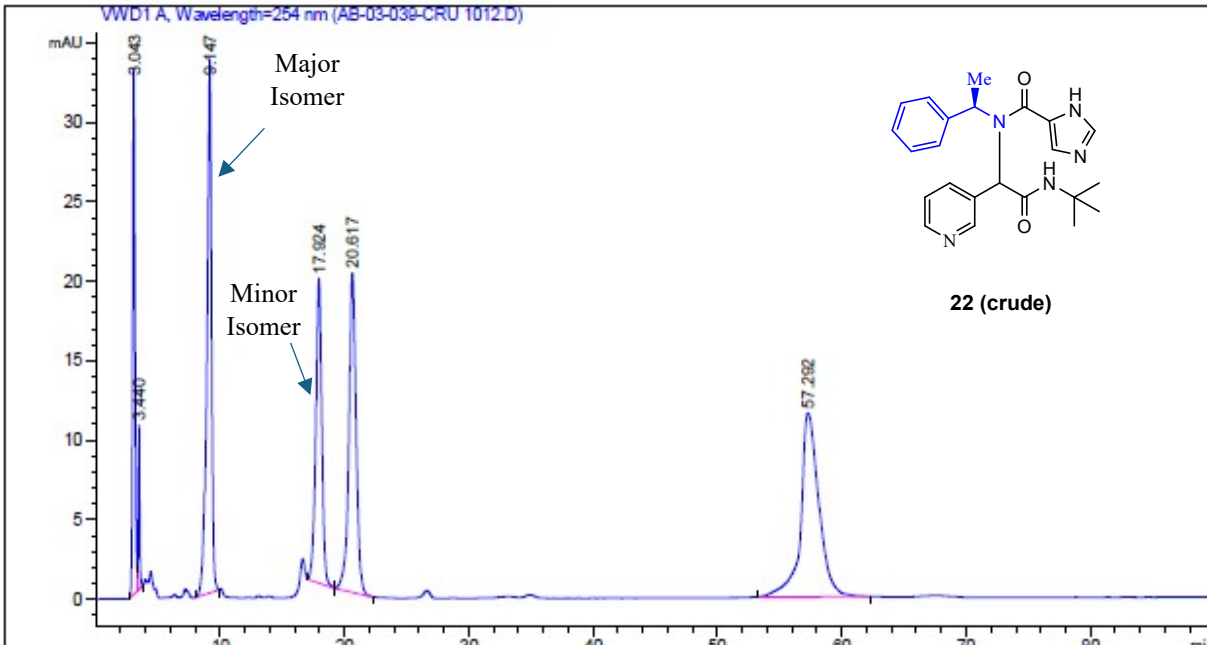
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.033	BB	0.0907	36.48205	5.85450	0.4666
2	6.675	BB	0.2057	73.90361	5.39817	0.9452
3	87.286	BB	1.0704	3798.01270	55.36224	48.5732
4	89.844	BB	1.1423	3910.75635	52.54787	50.0151
Totals :				7819.15470	119.16278	

*** End of Report ***



17

```
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : LC2                          Location :   1
Injection Date  : 8/23/2025 1:11:14 PM
                                               Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\AMLANMETHOD.M
Last changed    : 8/23/2025 1:10:10 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\AMLANMETHOD.M
Last changed    : 8/29/2025 7:46:47 PM by SYSTEM
                  (modified after loading)
Sample Info     : YMC Pak ODS-A
                  20% CH3CN:H2O (w/ 01.% TFA v/v)
                  1.0 mL/min
                  215  nm, 254 nm
                  5uL inj.
                  1 mg/mL
```

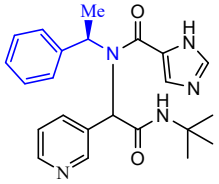


22 (crude)

Signal 1: VWD1 A, Wavelength=254 nm

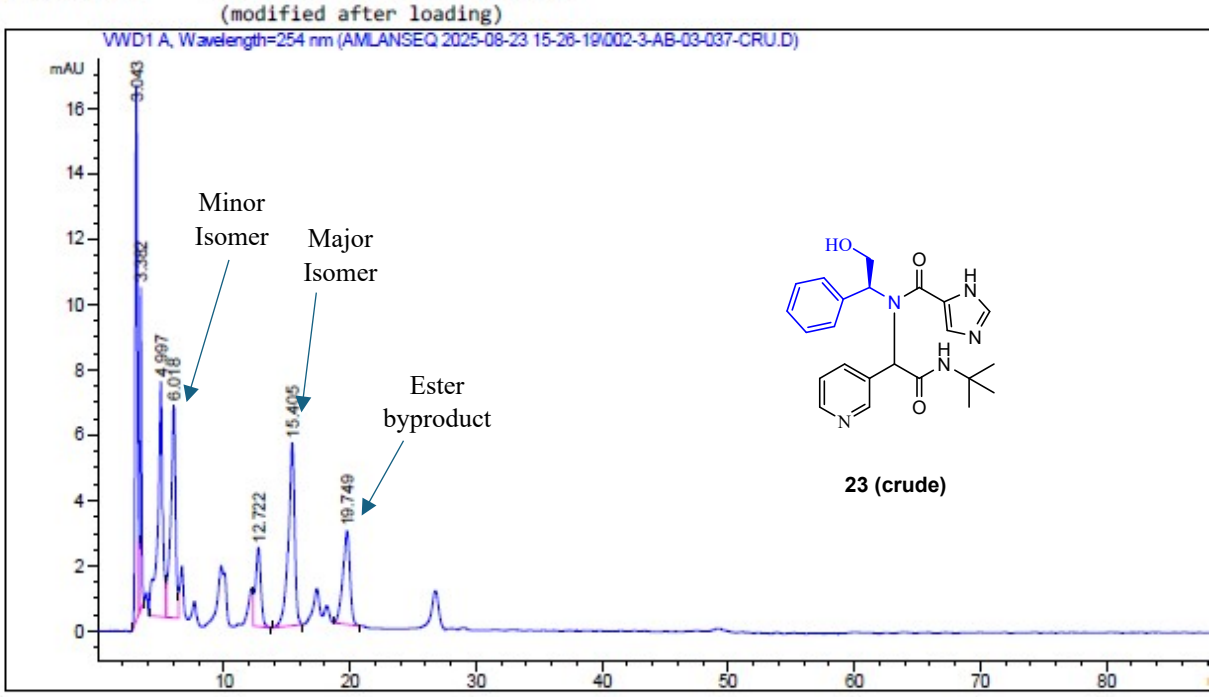
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.043	BV	0.2026	442.20242	32.94547	10.9723
2	3.440	VB	0.1047	71.94160	10.40597	1.7851
3	9.147	BB	0.3747	873.87115	33.46106	21.6831
4	17.924	BB	0.5035	641.15088	19.10703	15.9087
5	20.617	BB	0.6039	814.62933	20.13780	20.2132
6	57.292	BB	1.4959	1186.39063	11.55431	29.4376
Totals :				4030.18601	127.61164	

*** End of Report ***



22 (crude)

```
==================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   2
Acq. Instrument : LC2                               Location :   3
Injection Date  : 8/23/2025 4:58:06 PM                  Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Data\AMLANSEQ 2025-08-23 15-26-19\AMLANMETHOD.M
Last changed    : 8/23/2025 3:26:16 PM by SYSTEM
Analysis Method : C:\Chem32\1\Data\AMLANSEQ 2025-08-23 15-26-19\AMLANMETHOD.M (Sequence
                  Method)
Last changed    : 8/29/2025 7:47:47 PM by SYSTEM
                  (modified after loading)
```



23 (crude)

```
==================================================================
                        Area Percent Report
==================================================================

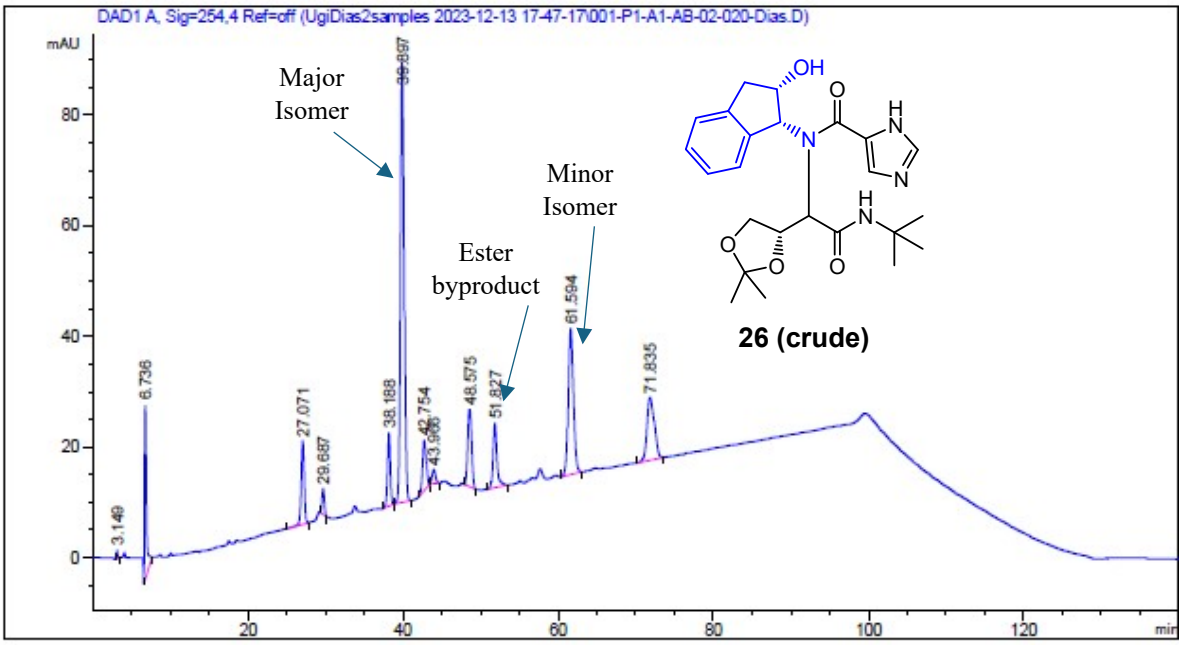
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
```

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-13 17-47-17\001-P1-A1-AB-02-020-Dias.D
Sample Name: AB-02-020-Dias

Acq. Operator	: SYSTEM	Seq. Line	: 1
Sample Operator	: SYSTEM		
Acq. Instrument	: GHOSH LC 1	Location	: P1-A-01
Injection Date	: 12/13/2023 5:48:16 PM	Inj	: 1
		Inj Volume	: 5.000 µl
Method	: C:\Chem32\1\Data\UgiDias2samples 2023-12-13 17-47-17\UgiDiastereomers.M (Sequence Method)		
Last changed	: 12/13/2023 5:47:14 PM by SYSTEM		
Method Info	: Amlan's Method		



Fraction Information

No Fractions found.

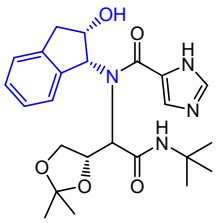
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=off

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-13 17-47-17\001-P1-A1-AB-02-020-Dias.D
Sample Name: AB-02-020-Dias

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.149	BB	0.1012	11.16004	1.60383	0.1521
2	6.736	BB	0.2827	564.83575	31.57578	7.6974
3	27.071	BB	0.4386	424.76291	15.07882	5.7885
4	29.687	BB	0.3501	104.63515	4.69307	1.4259
5	38.188	BB	0.3973	342.73904	13.27339	4.6707
6	39.897	BB	0.5124	2641.24658	79.74733	35.9940
7	42.754	BB	0.4970	293.15073	9.02326	3.9950
8	43.966	BB	0.4617	81.93283	2.55768	1.1166
9	48.575	BB	0.5207	475.80176	13.99265	6.4841
10	51.827	BB	0.5251	416.21133	11.64304	5.6720
11	61.594	BB	0.7049	1229.24561	26.31974	16.7518
12	71.835	BB	0.9326	752.28949	11.38943	10.2520
Totals :				7338.01122	220.89803	



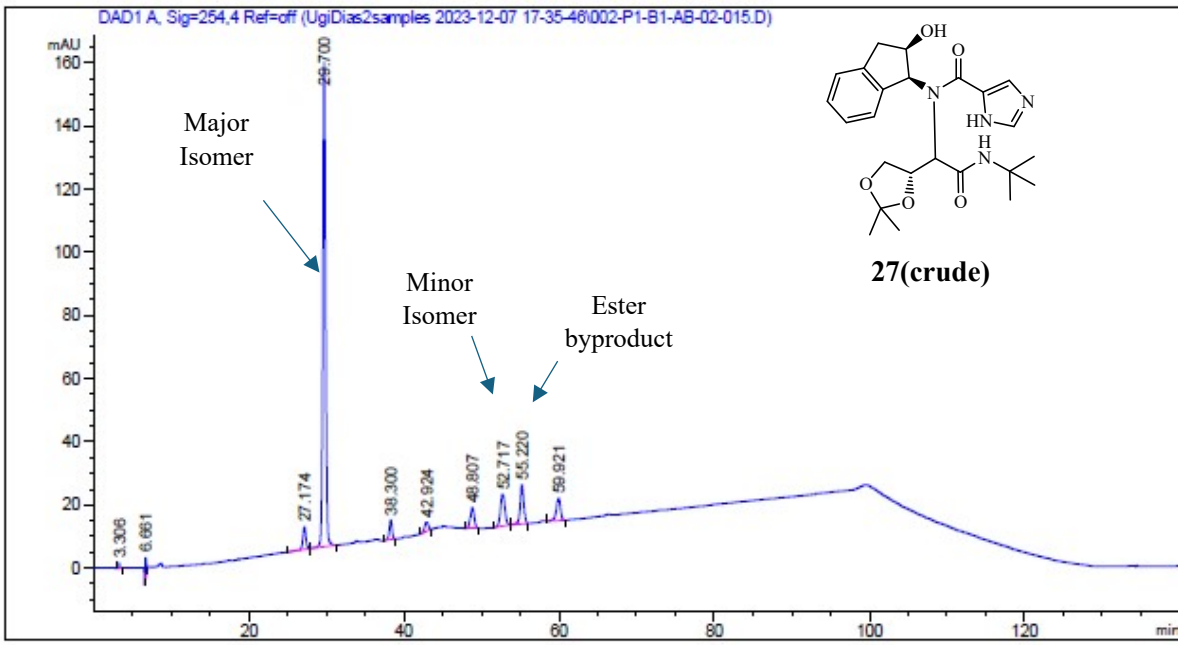
26 (crude)

==========

*** End of Report ***

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-07 17-35-46\002-P1-B1-AB-02-015.D
Sample Name: AB-02-015

```
======================================================================
Acq. Operator   : SYSTEM                       Seq. Line :   2
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                    Location :   P1-B-01
Injection Date  : 12/7/2023 7:57:56 PM             Inj :   1
                                               Inj Volume : 5.000 µl
Method          : C:\Chem32\1\Data\UgiDias2samples 2023-12-07 17-35-46\UgiDiastereomers.M (
                  Sequence Method)
Last changed    : 12/7/2023 5:35:43 PM by SYSTEM
Method Info     : Amlan's Method
```



27(crude)

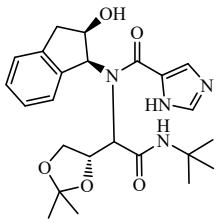
```
======================================================================
                        Fraction Information
======================================================================
No Fractions found.
======================================================================
======================================================================
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=off
```

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-07 17-35-46\002-P1-B1-AB-02-015.D
Sample Name: AB-02-015

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.306	BB	0.0790	9.95104	1.78633	0.1721
2	6.661	BB	0.1831	92.72414	7.56169	1.6040
3	27.174	BB	0.4227	199.99103	7.18683	3.4596
4	29.700	BB	0.3948	3957.14966	153.45776	68.4538
5	38.300	BB	0.3856	158.03642	6.27894	2.7338
6	42.924	BB	0.4572	92.07433	2.90966	1.5928
7	48.807	BB	0.5168	225.26241	6.65717	3.8968
8	52.717	BB	0.5704	385.73941	10.08187	6.6728
9	55.220	BB	0.4816	401.46445	12.53515	6.9448
10	59.921	BB	0.5345	258.36960	7.13433	4.4695
Totals :				5780.76248	215.58973	



27(crude)

Data File C:\Chem32\1\Data\2021\AB-02-054-CRU (1) 2024-02-15 19-34-46.D
Sample Name: AB-02-054-CRU

Acq. Operator : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1 Location : P1-A-01
Injection Date : 2/15/2024 7:35:41 PM Inj : 1
Inj Volume : 5.000 µl

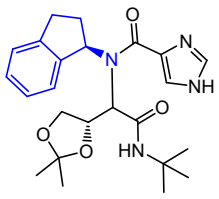
Major
Isomer

Minor
Isomer

Data File C:\Chem32\1\Data\2021\AB-02-054-CRU (1) 2024-02-15 19-34-46.D
Sample Name: AB-02-054-CRU

Signal 1: DAD1 A, Sig=254,4 Ref=off

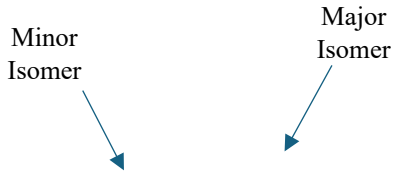
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.089	BB	0.1507	42.61708	4.05292	0.5919
2	6.655	BB	0.1865	86.90424	7.42986	1.2070
3	13.917	BB	0.2906	28.73410	1.45373	0.3991



28 (crude)

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30\002-P1-B1-AB-02-025.D
Sample Name: AB-02-025

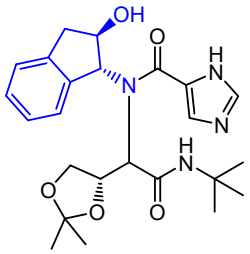
```
=====================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   2
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                       Location :   P1-B-01
Injection Date  : 12/18/2023 8:57:39 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30
                  \UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 12/18/2023 6:35:26 PM by SYSTEM
Analysis Method : C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30
                  \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
Last changed    : 8/29/2024 12:15:29 PM by SYSTEM
Method Info     : Amlan's Method
```


Minor
Isomer
Major
Isomer

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30\002-P1-B1-AB-02-025.D
Sample Name: AB-02-025

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	47.049	BB	0.6088	2983.76587	74.56726	51.2787
Totals :				5818.72580	187.40836	

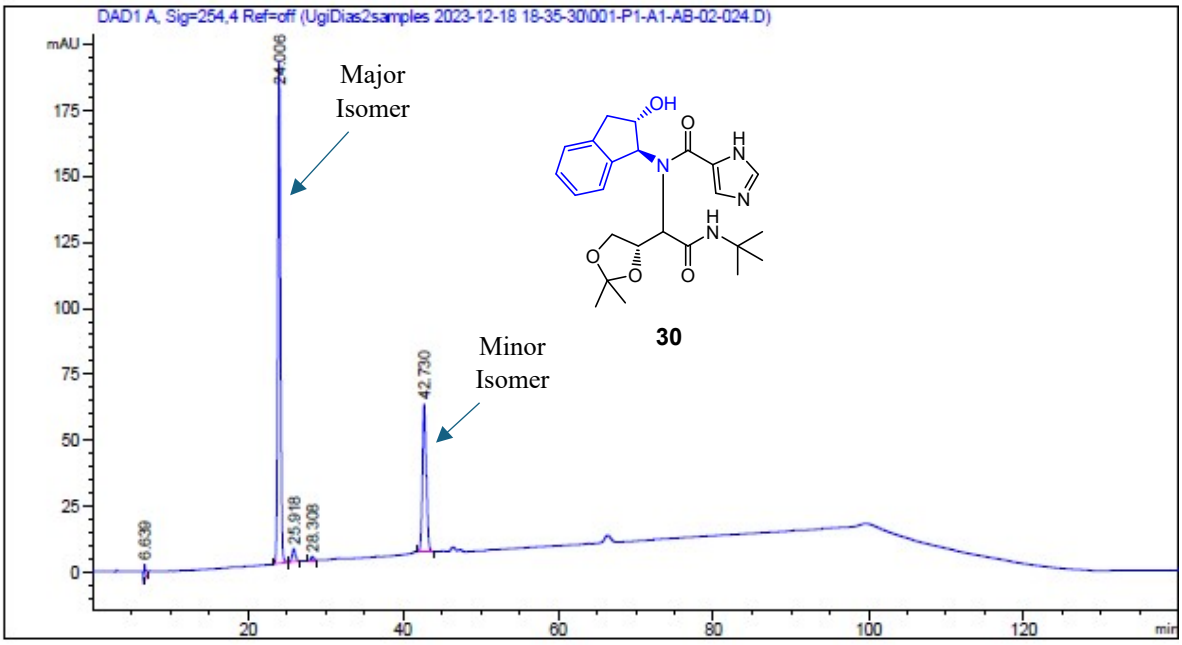
*** End of Report ***



29 (crude)

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30\001-P1-A1-AB-02-024.D
Sample Name: AB-02-024

```
Acq. Operator   : SYSTEM                          Seq. Line :   1
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                       Location :   P1-A-01
Injection Date  : 12/18/2023 6:36:28 PM               Inj :   1
                                                  Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30
                  \UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 12/18/2023 6:35:26 PM by SYSTEM
Analysis Method : C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30
                  \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
Last changed    : 8/29/2024 12:15:29 PM by SYSTEM
Method Info     : Amlan's Method
```



30

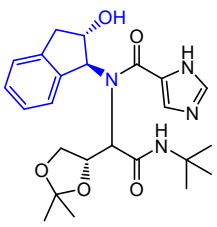
```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.639 BB    0.2048   90.43388    6.40177   1.3234
   2  24.006 BB    0.3764 4676.57227  190.48729  68.4340
```

Data File C:\Chem32\1\Data\UgiDias2samples 2023-12-18 18-35-30\001-P1-A1-AB-02-024.D
Sample Name: AB-02-024



30

```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   5  42.730 BB    0.5178 1890.15430   55.99797  27.6593

Totals :                  6833.69324  259.42868
```

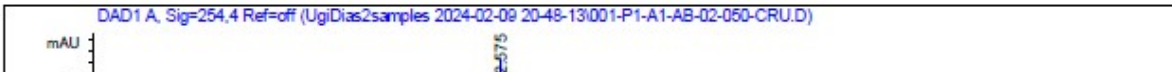
```
Data File C:\Chem32\1\Data\UgiDias2samples 2024-03-06 20-52-50\001-P1-A1-AB-02-064-CRU.D
Sample Name: AB-02-064-CRU
    ======================================================================
    Acq. Operator   : SYSTEM                          Seq. Line :   1
    Sample Operator : SYSTEM
    Acq. Instrument : GHOSH LC 1                       Location :   P1-A-01
    Injection Date  : 3/6/2024 8:53:49 PM                   Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\Chem32\1\Data\UgiDias2samples 2024-03-06 20-52-50
                      \UgiDiastereomersAmlanDONOTUSE.M
    Last changed    : 3/6/2024 8:52:46 PM by SYSTEM
    Analysis Method : C:\Chem32\1\Data\UgiDias2samples 2024-03-06 20-52-50
                      \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
    Last changed    : 8/29/2024 12:02:39 PM by SYSTEM
    Method Info     : Amlan's Method
```

Major
Isomer

Minor
Isomer

```
Data File C:\Chem32\1\Data\UgiDias2samples 2024-02-09 20-48-13\001-P1-A1-AB-02-050-CRU.D
Sample Name: AB-02-050-CRU

    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   1
    Sample Operator : SYSTEM
    Acq. Instrument : GHOSH LC 1                     Location :   P1-A-01
    Injection Date  : 2/9/2024 8:49:14 PM                Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\Chem32\1\Data\UgiDias2samples 2024-02-09 20-48-13
                      \UgiDiastereomersAmlanDONOTUSE.M
    Last changed    : 2/9/2024 8:48:09 PM by SYSTEM
    Analysis Method : C:\Chem32\1\Data\UgiDias2samples 2024-02-09 20-48-13
                      \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
    Last changed    : 8/29/2024 12:17:38 PM by SYSTEM
    Method Info     : Amlan's Method
```



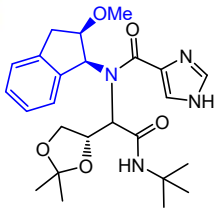
Major
Isomer

Minor
Isomer

Data File C:\Chem32\1\Data\UgiDias2samples 2024-02-09 20-48-13\001-P1-A1-AB-02-050-CRU.D
Sample Name: AB-02-050-CRU

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	40.981	BB	0.4257	70.17913	2.42446	1.1504
6	52.575	BB	0.6955	3490.79541	76.62241	57.2243
7	60.440	BB	0.6708	1823.74207	41.17014	29.8965
8	73.330	BB	0.8330	303.85922	5.11568	4.9811
Totals :				6100.19306	148.76310	

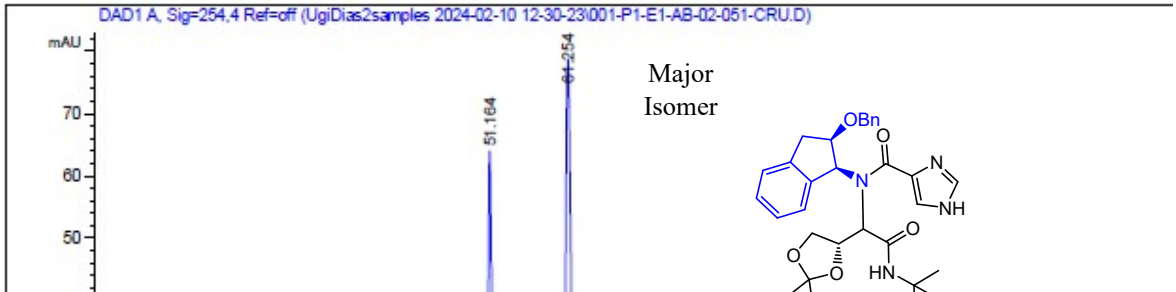
*** End of Report ***



32 (crude)

Data File C:\Chem32\1\Data\UgiDias2samples 2024-02-10 12-30-23\001-P1-E1-AB-02-051-CRU.D
Sample Name: AB-02-051-CRU

```
==================================================================
Acq. Operator   : SYSTEM                        Seq. Line :   1
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                     Location :   P1-E-01
Injection Date  : 2/10/2024 12:31:20 PM              Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Data\UgiDias2samples 2024-02-10 12-30-23
                  \UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 2/9/2024 8:48:09 PM by SYSTEM
Analysis Method : C:\Chem32\1\Data\UgiDias2samples 2024-02-10 12-30-23
                  \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
Last changed    : 8/29/2024 12:19:27 PM by SYSTEM
Method Info     : Amlan's Method
```



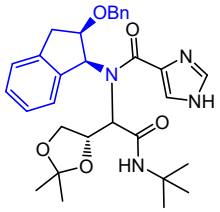
Major Isomer

Minor
Isomer

Data File C:\Chem32\1\Data\UgiDias2samples 2024-02-10 12-30-23\001-P1-E1-AB-02-051-CRU.D
Sample Name: AB-02-051-CRU

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	26.230	BB	0.4090	90.02829	3.31288	1.6020
6	51.164	BB	0.4983	1853.97974	56.57141	32.9899
7	61.254	BB	0.6946	3173.30737	69.77834	56.4662
8	73.290	BB	0.7591	305.52362	5.95006	5.4365
Totals :				5619.83738	154.68635	

*** End of Report ***

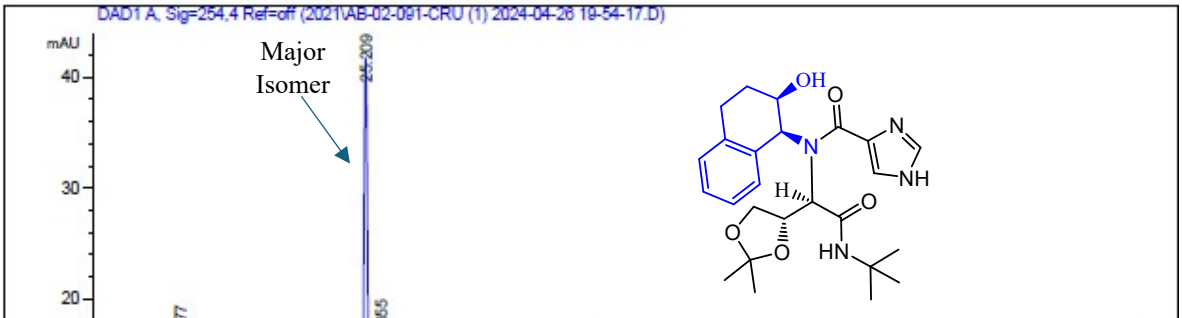


33 (crude)

Data File C:\Chem32\1\Data\2021\AB-02-091-CRU (1) 2024-04-26 19-54-17.D
Sample Name: AB-02-091-CRU

```
======================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
Injection Date  : 4/26/2024 7:55:13 PM              Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method     : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 4/26/2024 7:54:13 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 8/30/2024 7:14:48 PM by SYSTEM
Method Info     : Amlan's Method

Sample Info     : TOSOH BioSciences TSKgel CM-2SW
                  10% MeCN/H2O to 90% over 90 min, then to 10% MeCN/H2O over 30 min
                  0.5 mL/min
                  220 nm
                  254 nm
                  5 uL inj
                  2.2 mg/mL
```



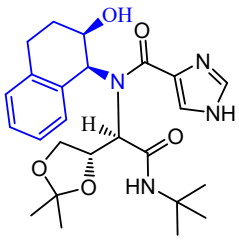
Minor
Isomer

Data File C:\Chem32\1\Data\2021\AB-02-091-CRU (1) 2024-04-26 19-54-17.D
Sample Name: AB-02-091-CRU

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.280	BB	0.1569	48.65250	3.97311	2.1745
2	6.626	BB	0.1437	70.36104	7.48266	3.1448
3	8.077	BB	0.2180	207.78911	14.60434	9.2871
4	11.031	BB	0.2681	27.70564	1.55291	1.2383
5	11.823	BB	0.2076	13.47590	1.01016	0.6023
6	17.161	BB	0.2790	51.15318	2.74990	2.2863
7	25.209	BB	0.4020	983.55829	37.74284	43.9600
8	26.655	BB	0.4128	291.38708	11.00782	13.0235
9	37.696	BB	0.3735	119.71264	4.79157	5.3505
10	42.102	BB	0.4507	89.20609	2.98422	3.9871
11	47.807	BB	0.4995	174.06444	5.24127	7.7798
12	49.495	BB	0.3450	32.96661	1.40867	1.4734
13	56.947	BB	0.5529	127.36320	3.25212	5.6925
Totals :				2237.39574	97.80161	

*** End of Report ***

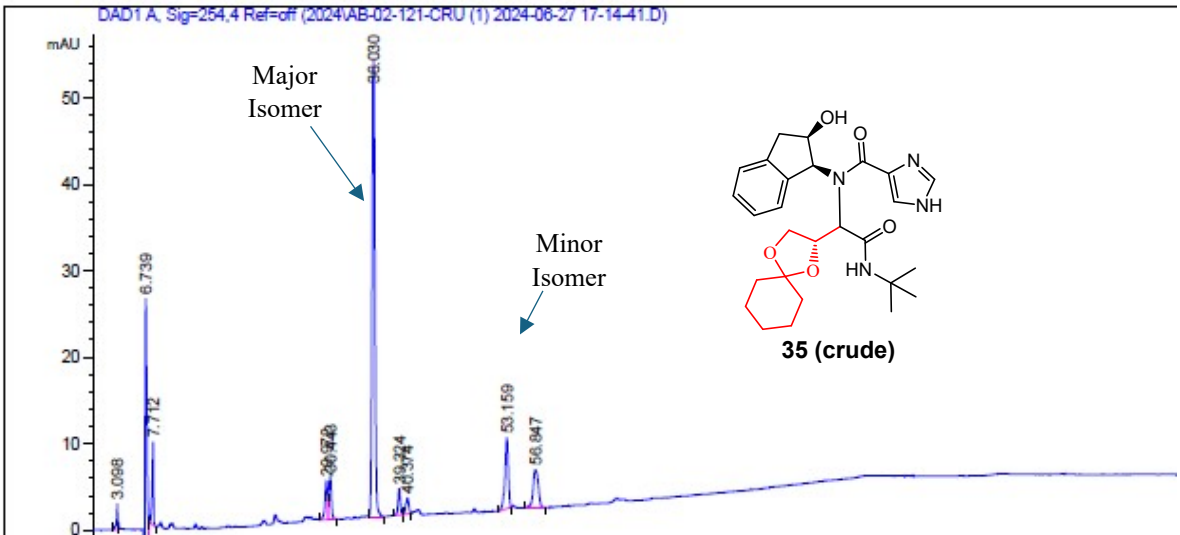


34 (crude)

Data File C:\Chem32\1\Data\2024\AB-02-121-CRU (1) 2024-06-27 17-14-41.D
Sample Name: AB-02-121-CRU

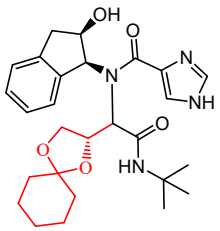
```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
Injection Date  : 6/27/2024 5:15:49 PM             Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method     : C:\CHEM32\1\METHODS\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 6/27/2024 4:30:49 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 8/30/2024 7:14:48 PM by SYSTEM
Method Info     : Amlan's Method

Sample Info     : TOSOH Bioscience TSKgel CM-2SW
                  10% TO 90% MeCN/H2O over 90 min
                  0.5 mL/min
                  215 nm
                  254 nm
                  5 uL inj
                  1 mg/mL
```



35 (crude)

Data File C:\Chem32\1\Data\2024\AB-02-121-CRU (1) 2024-06-27 17-14-41.D
Sample Name: AB-02-121-CRU



35 (crude)

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.098	BV	0.1380	31.63128	3.02403	1.1992
2	6.739	BB	0.2609	511.98129	31.28955	19.4109
3	7.712	BB	0.1758	122.15328	9.64137	4.6312
4	29.972	BV	0.3356	100.03532	4.42818	3.7927
5	30.443	VB	0.3277	108.47603	4.94872	4.1127
6	36.030	BB	0.3550	1207.08118	52.73700	45.7645
7	39.324	BB	0.3173	63.04088	3.04747	2.3901
8	40.374	BB	0.3865	48.15245	1.84494	1.8256
9	53.159	BB	0.4491	248.29874	8.15811	9.4138
10	56.847	BB	0.6376	196.74097	4.35074	7.4591
Totals :				2637.59141	123.47011	

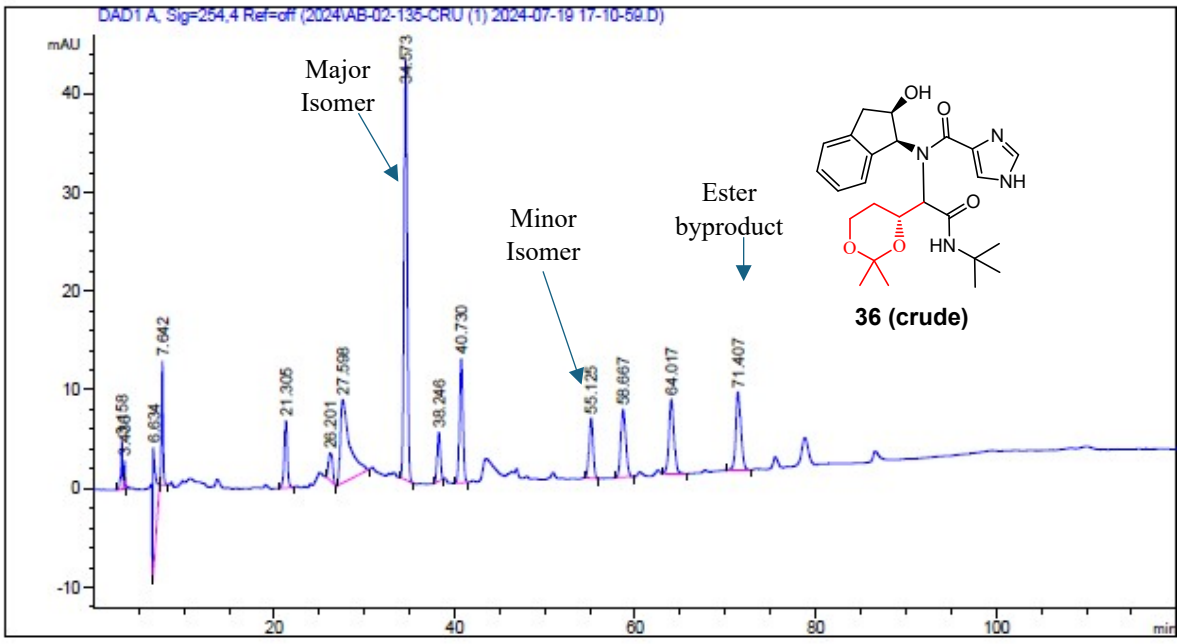
==========

*** End of Report ***

Data File C:\Chem32\1\Data\2024\AB-02-135-CRU (1) 2024-07-19 17-10-59.D
Sample Name: AB-02-135-CRU

```
=====================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
Injection Date  : 7/19/2024 5:11:56 PM              Inj :   1
                                                Inj Volume : 10.000 µl
Acq. Method     : C:\CHEM32\1\METHODS\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 7/19/2024 4:54:00 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 8/30/2024 7:14:48 PM by SYSTEM
Method Info     : Amlan's Method

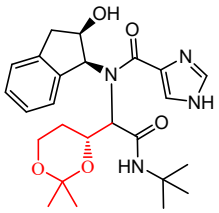
Sample Info     : TOSOH BioSciences TKgel CM-2SW
                  0.500 mL/min
                  215 nm
                  254 nm
                  10 uL inj
                  1.0 mg/mL
                  10 % MeCN/H2O to 90% MeCN/H2O over 90 min
```



36 (crude)

```
=====================================================================
                        Area Percent Report
=====================================================================
```

Data File C:\Chem32\1\Data\2024\AB-02-135-CRU (1) 2024-07-19 17-10-59.D
Sample Name: AB-02-135-CRU



36 (crude)

Signal 1: DAD1 A, Sig=254,4 Ref=off

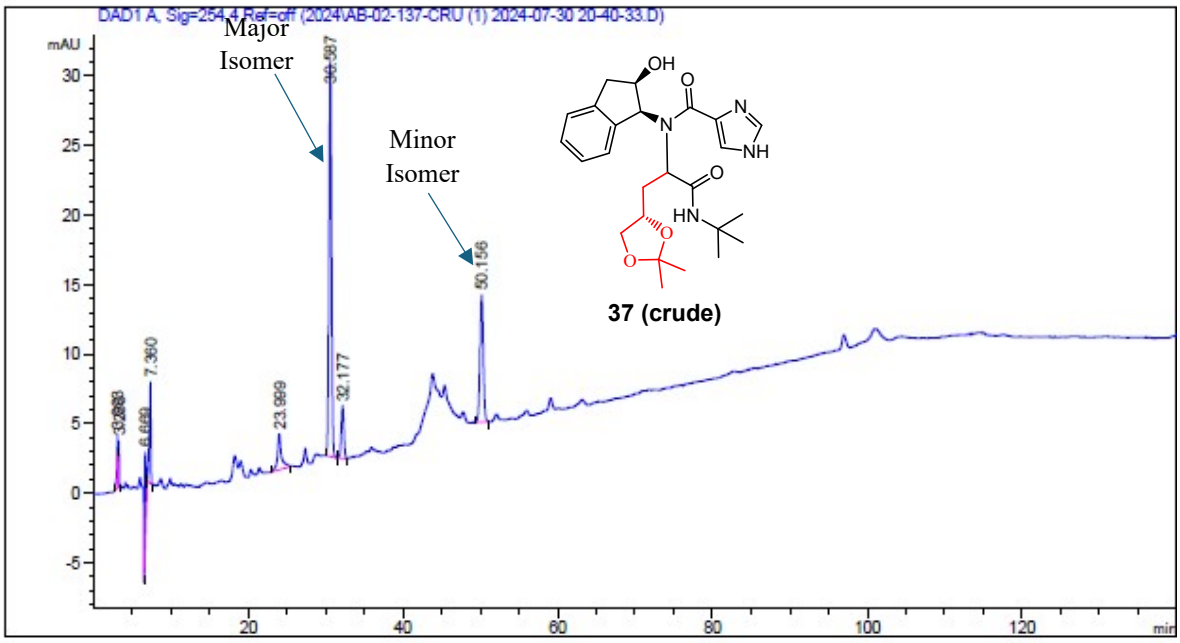
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.158	BV	0.1640	57.02198	5.03831	1.4714
2	3.436	VB	0.1397	27.42800	2.86486	0.7077
3	6.634	BB	0.2715	253.75496	12.36169	6.5477
4	7.642	BB	0.1889	162.58603	12.57017	4.1953
5	21.305	BB	0.3426	157.07512	6.87333	4.0531
6	26.201	BB	0.4543	91.29353	2.72873	2.3557
7	27.598	BB	0.9583	606.74426	8.48501	15.6560
8	34.573	BB	0.3610	1001.75513	42.49162	25.8486
9	38.246	BB	0.3747	118.77670	5.00812	3.0648
10	40.730	BB	0.4065	333.82474	12.62524	8.6138
11	55.125	BB	0.4630	187.19922	6.08351	4.8304
12	58.667	BB	0.5716	264.61063	6.83590	6.8278
13	64.017	BB	0.5957	300.54208	7.52956	7.7550
14	71.407	BB	0.5784	312.86172	7.96238	8.0729
Totals :				3875.47410	139.45844	

*** End of Report ***

Data File C:\Chem32\1\Data\2024\AB-02-137-CRU (1) 2024-07-30 20-40-33.D
Sample Name: AB-02-137-CRU

```
==========================================================================
Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
Injection Date  : 7/30/2024 8:41:28 PM             Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method     : C:\CHEM32\1\METHODS\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 7/30/2024 8:40:26 PM by SYSTEM
                  (modified after loading)
Analysis Method : C:\Chem32\1\Methods\UgiDiastereomersAmlanDONOTUSE.M
Last changed    : 8/30/2024 7:14:48 PM by SYSTEM
Method Info     : Amlan's Method

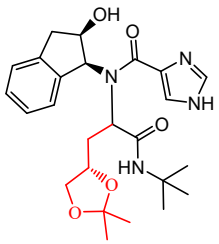
Sample Info     : TOSOH Bioscience CM-2SW
                  0.500 mL/min
                  10% MeCN/H2O to 90% MeCN/H2O over 90 min
                  215 nm
                  254 nm
                  5 uL inj
                  1.0 mg/mL
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs
```

Data File C:\Chem32\1\Data\2024\AB-02-137-CRU (1) 2024-07-30 20-40-33.D
Sample Name: AB-02-137-CRU



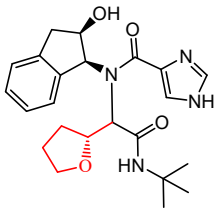
37 (crude)

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.093	BV	0.1119	32.65897	3.89053	2.4451
2	3.280	VB	0.1377	32.82311	3.31040	2.4574
3	6.669	BB	0.1725	77.87447	7.17991	5.8302
4	7.360	BB	0.1922	101.74294	7.31919	7.6172
5	23.999	BB	0.5072	94.17825	2.57194	7.0508
6	30.587	BB	0.3459	634.01392	28.46520	47.4666
7	32.177	BB	0.3809	92.86785	3.72408	6.9527
8	50.156	BB	0.4504	269.54709	9.13225	20.1801
Totals :				1335.70658	65.59350	

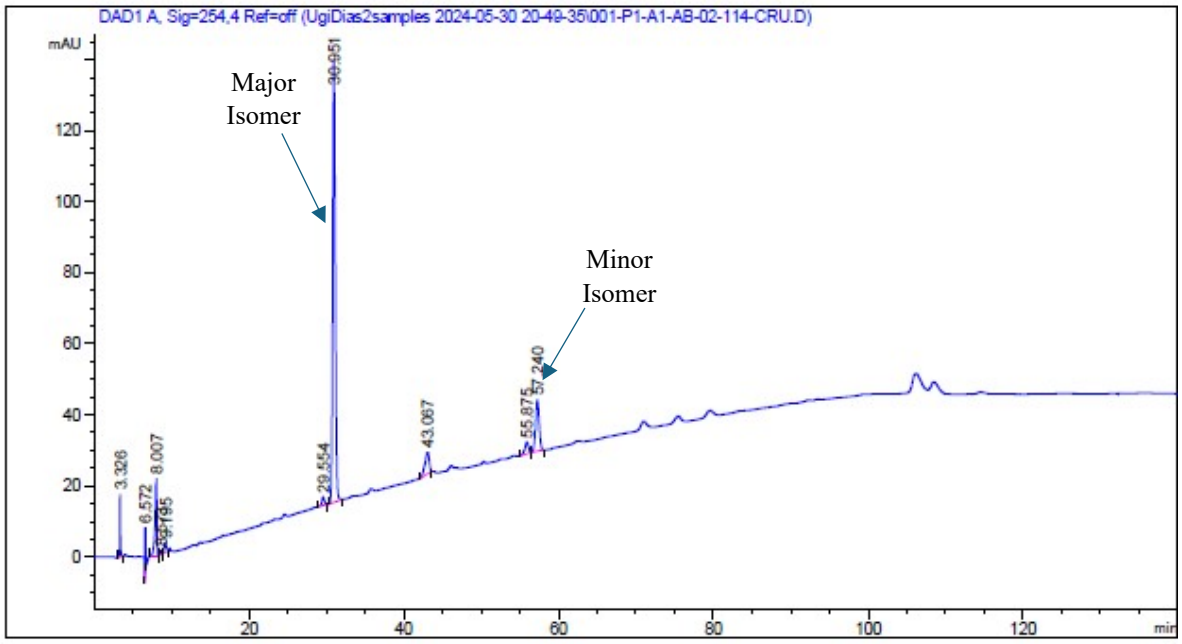
*** End of Report ***

Data File C:\Chem32\1\Data\UgiDias2samples 2024-05-30 20-49-35\001-P1-A1-AB-02-114-CRU.D
Sample Name: AB-02-114-CRU



38 (crude)

```
Acq. Operator   : SYSTEM                          Seq. Line :   1
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                       Location :   P1-A-01
Injection Date  : 5/30/2024 8:50:37 PM                 Inj :   1
                                                  Inj Volume : 10.000 µl
Method          : C:\Chem32\1\Data\UgiDias2samples 2024-05-30 20-49-35
                  \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
Last changed    : 5/30/2024 8:49:32 PM by SYSTEM
Method Info     : Amlan's Method
```



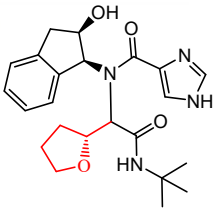

```
                          Area Percent Report

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.326 BB    0.0803  100.45779  17.66967   2.2895
   2   6.572 BB    0.1056   98.60744  14.09959   2.2474
   3   8.007 BB    0.1893  293.99890  21.79873   6.7006
   4   8.573 BB    0.2011   14.54679   1.13837   0.3315
   5   9.195 BB    0.3140   54.31709   2.68485   1.2379
```

Data File C:\Chem32\1\Data\UgiDias2samples 2024-05-30 20-49-35\001-P1-A1-AB-02-114-CRU.D
Sample Name: AB-02-114-CRU



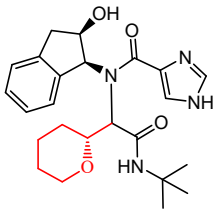
38 (crude)

```
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   8  43.067 BB    0.5383  224.97101   6.09959   5.1273
   9  55.875 BB    0.4703  102.94244   3.27839   2.3462
  10  57.240 BB    0.4874  460.78931  14.47330  10.5019
```

Data File C:\Chem32\1\Data\SATISH 2024-07-15 20-44-10\001-1-AB-02-132-CRU(AMLAN).D
Sample Name: AB-02-132-CRU(AMLAN)

Acq. Operator	: SYSTEM	Seq. Line :	1
Acq. Instrument	: LC2	Location :	1
Injection Date	: 7/15/2024 8:45:00 PM	Inj :	1
		Inj Volume :	5.000 µl
Method	: C:\Chem32\1\Data\SATISH 2024-07-15 20-44-10\AB-02-28A.M (Sequence Method)		
Last changed	: 7/15/2024 8:44:07 PM by SYSTEM		
Method Info	: Pump leak test method		
Additional Info	: Peak(s) manually integrated		

Major Isomer



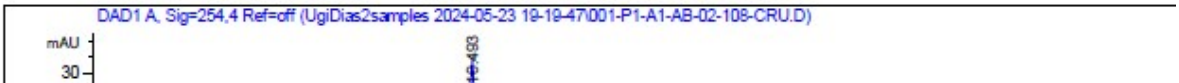
39 (crude)

Ester byproduct

Minor Isomer

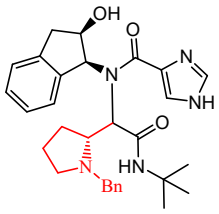
```
Data File C:\Chem32\1\Data\UgiDias2samples 2024-05-23 19-19-47\001-P1-A1-AB-02-108-CRU.D
Sample Name: AB-02-108-CRU

    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   1
    Sample Operator : SYSTEM
    Acq. Instrument : GHOSH LC 1                    Location :   P1-A-01
    Injection Date  : 5/23/2024 7:20:46 PM             Inj :   1
                                                   Inj Volume : 5.000 µl
    Method          : C:\Chem32\1\Data\UgiDias2samples 2024-05-23 19-19-47
                      \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
    Last changed    : 5/23/2024 7:19:43 PM by SYSTEM
    Method Info     : Amlan's Method
```



Major Isomer

Minor Isomer



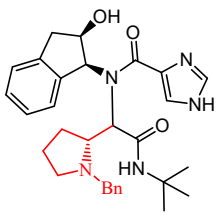
40 (crude)

```
Data File C:\Chem32\1\Data\UgiDias2samples 2024-05-23 19-19-47\001-P1-A1-AB-02-108-CRU.D
Sample Name: AB-02-108-CRU

   Peak RetTime Type  Width     Area      Height     Area
     #   [min]        [min]   [mAU*s]     [mAU]       %
   ----|-------|----|-------|----------|----------|--------|
      8  12.084 BV    0.3158  293.59470   14.04740  18.1840
      9  12.815 VB    0.3078  294.20706   13.96527  18.2219

   Totals :                  1614.58082   87.21445

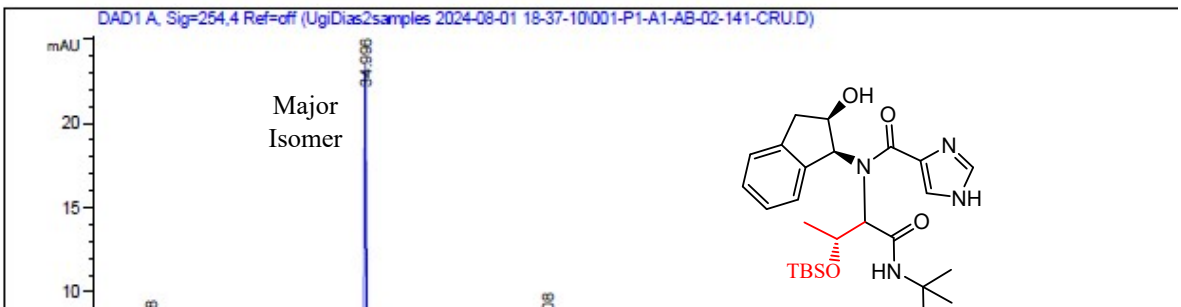

   ===================================================================
                          *** End of Report ***
```

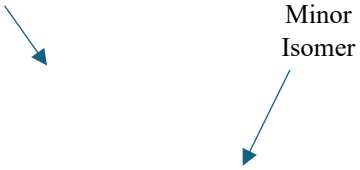


40 (crude)

Data File C:\Chem32\1\Data\UgiDias2samples 2024-08-01 18-37-10\001-P1-A1-AB-02-141-CRU.D
Sample Name: AB-02-141-CRU

```
======================================================================
Acq. Operator   : SYSTEM                          Seq. Line :   1
Sample Operator : SYSTEM
Acq. Instrument : GHOSH LC 1                       Location :   P1-A-01
Injection Date  : 8/1/2024 6:38:10 PM                  Inj :   1
                                                  Inj Volume : 5.000 µl
Method          : C:\Chem32\1\Data\UgiDias2samples 2024-08-01 18-37-10
                  \UgiDiastereomersAmlanDONOTUSE.M (Sequence Method)
Last changed    : 8/1/2024 6:37:06 PM by SYSTEM
Method Info     : Amlan's Method
```

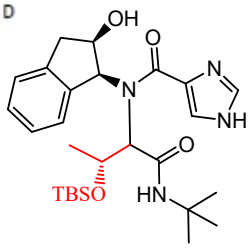




Data File C:\Chem32\1\Data\UgiDias2samples 2024-08-01 18-37-10\001-P1-A1-AB-02-141-CRU.D
Sample Name: AB-02-141-CRU

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
8	58.508	BB	0.3872	134.60574	5.28477	12.0522
9	67.440	BB	0.4486	76.18461	2.29885	6.8214
Totals :				1116.85260	58.17357	

*** End of Report ***



41 (crude)

X-ray crystallographic data

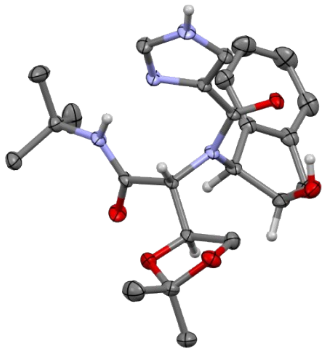


Figure S1: Deposition number: CCDC – 2474023 (Thermal ellipsoid drawing of compound **27a** at 50% probability).

Table S1. Crystallographic data for Ugi adduct **27a**.

Crystal data	
Chemical formula	$C_{24}H_{32}N_4O_5 \cdot C_4H_8O$
M_r	528.64

Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	150
***a*, *b*, *c* (Å)**	9.5836 (6), 11.8565 (8), 24.7268 (18)
***V* (Å^3)**	2809.7 (3)
Z	4
***F*(000)**	1136
D_x (Mg m^{-3})	1.250
Radiation type	Cu *Kα*
No. of reflections for cell measurement	9882
θ range (°) for cell measurement	3.6–77.4
μ (mm^{-1})	0.72
Crystal shape	Needle
Colour	Colourless
Crystal size (mm)	0.63 × 0.10 × 0.04
Data collection	
Diffractometer	Bruker AXS D8 Quest diffractometer with PhotonIII_C14 charge-integrating and photon counting pixel array detector
Radiation source	I-mu-S microsource X-ray tube
Monochromator	Laterally graded multilayer (Goebel) mirror
Detector resolution (pixels mm^{-1})	7.4074
Scan method	ω and phi scans
Absorption correction	Multi-scan *SADABS* 2016/2: Krause, L., Herbst-Irmer, R., Sheldrick G.M. & Stalke D., J. Appl. Cryst. 48 (2015) 3-10
T_{min}, T_{max}	0.499, 0.754
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	38467, 5964, 5714
R_{int}	0.059
θ values (°)	θ_{max} = 78.1, θ_{min} = 3.6
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.635
Range of *h*, *k*, *l*	*h* = −7→12, *k* = −15→14, *l* = −31→30
Refinement	
Refinement on	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.031, 0.083, 1.05
No. of reflections	5964
No. of parameters	396
No. of restraints	160
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement

Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0482P)^2 + 0.2596P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.008
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.18, −0.20
Absolute structure	Flack x determined using 2426 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	0.09 (4)

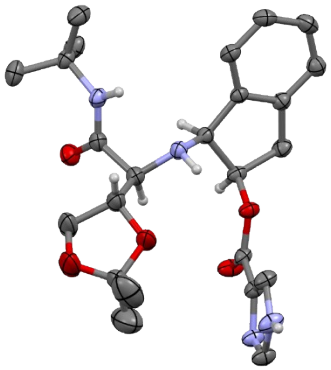


Figure S2: Deposition number: 2474024 (Thermal ellipsoid drawing of compound **27c** at 50% probability).

Table S2. Crystallographic data for Ugi adduct **27c**

Crystal data	
Chemical formula	$4(C_{24}H_{32}N_4O_5)\cdot C_5H_{12}$
M_r	1898.28
Crystal system, space	Orthorhombic, $P2_12_12$

group	
Temperature (K)	150
***a*, *b*, *c* (Å)**	12.2321 (5), 42.5089 (16), 10.0604 (4)
***V* (Å^3)**	5231.1 (4)
Z	2
Radiation type	Cu *K*α
μ (mm^{-1})	0.69
Crystal size (mm)	0.58 × 0.05 × 0.02
Data collection	
Diffractometer	Bruker AXS D8 Quest
Absorption correction	Multi-scan *SADABS* 2016/2: Krause, L., Herbst-Irmer, R., Sheldrick G.M. & Stalke D., J. Appl. Cryst. 48 (2015) 3-10
T_{min}, T_{max}	0.678, 0.754
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	111793, 11332, 10863
R_{int}	0.037
(sin θ/λ)$_{max}$ (Å^{-1})	0.639
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.030, 0.080, 1.03
No. of reflections	11332
No. of parameters	708
No. of restraints	145
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
Δρ$_{max}$, Δρ$_{min}$ (e Å^{-3})	0.31, −0.24
Absolute structure	Flack x determined using 4654 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	−0.02 (3)

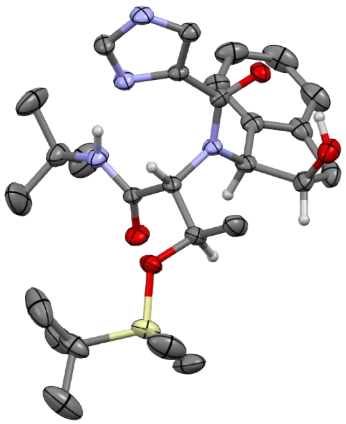


Figure S3: Deposition number: 2474025 (Thermal ellipsoid drawing of compound **41a** at 50% probability).

Table S3. Crystallographic data for Ugi adduct **41a**

Crystal data	
Chemical formula	$C_{27}H_{42}N_4O_4Si$
M_r	514.73
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Temperature (K)	150
a, b, c (Å)	9.6830 (6), 16.9749 (11), 18.0741 (11)
V (Å^3)	2970.8 (3)
Z	4
$F(000)$	1112
Radiation type	Cu $K\alpha$
No. of reflections for cell measurement	2087
θ range (°) for cell measurement	3.6–77.9
μ (mm^{-1})	0.99
Crystal shape	Needle
Colour	Colourless
Crystal size (mm)	0.14 × 0.02 × 0.01
Data collection	
Diffractometer	Bruker AXS D8 Quest
Radiation source	I-mu-S 3.0 microsource X-ray tube
Monochromator	HELIOS multilayer Montel optics
Scan method	ω and phi scans
Absorption correction	Multi-scan *SADABS* 2016/2: Krause, L., Herbst-Irmer, R., Sheldrick G.M. & Stalke D., J. Appl. Cryst. 48 (2015) 3-10
T_{min}, T_{max}	0.633, 0.754
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	15375, 5918, 4314
R_{int}	0.079
θ values (°)	θ_{max} = 80.2, θ_{min} = 3.6
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.639
Range of h, k, l	h = −12→10, k = −19→19, l = −19→23
Refinement	
Refinement on	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.054, 0.134, 1.02
No. of reflections	5918
No. of parameters	336
No. of restraints	0

H-atom treatment	**H atoms treated by a mixture of independent and constrained refinement**
Weighting scheme	**$w = 1/[\sigma^2(F_o^2) + (0.0526P)^2 + 0.2046P]$ where $P = (F_o^2 + 2F_c^2)/3$**
$(\Delta/\sigma)_{max}$	**< 0.001**
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	**0.26, −0.23**
Absolute structure	**Flack x determined using 1384 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).**
Absolute structure parameter	**0.03 (3)**

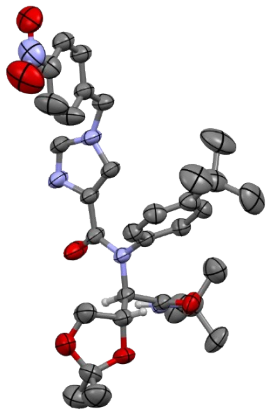


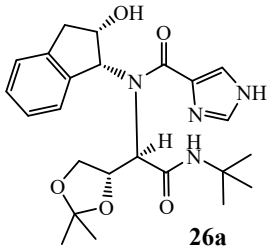
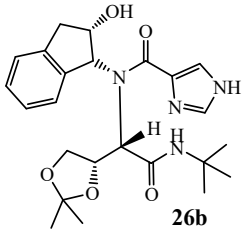
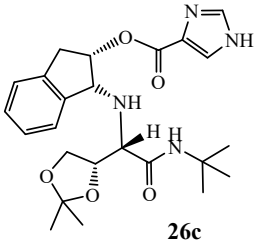
Figure S4: Deposition number: 2501300 (Thermal ellipsoid drawing of compound **10c** at 50% probability).

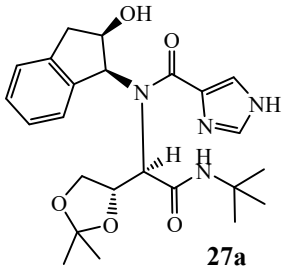
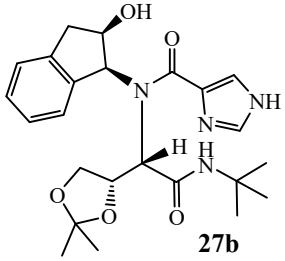
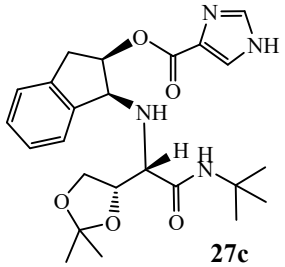
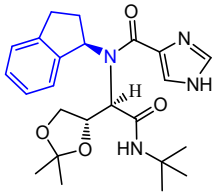
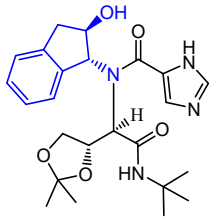
Table S4: Crystallographic data for Ugi adduct derivative **10c**.

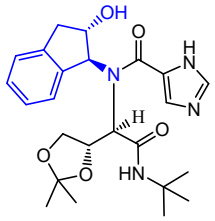
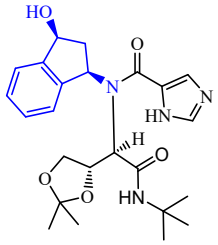
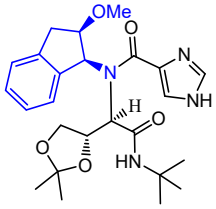
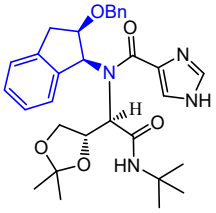
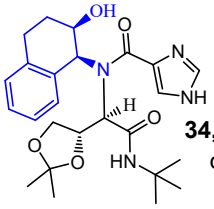
Crystal data	
Chemical formula	$C_{32}H_{41}N_5O_6$
***M*$_r$**	591.70

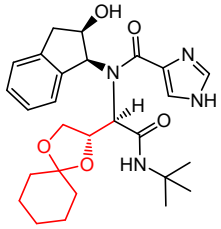
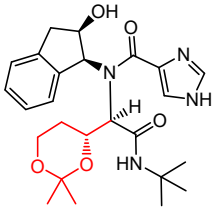
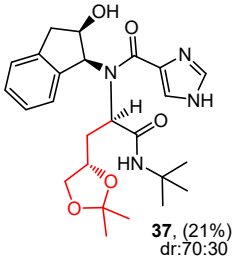
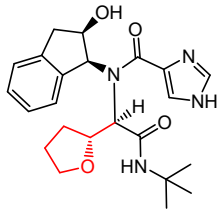
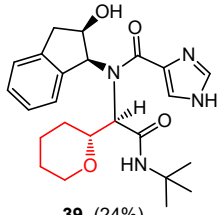
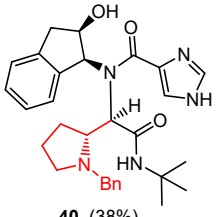
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	293
***a*, *b*, *c* (Å)**	9.6747 (5), 10.7211 (4), 15.9751 (6)
β (°)	92.949 (3)
***V* (Å³)**	1654.80 (12)
Z	2
Radiation type	Cu *K*α
μ (mm⁻¹)	0.68
Crystal size (mm)	0.43 × 0.04 × 0.02
Data collection	
Diffractometer	Bruker AXS D8 Quest
Absorption correction	Multi-scan *SADABS* 2016/2: Krause, L., Herbst-Irmer, R., Sheldrick G.M. & Stalke D., J. Appl. Cryst. 48 (2015) 3-10
T_{min}, T_{max}	0.658, 0.754
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	27249, 7037, 4961
R_{int}	0.086
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.640
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.046, 0.118, 1.06
No. of reflections	7037
No. of parameters	522
No. of restraints	470
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.19, −0.16
Absolute structure	Flack x determined using 1719 quotients [(I+)-(I-)]/[(I+)+(I-)] (Parsons, Flack and Wagner, Acta Cryst. B69 (2013) 249-259).
Absolute structure parameter	0.20 (18)

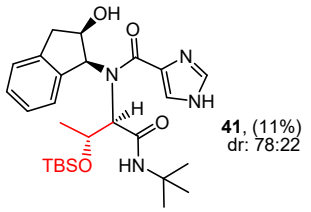
SARS-CoV-2 Mpro inhibition data

Compound Structures and compound numbers	IC_{50} Value (SARS-CoV-2 Mpro)
 **26a**	K_i > 100 μM
 **26b**	K_i > 100 μM
 **26c**	K_i > 100 μM

Compound Structures and compound numbers	IC_{50} Value (SARS-CoV-2 Mpro)
 **27a**	K_i > 100 μM
 **27b**	K_i > 100 μM
 **27c**	K_i > 100 μM
 **28**a,b (92%) dr: 69:31	K_i > 100 μM
 **29a,b**, (92%) dr: 54:46	K_i > 100 μM

Compound Structures and compound numbers	IC_{50} Value (SARS-CoV-2 Mpro)
 **30a,b**, (80%) dr: 71:29	K_i > 100 μM
 **31a,b**, (83%) dr: 72:28	K_i > 100 μM
 **32a,b**, (71%) dr: 66:34	K_i > 100 μM
 **33a,b**, (75%) dr: 63:37	K_i > 100 μM
 **34,a,b**, (15%) dr: 89:11	0% inhibition at 100μM

Compound Structures and compound numbers	IC_{50} Value (SARS-CoV-2 Mpro)
 **35**, (23%) dr:83:17	0% inhibition at 100μM
 **36**, (32%) dr: **84:16**	0% inhibition at 100μM
 **37**, (21%) dr:70:30	0% inhibition at 100μM
 **38**, (31%) dr: 87:13	5% inhibition at 100μM
 **39**, (24%) dr:86:14	4% inhibition at 100μM
 **40**, (38%) dr: 65:35	9% inhibition at 100μM

Compound Structures and compound numbers	IC_{50} Value (SARS-CoV-2 Mpro)
 **41**, (11%) dr: 78:22	20% inhibition at 100µM

SARS-CoV-2 3CLpro inhibition assays

Inhibition of SARS-CoV-2 3CLpro by designed compounds was assessed similar to our previously published methods using a continuous fluorescence assay and the FRET-based substrate UIVT3 (HiLyte Fluor488™–ESATLQSGLRKAK-QXL520™-NH_2) which was synthesized by Anaspec, Fremont, CA.[1,2] Briefly, the assay buffer consisted of 50 mM HEPES pH 7.5, 0.1 mg/mL BSA, 0.01% Triton X-100, 2 mM DTT, 1% DMSO and a final enzyme concentration of 50 nM to 200 nM depending on inhibitory potency. Kinetic assays were performed in Costar 3694 EIA/RIA 96-well half-area, flat bottom, black polystyrene plates (Corning, Corning, NY) at 25 °C. The increase in fluorescence intensity was measured at an emission wavelength of 528 nm (20 nm bandwidth) using an excitation wavelength of 485 (bandwidth 20 nm) using a CLARIOstar Plate Reader (BMG Labtech, Cary, NC). The initial rates of the reactions were determined from the slopes of the Relative Fluorescence Units (RFU) versus time (RFU min^{-1}). Inhibition data were collected and analyzed as described previously.[1]

References:

1. S. I. Hattori, N. Higashi-Kuwata, H. Hayashi, S. R. Allu, J. Raghavaiah, H. Bulut, D. Das, B. J. Anson, E. K. Lendy, Y. Takamatsu, N. Takamune. A small molecule compound with an indole moiety inhibits the main protease of SARS-CoV-2 and blocks virus replication. *Nature communications*, **2021**, *12*, 668.
2. A. K. Ghosh, J. Raghavaiah, D. Shahabi, M. Yadav, B. J. Anson, E. K. Lendy, S. I. Hattori, N. Higashi-Kuwata, H..Mitsuya, A. D. Mesecar. Indole Chloropyridinyl Ester-Derived SARS-CoV-2 3CLpro Inhibitors: Enzyme Inhibition, Antiviral Efficacy, Structure-Activity Relationship, and X-ray Structural Studies. *J Med Chem*, **2021**, *64*, 19, 14702-14714.