

# Pentafluorosulfanyl-Substituted Benzopyran Analogues as New Cyclooxygenase-2 Inhibitors with Improved Pharmacokinetics and Efficacy in Blocking Inflammation

Yanmei Zhang\*<sup>†</sup>, Yican Wang<sup>†</sup>, Chuang He<sup>†</sup>, Xiaorong Liu<sup>†</sup>, Yongzhi Lu<sup>†</sup>,  
Tingting Chen<sup>†</sup>, Qiong Pan<sup>†</sup>, Jingfang Xiong<sup>†</sup>, Miaoqin She<sup>†</sup>, Zhengchao Tu\*<sup>†</sup>,  
Xiaochu Qin<sup>†</sup>, Minke Li<sup>†</sup>, Micky D. Tortorella<sup>†</sup> and John J. Talley\*<sup>§</sup>

<sup>†</sup>Drug Discovery Pipeline, Guangzhou Institutes of Biomedicine and Health,  
ScienceCity, Guangzhou 510530, P.R.C.

<sup>§</sup>Euclises Pharmaceuticals, St. Louis, Missouri 63108, U.S.A.

Keywords: COX-2, PGE2, Pentafluorosulfanyl, Inflammation, Pain

## Supporting Information

### Table of Contents

S1: Table S1: Profile of Lead Compounds

S2: HPLC

S14: HRMS

S20: <sup>1</sup>H NMR

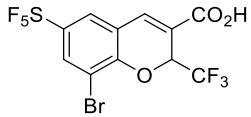
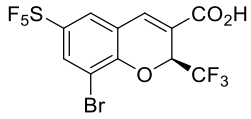
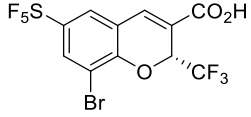
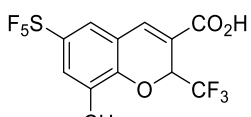
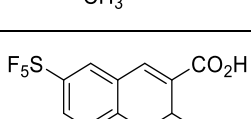
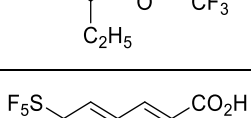
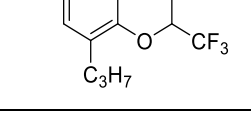
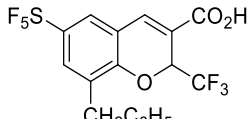
S28: <sup>13</sup>C NMR

S36: <sup>19</sup>F NMR

S46: Chiral HPLC

**Table S1: Profile of Lead Compounds:** Profile for compounds including the structures, HRMS and HPLC purity.

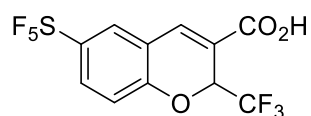
| Ex.           | IUPAC Name                                                                                           | Structure | HRMS<br>(M-H) | HPLC<br>Purity<br>(215nm) |
|---------------|------------------------------------------------------------------------------------------------------|-----------|---------------|---------------------------|
| <b>R,S-3a</b> | (R,S)-<br>6-(pentafluoro-λ <sup>6</sup> -sulfanyl)-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid |           | 368.9840      | 99.38%                    |
| <b>S-3a</b>   | (S)-<br>6-(pentafluoro-λ <sup>6</sup> -sulfanyl)-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid   |           | 368.9834      | 98.28                     |
| <b>R-3a</b>   | (R)-<br>6-(pentafluoro-λ <sup>6</sup> -sulfanyl)-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid   |           | 369.0002      | 99.56                     |
| <b>R,S-3b</b> | (R,S)-<br>7-(pentafluoro-λ <sup>6</sup> -sulfanyl)-2-(trifluoromethyl)-2H-chromene-3-carboxylic acid |           | 368.9842      | 99.43%                    |

|                |                                                                                                                           |                                                                                      |          |        |
|----------------|---------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------|--------|
| <b>R,S-7</b>   | ( <i>R,S</i> )-8-bromo-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid  |    | 446.9130 | 93.84  |
| <b>S-7</b>     | ( <i>S</i> )-8-bromo-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid    |    | 446.8957 | 98.29% |
| <b>R-7</b>     | ( <i>R</i> )-8-bromo-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid    |    | 446.9134 | 90.91  |
| <b>R,S-11a</b> | ( <i>R,S</i> )-8-methyl-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid |    | 383.0004 | 95.42% |
| <b>R,S-11b</b> | ( <i>R,S</i> )-8-ethyl-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid  |    | 397.0171 | 98.18% |
| <b>R,S-11c</b> | ( <i>R,S</i> )-8-propyl-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid |    | 411.0309 | 99.14% |
| <b>R,S-11d</b> | ( <i>R,S</i> )-8-benzyl-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid |   | 459.0308 | 99.37% |
| <b>R,S-11e</b> | ( <i>R,S</i> )-8-butyl-6-(pentafluoro- $\lambda^6$ -sulfanyl)-2-(trifluoromethyl)-2 <i>H</i> -chromene-3-carboxylic acid  |  | 425.0459 | 92.88  |

## HPLC

HPLC analyses were performed on an Agilent 1260 Infinity (Dikma, 250 × 4.6 nm, C18, 5  $\mu$ m, UV 215 nm, 1.0 mL/min). MeOH/H<sub>2</sub>O (0.1%TFA), 20%~30% 0-30 min.

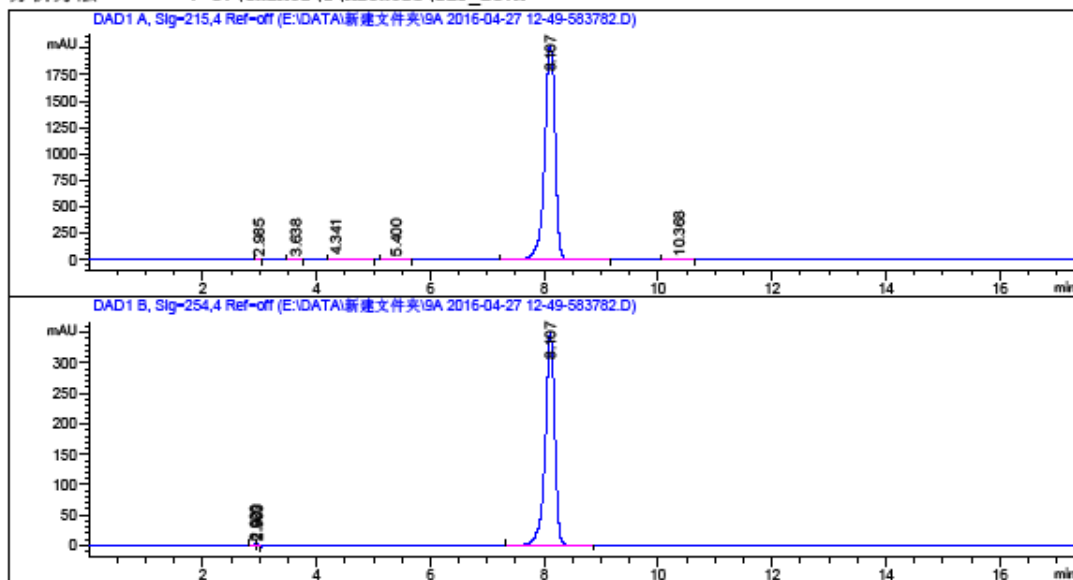
### (*R,S*)-3a



数据文件: E:\DATA\新建文件夹\9A 2016-04-27 12-49-583782.D  
 样品名称: 9a

=====

|      |                                |                |
|------|--------------------------------|----------------|
| 操作者  | : 系统                           |                |
| 仪器   | : HPLC1260                     | 位置 : F1-C-08   |
| 进样日期 | : 2016-4-27 12:50:42           |                |
|      |                                | 进样量 : 5.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |                |
| 最后修改 | : 2016-4-27 12:31:03 : 系统      |                |
|      | (调用后修改)                        |                |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |                |



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=215,4 Ref=off

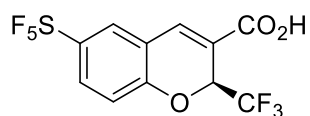
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|----|----------|-------------|------------|---------|
| 1   | 2.985      | BB | 0.0621   | 13.19051    | 3.33482    | 0.0509  |
| 2   | 3.638      | BB | 0.1176   | 8.10644     | 1.08013    | 0.0313  |
| 3   | 4.341      | VB | 0.1857   | 88.61333    | 6.90740    | 0.3422  |
| 4   | 5.400      | BB | 0.1684   | 22.19906    | 2.01627    | 0.0857  |
| 5   | 8.107      | BB | 0.1967   | 2.57359e4   | 2019.76343 | 99.3835 |
| 6   | 10.368     | BB | 0.2233   | 27.54211    | 1.89805    | 0.1064  |

总量 : 2.58956e4 2035.00009

HPLC1260 2016-4-27 14:07:07 系统

页 1/2

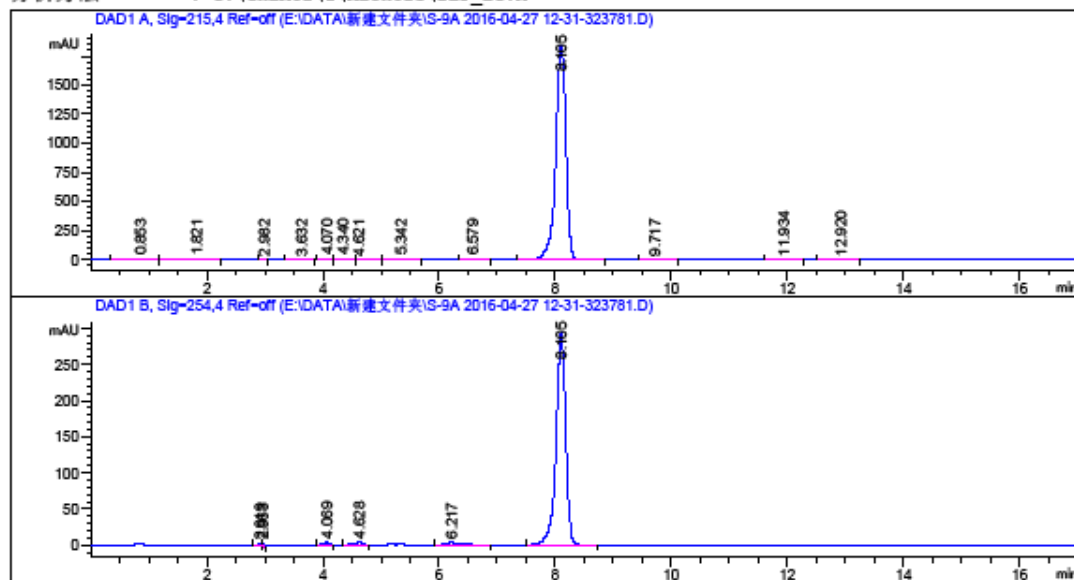
S-3a



数据文件: E:\DATA\新建文件夹\S-9A 2016-04-27 12-31-323781.D  
 样品名称: S-9a

=====

操作者 : 系统  
 仪器 : HPLC1260 位置 : P1-C-07  
 进样日期 : 2016-4-27 12:32:22 进样量 : 5.000 µl  
 采集方法 : C:\CHEM32\1\METHODS\DEF\_IC.M  
 最后修改 : 2016-4-27 12:31:03 : 系统  
 (调用后修改)  
 分析方法 : C:\CHEM32\1\METHODS\DEF\_IC.M



=====  
 面积百分比报告  
 =====

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

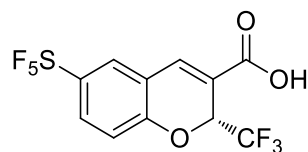
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 %  |
|-----|------------|----|----------|-------------|----------|--------|
| 1   | 0.853      | BB | 0.2759   | 60.19611    | 3.31385  | 0.2656 |
| 2   | 1.821      | BB | 0.3803   | 76.25819    | 2.84852  | 0.3365 |
| 3   | 2.982      | BB | 0.0572   | 10.87940    | 2.93605  | 0.0480 |
| 4   | 3.632      | BB | 0.1372   | 13.85271    | 1.48038  | 0.0611 |
| 5   | 4.070      | BV | 0.0938   | 14.16468    | 2.23827  | 0.0625 |
| 6   | 4.340      | VV | 0.1712   | 80.01286    | 6.90590  | 0.3531 |
| 7   | 4.621      | VB | 0.1305   | 18.19671    | 1.92140  | 0.0803 |
| 8   | 5.342      | BB | 0.1240   | 34.52759    | 4.02791  | 0.1524 |
| 9   | 6.579      | BB | 0.2331   | 27.11697    | 1.49865  | 0.1197 |

HPLC1260 2016-4-27 14:07:44 系统

页 1/2

**R-3a**

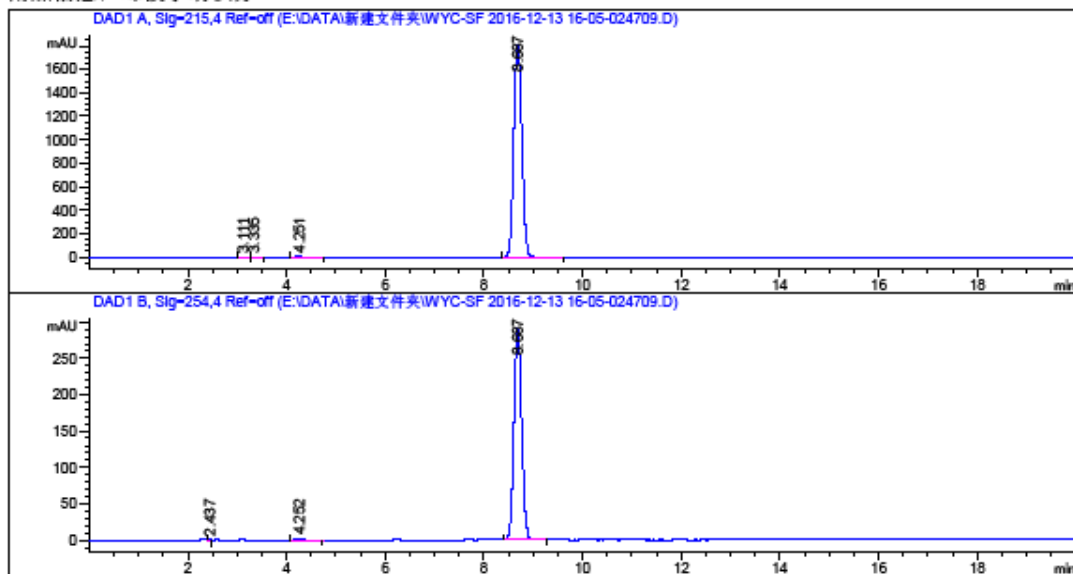


数据文件: E:\DATA\新建文件夹\WYC-SF 2016-12-13 16-05-024709.D  
 样品名称: WYC-SF

=====

|      |                                |     |            |
|------|--------------------------------|-----|------------|
| 操作者  | : 系统                           | 位置  | : P1-F-05  |
| 仪器   | : HPLC1260                     |     |            |
| 进样日期 | : 2016-12-13 16:05:43          | 进样量 | : 1.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_IC.M |     |            |
| 最后修改 | : 2016-12-13 16:06:28 : 系统     |     |            |
|      | (调用后修改)                        |     |            |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_IC.M |     |            |
| 最后修改 | : 2016-12-13 16:27:36 : 系统     |     |            |
|      | (调用后修改)                        |     |            |

附加信息: 峰被手动积分



=====  
 面积百分比报告  
 =====

|               |   |        |
|---------------|---|--------|
| 排序            | : | 信号     |
| 乘积因子          | : | 1.0000 |
| 稀释因子          | : | 1.0000 |
| 内标使用乘积因子和稀释因子 |   |        |

信号 1: DAD1 A, Sig=215,4 Ref=off

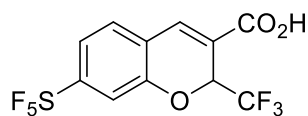
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|----|----------|-------------|------------|---------|
| 1   | 3.111      | BV | 0.0898   | 14.60410    | 2.51404    | 0.0704  |
| 2   | 3.335      | VB | 0.0670   | 4.68415     | 1.03067    | 0.0226  |
| 3   | 4.251      | BB | 0.1287   | 72.84741    | 8.11378    | 0.3510  |
| 4   | 8.687      | BB | 0.1819   | 2.06596e4   | 1800.28857 | 99.5560 |

总量 : 2.07517e4 1811.94706

HPLC1260 2016-12-13 16:27:43 系统

页 1/2

(R,S)-3b

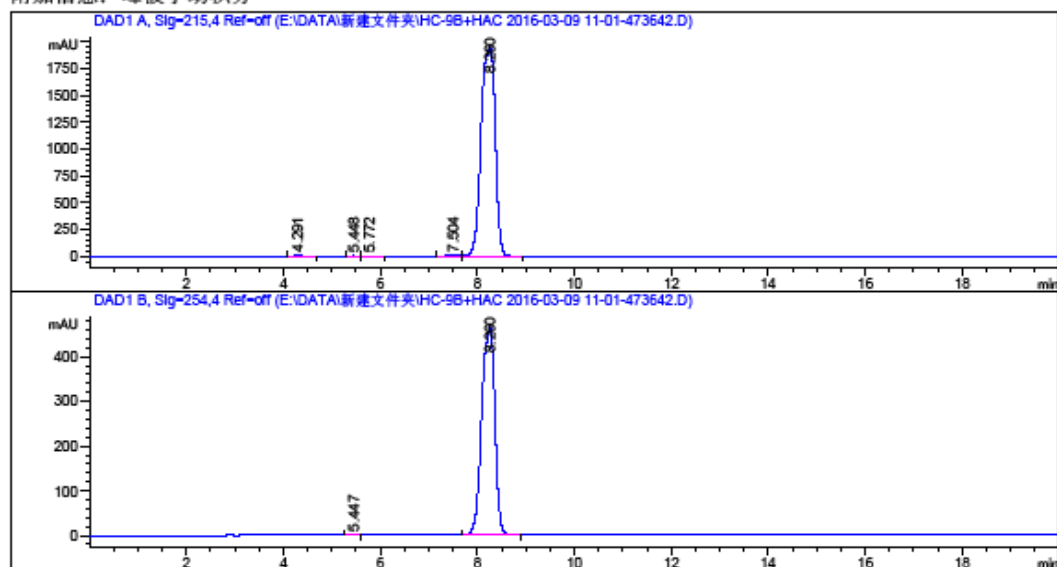


数据文件: E:\DATA\新建文件夹\HC-9B+HAC 2016-03-09 11-01-473642.D  
 样品名称: HC-9b+HAc

=====

|      |                                |     |            |
|------|--------------------------------|-----|------------|
| 操作者  | : 系统                           | 位置  | : F1-C-03  |
| 仪器   | : HPLC1260                     |     |            |
| 进样日期 | : 2016-3-9 11:02:31            | 进样量 | : 3.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |            |
| 最后修改 | : 2016-3-9 11:12:04 : 系统       |     |            |
|      | (调用后修改)                        |     |            |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |            |
| 最后修改 | : 2016-4-21 13:12:24 : 系统      |     |            |
|      | (调用后修改)                        |     |            |

附加信息: 峰被手动积分



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

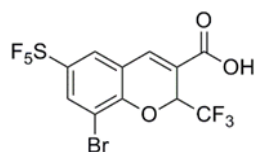
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|----|----------|-------------|------------|---------|
| 1   | 4.291      | BB | 0.1826   | 72.58504    | 5.85758    | 0.1832  |
| 2   | 5.448      | BV | 0.1552   | 25.37540    | 2.66277    | 0.0641  |
| 3   | 5.772      | VB | 0.1849   | 30.91427    | 2.67353    | 0.0780  |
| 4   | 7.504      | BV | 0.2459   | 97.19745    | 5.40263    | 0.2454  |
| 5   | 8.260      | VB | 0.2862   | 3.93842e4   | 1945.12366 | 99.4293 |

HPLC1260 2016-4-21 15:19:20 系统

页 1/2

(R,S)-7

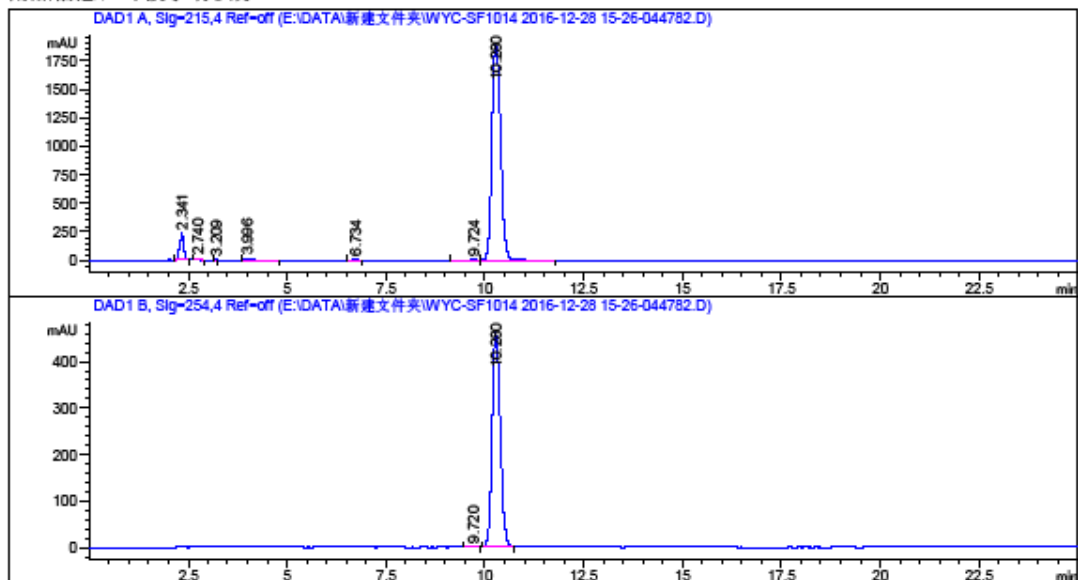


数据文件: E:\DATA\新建文件夹\WYC-SF1014 2016-12-28 15-26-044782.D  
 样品名称: WYC-SF1014

=====

|      |                                |                |
|------|--------------------------------|----------------|
| 操作者  | : 系统                           |                |
| 仪器   | : HPLC1260                     | 位置: P1-D-06    |
| 进样日期 | : 2016-12-28 15:26:50          |                |
|      |                                | 进样量: 10.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_IC.M |                |
| 最后修改 | : 2016-12-28 15:43:55 : 系统     |                |
|      | (调用后修改)                        |                |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_IC.M |                |
| 最后修改 | : 2016-12-26 10:51:08 : 系统     |                |
|      | (调用后修改)                        |                |

附加信息: 峰被手动积分



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

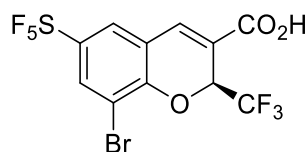
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %  |
|-----|------------|----|----------|-------------|-----------|--------|
| 1   | 2.341      | BB | 0.1015   | 1586.10144  | 232.67197 | 5.1268 |
| 2   | 2.740      | BB | 0.0870   | 35.66399    | 6.21072   | 0.1153 |
| 3   | 3.209      | BB | 0.0501   | 3.66288     | 1.18464   | 0.0118 |
| 4   | 3.996      | BB | 0.2217   | 147.18701   | 9.44933   | 0.4758 |
| 5   | 6.734      | BB | 0.1704   | 45.18993    | 4.30646   | 0.1461 |
| 6   | 9.724      | BV | 0.2323   | 86.90583    | 5.32865   | 0.2809 |

HPLC1260 2016-12-28 15:55:59 系统

页 1/2

S-7

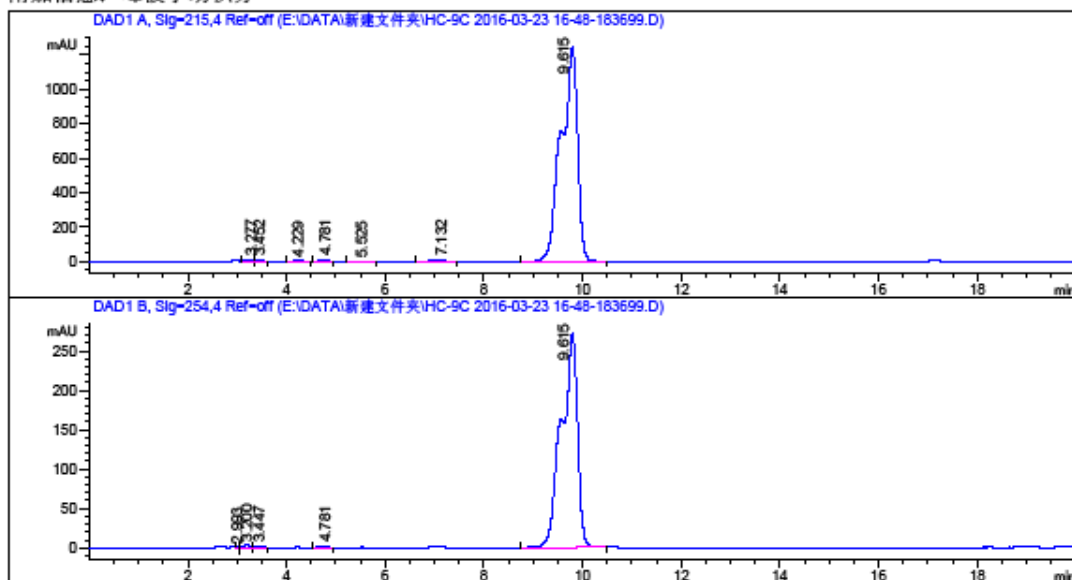


数据文件: E:\DATA\新建文件夹\HC-9C 2016-03-23 16-48-183699.D  
 样品名称: HC-9C

=====

|      |                                |     |            |
|------|--------------------------------|-----|------------|
| 操作者  | : 系统                           | 位置  | : P1-F-06  |
| 仪器   | : HPLC1260                     |     |            |
| 进样日期 | : 2016-3-23 16:49:00           | 进样量 | : 2.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_IC.M |     |            |
| 最后修改 | : 2016-3-23 16:41:09 : 系统      |     |            |
|      | (调用后修改)                        |     |            |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_IC.M |     |            |
| 最后修改 | : 2016-3-24 12:18:53 : 系统      |     |            |
|      | (调用后修改)                        |     |            |

附加信息: 峰被手动积分



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

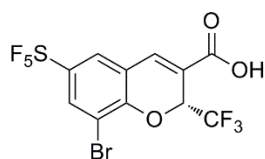
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 %  |
|-----|------------|----|----------|-------------|----------|--------|
| 1   | 3.277      | BV | 0.1267   | 90.57999    | 9.37365  | 0.3117 |
| 2   | 3.452      | VB | 0.1299   | 72.01148    | 7.93303  | 0.2478 |
| 3   | 4.229      | BV | 0.1932   | 56.61459    | 4.31099  | 0.1948 |
| 4   | 4.781      | VB | 0.1360   | 110.29639   | 11.28669 | 0.3795 |
| 5   | 5.525      | BB | 0.1699   | 13.05647    | 1.04399  | 0.0449 |
| 6   | 7.132      | BB | 0.2248   | 154.58348   | 9.45389  | 0.5319 |

HPLC1260 2016-3-24 12:19:04 系统

页 1/2

R-7

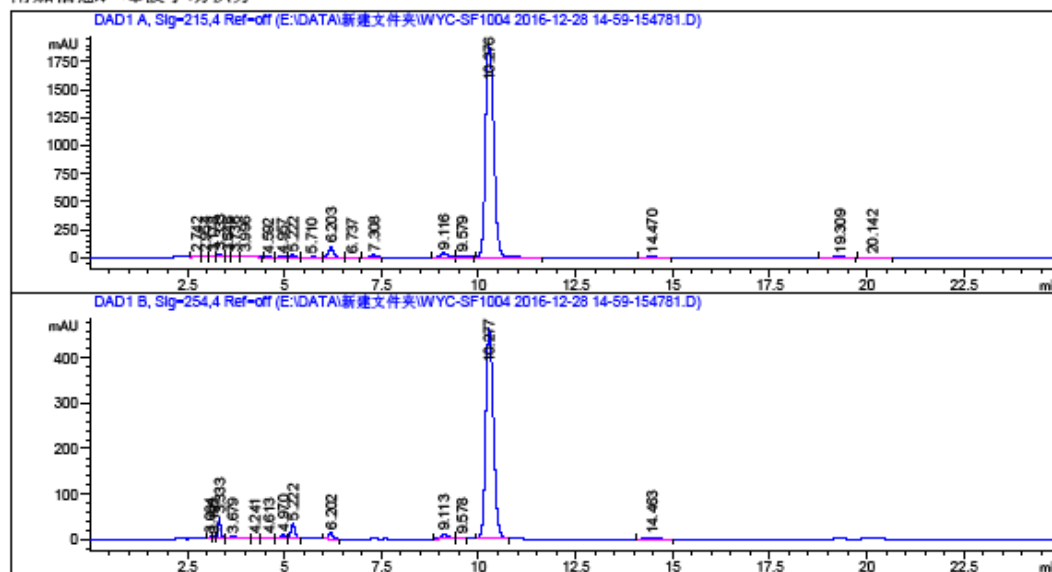


S8

数据文件: E:\DATA\新建文件夹\WYC-SF1004 2016-12-28 14-59-154781.D  
 样品名称: WYC-SF1004

操作者 : 系统  
 仪器 : HPLC1260 位置 : F1-D-05  
 进样日期 : 2016-12-28 15:00:00 进样量 : 10.000 µl  
 采集方法 : C:\CHEM32\1\METHODS\DEF\_LC.M  
 最后修改 : 2016-12-28 15:19:24 : 系统  
 (调用后修改)  
 分析方法 : C:\CHEM32\1\METHODS\DEF\_LC.M  
 最后修改 : 2016-12-26 10:51:08 : 系统  
 (调用后修改)

附加信息: 峰被手动积分



# 面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

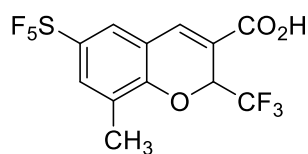
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 %  |
|-----|------------|----|----------|-------------|----------|--------|
| 1   | 2.742      | VV | 0.1017   | 45.72160    | 6.37296  | 0.1485 |
| 2   | 2.954      | VB | 0.0830   | 9.10013     | 1.68561  | 0.0296 |
| 3   | 3.178      | BV | 0.0963   | 11.68525    | 1.69753  | 0.0379 |
| 4   | 3.333      | VV | 0.0840   | 141.47829   | 25.78996 | 0.4594 |
| 5   | 3.546      | VB | 0.0850   | 22.41854    | 4.02679  | 0.0728 |
| 6   | 3.736      | BV | 0.1289   | 20.65101    | 2.59336  | 0.0671 |

HPLC1260 2016-12-28 15:26:59 系统

页 1/2

(R,S)-11a

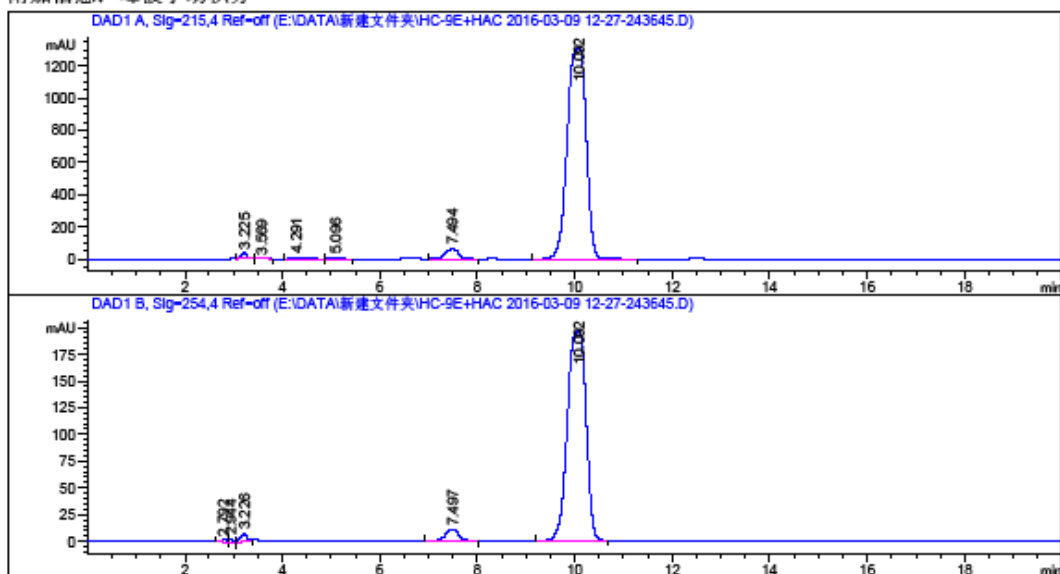


数据文件: E:\DATA\新建文件夹\HC-9E+HAC 2016-03-09 12-27-243645.D  
 样品名称: HC-9e+HAc

=====

|      |                                |     |             |
|------|--------------------------------|-----|-------------|
| 操作者  | : 系统                           | 位置  | : F1-C-05   |
| 仪器   | : HPLC1260                     |     |             |
| 进样日期 | : 2016-3-9 12:28:09            | 进样量 | : 10.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |             |
| 最后修改 | : 2016-3-9 12:42:15 : 系统       |     |             |
|      | (调用后修改)                        |     |             |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |             |
| 最后修改 | : 2016-4-21 13:12:24 : 系统      |     |             |
|      | (调用后修改)                        |     |             |

附加信息: 峰被手动积分



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

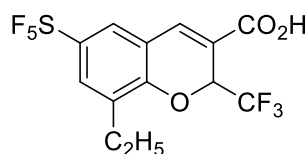
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|----|----------|-------------|------------|---------|
| 1   | 3.225      | VB | 0.1165   | 312.25629   | 37.74306   | 0.8497  |
| 2   | 3.569      | BB | 0.1777   | 19.52133    | 1.54150    | 0.0531  |
| 3   | 4.291      | BB | 0.2008   | 154.42552   | 11.34765   | 0.4202  |
| 4   | 5.096      | BB | 0.1759   | 80.51291    | 7.01704    | 0.2191  |
| 5   | 7.494      | BB | 0.2930   | 1115.22192  | 61.08814   | 3.0346  |
| 6   | 10.092     | BB | 0.3658   | 3.50685e4   | 1312.05786 | 95.4233 |

HPLC1260 2016-4-21 15:20:48 系统

页 1/2

(R,S)-11b

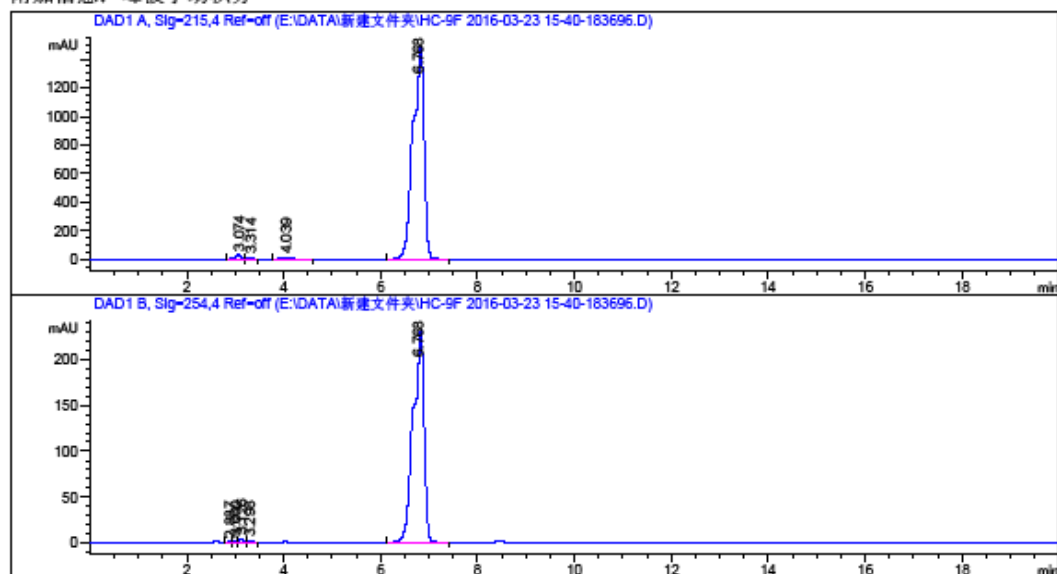


数据文件: E:\DATA\新建文件夹\HC-9F 2016-03-23 15-40-183696.D  
 样品名称: HC-9F

=====

|      |                                |               |
|------|--------------------------------|---------------|
| 操作者  | : 系统                           |               |
| 仪器   | : HPLC1260                     | 位置: P1-F-04   |
| 进样日期 | : 2016-3-23 15:41:02           |               |
|      |                                | 进样量: 5.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |               |
| 最后修改 | : 2016-3-23 15:30:37 : 系统      |               |
|      | (调用后修改)                        |               |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |               |
| 最后修改 | : 2016-3-24 12:20:12 : 系统      |               |
|      | (调用后修改)                        |               |

附加信息: 峰被手动积分



=====  
 面积百分比报告  
 =====

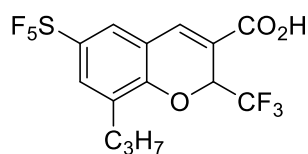
排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型   | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|------|----------|-------------|------------|---------|
| 1   | 3.074      | BV   | 0.1260   | 255.05031   | 28.07109   | 1.0634  |
| 2   | 3.314      | VB   | 0.1392   | 45.88972    | 5.18613    | 0.1913  |
| 3   | 4.039      | BB   | 0.1958   | 134.43462   | 9.34667    | 0.5605  |
| 4   | 6.768      | BB + | 0.2658   | 2.35486e4   | 1476.66309 | 98.1847 |

总量 : 2.39840e4 1519.26698

(R,S)-11c

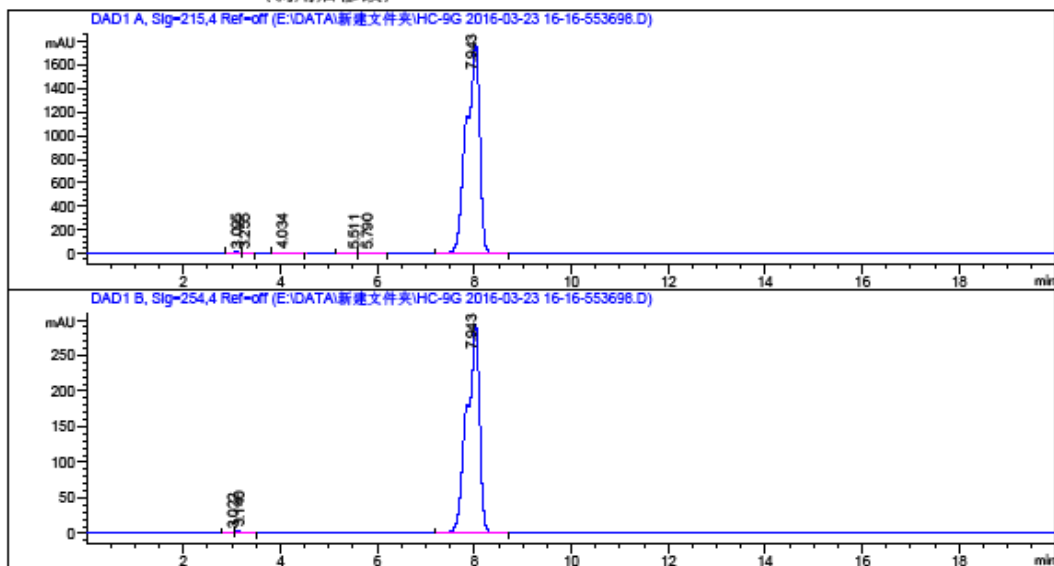


数据文件: E:\DATA\新建文件夹\HC-9G 2016-03-23 16-16-553698.D  
 样品名称: HC-9G

=====

|      |                                |     |            |
|------|--------------------------------|-----|------------|
| 操作者  | : 系统                           | 位置  | : F1-F-05  |
| 仪器   | : HPLC1260                     |     |            |
| 进样日期 | : 2016-3-23 16:17:38           | 进样量 | : 2.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |            |
| 最后修改 | : 2016-3-23 16:16:38 : 系统      |     |            |
|      | (调用后修改)                        |     |            |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |            |
| 最后修改 | : 2016-3-24 12:19:31 : 系统      |     |            |
|      | (调用后修改)                        |     |            |

=====



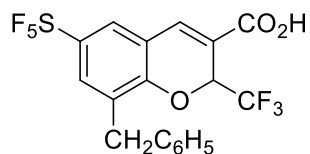
面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型   | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|------|----------|-------------|------------|---------|
| 1   | 3.095      | BV   | 0.1435   | 137.28810   | 13.62911   | 0.4031  |
| 2   | 3.255      | VB   | 0.1091   | 28.64284    | 3.92490    | 0.0841  |
| 3   | 4.034      | EB   | 0.1873   | 80.01785    | 5.86087    | 0.2349  |
| 4   | 5.511      | BV   | 0.1602   | 18.17498    | 1.53451    | 0.0534  |
| 5   | 5.790      | VB   | 0.1802   | 29.88677    | 2.29100    | 0.0877  |
| 6   | 7.943      | EB + | 0.3192   | 3.37672e4   | 1763.35461 | 99.1368 |

(R,S)-11d

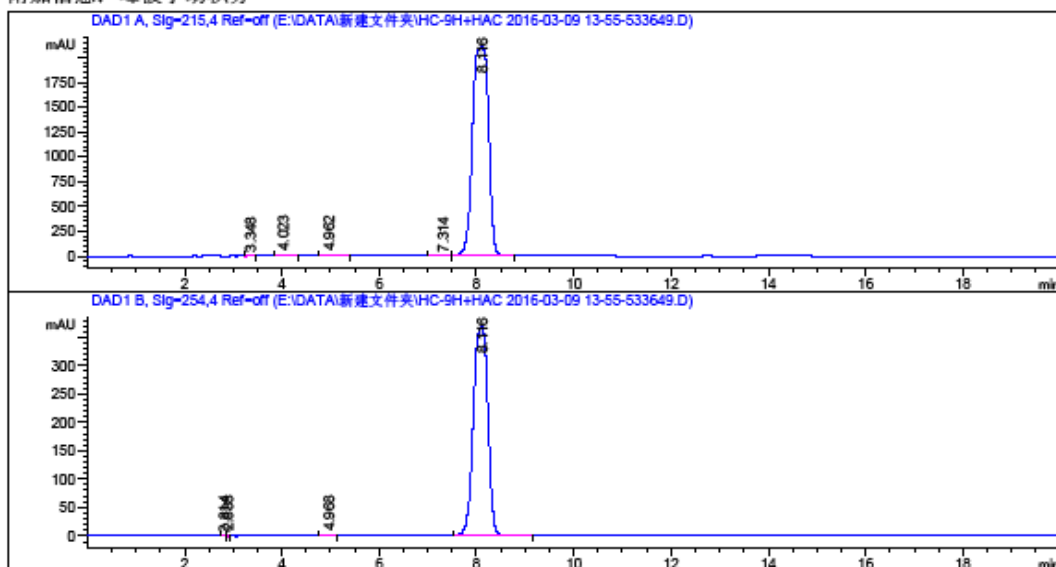


数据文件: E:\DATA\新建文件夹\HC-9H+HAC 2016-03-09 13-55-533649.D  
 样品名称: HC-9h+HAc

=====

|      |                                |     |             |
|------|--------------------------------|-----|-------------|
| 操作者  | : 系统                           | 位置  | : P1-C-06   |
| 仪器   | : HPLC1260                     |     |             |
| 进样日期 | : 2016-3-9 13:56:39            | 进样量 | : 10.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |             |
| 最后修改 | : 2016-3-9 13:43:47 : 系统       |     |             |
|      | (调用后修改)                        |     |             |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |     |             |
| 最后修改 | : 2016-4-21 13:12:24 : 系统      |     |             |
|      | (调用后修改)                        |     |             |

附加信息: 峰被手动积分



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

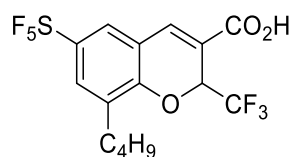
信号 1: DAD1 A, Sig=215,4 Ref=off

| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|----|----------|-------------|------------|---------|
| 1   | 3.348      | VB | 0.1330   | 31.32876    | 3.41457    | 0.0650  |
| 2   | 4.023      | BB | 0.1655   | 135.14691   | 12.36972   | 0.2803  |
| 3   | 4.962      | BB | 0.1709   | 88.56287    | 8.14313    | 0.1837  |
| 4   | 7.314      | BV | 0.2809   | 48.81304    | 2.80738    | 0.1012  |
| 5   | 8.116      | VB | 0.3140   | 4.79127e4   | 2101.32471 | 99.3698 |

HPLC1260 2016-4-21 15:22:48 系统

页 1/2

(R,S)-11e

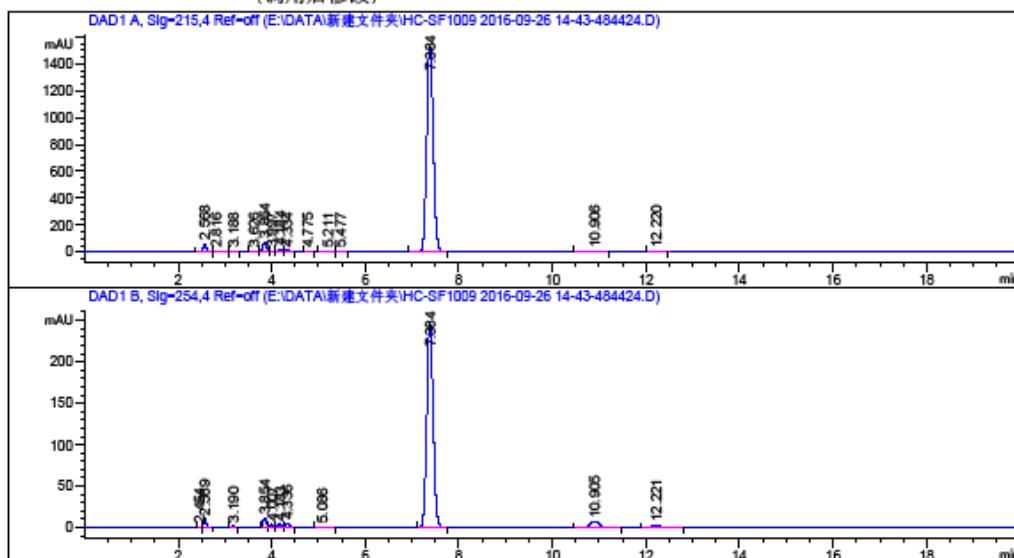


数据文件: E:\DATA\新建文件夹\HC-SF1009 2016-09-26 14-43-484424.D  
 样品名称: HC-SF1009

=====

|      |                                |               |
|------|--------------------------------|---------------|
| 操作者  | : 系统                           |               |
| 仪器   | : HPLC1260                     | 位置: F1-D-02   |
| 进样日期 | : 2016-9-26 14:44:30           |               |
|      |                                | 进样量: 3.000 µl |
| 采集方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |               |
| 最后修改 | : 2016-9-26 14:54:56 : 系统      |               |
|      | (调用后修改)                        |               |
| 分析方法 | : C:\CHEM32\1\METHODS\DEF_LC.M |               |
| 最后修改 | : 2016-9-26 14:14:35 : 系统      |               |
|      | (调用后修改)                        |               |

=====



面积百分比报告

排序 : 信号  
 乘积因子 : 1.0000  
 稀释因子 : 1.0000  
 内标使用乘积因子和稀释因子

信号 1: DAD1 A, Sig=215,4 Ref=off

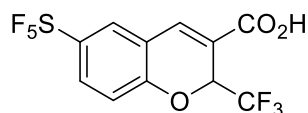
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU] | 峰面积 %  |
|-----|------------|----|----------|-------------|----------|--------|
| 1   | 2.568      | BV | 0.0733   | 309.01111   | 62.86721 | 1.9506 |
| 2   | 2.816      | VV | 0.1556   | 49.50758    | 4.08030  | 0.3125 |
| 3   | 3.188      | VV | 0.0853   | 39.53656    | 6.85015  | 0.2496 |
| 4   | 3.626      | BV | 0.1335   | 47.45886    | 5.45685  | 0.2996 |
| 5   | 3.854      | VV | 0.0788   | 369.83517   | 73.37326 | 2.3345 |
| 6   | 3.997      | VB | 0.0693   | 13.69423    | 3.11343  | 0.0864 |
| 7   | 4.184      | BV | 0.0792   | 65.33015    | 12.45834 | 0.4124 |

HPLC1260 2016-9-26 15:04:56 系统

页 1/2

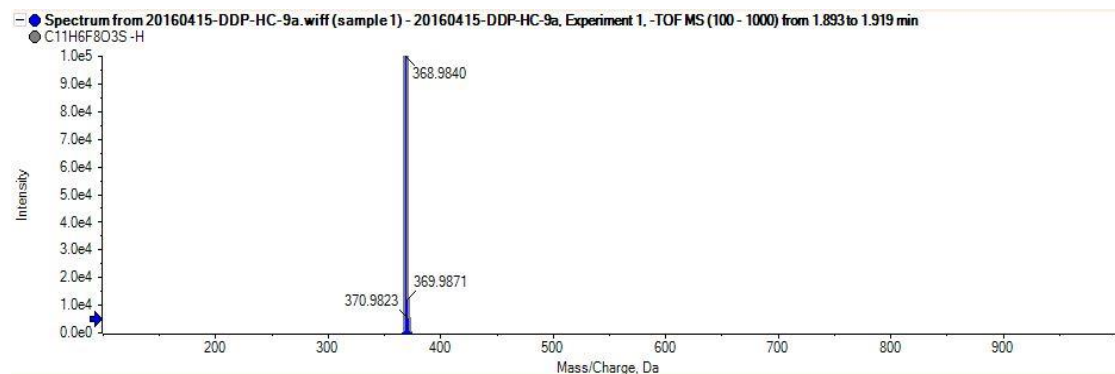
## HRMS

### (R,S)-3a

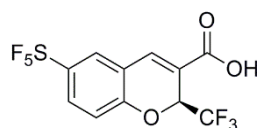


# HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.      | Formula (M)                                                    | Ion Formula                                                    | Measured m/z | Calc m/z | Error (ppm) |
|-----------------|----------------------------------------------------------------|----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-3a</b> | C <sub>11</sub> H <sub>6</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>5</sub> F <sub>8</sub> O <sub>3</sub> S | 368.9840     | 368.9837 | 0.9         |

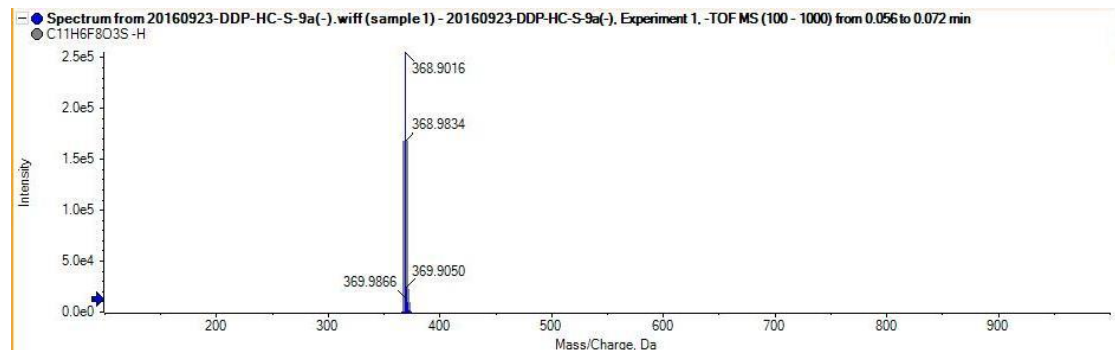


## S-3a

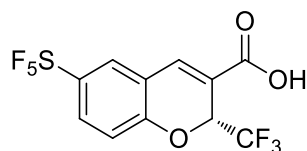


# HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.  | Formula (M)                                                    | Ion Formula                                                    | Measured m/z | Calc m/z | Error (ppm) |
|-------------|----------------------------------------------------------------|----------------------------------------------------------------|--------------|----------|-------------|
| <b>S-3a</b> | C <sub>11</sub> H <sub>6</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>5</sub> F <sub>8</sub> O <sub>3</sub> S | 368.9834     | 368.9837 | -0.7        |

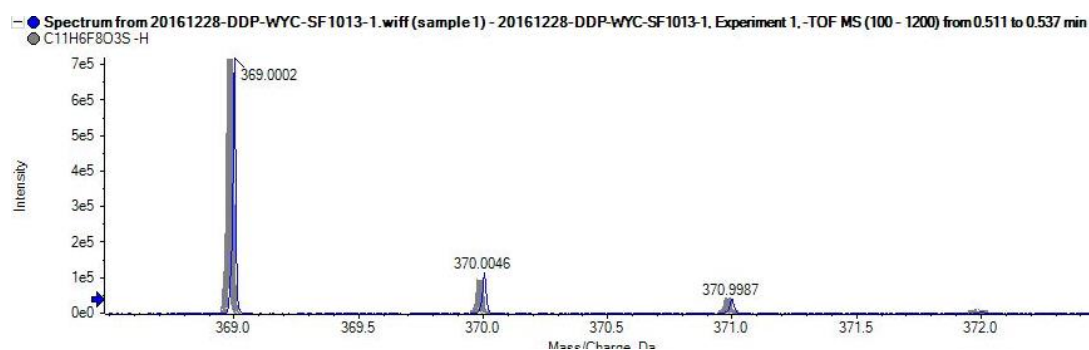


## R-3a

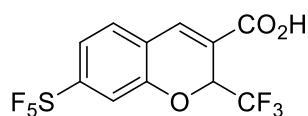


# HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.  | Formula (M)                                                    | Ion Formula                                                    | Measured m/z | Calc m/z | Error (ppm) |
|-------------|----------------------------------------------------------------|----------------------------------------------------------------|--------------|----------|-------------|
| <b>R-3a</b> | C <sub>11</sub> H <sub>6</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>5</sub> F <sub>8</sub> O <sub>3</sub> S | 369.0002     | 368.9837 | 44.8        |

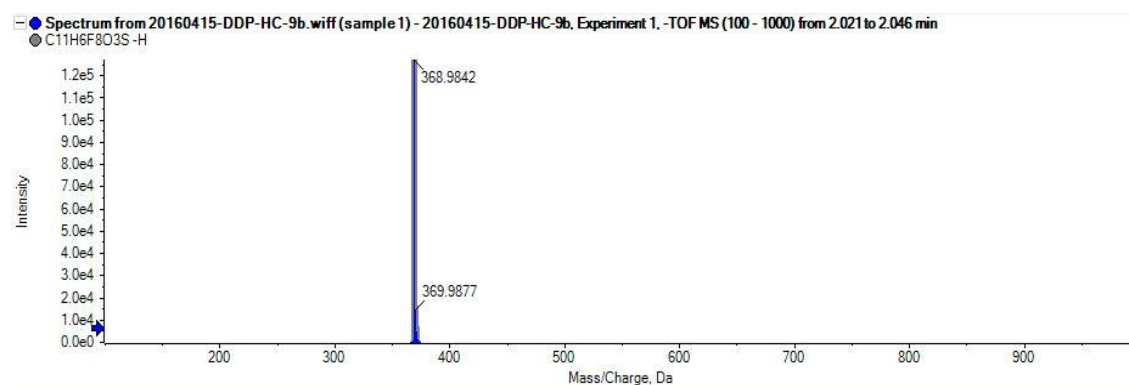


**(R,S)-3b**

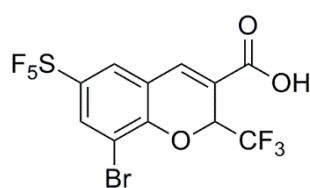


# HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.      | Formula (M)                                                    | Ion Formula                                                    | Measured m/z | Calc m/z | Error (ppm) |
|-----------------|----------------------------------------------------------------|----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-3b</b> | C <sub>11</sub> H <sub>6</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>5</sub> F <sub>8</sub> O <sub>3</sub> S | 368.9842     | 368.9837 | 1.4         |

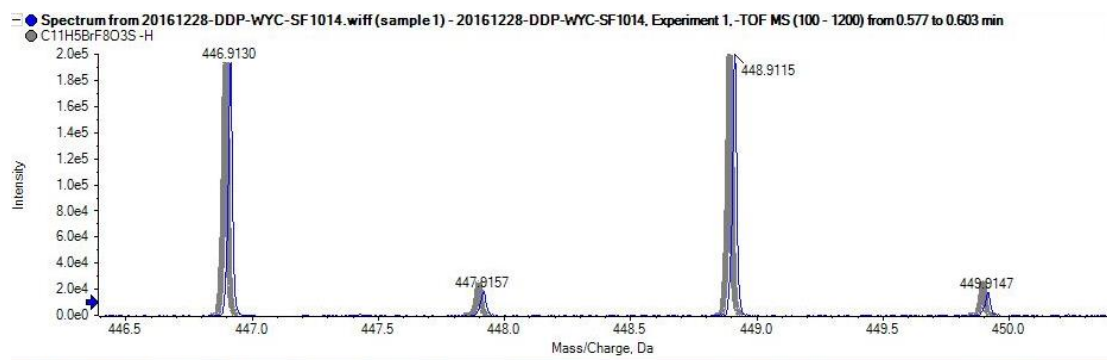


**(R,S)-7**

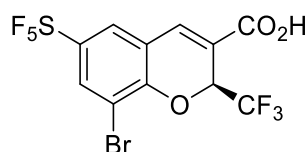


# HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.     | Formula (M)                                                      | Ion Formula                                                      | Measured m/z | Calc m/z | Error (ppm) |
|----------------|------------------------------------------------------------------|------------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-7</b> | C <sub>11</sub> H <sub>5</sub> BrF <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>4</sub> BrF <sub>8</sub> O <sub>3</sub> S | 446.9130     | 446.8942 | 42          |

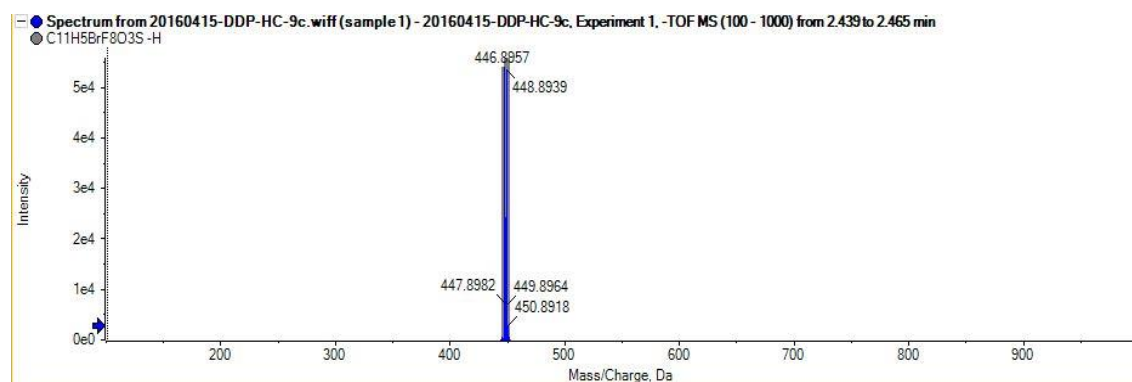


**S-7**

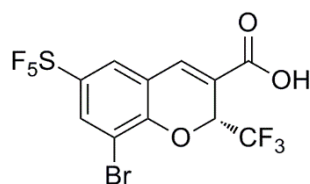


#### HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No. | Formula (M)                                                      | Ion Formula                                                      | Measured m/z | Calc m/z | Error (ppm) |
|------------|------------------------------------------------------------------|------------------------------------------------------------------|--------------|----------|-------------|
| <b>S-7</b> | C <sub>11</sub> H <sub>5</sub> BrF <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>4</sub> BrF <sub>8</sub> O <sub>3</sub> S | 446.8957     | 446.8942 | 3.3         |

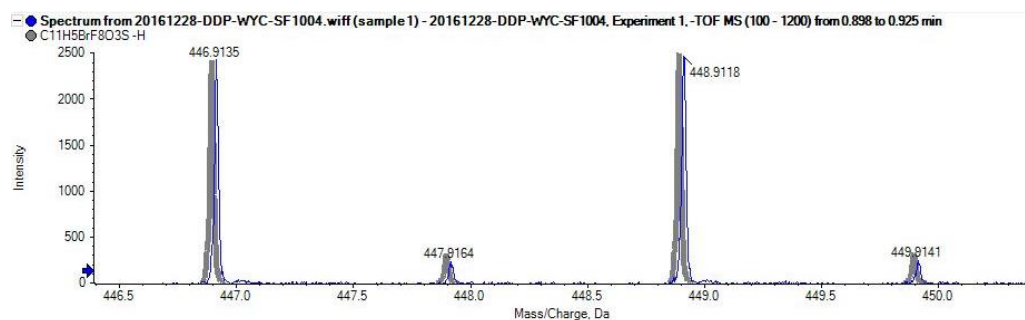


**R-7**

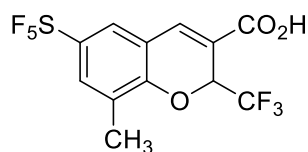


#### HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No. | Formula (M)                                                      | Ion Formula                                                      | Measured m/z | Calc m/z | Error (ppm) |
|------------|------------------------------------------------------------------|------------------------------------------------------------------|--------------|----------|-------------|
| <b>R-7</b> | C <sub>11</sub> H <sub>5</sub> BrF <sub>8</sub> O <sub>3</sub> S | C <sub>11</sub> H <sub>4</sub> BrF <sub>8</sub> O <sub>3</sub> S | 446.9134     | 446.8942 | 3.3         |

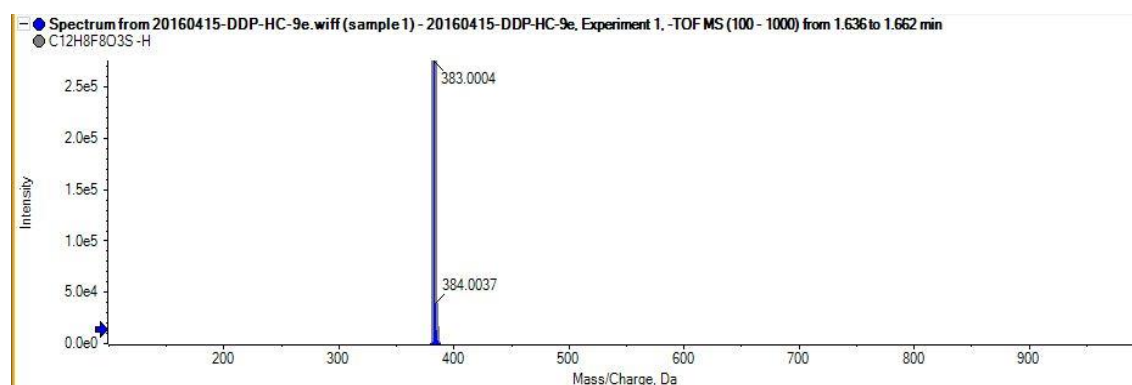


**(R,S)-11a**

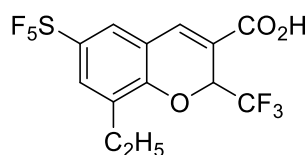


HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.       | Formula (M)                                                    | Ion Formula                                                    | Measured m/z | Calc m/z | Error (ppm) |
|------------------|----------------------------------------------------------------|----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-11a</b> | C <sub>12</sub> H <sub>8</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>12</sub> H <sub>7</sub> F <sub>8</sub> O <sub>3</sub> S | 383.0004     | 382.9994 | 2.8         |

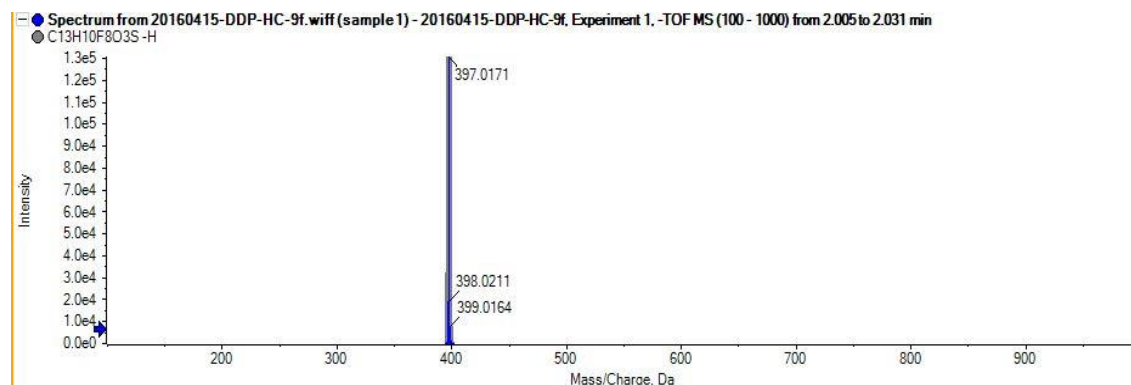


**(R,S)-11b**

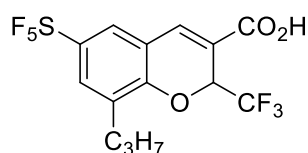


HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.       | Formula (M)                                                     | Ion Formula                                                    | Measured m/z | Calc m/z | Error (ppm) |
|------------------|-----------------------------------------------------------------|----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-11b</b> | C <sub>13</sub> H <sub>10</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>13</sub> H <sub>9</sub> F <sub>8</sub> O <sub>3</sub> S | 397.0171     | 397.0150 | 5.3         |

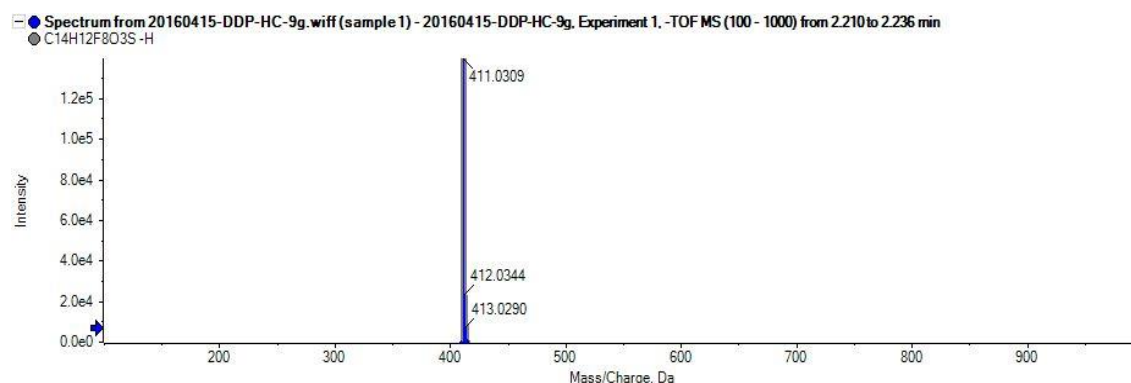


**(R,S)-11c**

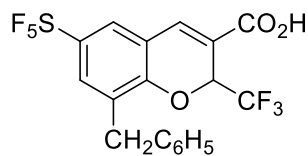


HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.       | Formula (M)                                                     | Ion Formula                                                     | Measured m/z | Calc m/z | Error (ppm) |
|------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-11c</b> | C <sub>14</sub> H <sub>12</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>14</sub> H <sub>11</sub> F <sub>8</sub> O <sub>3</sub> S | 411.0309     | 411.0307 | 0.5         |

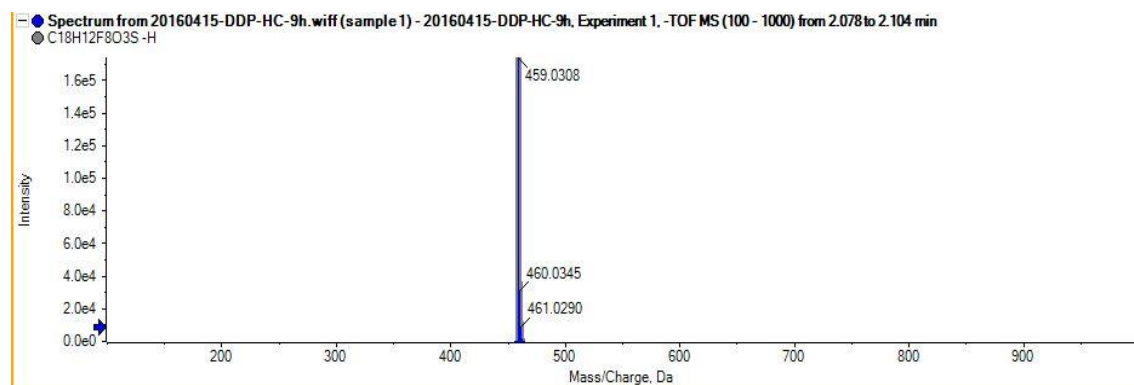


**(R,S)-11d**

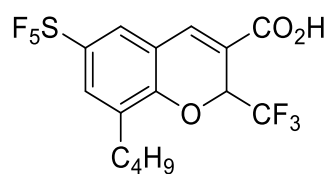


HIGH RESOLUTION MASS SPECTROMETRY REPORT

| Sample No.       | Formula (M)                                                     | Ion Formula                                                     | Measured m/z | Calc m/z | Error (ppm) |
|------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-11d</b> | C <sub>18</sub> H <sub>12</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>18</sub> H <sub>11</sub> F <sub>8</sub> O <sub>3</sub> S | 459.0308     | 459.0307 | 0.3         |

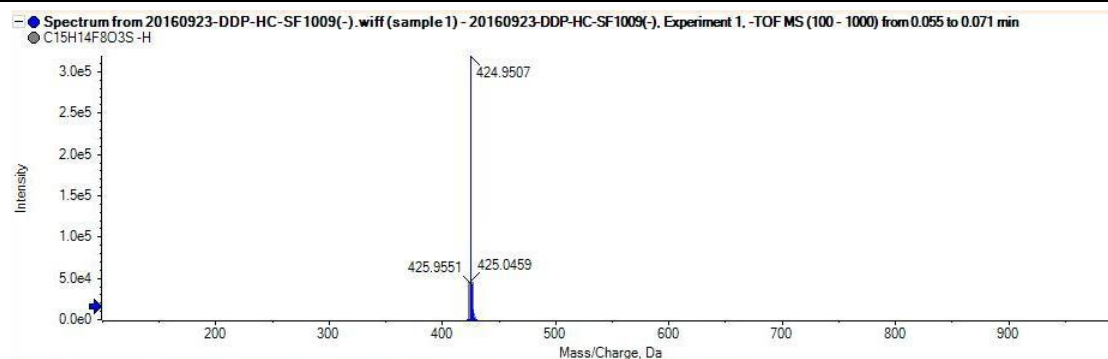


**(R,S)-11e**



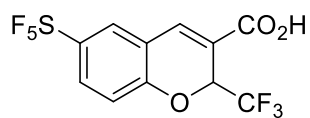
#### HIGH RESOLUTION MASS SPECTROMETRY REPORT

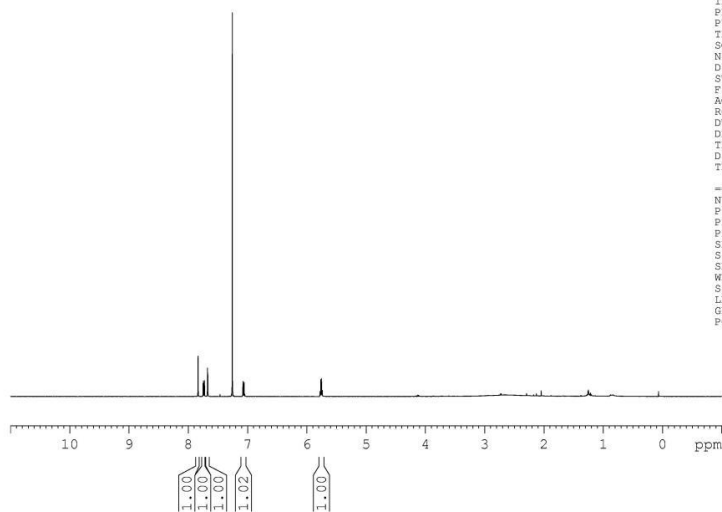
| Sample No.       | Formula (M)                                                     | Ion Formula                                                     | Measured m/z | Calc m/z | Error (ppm) |
|------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|--------------|----------|-------------|
| <b>(R,S)-11e</b> | C <sub>15</sub> H <sub>14</sub> F <sub>8</sub> O <sub>3</sub> S | C <sub>15</sub> H <sub>13</sub> F <sub>8</sub> O <sub>3</sub> S | 425.0459     | 425.0463 | -1.0        |



**<sup>1</sup>H NMR**

**(R,S)-3a**





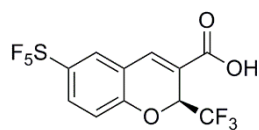
|         |                |      |
|---------|----------------|------|
| NAME    | 111111         |      |
| EXPNO   | 23             |      |
| PROCNO  |                |      |
| Date_   | 20160325       |      |
| Time    | 22.18          |      |
| INSTRUM | Spect          |      |
| PROBHD  | 5 mm PABBO BB- |      |
| PULPROG | zg30           |      |
| TD      | 65536          |      |
| SOLVENT | CDCl3          |      |
| NS      | 16             |      |
| DS      | 2              |      |
| SWH     | 10330.578      | Hz   |
| FTIDRS  | 0.157632       | Hz   |
| AQ      | 3.1719923      | sec  |
| RG      | 203            |      |
| DW      | 203            |      |
| DE      | 6.50           | usec |
| TE      | 295.4          | K    |
| D1      | 1.00000000     | sec  |
| TD0     | 1              |      |

```

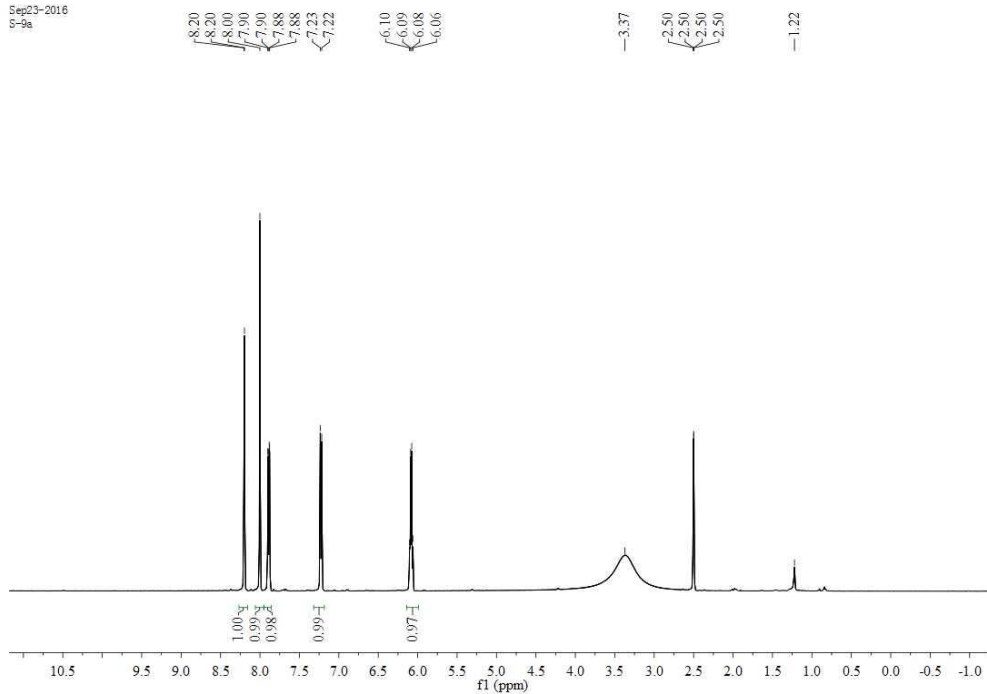
NUC1                      1H
P1                        14.00 usec
PL1                       2.50 dB
PL1W                     13.02359581 W
SFO1                    500.1330885 MHz
SI                         32768
SF                     500.1300227 MHz
WDW                       EM
SSB                        0
LB                        0.30 Hz
GB                        0
PC                         1.00

```

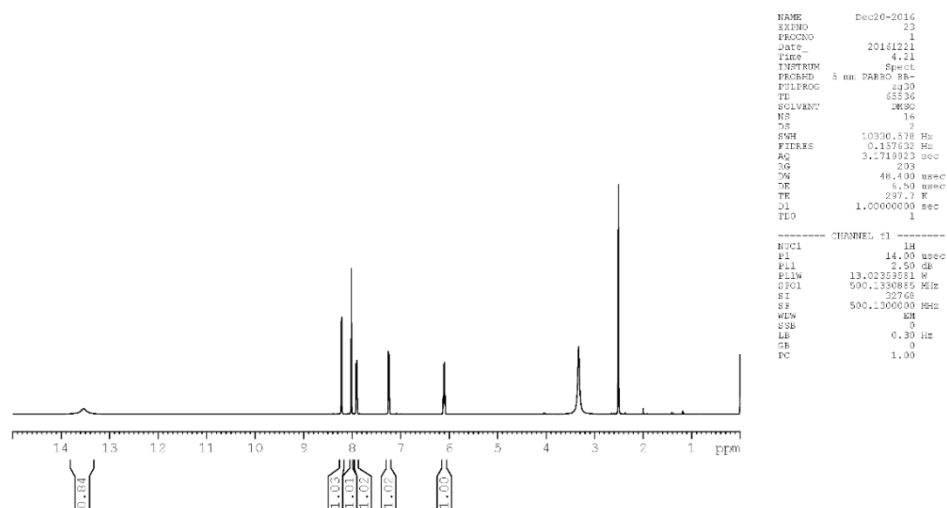
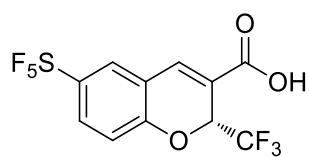
**S-3a**



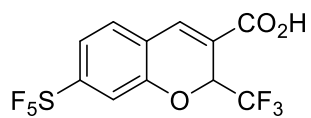
Sep23-2016  
S-9a



***R-3a***



**(R,S)-3b**



9b

<sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) of compound 9b. The spectrum shows peaks at 7.82, 7.43, 7.41, 7.37, 7.35, 7.26, 5.75, 5.74, and 1.25 ppm. Integration values are 1.00, 2.00, 1.05, and 1.00.

```

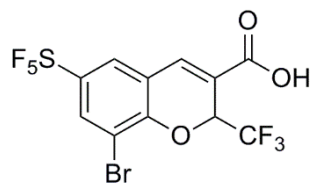
      _____
     /         \
    /             \
   /                 \
  /                     \
 /                         \
/                             \
_____

BRUKER

NAME          111111
EXPNO         26
PROCNO        1
F2          20160325
Time          23.22
INSTRUM       Spect
PROBHD        5 mm PABBO BB
PULPROG       zgpg30
SFO1          240
RG            6536
SOLVENT       CDCl3
NS            16
DS            2
SWH           10330.578 Hz
AQ            0.15762 Hz
DELTA         3.171993 sec
RG            203
WDW            48.400 usec
GB            0.50 usec
PC            295.4 K
TE            1.0000000 sec
D1            1
TDD           1
===== CHANNEL f1 =====
NUC1
P1            14.00 usec
PL1           2.50 dB
PL1W          13.02389881 MHz
SFO1          500.1330885 MHz
SF           32768
SFO2          500.1330226 MHz
NUC2          DM
NSB           0.00 usec
WDW           0.00 Hz
GB            0
PC            1.00

```

**(R,S)-7**



SF-1014

13.576  
13.544  
13.518  
13.499  
13.634  
13.601  
13.509

8.280  
8.273  
8.269  
8.263  
8.253

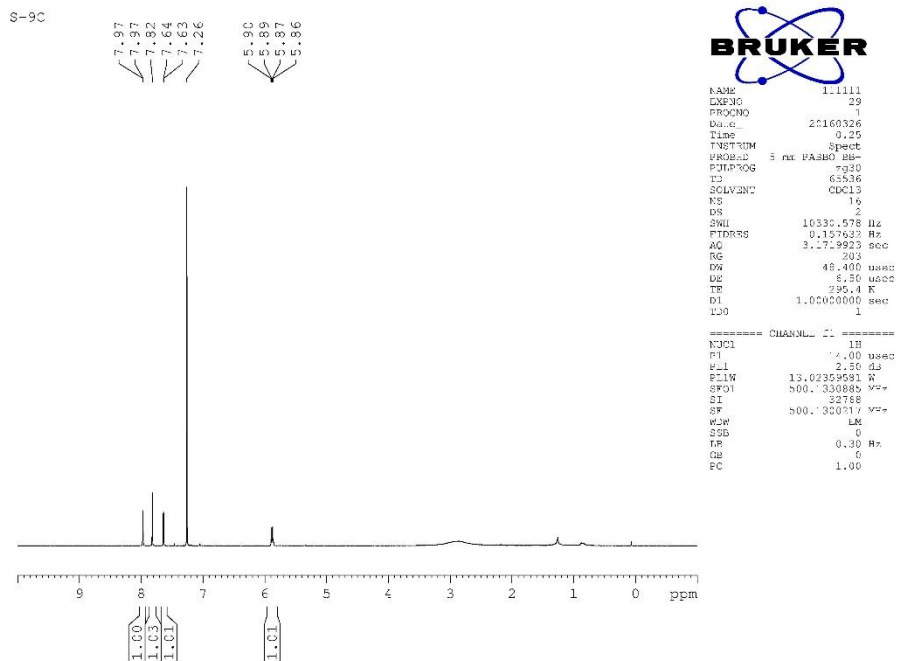
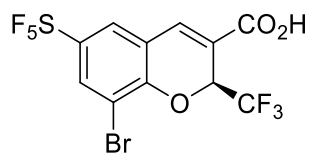
6.301  
6.253

3.344  
2.511  
2.506  
2.502

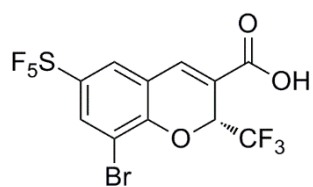
1.03  
1.94  
1.02  
1.00

ppm

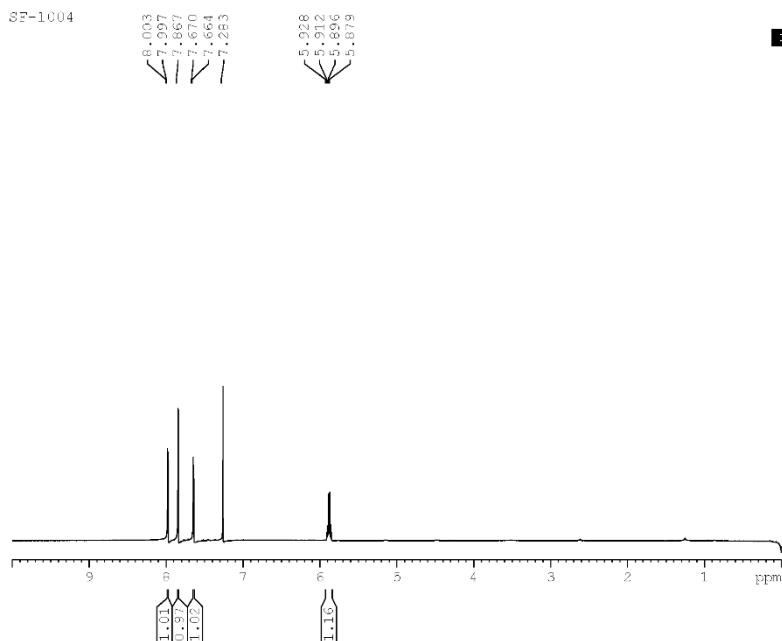
S-7



R-7



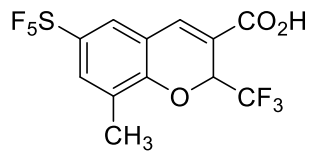
SP-1004



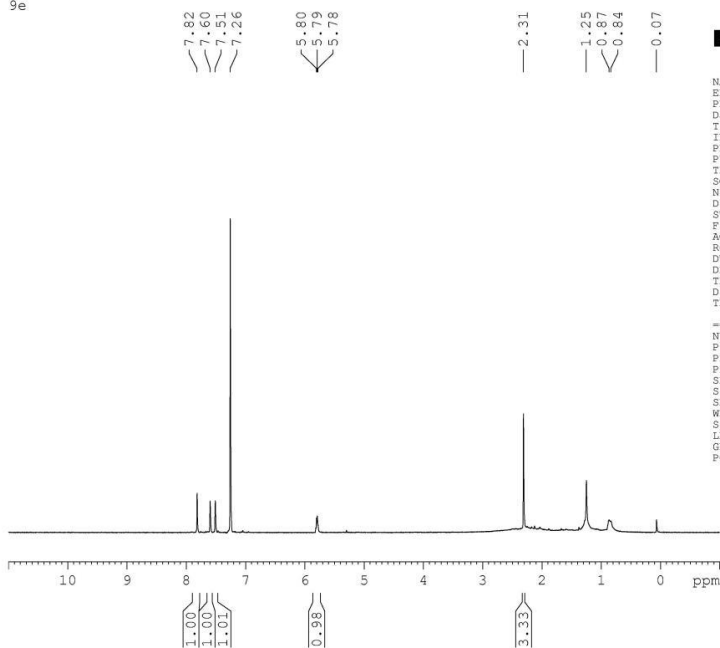
NAME Dec29-2016  
 EXPNO 6  
 PROCNO 1  
 Date\_ 20181229  
 Time 9.21  
 INSTRUM spect  
 PROBRD 5 mm DDZ-1  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 8278.146 Hz  
 FIDRES 0.126314 Hz  
 AQ 3.9584243 sec  
 RG 456.1  
 DW 50.400 usec  
 DE 1.50 usec  
 TE 295.2 K  
 D1 1.00000000 sec  
 TDO 1

----- CHANNEL f1 -----  
 NUC1 1H  
 P1 12.56 usec  
 PL1 0.00 dB  
 PL1W 10.8764866 W  
 SFO1 400.1324710 MHz  
 SI 32768  
 SF 400.1300094 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

(R,S)-11a



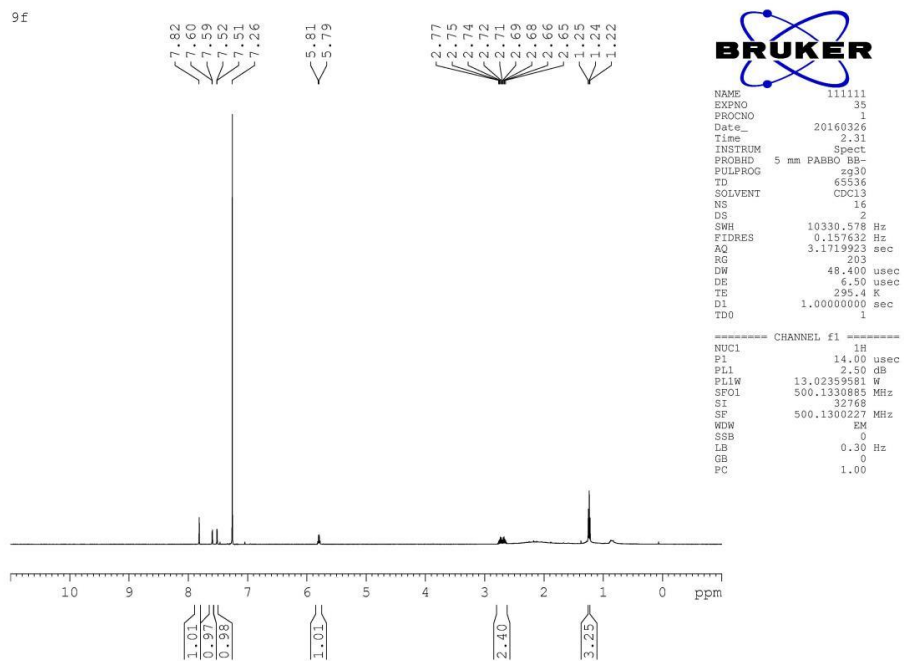
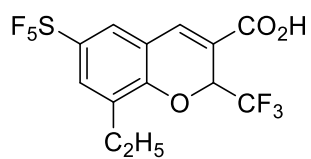
9e



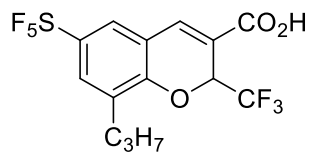
NAME 111111  
 EXPNO 32  
 PROCNO 1  
 Date\_ 20160326  
 Time 1.28  
 INSTRUM Spect  
 PROBRD 5 mm PABBO BB-  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10330.578 Hz  
 FIDRES 0.157632 Hz  
 AQ 3.1719923 sec  
 RG 203  
 DW 48.400 usec  
 DE 6.50 usec  
 TE 295.4 K  
 D1 1.00000000 sec  
 TDO 1

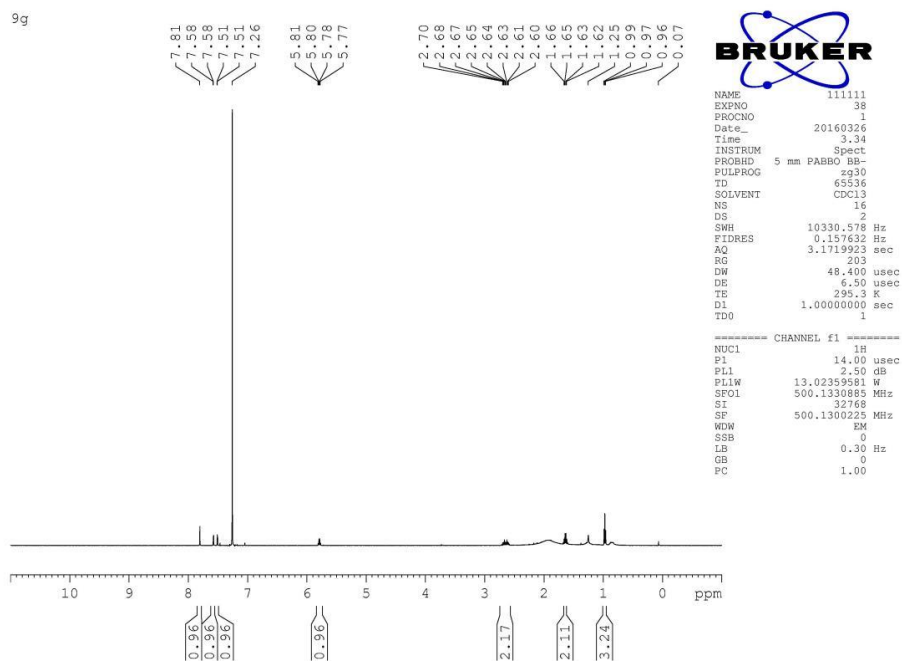
----- CHANNEL f1 -----  
 NUC1 1H  
 P1 14.00 usec  
 PL1 2.50 dB  
 PL1W 13.02359581 W  
 SFO1 500.1330885 MHz  
 SI 32768  
 SF 500.1300221 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

**(R,S)-11b**

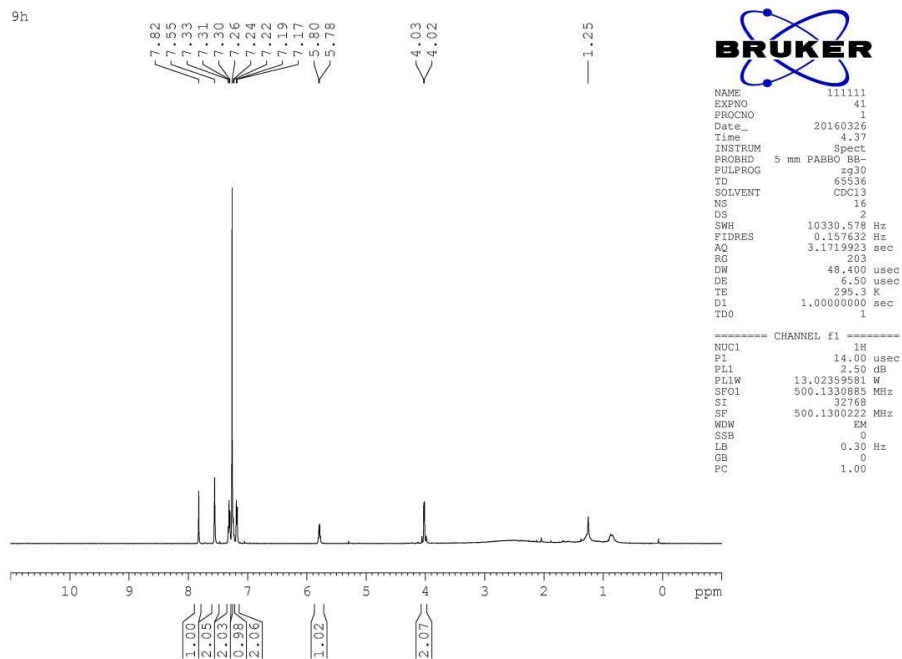
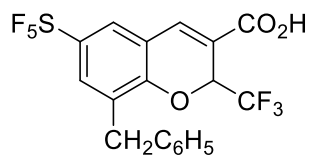


**(R,S)-11c**

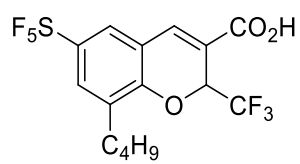




(R,S)-11d



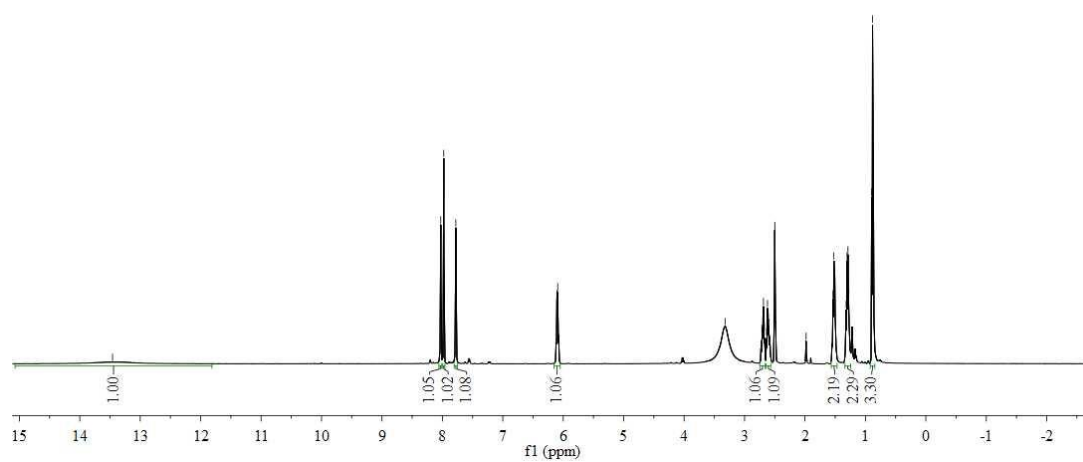
**(R,S)-11e**



Jun17-2016  
sf1009

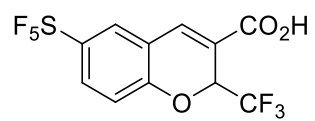
-13.46

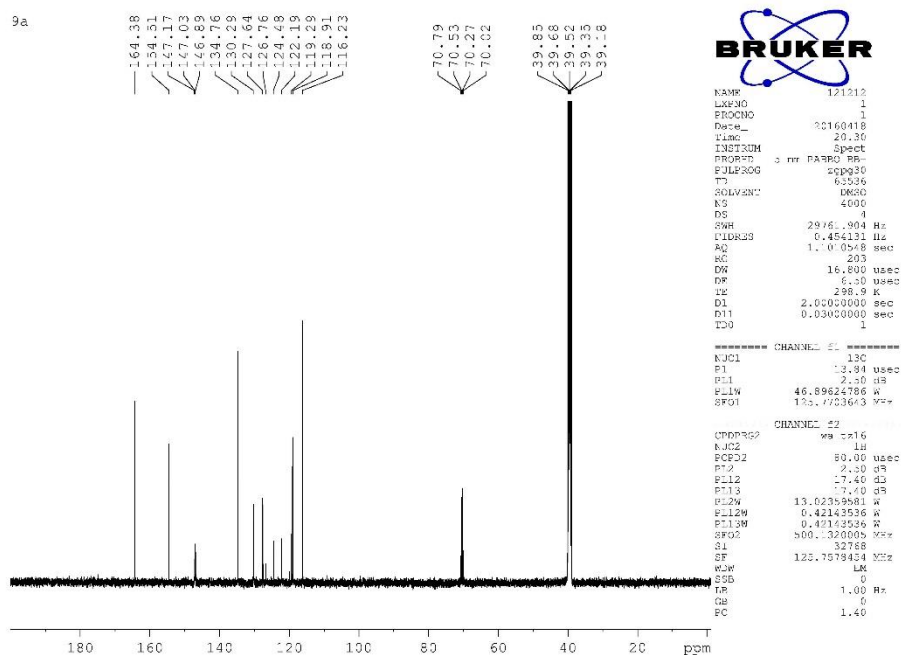
8.03 8.03 7.98 7.78 7.78 6.11 6.09 3.32 2.73 2.71 2.70 2.69 2.67 2.64 2.62 2.61 2.59 2.58 2.50 2.50 1.98 1.54 1.52 1.51 1.32 1.30 1.29 1.27 0.90 0.88 0.87



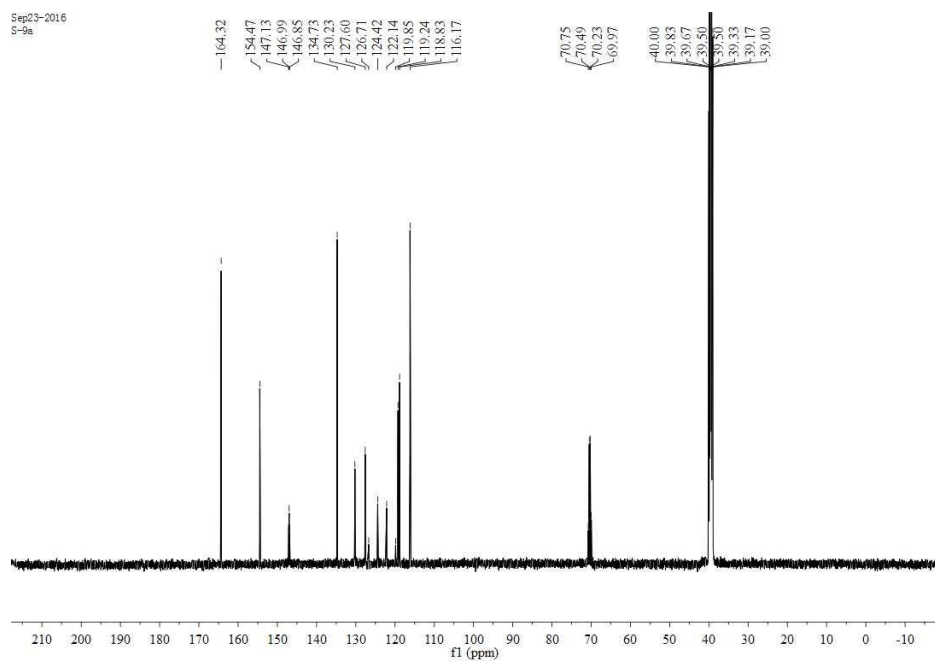
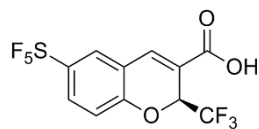
**<sup>13</sup>C NMR**

**(R,S)-3a**

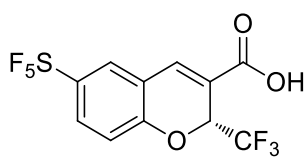




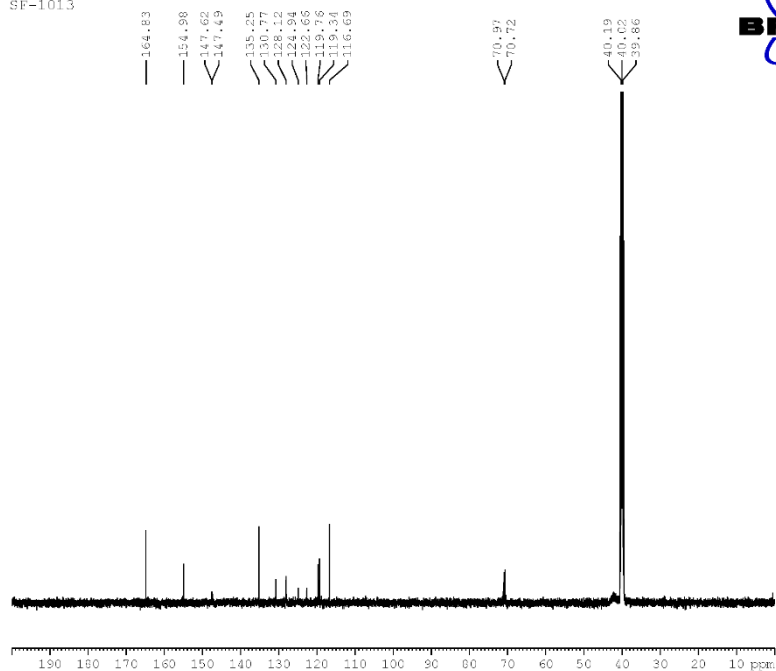
S-3a



# **R-3a**



SF-1013



```

NAME      Dec20-2016
EXPNO     2
PROCNO    1
Date_     20161221
Time      4.19
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         65536
SOLVENT   DMSO
NS         2048
DS         4
SWH        29761.904 Hz
FIDRES     0.454131 Hz
AQ         1.1010548 sec
RG         293
DW         16.800 usec
DE         6.50 usec
TE         298.2 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0        1
  
```

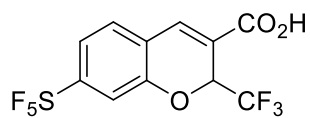
```

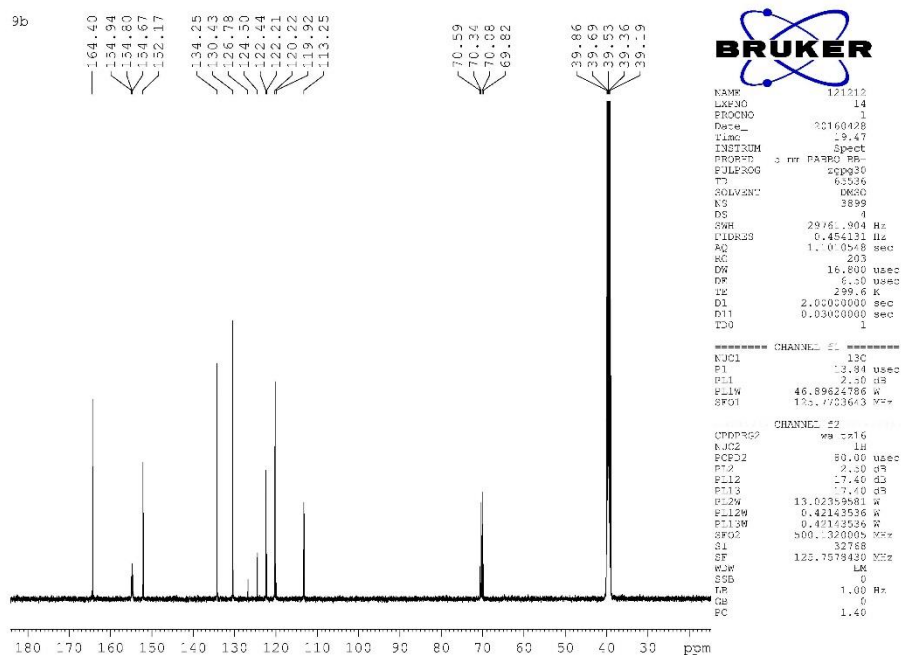
===== CHANNEL f1 =====
NUC1       13C
P1         12.84 usec
PL1        2.50 dB
PL1W       46.89624786 W
SFO1       125.7703643 MHz
  
```

```

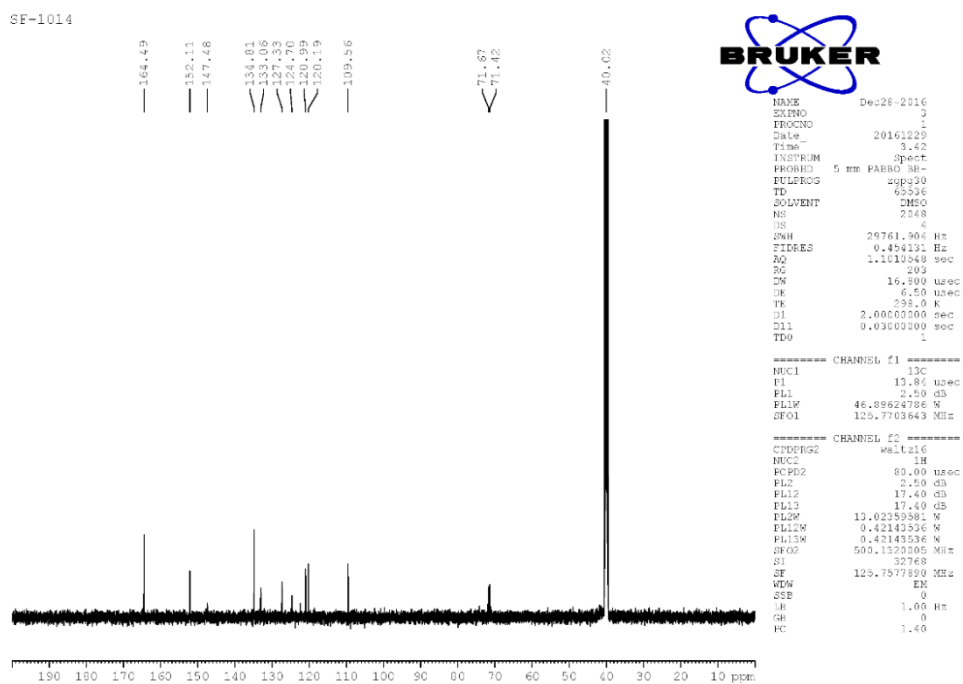
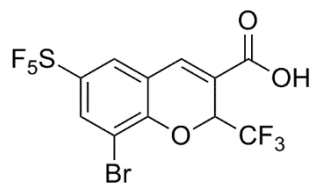
===== CHANNEL f2 =====
CPDPRG2    waltz16
NUC2       1H
P1         1H
P1P2       80.00 usec
PL2        2.50 dB
PL12       17.40 dB
PL13       17.40 dB
PL1W       13.02359581 W
PL1CW      0.42140536 W
PL1SW      0.42140536 W
SFO2       500.1320095 MHz
SI         32768
SF         125.7577890 MHz
WDW        EM
SSB         0
LB         1.00 Hz
GB         0
PC         1.40
  
```

# **(R,S)-3b**

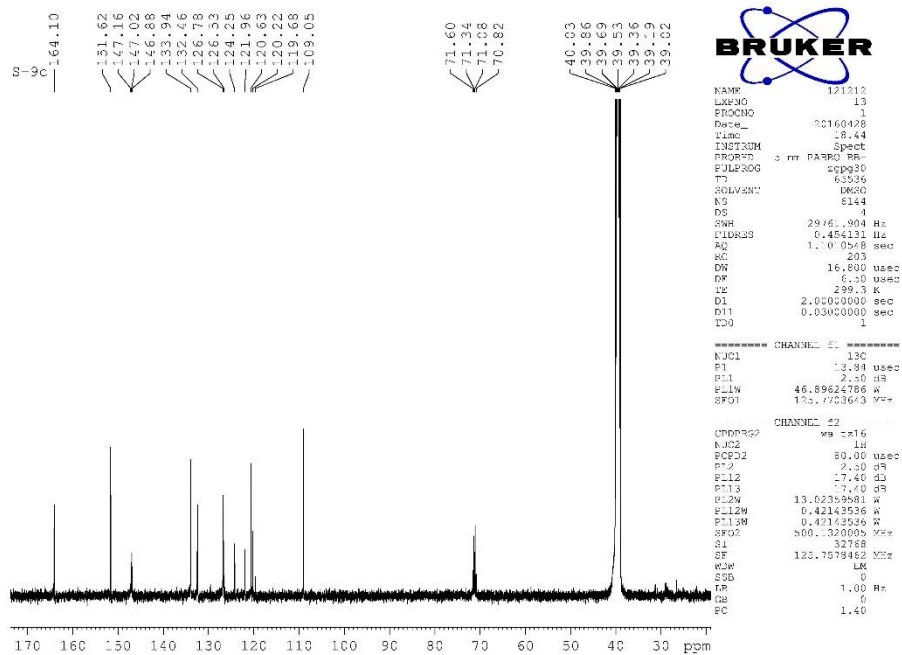
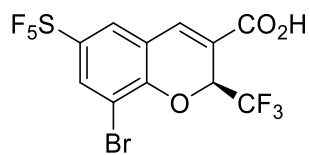




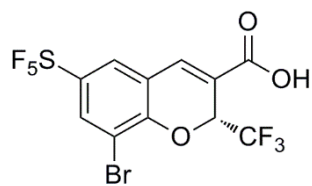
(R,S)-7



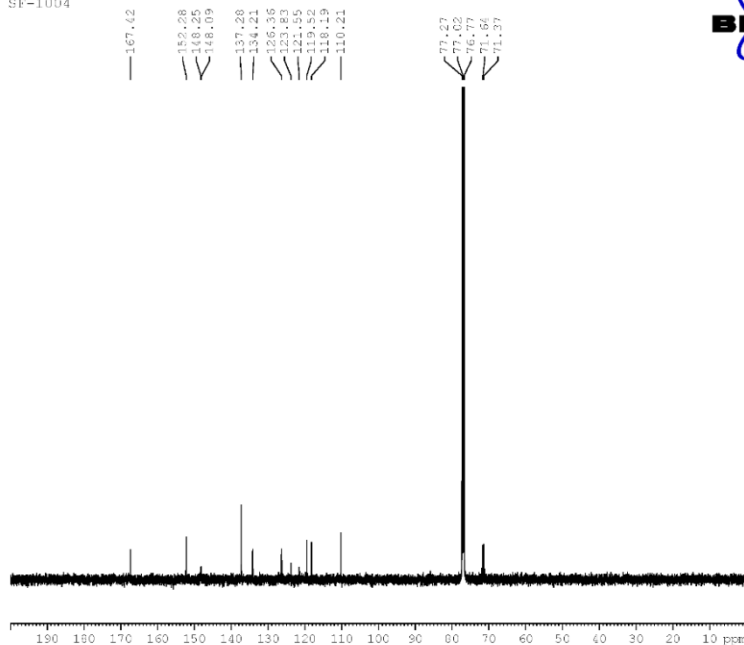
S-7



R-7



SF-1004

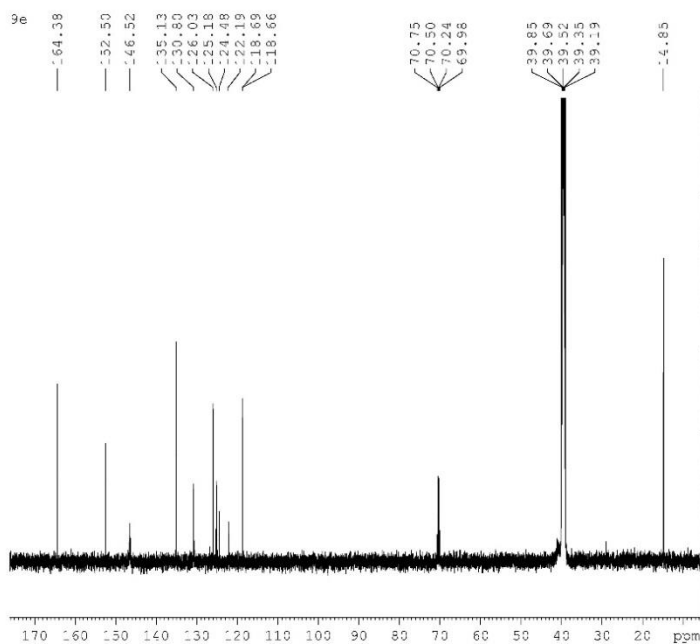
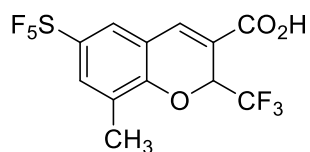


NAME Dec28-2016  
EXPNO 5  
PROCNO 1  
Date\_ 20161220  
Time\_ 5.39  
INSTRUM Spect  
PROBHD 5 mm PABBO BB-  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 2048  
DS 2  
SWH 29761.904 Hz  
FIDRES 0.454191 Hz  
AQ 1.1010048 sec  
RG 203  
CW 16.800 usec  
DE 6.50 usec  
TE 298.0 K  
D1 2.0000000 sec  
D11 0.0300000 sec  
TD0 1

===== CHANNEL f1 =====  
NUC1 13C  
P1 13.84 usec  
PL1 2.50 dB  
PL1W 46.89624786 W  
SFO1 125.7703643 MHz

===== CHANNEL f2 =====  
CPDPRG2 waltz16  
NUC2 1H  
PCPD2 80.00 usec  
PL2 2.50 dB  
PL12 17.40 dB  
PL13 17.40 dB  
PL1W 13.02359381 W  
PL12W 0.42143536 W  
PL13W 0.42143536 W  
SFO2 500.1320005 MHz  
SI 32768  
SF 125.7577890 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

(R,S)-11a

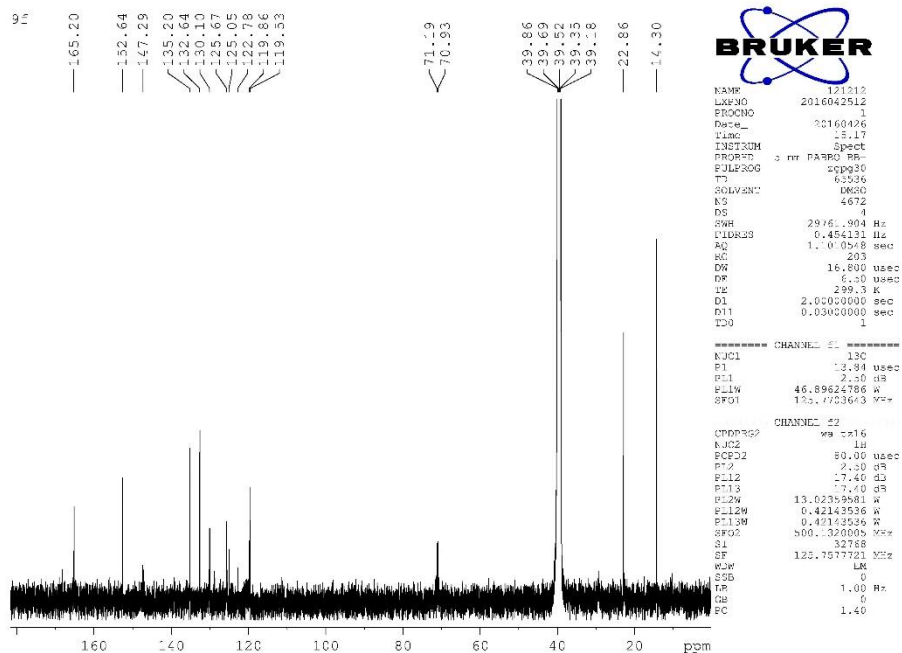
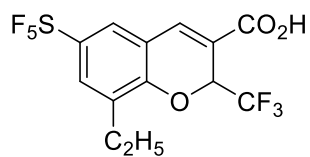


NAME 121212  
EXPNO 2  
PROCNO 1  
Date\_ 20160419  
Time\_ 9.57  
INSTRUM Spect  
PROBHD 5 mm PABBO BB-  
PULPROG zgpg30  
TD 65536  
SOLVENT DMSO  
NS 6144  
DS 4  
SWH 29761.904 Hz  
FIDRES 0.454191 Hz  
AQ 1.1010048 sec  
RG 203  
CW 16.800 usec  
DE 6.50 usec  
TE 298.0 K  
D1 2.0000000 sec  
D11 0.0300000 sec  
TD0 1

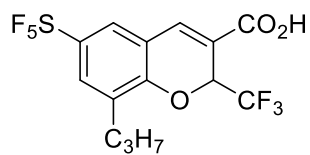
===== CHANNEL f1 =====  
NUC1 13C  
P1 13.84 usec  
PL1 2.50 dB  
PL1W 46.89624786 W  
SFO1 125.7703643 MHz

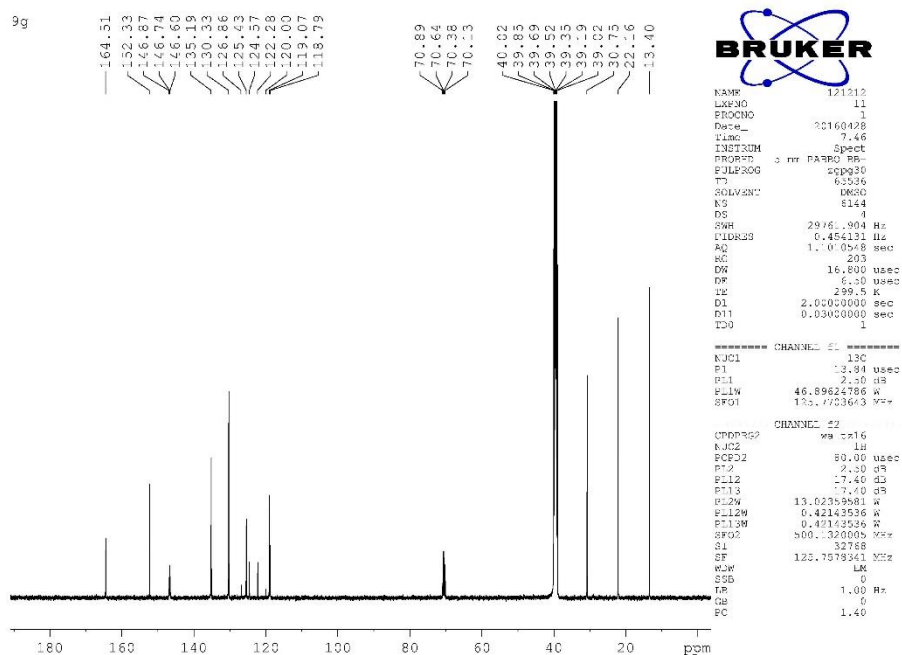
===== CHANNEL f2 =====  
CPDPRG2 waltz16  
NUC2 1H  
PCPD2 80.00 usec  
PL2 2.50 dB  
PL12 17.40 dB  
PL13 17.40 dB  
PL1W 13.07359381 W  
PL12W 0.42143536 W  
PL13W 0.42143536 W  
SFO2 500.1320005 MHz  
SI 32768  
SF 125.7578499 MHz  
WDW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 1.40

**(R,S)-11b**

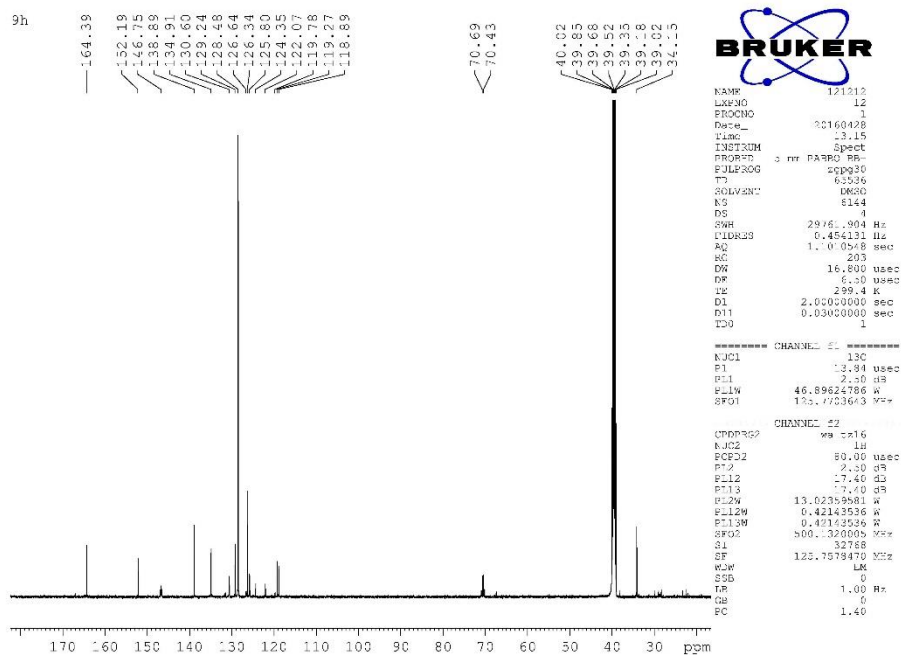
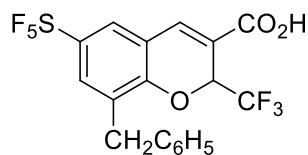


**(R,S)-11c**

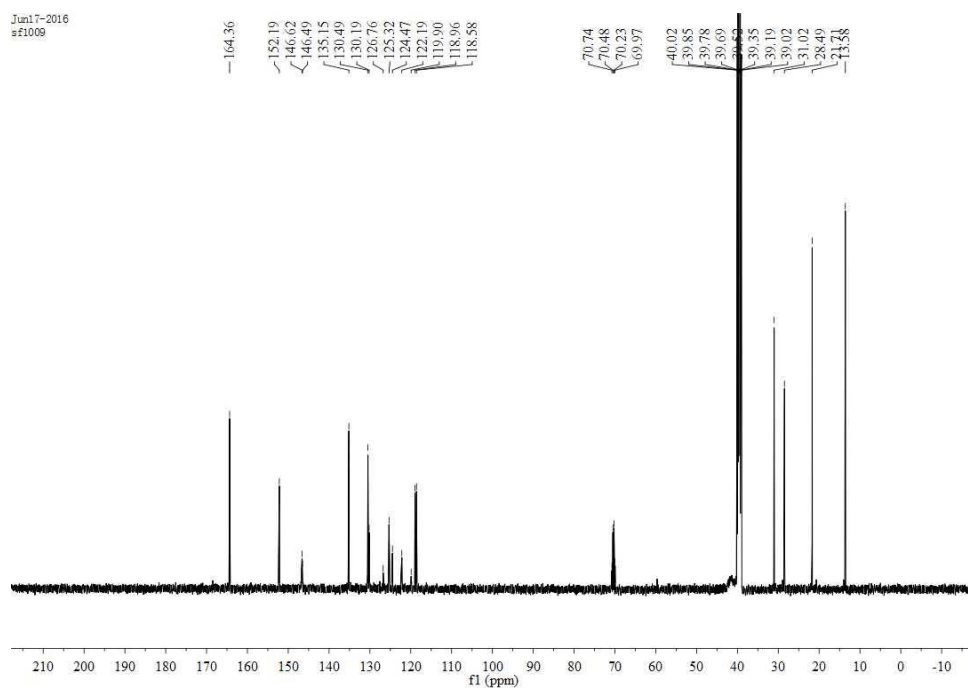
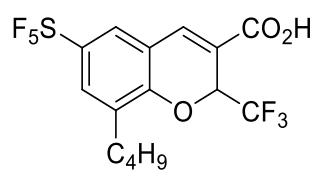




(R,S)-11d

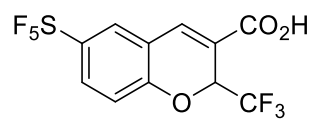


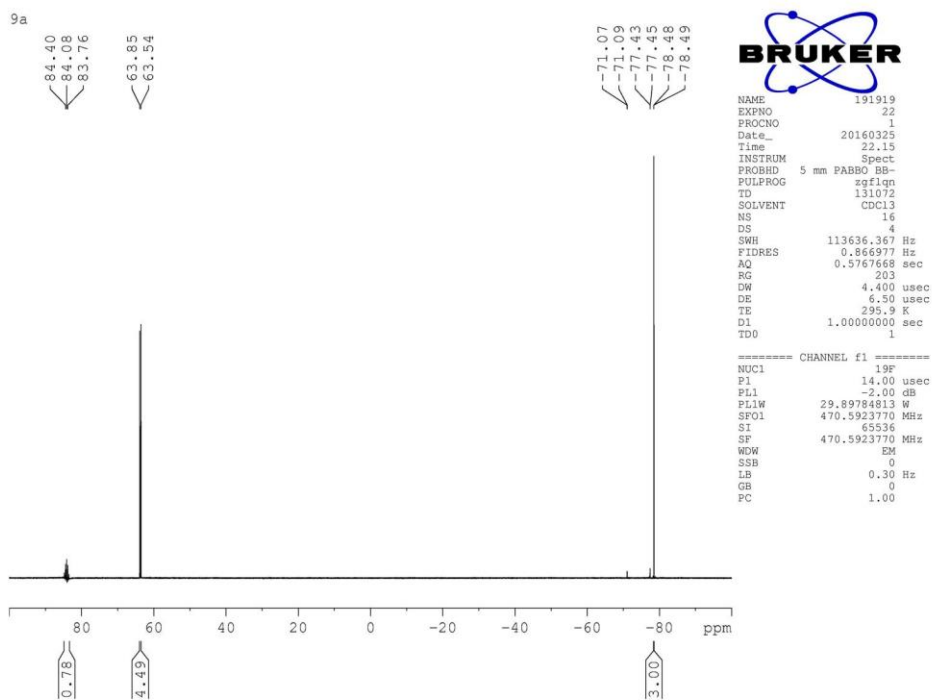
**(R,S)-11e**



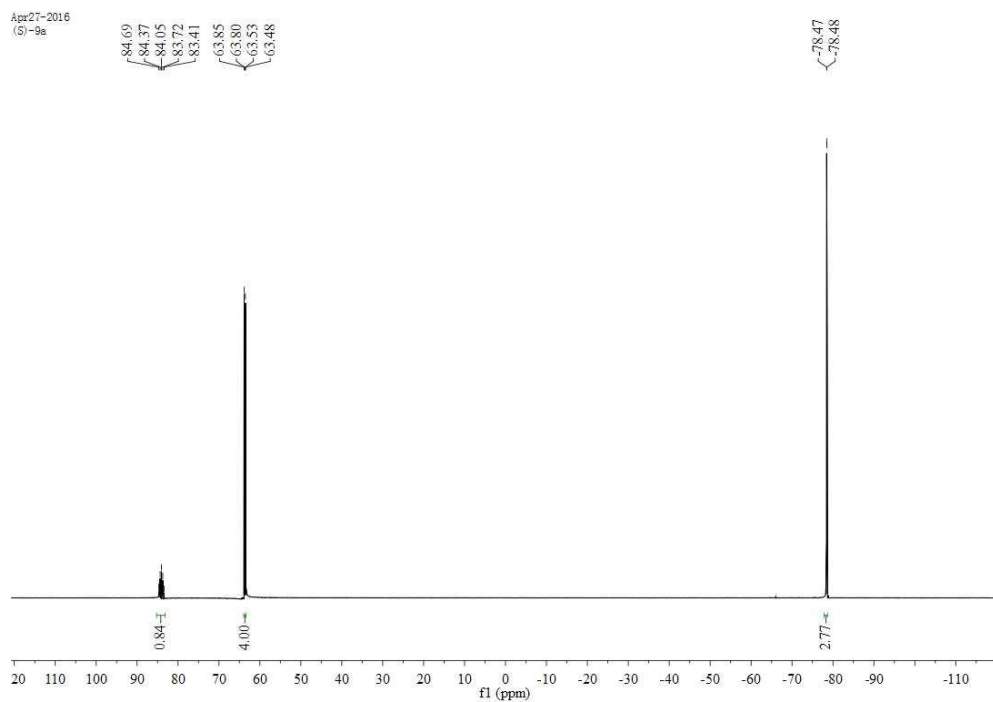
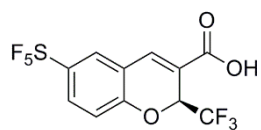
**<sup>19</sup>F NMR**

**(R,S)-3a**

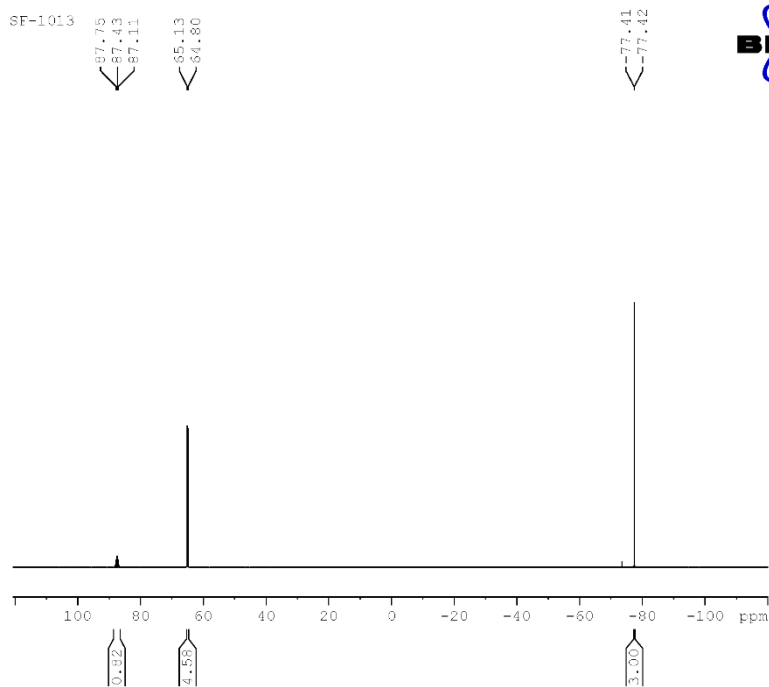
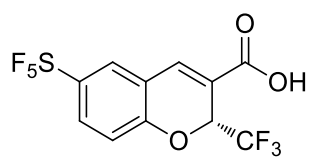




### S-3a



**R-3a**

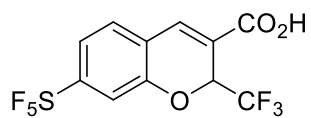


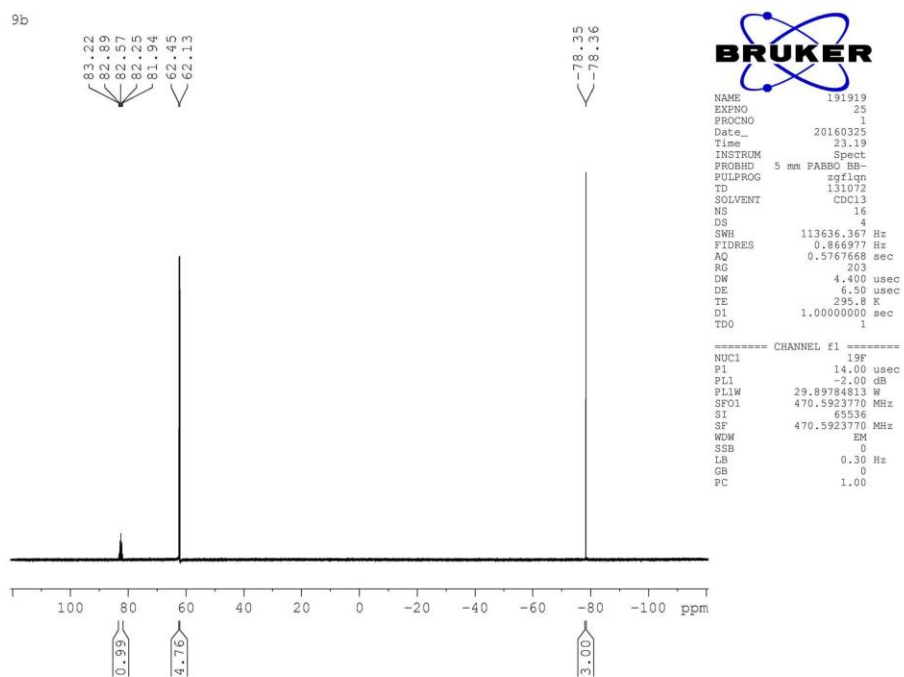
```

NAME      Dec20-2016
EXPNO     21
PROCNO    1
Date_     20161221
Time      2.29
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         131072
SOLVENT   DMSO
NS         16
DS         4
SWH        113636.367 Hz
FIDRES     0.166277 Hz
AQ         0.1767665 sec
RG         203
RW         4.400 usec
DE         6.50 usec
TE         298.0 K
DQ         1.00000000 sec
TDC        1

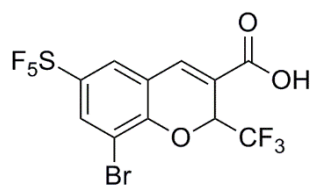
===== CHANNEL f1 =====
NUC1       19F
P1         14.00 usec
PL1        -2.00 dB
PL12       23.80784613 dB
SFO1       470.5923770 MHz
SI         65536
SF         470.5923770 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```

**(R,S)-3b**

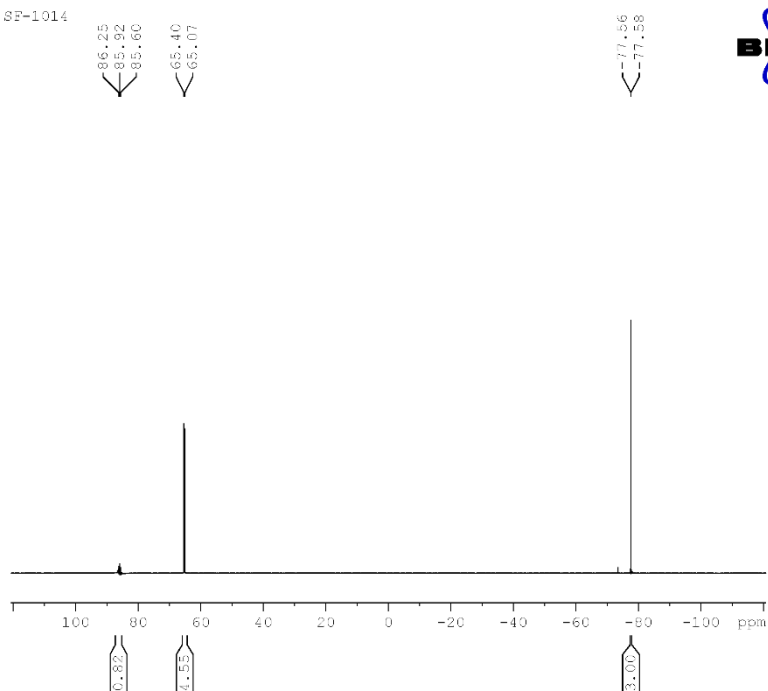




**(R,S)-7**



8F-1014

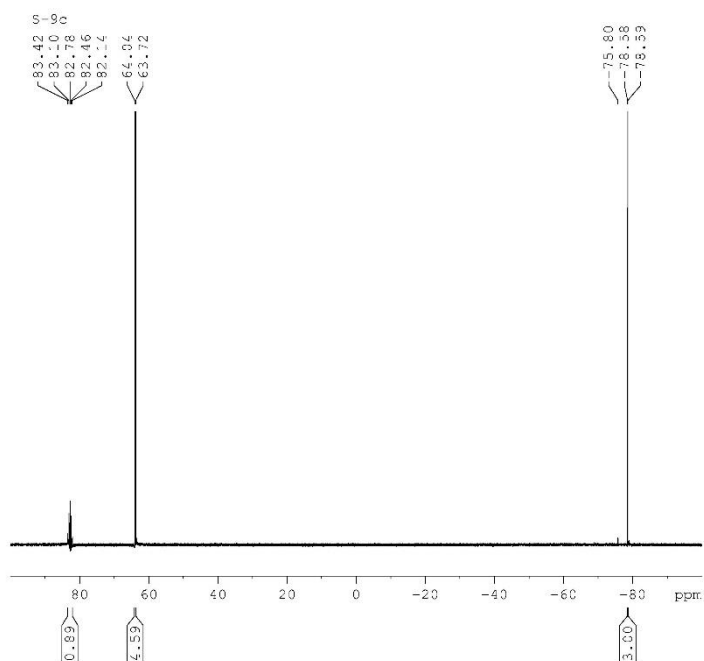
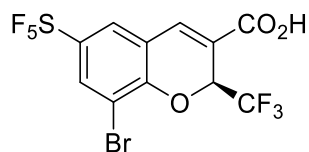


```

NAME      Des28-2016
EXPNO     4
PROCNO    1
Date_     20161229
Time      3.44
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         131072
SOLVENT   DMSO
NS         16
DS         4
SWH        113636.367 Hz
FIDRES     0.966977 Hz
AQ         0.5767668 sec
RG         203
DW         4.400 usec
DE         6.50 usec
TE         297.4 K
D1         1.00000000 sec
TDO        1

===== CHANNEL f1 =====
NUC1       19F
P1         14.00 usec
PL1        -2.00 dB
PL12       23.89784613 W
SFO1       470.5923770 MHz
SI         65536
SF         470.5923770 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```

S-7

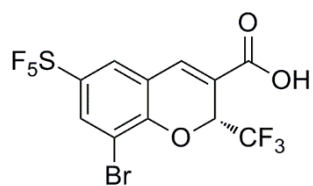


```

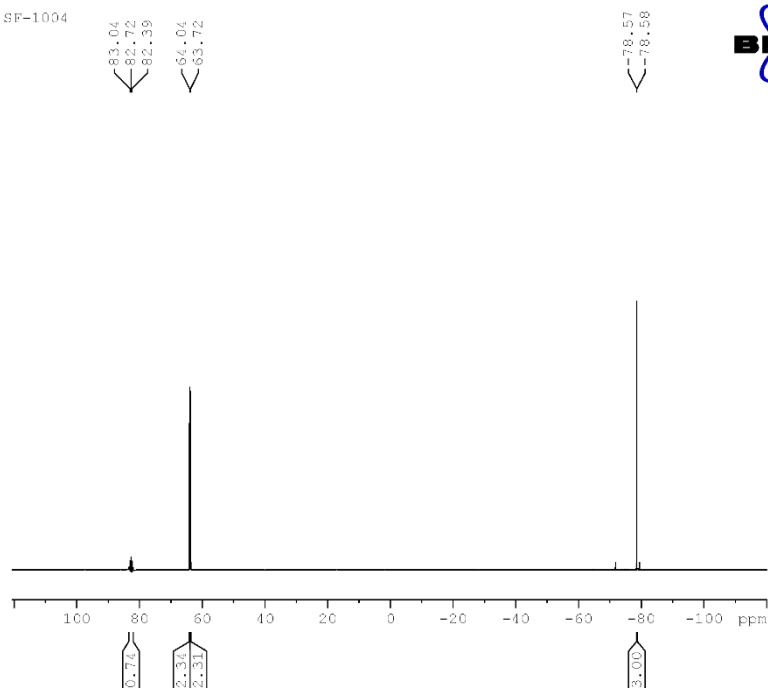
NAME      191919
EXPNO     28
PROCNO    1
Date_     20160326
Time      0.22
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         131072
SOLVENT   CDCl3
NS         16
DS         4
SWH        113636.367 Hz
FIDRES     0.866977 Hz
AQ         0.5767668 sec
RG         203
DW         4.400 usec
DE         6.50 usec
TE         295.9 K
D1         1.00000000 sec
TDO        1

===== CHANNEL f1 =====
NUC1       19F
P1         14.00 usec
PL1        -2.00 dB
PL12       23.89784613 W
SFO1       470.5923770 MHz
SI         65536
SF         470.5923770 MHz
WDW        EM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```

**R-7**



SF-1004

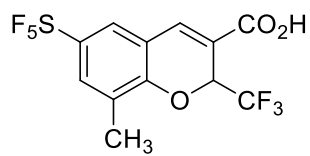


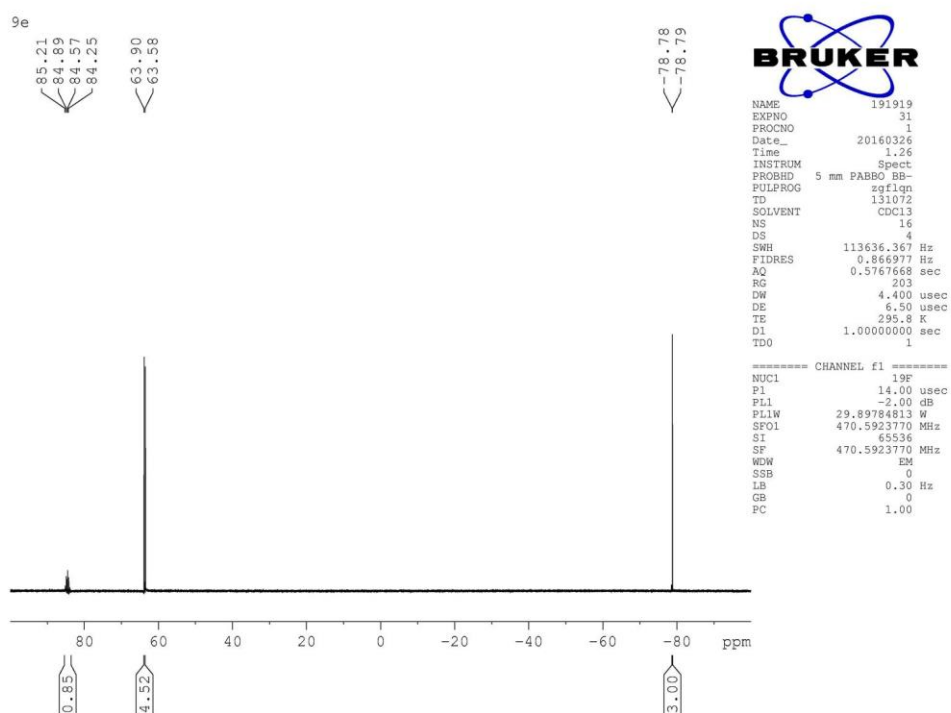
```

NAME      Des28-2016
EXPNO     6
PROCNO    1
Date_     20161229
Time      8.40
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zgpg30
TD         131072
SOLVENT   CDCl3
NS         16
DS         4
SWH        113636.367 Hz
FIDRES     0.366377 Hz
AQ         0.5787668 sec
RG          203
DS          4.400 usec
DE         6.50 usec
TE         297.4 K
DL         1.00000000 sec
TDC        1

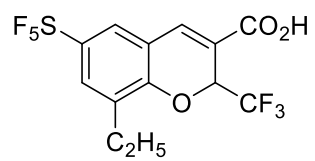
===== CHANNEL f1 =====
NUC1       13C
P1         14.00 usec
PL1        -2.00 dB
PL12       19.8978413 dB
SFO1       470.5923710 MHz
EL         85536
SF         470.5923710 MHz
WDW        RM
SSB        0
LB         0.30 Hz
GB         0
PC         1.00
  
```

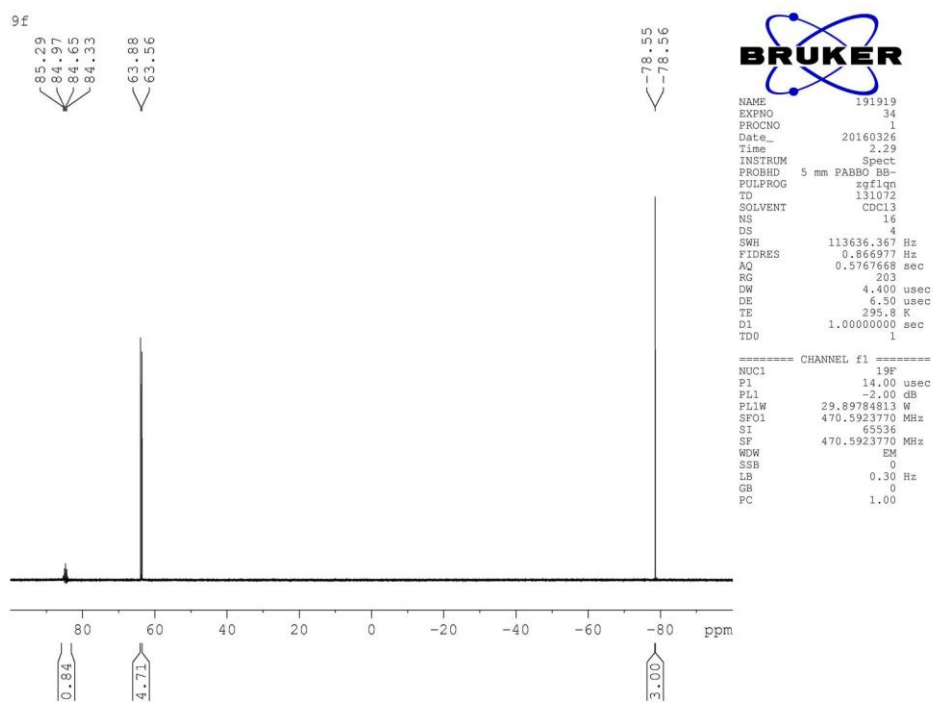
**(R,S)-11a**



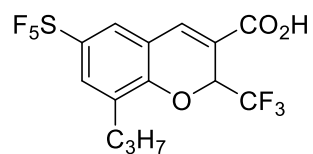


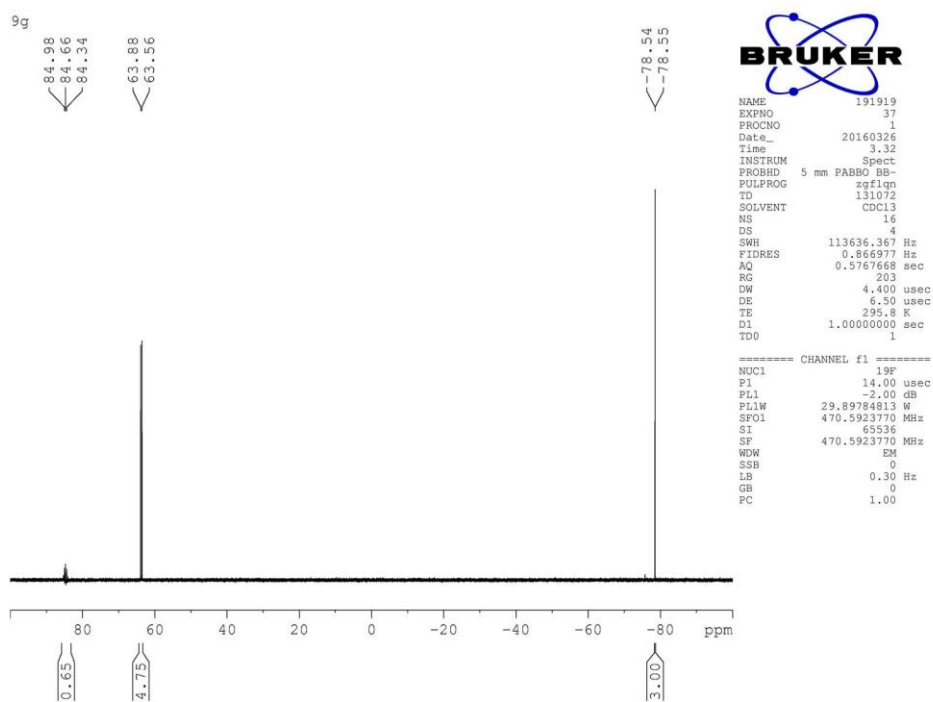
**(R,S)-11b**



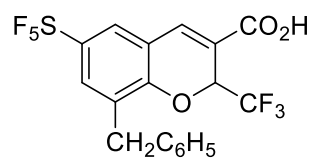


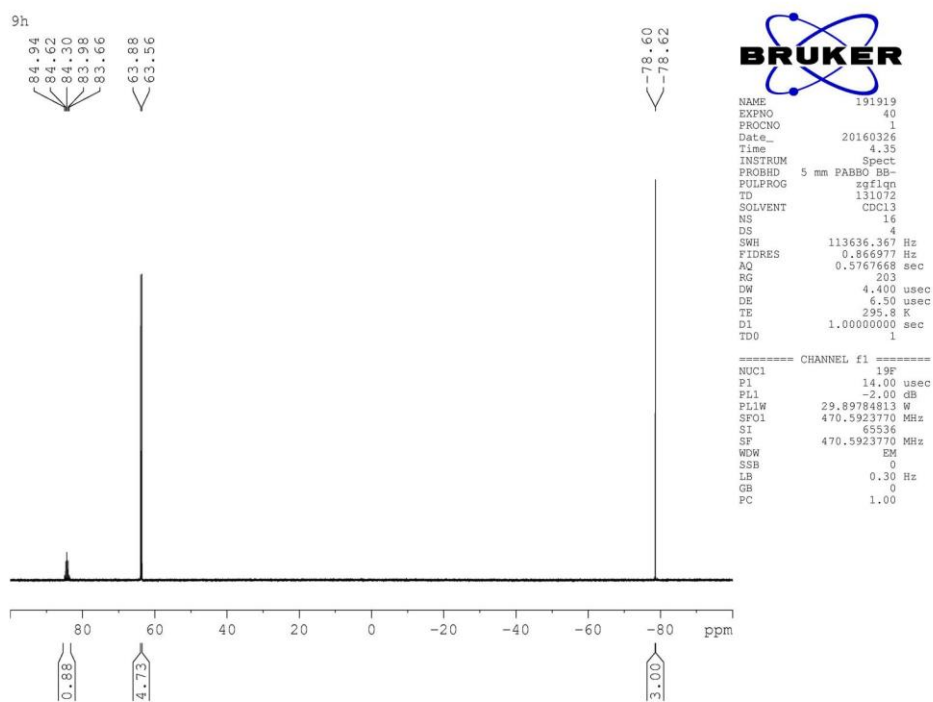
**(R,S)-11c**



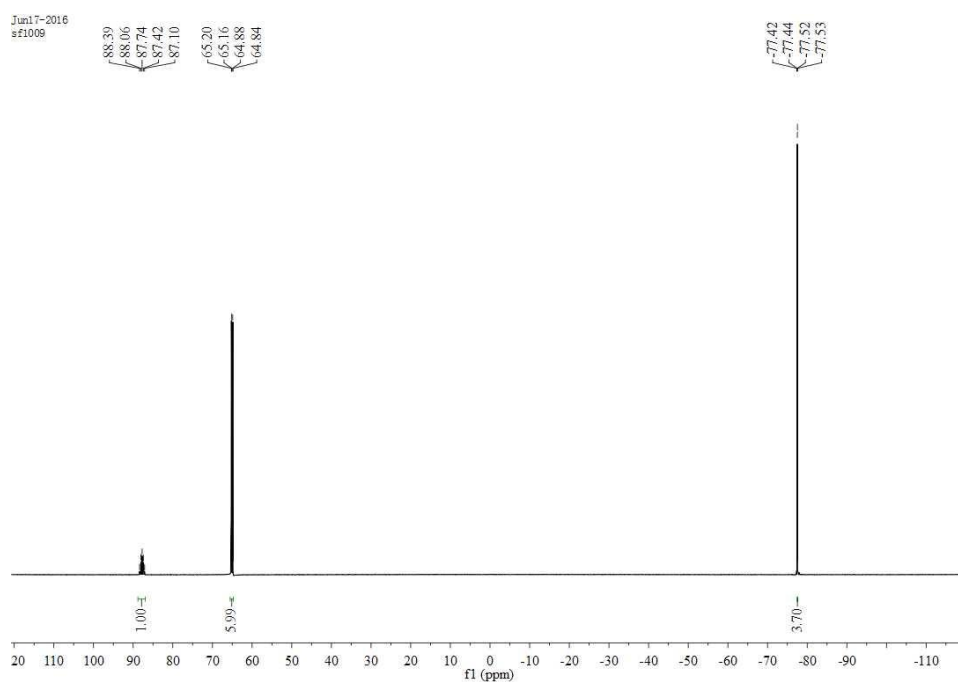
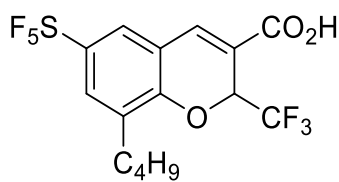


(R,S)-11d



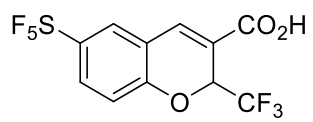


(R,S)-11e



## Chiral HPLC

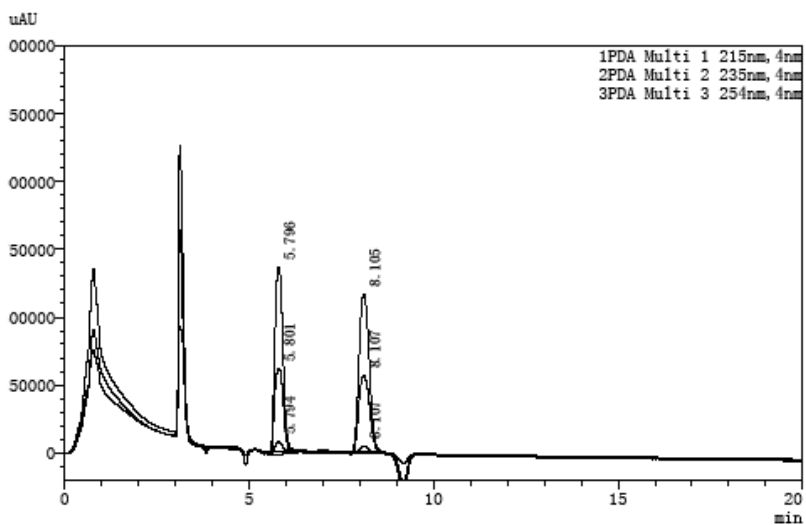
### (*R,S*)-3a



OD-H (*n*-hexane:*i*-PrOH:TFA 95:5:0.01); Flow rate 1.0 mL/min

## Data Report

**Sample Information**  
 Sample Name : 消旋体OD-H 5%  
 Tray# : 1  
 Vial# : 1  
 Injection Volume : 5  
 Data File : 消旋体OD 5%重复1.lcd  
 Method File : OD-H\_5%.lcm  
 Report Format File : 1.lsr  
 Sample Type : Unknown  
 Acquired by : System Administrator  
 Date Acquired : 2016/4/28 10:49:22  
 Date Processed : 2016/4/28 13:02:46



PDA Ch1 215nm

| NO. | Ret. Time | Height (uAU) | Area (uAU*min) | Rel. Area % | Resolution (USP) |
|-----|-----------|--------------|----------------|-------------|------------------|
| 1   | 5.801     | 314655       | 5238734        | 47.167      | —                |
| 2   | 8.107     | 287381       | 5868055        | 52.833      | 4.919            |

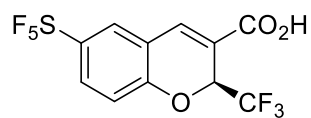
PDA Ch2 235nm

| NO. | Ret. Time | Height (uAU) | Area (uAU*min) | Rel. Area % | Resolution (USP) |
|-----|-----------|--------------|----------------|-------------|------------------|
| 1   | 5.796     | 680694       | 10364899       | 48.158      | —                |
| 2   | 8.105     | 581995       | 11157692       | 51.842      | 5.192            |

PDA Ch3 254nm

| NO. | Ret. Time | Height (uAU) | Area (uAU*min) | Rel. Area % | Resolution (USP) |
|-----|-----------|--------------|----------------|-------------|------------------|
| 1   | 5.794     | 35448        | 556657         | 52.615      | —                |
| 2   | 8.107     | 27444        | 501326         | 47.385      | 5.409            |

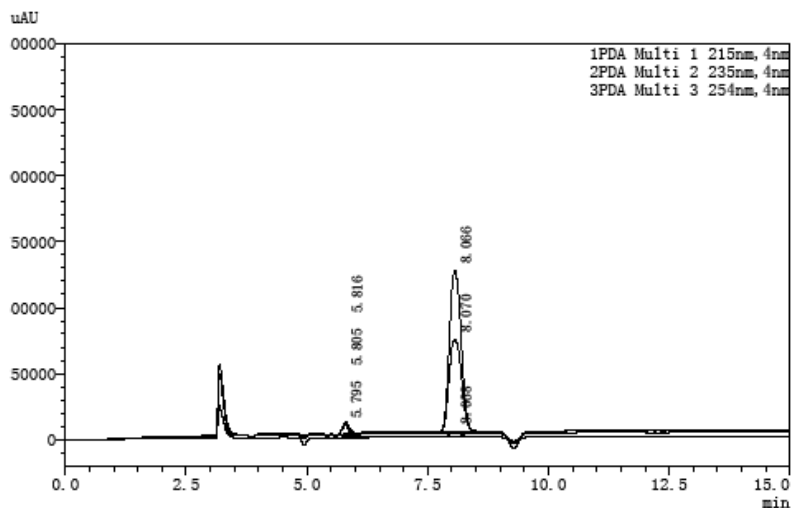
**S-3a**



OD-H (*n*-hexane:*i*-PrOH:TFA 95:5:0.01); Flow rate 1.0 mL/min

## Data Report

**Sample Information**  
 Sample Name : 手性OD-H 5%  
 Tray# : 1  
 Vial# : 2  
 Injection Volume : 2  
 Data File : 手性OD 5%重复1.lcd  
 Method File : OD-H,5%.lcm  
 Report Format File : 1.lsr  
 Sample Type : Unknown  
 Acquired by : System Administrator  
 Date Acquired : 2016/4/28 13:13:37  
 Date Processed : 2016/4/28 13:51:00



FDA Ch1 215nm

| NO. | Ret. Time | Height (uAU) | Area (uAU*min) | Rel. Area % | Resolution (USP) |
|-----|-----------|--------------|----------------|-------------|------------------|
| 1   | 5.795     | 31753        | 289697         | 4.440       | --               |
| 2   | 8.070     | 348915       | 6235308        | 95.560      | 6.294            |

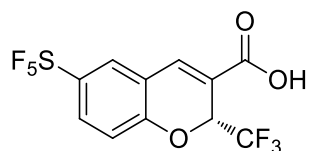
FDA Ch2 235nm

| NO. | Ret. Time | Height (uAU) | Area (uAU*min) | Rel. Area % | Resolution (USP) |
|-----|-----------|--------------|----------------|-------------|------------------|
| 1   | 5.805     | 48803        | 519697         | 4.744       | --               |
| 2   | 8.066     | 613427       | 10435369       | 95.256      | 6.157            |

FDA Ch3 254nm

| NO. | Ret. Time | Height (uAU) | Area (uAU*min) | Rel. Area % | Resolution (USP) |
|-----|-----------|--------------|----------------|-------------|------------------|
| 1   | 5.816     | 1607         | 22604          | 5.777       | --               |
| 2   | 8.068     | 23523        | 368697         | 94.223      | 5.424            |

### R-3a

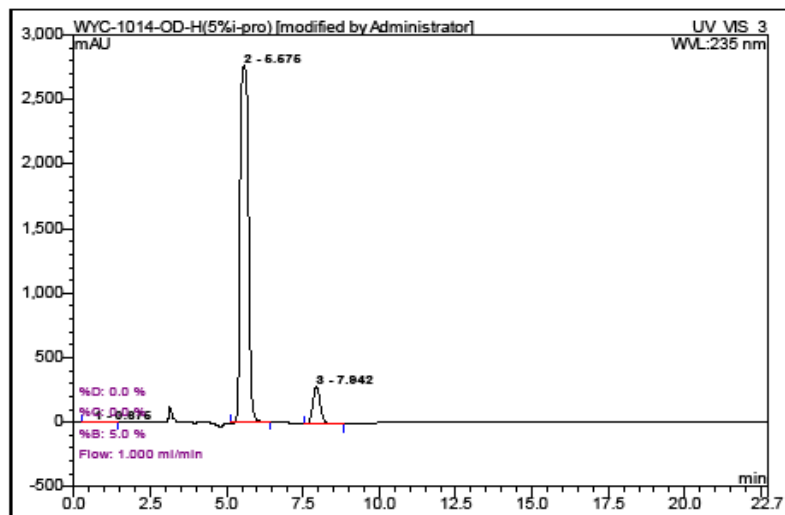


OD-H (*n*-hexane:*i*-PrOH:TFA 95:5:0.01); Flow rate 1.0 mL/min

**15 WYC-1014-OD-H(5%i-pro)**

Sample Name: WYC-1014-OD-H(5%i-pro)  
 Vial Number: RA4  
 Sample Type: unknown  
 Control Program: cl-090327-n  
 Quantif. Method: bhss  
 Recording Time: 4:05 AM  
 Run Time (min): 22.70

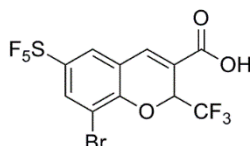
Injection Volume: 5.0  
 Channel: UV\_VIS\_3  
 Wavelength: n.a.  
 Bandwidth: n.a.  
 Dilution Factor: 1.0000  
 Sample Weight: 1.0000  
 Sample Amount: 1.0000



| No.    | Ret.Time<br>min | Peak Name | Height<br>mAU | Area<br>mAU*min | Rel.Area<br>% | Amount | Type |
|--------|-----------------|-----------|---------------|-----------------|---------------|--------|------|
| 1      | 0.68            | n.a.      | 1.698         | 1.022           | 0.11          | n.a.   | BMB  |
| 2      | 5.58            | n.a.      | 2787.169      | 859.471         | 91.70         | n.a.   | BMB* |
| 3      | 7.94            | n.a.      | 287.760       | 76.755          | 8.19          | n.a.   | BMB* |
| Total: |                 |           | 3056.627      | 937.249         | 100.00        | 0.000  |      |

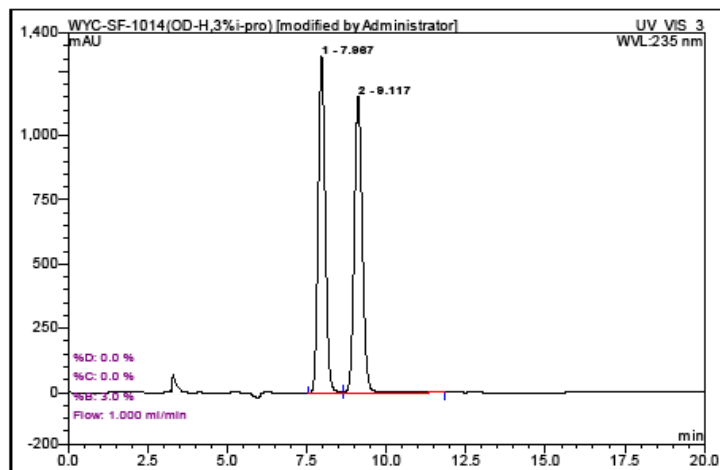
1014-2/1014-2

Chromeleon (c) Dionex 1996-2006  
 Version 6.80 Build 2212 (Demo-Installation)

**(R,S)-7**OD-H (*n*-hexane:*i*-PrOH:TFA 97:3:0.01); Flow rate 1.0 mL/min

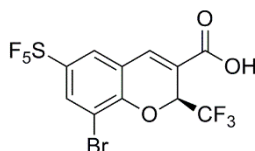
**22 WYC-SF-1014(OD-H,3%i-pro)**

|                  |                           |                   |          |
|------------------|---------------------------|-------------------|----------|
| Sample Name:     | WYC-SF-1014(OD-H,3%i-pro) | Injection Volume: | 2.0      |
| Vial Number:     | RA9                       | Channel:          | UV_VIS_3 |
| Sample Type:     | unknown                   | Wavelength:       | n.a.     |
| Control Program: | cl-090327-n               | Bandwidth:        | n.a.     |
| Quantif. Method: | bhss                      | Dilution Factor:  | 1.0000   |
| Recording Time:  | 4:21 PM                   | Sample Weight:    | 1.0000   |
| Run Time (min):  | 20.01                     | Sample Amount:    | 1.0000   |



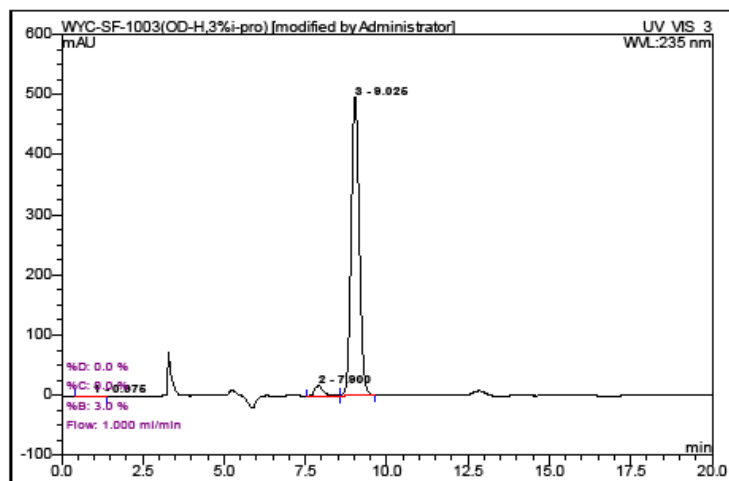
| No.    | Ret.Time<br>min | Peak Name | Height<br>mAU | Area<br>mAU*min | Rel.Area<br>% | Amount | Type |
|--------|-----------------|-----------|---------------|-----------------|---------------|--------|------|
| 1      | 7.97            | n.a.      | 1309.212      | 333.099         | 49.49         | n.a.   | BM * |
| 2      | 9.12            | n.a.      | 1153.120      | 340.016         | 50.51         | n.a.   | MB   |
| Total: |                 |           | 2462.333      | 673.115         | 100.00        | 0.000  |      |

SF-1014-2/SF-1014-2

Chromeleon (c) Dionex 1996-2006  
Version 6.80 Build 2212 (Demo-Installation)**S-7**OD-H (*n*-hexane:*i*-PrOH:TFA 97:3:0.01); Flow rate 1.0 mL/min

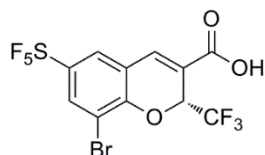
**21 WYC-SF-1003(OD-H,3%i-pro)**

|                  |                           |                   |          |
|------------------|---------------------------|-------------------|----------|
| Sample Name:     | WYC-SF-1003(OD-H,3%i-pro) | Injection Volume: | 2.0      |
| Vial Number:     | RA8                       | Channel:          | UV_VIS_3 |
| Sample Type:     | unknown                   | Wavelength:       | n.a.     |
| Control Program: | cl-090327-n               | Bandwidth:        | n.a.     |
| Quantif. Method: | bhss                      | Dilution Factor:  | 1.0000   |
| Recording Time:  | 4:00 PM                   | Sample Weight:    | 1.0000   |
| Run Time (min):  | 20.01                     | Sample Amount:    | 1.0000   |



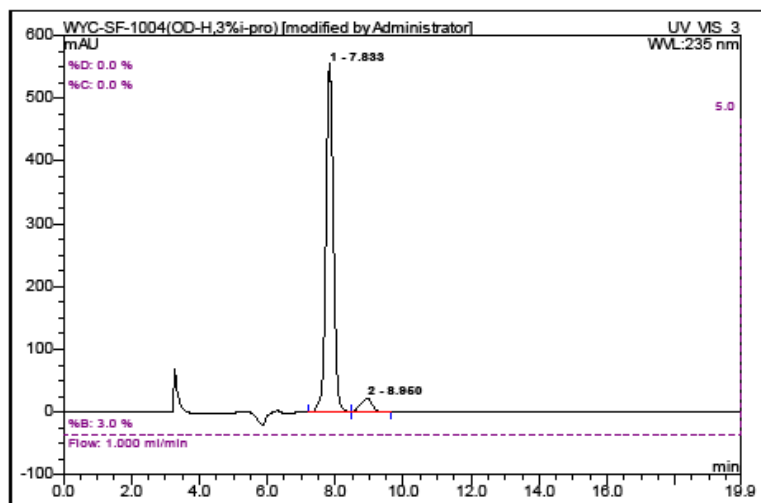
| No.    | Ret. Time<br>min | Peak Name | Height<br>mAU | Area<br>mAU*min | Rel. Area<br>% | Amount | Type |
|--------|------------------|-----------|---------------|-----------------|----------------|--------|------|
| 1      | 0.98             | n.a.      | 1.211         | 0.584           | 0.39           | n.a.   | BMB  |
| 2      | 7.90             | n.a.      | 17.494        | 5.079           | 3.44           | n.a.   | BM * |
| 3      | 9.03             | n.a.      | 495.624       | 142.180         | 96.17          | n.a.   | MB   |
| Total: |                  |           | 514.328       | 147.843         | 100.00         | 0.000  |      |

1003-2/1003-2

Chromleon (c) Dionex 1996-2006  
Version 6.80 Build 2212 (Demo-Installation)**R-7**OD-H (*n*-hexane:*i*-PrOH:TFA 97:3:0.01); Flow rate 1.0 mL/min

**20 WYC-SF-1004(OD-H,3%i-pro)**

|                  |                           |                   |          |
|------------------|---------------------------|-------------------|----------|
| Sample Name:     | WYC-SF-1004(OD-H,3%i-pro) | Injection Volume: | 2.0      |
| Vial Number:     | RA7                       | Channel:          | UV_VIS_3 |
| Sample Type:     | unknown                   | Wavelength:       | n.a.     |
| Control Program: | cl-090327-n               | Bandwidth:        | n.a.     |
| Quantif. Method: | bhss                      | Dilution Factor:  | 1.0000   |
| Recording Time:  | 3:04 PM                   | Sample Weight:    | 1.0000   |
| Run Time (min):  | 19.91                     | Sample Amount:    | 1.0000   |



| No.    | Ret. Time<br>min | Peak Name | Height<br>mAU | Area<br>mAU*min | Rel. Area<br>% | Amount | Type |
|--------|------------------|-----------|---------------|-----------------|----------------|--------|------|
| 1      | 7.83             | n.a.      | 553.799       | 139.502         | 95.11          | n.a.   | BMB* |
| 2      | 8.95             | n.a.      | 20.922        | 7.166           | 4.89           | n.a.   | bMB  |
| Total: |                  |           | 574.721       | 146.668         | 100.00         | 0.000  |      |