Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.


# Supporting Information

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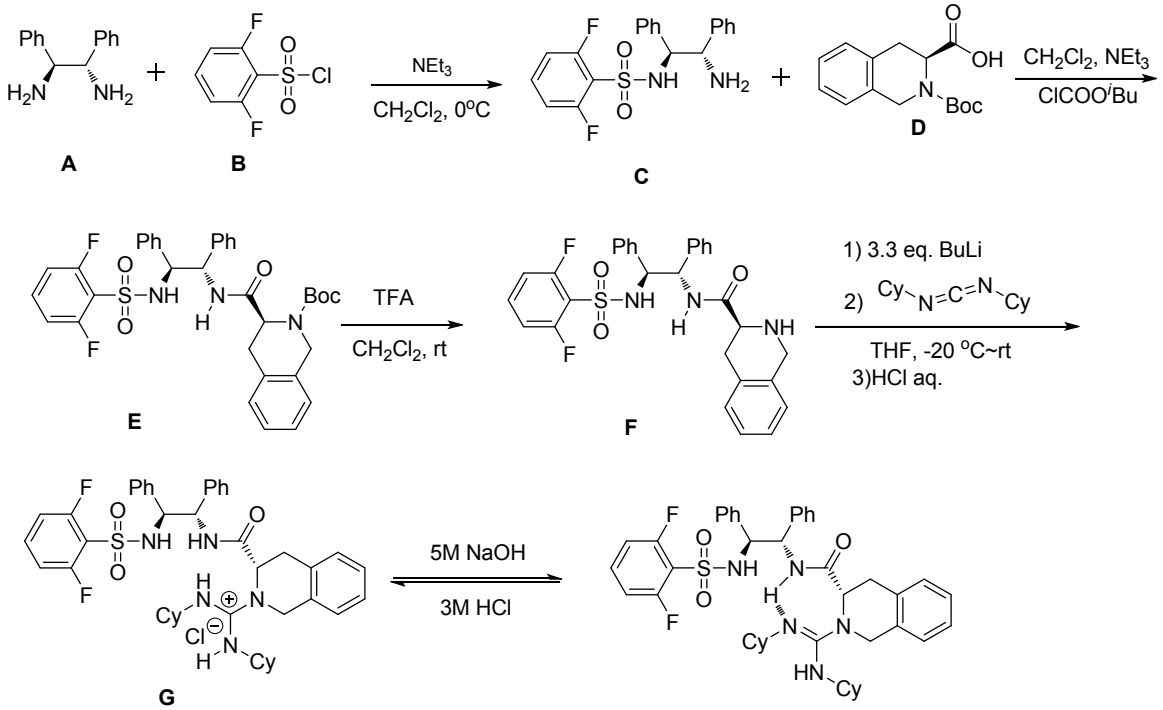
## 1. General information

$^1$H NMR spectra were recorded on commercial instruments (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26), ($(CD_3)_2SO$, δ = 2.5), (MeOD, δ = 2.64), ($(CD_3)_2CO$, δ = 2.05), Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration and assignment. $^{13}$CNMR spectra were collected on commercial instruments (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0), ($(CD_3)_2SO$, δ = 39.5), (MeOD, δ = 49.0), ($(CD_3)_2CO$, δ = 206.3， δ = 29.8). Enantiomeric excesses (*ee*) were determined by UPC2 analysis using the corresponding commercial chiralpak column as stated in the experimental procedures at 35℃. Optical rotations were reported as follows: $[\alpha]_D^{18}$ (*c*: g/100 mL, in solvent). HRMS was recorded on a commercial apparatus (ESI Source). All catalytic reactions were run in dried glassware. THF, toluene and diethyl ether ($Et_2O$) were distilled from sodium benzophenone ketyl. Ethyl acetate, $CH_2Cl_2$ was distilled over $CaH_2$.

## 2. Typical procedure for guanidines preparation



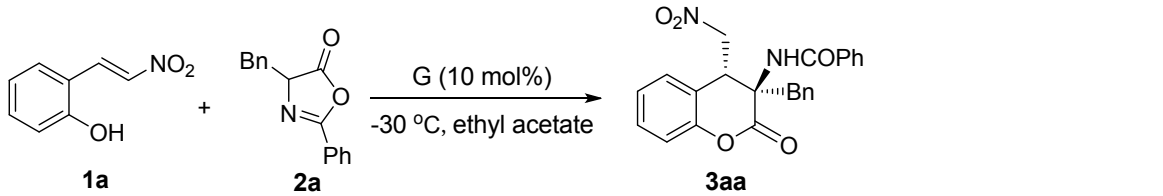

A solution of sulfonyl chloride **B** (10 mmol) was slowly added to a stirred solution of diamine **A** (10 mmol), $NEt_3$ (11 mmol) in dichloromethane (25 mL). The resulting mixture was stirred for another 2 hours, washed twice with water (25 mL) and dried over $Na_2SO_4$. The solvent was removed *in vacuo* to give a white solid **C**. To a solution of **D** in $CH_2Cl_2$ (40 mL) was added $NEt_3$ (11 mmol), isobutyl carbonochloridate (11 mmol) at 0 °C under stirring. After 10 min, **C** was added. The reaction was allowed to warm to room temperature for another 2 hours. The mixture was washed with 1 N $KHSO_4$ solution, saturated $NaHCO_3$ solution, and brine, dried over anhydrous $Na_2SO_4$ and concentrated to get a white solid **E**. Then, TFA (10 mL) was added to the $CH_2Cl_2$ (10 mL) solution of **E**, and stirred until the reaction finished (1 h). The *p*H value of the mixture was brought into the range of 10–12 by the addition of 2 N NaOH solution. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 30 mL). The

combined organic phase was washed with brine, dried over anhydrous $Na_2SO_4$ and concentrated and purified through flash chromatograph as a white solid **F** (70% yield).

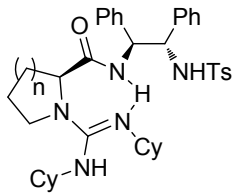
*n*BuLi (2.4 M in *n*-hexane, 3.3 eq., 16.5 mmol) was injected into a solution of **F** (5.0 mmol) in THF (30 mL) dropwise over 10 mins under nitrogen atmosphere at −20 ºC with well stirring. After additional 10 mins, a solution of *N*,*N*-dicyclohexylcarbodiimide (1.2 eq., 6.0 mmol) in 10 mL of THF was added dropwise within 10 mins. The reaction was allowed to warm to room temperature and detected by TLC. After 12 h, the mixture was evaporated under reduced pressure to get rid of THF, and the pH value of the mixture was brought into the range of 0–1 by the addition of 3 M HCl. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic phase was washed with 3M HCl in brine, dried over anhydrous $Na_2SO_4$ and evaporated in vacuum, and purified through flash chromatograph on silica gel to produce guanidinium salt **G**. The purified guanidinium salt **G** can be given through recrystallization in $CH_2Cl_2$ and ethyl acetate. Then, guanidinium salt **G** in $CH_2Cl_2$ (20 mL) was added 5 M NaOH (20 mL) and stirred until the basification finished (10 mins). The pH value of the mixture was kept in the range of 11–12. The aqueous phase was extracted with $CH_2Cl_2$ (5 × 20 mL). The combined organic phase was washed with 5 M NaOH, dried over anhydrous $Na_2SO_4$ and evaporated in vacuum. Finally, a white solid was obtained. Then it was dissolved in $CH_2Cl_2$ and filtration through Celite to remove the silicone gel,concentrate to get a kind of white foam (22% yield). For other catalysts, the synthesis method could be found in the literature.[1]

## 3. Optimization of the reaction conditions

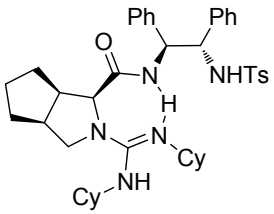
Table 1: Screening of guanidines[a]



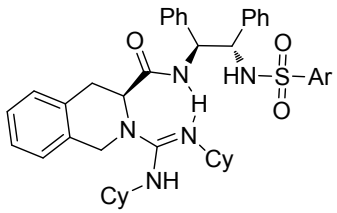

**1a** + **2a** → **3aa**



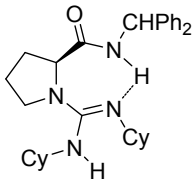

**G-1**: n = 0
**G-2**: n = 1
(Cy = Cyclohexyl)



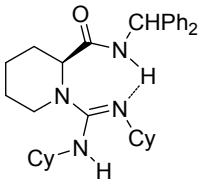

**G-3**



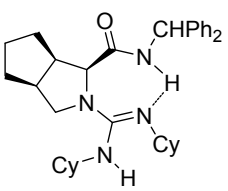

**G-4:** Ar = 4-$MeC_6H_4$ **G-5:** Ar = 2,6-$F_2C_6H_3$
**G-6**: Ar = 4-$MeOC_6H_4$ **G-7**: Ar = 4-$CF_3C_6H_4$
**G-8**: Ar = 4-t-$BuC_6H_4$ **G-9**: Ar = 4-$BrC_6H_4$
**G-10**: Ar = 2,6-$Cl_2C_6H_3$ **G-11**: Ar = $C_6H_5$



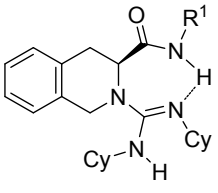

**G-12**



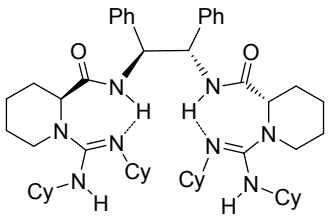

**G-13**



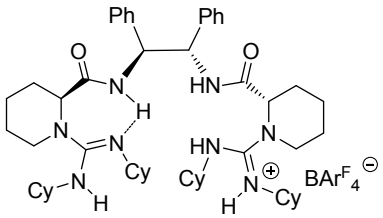

**G-14**




**G-15:** $R^1$ = $Ph_2CH$
**G-16:** $R^1$ = $Ph_3C$
**G-17:** $R^1$ = Ph



**BG-1**

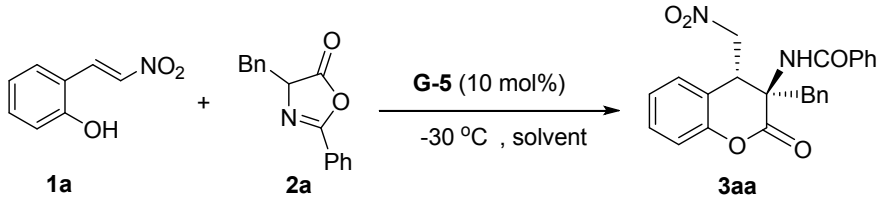


**BG-1**•$HBAr^F_4$

| entry | cat | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|
| 1 | **G-1** | 98 | >19:1 | 47 |
| 2 | **G-2** | 94 | >19:1 | 52 |
| 3 | **G-3** | 97 | >19:1 | 41 |
| 4 | **G-4** | 95 | >19:1 | 74 |
| 5 | **G-5** | 99 | >19:1 | 85 |
| 6 | **G-6** | 99 | >19:1 | 76 |
| 7 | **G-7** | 99 | >19:1 | 75 |
| 8 | **G-8** | 99 | >19:1 | 80 |
| 9 | **G-9** | 99 | >19:1 | 82 |
| 10 | **G-10** | 99 | >19:1 | 74 |
| 11 | **G-11** | 99 | >20:1 | 79 |
| 12 | **G-12** | 81 | 8:1 | 36 |
| 13 | **G-13** | 84 | 12:1 | 17 |
| 14 | **G-14** | 77 | 5:1 | 13 |
| 15 | **G-15** | 88 | 14:1 | 58 |
| 16 | **G-16** | 81 | 5:1 | 50 |
| 17 | **G-17** | 85 | 6:1 | 46 |
| 18 | **BG-1** | 86 | 2.5:1 | 24/14 |
| 19 | **BG-1•HBAr$^F_4$** | 75 | 2:1 | 23/11 |

[a] Unless otherwise noted, the reactions were carried out with the catalyst (10 mol%), **1a** (0.10 mmol) and **2a** (0.12 mmol) in ethyl acetate (1.0 mL) at -30 °C for 24 h. [b] Isolated yield. [c] Determined by NMR analysis. [d] Determined by UPC2 analysis.

Table 2: Screening of the solvents[a]

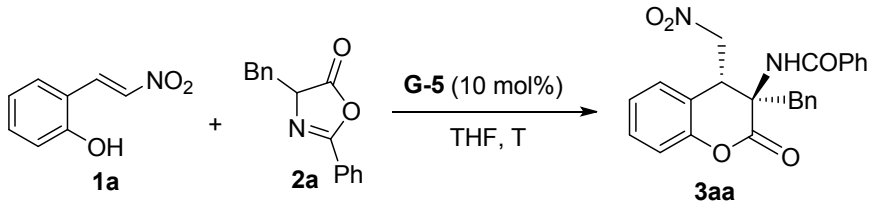



**1a** **2a** **3aa**

| entry | solvent | yield (%)[b] | dr | ee (%)[c] |
|---|---|---|---|---|
| 1 | Toluene | 72 | >19:1 | 54 |
| 2 | THF | 99 | >19:1 | 88 |
| 3 | $CH_2Cl_2$ | 94 | >19:1 | 79 |
| 4 | $Et_2O$ | 80 | >19:1 | 77 |
| 5 | $CH_3CN$ | 86 | >19:1 | 65 |
| 6 | Ethyl acetate | 99 | >19:1 | 85 |

[a] Unless otherwise noted, the reactions were carried out with **G-5** (10 mol%), **1a** (0.10 mmol) and **2a** (0.12 mmol) in solvent (1.0 mL) at -30 °C for 24 h. [b] Isolated yield. [c] Determined by NMR analysis. [d] Determined by UPC2 analysis.

Table 3: Screening of the temperature[a]

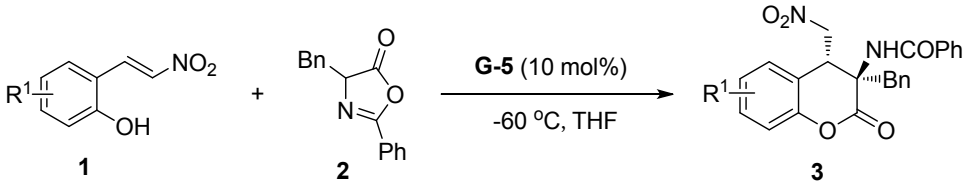



| entry | T (°C ) | t (h) | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|---|
| 1 | -30 | 24 | 99 | >19:1 | 88 |
| 2 | -40 | 24 | 99 | >19:1 | 91 |
| 3 | -50 | 72 | 99 | >19:1 | 93 |
| 4 | -60 | 72 | 99 | >19:1 | 95 |
| 5[e] | -60 | 72 | 99 | >19:1 | 93 |
| 6 | -70 | 96 | 99 | >19:1 | 96 |
| 7 | -78 | 96 | trace | — | — |

[a] Unless otherwise noted, the reactions were carried out **G-5** (10 mol%), **1a** (0.10 mmol) and **2a** (0.12 mmol) in solvent (1.0 mL) at the indicated temperature. [b] Isolated yield. [c] Determined by NMR analysis. [d] Determined by UPC2 analysis. [e] **G-5** (5 mol%).

## 4. Substrate scope

Table 4: Substrate scope of (*E*)-2-(2-nitrovinyl) phenols **1**[a]

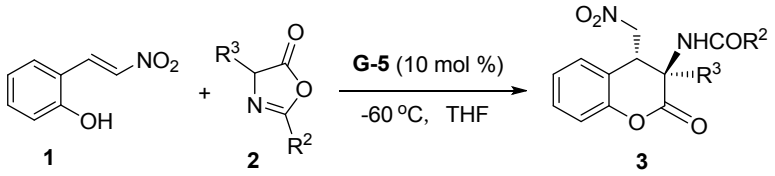



| entry | **1**: $R^1$ | t (h) | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|---|
| 1 | **1a**: H | 72 | 99 (**3aa**) | >19:1 | 95 |
| 2 | **1b**: 4-F | 72 | 99 (**3ba**) | >19:1 | 95 |
| 3 | **1c**: 4-Cl | 72 | 90 (**3ca**) | >19:1 | 95 |
| 4 | **1d**: 4-Br | 72 | 84 (**3da**) | >19:1 | 96 |
| 5 | **1e**: 5-Me | 72 | 80 (**3ea**) | >19:1 | 92 |
| 6 | **1f**: 5-Cl | 72 | 85 (**3fa**) | >19:1 | 92 |
| 7 | **1g**: 5-OH, 6-Me | 72 | 80 (**3ga**) | >19:1 | 96 |
| 8 | **1h**: 6- F | 72 | 83 (**3ha**) | >19:1 | 94 |
| 9 | **1i**: 6-Cl | 72 | 82 (**3ia**) | >19:1 | 91 |
| 10 | **1j**: 6-Br | 72 | 80 (**3ja**) | >19:1 | 91 |
| 11 | **1k**: 6-Me | 72 | 92 (**3ka**) | >19:1 | 95 |

| | | | | | |
|---|---|---|---|---|---|
| 12 | **1l**: 6-MeO | 72 | 99 (**3la**) | >19:1 | 92 |
| 13 | **1m**: 6-EtO | 72 | 95 (**3ma**) | >19:1 | 93 |
| 14 | **1n**: 6-*t*-Bu | 72 | 99 (**3na**) | >19:1 | 95 |

[a] Unless otherwise noted, the reactions were carried out **G-5** (10 mol%), **1a** (0.10 mmol) and **2a** (0.12 mmol) in solvent (1.0 mL) at the indicated temperature. [b] Isolated yield. [c] Determined by NMR analysis. [d] Determined by UPC2 analysis.

Table 5: Substrate scope of azlactones **2**[a]




**1** **2** **3**

| entry | **2**: $R^2/R^3$ | t (h) | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|---|
| 15 | 4-$ClC_6H_4$ / Bn | 48 | 87 (**3ab**) | >19:1 | 95 |
| 16 | 4-$BrC_6H_4$ / Bn | 48 | 87 (**3ac**) | >19:1 | 96 |
| 17 | 4-$MeC_6H_4$ / Bn | 48 | 99 (**3ad**) | >19:1 | 95 |
| 18 | 4-$MeOC_6H_4$ / Bn | 48 | 99 (**3ae**) | >19:1 | 95 |
| 19 | 4-$EtC_6H_4$ / Bn | 48 | 99 (**3af**) | >19:1 | 98 |
| 20 | 4-$NCC_6H_4$ / Bn | 72 | 63 (**3ag**) | >19:1 | 93 |
| 21 | Ph / 4-$ClC_6H_4CH_2$ | 48 | 99 (**3ah**) | >19:1 | 96 |
| 22 | Ph / Me | 24 | 94 (**3ai**) | >19:1 | 98 |
| 23 | Ph / *i*-Bu | 72 | 97 (**3aj**) | >19:1 | 97 |
| 24 | Ph / $CH_2CH_2Ph$ | 72 | 97 (**3ak**) | >19:1 | 98 |
| 25 | Ph / 3-Indolylmethyl | 72 | 99 (**3al**) | >19:1 | 99 |

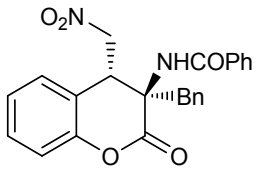
[a] Unless otherwise noted, the reactions were carried out **G-5** (10 mol%), **1a** (0.10 mmol) and **2a** (0.12 mmol) in solvent (1.0 mL) at the indicated temperature. [b] Isolated yield. [c] Determined by NMR analysis. [d] Determined by UPC2 analysis.

## 5. Typical procedure for the cascade Michael reaction

2-nitrovinylphenol **1** (0.10 mmol), azlactone **2** (1.2-2 equiv) and the catalyst **G-5** (7.5 mg, 10 mol%) were added into the test tube, followed by the addition of THF (1.0 mL). Then the mixture was stirred at -60 °C. After completion, the reaction mixture was purified by silica gel column chromatography (ethyl acetate/petroleum ether 1/4-1/2) to afford the desired products. Then the product was directed for UPC2 analysis.

## 6. The analytical and spectral characterization data of the product

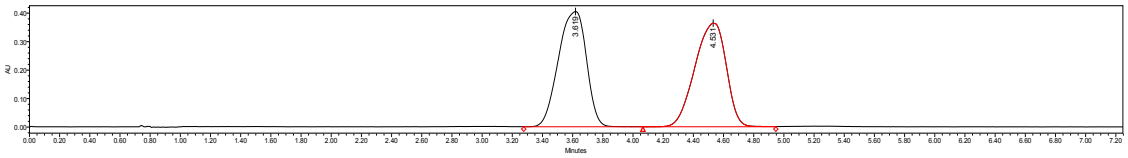
***N*-((3*R*,4*R*)-3-benzyl-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3aa)**



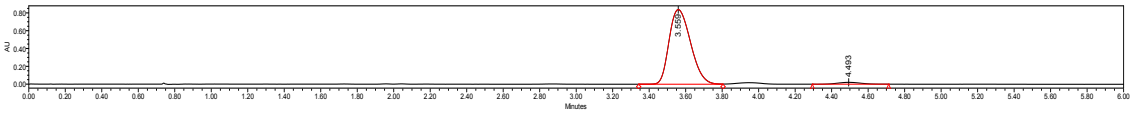

**3aa**

White solid, $[\alpha]^{18}$ = +1.99 (*c*: 1.11, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 3.56 min, t (minor) = 4.49 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.36 (m, 3H), 7.32 – 7.20 (m, 6H), 7.14 – 6.99 (m, 5H), 6.32 (s, 1H), 5.24 – 5.04 (dd, *J* = 13.6, 3.2 Hz, 1H), 4.92 (d, *J* = 8.8 Hz, 1H), 4.80

(dd, $J$ = 13.2, 9.6 Hz, 1H), 3.21 (d, $J$ = 14.4 Hz, 1H), 3.03 (d, $J$ = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.9, 150.1, 133.3, 132.7, 132.3, 130.1, 130.1, 129.1, 128.8, 128.3, 127.0, 126.4, 125.5, 121.4, 116.9, 74.3, 60.5, 40.5, 35.6. HRMS (ESI-TOF) caled for **$C_{24}H_{20}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 439.1270, observed: 439.1271.

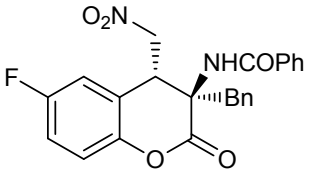



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.619 | 5231842 | 49.91 |
| 2 | 4.531 | 5249890 | 50.09 |



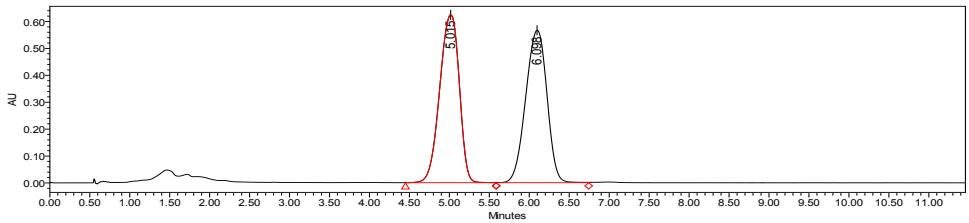

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.559 | 6850779 | 97.50 |
| 2 | 4.493 | 175929 | 2.50 |

***N*-((3*R*,4*R*)-3-benzyl-6-fluoro-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ba)**

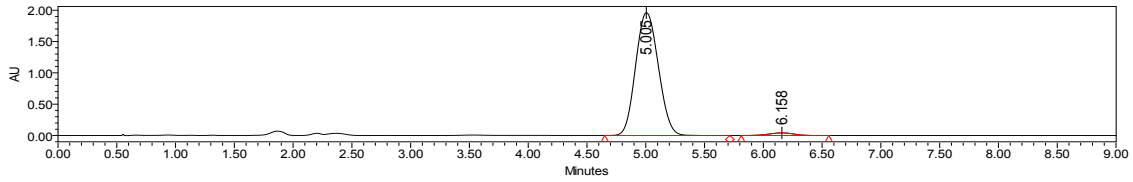



**3ba**

White solid, $[\alpha]^{18}$ = +44.5 (*c*: 0.27, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 80/20, 2 mL/min, λ = 232.0 nm, t (major) = 5.01 min, t (minor) = 6.16 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.52 (m, 2H), 7.51 – 7.44 (m, 1H), 7.40 – 7.33 (m, 2H), 7.31 – 7.25 (m, 3H), 7.10 – 6.99 (m, 4H), 6.85 (dd, $J$ = 8.4, 2.4 Hz, 1H), 6.46 (s, 1H), 5.17 (dd, $J$ = 13.6, 3.2 Hz, 1H), 5.08 (d, $J$ = 8.8 Hz, 1H), 4.84 (dd, $J$ = 13.2, 9.2 Hz, 1H), 3.22 (d, $J$ = 14.4 Hz, 1H), 3.04 (d, $J$ = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.5, 160.7, 158.2, 146.1, 133.0, 132.5, 132.2, 130.0, 129.2, 128.8, 128.4, 127.0, 123.2( $J$ = 7.5 Hz, 1C), 118.4( $J$ = 8.5 Hz, 1C), 118.3, 116.6( $J$ = 23.2 Hz, 1C), 113.5( $J$ = 25.3 Hz, 1C), 74.0, 60.3, 40.1, 36.1. HRMS (ESI-TOF) caled for **$C_{24}H_{19}FN_2O_5Na^+$ (M+Na)$^+$**, m/z: 457.1176, observed: 457.1179.

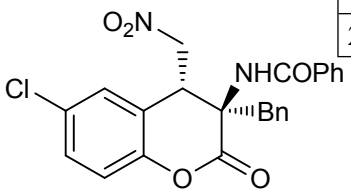



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 5.015 | 10606801 | 50.32 |
| 2 | 6.098 | 10472280 | 49.68 |



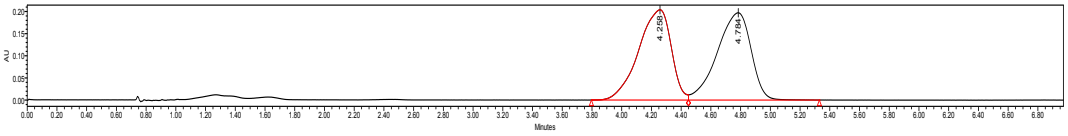

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 5.005 | 26296987 | 97.75 |
| 2 | 6.158 | 605124 | 2.25 |

***N*-((3*R*,4*R*)-3-benzyl-6-chloro-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ca)**

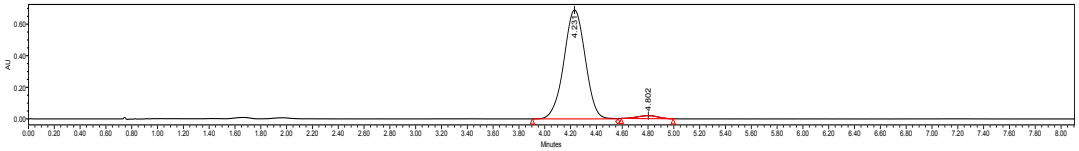



**3ca**

White solid, $[\alpha]^{18}$ = +54.5 (*c*: 0.62, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 70/30,1.5 mL/min, λ = 254 nm, t (major) = 4.23 min, t (minor) = 4.80 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.35 (m, 3H), 7.32 – 7.20 (m, 6H), 7.08 – 6.88 (m, 4H), 6.32 (s, 1H), 5.09 (dd, *J* = 13.6, 3.2 Hz, 1H), 4.96 (d, *J* = 8.4 Hz, 1H), 4.77 (dd, *J* = 13.6, 9.6Hz, 1H), 3.18 (d, *J* = 14.4 Hz, 1H), 2.97 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.3, 148.6, 132.9, 132.5, 132.2, 130.6, 130.1, 130.0, 129.2, 128.8, 128.5, 127.0, 126.4, 123.2, 118.3, 73.9, 60.1, 40.0, 36.1. HRMS (ESI-TOF) caled for **$C_{24}H_{19}ClN_2O_5Na^+$ (M+Na)$^+$**, m/z: 473.0880, 475.0851; observed: 473.0879, 475.0874.

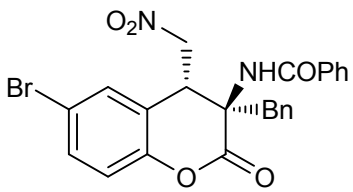



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.258 | 3111263 | 49.93 |
| 2 | 4.784 | 3119541 | 50.07 |




| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.231 | 7930074 | 97.46 |
| 2 | 4.802 | 206699 | 2.54 |

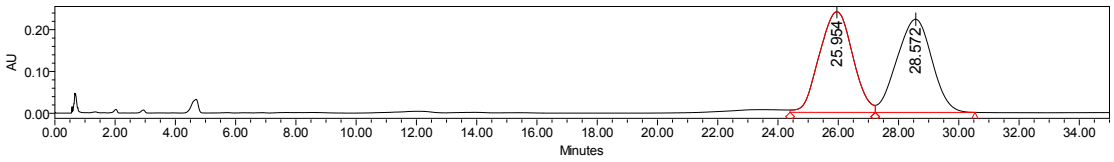
***N*-((3*R*,4*R*)-3-benzyl-6-bromo-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3da)**



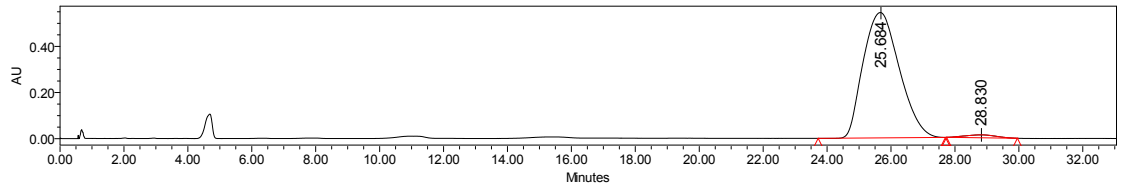

**3da**

White solid, [α]$^{18}$ = +56.9 (*c*: 0.58, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 90/10, 2 mL/min, λ = 224.0 nm, t (major) = 25.68 min, t (minor) = 28.83 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.42 (m, 4H), 7.41 – 7.27 (m, 5H), 7.22 (d, *J* = 1.2 Hz, 1H), 7.13 – 7.04 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.38 (s, 1H), 5.16 (dd, *J* = 13.6, 3.2 Hz, 1H), 5.03 (d, *J* = 7.6 Hz, 1H), 4.84 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.27(d, *J* =14.4 Hz, 1H), 3.05(d, *J* =14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.3, 149.1, 133.0, 132.9, 132.5, 132.2, 130.0, 129.2, 129.2, 128.8, 128.4, 127.1, 123.6, 118.6, 118.0, 73.9, 60.2, 39.9, 36.3. HRMS

(ESI-TOF) calcd for **[M+Na]$^+$ $C_{24}H_{19}BrN_2O_5Na^+$**, m/z: 517.0375, 519.0355; observed: 517.0374, 519.0358.

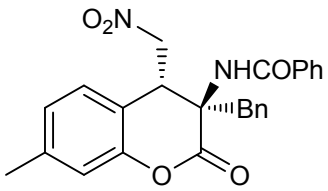



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 25.954 | 18457768 | 50.63 |
| 2 | 28.572 | 17999838 | 49.37 |



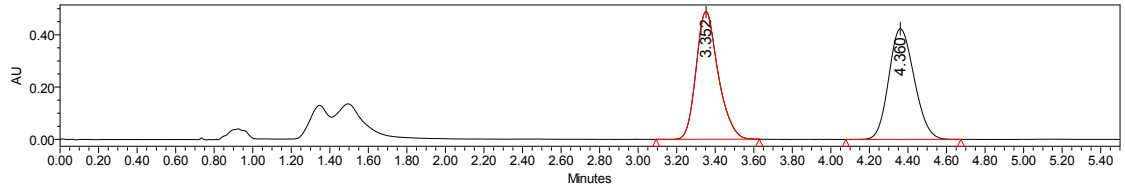

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 25.684 | 42702976 | 98.05 |
| 2 | 28.830 | 849785 | 1.95 |

***N*-((3*R*,4*R*)-3-benzyl-7-methyl-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ea)**

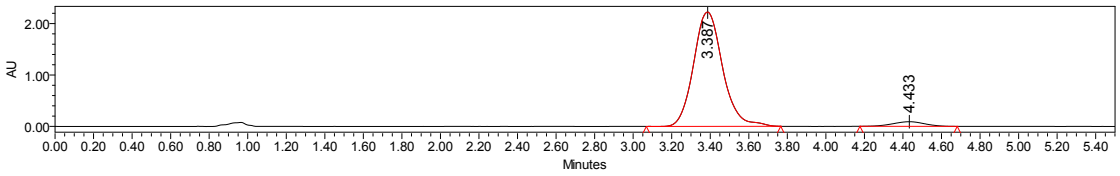



**3ea**

White solid, $[\alpha]^{18}$ = -44.8 (*c*: 0.21, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 218 nm, t (major) = 3.39 min, t (minor) = 4.43 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.37 (m, 3H), 7.32 – 7.20 (m, 5H), 7.10 – 6.97 (m, 2H), 6.90 (t, *J* = 8.4 Hz, 3H), 6.30 (s, 1H), 5.14 (dd, *J* = 12.4, 2.4 Hz, 1H), 4.90 – 4.67 (m, 2H), 3.22 (d, *J* = 14.4 Hz, 1H), 3.05 (d, *J* = 14.4 Hz, 1H), 2.28 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.2, 150.0, 140.7, 133.4, 132.8, 132.3, 130.1, 129.1, 128.8, 128.2, 127.0, 126.1, 118.2, 117.4, 74.5, 60.6, 40.4, 35.3, 21.2. HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 453.1426, observed: 453.1428.

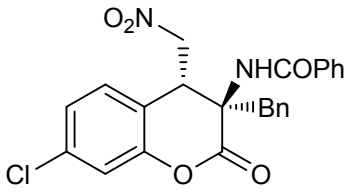



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.352 | 3876064 | 49.97 |
| 2 | 4.360 | 3880195 | 50.03 |



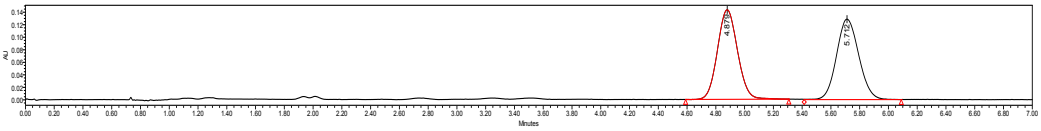

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.387 | 23319041 | 95.80 |
| 2 | 4.433 | 1023041 | 4.20 |

**_N_-((3_R_,4_R_)-3-benzyl-7-chloro-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3fa)**

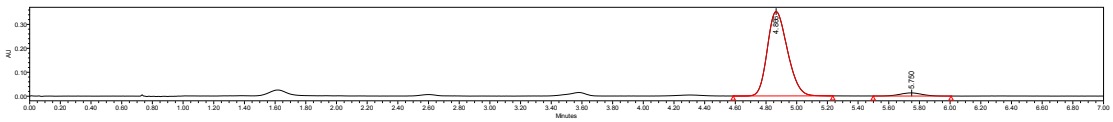



**3fa**

White solid, $[\alpha]^{18}$ = -25.7 (*c*: 0.68, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 4.87 min, t (minor) = 5.75 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.29 – 7.22 (m, 4H), 7.16 – 6.95 (m, 5H), 6.47 (s, 1H), 5.14 (dd, *J* = 13.6, 2.8 Hz, 1H), 5.00 (d, *J* = 8.8 Hz, 1H), 4.82 (dd, *J* = 13.2, 10.0 Hz, 1H), 3.24 (d, *J* = 14.4 Hz, 1H), 3.03 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.3, 150.5, 135.5, 132.9, 132.5, 132.3, 130.1, 129.2, 128.8, 128.4, 127.4, 127.0, 125.5, 120.0, 117.4, 74.2, 60.3, 39.9, 36.2. HRMS (ESI-TOF) caled for **$C_{24}H_{19}ClN_2O_5Na^+$ (M+Na)$^+$**, m/z: 473.0880, 475.0851; observed: 473.0882, 475.0875.



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.879 | 1383060 | 50.03 |
| 2 | 5.712 | 1381222 | 49.97 |

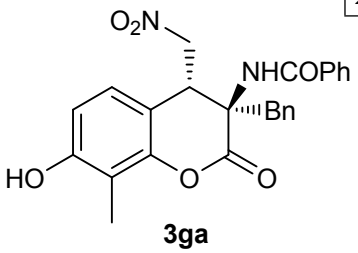


**_N_-((3_R_,4_R_)-3-benzyl-7-(nitromethyl)-2-yl)benzamide (3ga)**

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.866 | 3199646 | 96.08 |
| 2 | 5.750 | 130506 | 3.92 |

**hydroxy-8-methyl-4-oxochroman-3-**

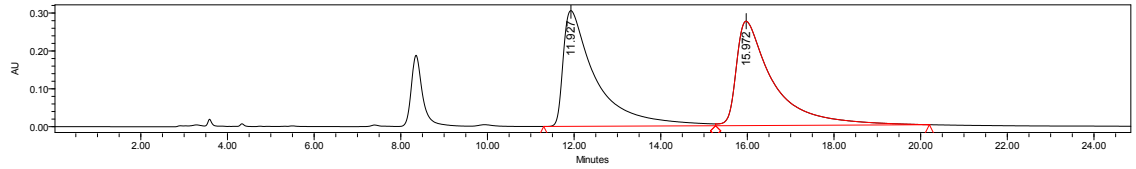
White solid, $[\alpha]^{18}$ = -61.4 (*c*: 0.69, λ = 405 nm, $CH_2Cl_2$);



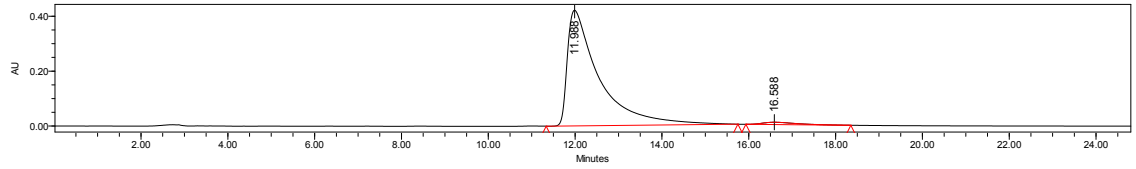

**3ga**

Determined by HPLC analysis [Daicel Chiralpak IA, *n*-hexane/ $^i$PrOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 11.99 min, t (minor) = 16.59 min]; $^1$H NMR(400 MHz, MeOD) δ 7.46 (dd, *J* = 16.0, 7.6 Hz, 3H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.18 (m, 5H), 6.72 (d, *J* = 8.4Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 5.28 (dd, *J* = 12.8, 3.2 Hz, 1H), 4.67 (t, *J* = 11.2 Hz, 1H), 4.37 (s, 1H), 3.59 (d, *J* = 14.4 Hz, 1H), 3.15 (d, *J* = 14.4 Hz, 1H), 2.02 (s, 3H). $^{13}$C NMR (100 MHz, MeOD) δ 170.3, 168.3, 158.0, 151.1,

135.8, 135.0 133.0, 131.7, 129.5, 129.5, 128.4, 126.6, 113.8, 113.0, 111.5, 76.9, 61.1, 42.1, 37.5, 8.4. HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_6Na^+$ (M+Na)$^+$**, m/z: 469.1376, observed: 469.1371.

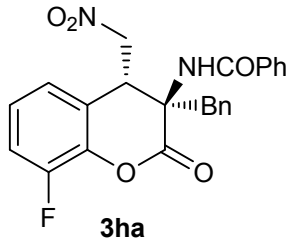



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 11.927 | 16096645 | 49.64 |
| 2 | 15.972 | 16329890 | 50.36 |



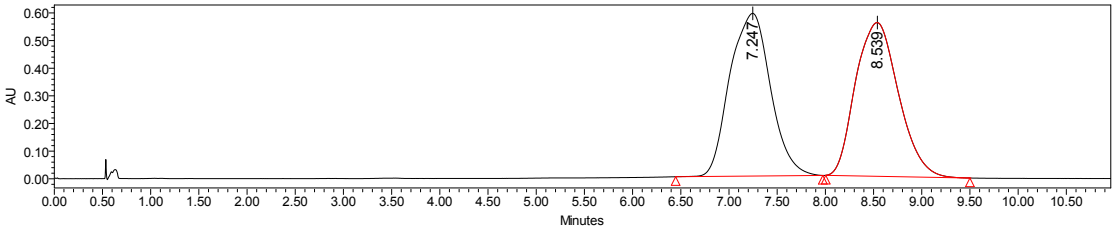

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 11.988 | 21455763 | 98.14 |
| 2 | 16.588 | 406858 | 1.86 |

***N*-((3*R*,4*R*)-3-benzyl-8-fluoro-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ha)**

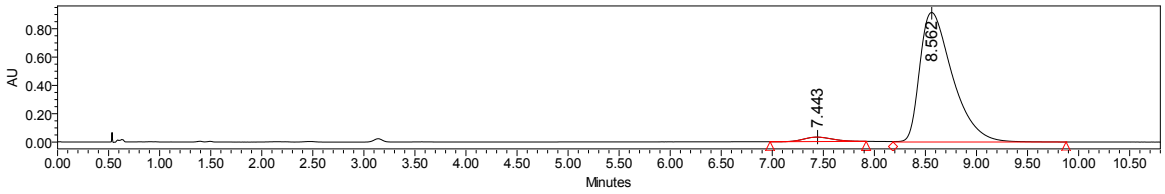


**3ha**

White solid, $[\alpha]^{18}$ = +20.3 (*c*: 0.48, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OD-3, $scCO_2$/$^i$PrOH = 85/15, 2 mL/min, λ = 226 nm, t (major) = 8.56 min, t (minor) = 7.44 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.23 – 7.16 (m, 3H), 7.13 – 6.96 (m, 4H), 6.78 (d, *J* = 7.2 Hz, 1H), 6.43 (s, 1H),5.18 – 5.01 (m, 2H), 4.82 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.16 (d, *J* = 14.4 Hz, 1H), 2.97 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 164.7, 149.8(*J* = 25.1 Hz, 1C), 138.1 (*J* = 11.6 Hz, 1C). 133.0, 132.5, 132.1, 130.0, 129.9 (*J* = 21.6 Hz, 1C),129.1 (*J* = 13.8 Hz, 1C), 128.8 (*J* = 9.5 Hz, 1C), 128.5, 127.0, 125.6 (*J* = 7.0 Hz, 1C),124.0, 121.0, 117.3, 117.1, 74.1, 60.4, 40.2, 36.3. HRMS (ESI-TOF) caled for **$C_{24}H_{19}FN_2O_5Na^+$ (M+Na)$^+$**, m/z: 457.1176, observed: 457.1176.

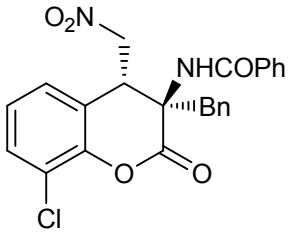



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 7.247 | 17289978 | 50.13 |
| 2 | 8.539 | 17200754 | 49.87 |



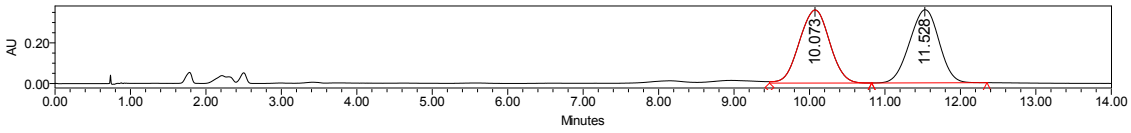

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 7.443 | 619787 | 2.99 |
| 2 | 8.562 | 20125463 | 97.01 |

***N*-((3*R*,4*R*)-3-benzyl-8-chloro-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ia).**

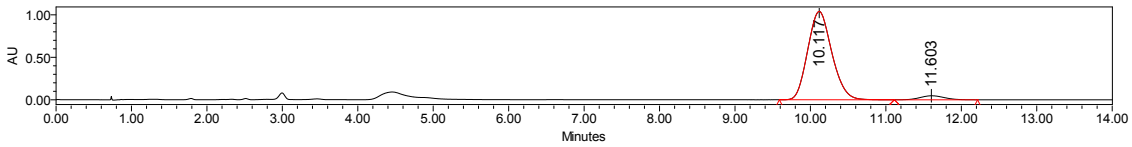



**3ia**

White solid, $[\alpha]^{18}$ = -28.3 (*c*: 0.27, λ = 365 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 80/20, 1.5 mL/min, λ = 236 nm, t (major) = 10.18 min, t (minor) = 11.60 min]; $^1$H NMR (400 MHz, $CDCl_3$) $^1$H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 2H), 7.53 – 7.47 (m, 1H), 7.44 – 7.36 (m, 3H), 7.34 – 7.28 (m, 3H), 7.14 – 7.07 (m, 3H), 7.05 – 6.97 (m, 1H), 6.38 (s, 1H), 5.20 (dd, *J* = 13.6, 3.2 Hz, 1H), 5.10 (d, *J* = 9.6 Hz, 1H), 4.89 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.24 (d, *J* = 14.4 Hz, 1H), 3.11 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 164.9, 146.1, 133.1, 132.5, 132.2, 130.9, 130.0, 129.2, 128.8, 128.5, 127.0, 125.7, 124.4, 123.4, 122.3, 74.1, 60.4, 40.6, 35.9. HRMS (ESI-TOF) caled for **$C_{24}H_{19}ClN_2O_5Na^+$ (M+Na)$^+$**, m/z: 473.0880, 475.0851; observed: 473.0883, 475.0863.

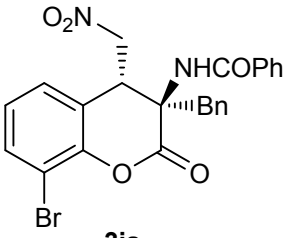



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 10.073 | 10033002 | 50.66 |
| 2 | 11.528 | 9773066 | 49.34 |




| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 10.117 | 23002669 | 95.67 |
| 2 | 11.603 | 1039861 | 4.33 |

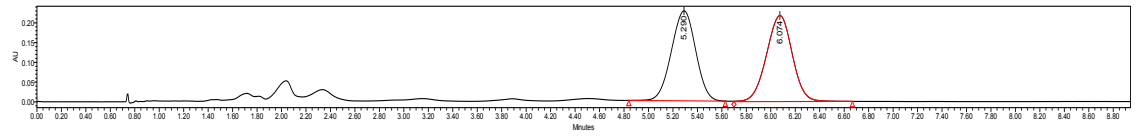
***N*-((3*R*,4*R*)-3-benzyl-8-bromo-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ja)**



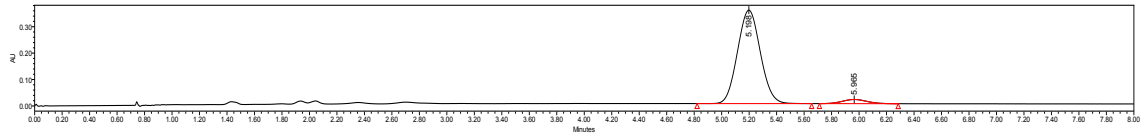

**3ja**

White solid, $[\alpha]^{18}$ = -32.7 (*c*: 0.62, λ =405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 70/30, 1.5 mL/min, λ = 254 nm, t (major) = 5.20 min, t (minor) = 5.97 min]; $^1$H NMR (400 MHz, $(CD_3)_2SO$) δ 8.70 (s, 1H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6

Hz, 2H), 7.46 (t, $J$ = 7.6 Hz, 2H), 7.28 – 7.14 (m, 5H), 7.12 – 7.00 (m, 2H), 5.54 (dd, $J$ = 14.4, 2.8 Hz, 1H), 5.10 (t, $J$ = 10.4 Hz, 1H), 4.69 (t, $J$ = 8.4 Hz, 1H), 3.33 (d, $J$ = 14.4 Hz, 1H), 3.23 (d, $J$ = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 166.7, 164.9, 147.0, 133.9, 133.1, 132.7, 131.9, 130.3, 128.3, 128.0, 127.4, 127.1, 125.4, 123.8, 108.9, 74.7, 59.5, 36.3. HRMS (ESI-TOF) calcd for **[M+Na]$^+$ $C_{24}H_{19}BrN_2O_5Na^+$**, m/z: 517.0375, 519.0355; observed: 517.0387, 519.0369.

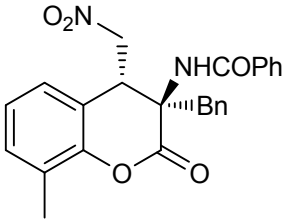



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 6.074 | 3190549 | 50.33 |
| 2 | 5.290 | 3148165 | 49.67 |



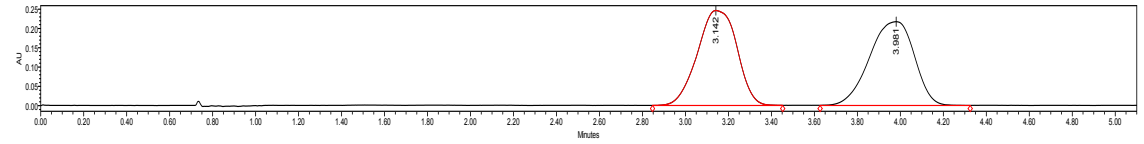

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 5.198 | 4075029 | 95.44 |
| 2 | 5.965 | 194720 | 4.56 |

***N*-((3*R*,4*R*)-3-benzyl-8-methyl-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ka).**

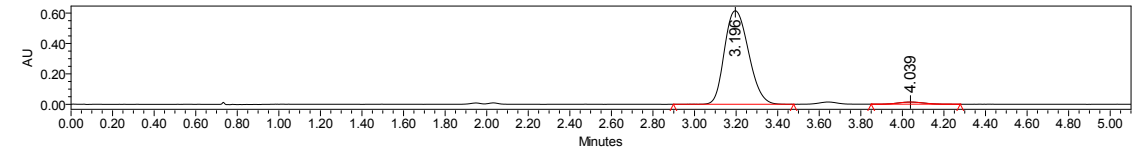



**3ka**

White solid, $[\alpha]^{18}$ = -26.1 (*c*: 0.66, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 3.20 min, t (minor) = 4.04 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 2H), 7.53 – 7.47 (m, 1H), 7.44 – 7.36 (m, 3H), 7.34 – 7.28 (m, 3H), 7.14 – 7.07 (m, 3H), 7.05 – 6.97 (m, 1H), 6.38 (s, 1H), 5.20 (dd, $J$ = 13.6, 3.2 Hz, 1H), 5.10 (d, $J$ = 9.6 Hz, 1H), 4.89 (dd, $J$ = 13.6, 9.6 Hz, 1H), 3.24 (d, $J$ = 14.4 Hz, 1H), 3.11 (d, $J$ = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 164.9, 146.1, 133.1, 132.5, 132.2, 130.9, 130.0, 129.2, 128.8, 128.5, 127.0, 125.7, 124.4, 123.4, 122.3, 74.1, 60.4, 40.6, 35.9. HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 453.1426, observed: 453.1429.

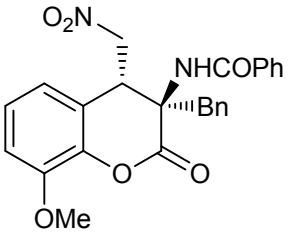



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.142 | 3156252 | 49.98 |
| 2 | 3.981 | 3159388 | 50.02 |



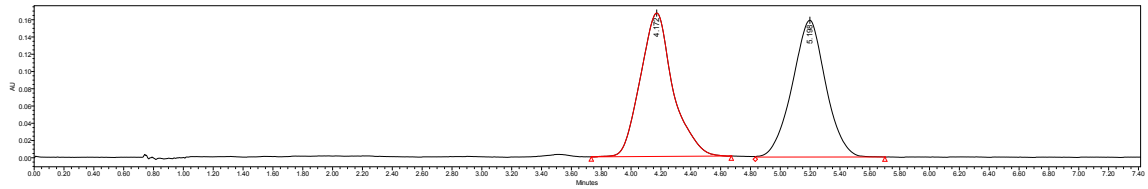
| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.196 | 4944001 | 97.62 |
| 2 | 4.039 | 120510 | 2.38 |

***N*-((3*R*,4*R*)-3-benzyl-8-methoxy-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3la)**

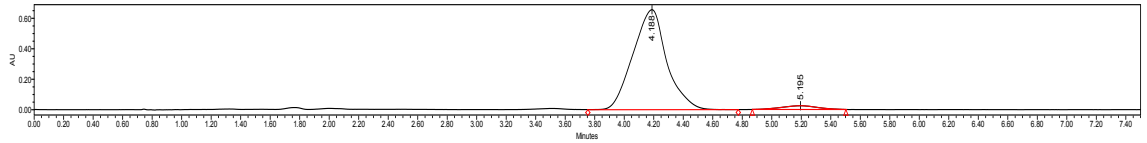



**3la**

White solid, $[\alpha]^{18}$ = -10.5 (*c*: 0.71, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 4.19 min, t (minor) = 5.20 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.19 – 7.04 (m, 3H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.46 (s, 1H), 5.24 (dd, *J* = 13.6, 3.2 Hz, 1H), 5.06 (d, *J* = 9.2 Hz, 1H), 4.90 (dd, *J* = 13.6, 9.6 Hz, 1H), 3.90 (s, 3H), 3.27 (d, *J* = 14.4 Hz, 1H), 3.13 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.6, 147.6, 139.1, 133.4, 132.7, 132.3, 130.1, 129.1, 128.7, 128.2, 127.0, 125.6, 122.6, 117.2, 113.0, 74.3, 60.5, 56.3, 40.6, 35.4. HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_6Na^+$ (M+Na)$^+$**, m/z: 469.1376, observed:469.1373.

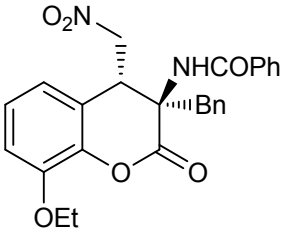



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.172 | 2518490 | 50.50 |
| 2 | 5.198 | 2468472 | 49.50 |



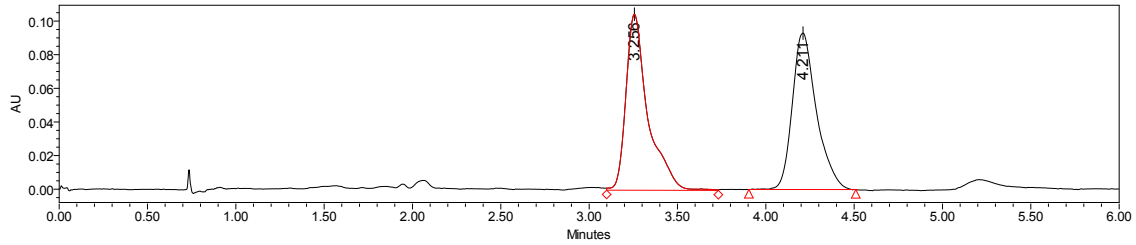

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.188 | 10445265 | 96.17 |
| 2 | 5.195 | 415795 | 3.83 |

***N*-((3*R*,4*R*)-3-benzyl-8-ethoxy-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ma)**

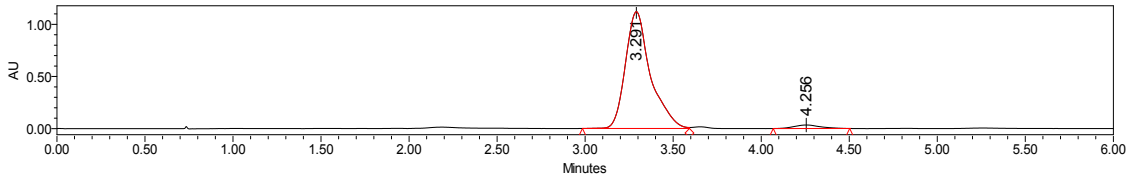



**3ma**

White solid, $[\alpha]^{18}$ = -16.3 (*c*: 0.64, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 239 nm, t (major) = 3.29 min, t (minor) = 4.26 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 6.0 Hz, 3H), 7.11 – 7.02 (m, 3H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 6.57 (d, *J* = 15.6 Hz, 1H), 5.18 (dd, *J* = 13.6, 2.8 Hz, 1H), 5.04 (d, *J* = 8.8 Hz, 1H), 4.87 (dd, *J* = 13.6, 10.0 Hz, 1H), 4.09 (q, *J* =7.2 Hz, 2H), 3.26 (d, *J* = 14.4 Hz, 1H), 3.12 (d, *J* = 14.4 Hz, 1H), 1.41 (t, *J* = 7.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.7, 146.8, 139.5, 133.4, 132.8, 132.2, 130.1, 129.0, 128.7, 128.1, 127.1, 125.5, 122.7, 117.3, 114.4, 74.4, 65.1, 60.5, 40.5, 35.6, 14.7. HRMS (ESI-TOF) caled for **$C_{26}H_{24}N_2O_6Na^+$ (M+Na)$^+$**, m/z: 483.1532, observed: 483.1536.

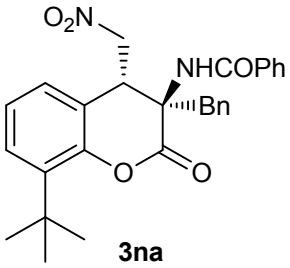



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.256 | 905866 | 50.60 |
| 2 | 4.210 | 884331 | 49.40 |



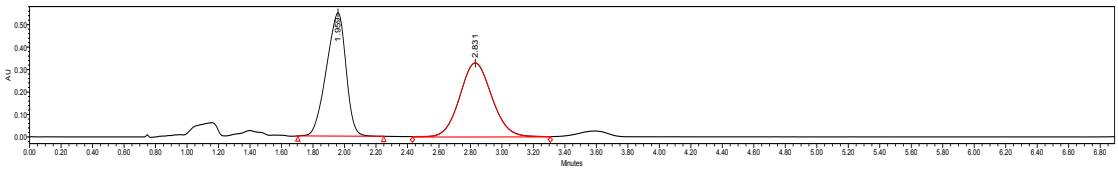

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.291 | 11057721 | 96.93 |
| 2 | 4.256 | 350354 | 3.07 |

**_N_-((3_R_,4_R_)-3-benzyl-8-(tert-butyl)-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3na)**

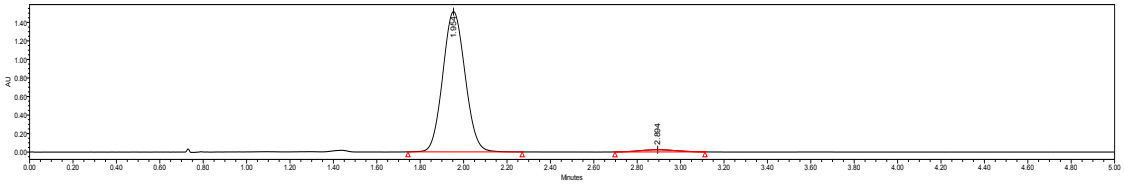



**3na**

White solid, $[\alpha]^{18}$ = -128.9 (*c*: 0.48, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 70/30, 1.5 mL/min, λ = 254 nm, t (major) = 1.95 min, t (minor) = 2.89 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.40 (m, 3H), 7.38 – 7.29 (m, 6H), 7.16 – 7.11 (m, 2H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.06 (s, 1H), 5.16 (dd, *J* = 13.2, 3.2 Hz, 1H), 4.80 (dd, *J* = 13.2, 10.4 Hz, 1H), 4.65 (s, 1H), 3.46 (d, *J* = 14.4 Hz, 1H), 3.09 (d, *J* = 14.4 Hz, 1H), 1.41 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.5, 149.2, 138.3, 133.2, 133.1, 132.3, 130.2, 129.1, 128.8, 128.1, 127.9, 126.9, 125.0, 124.8, 121.5, 74.7, 59.2, 41.0, 35.2, 35.0, 29.9. HRMS (ESI-TOF) caled for **$C_{28}H_{28}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 495.1896, observed: 495.1993.

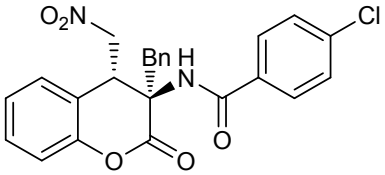



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 1.959 | 4722127 | 50.09 |
| 2 | 2.831 | 4704480 | 49.91 |



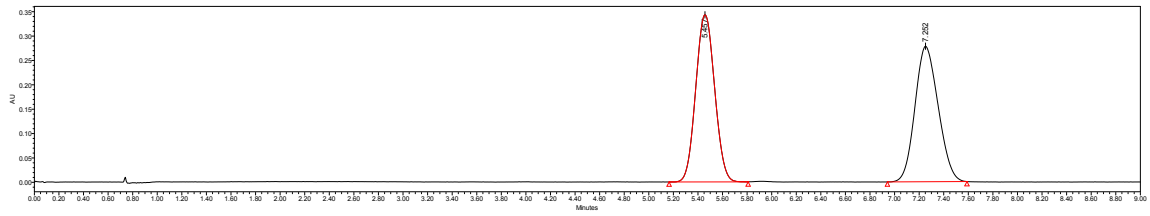
| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 1.954 | 10782399 | 97.54 |
| 2 | 2.894 | 272008 | 2.46 |

***N*-((3*R*,4*R*)-3-benzyl-4-(nitromethyl)-2-oxochroman-3-yl)-4-chlorobenzamide (3ab)**

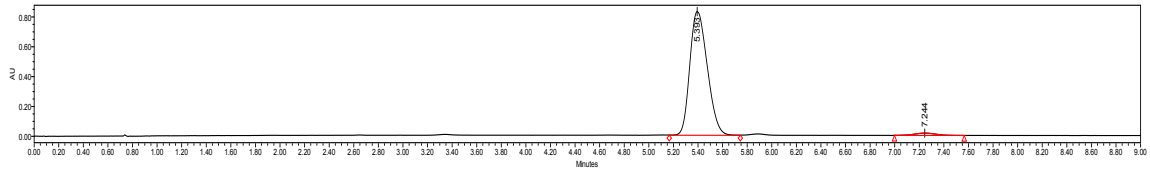


**3ab**

White solid, $[\alpha]_D^{18}$ = +14.9 (*c*: 0.74, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 5.40 min, t (minor) = 7.24 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.4 Hz, 2H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.19 (dd, *J* = 6.0, 3.2 Hz, 5H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.05 – 6.93 (m, 4H), 6.42 (s, 1H), 5.10 (dd, *J* = 13.6, 3.6 Hz, 1H), 4.98 (d, *J* = 8.8 Hz, 1H), 4.81 (dd, *J* = 13.6, 9.2 Hz, 1H), 3.14 (d, *J* = 14.4 Hz, 1H), 2.97 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 167.1, 165.8, 145.0, 138.7, 132.5, 131.6, 130.1, 130.0, 129.12, 129.0, 128.4, 128.3, 126.2, 125.5, 121.3, 116.9, 74.3, 60.7, 40.2, 35.8. HRMS (ESI-TOF) caled for **$C_{24}H_{19}ClN_2O_5Na^+$ (M+Na)$^+$**, m/z: 473.0880, 475.0851; observed: 473.0880, 475.0860.

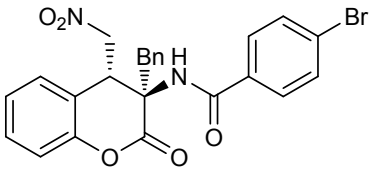


| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 5.457 | 3668391 | 50.15 |
| 2 | 7.252 | 3645882 | 49.85 |



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 5.393 | 8208001 | 97.79 |
| 2 | 7.244 | 185873 | 2.21 |

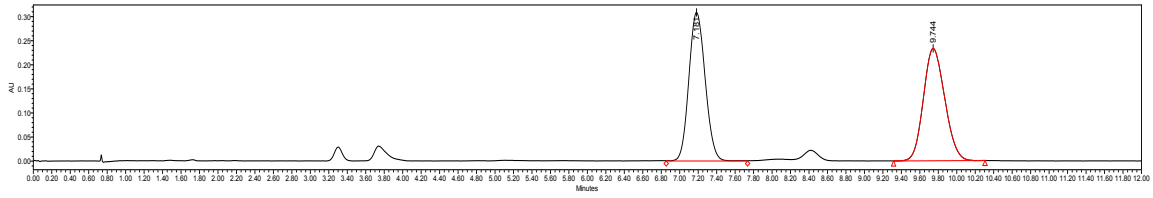
***N*-((3*R*,4*R*)-3-benzyl-4-oxochroman-3-yl)-4-(nitromethyl)-2-bromobenzamide (3ac)**



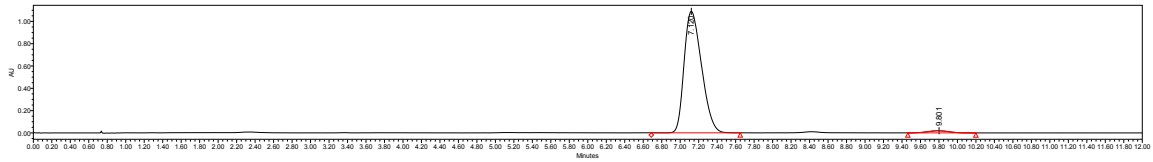
**3ac**

White solid, $[\alpha]_D^{18}$ = +18.5 (*c*: 0.80, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 7.12 min, t (minor) = 9.80 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.32 (m,2H), 7.26 (d, *J* = 8.4

Hz, 2H), 7.22 – 7.17 (m, 4H), 7.13 – 6.96 (m, 5H), 6.44 (s, 1H), 5.09 (dd, *J* = 13.6, 3.2 Hz, 1H), 4.97 (d, *J* = 8.0 Hz, 1H), 4.80 (dd, *J* = 12.8, 10.0Hz, 1H), 3.14 (d, *J* = 14.4 Hz, 1H), 2.97 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 167.2, 165.8, 150.0, 132.5, 132.0, 132.0, 130.1, 130.0, 129.1, 128.6, 128.4, 127.2, 126.2, 125.6, 121.3, 116.9, 74.3, 60.6, 40.2, 35.8. HRMS (ESI-TOF) calcd for **[M+Na]$^+$ $C_{24}H_{19}BrN_2O_5Na^+$**, m/z: 517.0375, 519.0355; observed: 517.0375, 519.0380.

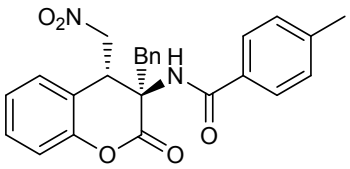



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 7.181 | 3786610 | 50.27 |
| 2 | 9.744 | 3745457 | 49.73 |



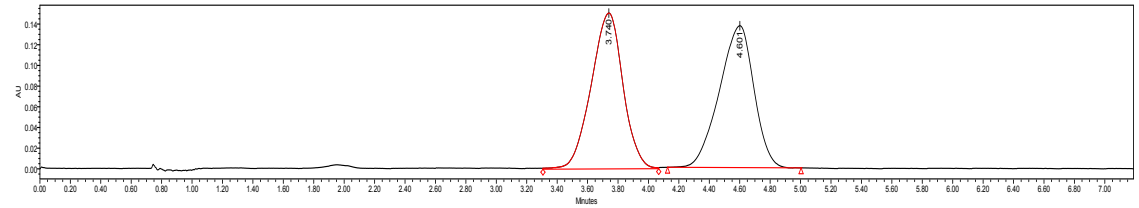

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 7.120 | 14250899 | 97.90 |
| 2 | 9.801 | 306299 | 2.10 |

***N*-((3*R*,4*R*)-3-benzyl-4-(nitromethyl)-2-oxochroman-3-yl)-4-methylbenzamide (3ad)**

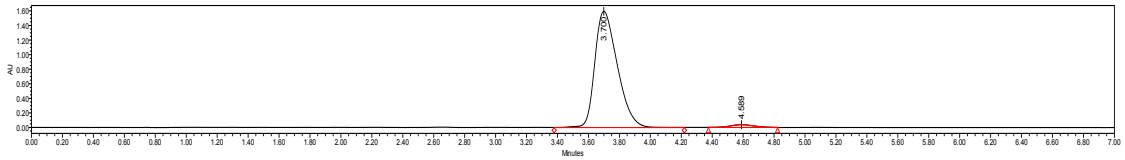



**3ad**

White solid, $[\alpha]^{18}$ = +19.8 (*c*: 0.80, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 3.70 min, t (minor) = 4.59 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.27 (m, 4H), 7.20 – 7.05 (m, 7H), 6.33 (s, 1H), 5.22 (dd, *J* = 13.6, 2.8 Hz, 1H), 4.96 (d, *J* = 9.2 Hz, 1H), 4.86 (dd, *J* = 12.8, 10.0 Hz, 1H), 3.28 (d, *J* = 14.4 Hz, 1H), 3.11 (d, *J* = 14.4 Hz, 1H), 2.35 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.0, 166.0, 150.2, 143.0, 132.8, 130.4, 130.1, 130.1, 129.4, 129.1, 128.2, 127.0, 126.4, 125.4, 121.4, 116.9, 74.4, 60.4, 40.5, 35.5, 21.5. HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 453.1426, observed: 453.1427.

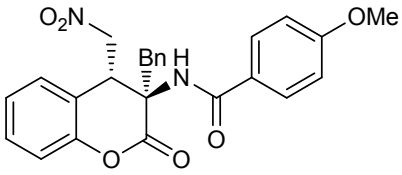



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.740 | 2192509 | 50.33 |
| 2 | 4.601 | 2163406 | 49.67 |



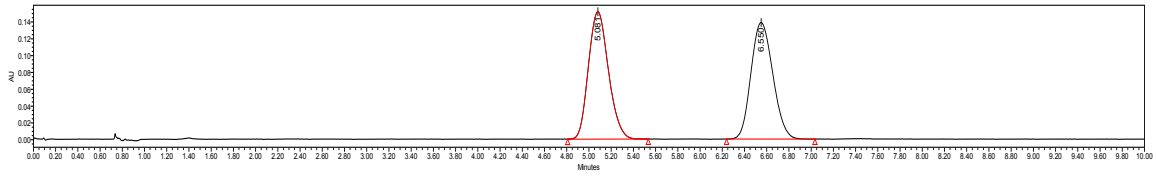
| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.700 | 16123064 | 97.61 |
| 2 | 4.589 | 395562 | 2.39 |

***N*-((3*R*,4*R*)-3-benzyl-4-(nitromethyl)-2-oxochroman-3-yl)-4-methoxybenzamide (3ae)**

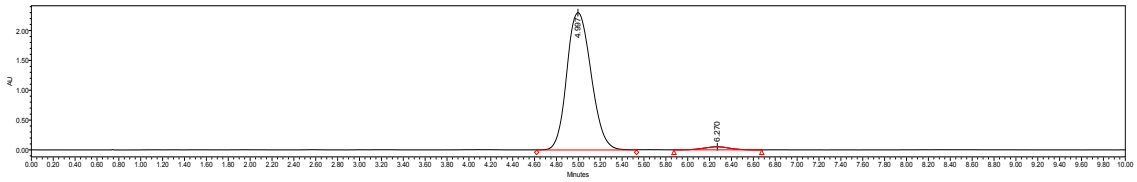


**3ae**

White solid, $[\alpha]^{18}$ = +39.0 (*c*: 0.70, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 5.00 min, t (minor) = 6.27 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.8 Hz, 2H), 7.43 – 7.23 (m, 4H), 7.21 – 7.03 (m, 5H), 6.95 – 6.75 (m, 2H), 6.28 (s, 1H), 5.22 (dd, *J* = 13.6, 3.2 Hz, 1H), 4.98 (d, *J* = 8.4 Hz, 1H), 4.86 (dd, *J* = 13.2, 10.0 Hz, 1H), 3.81 (s, 1H), 3.27 (d, *J* = 14.4 Hz, 1H), 3.10 (d, *J* = 14.4 Hz, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 167.5, 166.1, 162.9, 150.2, 132.8, 130.1, 129.1, 129.0, 128.3, 126.4, 125.4, 125.4, 121.5, 116.9, 114.0, 74.4, 60.4, 55.5, 40.5, 35.6. HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_6Na^+$ (M+Na)$^+$**, m/z: 469.1376, observed: 469.1374.

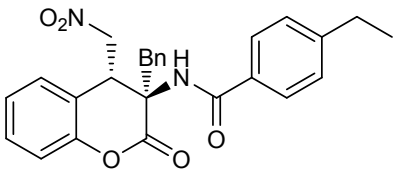


| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 5.081 | 1892455 | 50.00 |
| 2 | 6.550 | 1892191 | 50.00 |



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.998 | 17148322 | 97.77 |
| 2 | 6.272 | 390519 | 2.23 |

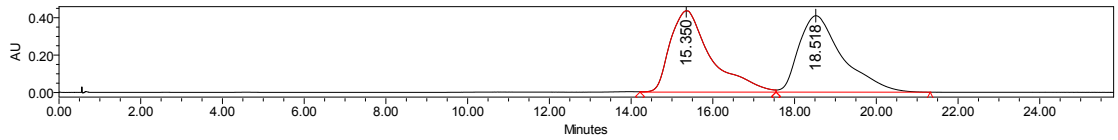
***N*-((3*R*,4*R*)-3-benzyl-4-(nitromethyl)-2-oxochroman-3-yl)-4-ethylbenzamide (3af)**



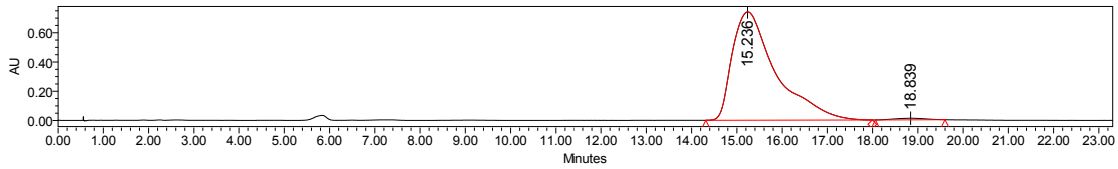
**3af**

White solid, $[\alpha]^{18}$ = +27.0 (*c*: 0.64, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3,

$scCO_2$/$^i$PrOH = 90/10, 2 mL/min, λ = 237.0 nm, t (major) = 15.24 min, t (minor) = 18.84 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.40 – 7.28 (m, 4H), 7.23 – 7.04 (m, 7H), 6.36 (s, 1H), 5.22 (dd, *J* = 13.2, 3.2 Hz, 1H), 5.08 – 4.74 (m, 2H), 3.20 (dd, *J* = 74.8, 14.4 Hz, 2H), 2.80 – 2.49 (m, 2H), 1.21 (t, *J* = 7.6 Hz, 3H). $^{13}$C NMR (100 Hz, $CDCl_3$) δ 1680 1660 150.2, 149.2, 132.8 130.6, 130.1 130.1 129.1, 128.3 127.1, 126.4, 125.4, 121.4, 116.9, 74.4 60.3, 40.6 35.5 28.8, 15.2. HRMS (ESI-TOF) caled for **$C_{26}H_{24}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 467.1583, observed: 467.1587.

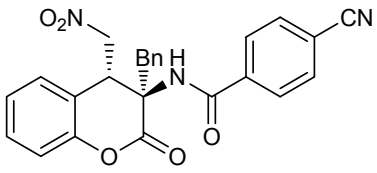



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 15.350 | 30277677 | 49.92 |
| 2 | 18.518 | 30376356 | 50.08 |



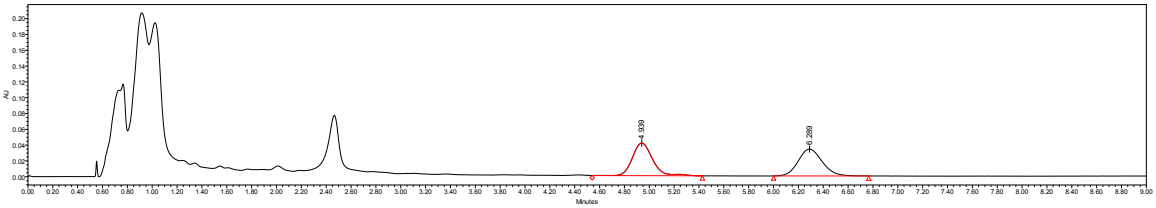

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 15.236 | 49393675 | 98.98 |
| 2 | 18.839 | 510020 | 1.02 |

**_N_-((3_R_,4_R_)-3-benzyl-4-(nitromethyl)-2-oxochroman-3-yl)-4-cyanobenzamide (3ag)**

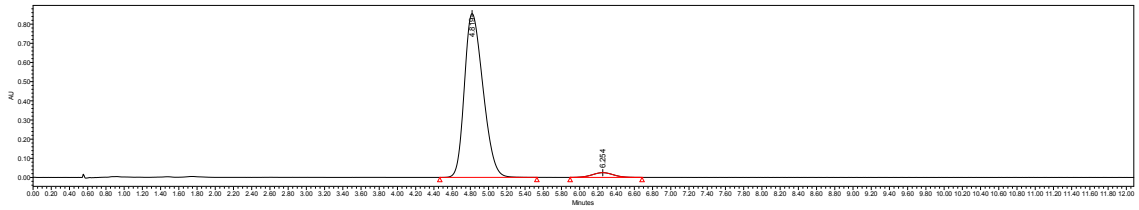



**3ag**

White solid, [α]$^{18}$ = +64.1 (*c*: 0.26, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 254 nm, t (major) = 4.82 min, t (minor) = 6.26 min]; $^1$H NMR (400 MHz, $(CD_3)_2SO$) δ 8.88 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.07 (m, 7H), 7.02 (d, *J* = 8.0 Hz, 1H), 5.52 (dd, *J* = 14.0, 2.8 Hz, 1H), 5.09 – 4.92 (t, *J* = 10.8 Hz, 1H), 4.65 (d, *J* = 6.8 Hz, 1H), 3.25 (dd, *J* = 28.4, 14.4 Hz, 2H).$^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 165.3, 165.1, 150.1, 137.1, 134.1, 132.4, 130.4, 129.5, 128.2, 128.1, 127.9, 127.1, 124.5, 121.6, 118.1, 115.8, 114.2, 74.9, 59.9, 36.0. HRMS (ESI-TOF) caled for **$C_{25}H_{19}N_3O_5Na^+$ (M+Na)$^+$**, m/z: 464.1222, observed: 464.1221.

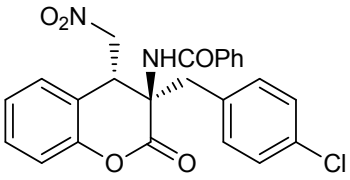


| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.939 | 465485 | 50.54 |
| 2 | 6.289 | 455517 | 49.46 |



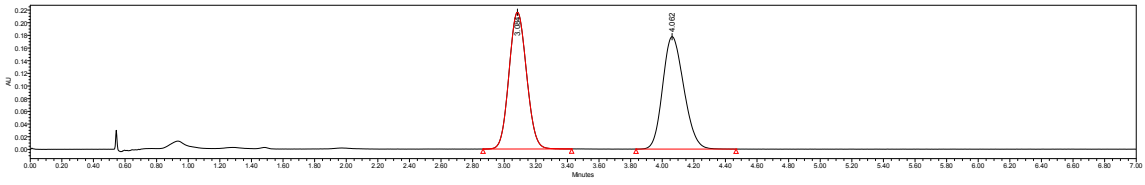
| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 4.819 | 12090792 | 96.80 |
| 2 | 6.254 | 399101 | 3.20 |

***N*-((3*R*,4*R*)-3-(4-methylbenzyl)-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ah)**

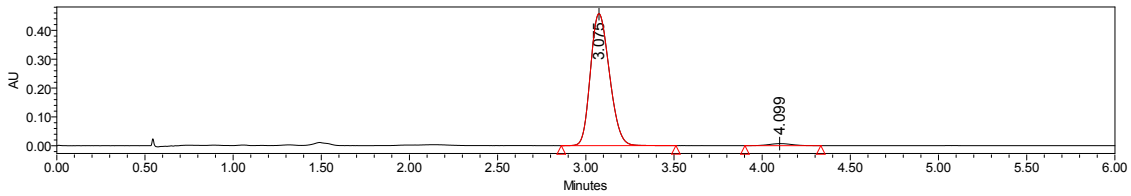


**3ah**

White solid, $[\alpha]^{18}$ = -78.3 (*c*: 0.58, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 70/30, 2.0 mL/min, λ = 254 nm, t (major) = 3.08 min, t (minor) = 4.10 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.44 (m, 3H), 7.43 – 7.32 (m, 3H), 7.25 – 7.15 (m, 3H), 7.14 – 7.08 (m, 2H), 7.05 – 6.95 (m, 2H), 6.45 (s, 1H), 5.26 (q, *J* = 9.2 Hz, 1H), 4.98 – 4.74 (m, 2H), 3.29 – 3.17 (dd, *J* = 20.4, 14.4 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 168.1, 166.0, 150.0, 134.2, 133.2, 132.5, 131.3, 130.3, 129.2, 128.9, 127.0, 126.4, 125.6, 121.2, 117.0, 74.4, 60.7, 41.0, 34.5. HRMS (ESI-TOF) caled for **$C_{24}H_{19}ClN_2O_5Na^+$ (M+Na)$^+$**, m/z: 473.0880, 475.0851; observed: 473.0882, 475.0872.

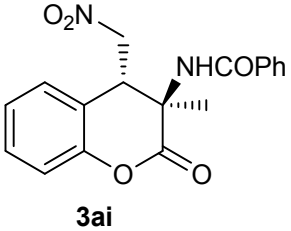


| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.084 | 4804485 | 50.04 |
| 2 | 4.063 | 4797632 | 49.96 |




| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 3.075 | 4138639 | 98.19 |
| 2 | 4.099 | 76371 | 1.81 |

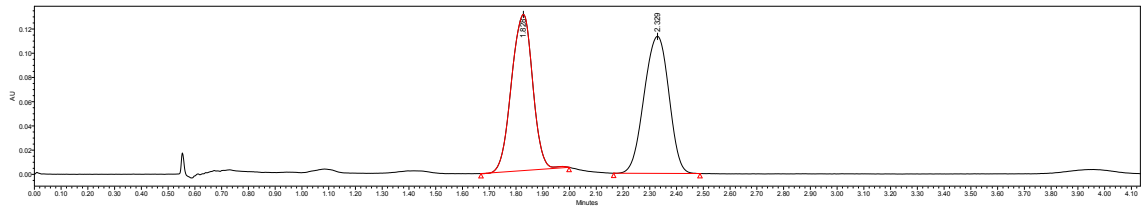
***N*-((3*R*,4*R*)-3-methyl-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3ai)**



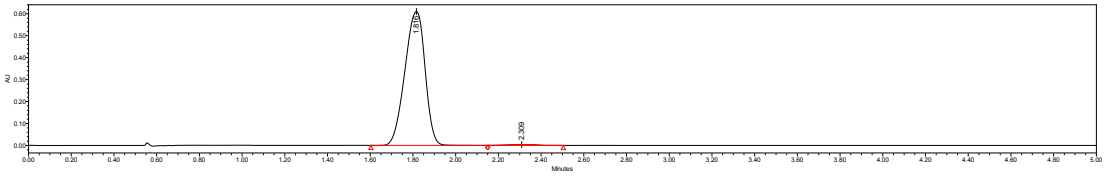
**3ai**

White solid, $[\alpha]^{18}$ = -52.5 (*c*: 0.52, λ = 405 nm, MeOH); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 232.0 nm, t (major) = 1.82 min, t (minor) = 2.33 min]; $^1$H NMR (400 MHz, $(CD_3)_2SO$) δ 8.91 (s, 1H), 7.82 – 7.73 (m, 2H), 7.60 – 7.53 (m, 1H),

7.53– 7.44 (m, 2H), 7.44 – 7.35 (m, 3H), 7.33 – 7.07 (m, 3H), 5.24 (dd, *J* = 14.4, 8.0 Hz, 1H), 5.10 (dd, *J* = 14.4, 4.8 Hz, 1H), 4.93 (dd, *J* = 8.4, 4.4 Hz, 1H), 1.35 (s, 4H). $^{13}$C NMR (100 MHz, $(CD_3)_2SO$) δ 167.5, 167.0, 149.9, 133.4, 131.8, 129.4, 128.2, 127.6, 126.7, 125.0, 121.9, 116.4, 74.2, 56.5, 18.1. HRMS (ESI-TOF) caled for **$C_{18}H_{16}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 363.0956, observed: 363.0963.

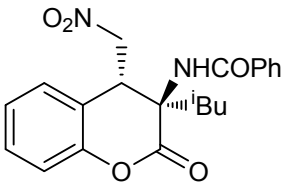



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 1.828 | 712576 | 49.48 |
| 2 | 2.329 | 727630 | 50.52 |



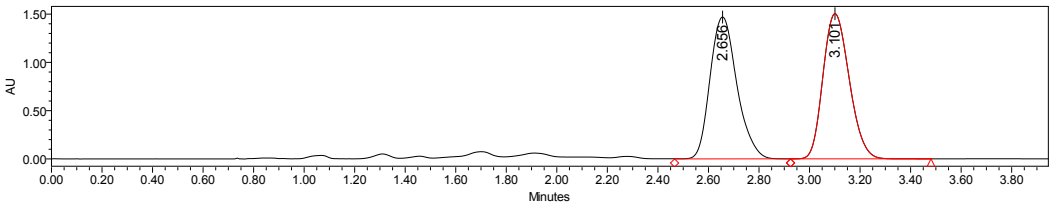

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 1.816 | 4003826 | 99.14 |
| 2 | 2.309 | 34535 | 0.86 |

***N*-((3R,4R)-3-isobutyl-4-(nitromethyl)-2-oxochroman-3-yl)benzamide(3aj)**

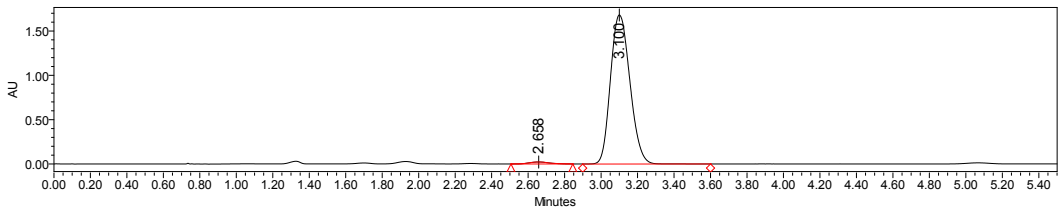



**3aj**

White solid, $[\alpha]^{18}$ = +19.4 (*c*: 0.52, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 85/15, 1.5 mL/min, λ = 238 nm, t (major) = 3.10 min, t (minor) = 2.69 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* =8.0 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.45 – 7.33 (m, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 6.8 Hz, 1H), 6.74 (s, 1H), 5.23 – 5.12 (m, 1H), 5.03 (dd, *J* = 13.6, 3.2 Hz, 1H), 4.85 (dd, *J* = 13.6, 9.2 Hz, 1H), 1.77 – 1.57 (m, 3H), 1.00 (d, *J* = 5.2 Hz, 3H), 0.81 (d, *J* = 5.2 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 167.9, 166.3, 149.8, 133.5, 132.3, 129.8, 128.8, 127.0, 125.7, 125.5, 121.8, 117.0, 74.2, 60.7, 40.7, 38.1, 24.4, 23.9, 23.7. HRMS (ESI-TOF) caled for **$C_{21}H_{22}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 405.1426, observed: 405.1427.

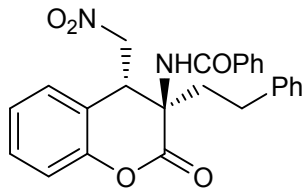



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 2.656 | 10841745 | 50.00 |
| 2 | 3.101 | 10841334 | 50.00 |



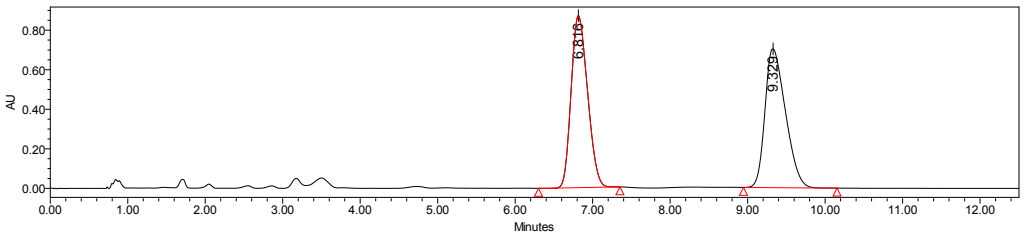

| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 2.658 | 167314 | 1.33 |
| 2 | 3.100 | 12449065 | 98.67 |

***N*-((3*R*,4*R*)-4-(nitromethyl)-2-oxo-3-phenethylchroman-3-yl)benzamide (3ak)**

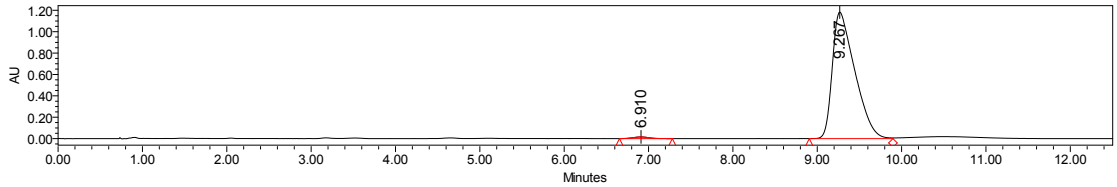



**3ak**

White solid, $[\alpha]^{18}$ = -16.4 (*c*: 0.52, λ = 405 nm, $CH_2Cl_2$); Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/MeOH = 80/20, 1.5 mL/min, λ = 229 nm, t (major) = 9.27 min, t (minor) = 6.91 min]; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 1H), 7.41 – 7.37 (m, 2H), 7.37 – 7.26 (m, 4H), 7.25 – 7.13 (m, 5H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.61 (s, 1H), 5.17 (dd, *J* = 9.2, 3.6Hz, 1H), 5.00 (dd, *J* = 13.6, 4.0 Hz, 1H), 4.87 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.83 – 2.61 (m, 2H), 2.31 – 2.18 (m, 1H), 2.17 – 2.08 (m, 1H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 167.9, 166.0, 149.9, 139.6, 132.9, 132.3, 129.9, 129.1, 128.6, 128.5, 127.0, 126.8, 125.9, 125.6, 121.5, 117.0, 74.2, 61.1, 40.4, 30.8, 29.9.
HRMS (ESI-TOF) caled for **$C_{25}H_{22}N_2O_5Na^+$ (M+Na)$^+$**, m/z: 453.1426, observed: 453.1427.

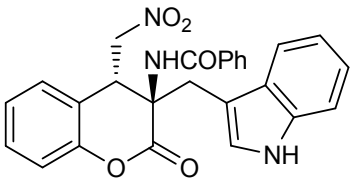



| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 6.816 | 12765955 | 49.82 |
| 2 | 9.329 | 12857210 | 50.18 |




| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 6.910 | 204320 | 0.93 |
| 2 | 9.267 | 21867126 | 99.07 |

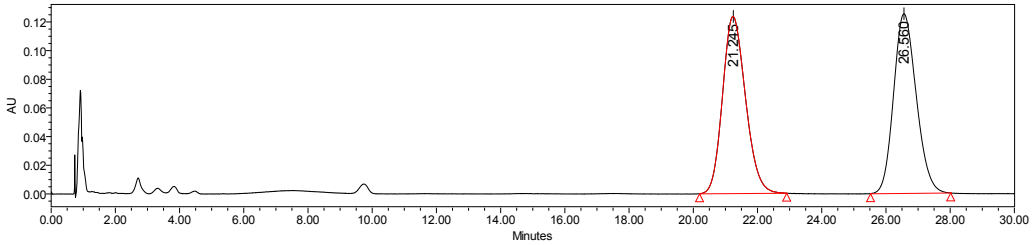
***N*-((3*R*,4*R*)-3-((1H-indol-3-yl)methyl)-4-(nitromethyl)-2-oxochroman-3-yl)benzamide (3al)**



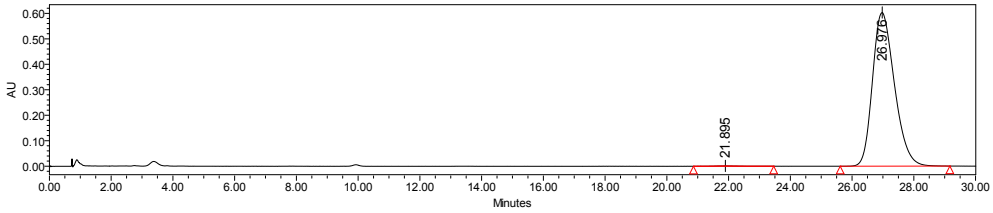

**3al**

White solid, $[\alpha]^{18}$ = -196.6 (*c*: 0.47, λ = 405 nm, $CH_3COCH_3$);

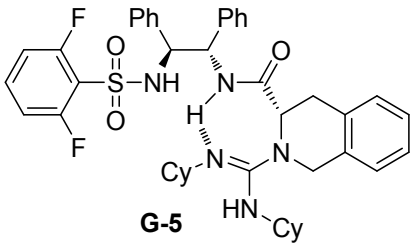
Determined by UPC2 analysis [Daicel chiralcel OJ-3, $scCO_2$/$^i$PrOH = 70/30, 1.5 mL/min, λ = 222.5 nm, t (major) = 26.98 min, t (minor) = 21.90 min]; $^1$H NMR (400 MHz, $(CD_3)_2CO$) δ 10.17 (s, 1H), 7.50 (s, 1H), 7.40 – 7.27 (m, 5H), 7.26 – 7.11 (m, 4H), 7.05 – 6.86 (m, 4H), 6.73 (t, *J* = 7.6 Hz, 1H), 5.66 – 5.35 (m, 1H), 4.97 – 4.59 (m, 2H), 3.65 (d, *J* = 15.6 Hz, 1H), 3.26 (d, *J* = 15.6 Hz, 1H). $^{13}$C NMR (100 MHz, $(CD_3)_2CO$) δ 168.0, 166.9, 152.1, 137.3, 134.8, 132.5, 130.4, 129.4, 129.2, 129.0, 128.2, 125.9, 125.2, 123.0, 122.4, 119.9, 119.3, 116.9, 112.3, 107.6, 76.2, 60.5, 41.3, 27.1. HRMS (ESI-TOF) caled for **$C_{26}H_{21}N_3O_5Na^+$ (M+Na)$^+$**, m/z: 478.1379, observed: 478.1374.




| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 21.245 | 6154771 | 50.04 |
| 2 | 26.560 | 6145168 | 49.96 |




| | Retention Time | Area | % Area |
|---|---|---|---|
| 1 | 21.895 | 60721 | 0.20 |
| 2 | 26.976 | 29758704 | 99.80 |

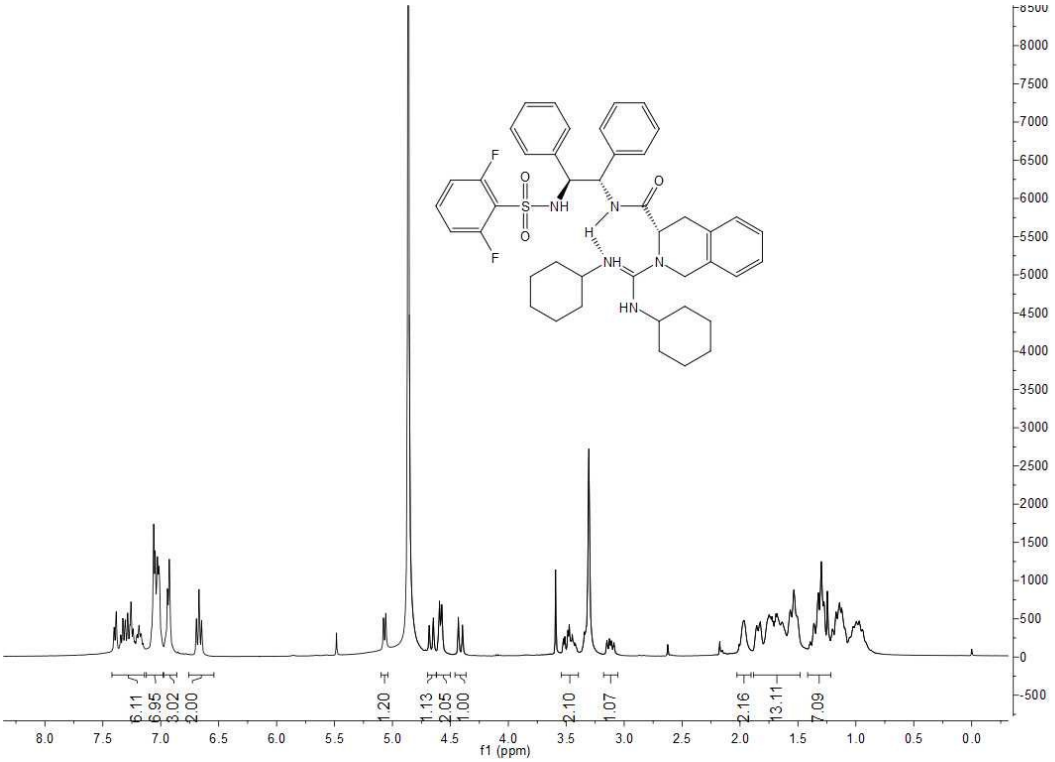


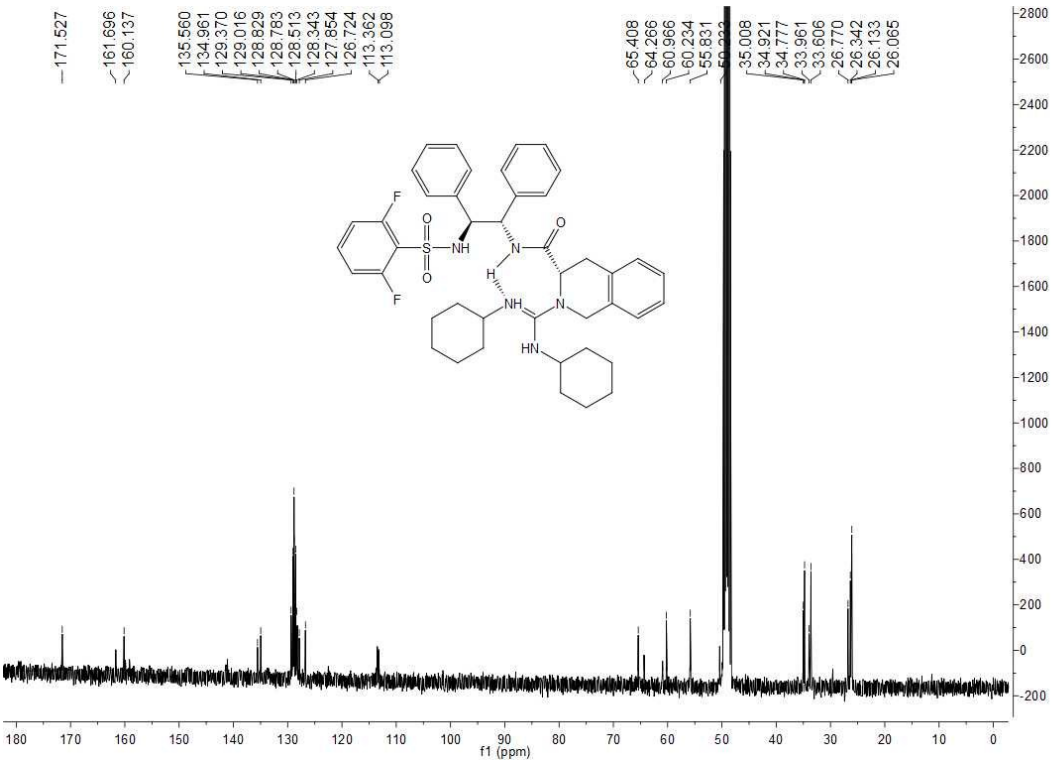

**G-5**

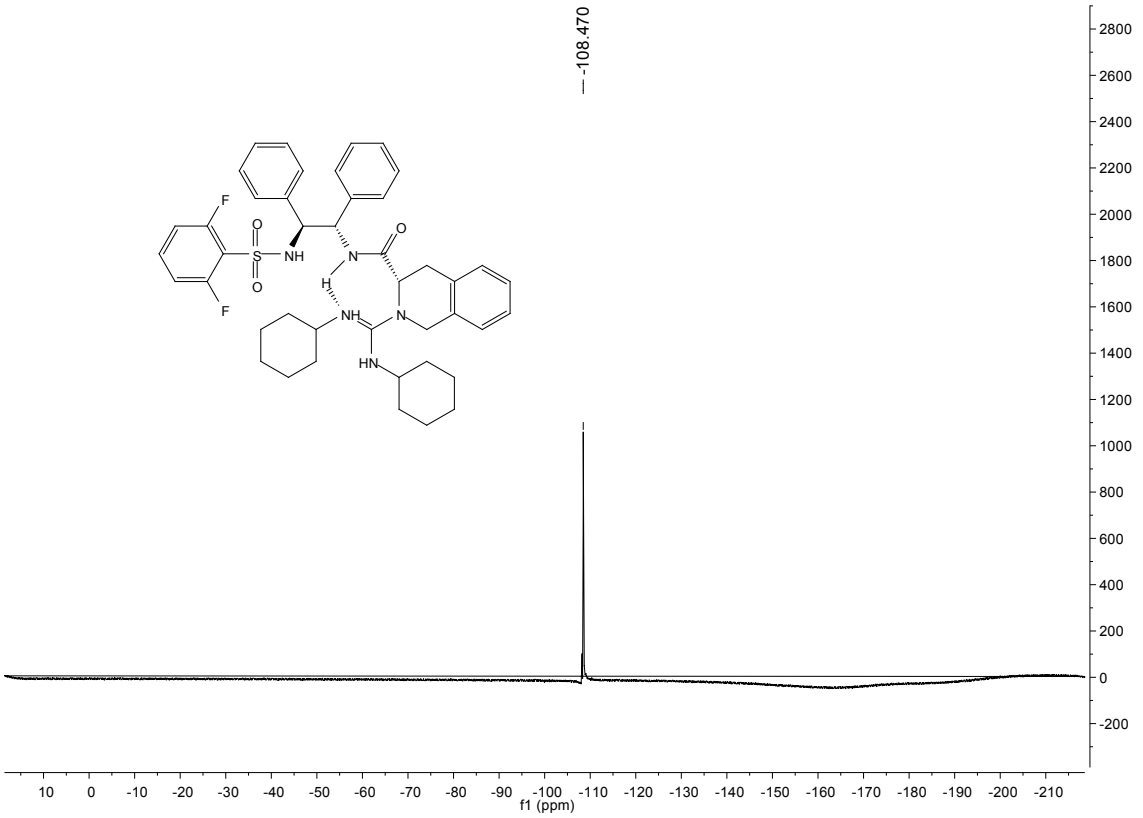
White solid, $[\alpha]_D^{18}$ = +36.3 (*c*: 0.20, $CH_2Cl_2$); HRMS (ESI-TOF) caled for **$C_{43}H_{49}F_2N_5O_3SH^+$ (M+H)$^+$**, m/z: 754.3602, observed: 754.3599. $^1$H NMR (400 MHz, MeOD) δ 7.44 – 7.14 (m, 6H), 7.04 (dd, *J* = 12.8, 5.2 Hz, 7H), 6.93 (d, *J* = 6.4 Hz, 3H), 6.67 (t, *J* = 8.8 Hz, 1H), 5.07 (d, *J* = 8.0 Hz, 1H), 4.66 (d, *J* = 14.0 Hz, 1H), 4.58 (d, *J* = 7.6 Hz, 2H), 4.41 (d, *J* = 14.0 Hz, 1H), 3.54 – 3.39 (m, 2H), 3.12 (dd, *J* = 15.2, 8.8 Hz, 1H), 1.97 (s, 2H), 1.88 – 1.46 (m, 13H), 1.42 – 1.22 (m, 7H). $^{13}$C NMR (100 MHz, MeOD) δ 171.5, 161.7, 160.1, 135.6, 135.0, 129.4, 129.0, 128.8, 128.8, 128.5, 128.3, 127.9, 126.7, 113.4, 113.1, 65.4, 64.3, 61.0, 60.2, 55.8, 50.2, 35.0, 34.9, 34.8, 34.0, 33.6, 26.8, 26.3, 26.1, 26.

## 7. NMR spectra

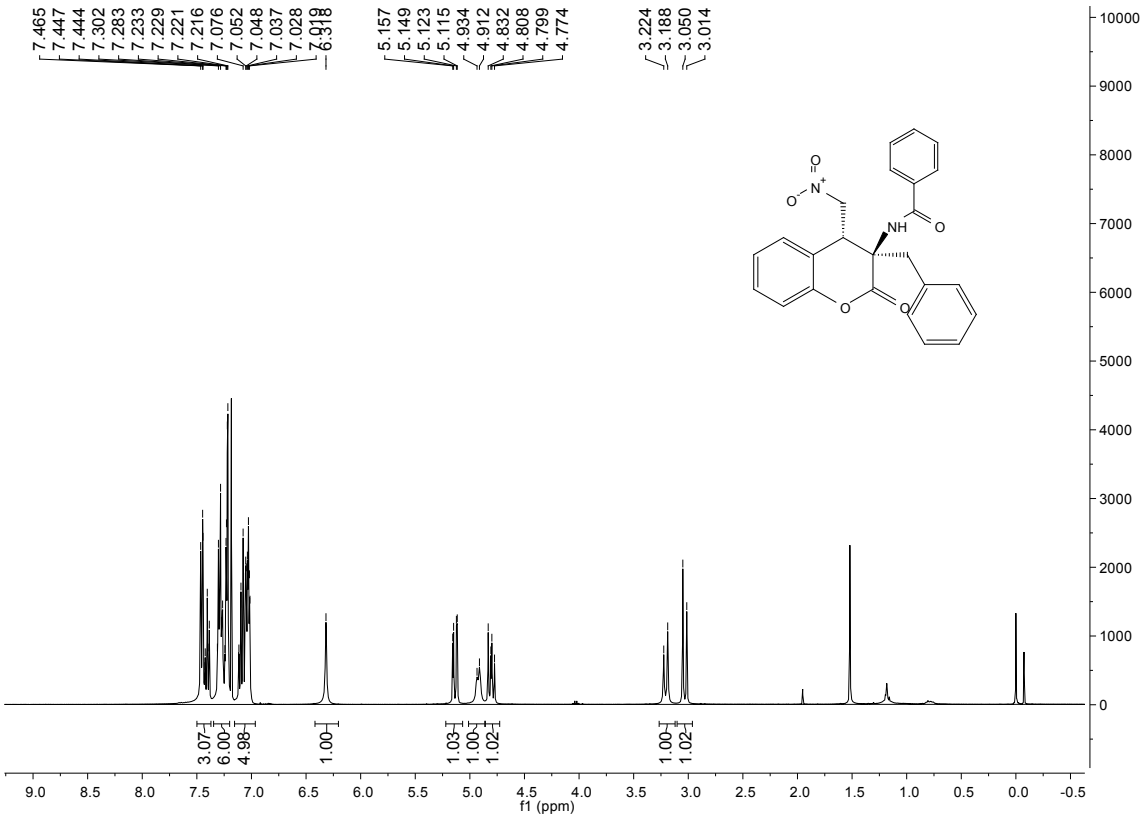
# G-5

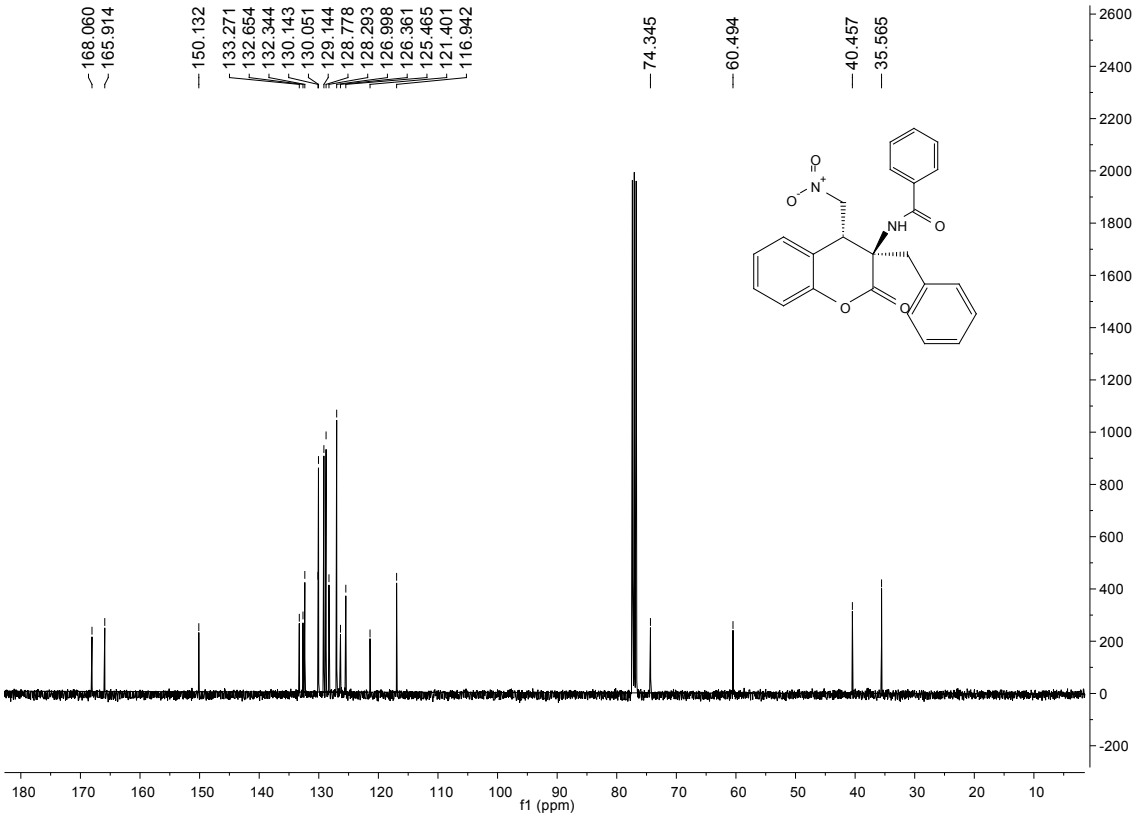


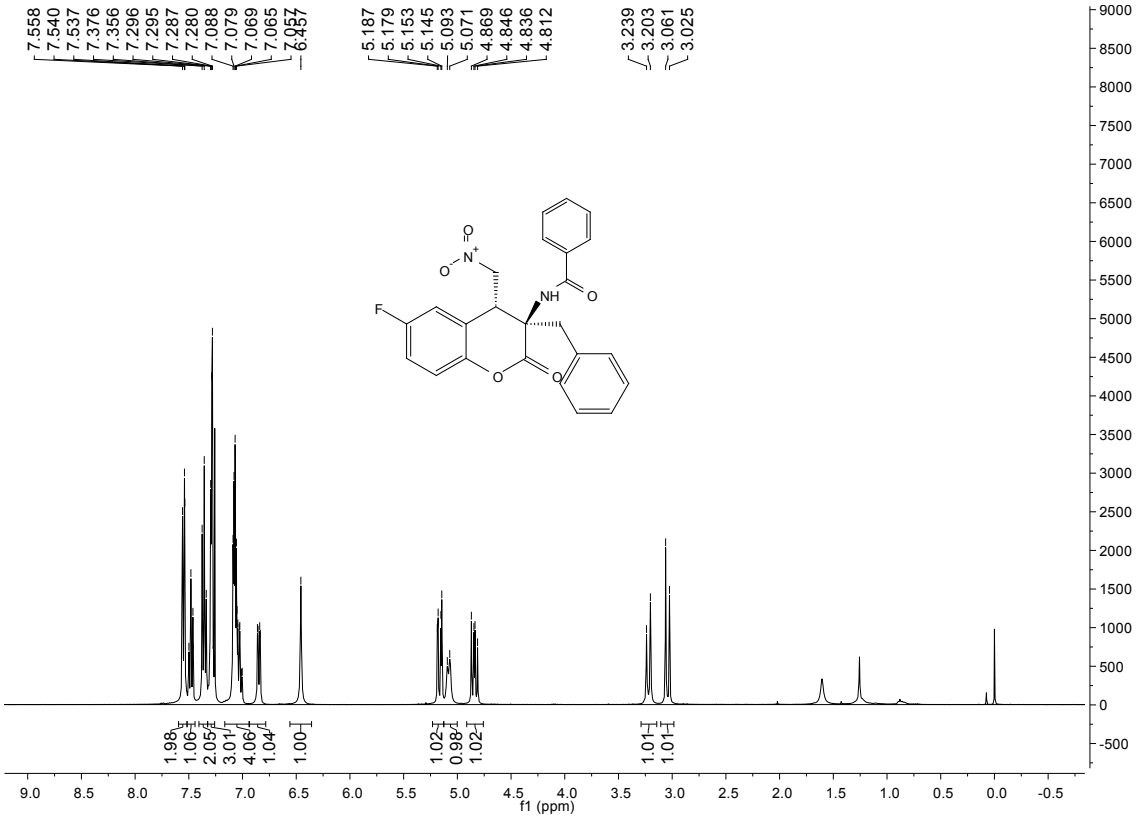

-108.470
F
O
S
NH
O
F
N
O
H
NH
N
HN
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

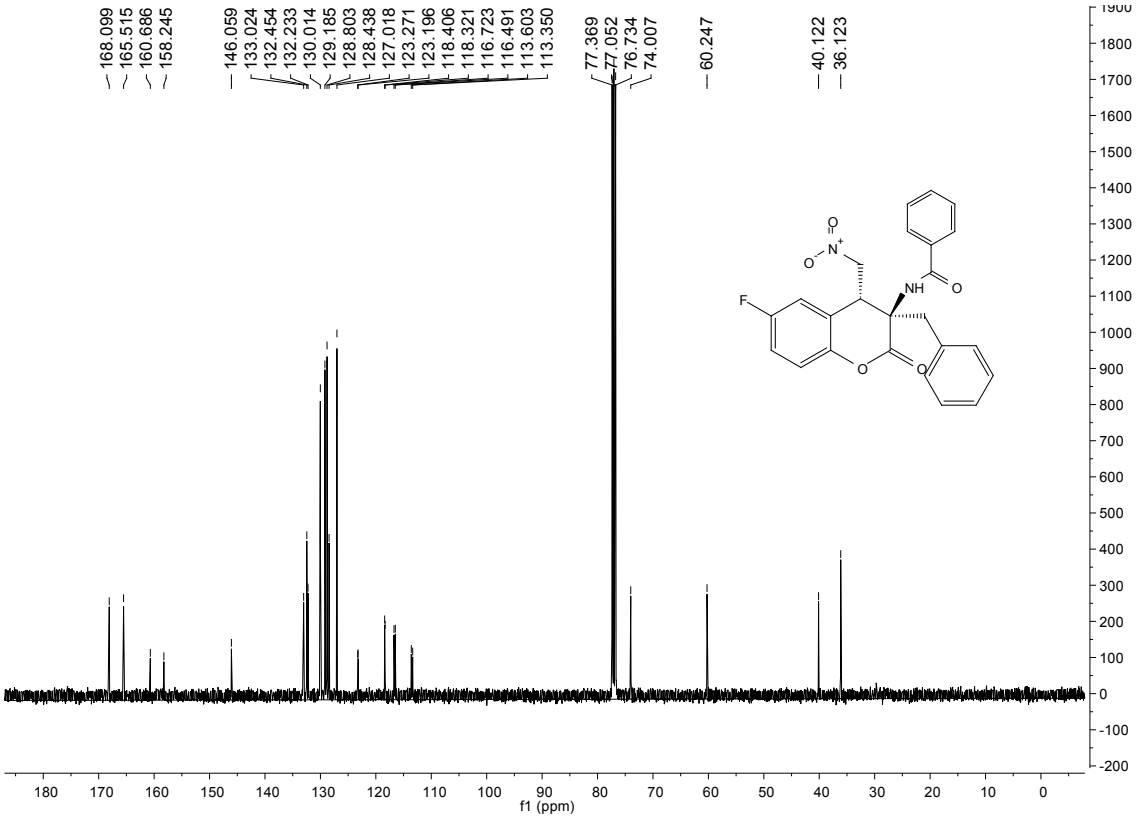
## 3aa


7.465
7.447
7.444
7.302
7.283
7.233
7.229
7.221
7.216
7.076
7.052
7.048
7.037
7.028
7.019
6.318
5.157
5.149
5.123
5.115
4.934
4.912
4.832
4.808
4.799
4.774
3.224
3.188
3.050
3.014
O
N+
O
NH
O
O
O
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
3.07
6.00
4.98
1.00
1.03
1.00
1.02
1.00
1.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


168.060
165.914
150.132
133.271
132.654
132.344
130.143
130.051
129.144
128.778
128.293
126.998
126.361
125.465
121.401
116.942
74.345
60.494
40.457
35.565
f1 (ppm)

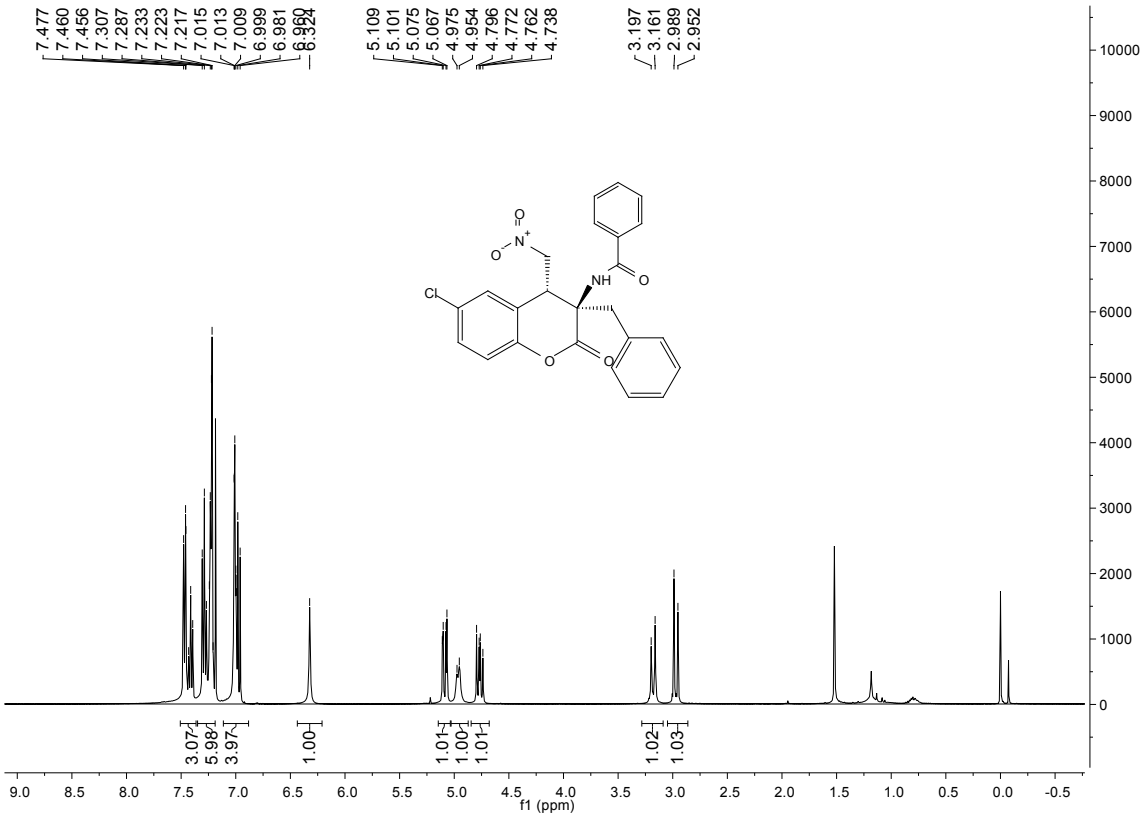
## 3ba

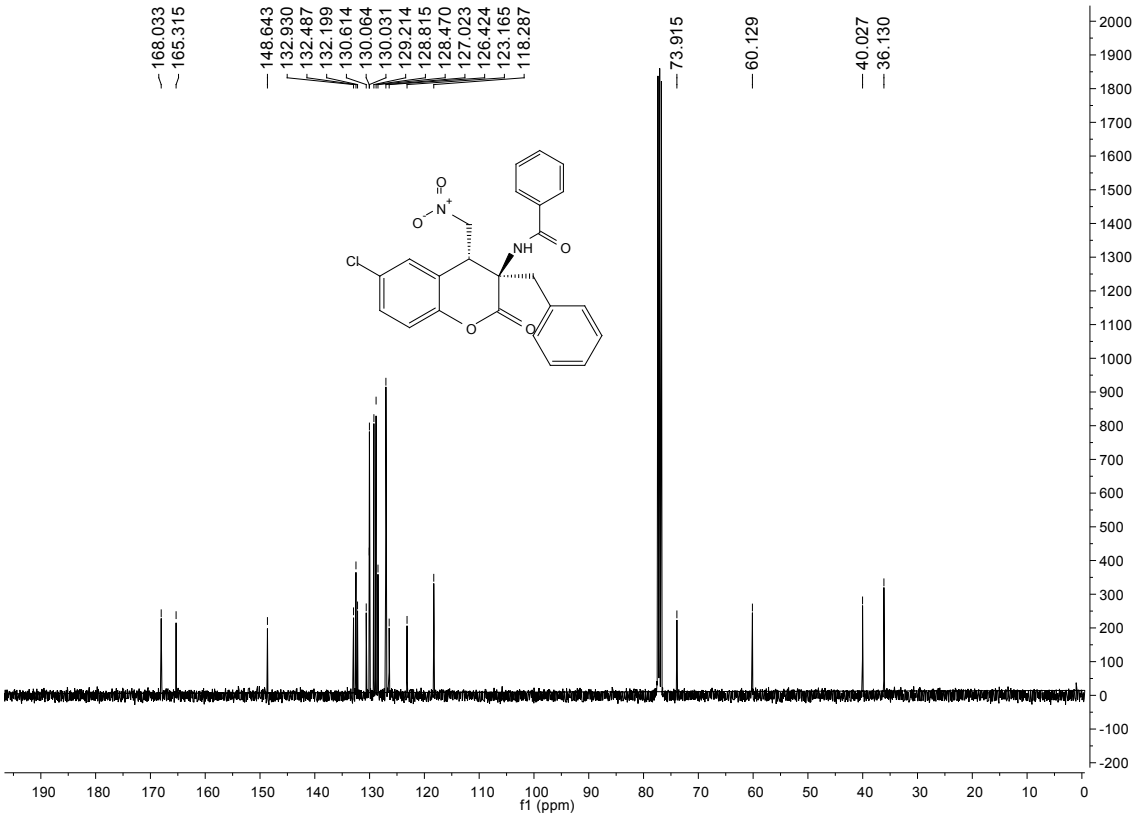

7.558
7.540
7.537
7.376
7.356
7.296
7.295
7.287
7.280
7.088
7.079
7.069
7.065
7.057
6.457
5.187
5.179
5.153
5.145
5.093
5.071
4.869
4.846
4.836
4.812
3.239
3.203
3.061
3.025
1.98
1.06
2.05
3.01
4.06
1.04
1.00
1.02
0.98
1.02
1.01
1.01
f1 (ppm)


168.099
165.515
160.686
158.245
146.059
133.024
132.454
132.233
130.014
129.185
128.803
128.438
127.018
123.271
123.196
118.406
118.321
116.723
116.491
113.603
113.350
77.369
77.052
76.734
74.007
60.247
40.122
36.123
f1 (ppm)

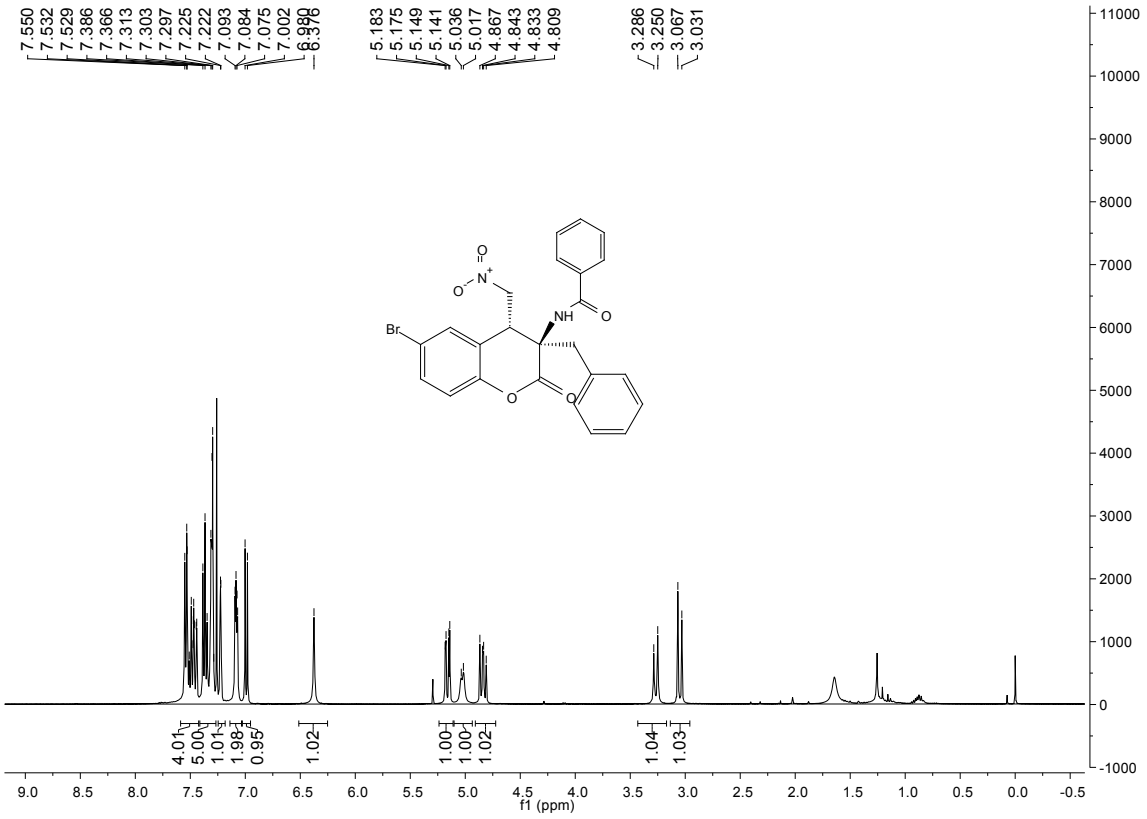

-115.646
f1 (ppm)

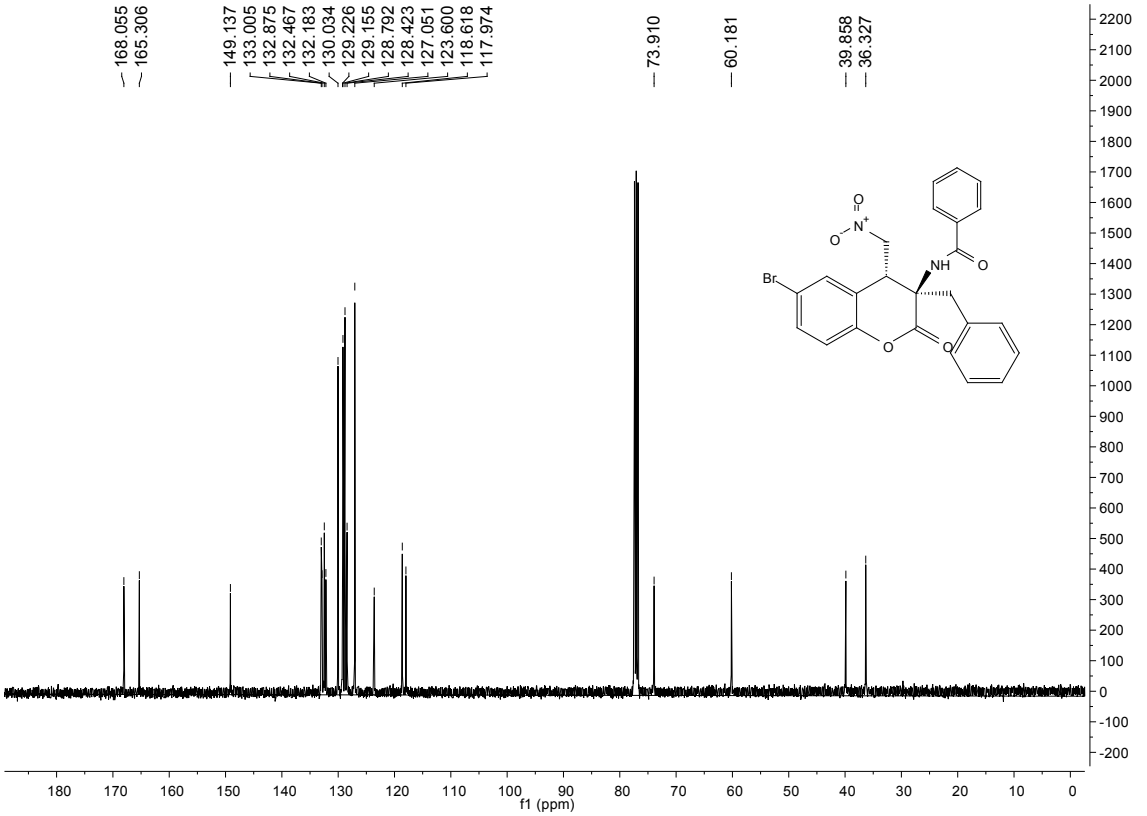
# 3ca


7.477
7.460
7.456
7.307
7.287
7.233
7.223
7.217
7.015
7.013
7.009
6.999
6.981
6.960
6.324
5.109
5.101
5.075
5.067
4.975
4.954
4.796
4.772
4.762
4.738
3.197
3.161
2.989
2.952
3.07
5.98
3.97
1.00
1.01
1.00
1.01
1.02
1.03
f1 (ppm)

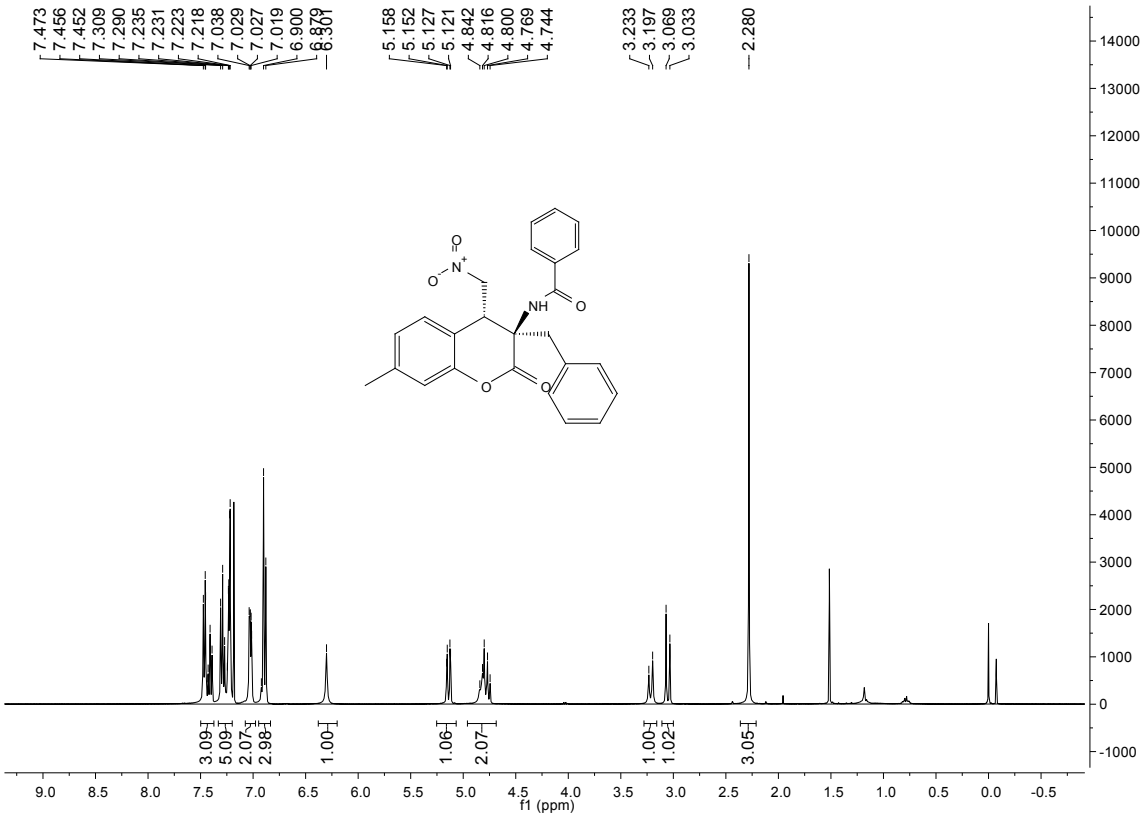

168.033
165.315
148.643
132.930
132.487
132.199
130.614
130.064
130.031
129.214
128.815
128.470
127.023
126.424
123.165
118.287
73.915
60.129
40.027
36.130
f1 (ppm)

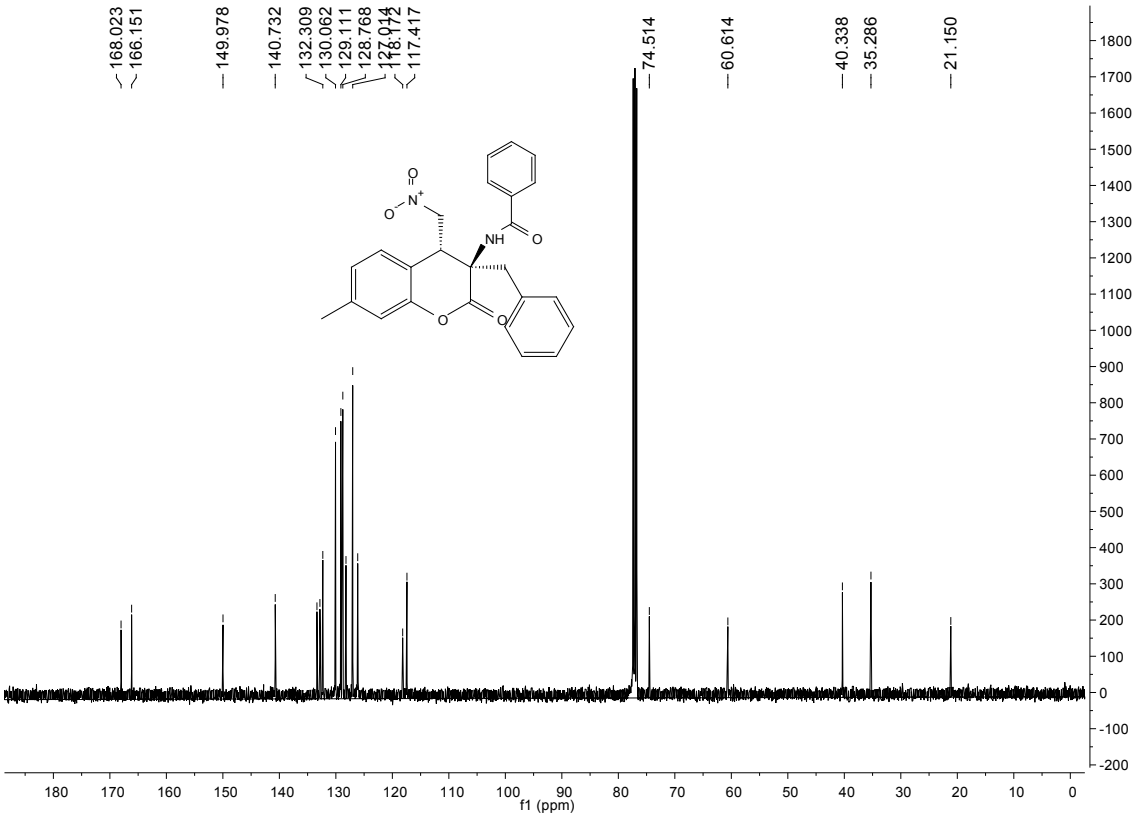
# 3da


7.550
7.532
7.529
7.386
7.366
7.313
7.303
7.297
7.225
7.222
7.093
7.084
7.075
7.002
6.980
6.976
5.183
5.175
5.149
5.141
5.036
5.017
4.867
4.843
4.833
4.809
3.286
3.250
3.067
3.031
4.01
5.00
1.01
1.98
0.95
1.02
1.00
1.00
1.02
1.04
1.03
f1 (ppm)

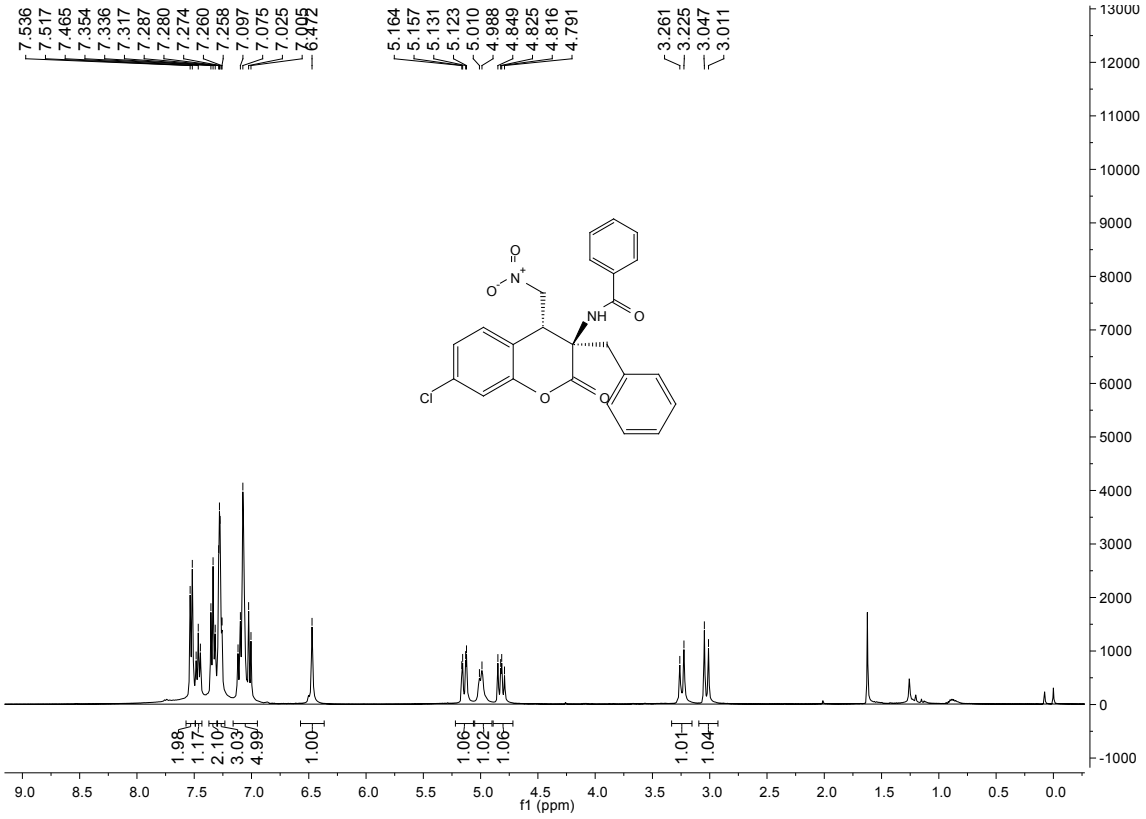

168.055
165.306
149.137
133.005
132.875
132.467
132.183
130.034
129.226
129.155
128.792
128.423
127.051
123.600
118.618
117.974
73.910
60.181
39.858
36.327
f1 (ppm)

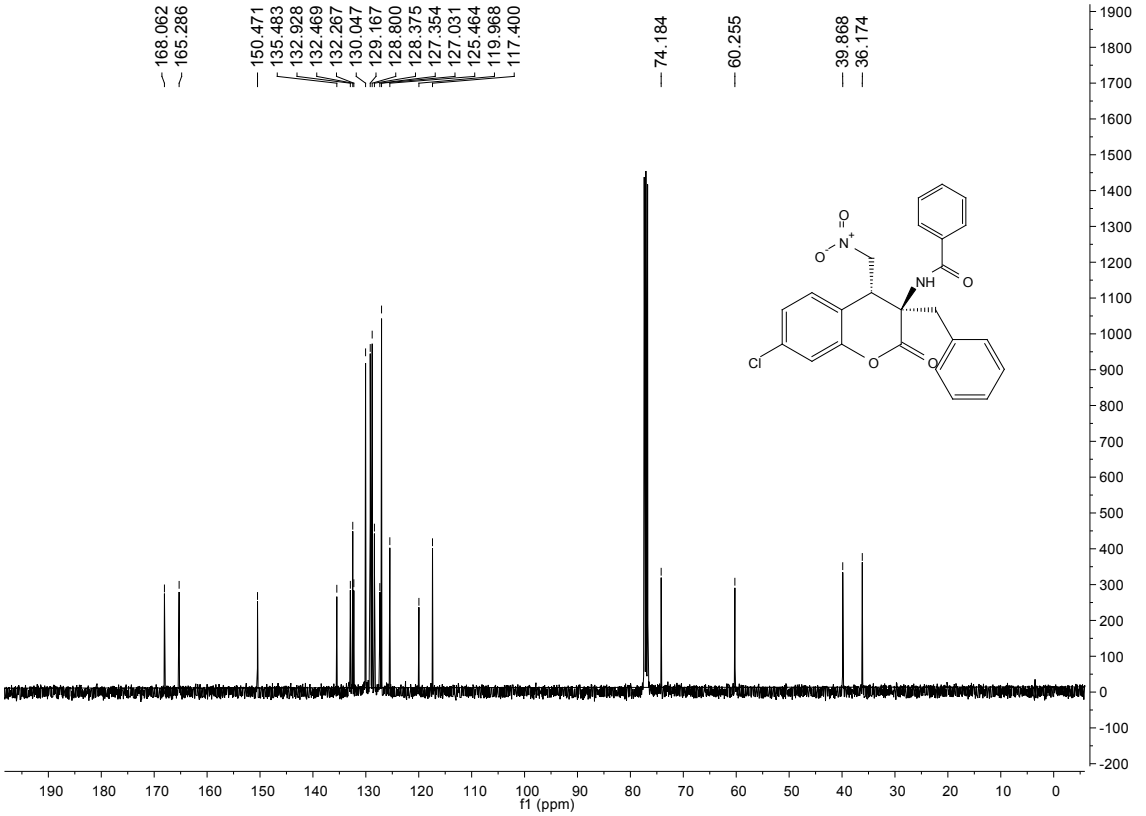
# 3ea


7.473
7.456
7.452
7.309
7.290
7.235
7.231
7.223
7.218
7.038
7.029
7.027
7.019
6.900
6.879
6.307
5.158
5.152
5.127
5.121
4.842
4.816
4.800
4.769
4.744
3.233
3.197
3.069
3.033
2.280
3.09
5.09
2.07
2.98
1.00
1.06
2.07
1.00
1.02
3.05
f1 (ppm)

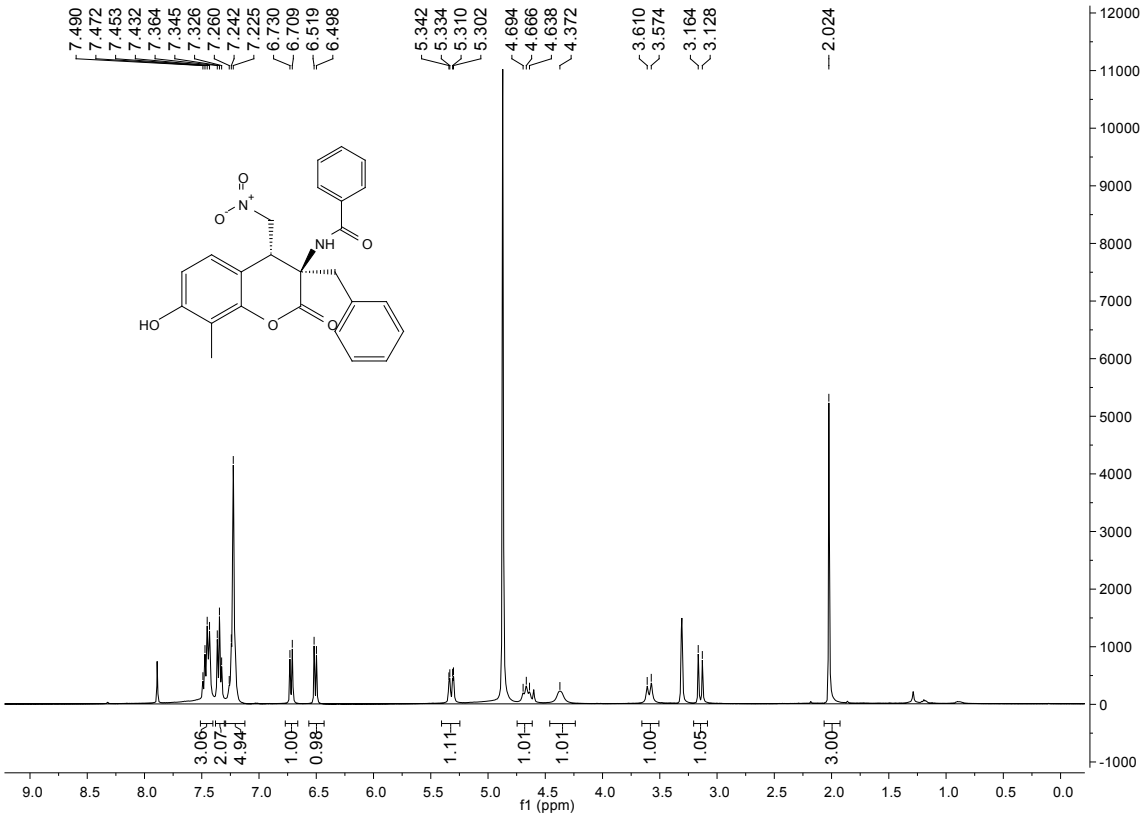

168.023
166.151
149.978
140.732
132.309
130.062
129.111
128.768
127.014
118.172
117.417
74.514
60.614
40.338
35.286
21.150
f1 (ppm)

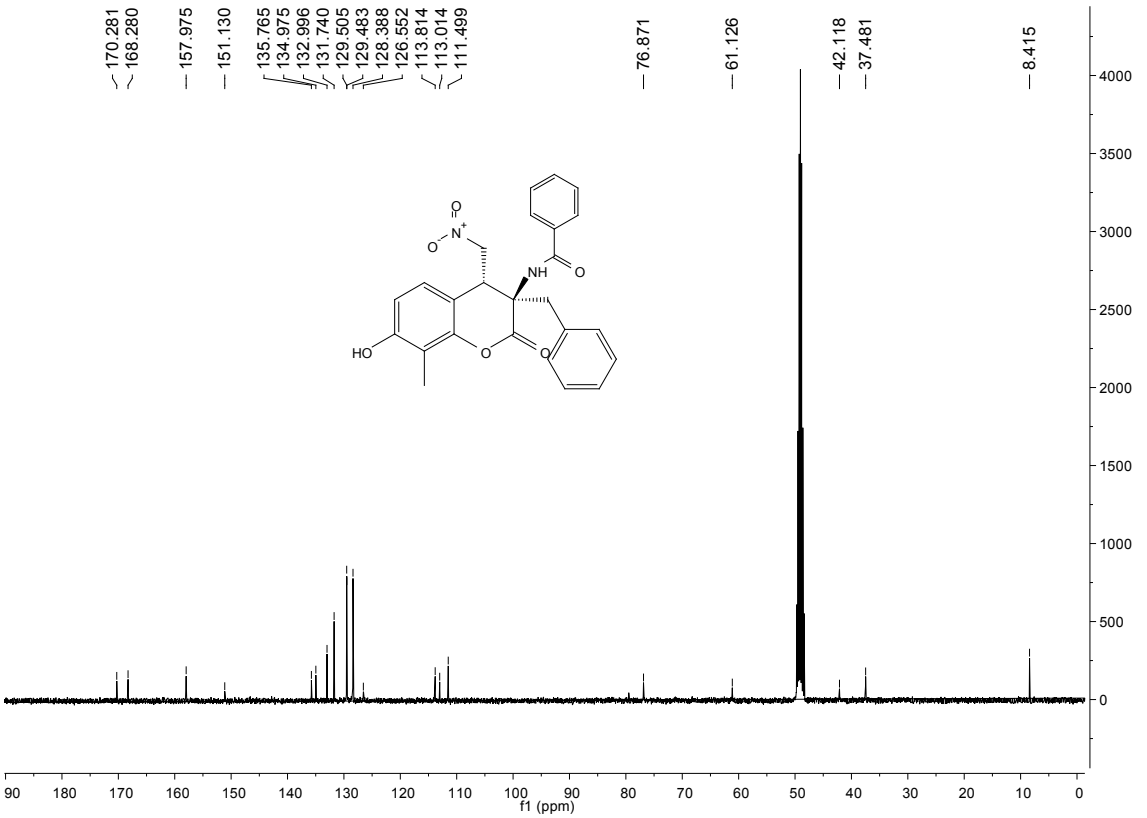
# 3fa


7.536
7.517
7.465
7.354
7.336
7.317
7.287
7.280
7.274
7.260
7.258
7.097
7.075
7.025
7.005
6.472
5.164
5.157
5.131
5.123
5.010
4.988
4.849
4.825
4.816
4.791
3.261
3.225
3.047
3.011
1.98
1.17
2.10
3.03
4.99
1.00
1.06
1.02
1.06
1.01
1.04
f1 (ppm)

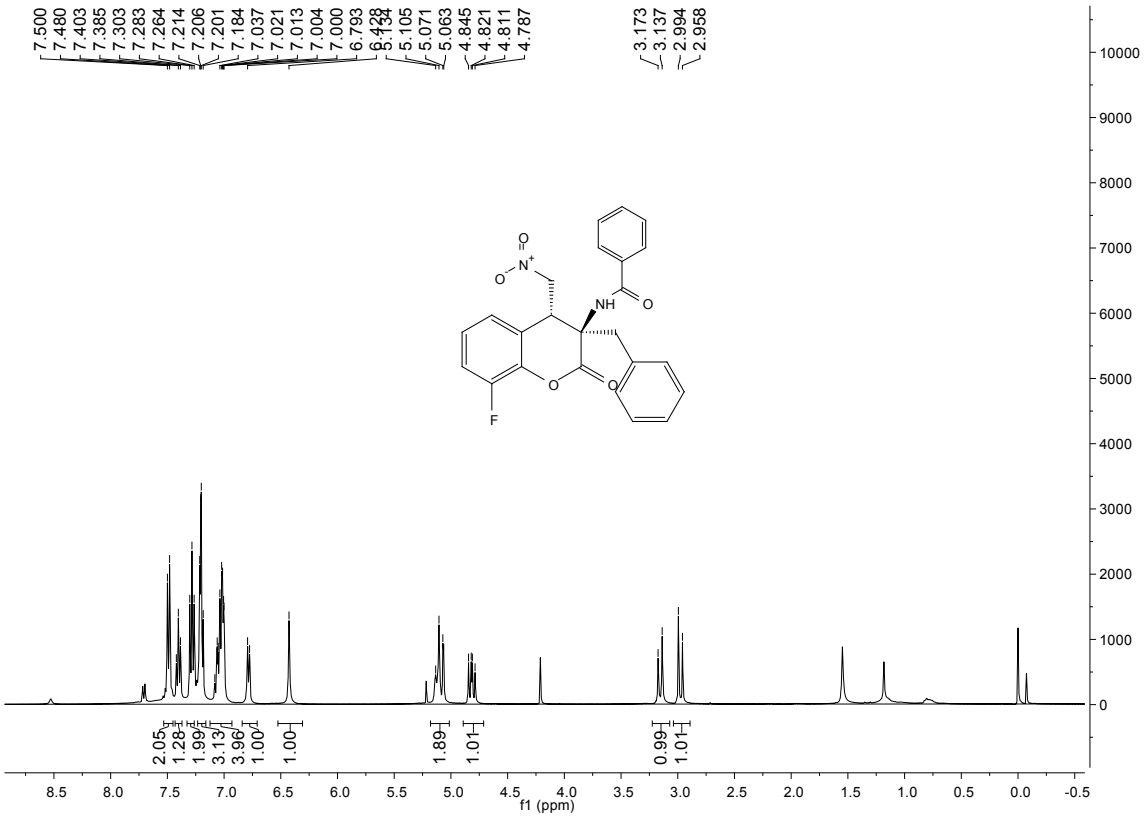

168.062
165.286
150.471
135.483
132.928
132.469
132.267
130.047
129.167
128.800
128.375
127.354
127.031
125.464
119.968
117.400
74.184
60.255
39.868
36.174
f1 (ppm)

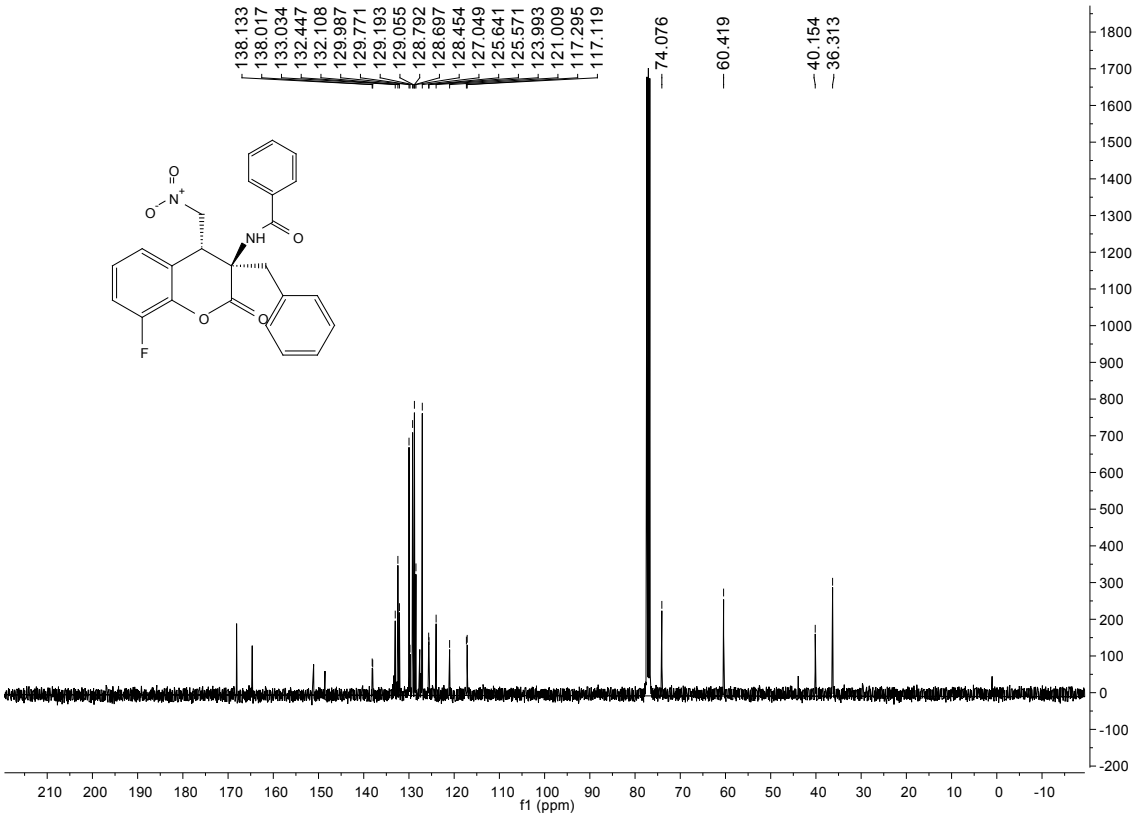
# 3ga

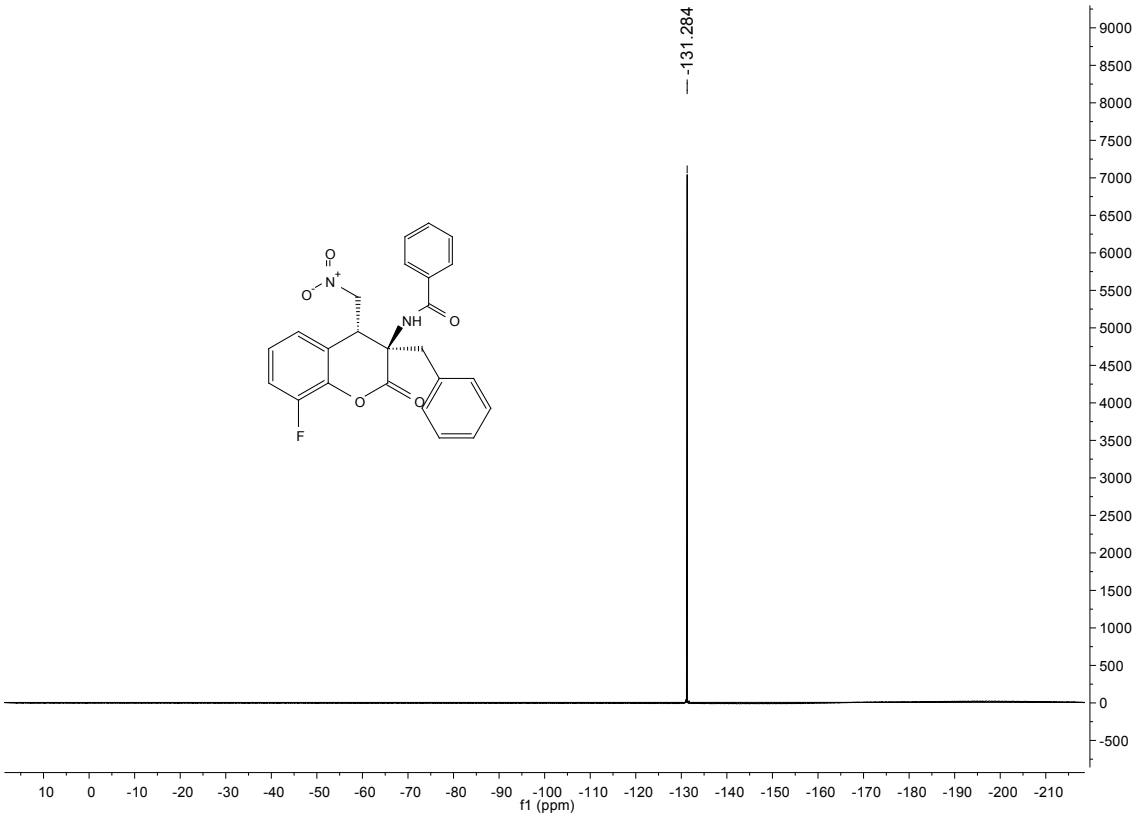

7.490
7.472
7.453
7.432
7.364
7.345
7.326
7.260
7.242
7.225
6.730
6.709
6.519
6.498
5.342
5.334
5.310
5.302
4.694
4.666
4.638
4.372
3.610
3.574
3.164
3.128
2.024
3.06
2.07
4.94
1.00
0.98
1.11
1.01
1.01
1.00
1.05
3.00
f1 (ppm)


170.281
168.280
157.975
151.130
135.765
134.975
132.996
131.740
129.505
129.483
128.388
126.552
113.814
113.014
111.499
76.871
61.126
42.118
37.481
8.415
f1 (ppm)

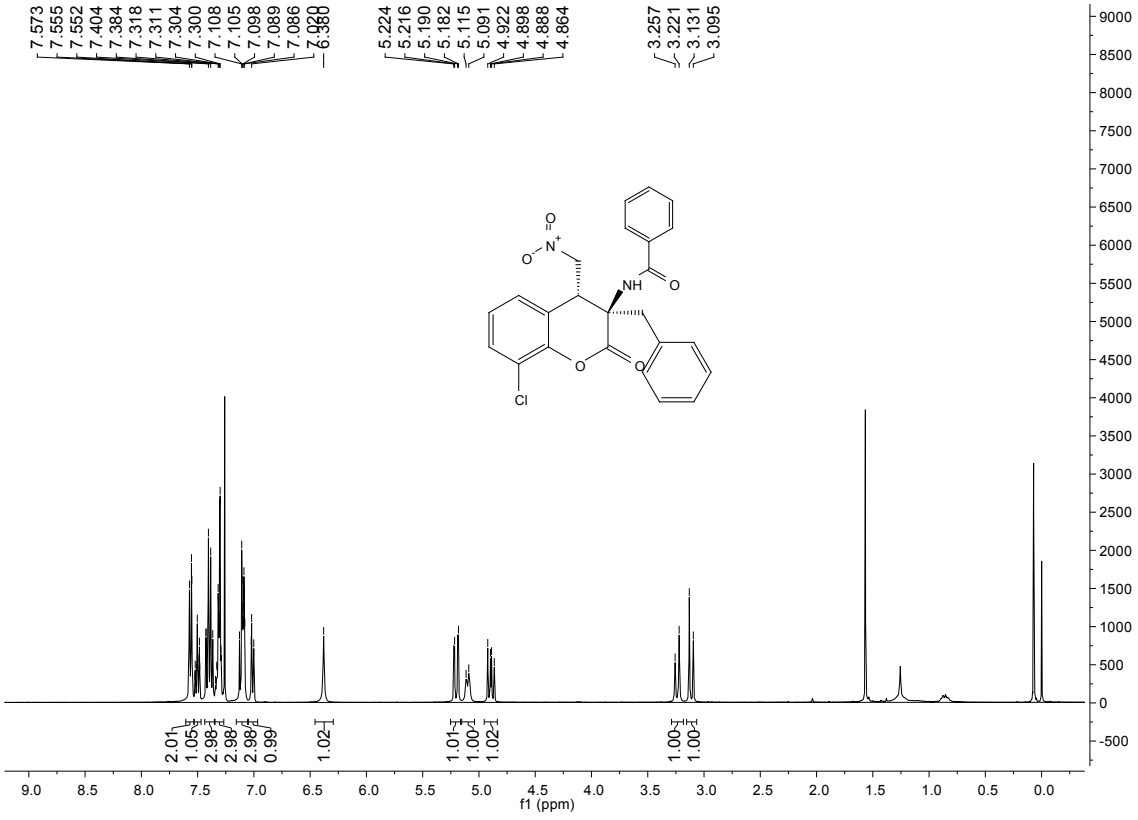
# 3ha

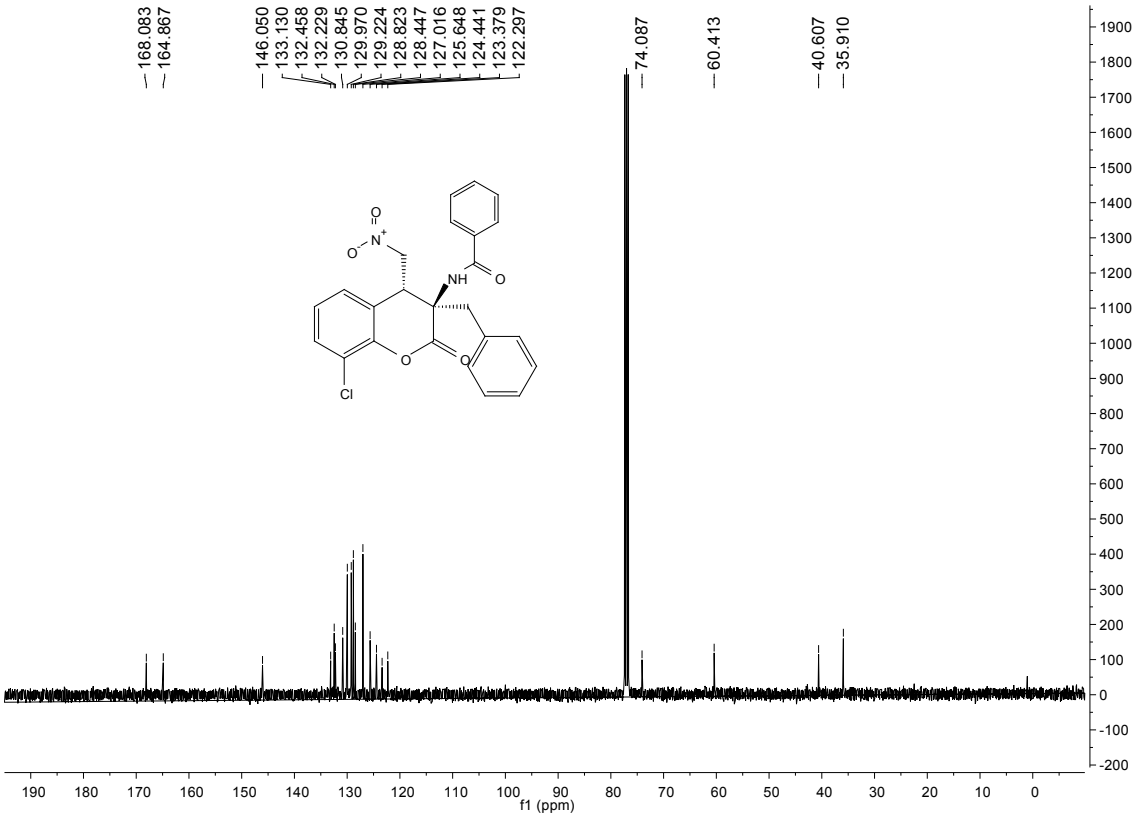

7.500
7.480
7.403
7.385
7.303
7.283
7.264
7.214
7.206
7.201
7.184
7.037
7.021
7.013
7.004
7.000
6.793
5.105
5.071
5.063
4.845
4.821
4.811
4.787
3.173
3.137
2.994
2.958
2.05
1.28
1.99
3.13
3.96
1.00
1.00
1.89
1.01
0.99
1.01
f1 (ppm)


138.133
138.017
133.034
132.447
132.108
129.987
129.771
129.193
129.055
128.792
128.697
128.454
127.049
125.641
125.571
123.993
121.009
117.295
117.119
74.076
60.419
40.154
36.313
f1 (ppm)

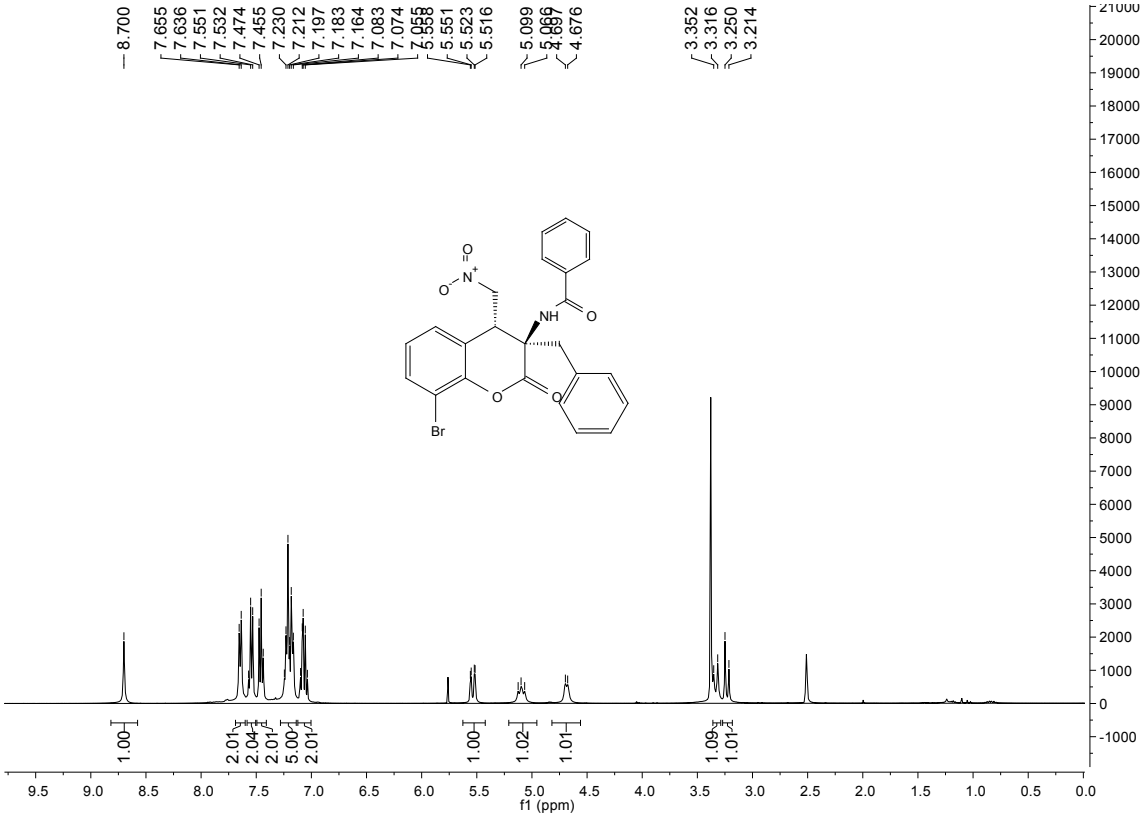

-131.284
F
NH
O
f1 (ppm)

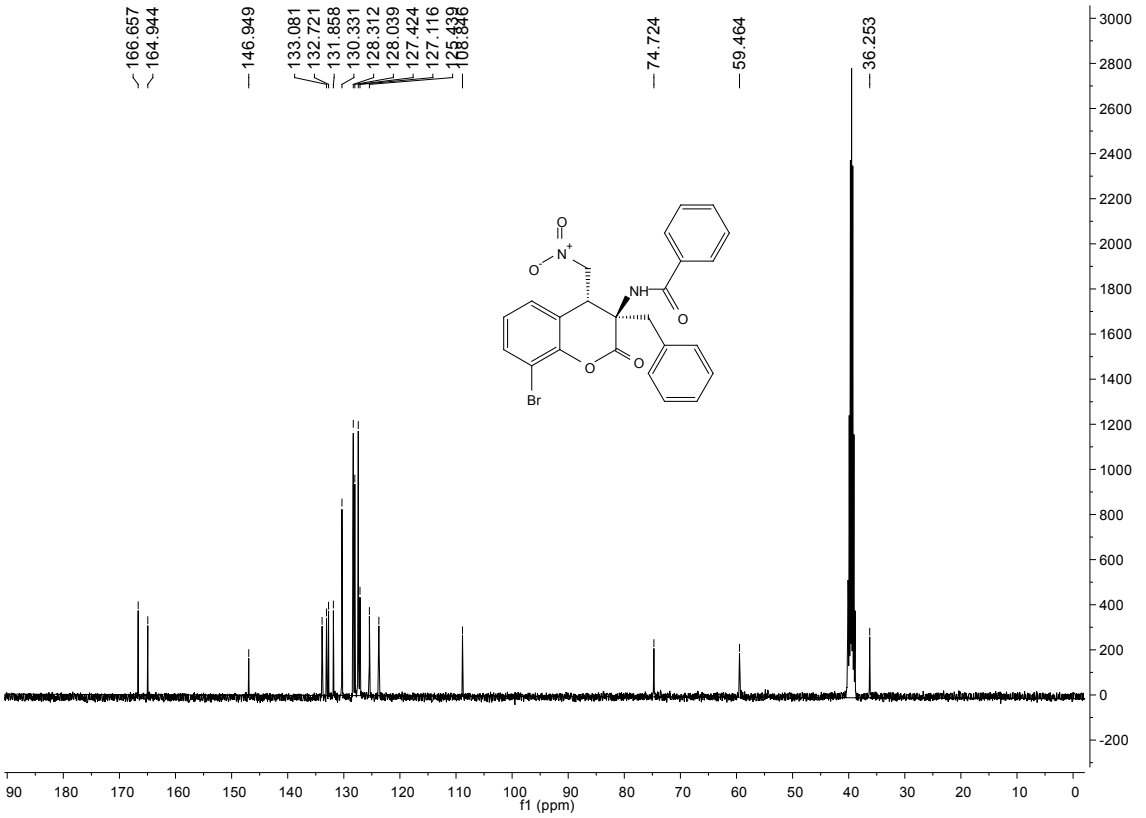
# 3ia


7.573
7.555
7.552
7.404
7.384
7.318
7.311
7.304
7.300
7.108
7.105
7.098
7.089
7.086
6.380
5.224
5.216
5.190
5.182
5.115
5.091
4.922
4.898
4.888
4.864
3.257
3.221
3.131
3.095
Cl
NH
O
2.01
1.05
2.98
2.98
2.98
0.99
1.02
1.01
1.00
1.02
1.00
1.00
f1 (ppm)

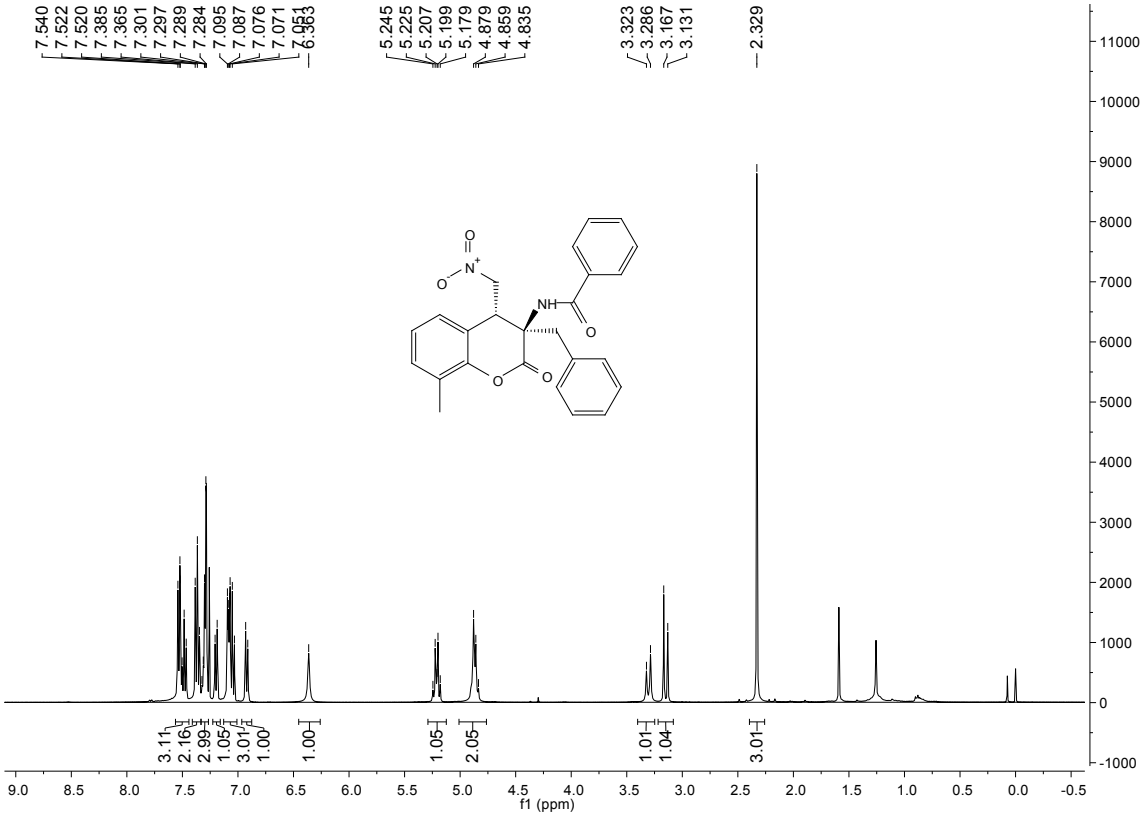

168.083
164.867
146.050
133.130
132.458
132.229
130.845
129.970
129.224
128.823
128.447
127.016
125.648
124.441
123.379
122.297
74.087
60.413
40.607
35.910
NH
O
Cl
f1 (ppm)

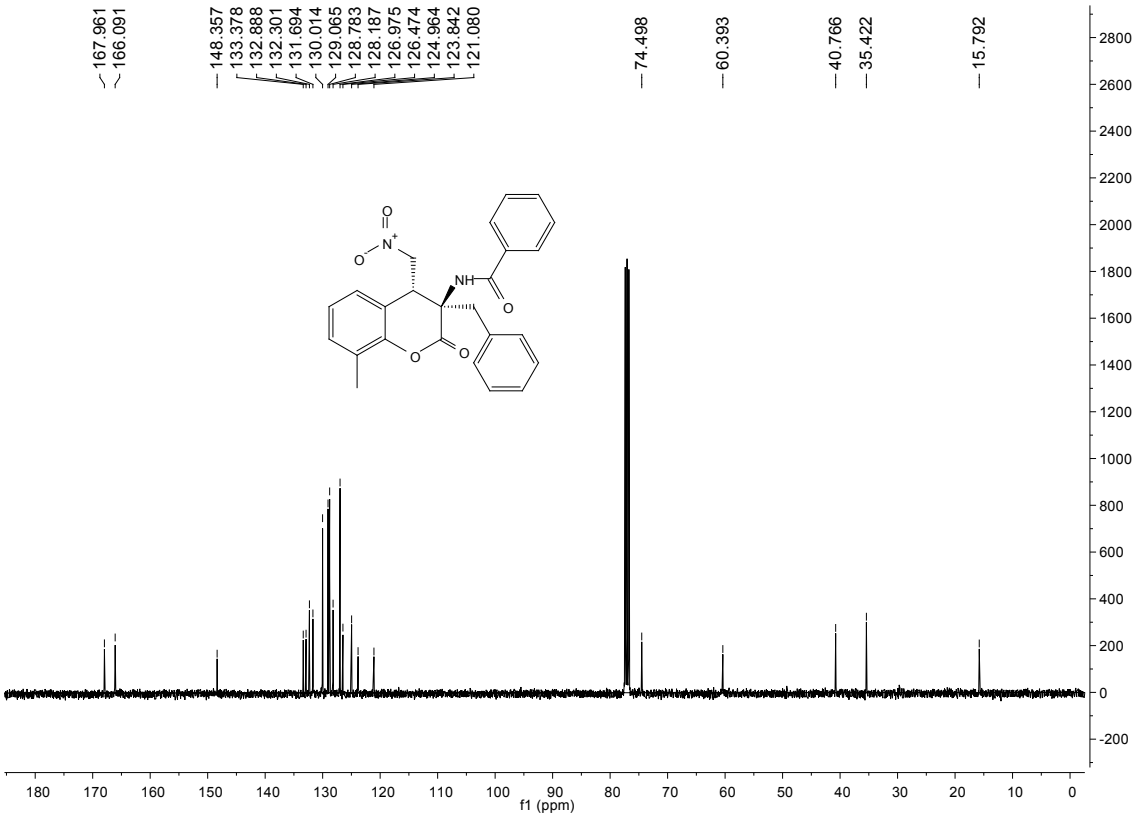
# 3ja


8.700
7.655
7.636
7.551
7.532
7.474
7.455
7.230
7.212
7.197
7.183
7.164
7.083
7.074
5.551
5.523
5.516
5.099
4.676
3.352
3.316
3.250
3.214
NH
O
Br
1.00
2.01
2.04
2.01
5.00
2.01
1.00
1.02
1.01
1.09
1.01
f1 (ppm)

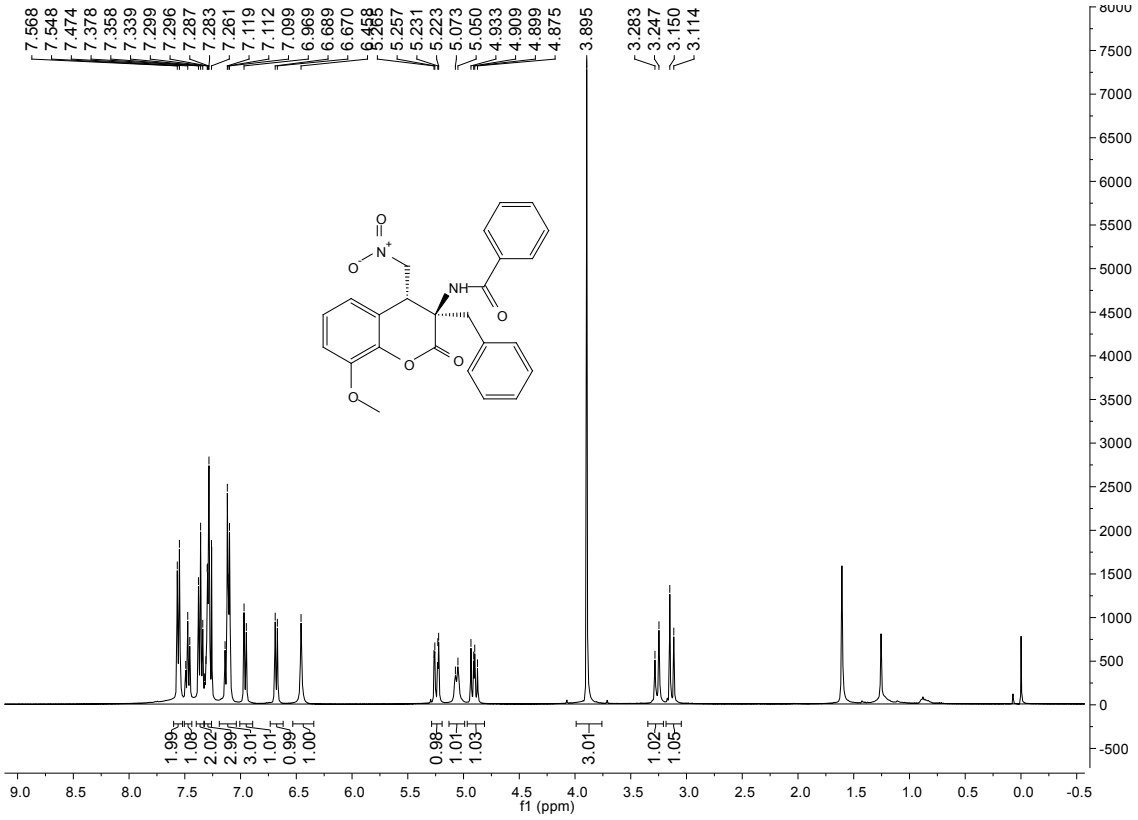

166.657
164.944
146.949
133.081
132.721
131.858
130.331
128.312
128.039
127.424
127.116
74.724
59.464
36.253
NH
O
Br
f1 (ppm)

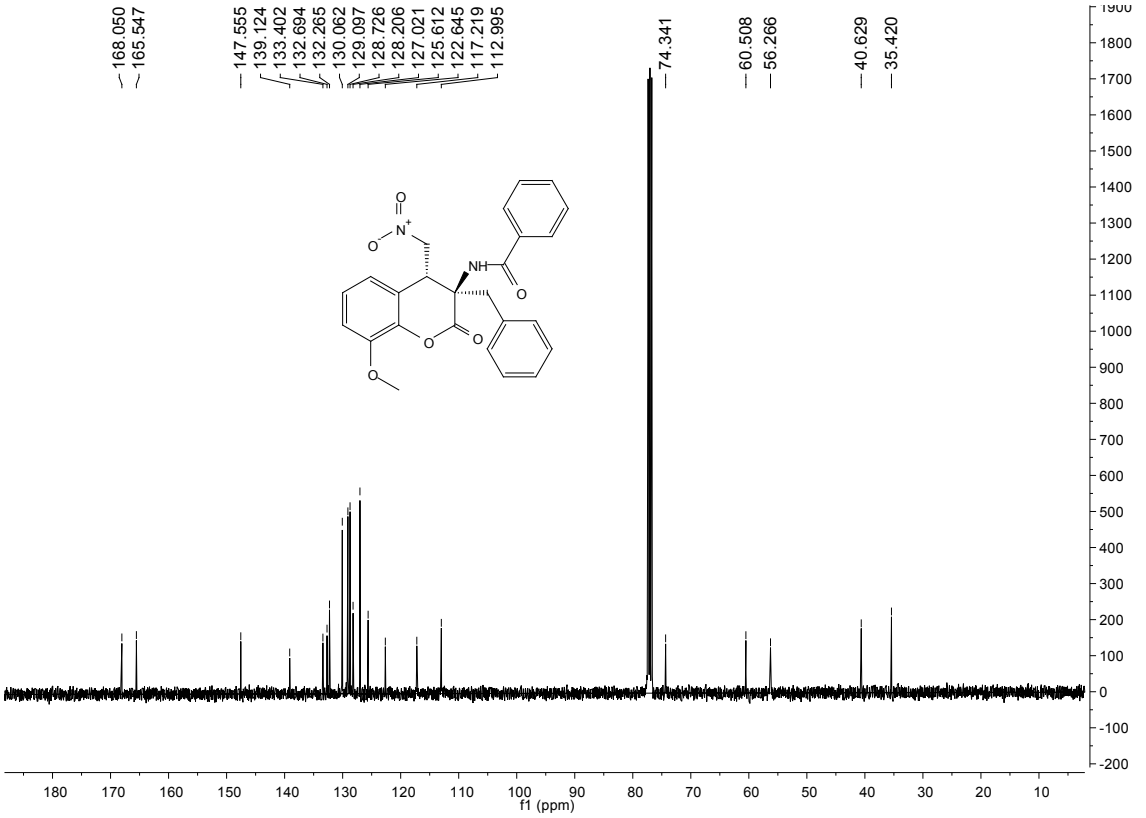
## 3ka


7.540
7.522
7.520
7.385
7.365
7.301
7.297
7.289
7.284
7.095
7.087
7.076
7.071
6.363
5.245
5.225
5.207
5.199
5.179
4.879
4.859
4.835
3.323
3.286
3.167
3.131
2.329
NH
O
3.11
2.16
2.99
1.05
3.01
1.00
1.00
1.05
2.05
1.01
1.04
3.01
f1 (ppm)

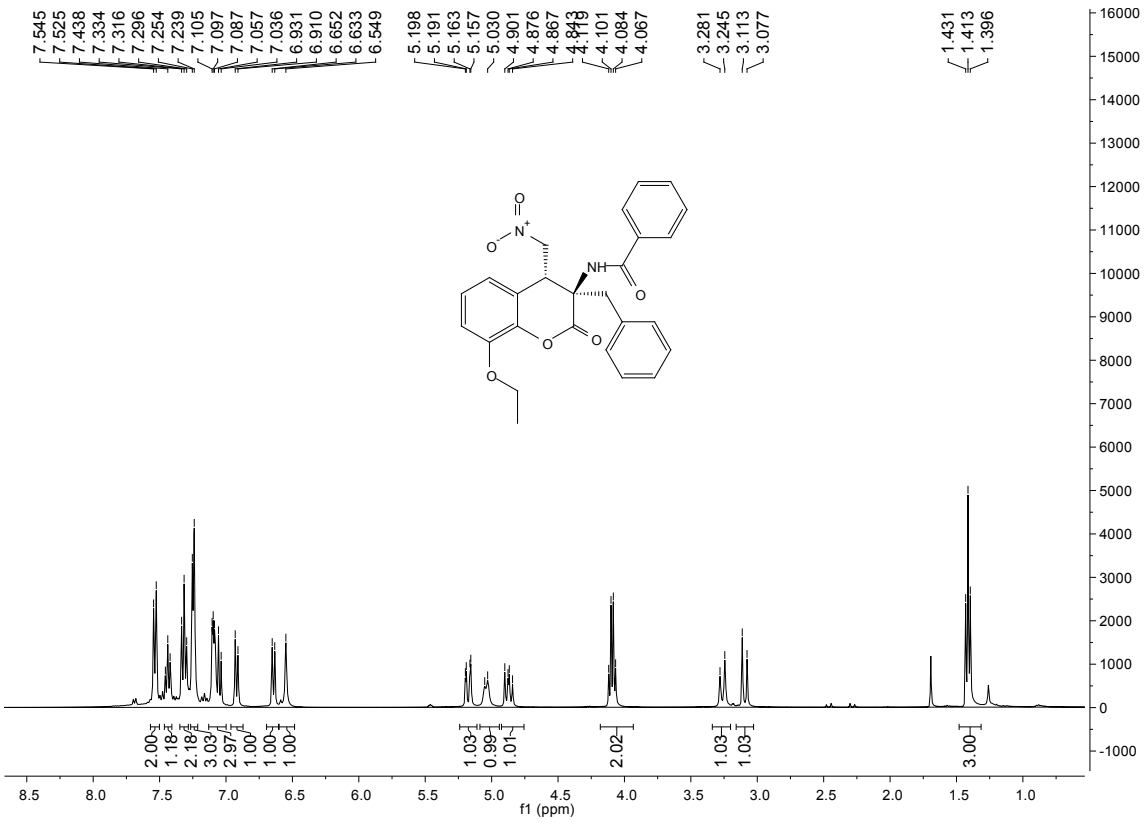

167.961
166.091
148.357
133.378
132.888
132.301
131.694
130.014
129.065
128.783
128.187
126.975
126.474
124.964
123.842
121.080
74.498
60.393
40.766
35.422
15.792
f1 (ppm)

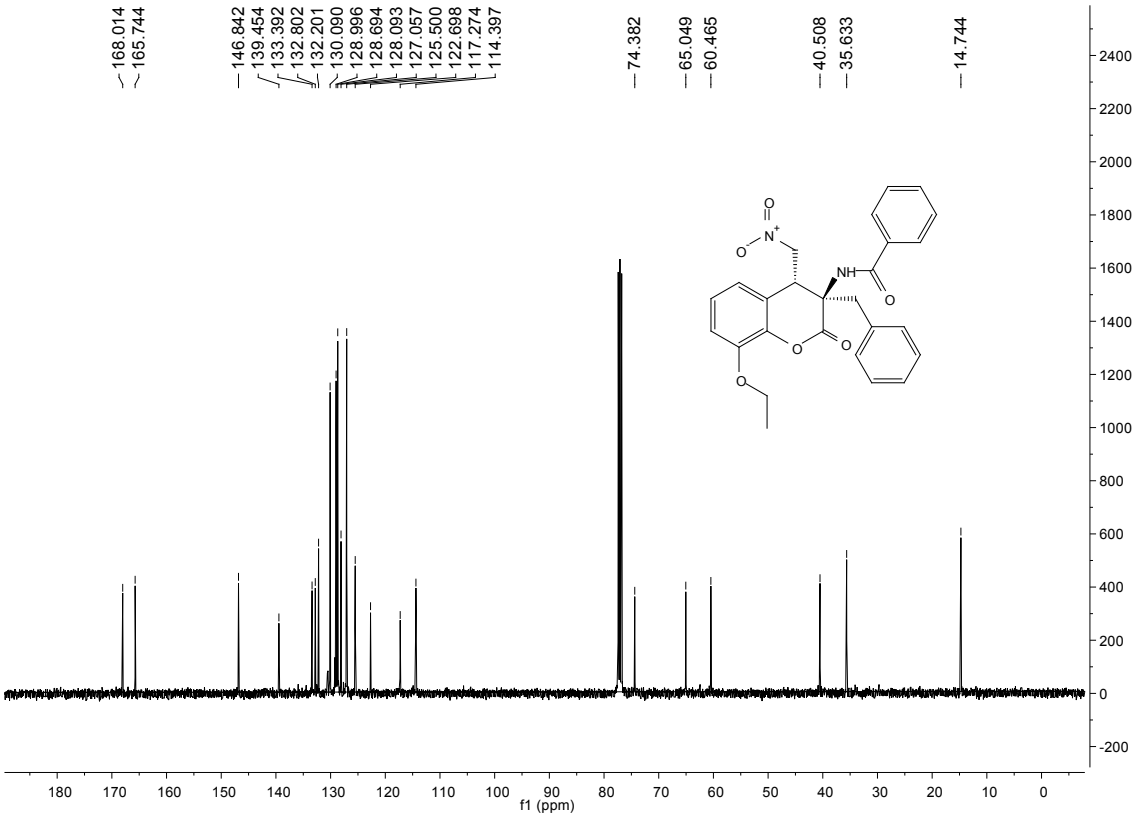
## 3la


7.568
7.548
7.474
7.378
7.358
7.339
7.299
7.296
7.287
7.283
7.261
7.119
7.112
7.099
6.969
6.689
6.670
5.257
5.231
5.223
5.073
5.050
4.933
4.909
4.899
4.875
3.895
3.283
3.247
3.150
3.114
1.99
1.08
2.02
2.99
3.01
1.01
0.99
1.00
0.98
1.01
1.03
3.01
1.02
1.05
f1 (ppm)

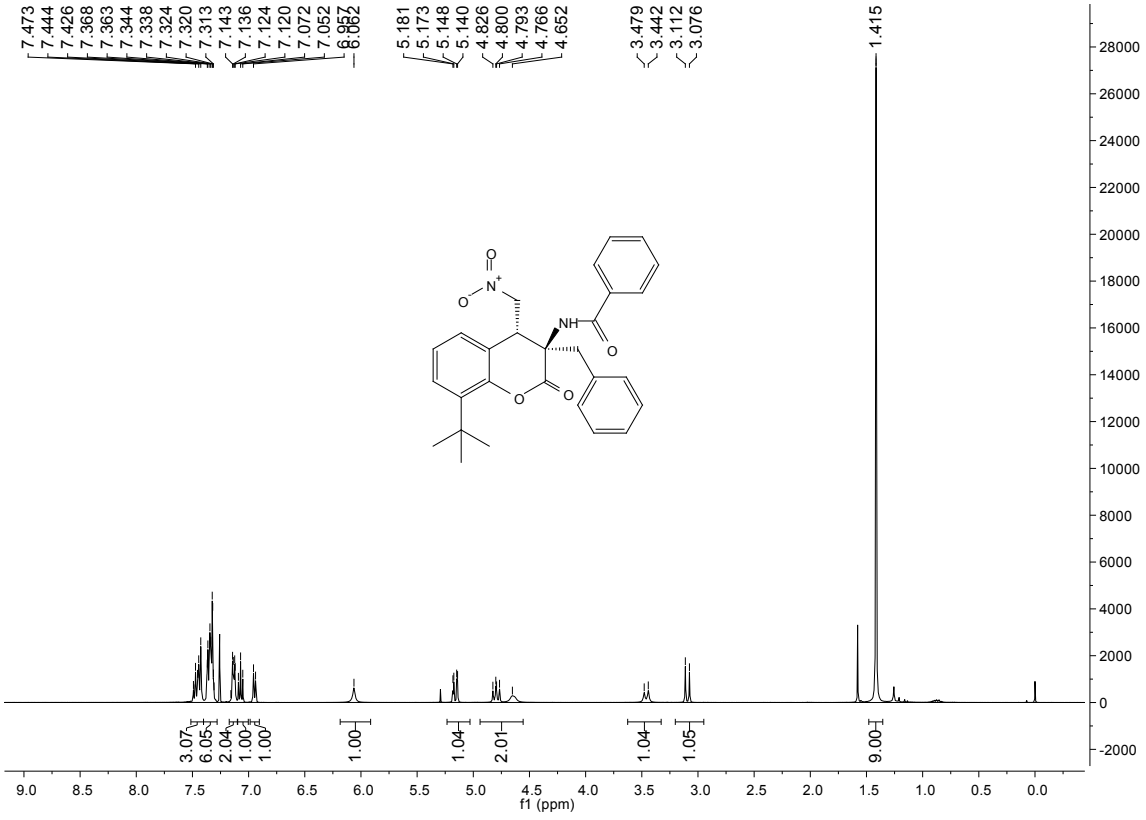

168.050
165.547
147.555
139.124
133.402
132.694
132.265
130.062
129.097
128.726
128.206
127.021
125.612
122.645
117.219
112.995
74.341
60.508
56.266
40.629
35.420
f1 (ppm)

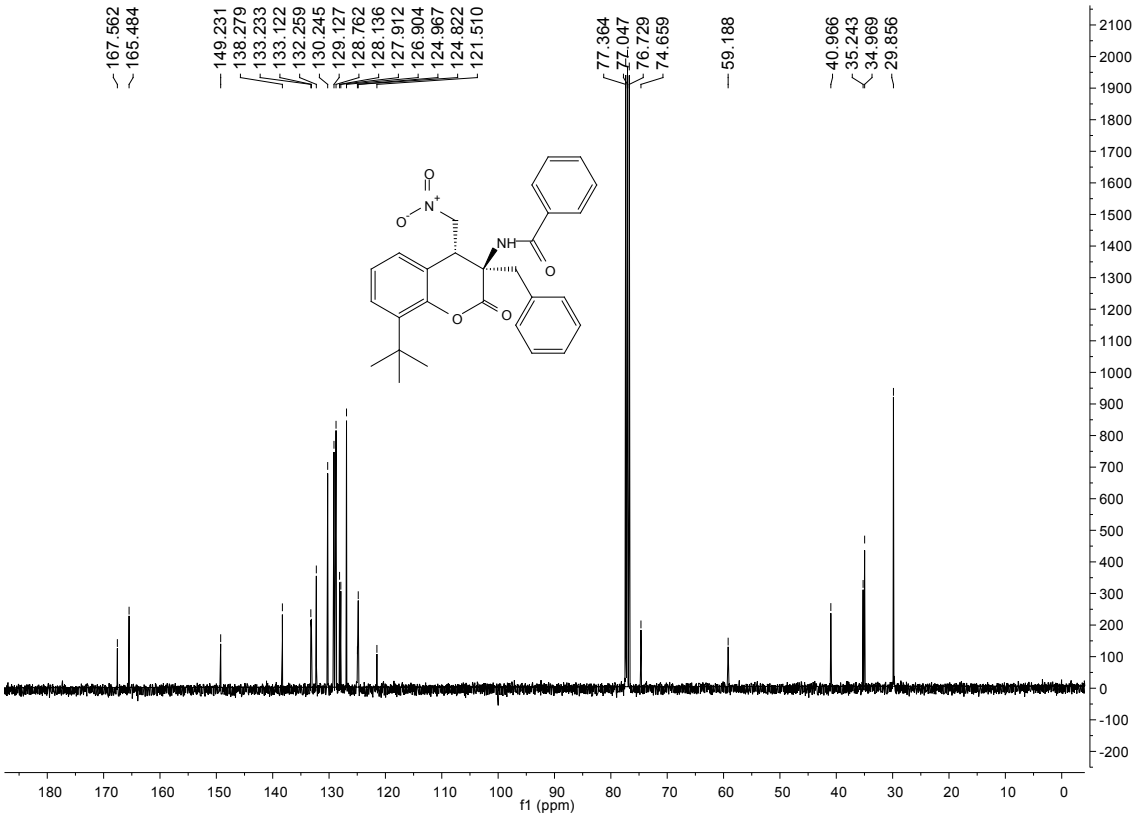
## 3ma


7.545
7.525
7.438
7.334
7.316
7.296
7.254
7.239
7.105
7.097
7.087
7.057
7.036
6.931
6.910
6.652
6.633
6.549
5.198
5.191
5.163
5.157
5.030
4.901
4.876
4.867
4.101
4.084
4.067
3.281
3.245
3.113
3.077
1.431
1.413
1.396
2.00
1.18
2.18
3.03
2.97
1.00
1.00
1.00
1.03
0.99
1.01
2.02
1.03
1.03
3.00
f1 (ppm)

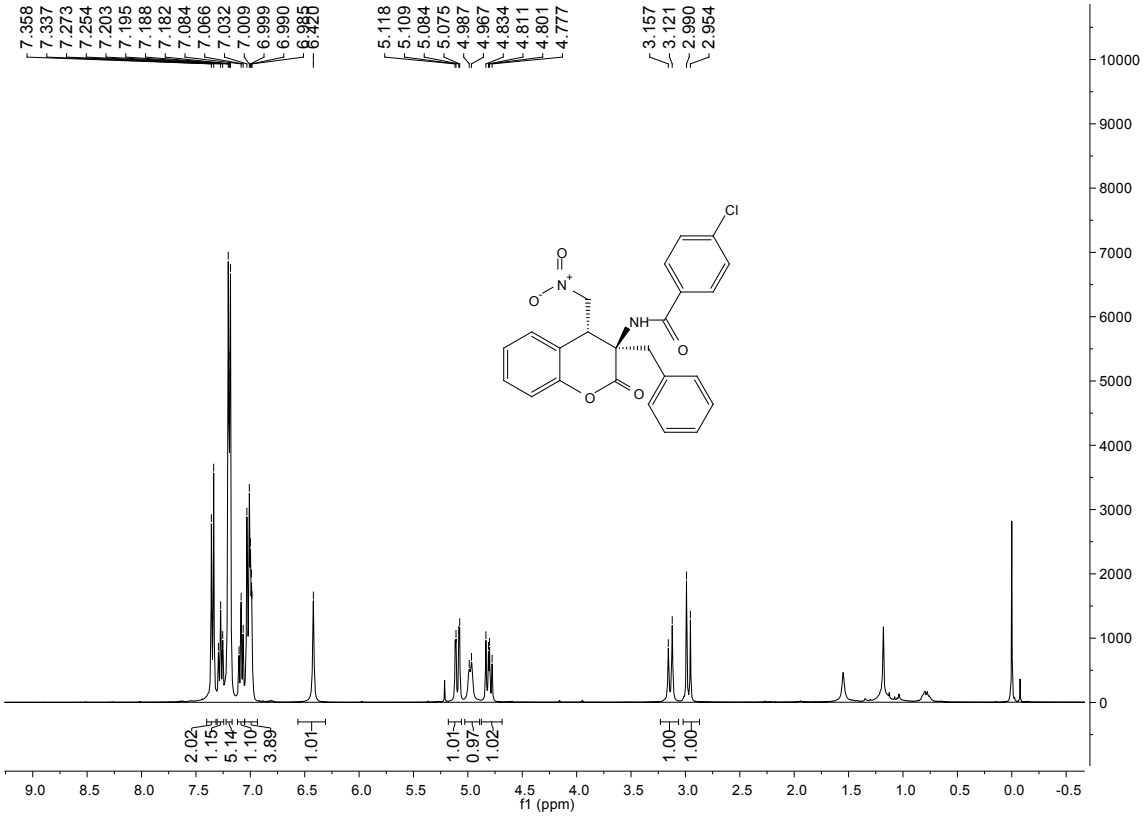

168.014
165.744
146.842
139.454
133.392
132.802
132.201
130.090
128.996
128.694
128.093
127.057
125.500
122.698
117.274
114.397
74.382
65.049
60.465
40.508
35.633
14.744
f1 (ppm)

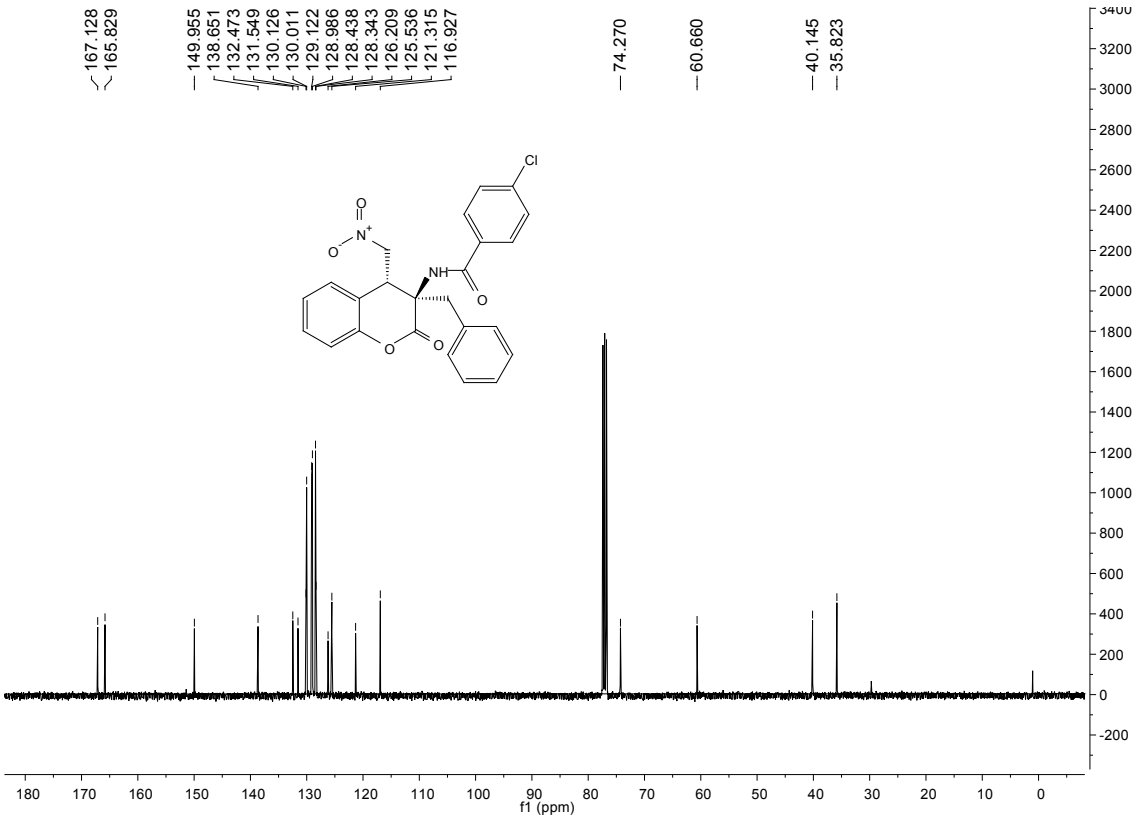
## 3na


7.473
7.444
7.426
7.368
7.363
7.344
7.338
7.324
7.320
7.313
7.143
7.136
7.124
7.120
7.072
7.052
6.957
6.862
5.181
5.173
5.148
5.140
4.826
4.800
4.793
4.766
4.652
3.479
3.442
3.112
3.076
1.415
3.07
6.05
2.04
1.00
1.00
1.00
1.04
2.01
1.04
1.05
9.00
f1 (ppm)

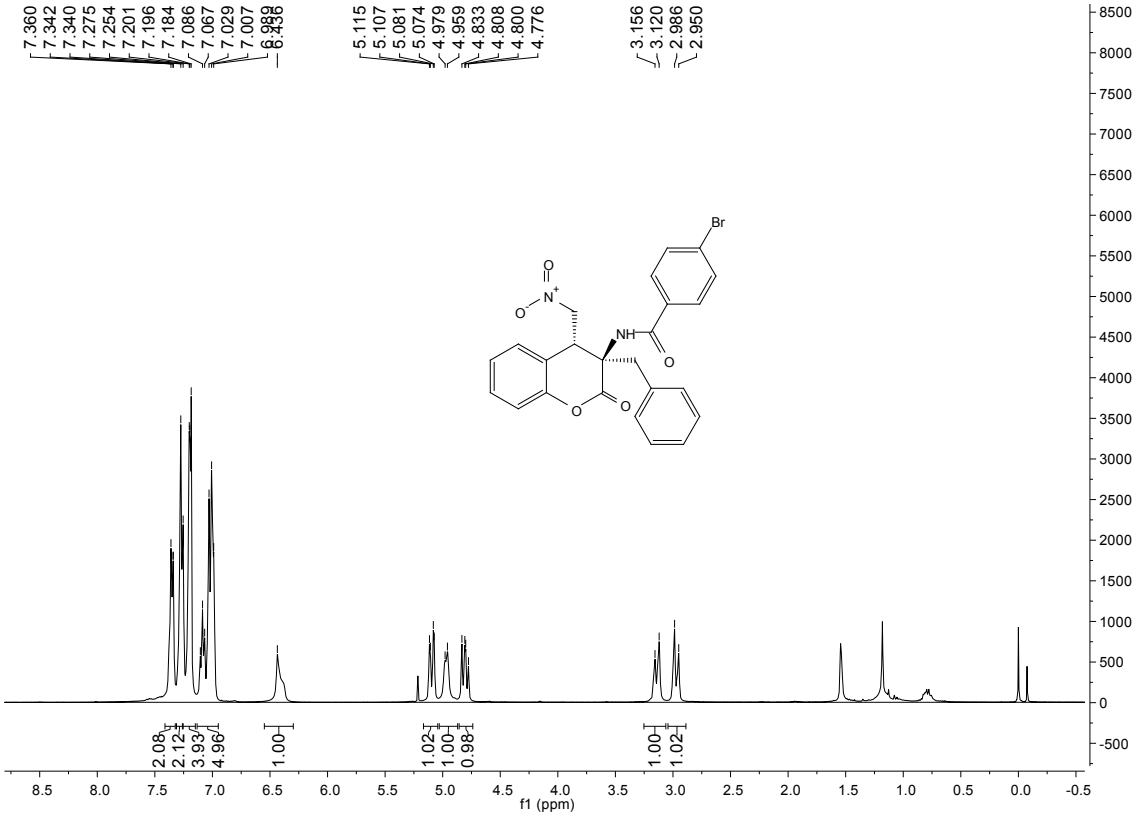

167.562
165.484
149.231
138.279
133.233
133.122
132.259
130.245
129.127
128.762
128.136
127.912
126.904
124.967
124.822
121.510
77.364
77.047
76.729
74.659
59.188
40.966
35.243
34.969
29.856
f1 (ppm)

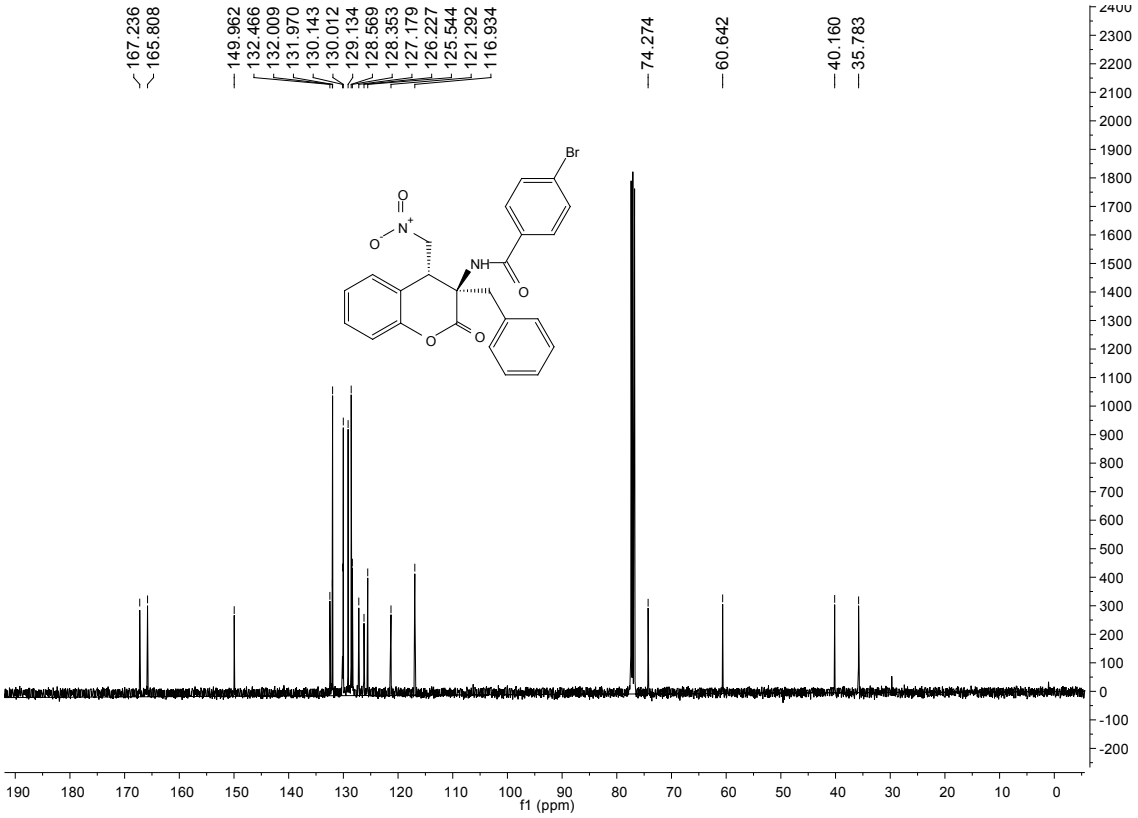
# 3ab


7.358
7.337
7.273
7.254
7.203
7.195
7.188
7.182
7.084
7.066
7.032
7.009
6.999
6.990
6.985
6.420
5.118
5.109
5.084
5.075
4.987
4.967
4.834
4.811
4.801
4.777
3.157
3.121
2.990
2.954
2.02
1.15
5.14
1.10
3.89
1.01
1.01
0.97
1.02
1.00
1.00
f1 (ppm)

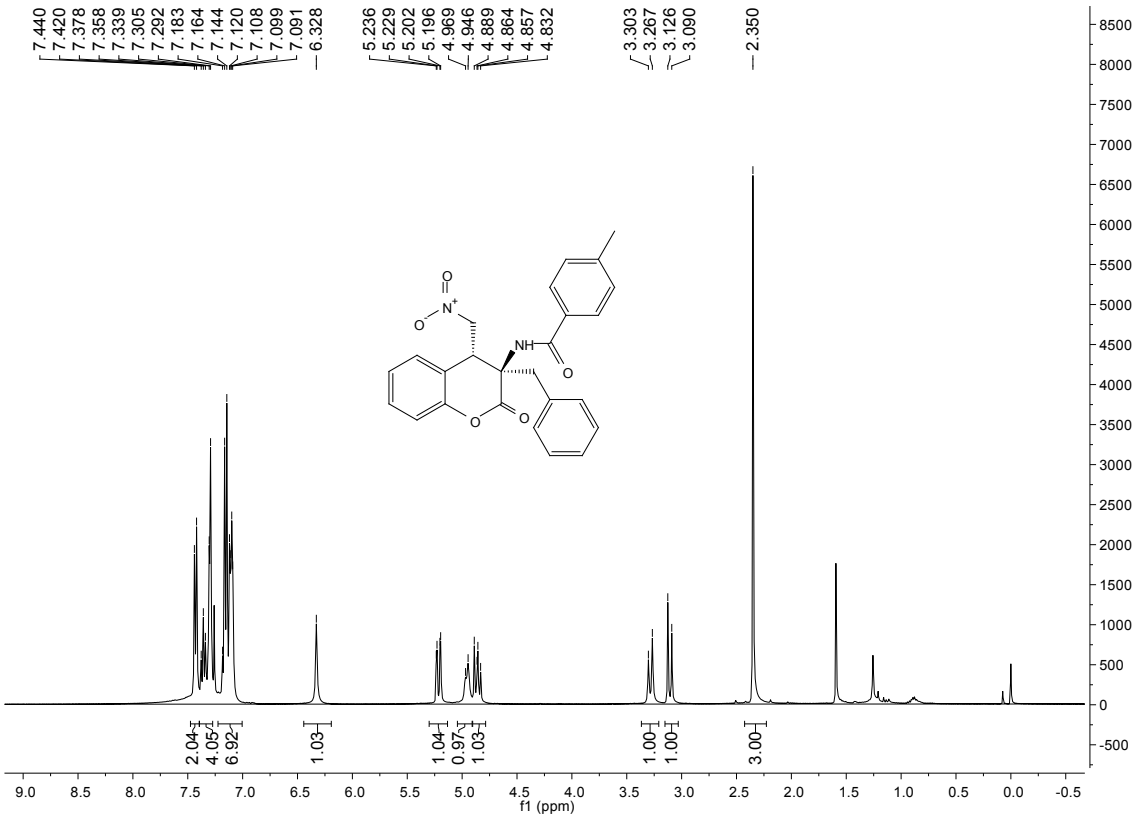

167.128
165.829
149.955
138.651
132.473
131.549
130.126
130.011
129.122
128.986
128.438
128.343
126.209
125.536
121.315
116.927
74.270
60.660
40.145
35.823
Cl
NH
O
f1 (ppm)

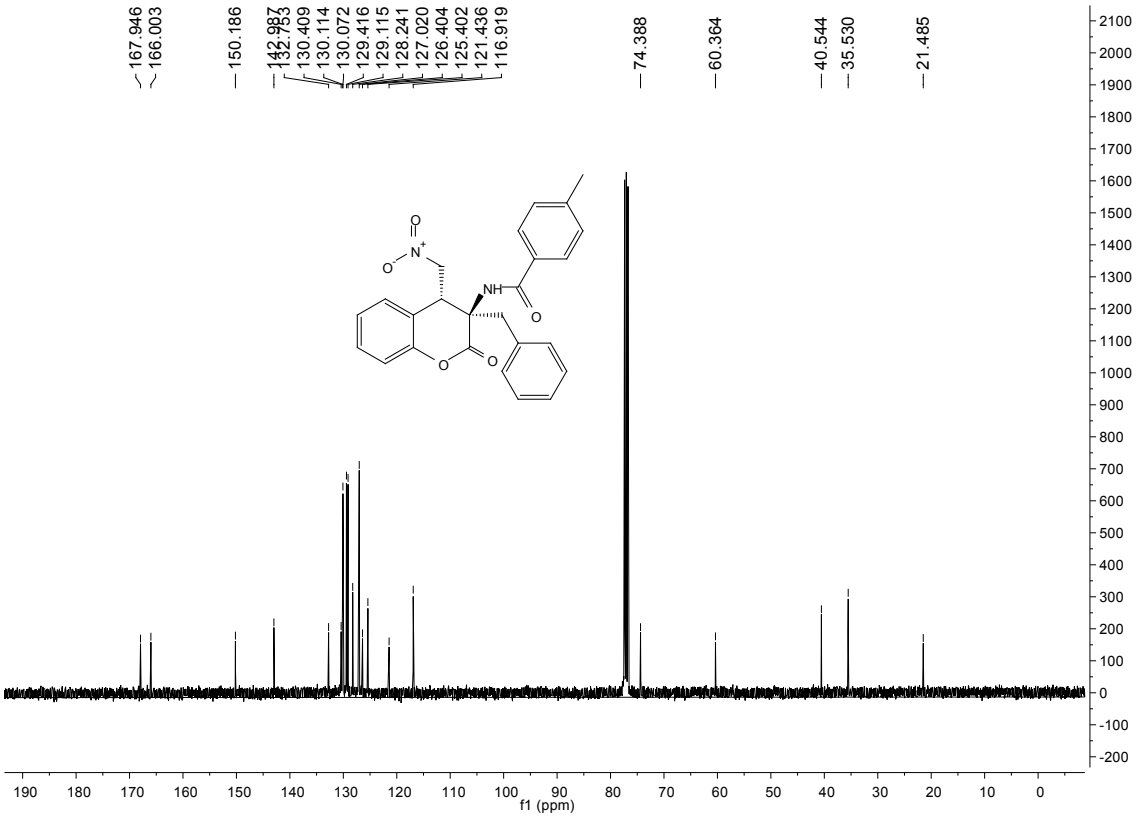
## 3ac


7.360
7.342
7.340
7.275
7.254
7.201
7.196
7.184
7.086
7.067
7.029
7.007
6.989
6.936
5.115
5.107
5.081
5.074
4.979
4.959
4.833
4.808
4.800
4.776
3.156
3.120
2.986
2.950
Br
NH
O
2.08
2.12
3.93
4.96
1.00
1.02
1.00
0.98
1.00
1.02
f1 (ppm)

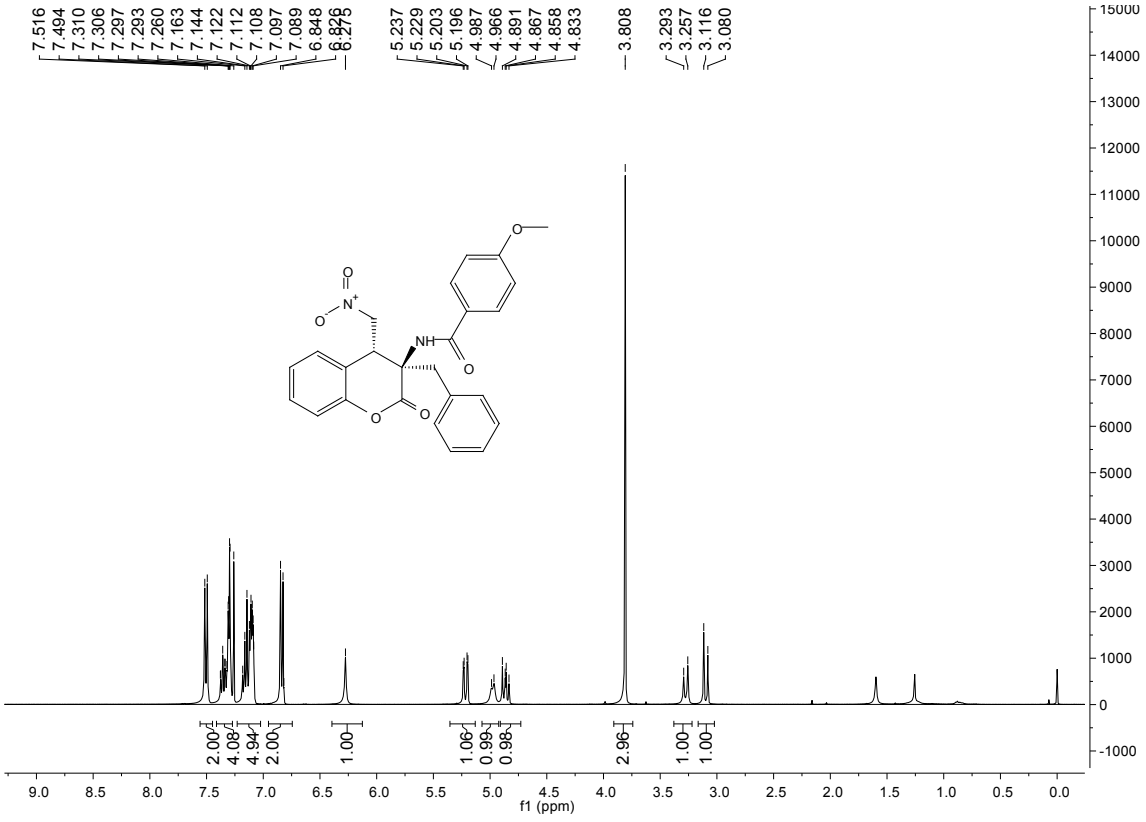

167.236
165.808
149.962
132.466
132.009
131.970
130.143
130.012
129.134
128.569
128.353
127.179
126.227
125.544
121.292
116.934
74.274
60.642
40.160
35.783
Br
NH
O
f1 (ppm)

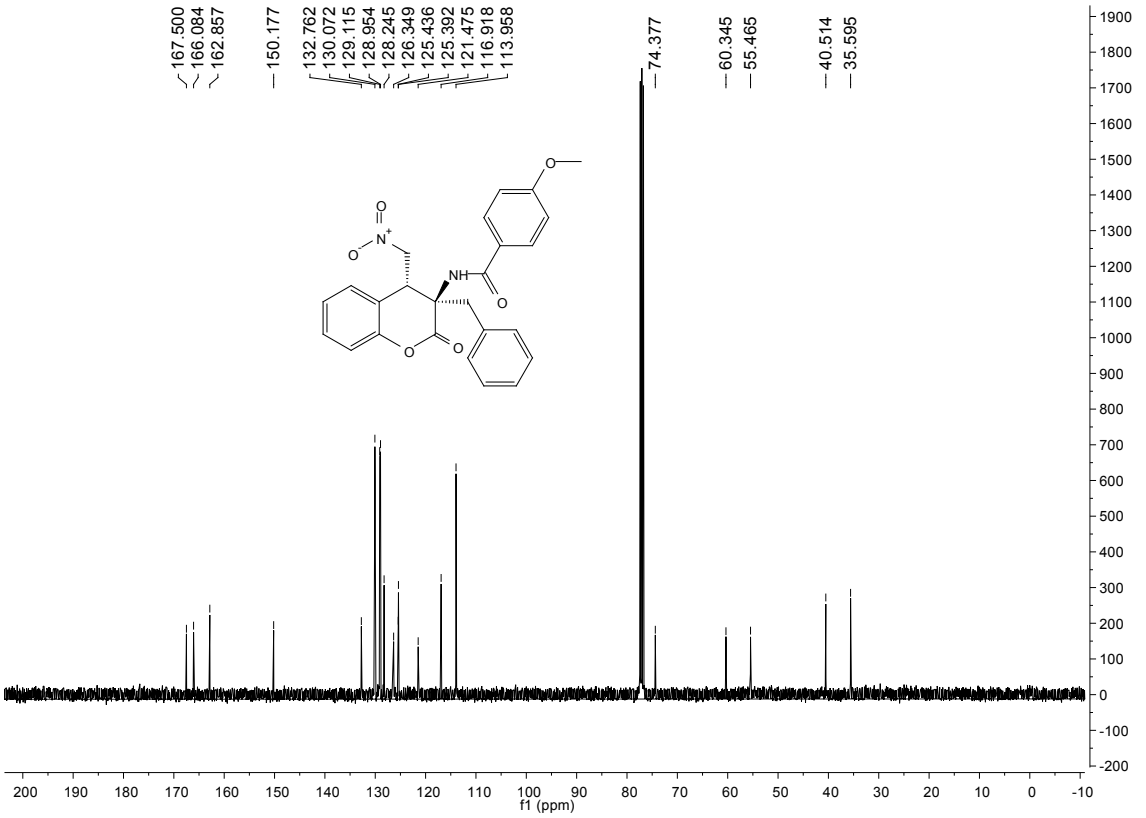
# 3ad


7.440
7.420
7.378
7.358
7.339
7.305
7.292
7.183
7.164
7.144
7.120
7.108
7.099
7.091
6.328
5.236
5.229
5.202
5.196
4.969
4.946
4.889
4.864
4.857
4.832
3.303
3.267
3.126
3.090
2.350
2.04
4.05
6.92
1.03
1.04
0.97
1.03
1.00
1.00
3.00
NH
O
f1 (ppm)

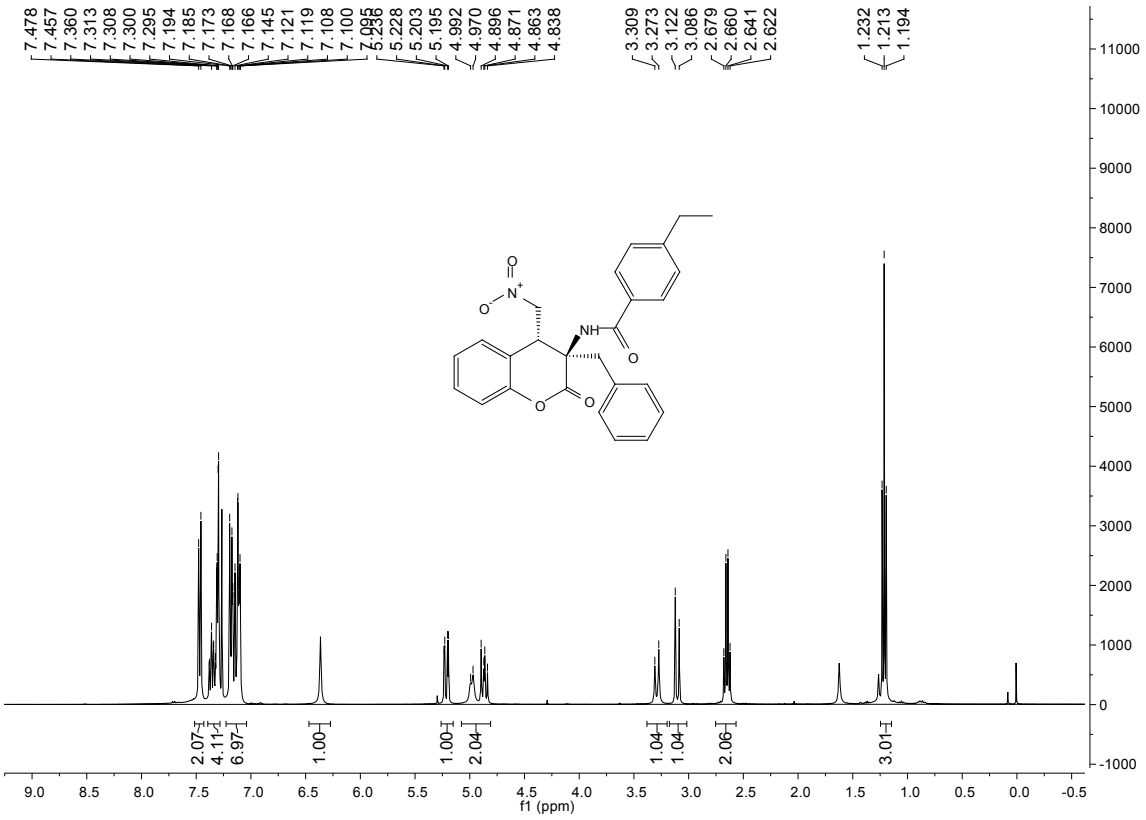

167.946
166.003
150.186
142.987
132.753
130.409
130.114
130.072
129.416
129.115
128.241
127.020
126.404
125.402
121.436
116.919
74.388
60.364
40.544
35.530
21.485
f1 (ppm)

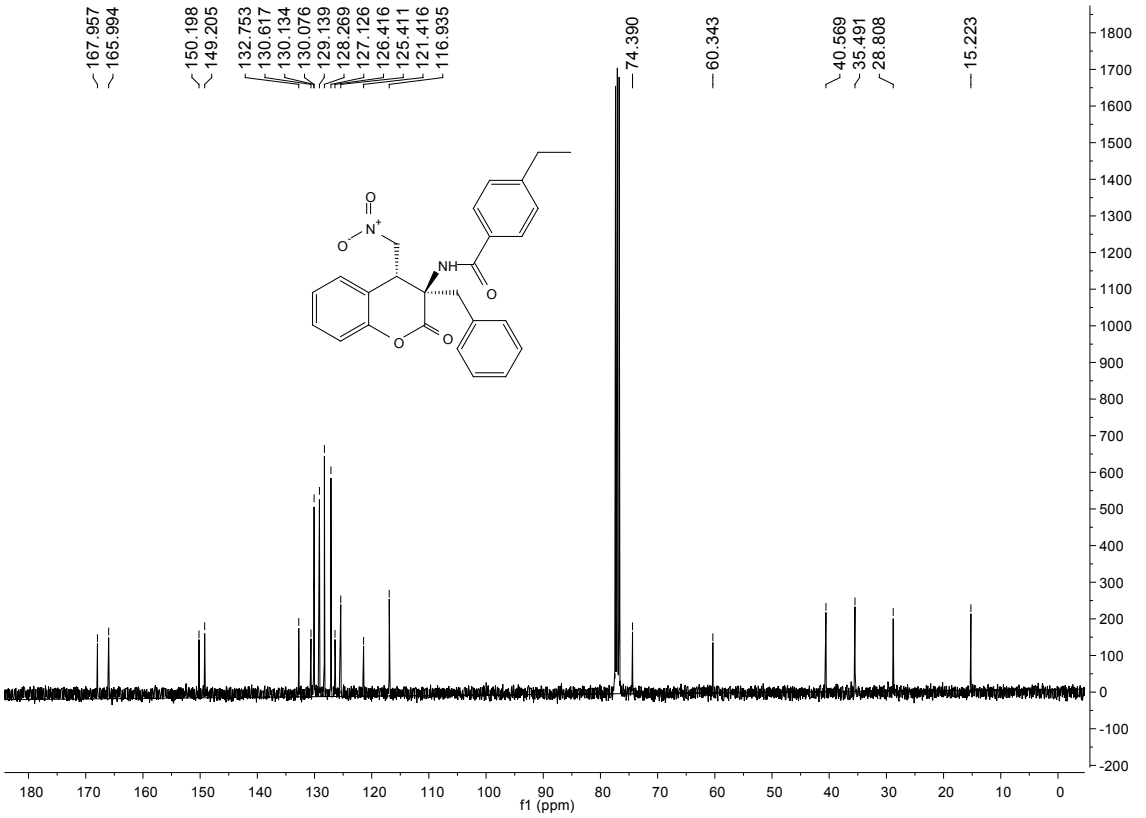
## 3ae


7.516
7.494
7.310
7.306
7.297
7.293
7.260
7.163
7.144
7.122
7.112
7.108
7.097
7.089
6.848
6.275
5.237
5.229
5.203
5.196
4.987
4.966
4.891
4.867
4.858
4.833
3.808
3.293
3.257
3.116
3.080
2.00
4.08
4.94
2.00
1.00
1.06
0.99
0.98
2.96
1.00
1.00
f1 (ppm)

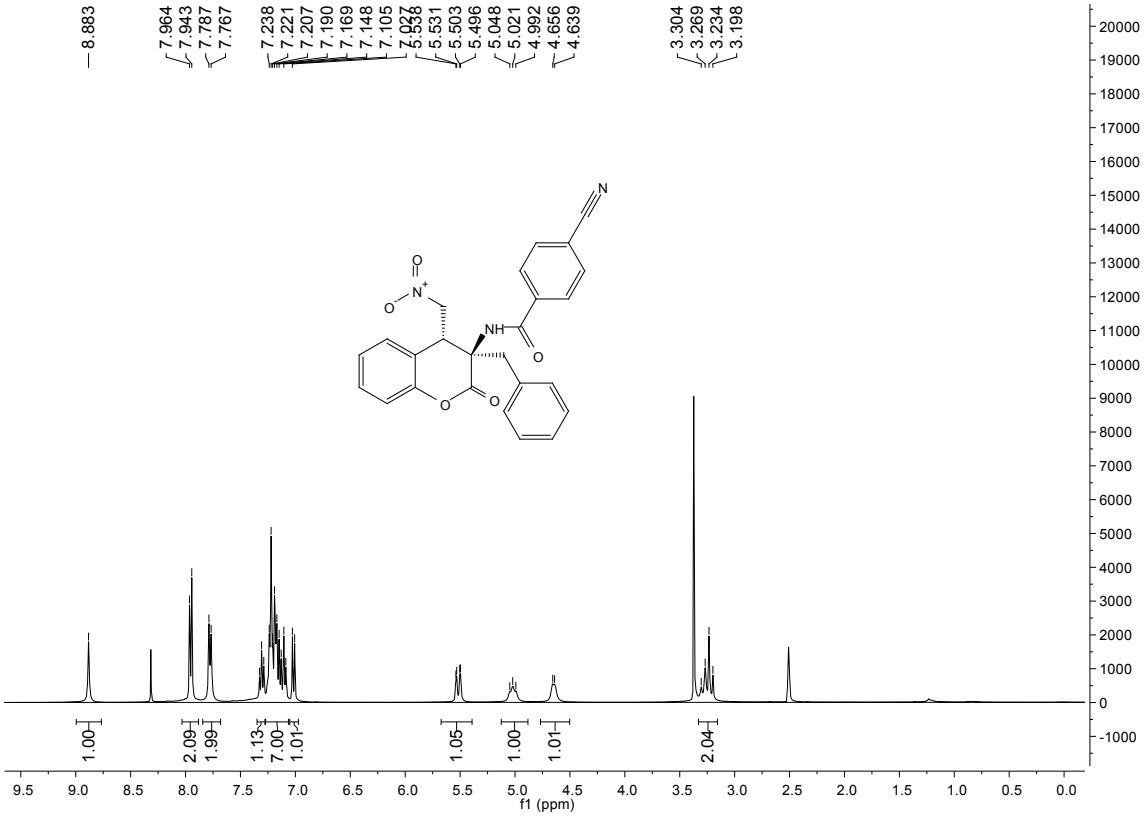

167.500
166.084
162.857
150.177
132.762
130.072
129.115
128.954
128.245
126.349
125.436
125.392
121.475
116.918
113.958
74.377
60.345
55.465
40.514
35.595
f1 (ppm)

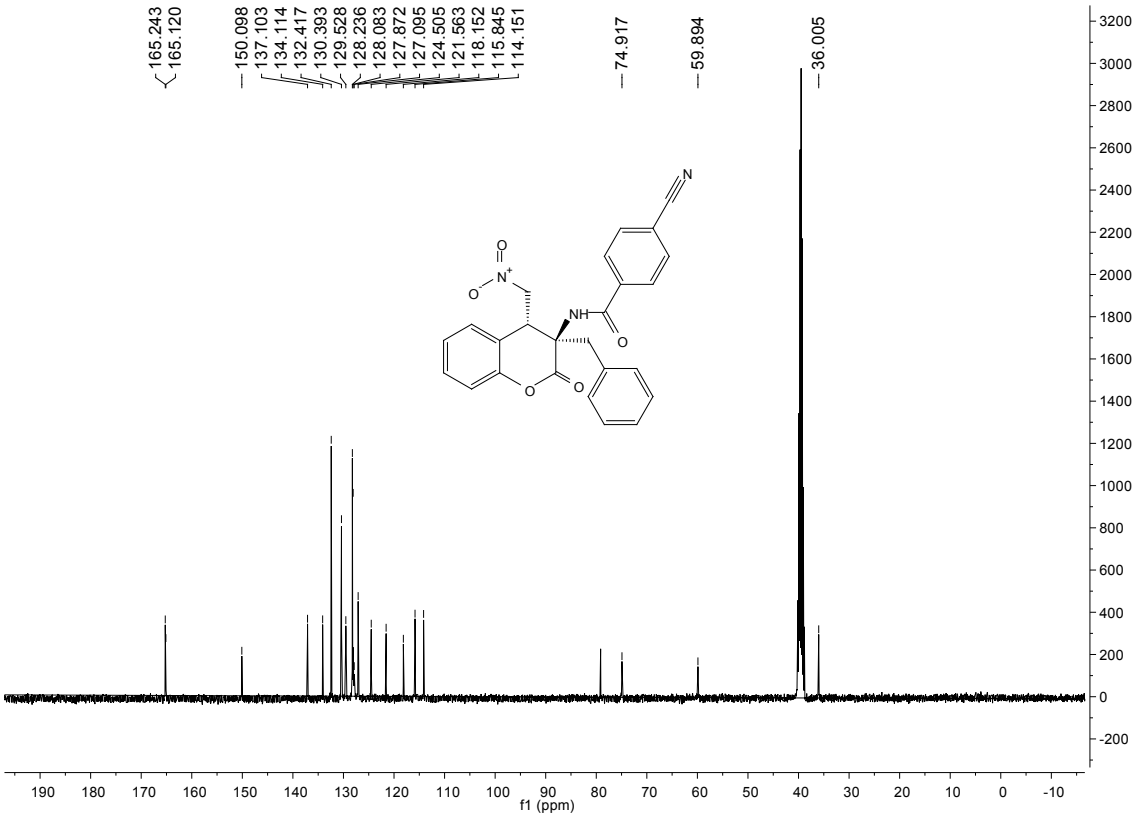
# 3af


7.478
7.457
7.360
7.313
7.308
7.300
7.295
7.194
7.185
7.173
7.168
7.166
7.145
7.121
7.119
7.108
7.100
5.228
5.203
5.195
4.992
4.970
4.896
4.871
4.863
4.838
3.309
3.273
3.122
3.086
2.679
2.660
2.641
2.622
1.232
1.213
1.194
2.07
4.11
6.97
1.00
1.00
2.04
1.04
1.04
2.06
3.01
f1 (ppm)

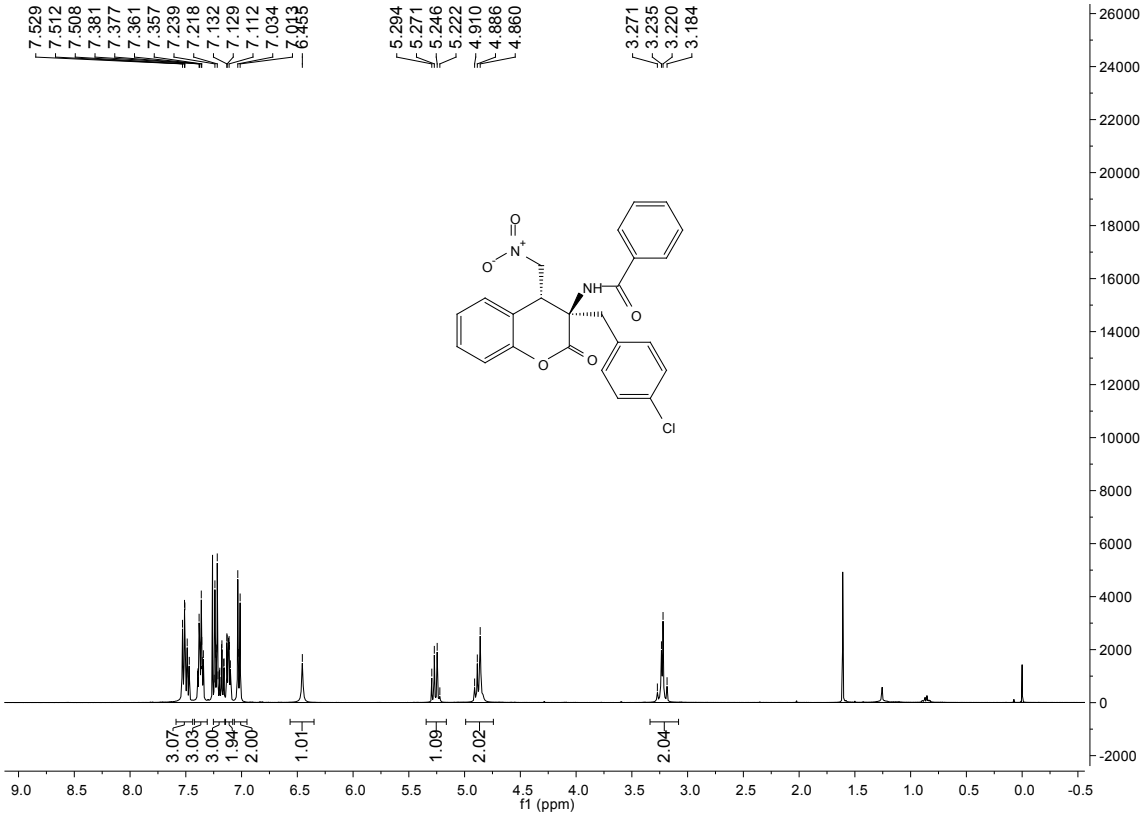

167.957
165.994
150.198
149.205
132.753
130.617
130.134
130.076
129.139
128.269
127.126
126.416
125.411
121.416
116.935
74.390
60.343
40.569
35.491
28.808
15.223
NH
f1 (ppm)

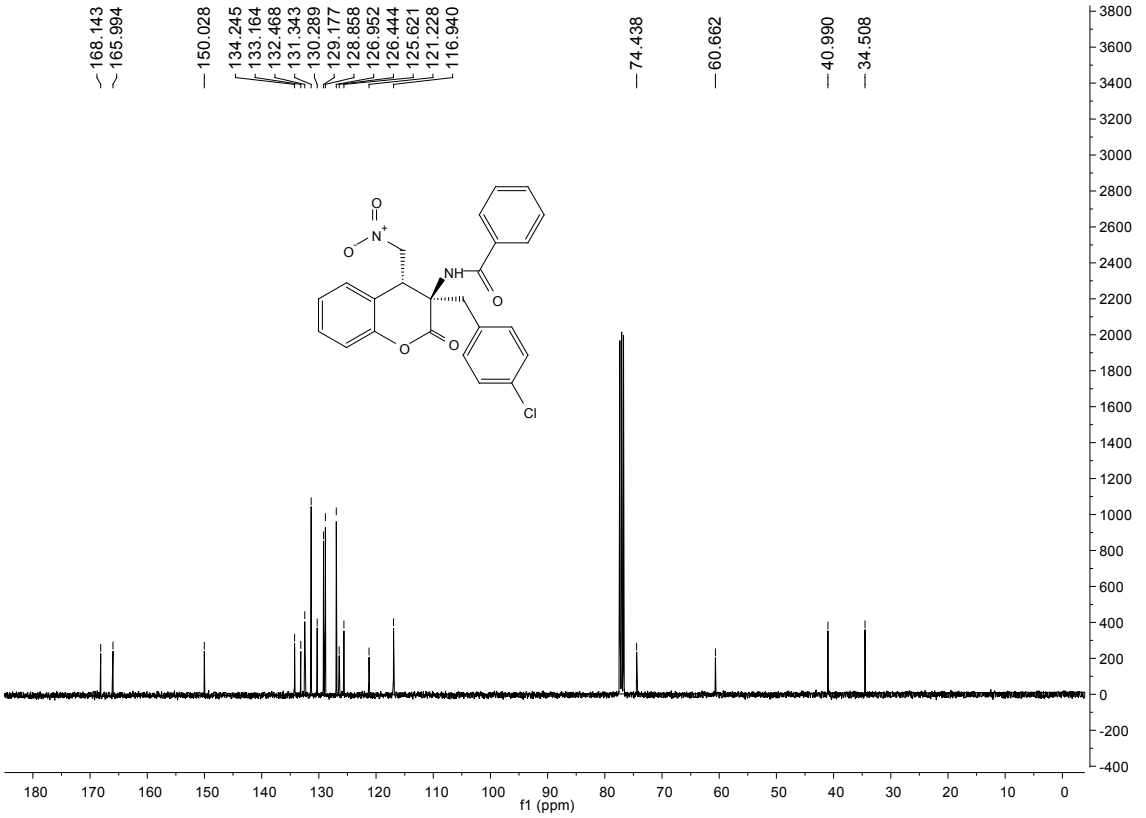
**3ag**


8.883
7.964
7.943
7.787
7.767
7.238
7.221
7.207
7.190
7.169
7.148
7.105
5.531
5.503
5.496
5.048
5.021
4.992
4.656
4.639
3.304
3.269
3.234
3.198
1.00
2.09
1.99
1.13
7.00
1.01
1.05
1.00
1.01
2.04
NH
N
f1 (ppm)

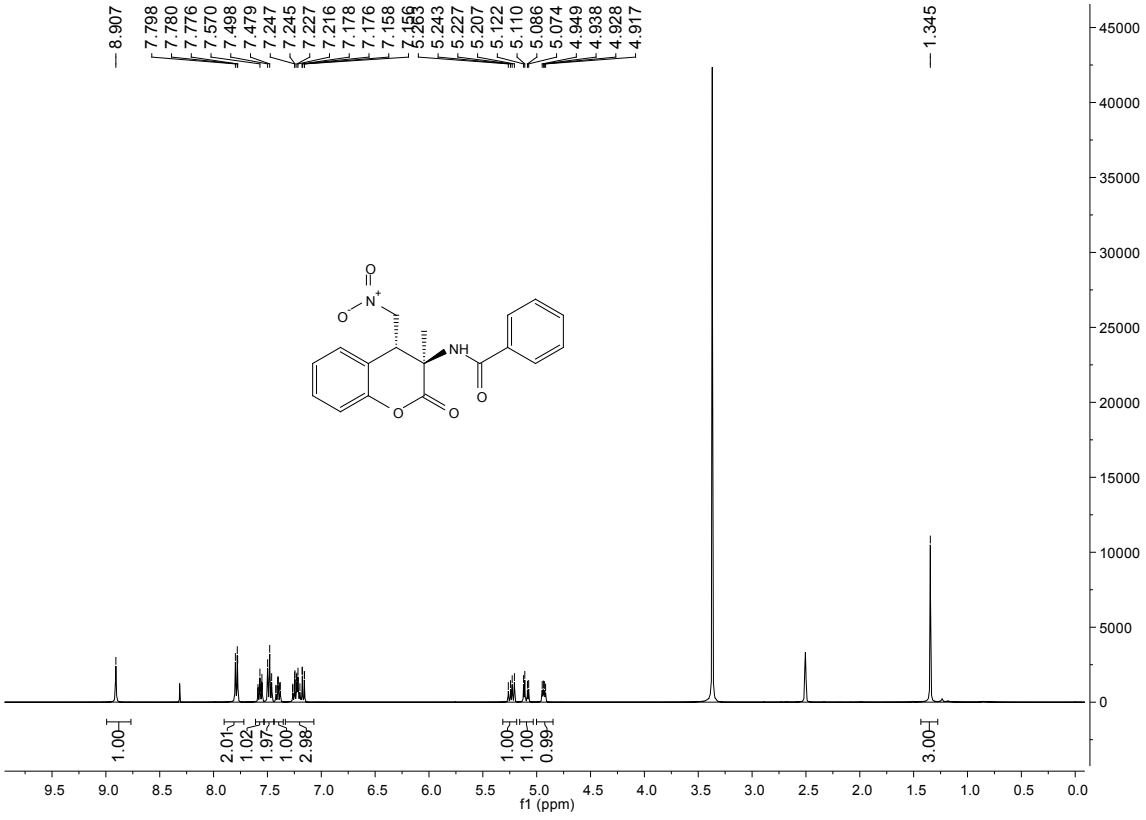

165.243
165.120
150.098
137.103
134.114
132.417
130.393
129.528
128.236
128.083
127.872
127.095
124.505
121.563
118.152
115.845
114.151
74.917
59.894
36.005
f1 (ppm)

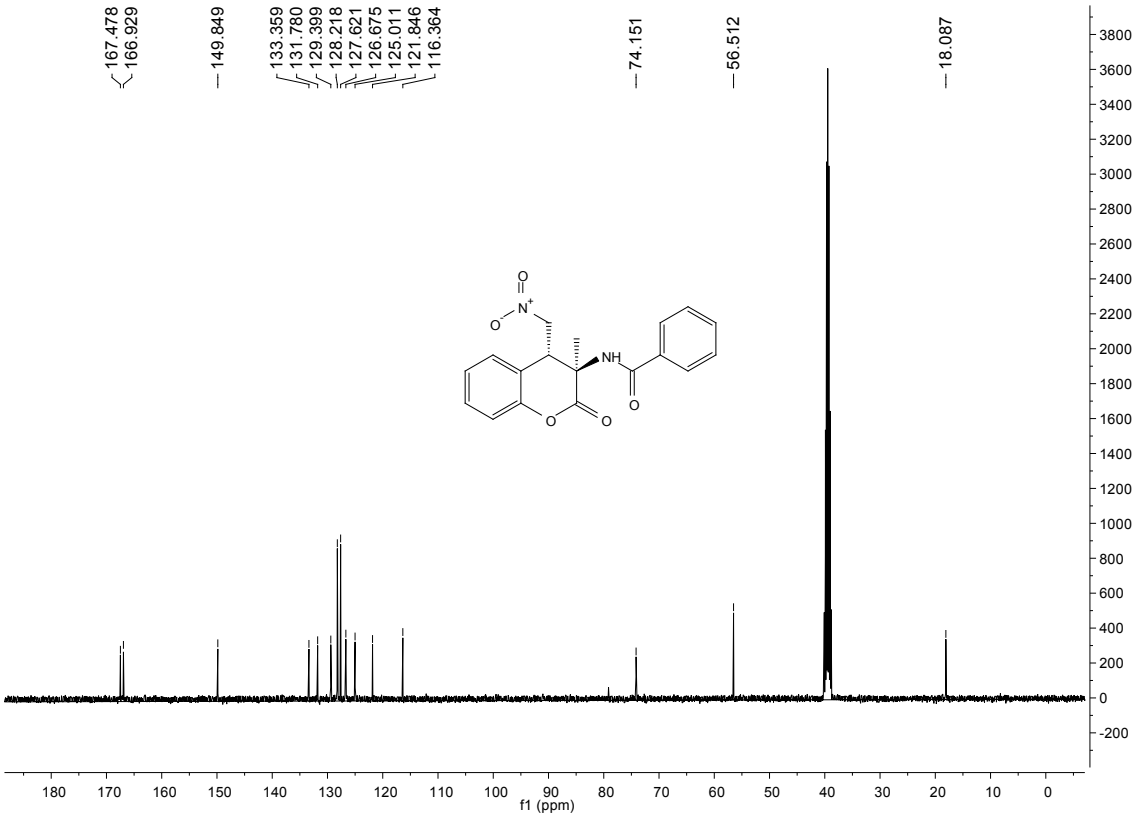
## 3ah


7.529
7.512
7.508
7.381
7.377
7.361
7.357
7.239
7.218
7.132
7.129
7.112
7.034
7.013
6.453
5.294
5.271
5.246
5.222
4.910
4.886
4.860
3.271
3.235
3.220
3.184
3.07
3.03
3.00
1.94
2.00
1.01
1.09
2.02
2.04
f1 (ppm)

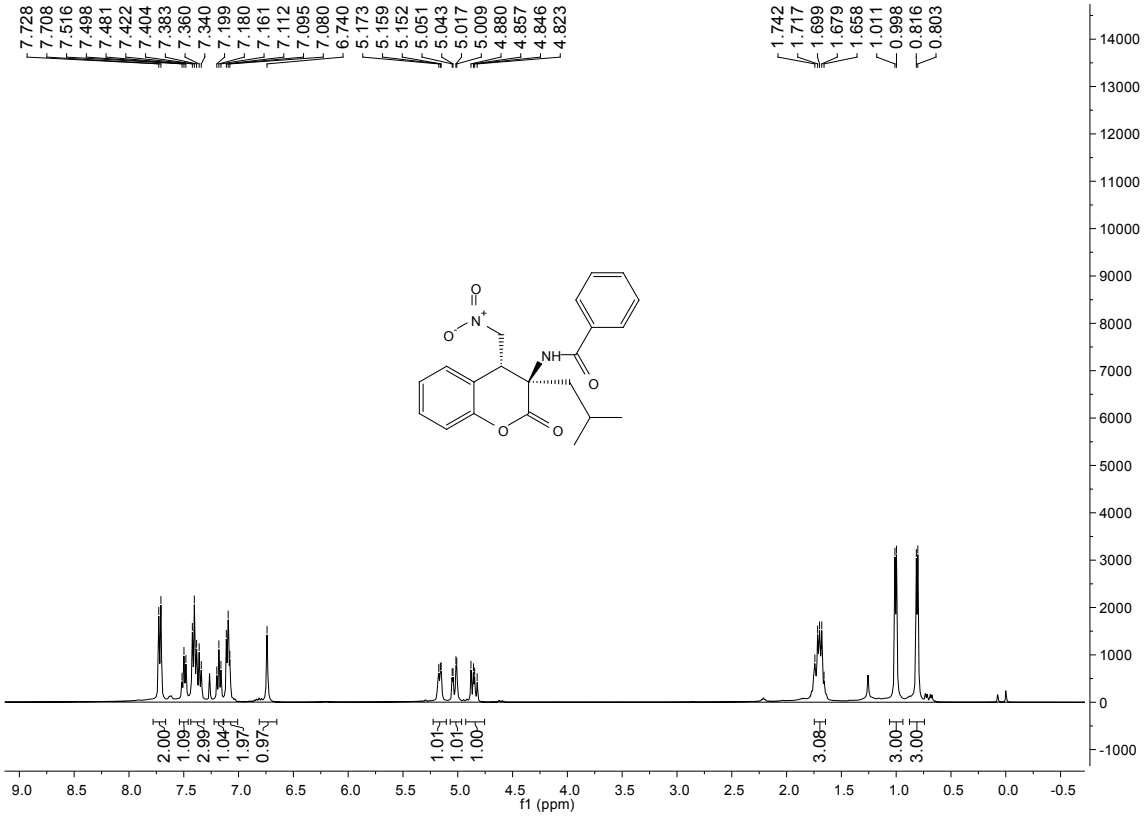

168.143
165.994
150.028
134.245
133.164
132.468
131.343
130.289
129.177
128.858
126.952
126.444
125.621
121.228
116.940
74.438
60.662
40.990
34.508
NH
O
Cl
f1 (ppm)

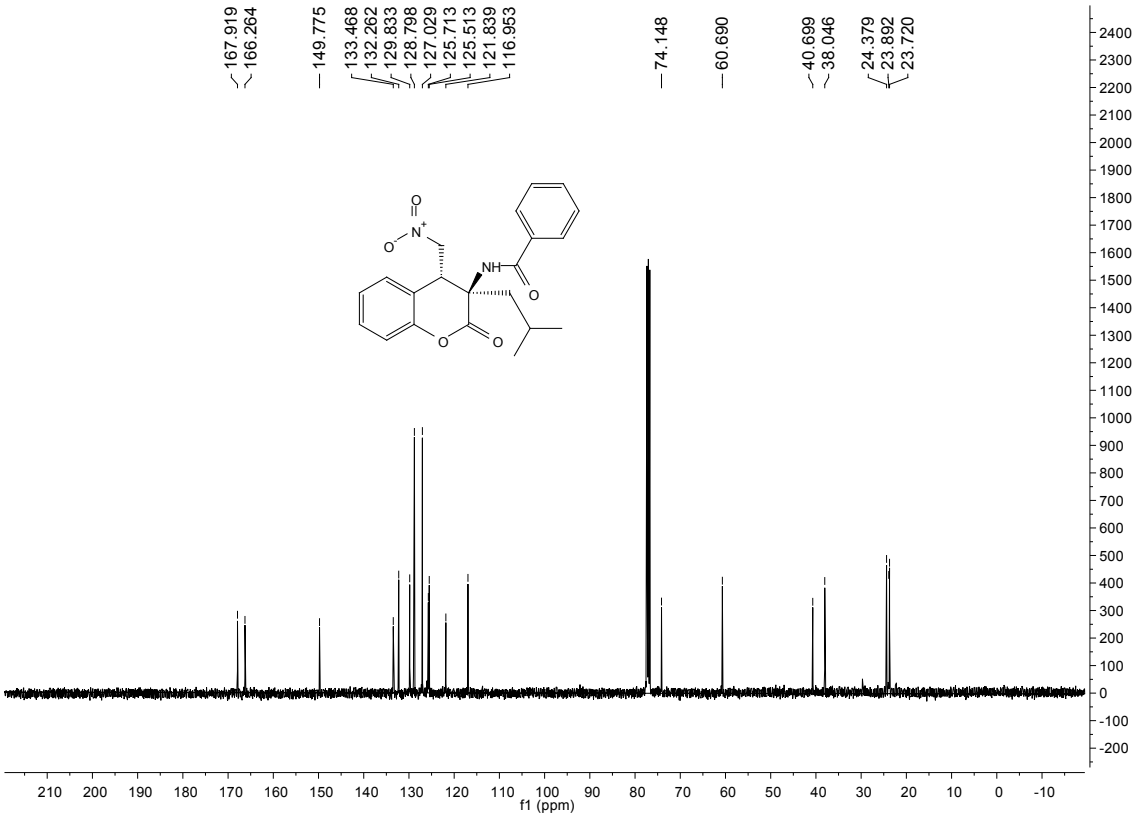
**3ai**


8.907
7.798
7.780
7.776
7.570
7.498
7.479
7.247
7.245
7.227
7.216
7.178
7.176
7.158
5.263
5.243
5.227
5.207
5.122
5.110
5.086
5.074
4.949
4.938
4.928
4.917
1.345
NH
O
1.00
2.01
1.02
1.97
1.00
2.98
1.00
1.00
0.99
3.00
f1 (ppm)

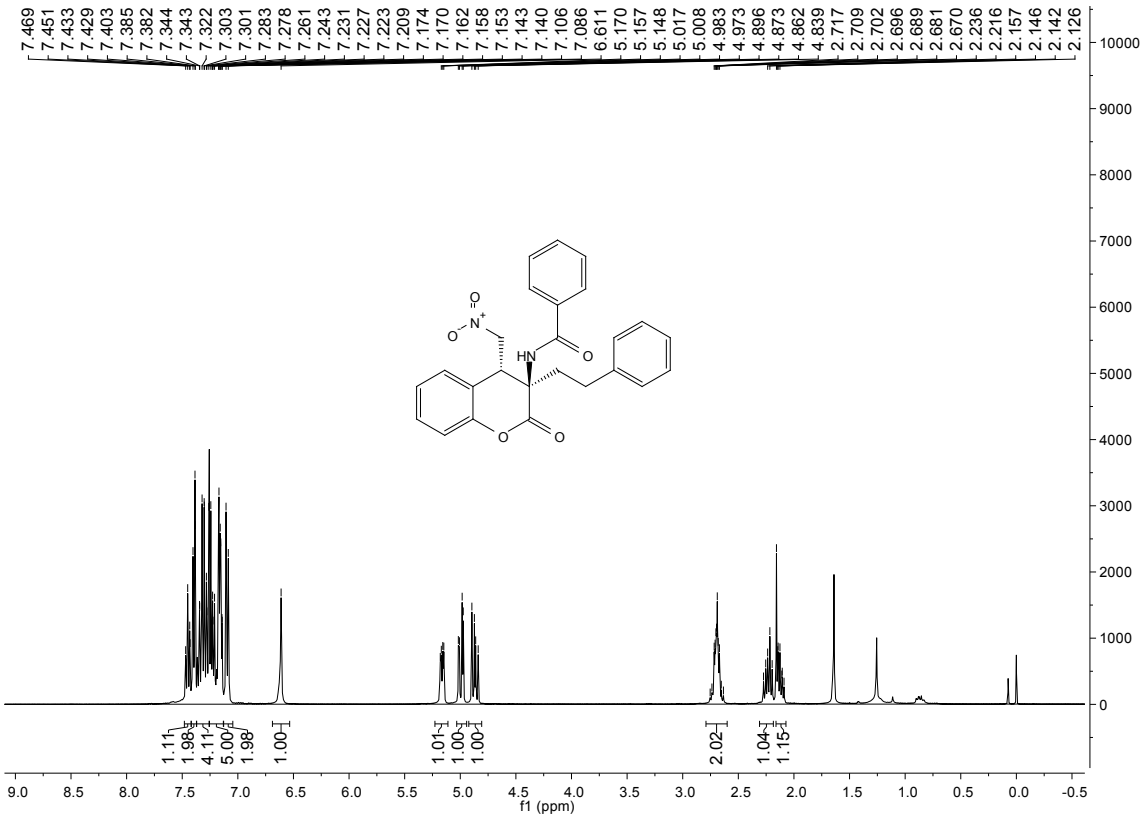

167.478
166.929
149.849
133.359
131.780
129.399
128.218
127.621
126.675
125.011
121.846
116.364
74.151
56.512
18.087
f1 (ppm)

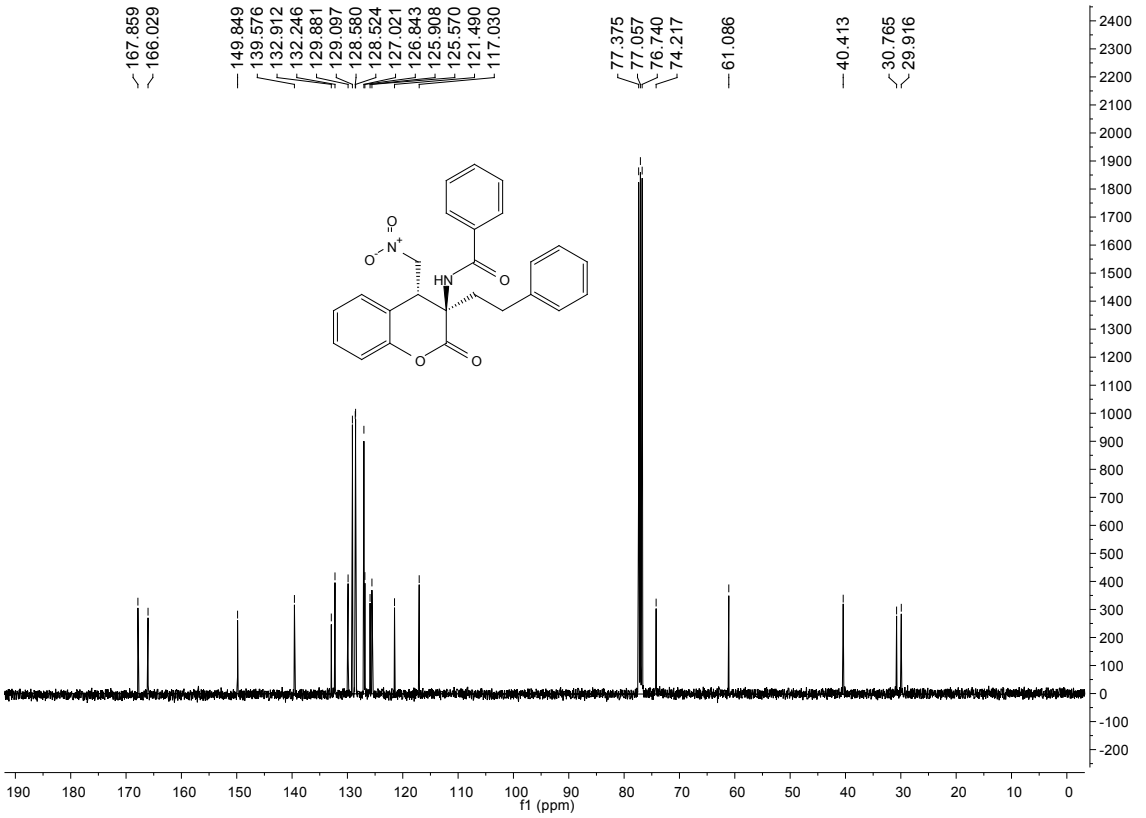
**3aj**


7.728
7.708
7.516
7.498
7.481
7.422
7.404
7.383
7.360
7.340
7.199
7.180
7.161
7.112
7.095
7.080
6.740
5.173
5.159
5.152
5.051
5.043
5.017
5.009
4.880
4.857
4.846
4.823
1.742
1.717
1.699
1.679
1.658
1.011
0.998
0.816
0.803
2.00
1.09
2.99
1.04
1.97
0.97
1.01
1.01
1.00
3.08
3.00
3.00
f1 (ppm)

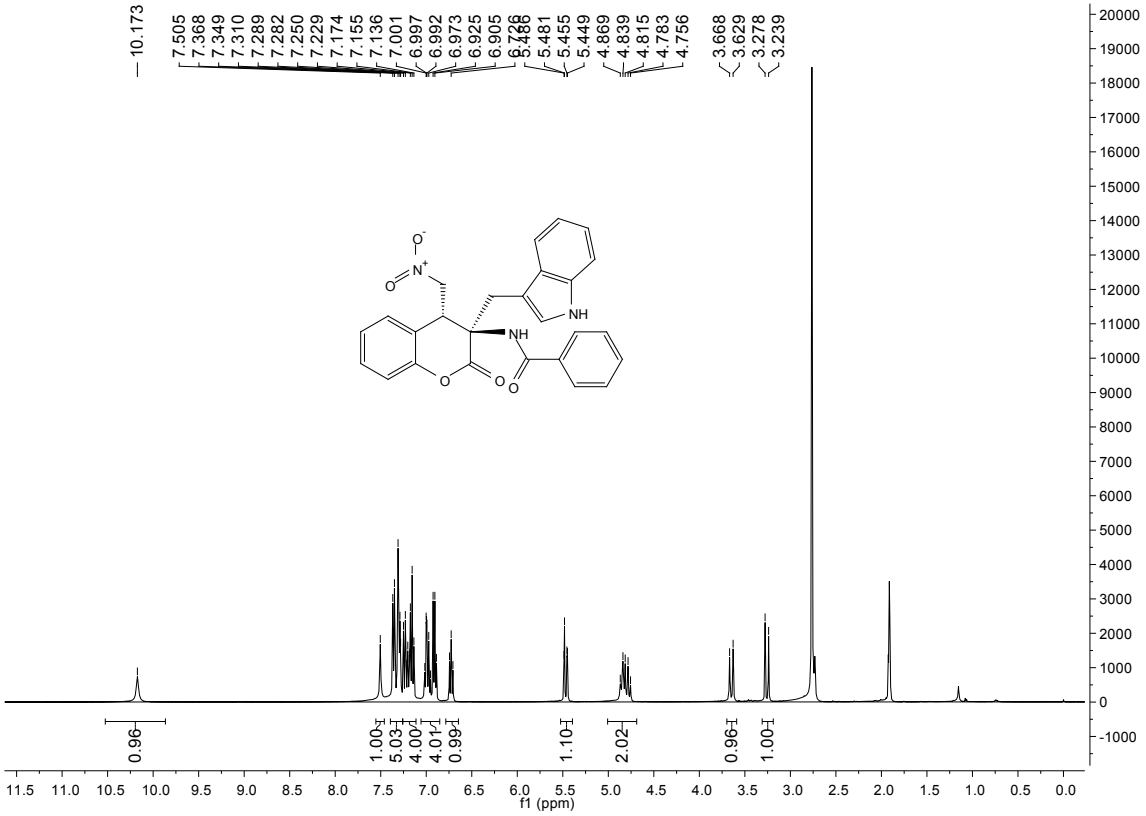

167.919
166.264
149.775
133.468
132.262
129.833
128.798
127.029
125.713
125.513
121.839
116.953
74.148
60.690
40.699
38.046
24.379
23.892
23.720
f1 (ppm)

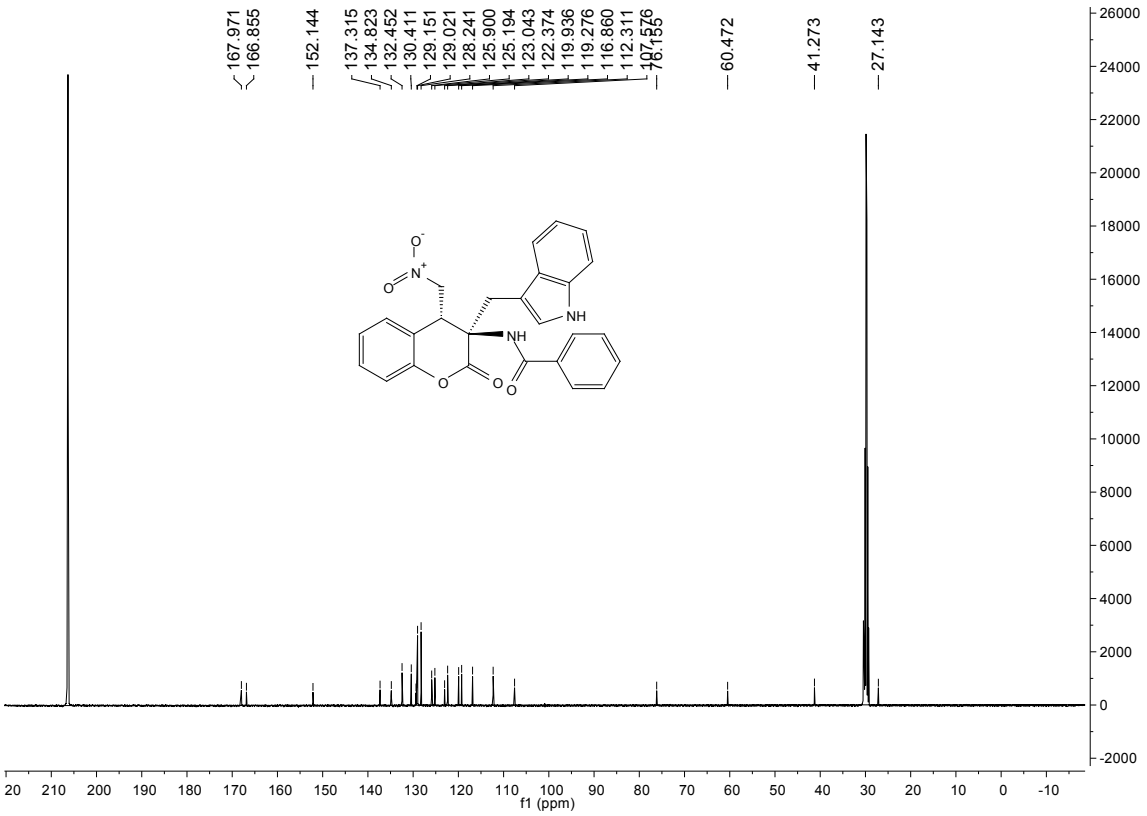
# 3ak


7.469
7.451
7.433
7.429
7.403
7.385
7.382
7.344
7.343
7.322
7.303
7.301
7.283
7.278
7.261
7.243
7.231
7.227
7.223
7.209
7.174
7.170
7.162
7.158
7.153
7.143
7.140
7.106
7.086
6.611
5.170
5.157
5.148
5.017
5.008
4.983
4.973
4.896
4.873
4.862
4.839
2.717
2.709
2.702
2.696
2.689
2.681
2.670
2.236
2.216
2.157
2.146
2.142
2.126
1.11
1.98
4.11
5.00
1.98
1.00
1.01
1.00
1.00
2.02
1.04
1.15
f1 (ppm)


167.859
166.029
149.849
139.576
132.912
132.246
129.881
129.097
128.580
128.524
127.021
126.843
125.908
125.570
121.490
117.030
77.375
77.057
76.740
74.217
61.086
40.413
30.765
29.916
HN
O
O
O
O
O
f1 (ppm)

## 3al

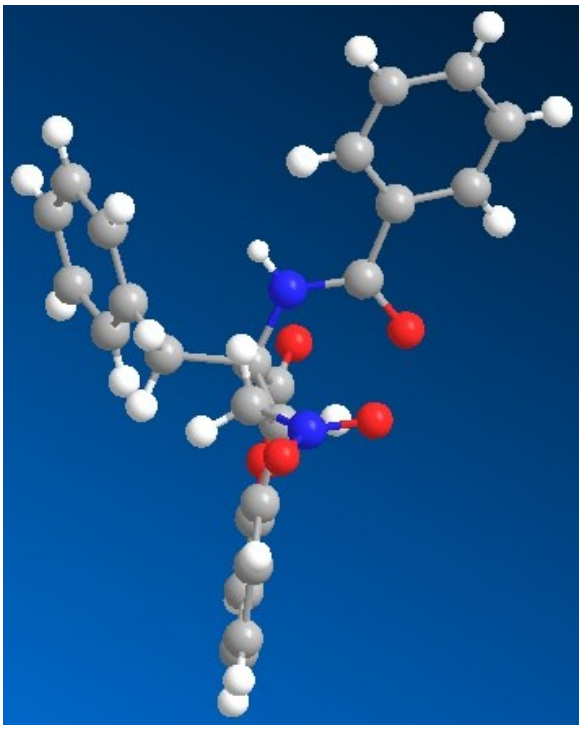

10.173
7.505
7.368
7.349
7.310
7.289
7.282
7.250
7.229
7.174
7.155
7.136
7.001
6.997
6.992
6.973
6.925
6.905
5.481
5.455
5.449
4.869
4.839
4.815
4.783
4.756
3.668
3.629
3.278
3.239
NH
NH
O
O
O
0.96
1.00
5.03
4.00
4.01
0.99
1.10
2.02
0.96
1.00
f1 (ppm)

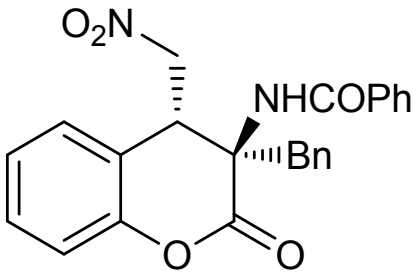



## 8. X-ray crystal structure of the product 3aa

| | |
|---|---|
| Identification code | fxm-ruan2 |
| Empirical formula | $C_{48}H_{40}N_2O_5$ |
| Formula weight | 832.84 |
| Temperature/K | 135 |
| Crystal system | monoclinic |
| Space group | P21 |
| a/Å | 10.31419(17) |
| b/Å | 19.2062(3) |
| c/Å | 11.0205(2) |
| α/° | 90 |
| β/° | 109.532(2) |
| γ/° | 90 |
| Volume/Å3 | 2057.48(6) |
| Z | 2 |
| ρcalcg/cm3 | 1.344 |
| μ/mm-1 | 0.785 |
| F(000) | 872.0 |
| Crystal size/mm3 | 0.6 × 0.45 × 0.35 |
| Radiation | Cu Kα (λ = 1.54184) |
| 2Θ range for data collection/° | 9.098 to 145.514 |
| Index ranges | $-12 \le h \le 9$, $-23 \le k \le 23$, $-13 \le l \le 13$ |

| | |
|---|---|
| Reflections collected | 30369 |
| Independent reflections | 8035 [Rint = 0.0349, Rsigma = 0.0275] |
| Data/restraints/parameters | 8035/1/559 |
| Goodness-of-fit on F2 | 1.061 |
| Final R indexes [I>=2σ (I)] | R1 = 0.0414, wR2 = 0.1079 |
| Final R indexes [all data] | R1 = 0.0427, wR2 = 0.1097 |
| Largest diff. peak/hole / e Å-3 | 0.21/-0.30 |
| Flack parameter | -0.07(6) |

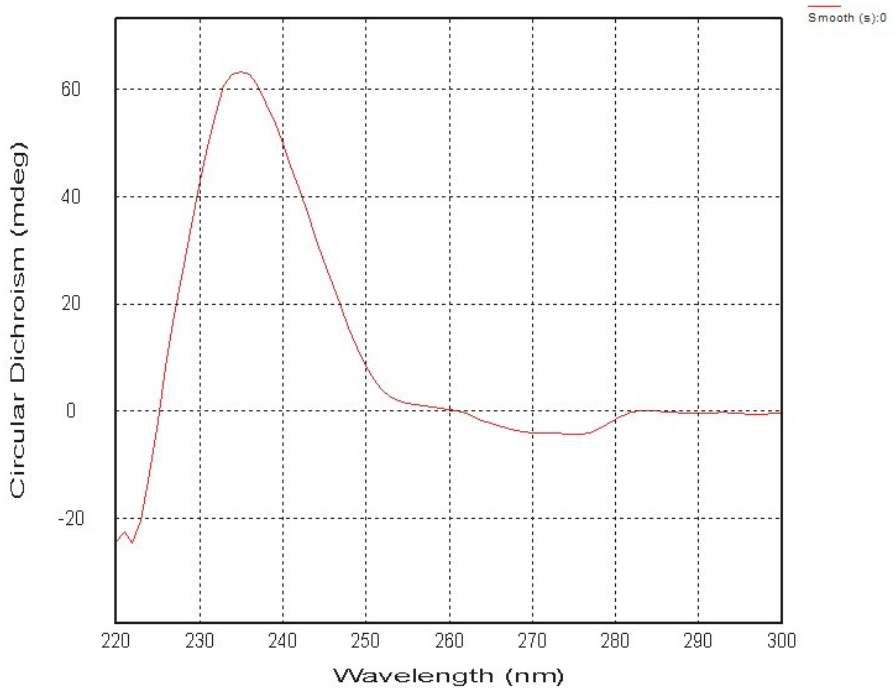


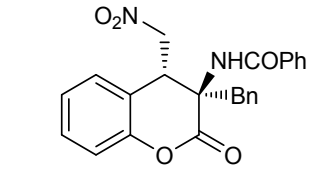



**3aa**

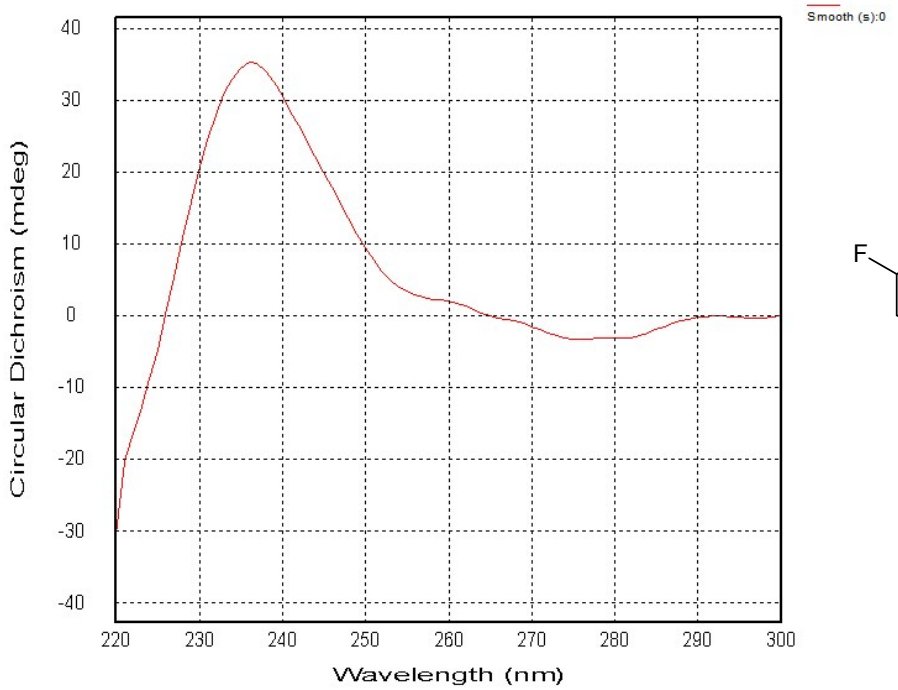
**9.** Copies of the CD spectra of the products 3

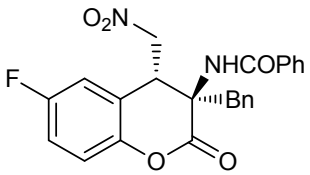
(*R,R*)-**3aa (standard)**



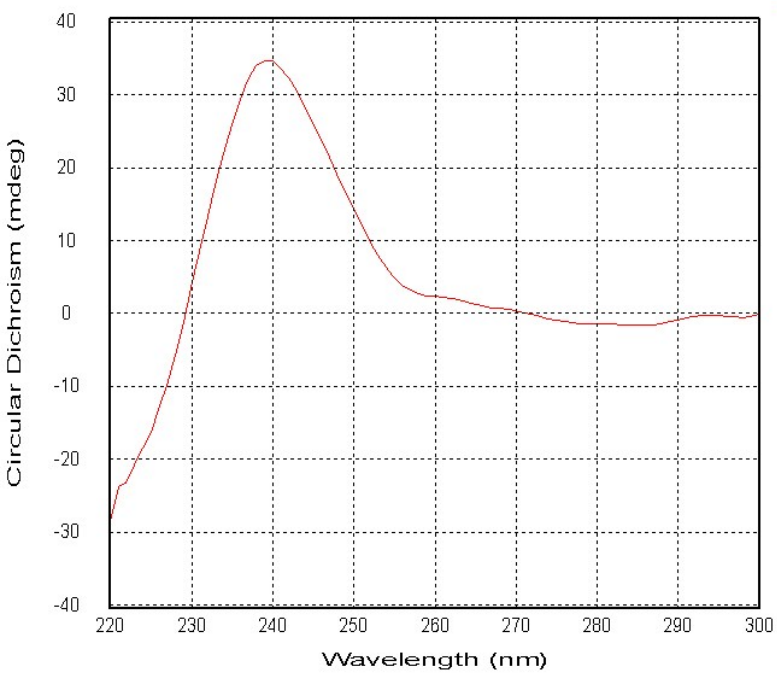



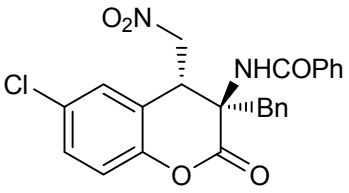

**3aa**



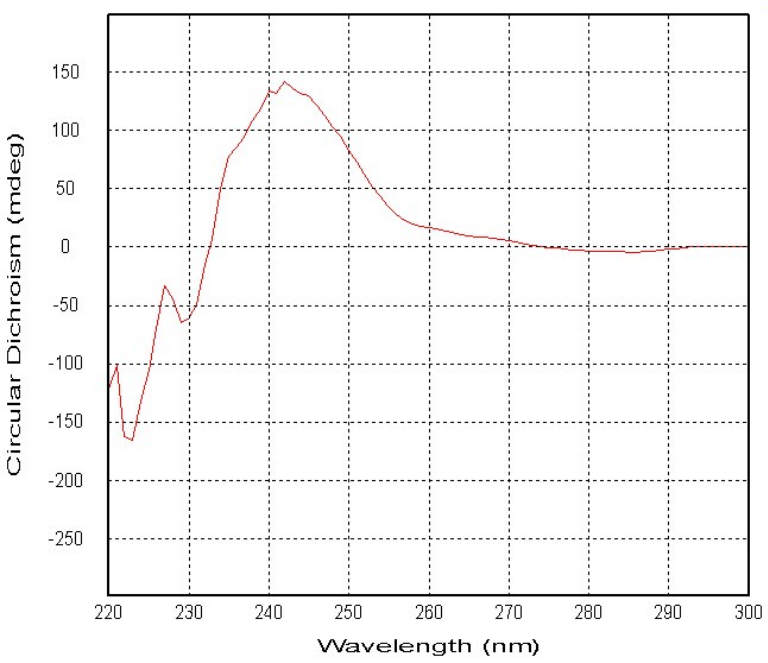



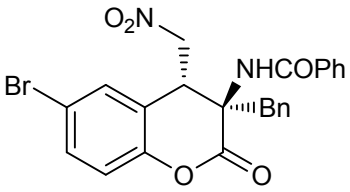

**3ba**


Smooth (s):0
Circular Dichroism (mdeg)
40
30
20
10
0
-10
-20
-30
-40
220
230
240
250
260
270
280
290
300
Wavelength (nm)

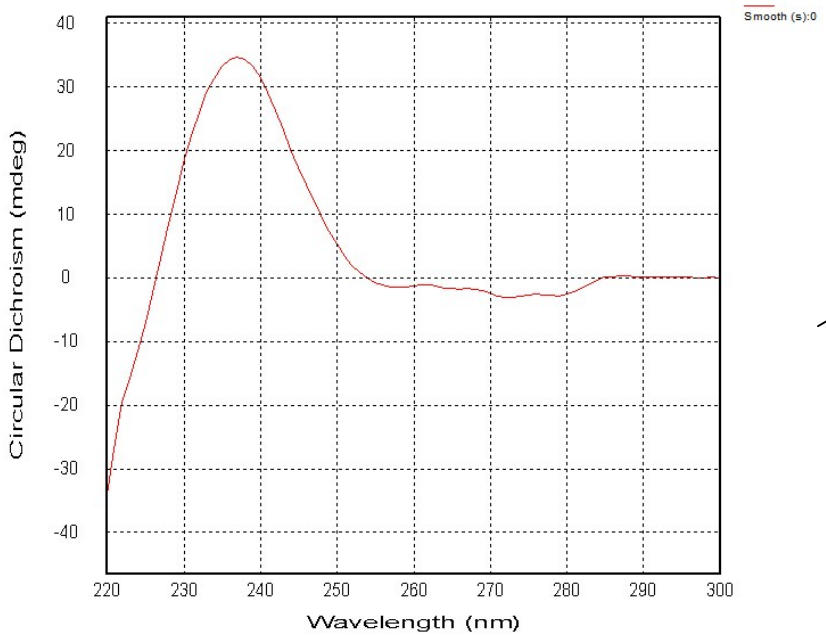

O2N
NHCOPh
Cl
Bn
O
O

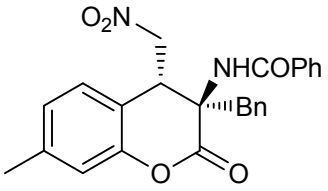
**3ca**


Smooth (s):0
Circular Dichroism (mdeg)
150
100
50
0
-50
-100
-150
-200
-250
220
230
240
250
260
270
280
290
300
Wavelength (nm)

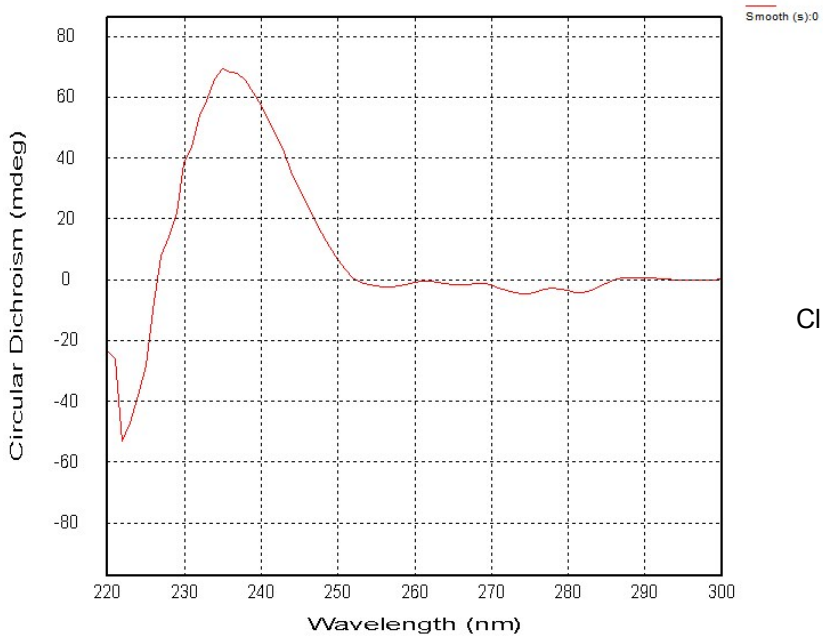

O2N
NHCOPh
Br
Bn
O
O

**3da**


Smooth (s):0
Circular Dichroism (mdeg)
40
30
20
10
0
-10
-20
-30
-40
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
NHCOPh
Bn
O
O

**3ea**


Smooth (s):0
Circular Dichroism (mdeg)
80
60
40
20
0
-20
-40
-60
-80
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230
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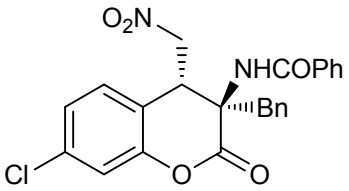
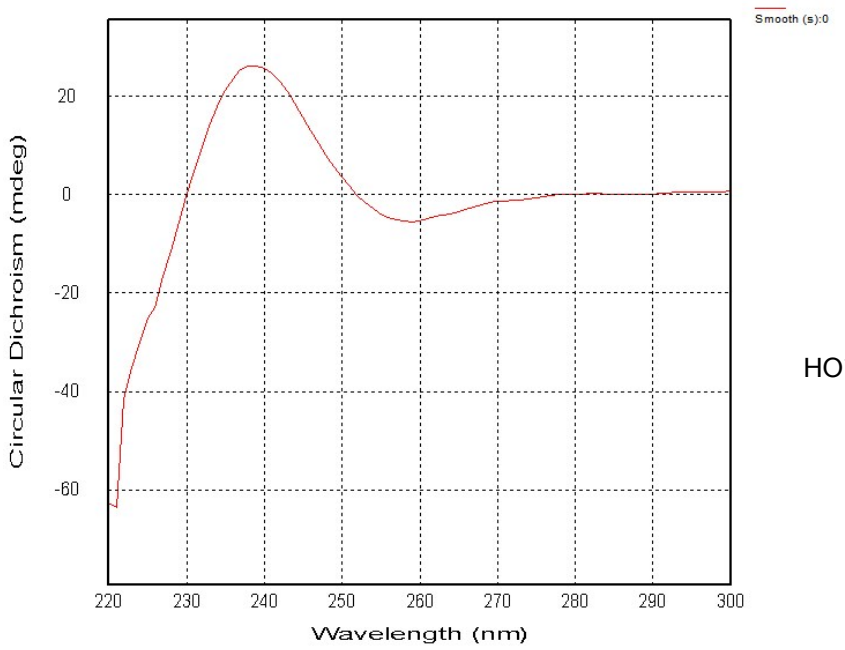
250
260
270
280
290
300
Wavelength (nm)


O2N
NHCOPh
Bn
Cl
O
O

**3fa**


Smooth (s):0
Circular Dichroism (mdeg)
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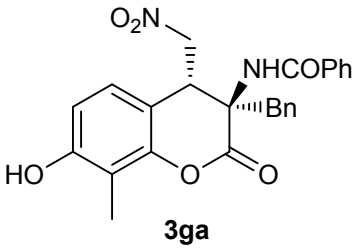
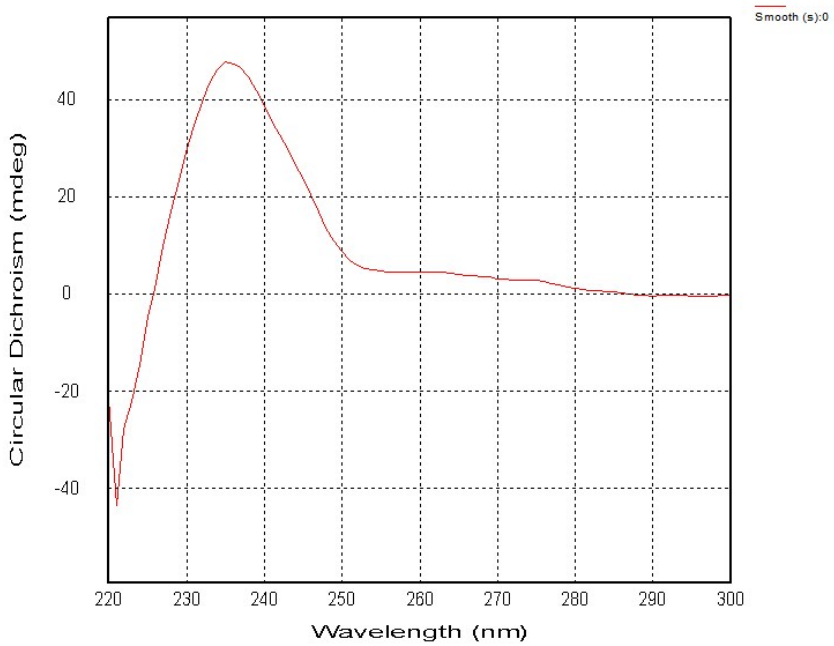
0
-20
-40
-60
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
NHCOPh
Bn
HO
O
O

**3ga**


Smooth (s):0
Circular Dichroism (mdeg)
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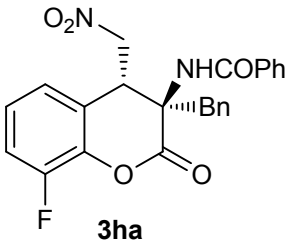
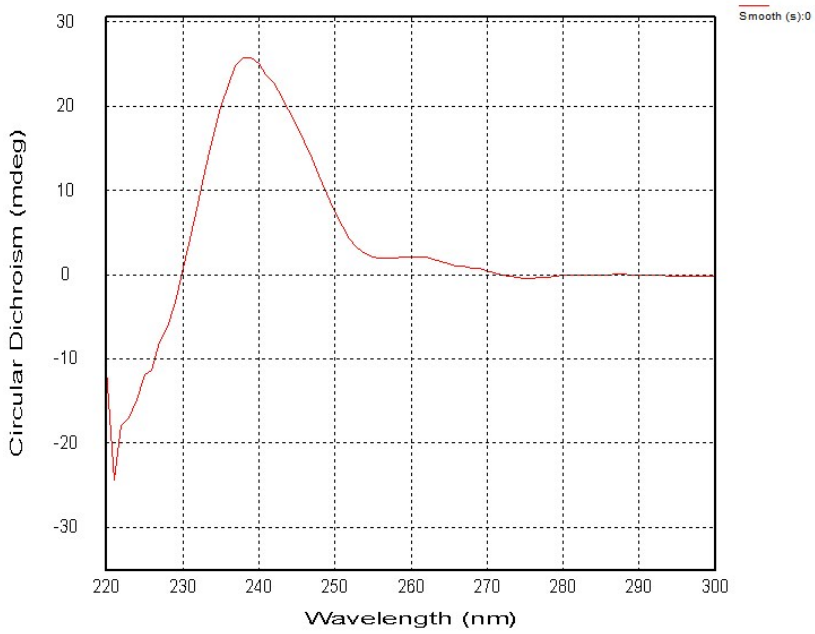
20
0
-20
-40
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
NHCOPh
Bn
O
O
F

**3ha**


Smooth (s):0
Circular Dichroism (mdeg)
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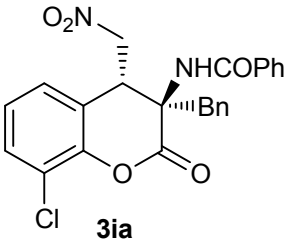
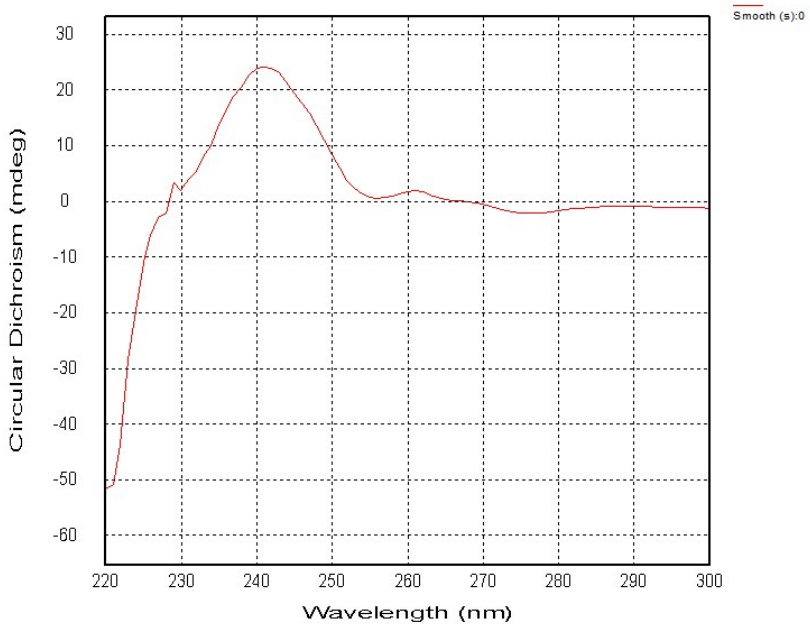
10
0
-10
-20
-30
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
NHCOPh
Bn
O
O
Cl

**3ia**


Smooth (s):0
Circular Dichroism (mdeg)
30
20
10
0
-10
-20
-30
-40
-50
-60
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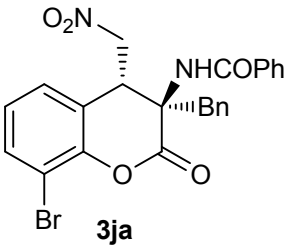
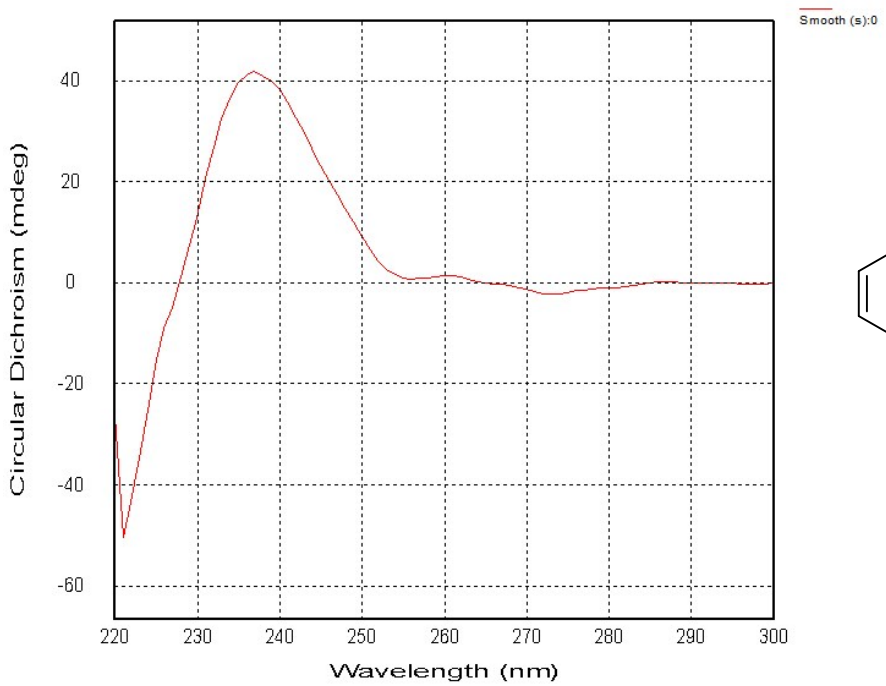
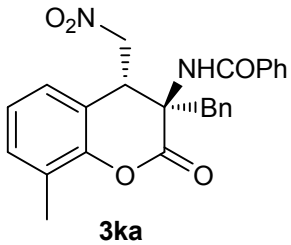
240
250
260
270
280
290
300
Wavelength (nm)

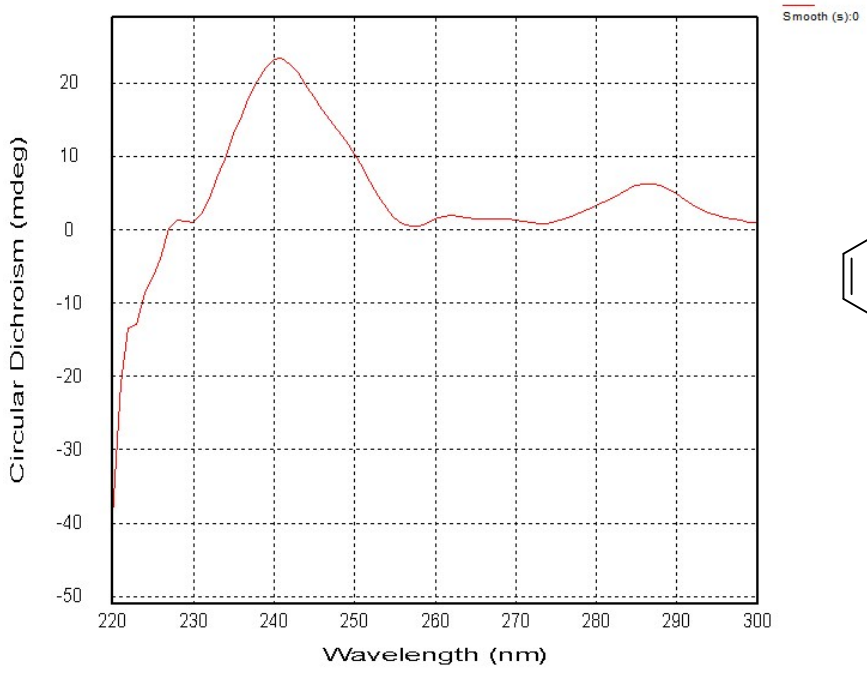

O2N
NHCOPh
Bn
O
O
Br

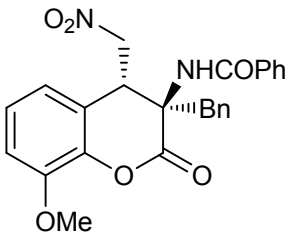
**3ja**


Smooth (s):0
Circular Dichroism (mdeg)
40
20
0
-20
-40
-60
220
230
240
250
260
270
280
290
300
Wavelength (nm)

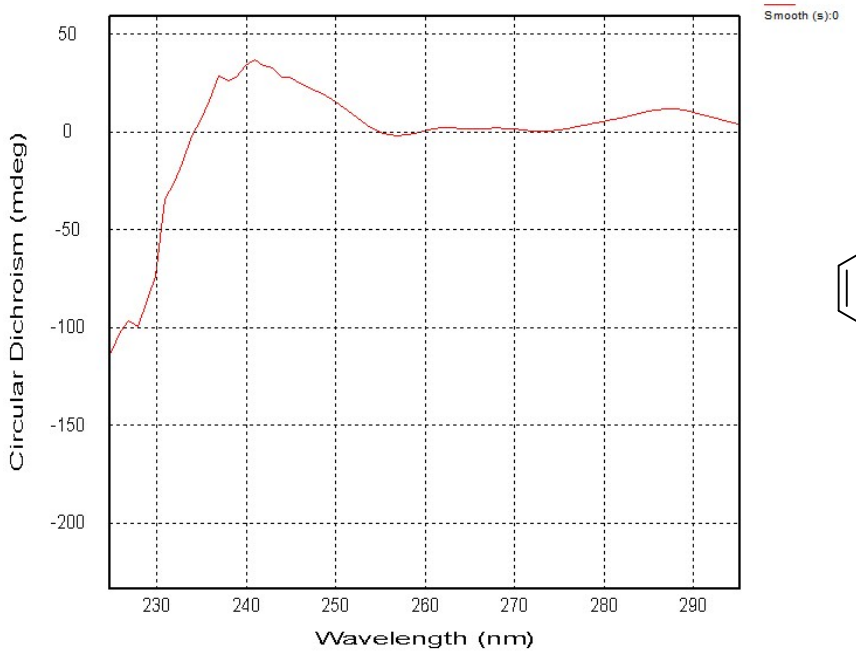

O2N
NHCOPh
Bn
O
O

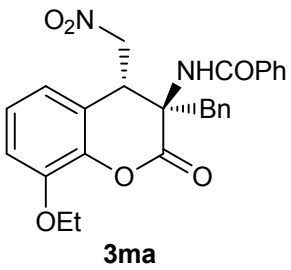
**3ka**


Smooth (s):0
Circular Dichroism (mdeg)
20
10
0
-10
-20
-30
-40
-50
220
230
240
250
260
270
280
290
300
Wavelength (nm)

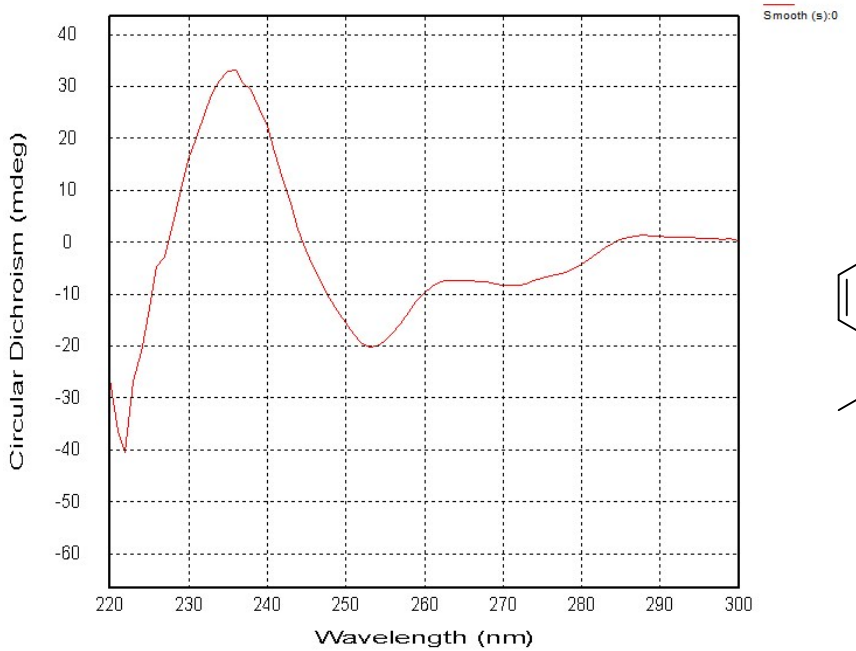

O2N
NHCOPh
Bn
O
O
OMe

**3la**


Smooth (s):0
Circular Dichroism (mdeg)
50
0
-50
-100
-150
-200
230
240
250
260
270
280
290
Wavelength (nm)


O2N
NHCOPh
Bn
O
O
OEt

**3ma**


Smooth (s):0
Circular Dichroism (mdeg)
40
30
20
10
0
-10
-20
-30
-40
-50
-60
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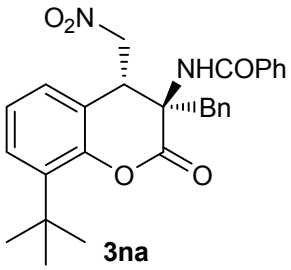
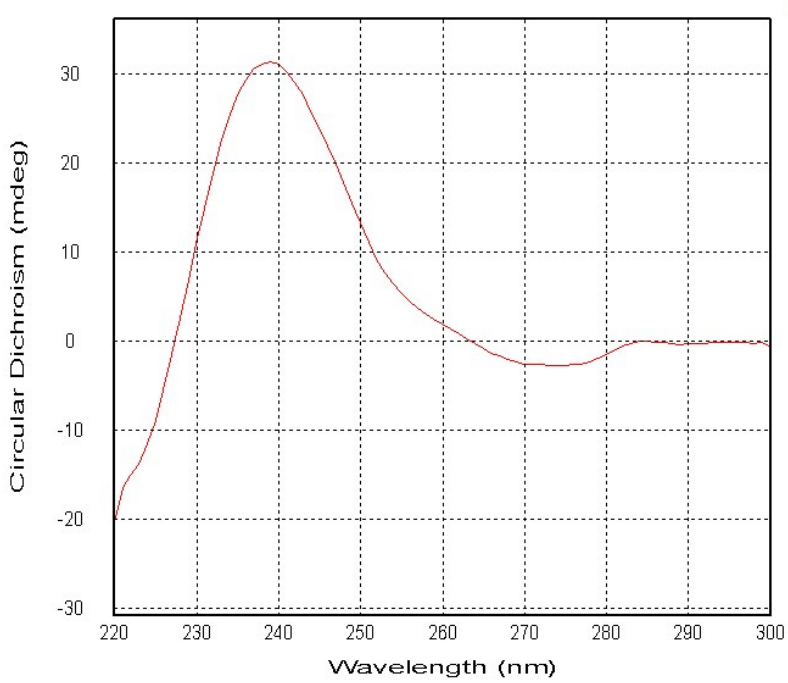
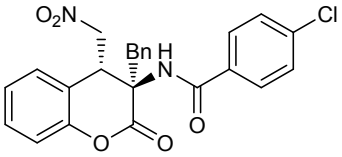
230
240
250
260
270
280
290
300
Wavelength (nm)

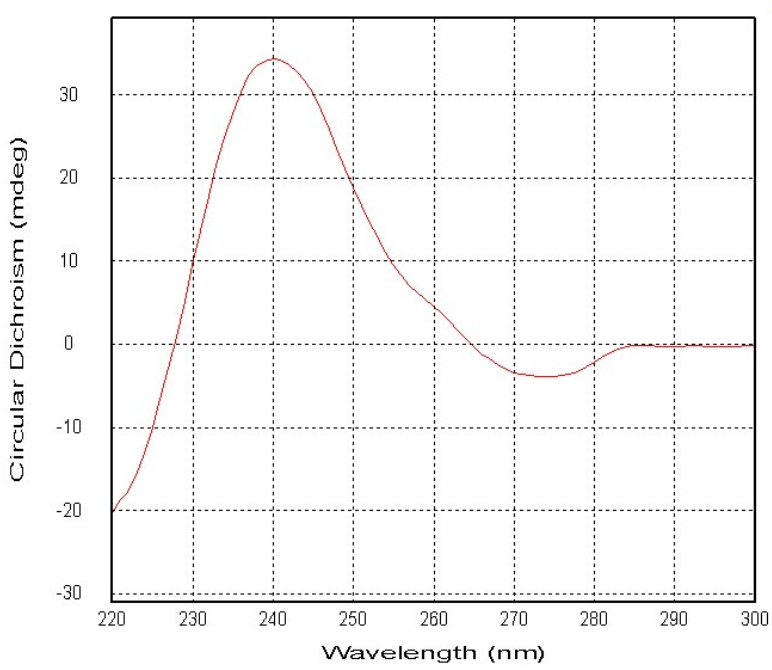

O2N
NHCOPh
Bn
O
O

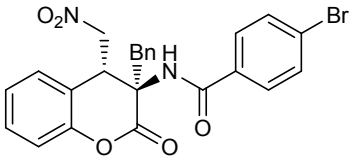
**3na**


Smooth (s):0
Circular Dichroism (mdeg)
30
20
10
0
-10
-20
-30
220
230
240
250
260
270
280
290
300
Wavelength (nm)

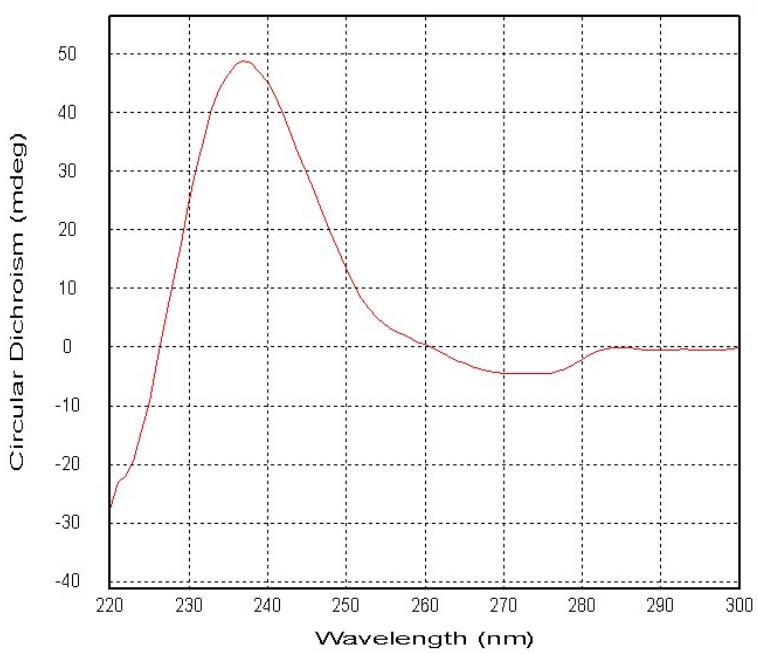

O2N
Bn
H
N
Cl
O
O
O

**3ab**


Smooth (s):0
Circular Dichroism (mdeg)
30
20
10
0
-10
-20
-30
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
Bn
H
N
Br
O
O
O

**3ac**


Smooth (s):0
Circular Dichroism (mdeg)
50
40
30
20
10
0
-10
-20
-30
-40
220
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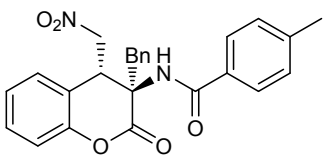
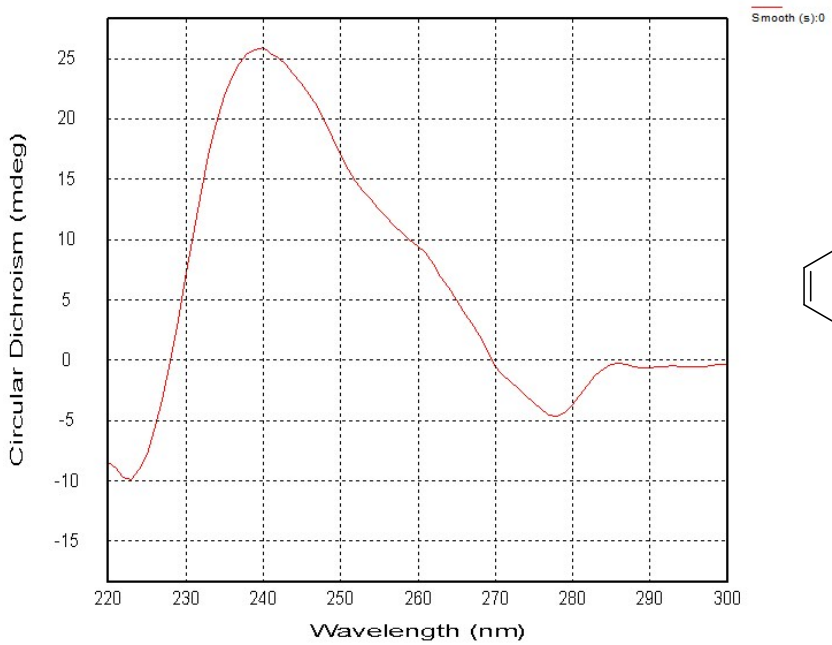
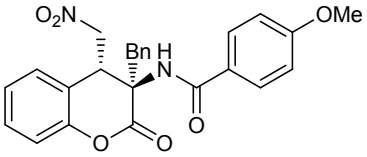
240
250
260
270
280
290
300
Wavelength (nm)

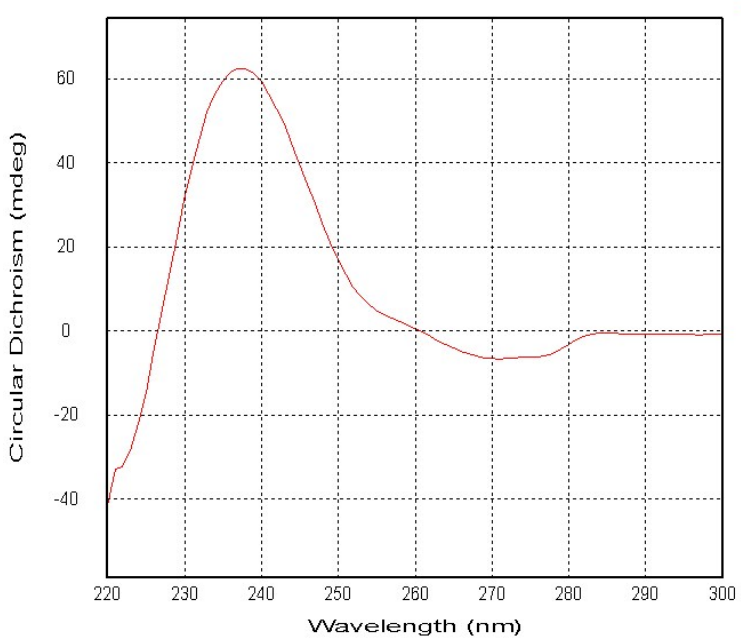

O2N
Bn H
N
O
O
O

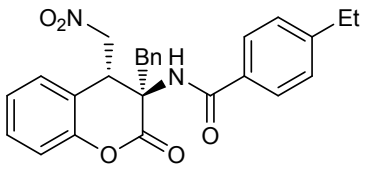
**3ad**


Smooth (s):0
Circular Dichroism (mdeg)
25
20
15
10
5
0
-5
-10
-15
220
230
240
250
260
270
280
290
300
Wavelength (nm)

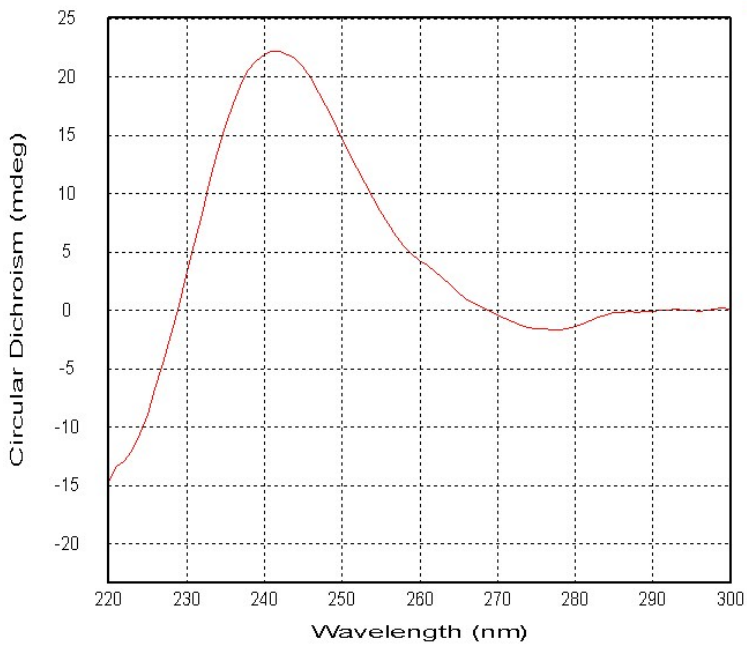

O2N
Bn H
N
OMe
O
O
O

**3ae**


Smooth (s):0
Circular Dichroism (mdeg)
60
40
20
0
-20
-40
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
Bn H
N
Et
O
O
O

**3af**


Smooth (s):0
Circular Dichroism (mdeg)
25
20
15
10
5
0
-5
-10
-15
-20
220
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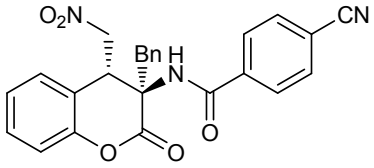
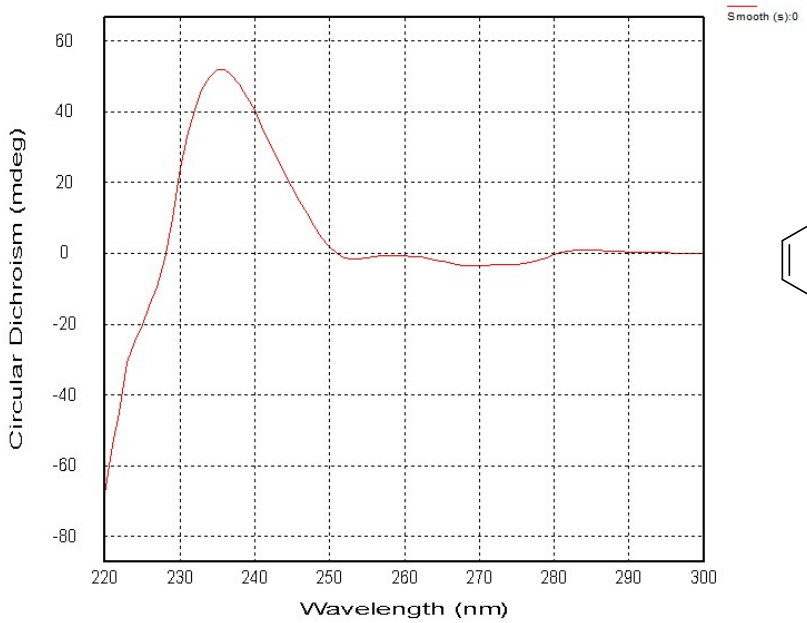
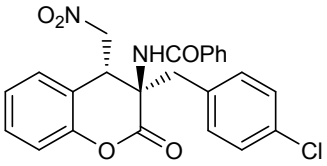
240
250
260
270
280
290
300
Wavelength (nm)

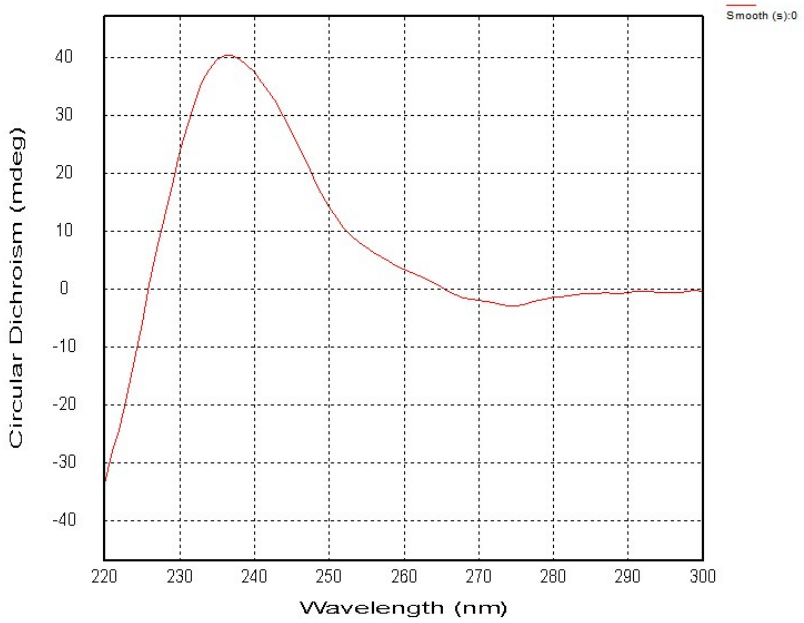

O2N
Bn H
N
CN
O
O
O

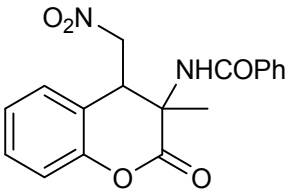
**3ag**


Smooth (s):0
Circular Dichroism (mdeg)
60
40
20
0
-20
-40
-60
-80
220
230
240
250
260
270
280
290
300
Wavelength (nm)

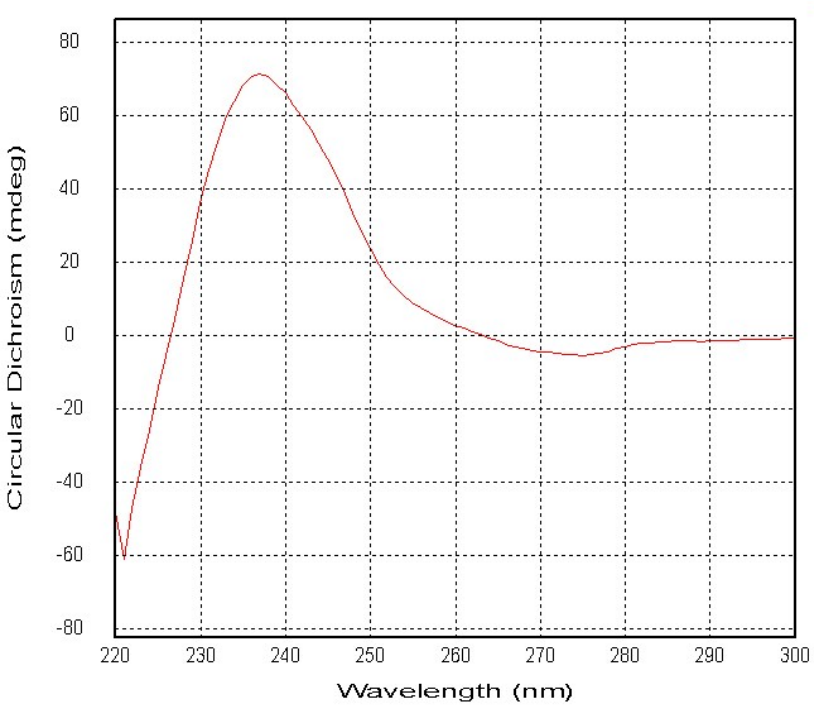

O2N
NHCOPh
O
O
Cl

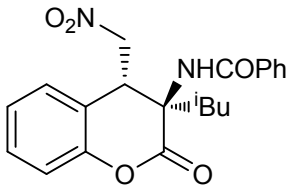
**3ah**


Smooth (s):0
Circular Dichroism (mdeg)
40
30
20
10
0
-10
-20
-30
-40
220
230
240
250
260
270
280
290
300
Wavelength (nm)

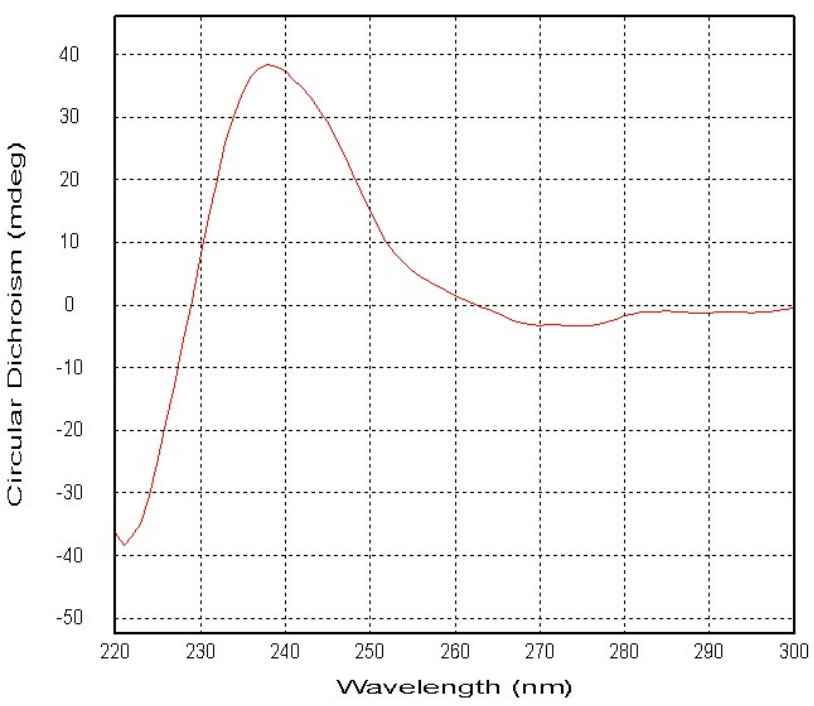

O2N
NHCOPh
O
O

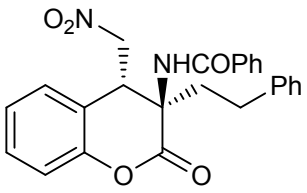
**3ai**


Smooth (s):0
Circular Dichroism (mdeg)
80
60
40
20
0
-20
-40
-60
-80
220
230
240
250
260
270
280
290
300
Wavelength (nm)

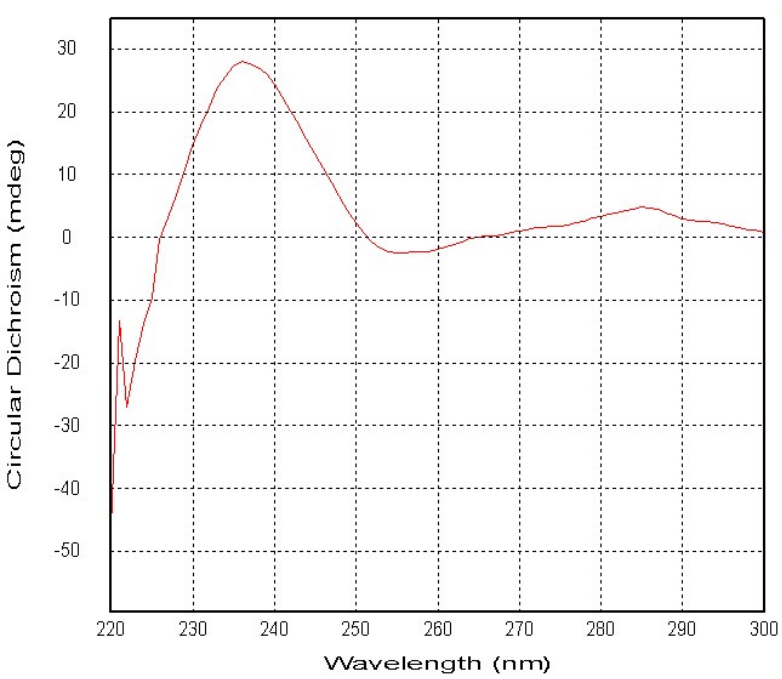

O2N
NHCOPh
iBu
O
O

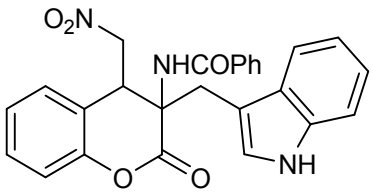
**3aj**


Smooth (s):0
Circular Dichroism (mdeg)
40
30
20
10
0
-10
-20
-30
-40
-50
220
230
240
250
260
270
280
290
300
Wavelength (nm)


O2N
NHCOPh
Ph
O
O

**3ak**




**3al**

## **10.** References

1. (a) Z. P. Yu, X. H. Liu, L. Zhou, L. L. Lin and X. M. Feng, *Angew. Chem. Int. Ed.*, 2009, **48**, 5195; (b) S. X. Dong, X. H. Liu, X. H. Chen, F. Mei, Y. L. Zhang, B. Gao, L. L. Lin and X. M. Feng, *J. Am. Chem. Soc.*, 2010, **132**, 10650; (c) S. X. Dong, X. H. Liu, Y. L. Zhang, L. L. Lin and X. M. Feng, *Org. Lett.*, 2011, **13**, 5060.