Supporting Information for

Original Article

Rational drug design, synthesis, and biological evaluation of novel chiral tetrahydronaphthalene-fused spirooxindole as MDM2-CDK4 dual inhibitor against glioblastoma

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1. The IC_{50} values of compounds 4a–4j against MDM2 and CDK4

Table S1 The IC_{50} values of compounds **4a**–**4j** against MDM2 and CDK4[a].

Compd.	IC_{50} (μmol/L)	
	MDM2	CDK4
4a	0.82±0.10	4.20±0.37
4b	0.57±0.08	1.10±0.09
4c	0.77±0.09	0.99±0.12
4d	0.52±0.07	0.78±0.11
4e	0.79±0.09	0.94±0.06
4f	1.40±0.13	2.90±0.33
4g	0.28±0.06	0.32±0.05
4h	0.85±0.11	1.10±0.14
4i	2.6±0.34	3.31±0.28
4j	0.98±0.07	0.91±0.08
Nutlin-3a	0.49±0.12	N.D.
Palbociclib	N.D.	0.007±0.002

[a]Each compound was tested in triplicate; data are mean ± SD (n = 3). N.D., not detected.

2. Selected isomers of compound 4g inhibited MDM2 and CDK4

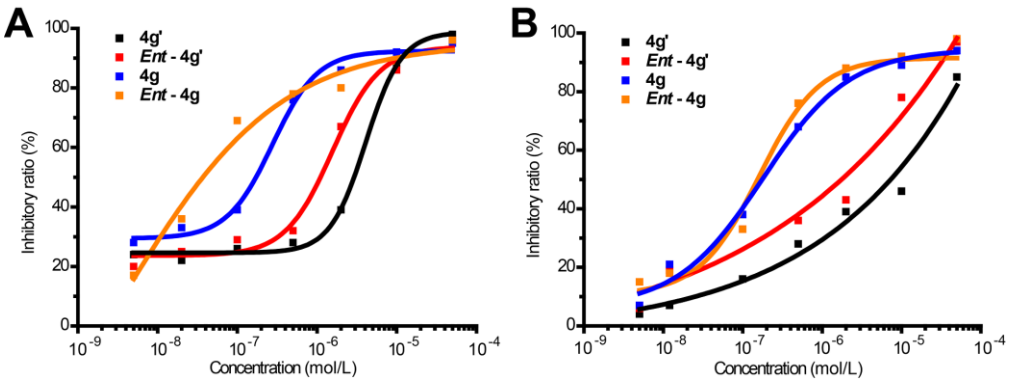


Figure S1 Selected isomers were serially diluted from 50 μmol/L to 5 nmol/L and tested against MDM2 (A) and CDK4 (B) in TR-FRET assays.

3. The kinase selectivity of *ent*-4g screened by KINOMEscan®

Table S2 The kinase selectivity of ***ent*-4g** screened by KINOMEscan.

Gene symbol	Ctrl. at 100 nmol/L (%)	Gene symbol	Ctrl. at 100 nmol/L (%)
ABL1(E255K)-phosphorylated	60	KIT(D816V)	84
ABL1(T315I)-phosphorylated	84	KIT(V559D, T670I)	95
ABL1-nonphosphorylated	74	LKB1	54
ABL1-phosphorylated	90	MAP3K2	25
ACVR1B	89	MAP3K4	97
ADCK3	100	MARK3	16
AKT1	76	MEK1	55
AKT2	51	MEK2	47
ALK	55	MET	57
AURKA	57	MKNK1	94
AURKB	83	MKNK2	100
AXL	53	MLK1	53
BMPR2	100	P38-alpha	95
BRAF	88	P38-beta	99
BRAF(V600E)	72	PAK1	81
BTK	74	PAK2	85
CDK2	4	PAK4	93
CDK3	41	PCTK1	89
CDK4-CyclinD1	0.8	PDGFRA	100
CDK4	2.2	PDGFRB	81
CDK7	58	PDPK1	48
CDK9	76	PIK3C2B	99
CSF1R	92	PIK3CA	100
CSNK1D	61	PIK3CG	58
CSNK1G2	91	PIM1	41
DCAMKL1	46	PIM2	52
DYRK1B	99	PIM3	46
EGFR	87	PKAC-alpha	100
EGFR(L858R)	98	PLK1	69
EPHA2	100	PLK3	55
ERBB2	47	PLK4	45
ERBB4	58	PRKCE	71
ERK1	46	RAF1	93
FAK	63	RET	40
FGFR2	51	RIOK2	97
FGFR3	75	ROCK2	24
FLT3	60	RSK2	84
GSK3B	44	SNARK	54
IGF1R	72	SRC	88
IKK-alpha	47	SRPK3	71

IKK-beta	100	TGFBR1	100
INSR	77	TIE2	98
JAK2	11	TRKA	68
JAK3	46	TSSK1B	82
JNK1	100	TYK2	72
JNK2	100	ULK1	59
JNK3	75	ULK2	100
KIT	57	VEGFR2	100
ZAP70	74	WEE1	78
		YANK3	67

4. Molecular docking and dynamics studies

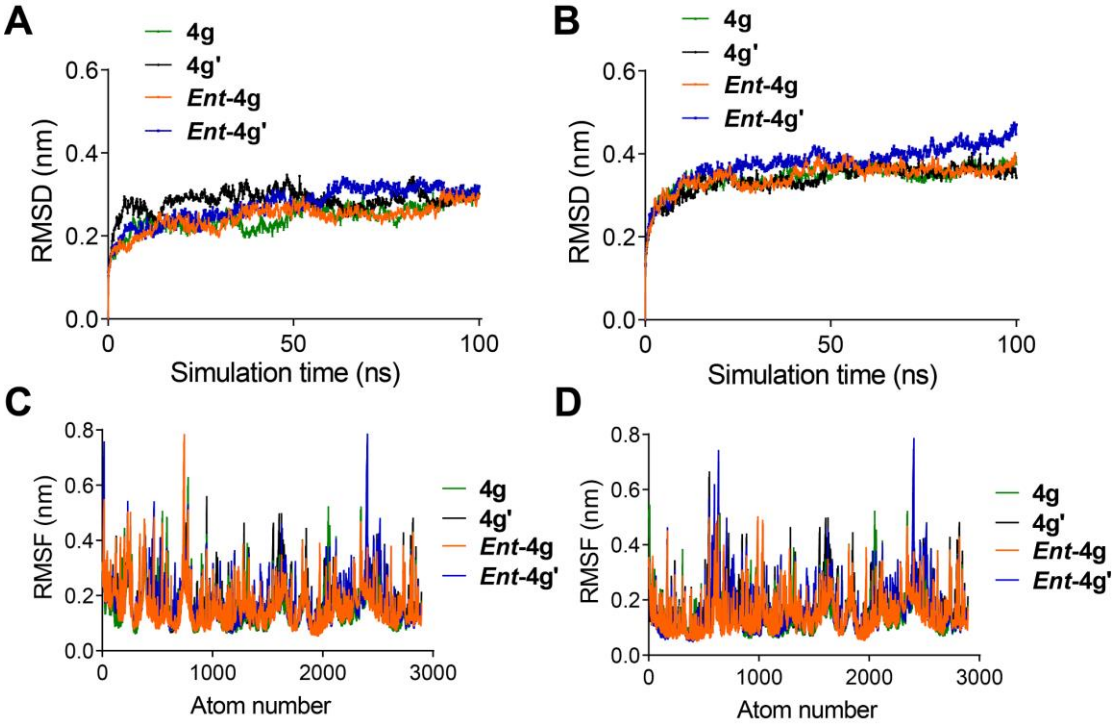


Figure S2 The root-mean-square deviations (RMSD) of the backbone atoms relative to their initial minimized complex structures as a function of time for **4g** (green), **4g′** (black), ***ent*-4g** (orange) and ***ent*-4g′** (blue) against MDM2 (A) and CDK4 (B), respectively; and the root-mean-square fluctuation (RMSF) of the backbone atom *versus* atom numbers for the MDM2-inhibitor complexes (C) and CDK4-inhibitor complexes (D).

Table S3 Binding free energies and individual energy terms of inhibitors in complex with MDM2 and CDK4 (kcal/mol).

Contribution	MDM2				CDK4			
	4g	**4g′**	***Ent*–4g**	***Ent*–4g′**	**4g**	**4g′**	***Ent*–4g**	***Ent*–4g′**
$\Delta E_{\text{int}}^{\text{ele}}$ (kcal/mol)	–37.38	–29.24	–35.17	–33.60	–36.88	–34.73	–34.12	–36.44
$\Delta E_{\text{int}}^{\text{vdw}}$ (kcal/mol)	–27.43	–25.84	–29.49	–32.01	–28.71	–30.84	–30.31	–33.98
$\Delta G_{\text{sol}}^{\text{nopole}}$ (kcal/mol)	–4.26	–6.13	–4.74	–5.03	–3.9	–5.67	–4.74	–4.20
$\Delta G_{\text{sol}}^{\text{ele}}$ (kcal/mol)	50.83	55.06	43.35	54.66	40.80	47.49	41.35	47.74
ΔG_{sol} (kcal/mol)	46.57	48.92	38.61	49.62	36.90	41.81	36.60	43.53
ΔG_{ele} (kcal/mol)	13.45	25.81	8.18	21.05	3.92	12.76	7.22	11.29
$-T\Delta S$ (kcal/mol)	–7.67	–8.70	–8.08	–8.22	–9.81	–8.34	–9.91	–9.01
ΔG_{bind} (kcal/mol)	–25.90	–14.86	–34.14	–24.21	–38.50	–32.10	–37.73	–35.91
IC_{50} (μmol/L)[a]	0.28	2.5	0.078	1.3	0.32	10.6	0.25	3.7

[a]Experimental mean IC_{50} values.

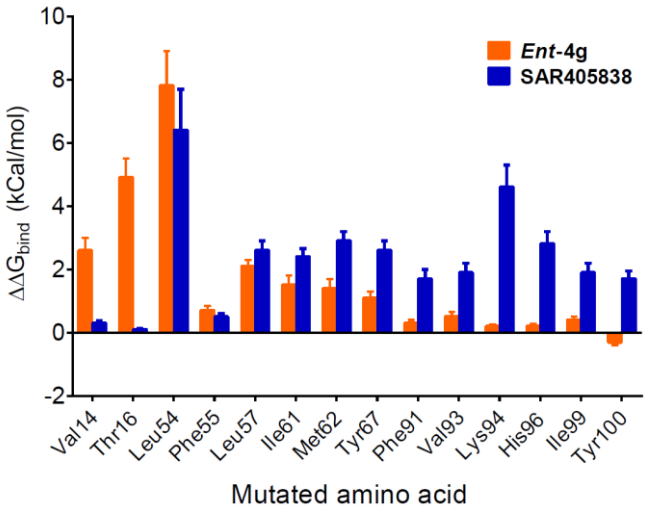


Figure S3 Effects of selected amino acid residues of the MDM2 binding pocket on the calculated free energies (kcal/mol) for the binding of ***ent*-4g** or SAR405838 to MDM2 in the MM/GBSA computational alanine scanning ($\Delta\Delta G_{\text{bind}} = \Delta G_{\text{mut}} - \Delta G_{\text{wt}}$).

5. Analyzing the changes in gene expression *via* Illumina Hiseq4000 platform

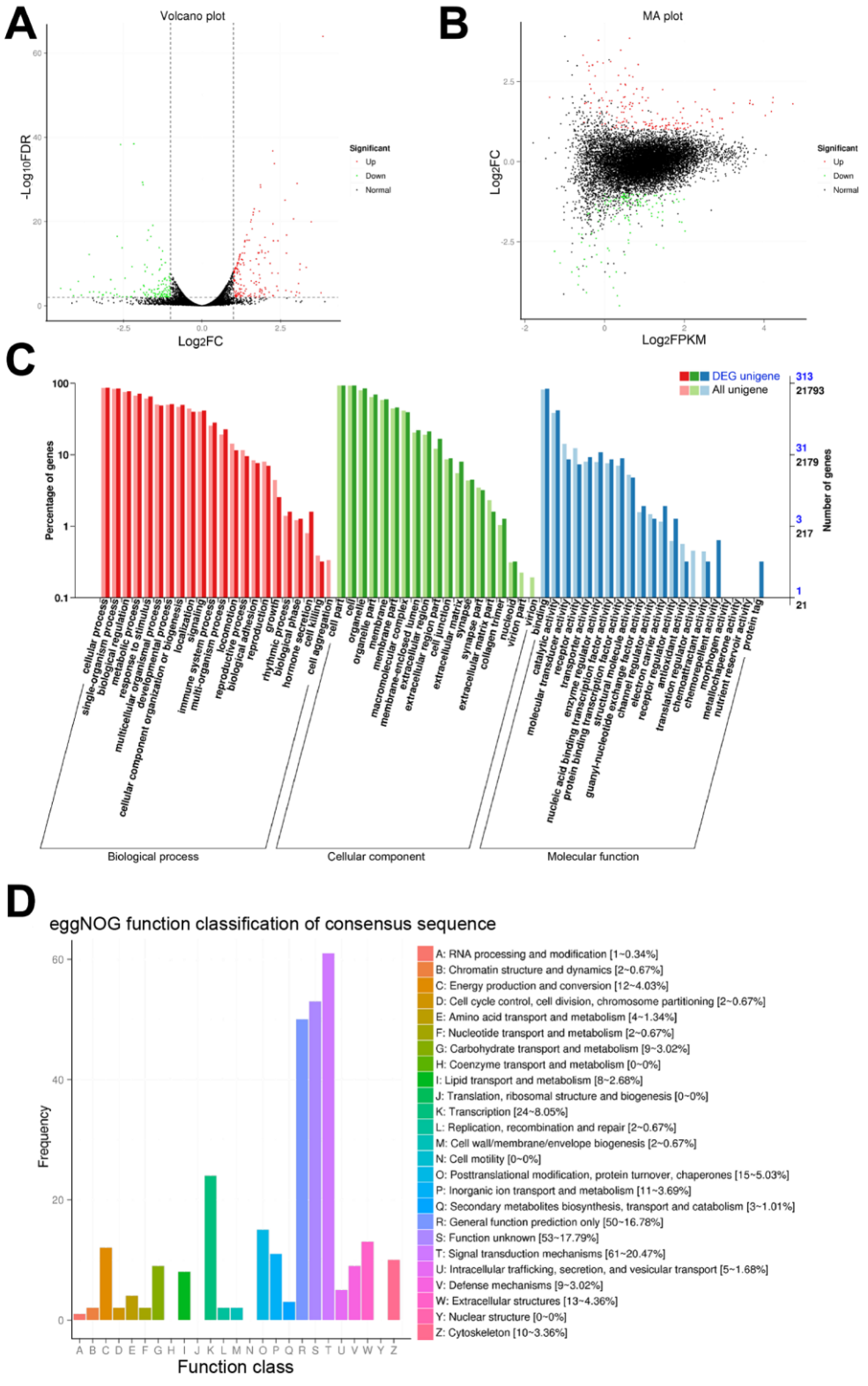


Figure S4 (A) The volcano plot of differential expressed mRNAs of ***ent*-4g** treated U251 cells. (B) The MA plot of differential expressed mRNAs of ***ent*-4g** treated U251 cells. (C) GO annotation and enriched GO terms of DEG in ***ent*-4g** treated U251 cells. (D) The eggNOG annotation of DEG in ***ent*-4g** treated U251 cells.

6. Compound *ent*-4g induced nuclei morphology change in glioblastoma cells

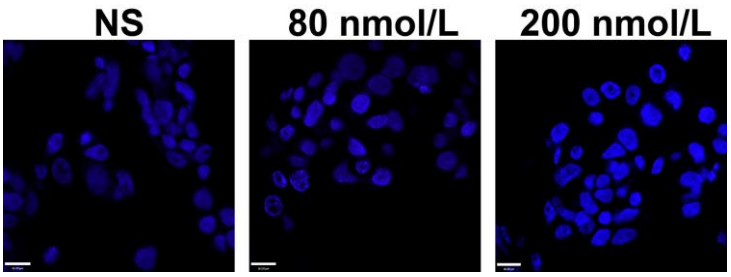


Figure S5 The nuclei morphology of U251 cells incubated with different concentration of ***ent*-4g** for 24 h.

7. The histopathological analysis of main organs in xenograft models

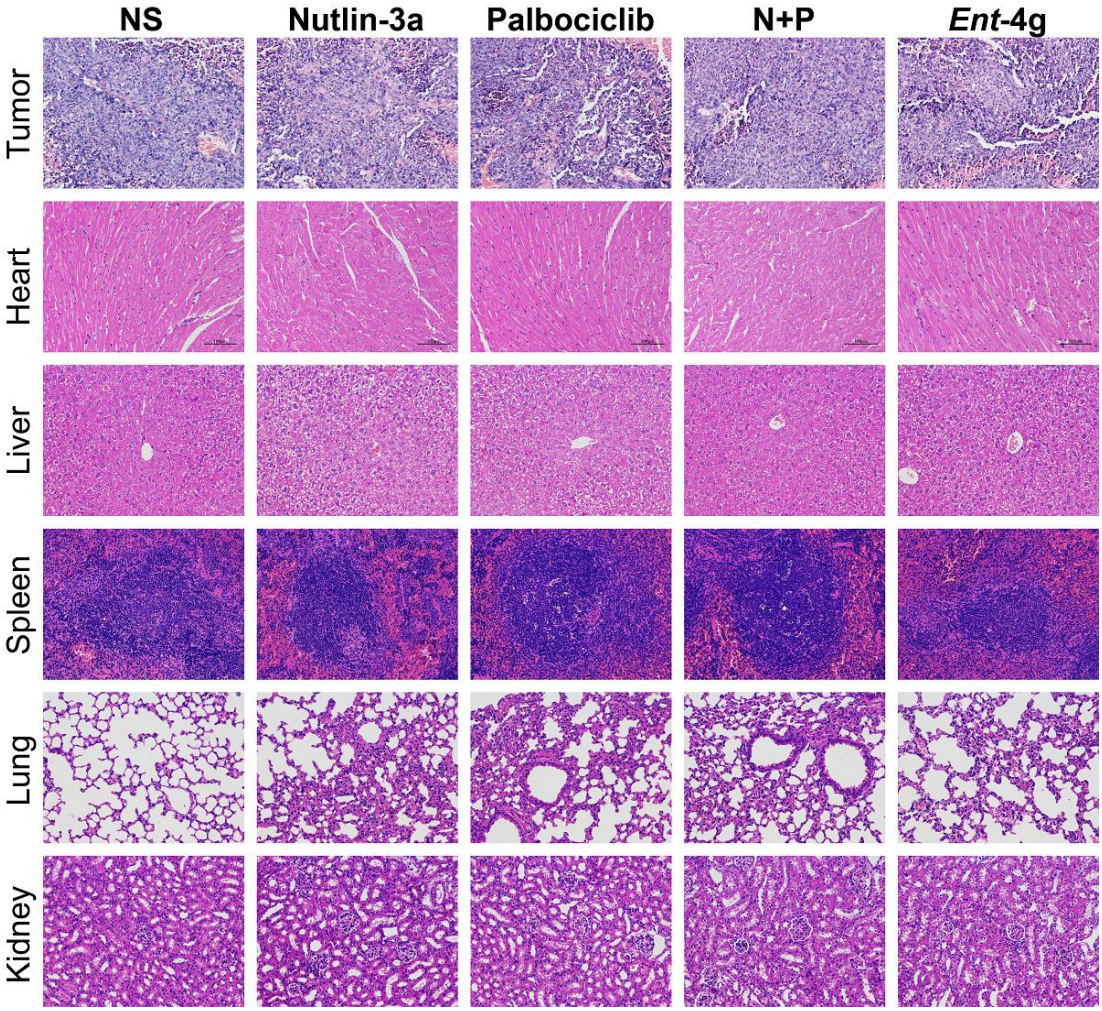


Figure S6 The representative H&E staining images of tumor and main organ tissues in each group of xenograft models.

8. The compound *ent*-4g concentrations in tumor tissues and plasma

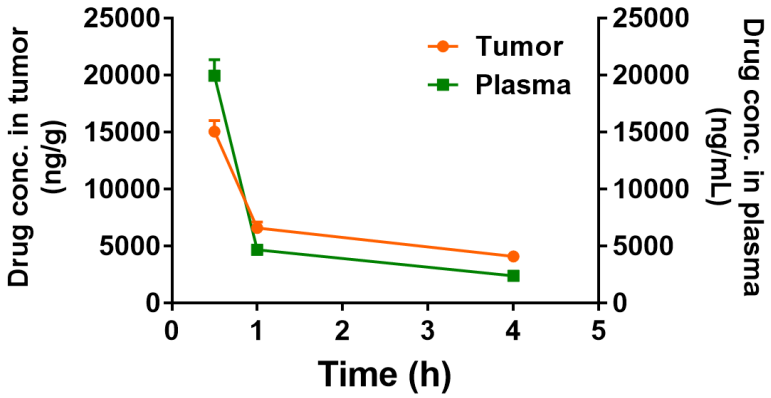


Figure S7 The drug concentrations in tumor tissues and plasma. The tumor and plasma concentrations of compound ***ent*-4g** in mice were measured after the last of four-days i.p. administration (30 mg/kg per day). Mice were sacrificed at 0.5, 1.0 and 4.0 h respectively after administration, then blood and tumor samples were collected.

9. Experimental details

9.1. Biochemical assays and KINOMEScan® experiment

The *in vitro* MDM2 and CDK4 assays were performed according to the previous reports and manufacturer's protocols. For the MDM2 assay, the HTRF assay used a GST-tagged MDM2 protein, and then, the biotinylated substrate peptide of P53 and two HTRF detection reagents were added. The HTRF signal was proportional to the amount of interaction between GST-tagged MDM2 protein and biotinylated P53 substrate peptide. For the CDK4 assays, kinase activity was measured using Lantha Screen technology from Invitrogen. In brief, GST-tagged truncated CDK4 kinase domain was incubated with fluorescein-labeled peptide substrate in the presence of a dose response of compound. Upon completion, the assay was stopped and detected with a terbium labeled anti-phosphorylated antibody. After an incubation of 1 h at room temperature, the plate was read on an Envision with an excitation wavelength of 340 nm and a reading emission at both 520 and 495 nm. The ratio of the 520 and 495 nm emission was used to analyze the data. The protein kinase selectivity of compound ***ent*-4g** (100 nmol/L) was detected in a high-throughput binding assay (KINOMEscan, DiscoveRx, Fremont, CA, USA) against a panel of 99 kinases. For the human kinase dendrogram, red circles indicated the main hits (< 5% of control), weak or no hits were labeled with small red circles (10%–35% of control) and smaller green circles (>

35% of control). TREEspot is a proprietary data visualization software developed by KINOMEscan that shows the protein kinase binding affinity.

9.2. Homology modeling and molecular dynamics simulation

The Accelrys Discovery Studio (DS3.5, Accelrys, San Diego, CA, USA) is utilized for the homology modeling of CDK4 binds to allosteric inhibitors. The brief procedures are listed as follows: in brief, the protein sequence of CDK4 kinase domain (Arg10 to Leu300) is retrieved from the UniProt database (UniProt entry P11802). The PSI-BLAST search module in Discovery Studio is used for the template search, and CDK2 (PDB No. 3PXZ) showed good identity to CDK4 kinase domain (56% of identity), then it is chosen as template for homology modeling. Then the initial model is optimized by the standard molecular dynamics protocol in AMBER12 package. The MDM2 in complex with SAR405838 (PDB No. 5 TRF) was utilized to perform MD simulation between inhibitors and MDM2 protein. The inhibitors **4g**, **4g′**, ***ent*-4g** and ***ent*-4g′** were constructed by using the DS3.5 molecular modeling software based on the X-ray crystallized confirmation. All compounds were energy minimized with the MMFF94 force field. The missing hydrogen atoms of the inhibitors were added while the missing atoms of CDK4 and MDM2 proteins were added using the tleap program in AMBER 12.0. The inhibitors were minimized using the Hartree-Fock (HF)/6-31G* optimization in Gaussian09, and the atom partial charges were obtained by fitting the electrostatic potentials derived by Gaussian *via* the RESP fitting technique in AMBER 12.0. The generations of the partial charges and the force field parameters for the inhibitors were accomplished by the antechamber program in AMBER 12.0. In the following molecular mechanics (MM) minimizations and MD simulations, the AMBER99 force field and the general AMBER force field (gaff) were used to establish the potential of proteins and inhibitors, respectively. An appropriate number of chloride counter ions were placed around four CDK4–inhibitor complexes (or MDM2-inhibitor complexes) to neutralize the charges of the systems. Finally, the whole system was solvated in a cubic periodic box of TIP3P water molecules, and the distance between the edges of the water box and the closest atom of the solutes was at least 10 Å. To avoid edge effects, periodic boundary conditions were applied during the whole molecular dynamics (MD) simulation.

For each system, energy minimization and MD simulation were performed by using the Sander module of the Amber12. Prior to MD simulations, the entire system was subject to energy minimization in two stages to remove bad contacts between the complex and the solvent molecules. Firstly, the water molecules and counterions were minimized by freezing the solute using a harmonic constraint of a strength of 100 kcal/mol Å. Secondly, the entire system was minimized without restriction. Each stage was consisted of a 5000-step steepest descent and a 5000-step conjugate gradient minimization. In MD simulations, Particle Mesh Ewald (PME) was employed to deal with the long-range electrostatic interactions. The cutoff distances for the long-range electrostatic and van der Waals energy interaction were set to 10 Å. The systems were gradually heated in the NVT ensemble from 0 to 300 K over 1000 ps. Finally, 100ns MD simulations were carried out for each system in an isothermal isobaric ensemble (NPT) with periodic boundary conditions. The SHAKE method, with a tolerance of 10^{-5} Å, was applied to constrain all covalent bonds involving hydrogen atoms. Each simulation was coupled to a 300 K thermal bath at 1.0 atm (1 atm = 101.3 kPa) by applying the Langevin algorithm. The temperature and pressure coupling parameters were set as 1.0 ps. During the sampling process, the coordinates were saved every 1.0 ps and the conformations generated from the simulations were used for further binding free energy calculations and decomposition analysis.

Based on the previous MD simulation studies, we extracted a total number of 300 snapshots from the last 30 ns trajectory with an interval of 100 ps for binding free energy calculations. The MM/GBSA method and Nmod module included in the Amber 12 were applied to compute the binding free energies of four inhibitors to CDK4 or MDM2 according to the following Eq. (1):

$$\Delta G_{\mathrm{b}} = \Delta E_{\mathrm{MM}} + \Delta G_{\mathrm{sol}} - T\Delta S \quad (1)$$

Where ΔE_{MM} is the difference in molecular mechanics energy between the complex and each binding partner in the gas phase, ΔG_{sol} is the solvation free energy contribution to binding and $T\Delta S$ is the contribution of entropy changes to the binding free energy. ΔE_{MM} is further divided into two parts:

$$\Delta E_{\mathrm{MM}} = \Delta E_{\mathrm{int}}^{\mathrm{ele}} + \Delta E_{\mathrm{int}}^{\mathrm{vdw}} \quad (2)$$

Where $\Delta E_{\mathrm{int}}^{\mathrm{ele}}$ and $\Delta E_{\mathrm{int}}^{\mathrm{vdw}}$ are described as the electrostatic interaction and van der Waals energy in the gas phase, respectively. The solvation free energy is expressed as Eq. (3):

$$\Delta G_{\mathrm{sol}} = \Delta G_{\mathrm{sol}}^{\mathrm{ele}} + \Delta G_{\mathrm{sol}}^{\mathrm{nopol}} \quad (3)$$

The electrostatic contribution to the solvation free energy ($\Delta G_{\mathrm{sol}}^{\mathrm{ele}}$) was calculated using the generalized Born (GB) model of Onufriev et al[1]. The hydrophobic contribution to the solvation free energy ($\Delta G_{\mathrm{sol}}^{\mathrm{nopol}}$) was determined with a function of the solvEnt-accessible surface area:

$$\Delta G_{\mathrm{sol}}^{\mathrm{nopol}} = \gamma \mathrm{SASA} + \beta \quad (4)$$

In which SASA is the solvEnt-accessible surface area and was calculated with the MSMS program. In our calculations, the values for γ and β were set to 0.0072 and 0 kcal/mol, respectively. The normal-mode analysis was performed to estimate the change of the conformational entropy upon the ligand binding ($-T\Delta S$) *via* the nmode program in AMBER 12.0. The protein–ligand binding free energy was calculated based on 300 snapshots taken from 70 to 100 ns MD simulation trajectories of the complex. Considering the high computational demand, only 100 snapshots for each complex were used to estimate the binding entropy.

9.3. Computational alanine scanning

To study the detailed mechanisms of the inhibitor–residue interaction at the energetic and atomic levels, computational alanine scanning was carried out on MDM2, and the binding free energies of compound ***ent*-4g** and SAR405838 to the protein mutants were calculated by using the MM/GBSA method. For alanine-scanning, snapshots were generated every 100 ps from 50 to 100 ns in the wild type trajectory. Mutations to alanine were performed only on selected residues in the active site. Alanine mutations were generated by truncation of residues after the Cβ and adding a hydrogen atom in the same direction as the Cγ. Partial charges for the mutated residue were then changed to those of alanine. None of the residues mutated in this study were glycines. The binding free energy difference between the mutant and wild-type complexes is defined as:

$$\Delta\Delta G_{\mathrm{bind}} = \Delta G_{\mathrm{mut}} - \Delta G_{\mathrm{wt}} \quad (5)$$

The polar contribution (ΔG_{GB}) of ΔG_{sol}^{ele} was computed using the generalized Born model, and the parameters for GB calculations were developed by Onufriev et al. The charges used in GB calculations were taken from the AMBER parameter set. All energy components in Eq. (1) were calculated using 500 snapshots taken from 50 to 100 ns of MD trajectory with the time interval of 100 ps were used. The key residues of MDM2: Val14, Thr16, Leu54, Phe55, Leu57, Ile61, Met63, Tyr67, Phe91, Val93, Lys94, His96, Ile99 and Tyr100 were chosen for mutating.

9.4. Cell proliferation and apoptosis assays

The glioblastoma cell lines U87MG, U251 and T98G were obtained from the ATCC (American Type Culture Collection) and cultured in the state key laboratory of biotherapy, west china hospital, Sichuan University. All cells were cultured in DMEM supplemented with 10% fetal bovine serum and maintained at 37 °C with 5% CO_2 in atmosphere. The cell proliferation assay was measured by using the MTT method. Cells treated with DMSO were set as negative control. In brief, about 5×10^3 cells were incubated with test compounds in 96-well plate for 24–48 h, then 10 μL MTT (5 mg/mL) was added and incubated for an additional 4 h, added the extraction buffer and incubated overnight, the absorbance values were measured at 570 nm on a microplate reader (Thermo Scientific Multiskan, Finland). The annexin V-propidium iodide (PI) dual-staining method was used as apoptosis assay. U251 cells with or without compounds incubated were harvested and washed twice with cold PBS. The early and late apoptosis cells were identified on a flowcytometry instrument (BD Biosciences, San Jose, CA, USA) by staining with FITC-conjugated annexin V-PI kit according to the manufacturer's instructions (Keygen, Nanjing, China). In addition, U251 cells were plated in six-well plates, the cells were grown and adhered for 24 h, then incubated with 80 or 200 nmol/L of ***ent*-4g** for an additional 12 h followed by Hoechst 33258 addition. The morphology of nuclei was visualized under an Olympus fluorescence microscope.

The Western blot (WB) analysis were performed according to our previously reports. In brief, the equivalent concentrations of total proteins in cell lysate were separated by SDS-PAGE and then transferred to PVDF (poly-vinylidene difluoride membrane, Millipore, MA, USA). After blocked by 0.5%–1% of BSA under 4 °C overnight, the PVDF membranes were incubated by corresponding primary antibodies

at 4 °C overnight or room temperature for two hours. The PVDF membranes were washed twice by TBST solution and then incubated with HRP-conjugated second antibodies. The immunoblotting slides were collected by using ECL (enhanced chemiluminescence) method according to the manufacturer's instruction.

9.5. RNA sequencing, data collection and bioinformatics analysis

Total RNA from U251 cells with or without ***ent*-4g** incubation were extracted using the Trizol reagent according to the manufacturer's protocol. RNA concentrations were quantified using a Nano-drop Spectrophotometer (Thermo Scientific Technologies) at a wavelength of 260 nm. RNA samples were analyzed by Bioanalyzer at a concentration of 100–200 ng/μL to verify the concentration and the purity of samples. Only the samples with RNA integrity values of >7.0 were used for mRNA sequencing at the Genomic Core Facility at Novogene Co., Ltd. (Beijing, China). The RNA-seq data were analyzed by following the procedure described below. Briefly, after sequence quality filtering at a cutoff of a minimum quality score Q20 in at least 90% bases, the good-quality reads aligned to Reads were processed and aligned to the University of California Santa Cruz (UCSC) human reference genome and transcriptome (build hg38) using the Burrows-Wheeler Aligner (BWA). The reads that are uniquely aligned to the exon and splicing junction sites for each transcript were combined to calculate an expression level for a corresponding transcript and further normalized based on reads per kilobase per million reads in order to compare transcription levels among samples. The transcripts with a low raw read count < 100 in all the samples were excluded for downstream analysis. Gene expression value was transformed to the log 2 base scale.

9.6. Xenograft models and immunohistochemical analysis

The *in vivo* antitumor activity and preliminary safety of ***ent*-4g** were carried out according to the Guidelines for the Care and Use of Laboratory Animals that were approved by the by the Committee of Ethics of Animal Experimentation of Sichuan University, China. The six to eight weeks old SPF (specific pathogen-free) nude mice were purchased from Beijing Huafukang Biotechnology Co., Ltd, and were randomly grouped by weighed and coded (n = 8). After five to eight days adaptation, the mice were grafted s.c. into the dorsal flank with 0.1 mL of phosphate buffer containing 2×10^6 U251 cells. When the tumors grew to a size of approximate leg diameter of 6

mm, the mice were initially treated and orally administered with ***ent*-4g**, nulin-3a, palbociclib, N+P or saline on days 1–21, and were monitored on a daily basis during treatment (tumor volume and body weights). On the last day, the animals were sacrificed; tumors and main organs were isolated and weighed. The tumor and various organs tissues were sectioned, then fixed in 4% paraformaldehyde in PBS for immunohistochemistry analysis and stained with H&E, TUNEL, Ki67, MDM2, P53, P21, phos-CDK4 and phos-RB antibodies as the previous studies stated.

9.7. Determination of drug concentrations in plasma and tumor, and the ADMET properties

When the volume of xenograft tumors beyond 100 mm^3, the BALB/c nude mice were randomly divided to treatment and control groups. The treatment groups received specified concentrations of compounds by intraperitoneal administration, and the control group received i.p. administration of equal volume of PBS (5% DMSO). After four-day treatment of compound ***ent*-4g**, mice were sacrificed at 0.5, 1.0 and 4.0 h respectively after administration and dissected to collect the blood and weigh the tumor tissues at the specific time points. Plasma was separated from the blood by centrifugation and stored in a freezer at –80 °C. The tumor tissues were homogenized with normal saline (5:1 *v*/*w*) before ultrasound treatment. The protein components in plasma and tumor samples were removed by methanol containing an internal standard. After centrifugation, the supernatants were diluted with methanol and acetonitrile and then centrifugation again. The compound concentrations in the supernatants were analyzed by a Waters UPLC–MS instrument.

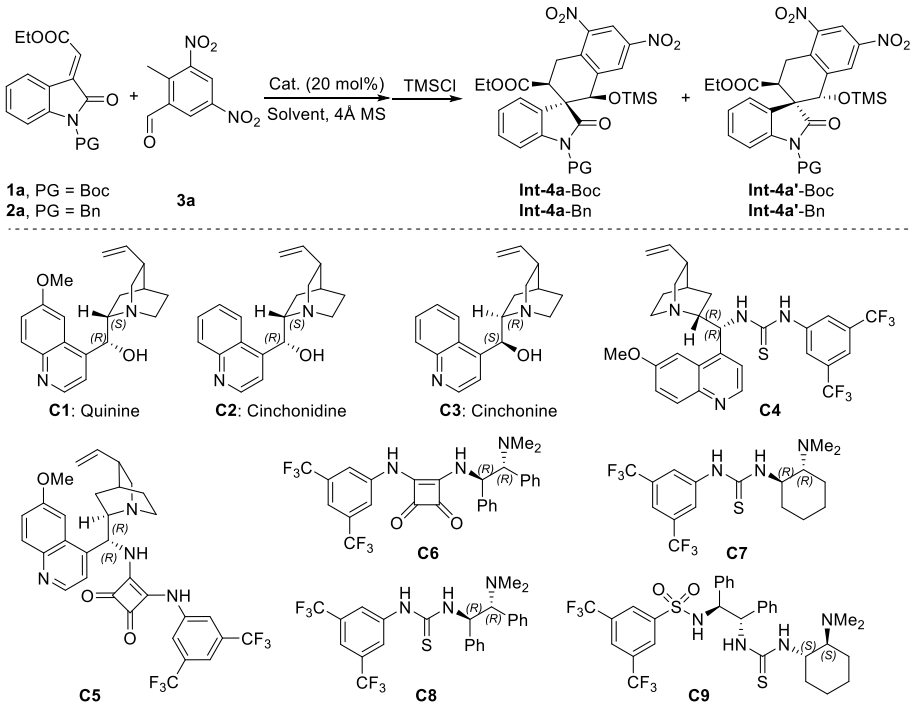
Pharmacokinetic properties of compound ***ent*-4g** were assessed in Sprague–Dawley rats (350–400 g). The compound was prepared as a solution in 10:10:80 dimethyl sulfoxide/Tween 80/water (*v*/*v*/*v*) at a concentration of 1 mg/mL for i.v. and *p.o.* administration of 7.5 and 15 mg/kg, respectively. All procedures and handling were according to standard operating procedures approved by the Institutional Animal Care and Use Committee (IACUC). Compound concentrations were determined using peripheral whole blood. At selected time points (5 min for i.v. only, 0.25, 0.5, 1, 2, 4, 8, and 24 h post-dose), blood was collected from jugular vein cannulas for pooled plasma analysis.

For the liver microsomes stability assay, compounds were prepared as 5 mmol/L stock solutions in DMSO then diluted to 500 μmol/Lwith acetonitrile. Microsomes

were separated from mice liver and then diluted with warm KPhos buffer to prepare a 5% microsomal mixture. The compound stock solution was then added to each well and turbidity was assessed after each addition. The microsomal preparation was then added to each well and shaken gently and warmed at 37 °C. Sample aliquots were taken out of the mixtures at T = 0, 10, 20, 30, 60, and 90 min and quenched immediately with acetonitrile containing bioanalytical internal standards and maintained at 5 °C. The samples were centrifuged for 5 min at 5 °C and then the supernatant was assessed by the UPLC/MS described in the MDCK procedure. The percent remaining was calculated relative to T = 0 using peak area ratios.

10. Asymmetric synthesis of THN-fused spirooxindole derivatives 4 and 4′

10.1. Optimization of reaction conditions (Table S4)[a]



PG	Cat.	Solvent	Product	Yield (%)[b]	dr[c]	ee[d] (%)
Boc	**C1**	CH_2Cl_2	**int-4a**	47	65:35	24
Boc	**C2**	CH_2Cl_2	**int-4a**	54	73:27	8
Boc	**C3**	CH_2Cl_2	**int-4a**	52	75:25	7
Boc	**C4**	CH_2Cl_2	**int-4a**	65	71:29	72
Boc	**C5**	CH_2Cl_2	**int-4a**	59	78:22	78
Boc	**C6**	CH_2Cl_2	**int-4a**	66	55:45	82
Boc	**C7**	CH_2Cl_2	**int-4a**	73	80:20	96
Boc	**C8**	CH_2Cl_2	**int-4a**	63	70:30	92
Boc	**C9**	CH_2Cl_2	**int-4a**	45	81:19	95
Boc	**C7**	Toluene	**int-4a**	47	60:40	92
Boc	**C7**	THF	**int-4a**	49	55:45	65
Boc	**C7**	MeCN	**int-4a**	84	50:50	71
Boc	**C7**	CH_2Cl_2	**int-4a**[e]	80	88:12	99
Boc	**C7**	CH_2Cl_2	**int-4a**[f]	65	90:10	99
Bn	**C7**	CH_2Cl_2	**int-4a′**[g]	51	91:9	89

We commenced our research by screening the reaction between Boc-protected 3-ylideneoxindole **1a** and nitro-substituted 2-methyl-3,5-dinitrobenzaldehyde (**3a**, Table S4), promoted by a range of bifunctional hydrogen-bonding catalysts or chiral tertiary amine catalysts (**C1**−**C9**). We planned to convert the intermediate product to its analogue **int-4a** and isomer **int-4a′** in order to protect the hydroxyl group and thereby ensure solubility in $CDCl_3$ for clear NMR spectra.

First, we investigated a series of cinchona alkaloid-based thiourea or squaramide catalysts (**C1**−**C6**), providing **int-4a** as the major diastereoisomer with dr values of 55:45 to 78:22 and moderate ee values (Table S4, entries 1−6). We also evaluated several chiral amine catalysts (**C7**−**C9**), which did not increase stereoselectivity (Table S4, entries 8 and 9).

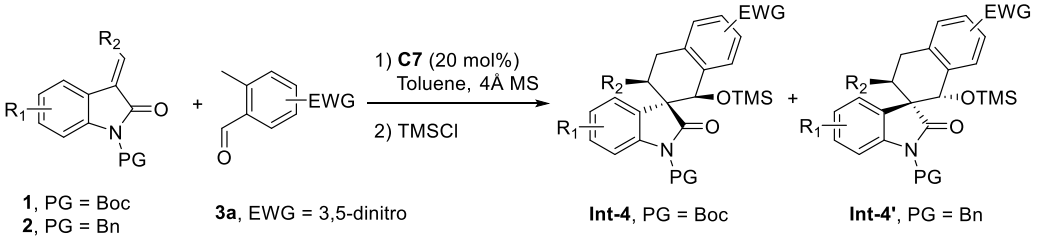
To our satisfaction, using Takemoto's bifunctional chiral thiourea catalyst **C7** gave high diastereo- and enantioselectivities (Table S4, entry 7). Then we explored more reaction parameters in order to improve yield (Table S4, entries 10−14). The optimal conditions were found to be reaction in anhydrous CH_2Cl_2 at −10 °C for 48 h (entry 13). Applying these optimized conditions to the Bn-protected substrate **2a** led to inverted diastereoselectivity, generating **int-4a′** as the major product in 51% yield with 91:9 dr and 89% ee (entry 15).

Hence, the optimal reaction conditions were established: (i) for the Boc-protected substrates **1**, 20 mol% of C7 and 4 Å MS in CH_2Cl_2 at −10 °C for 48 h under N_2; (ii) for the Bn-protected substrates **2**, 20 (mol/mol %) of **C7** and 4 Å MS in CH_2Cl_2 at −10 °C for 7 days under N_2.

10.2. General information for synthesis

Nuclear Magnetic Resonance (NMR) data were obtained for ^1H at 400 MHz and for ^{13}C at 100 MHz or for ^1H at 600 MHz and for ^{13}C at 150 MHz. Chemical shifts were reported in parts per million (ppm) with tetramethylsilane resonance as the internal standard in $CDCl_3$ or DMSO-d_6 solution. Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant (s, Hz), integration]. ESI high resolution mass spectra (HRMS) were recorded using electrospray ionization on a Waters SYNAPT G2 (Q-TOF) instrument. The enantiomeric ratio was determined by High Performance Liquid Chromatography (HPLC) analysis on chiral column in comparison with authentic racemates, using the Daicel Chiralpak AD/OD/IE (250 mm × 4.6 mm). UV detection was monitored at 254 nm. Purity of compounds **4** and **4′** was determined by reverse-phase HPLC analysis to be >95% at 254 nm. HPLC instrument: Dionex Summit HPLC (column: Thermo Scientific Technologies, Hypersil GOLD™, 5 μm, 250 mm × 4.6 mm), detector: PDA-100 photodiode array, injector: ASI-100 auto sample injector, pump: p-680A LPG-4. A flow rate of 1.0 mL/min was used with mobile phase of MeOH in H_2O. Optical rotation data were examined in CH_2Cl_2 solution at 25 °C and λ = 589 nm. Column chromatography was performed on a silica gel (200−300 mesh) using an eluent of ethyl acetate and petroleum ether. TLC was performed on glass backed silica plates; products were visualized using UV light. Melting points were determined on a Mel-Temp apparatus.

*10.3. General procedure for the asymmetric synthesis of **int-4** and **int-4′** (Scheme S1)*



Scheme S1 General procedure for the asymmetric synthesis of **int-4** and **int-4′**.

The reaction was carried out with 3-ylideneoxidole **1** or **2** (0.3 mmol), 2-methylbenzaldehyde (**3**, 0.36 mmol) and **C7** (49.6 mg, 0.06 mmol) with 4Å MS in anhydrous CH_2Cl_2 (4.0 mL) at −10 °C for 48 h or 7 days under N_2. The reaction mixture was direct purified by flash chromatography on a silica gel to afford the unprotected intermediate.

Next, the protection hydroxyl group of the intermediate gave the corresponding easily separable THN-fused spirooxindole derivative **int-4** or **int-4′**. To a solution of intermediate in CH_2Cl_2 (4 mL) was added TMSCl (25.9 μL, 0.3 mmol) and imidazole (45.8 mg, 0.6 mmol). The mixture was stirred at 0 °C until the reaction was completed based on TLC. The reaction was quenched with aqueous $NaHCO_3$ (aq) and CH_2Cl_2. The organic layer was dried by Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel to give the major isomer product **int-4** or **int-4′** which were dried under vacuum and further analyzed by ^{1}H-NMR, ^{13}C-NMR, HPLC and HRMS.

*10.3.1. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4a**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1a**, 95.2 mg, 0.3 mmol), 2-methyl-3,5-dinitrobenzaldehydes (**3a**, 75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4a** as a white solid in 80% yield (144.5 mg, 0.26 mmol) for two steps after flash chromatography. The dr was calculated to be 88:12 by crude ^{1}H-NMR analysis and the ee was determined to be 99% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 7.75 min, t_{major} = 10.31 min, $[\alpha]_D^{25}$ = +62.64 (*c* 1.00 in CH_2Cl_2), m.p. 158−160 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.51 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 5.01 (s, 1H), 3.93 (dd, *J* = 12.8 Hz, 1H), 3.76−3.63 (m, 2H), 3.24 (q, *J* = 12.4 Hz, 2H), 1.64 (s, 9H), 0.73 (t, *J* = 7.2 Hz, 3H), −0.16 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 174.8, 170.3, 149.1, 148.4, 146.8, 143.6, 141.6, 137.6, 129.9, 128.8, 124.8, 124.0, 123.1, 119.0, 115.5, 85.0, 75.8, 61.4, 55.9, 47.2, 28.3, 25.7, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{33}N_3O_{10}SiNa$ $[M + Na]^+$: 622.1833, Found: 622.1832.

*10.3.2. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-5-fluoro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4b**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-5-fluoro-2-oxoindoline-1-carboxylate (**1b**, 100.6 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4b** as a white solid in 79% yield (145.8 mg, 0.24 mmol) for two steps after flash chromatography. The dr was calculated to be 84:16 by crude ^{1}H-NMR analysis and the ee was determined to be 99% by HPLC on Chiralpak IE column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 7.11 min, t_{minor} = 8.08 min, $[\alpha]_D^{25}$ = −14.55 (*c* 1.00 in CH_2Cl_2), m.p. 140–142 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.82 (s, 1H), 8.28 (s, 1H), 7.88 (dd, *J* = 9.2, 4.8 Hz, 1H), 7.07 (td, *J* = 8.8, 2.8 Hz, 1H), 6.78 (dd, *J* = 8.0, 2.8 Hz, 1H), 4.83 (s, 1H), 4.03−3.97 (m, 2H), 3.79 (dd, *J* = 17.2, 5.6 Hz, 1H), 3.72−3.60 (m, 2H), 1.60 (s, 9H), 1.06 (t, *J* = 7.2 Hz, 3H), 0.03 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 172.8, 170.1, 158.9 (d, J_{CF} = 242.1 Hz), 148.3, 148.0, 145.3, 140.5, 137.6, 135.5 (d, J_{CF} = 2.5 Hz), 129.1 (d, J_{CF} = 8.2 Hz), 126.8, 119.2, 115.6 (d, J_{CF} = 7.9 Hz), 115.1 (d, J_{CF} = 22.5 Hz), 112.0 (d, J_{CF} = 25.0 Hz), 84.4, 72.2, 61.1, 52.1, 42.8, 27.5, 26.0, 13.1, –0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}FN_3O_{10}SiNa$ $[M + Na]^+$: 640.1739, Found: 640.1738.

*10.3.3. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-7-fluoro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4c**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-7-fluoro-2-oxoindoline-1-carboxylate (**1c**, 100.6 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4c** as a white solid in 76% yield (140.1 mg, 0.23 mmol) for two steps after flash chromatography. The dr was calculated to be 83:17 by crude ^{1}H-NMR analysis and the ee was determined to be 91% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 5.92 min, t_{major} = 10.80 min, $[\alpha]_D^{25}$ = +15.40 (*c* 1.00 in CH_2Cl_2), m.p. 83–85 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.81 (s, 1H), 8.29 (s, 1H), 7.16−7.06 (m, 2H), 6.77 (dd, *J* = 7.2, 0.8 Hz, 1H),

4.89 (s, 1H), 4.08−3.95 (m, 2H), 3.80 (dd, J = 16.0, 4.0 Hz, 1H), 3.70−3.59 (m, 2H), 1.59 (s, 9H), 1.05 (t, J = 7.2 Hz, 3H), 0.03 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.4, 170.5, 148.5, 148.4 (d, J_{CF} = 249.4 Hz), 147.2, 145.9, 141.3, 138.7 (d, J_{CF} = 1.8 Hz), 138.1, 131.3 (d, J_{CF} = 1.9 Hz), 127.0, 125.0 (d, J_{CF} = 6.8 Hz), 120.6 (d, J_{CF} = 3.6 Hz), 119.7, 117.6 (d, J_{CF} = 20.4 Hz), 85.4, 72.7, 61.8, 53.5, 43.8, 27.7, 26.4, 13.6, 0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}FN_3O_{10}SiNa$ $[M + Na]^+$: 640.1739, Found: 640.1738.

*10.3.4. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-5-chloro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4d**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-5-chloro-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1d**, 105.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4d** as a white solid in 81% yield (154.7 mg, 0.24 mmol) for two steps after flash chromatography. The dr was calculated to be 91:9 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak IE column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 7.33 min, $[\alpha]_D^{25}$ = –25.85 (*c* 1.00 in CH_2Cl_2), m.p. 141–143 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.54 (s, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.38 (dd, J = 8.8, 2.4 Hz, 1H), 7.21 (d, J = 2.0 Hz, 1H), 5.08 (s, 1H), 4.01−3.92 (m, 3H), 3.60 (dd, J = 18.8, 6.0 Hz, 1H), 3.44 (dd, J = 12.0, 6.4 Hz, 1H), 1.59 (s, 9H), 1.01 (t, J = 7.2 Hz, 3H), −0.08 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.7, 169.6, 148.7, 148.0, 146.4, 142.1, 140.3, 136.6, 130.1, 129.8, 129.4, 125.9, 122.2, 119.1, 116.8, 84.7, 76.2, 61.7, 52.5, 46.1, 28.0, 26.8, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}ClN_3O_{10}SiNa$ $[M + Na]^+$: 656.1443, Found: 656.1440.

*10.3.5. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-6-chloro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4e**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-6-chloro-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1e**, 105.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4e** as a white solid in 78% yield (148.6 mg, 0.23 mmol)

for two steps after flash chromatography. The dr was calculated to be 87:13 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 7.13 min, $[\alpha]_D^{25}$ = –58.19 (*c* 1.00 in CH_2Cl_2), m.p. 130–132 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.42 (s, 1H), 7.99 (s, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 5.88 (d, *J* = 8.0 Hz, 1H), 5.23 (s, 1H), 3.93−3.82 (m, 3H), 3.78 (t, *J* = 8.4 Hz, 1H), 3.61 (dd, *J* = 19.2, 8.0 Hz, 1H), 1.67 (s, 9H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.20 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 175.8, 169.2, 148.4, 148.3, 146.3, 143.0, 142.0, 135.8, 134.9, 124.4, 123.9, 123.8, 122.9, 118.9, 115.3, 84.9, 74.8, 61.5, 54.6, 44.1, 27.8, 25.0, 13.2, –0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}ClN_3O_{10}SiNa$ $[M + Na]^+$: 656.1443, Found: 656.1445.

*10.3.6. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-4-bromo-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4f**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-4-bromo-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1f**, 118.9 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4f** as a white solid in 81% yield (166.2 mg, 0.24 mmol) for two steps after flash chromatography. The dr was calculated to be >95:5 by crude ^{1}H-NMR analysis and the ee was determined to be 37% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 5.70 min, t_{minor} = 7.39 min, $[\alpha]_D^{25}$ = +28.80 (*c* 1.00 in CH_2Cl_2), m.p. 161–163 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.52 (s, 1H), 7.93 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.38 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 5.70 (s, 1H), 4.26 (dd, *J* = 8.8, 6.4 Hz, 1H), 4.05 (dd, *J* = 18.0, 8.8 Hz, 1H), 3.95 (q, *J* = 7.2 Hz, 2H), 3.49 (dd, *J* = 17.6, 6.4 Hz, 1H), 1.58 (s, 9H), 1.01 (t, *J* = 7.2 Hz, 3H), −0.07 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.7, 170.1, 148.4, 148.2, 146.2, 143.7, 142.7, 137.2, 130.8, 128.9, 126.4, 125.3, 118.6, 117.8, 114.4, 84.8, 71.7, 61.5, 55.8, 43.1, 27.9, 25.9, 13.5, –0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}BrN_3O_{10}SiNa$ $[M + Na]^+$: 700.0938, Found: 700.0941.

*10.3.7. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-5-bromo-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4g**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-5-bromo-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1g**, 118.9 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4g** as a white solid in 79% yield (161.4 mg, 0.24 mmol) for two steps after flash chromatography. The dr was calculated to be 90:10 by crude ^{1}H-NMR analysis and the ee was determined to be 95% by HPLC on Chiralpak IE column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 7.65 min, t_{minor} = 8.58 min, $[\alpha]_D^{25}$ = –38.84 (*c* 1.00 in CH_2Cl_2), m.p. 123–125 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.54 (s, 1H), 7.82 (d, *J* = 8.8 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 5.07 (s, 1H), 4.01−3.93 (m, 3H), 3.60 (dd, *J* = 18.8, 6.0 Hz, 1H), 3.44 (dd, *J* = 12.0, 6.4 Hz, 1H), 1.59 (s, 9H), 1.01 (t, *J* = 7.2 Hz, 3H), −0.08 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.6, 169.6, 148.7, 148.1, 146.3, 142.1, 140.8, 136.8, 132.3, 130.5, 125.8, 125.0, 119.1, 117.2, 117.1, 84.8, 76.3, 61.7, 52.5, 46.1, 28.0, 26.8, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}BrN_3O_{10}SiNa$ $[M + Na]^+$: 700.0938, Found: 700.0939.

*10.3.8. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-6-bromo-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4h**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-6-bromo-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1h**, 118.9 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4h** as a white solid in 78% yield (158.3 mg, 0.23 mmol) for two steps after flash chromatography. The dr was calculated to be 85:15 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 7.23 min, $[\alpha]_D^{25}$ = –30.75 (*c* 1.00 in CH_2Cl_2), m.p. 128–130 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.42 (s, 1H), 8.14 (s, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 5.82 (d, *J* = 8.0 Hz, 1H), 5.22 (s, 1H), 3.93−3.83 (m, 3H), 3.78 (t, *J* = 8.4 Hz, 1H), 3.61 (dd, *J* = 19.2, 8.0 Hz, 1H), 1.67 (s, 9H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.20 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 175.7, 169.1, 148.4, 148.3, 146.3, 143.0, 142.1, 135.8, 126.8, 124.4, 124.1, 123.4, 122.8, 118.9, 118.1, 84.9, 74.8, 61.5, 54.6, 44.0, 27.8, 25.0, 13.2, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}BrN_3O_{10}SiNa$ $[M + Na]^+$: 700.0938, Found: 700.0938.

*10.3.9. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-5,5',7'-trinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4i**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-5-nitro-2-oxoindoline-1-carboxylate (**1i**, 108.7 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4i** as a white solid in 74% yield (143.3 mg, 0.22 mmol) for two steps after flash chromatography. The dr was calculated to be 87:13 by crude ^{1}H-NMR analysis and the ee was determined to be 79% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 8.63 min, t_{major} = 10.87 min, $[\alpha]_D^{25}$ = –13.05 (*c* 1.00 in CH_2Cl_2), m.p. 109–111 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.79 (s, 1H), 8.54 (s, 1H), 8.35 (dd, *J* = 9.2, 2.4 Hz, 1H), 8.15 (d, *J* = 2.0 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 5.18 (s, 1H), 4.02−3.93 (m, 3H), 3.68 (dd, *J* = 18.8, 6.0 Hz, 1H), 3.58 (dd, *J* = 11.6, 6.4 Hz, 1H), 1.61 (s, 9H), 1.04 (t, *J* = 7.2 Hz, 3H), −0.11 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 175.5, 169.0, 148.3, 146.4, 142.7, 140.2, 135.6, 131.9, 126.7, 126.1, 124.7, 119.1, 116.8, 116.1, 84.7, 74.9, 61.6, 54.6, 44.1, 27.8, 25.1, 13.2, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{32}N_4O_{12}SiNa$ $[M + Na]^+$: 667.1684, Found: 667.1685.

*10.3.10. 1-(tert-Butyl) 3'-ethyl (1'R,3R,3'S)-5-methyl-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4j**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-5-methyl-2-oxoindoline-1-carboxylate (**1j**, 99.4 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4j** as a white solid in 73% yield (135.1 mg, 0.22 mmol) for two steps after flash chromatography. The dr was calculated to be 84:16 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 8.33 min, $[\alpha]_D^{25}$ = –74.09 (*c* 1.00 in CH_2Cl_2), m.p. 146–148 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.44 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.74 (d, *J* = 1.2 Hz, 1H), 5.24 (s, 1H), 3.94 (dd, *J* = 19.2, 8.4 Hz, 1H), 3.85−3.74 (m, 3H), 3.59 (dd, *J*

= 19.2, 8.0 Hz, 1H), 2.07 (s, 3H), 1.66 (s, 9H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.19 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): *δ* 176.3, 169.3, 148.6, 148.3, 146.2, 143.4, 138.7, 136.1, 133.3, 129.4, 124.4, 124.3, 123.7, 118.7, 114.2, 84.1, 74.9, 61.3, 54.8, 44.1, 27.8, 25.0, 20.9, 13.1, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{29}H_{35}N_3O_{10}SiNa$ $[M + Na]^+$: 636.1989, Found: 636.1987.

*10.3.11. tert-Butyl (1'R,3R,3'S)-3'-benzoyl-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1-carboxylate (**int-4k**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-2-oxo-3-(2-oxo-2-phenylethylidene)indoline-1-carboxylate (**1k**, 104.8 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4k** as a white solid in 76% yield (143.6 mg, 0.23 mmol) for two steps after flash chromatography. The dr was calculated to be 88:12 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 4.99 min, t_{major} = 10.46 min, $[\alpha]_D^{25}$ = +121.73 (*c* 1.00 in CH_2Cl_2), m.p. 178–180 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): *δ* 8.84 (s, 1H), 8.37 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.43−7.35 (m, 3H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 8.4 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 5.57 (d, *J* = 7.2 Hz, 1H), 5.36 (s, 1H), 4.74 (dd, *J* = 7.6, 5.6 Hz, 1H), 4.10 (dd, *J* = 17.6, 5.6 Hz, 1H), 3.36 (dd, *J* = 17.6, 7.6 Hz, 1H), 1.61 (s, 9H), 0.15 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): *δ* 197.8, 176.9, 148.4, 148.0, 146.1, 143.7, 140.5, 137.7, 135.9, 133.0, 128.6, 128.2, 127.6, 124.4, 123.9, 123.8, 118.8, 114.0, 84.3, 74.6, 55.8, 48.1, 27.8, 25.1, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{32}H_{33}N_3O_9SiNa$ $[M + Na]^+$: 654.1884, Found: 654.1886.

*10.3.12. tert-Butyl (1'R,3R,3'S)-3'-(2-fluorobenzoyl)-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1-carboxylate (**int-4l**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-(2-fluorophenyl)-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1l**, 110.2 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4l** as a white solid in 75% yield (145.4 mg, 0.22 mmol) for two steps after flash chromatography. The dr was calculated to be 87:13 by crude

^{1}H-NMR analysis and the ee was determined to be 87% by HPLC on Chiralpak OD column (20% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 8.54 min, t_{minor} = 12.27 min, $[\alpha]_D^{25}$ = +16.80 (*c* 1.00 in CH_2Cl_2), m.p. 191–193 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.58 (s, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.56−7.53 (m, 2H), 7.32 (t, *J* = 8.4 Hz, 1H), 7.18−7.12 (m, 3H), 7.09 (t, *J* = 7.2 Hz, 1H), 5.23 (s, 1H), 4.54 (dd, *J* = 12.6, 6.0 Hz, 1H), 3.88 (dd, *J* = 19.2, 12.6 Hz, 1H), 3.62 (dd, *J* = 19.2, 6.0 Hz, 1H), 1.64 (s, 9H), −0.12 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 195.4, 173.2, 160.5, 149.1, 147.2 (d, J_{CF} = 253.7 Hz), 142.8, 142.1, 137.3, 135.7 (d, J_{CF} = 10.2 Hz), 131.5, 129.3, 128.6, 126.2, 125.1, 124.2, 121.2, 119.0, 116.7 (d, J_{CF} = 24.5 Hz), 115.8, 84.3, 52.3, 52.0 (d, J_{CF} = 8.7 Hz), 28.1, 26.8, −0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{32}H_{32}N_3O_9FSiNa$ $[M + Na]^+$: 672.1790, Found: 672.1793.

*10.3.13. tert-Butyl (1'R,3R,3'S)-3'-(4-fluorobenzoyl)-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1-carboxylate (**int-4m**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-(4-fluorophenyl)-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1m**, 110.2 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4m** as a white solid in 79% yield (153.9 mg, 0.23 mmol) for two steps after flash chromatography. The dr was calculated to be 90:10 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak IE column (20% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 17.04 min, $[\alpha]_D^{25}$ = –57.69 (*c* 2.00 in CH_2Cl_2), m.p. 173–175 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.59 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.83 (dd, *J* = 9.0, 5.4 Hz, 2H), 7.32 (t, *J* = 8.4 Hz, 1H), 7.13 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.12−7.09 (m, 3H), 5.25 (s, 1H), 4.52 (dd, *J* = 12.0, 6.0 Hz, 1H), 3.93 (dd, *J* = 18.6, 12.0 Hz, 1H), 3.57 (dd, *J* = 19.2, 6.0 Hz, 1H), 1.63 (s, 9H), −0.11 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 195.3, 173.2, 166.3 (d, J_{CF} = 255.9 Hz), 149.0, 148.0, 146.4, 142.8, 142.1, 137.2, 131.4, 131.2 (d, J_{CF} = 9.3 Hz), 129.5, 128.5, 126.1, 124.3, 120.8, 119.0, 116.3 (d, J_{CF} = 22.2 Hz), 115.9, 84.3, 76.7, 52.2, 47.7, 28.1, 27.8, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{32}H_{32}N_3O_9FSiNa$ $[M + Na]^+$: 672.1790, Found: 672.1792.

*10.3.14. tert-Butyl (1'R,3R,3'S)-3'-(3,4-dichlorobenzoyl)-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1-carboxylate (**int-4n**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-(3,4-dichlorophenyl)-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1n**, 125.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4n** as a white solid in 75% yield (157.9 mg, 0.22 mmol) for two steps after flash chromatography. The dr was calculated to be 88:12 by crude ^{1}H-NMR analysis and the ee was determined to be 89% by HPLC on Chiralpak OD column (20% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 11.90 min, t_{minor} = 16.56 min, $[\alpha]_D^{25}$ = –50.69 (*c* 1.00 in CH_2Cl_2), m.p. 183–185 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.58 (s, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 1.8 Hz, 1H), 7.60 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.35 (t, *J* = 6.6 Hz, 1H), 7.16−7.12 (m, 2H), 5.25 (s, 1H), 4.46 (dd, *J* = 12.0, 6.0 Hz, 1H), 3.94 (dd, *J* = 19.2, 12.0 Hz, 1H), 3.55 (dd, *J* = 18.6, 6.0 Hz, 1H), 1.62 (s, 9H), −0.12 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 194.9, 172.9, 148.9, 148.0, 146.4, 142.7, 142.0, 139.0, 136.9, 134.5, 133.9, 131.2, 130.3, 129.7, 128.4, 127.3, 126.0, 124.4, 120.8, 119.1, 115.9, 84.4, 76.5, 52.3, 47.9, 28.1, 27.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{32}H_{31}N_3O_9Cl_2SiNa$ $[M + Na]^+$: 722.1104, Found: 722.1102.

*10.3.15. tert-Butyl (1'R,3R,3'S)-3'-(4-bromobenzoyl)-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1-carboxylate (**int-4o**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-(4-bromophenyl)-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1o**, 128.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4o** as a white solid in 80% yield (169.8 mg, 0.24 mmol) for two steps after flash chromatography. The dr was calculated to be 92:8 by crude ^{1}H-NMR analysis and the ee was determined to be 96% by HPLC on Chiralpak IE column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 14.23 min, t_{minor} = 16.58 min, $[\alpha]_D^{25}$ = –78.14 (*c* 2.00 in CH_2Cl_2), m.p. 204–206 °C.^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.58 (s, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.33 (t, *J* = 8.4 Hz, 1H), 7.13−7.09 (m, 2H), 5.24 (s, 1H),

4.50 (dd, J = 12.0, 6.0 Hz, 1H), 3.93 (dd, J = 18.6, 12.0 Hz, 1H), 3.56 (dd, J = 19.2, 6.0 Hz, 1H), 1.62 (s, 9H), −0.12 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 195.9, 173.1, 149.0, 148.0, 146.4, 142.8, 142.0, 137.1, 133.6, 132.4, 129.8, 129.6, 129.5, 128.5, 126.1, 124.3, 120.8, 119.0, 115.9, 84.3, 76.6, 52.2, 47.8, 28.1, 27.7, −0.3; HRMS (ESI): m/z Calcd. for $C_{32}H_{32}N_3O_9BrSiNa$ $[M + Na]^+$: 732.0989, Found: 732.0991.

*10.3.16. tert-Butyl (1'R,3R,3'S)-3'-(4-methoxybenzoyl)-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1-carboxylate (**int-4p**)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-(4-methoxyphenyl)-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1p**, 113.8 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.12 mol). Purification of the crude product obtained **int-4p** as a white solid in 79% yield (158.2 mg, 0.24 mmol) for two steps after flash chromatography. The dr was calculated to be 89:11 by crude ^{1}H-NMR analysis and the ee was determined to be >99% by HPLC on Chiralpak OD column (20% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 8.33 min, $[\alpha]_D^{25}$ = –171.87 (c 2.00 in CH_2Cl_2), m.p. 178–180 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.59 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 9.0 Hz, 2H), 7.30 (t, J = 8.4 Hz, 1H), 7.12 (d, J = 6.6 Hz, 1H), 7.08 (t, J = 7.2 Hz, 1H), 6.90 (d, J = 8.4 Hz, 2H), 5.25 (s, 1H), 4.52 (dd, J = 12.6, 6.0 Hz, 1H), 3.92 (dd, J = 19.2, 12.2 Hz, 1H), 3.86 (s, 3H), 3.58 (dd, J = 19.2, 6.0 Hz, 1H), 1.63 (s, 9H), −0.12 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 195.1, 173.4, 164.3, 149.1, 148.0, 146.3, 142.9, 142.1, 137.5, 130.8, 129.3, 128.8, 127.8, 126.1, 124.2, 120.8, 118.9, 115.9, 114.3, 84.1, 55.6, 52.1, 47.4, 28.1, 28.1, −0.2; HRMS (ESI): m/z Calcd. for $C_{33}H_{35}N_3O_{10}SiNa$ $[M + Na]^+$: 684.1989, Found: 684.1987.

*10.3.17. 1-(tert-Butyl) 3'-ethyl 5'-nitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4q** racemate)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1a**, 95.2 mg, 0.3 mmol), 2-methyl-3-nitrobenzaldehydes (**3b**, 75.7 mg, 0.36 mmol) and DBU (9.13 mg, 0.06 mmol). Purification of the crude product obtained **int-4q** racemate as a semisolid in 47% yield (78.1 mg, 0.14 mmol) for two steps after flash chromatography.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.26 (d, J = 1.6 Hz, 1H), 8.07 (dd, J = 8.4, 2.4 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.39−7.35 (m, 1H), 7.32 (d, J = 8.4 Hz, 1H), 7.23 (d, J = 4.0 Hz, 2H), 5.10 (s, 1H), 3.94−3.81 (m, 3H), 3.49 (dd, J = 12.4, 5.6 Hz, 1H), 3.25 (dd, J = 17.2, 5.6 Hz, 1H), 1.60 (s, 9H), 0.94 (t, J = 7.2 Hz, 3H), −0.14 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 172.6, 170.3, 149.1, 146.9, 142.0, 141.7, 138.5, 129.2, 128.9, 128.6, 124.2, 122.5, 122.0, 121.8, 115.3, 84.0, 61.1, 52.9, 46.7, 29.3, 28.0, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{34}N_2O_8Si$+Na [M + Na]$^+$: 577.1982, Found: 577.1984.

*10.3.18. 1-(tert-Butyl) 3'-ethyl 7'-nitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-1,3'-dicarboxylate (**int-4r** racemate)*

Prepared according to the general procedure using *tert*-butyl (*E*)-3-(2-ethoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate (**1a**, 95.2 mg, 0.3 mmol), 2-methyl-5-nitrobenzaldehydes (**3c**, 75.7 mg, 0.36 mmol) and DBU (9.13 mg, 0.06 mmol). Purification of the crude product obtained **int-4r** racemate as a semisolid in 47% yield (78.1 mg, 0.14 mmol) for two steps after flash chromatography. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.18 (dd, J = 8.4, 2.0 Hz, 1H), 8.15 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 5.96 (d, J = 7.6 Hz, 1H), 5.25 (s, 1H), 3.86−3.72 (m, 3H), 3.60 (dd, J = 18.4, 8.0 Hz, 1H), 3.40 (dd, J = 18.4, 9.2 Hz, 1H), 1.67 (s, 9H), 0.90 (t, J = 7.2 Hz, 3H), 0.18 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.8, 170.1, 148.7, 146.9, 141.5, 141.0, 139.3, 128.5, 128.4, 125.1, 123.6, 123.3, 122.3, 121.0, 114.1, 83.9, 75.0, 61.0, 55.5, 44.2, 27.8, 27.4, 13.0, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{28}H_{34}N_2O_8Si$+Na [M + Na]$^+$: 577.1982, Found: 577.1980.

*10.3.19. Ethyl (1'S,3S,3'S)-1-benzyl-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro [indoline-3,2'-naphthalene]-3'-carboxylate (**int-4a'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-2-oxoindolin-3-ylidene)acetate (**2a**, 92.2 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4a'** as a white solid in 51% yield (90.8 mg, 0.15 mmol) for two steps after flash

chromatography. The dr was calculated to be 91:9 by crude ^{1}H-NMR analysis and the ee was determined to be 89% by HPLC on Chiralpak OD column (25% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 10.40 min, t_{major} = 16.35 min, $[\alpha]_D^{25}$ = +55.09 (*c* 1.00 in CH_2Cl_2), m.p. 133–135 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.56 (s, 1H), 7.38−7.22 (m, 7H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 5.17 (s, 1H), 4.88 (s, 2H), 3.96 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.68 (q, *J* = 7.2 Hz, 2H), 3.33−3.20 (m, 2H), 0.60 (t, *J* = 7.2 Hz, 3H), −0.21 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.5, 170.9, 148.4, 146.8, 144.7, 144.3, 137.5, 135.8, 129.6, 129.6, 128.9, 128.1, 127.9, 123.8, 123.6, 122.9, 118.8, 109.5, 74.6, 61.3, 54.8, 46.8, 44.4, 25.7, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{31}N_3O_8SiNa$ $[M + Na]^+$: 612.1778, Found: 612.1779.

*10.3.20. Ethyl (1'S,3S,3'S)-1-benzyl-5-fluoro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro -1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4b'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-5-fluoro-2-oxoindolin-3-ylidene)acetate (**2b**, 97.6 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4b'** as a white solid in 59% yield (107.6 mg, 0.18 mmol) for two steps after flash chromatography. The dr was calculated to be 90:10 by crude ^{1}H-NMR analysis and the ee was determined to be 89% by HPLC on Chiralpak OD column (25% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 10.23 min, t_{major} = 16.64 min, $[\alpha]_D^{25}$ = +84.39 (*c* 1.00 in CH_2Cl_2), m.p. 105–107 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.55 (s, 1H), 7.34−7.28 (m, 5H), 7.04 (dd, *J* = 8.0, 2.8 Hz, 1H), 6.96 (td, *J* = 8.8, 2.4 Hz, 1H), 6.69 (q, *J* = 4.4 Hz, 1H), 5.17 (s, 1H), 4.87 (s, 2H), 3.98 (dd, *J* = 15.6, 3.2 Hz, 1H), 3.84−3.72 (m, 2H), 3.32−3.21 (m, 2H), 0.70 (t, *J* = 7.2 Hz, 3H), −0.16 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.1, 170.7, 159.2 (d, J_{CF} = 241.1 Hz), 148.4, 146.8, 143.8, 140.7, 137.2, 135.4, 131.1 (d, J_{CF} = 7.4 Hz), 129.0, 128.1, 127.8, 123.9, 118.9, 115.7 (d, J_{CF} = 23.2 Hz), 112.0 (d, J_{CF} = 24.3 Hz), 110.0 (d, J_{CF} = 7.6 Hz), 74.4, 61.4, 55.1, 46.5, 44.5, 25.8, 13.6, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{30}N_3O_8FSiNa$ $[M + Na]^+$: 630.1684, Found: 630.1683.

*10.3.21. Ethyl (1'S,3S,3'S)-1-benzyl-7-fluoro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro -1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4c'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-7-fluoro-2-oxoindolin-3-ylidene)acetate (**2c**, 97.6 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4c'** as a white solid in 55% yield (100.7 mg, 0.17 mmol) for two steps after flash chromatography. The dr was calculated to be 89:11 by crude ^{1}H-NMR analysis and the ee was determined to be 73% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 7.00 min, t_{major} = 14.37 min, $[\alpha]_D^{25}$ = +49.74 (*c* 1.00 in CH_2Cl_2), m.p. 84–86 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.54 (s, 1H), 7.41−7.28 (m, 5H), 7.0−7.01 (m, 3H), 5.13 (s, 1H), 5.02 (dd, *J* = 23.2, 15.2 Hz, 2H), 3.95 (dd, *J* = 15.6, 3.2 Hz, 1H), 3.72−3.62 (m, 2H), 3.30−3.18 (m, 2H), 0.61 (t, *J* = 7.2 Hz, 3H), −0.19 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.3, 170.6, 148.4, 147.6 (d, J_{CF} = 243.6 Hz), 146.8, 143.9, 137.3, 137.0, 132.8 (d, J_{CF} = 3.5 Hz), 131.4 (d, J_{CF} = 8.5 Hz), 128.7, 128.2 (d, J_{CF} = 1.5 Hz), 128.0, 123.8, 123.6, 123.6, 119.4 (d, J_{CF} = 3.2 Hz), 118.9, 117.8 (d, J_{CF} = 19.5 Hz), 74.8, 61.3, 46.9, 45.9 (d, J_{CF} = 4.5 Hz), 25.8, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{30}N_3O_8FSiNa$ $[M + Na]^+$: 630.1684, Found: 630.1685.

*10.3.22. Ethyl (1'S,3S,3'S)-1-benzyl-5-chloro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro -1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4d'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)acetate (**2d**, 102.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4d'** as a white solid in 58% yield (107.2 mg, 0.17 mmol) for two steps after flash chromatography. The dr was calculated to be 94:6 by crude ^{1}H-NMR analysis and the ee was determined to be 86% by HPLC on Chiralpak OD column (10% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 15.31 min, t_{major} = 18.68 min, $[\alpha]_D^{25}$ = +153.03 (*c* 1.00 in CH_2Cl_2), m.p. 104–106 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.55 (s, 1H), 7.34−7.21 (m, 7H), 6.69 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 1H), 4.86 (s, 2H), 3.98 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.85−3.74 (m, 2H), 3.32−3.20 (m, 2H),

0.72 (t, J = 7.2 Hz, 3H), −0.16 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 175.9, 170.6, 148.3, 146.7, 143.7, 143.1, 137.2, 135.2, 131.3, 129.3, 129.0, 128.2, 128.2, 127.8, 124.1, 123.6, 119.0, 110.4, 74.3, 61.5, 54.8, 46.5, 44.5, 25.8, 13.6, −0.3; HRMS (ESI): m/z Calcd. for $C_{30}H_{30}N_3O_8ClSiNa$ $[M + Na]^+$: 646.1388, Found: 646.1390.

*10.3.23. Ethyl (1'S,3S,3'S)-1-benzyl-6-chloro-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4e'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-6-chloro-2-oxoindolin-3-ylidene)acetate (**2e**, 102.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4e'** as a white solid in 54% yield (101.4 mg, 0.16 mmol) for two steps after flash chromatography. The dr was calculated to be 92:8 by crude ^{1}H-NMR analysis and the ee was determined to be 75% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 9.18 min, t_{major} = 11.66 min, $[\alpha]_D^{25}$ = +59.34 (c 1.00 in CH_2Cl_2), m.p. 106–108 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.54 (s, 1H), 7.3−7.29 (m, 5H), 7.16 (d, J = 8.0 Hz, 1H), 7.04 (dd, J = 8.0, 2.0 Hz, 1H), 6.77 (d, J = 1.6 Hz, 1H), 5.13 (s, 1H), 4.85 (s, 2H), 3.96 (dd, J = 16.0, 3.6 Hz, 1H), 3.74 (q, J = 7.2 Hz, 2H), 3.31−3.19 (m, 2H), 0.70 (t, J = 7.2 Hz, 3H), −0.16 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.3, 170.6, 148.3, 146.7, 145.9, 143.8, 137.2, 135.4, 135.1, 129.0, 128.2, 127.9, 127.7, 124.4, 123.8, 122.4, 118.9, 109.9, 74.3, 61.4, 54.4, 46.5, 44.4, 25.7, 13.6, −0.3; HRMS (ESI): m/z Calcd. for $C_{30}H_{30}N_3O_8ClSiNa$ $[M + Na]^+$: 646.1388, Found: 646.1385.

*10.3.24. Ethyl (1'S,3S,3'S)-1-benzyl-4-bromo-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4f'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-4-bromo-2-oxoindolin-3-ylidene)acetate (**2f**, 115.9 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4f'** as a white solid in 55% yield (110.3 mg, 0.16 mmol) for two steps after flash chromatography. The dr was calculated to be >95:5 by crude ^{1}H-NMR analysis and the ee was determined to be 85% by HPLC on Chiralpak AD column (30%

2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 5.15 min, t_{minor} = 23.35 min, $[\alpha]_D^{25}$ = –45.14 (*c* 1.00 in CH_2Cl_2), m.p. 152–154 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.75 (s, 1H), 8.56 (s, 1H), 7.35−7.08 (m, 7H), 6.68 (d, *J* = 6.8 Hz, 1H), 5.80 (s, 1H), 5.12 (d, *J* = 15.6 Hz, 1H), 4.56 (d, *J* = 16.0 Hz, 1H), 4.32 (dd, *J* = 10.0, 6.4 Hz, 1H), 4.13−4.10 (m, 1H), 3.99−3.90 (m, 2H), 3.54 (dd, *J* = 18.0, 6.4 Hz, 1H), 0.97 (t, *J* = 7.2 Hz, 3H), −0.11 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.8, 170.4, 148.1, 146.8, 146.3, 143.0, 137.4, 135.1, 130.8, 128.7, 127.7, 127.4, 126.9, 126.8, 125.3, 118.7, 118.2, 108.5, 71.7, 61.3, 54.9, 43.9, 42.4, 26.2, 13.7, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{30}N_3O_8BrSiNa$ $[M + Na]^+$: 690.0883, Found: 690.0881.

*10.3.25. Ethyl (1'S,3S,3'S)-1-benzyl-5-bromo-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4g'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)acetate (**2g**, 115.9 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4g'** as a white solid in 60% yield (120.1 mg, 0.18 mmol) for two steps after flash chromatography. The dr was calculated to be 93:7 by crude ^{1}H-NMR analysis and the ee was determined to be 85% by HPLC on Chiralpak OD column (10% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 14.65 min, t_{major} = 19.58 min, $[\alpha]_D^{25}$ = +26.15 (*c* 1.00 in CH_2Cl_2), m.p. 161–163 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.78 (s, 1H), 8.55 (s, 1H), 7.39−7.28 (m, 7H), 6.64 (d, *J* = 8.4 Hz, 1H), 5.18 (s, 1H), 4.86 (s, 2H), 3.98 (dd, *J* = 16.4, 4.0 Hz, 1H), 3.86−3.75 (m, 2H), 3.32−3.18 (m, 2H), 0.73 (t, *J* = 7.2 Hz, 3H), −0.16 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 175.8, 170.6, 148.3, 146.7, 143.7, 143.6, 137.2, 135.2, 132.3, 131.7, 129.0, 128.2, 127.7, 126.8, 123.8, 119.0, 115.2, 110.8, 74.3, 61.5, 54.7, 46.5, 44.4, 25.8, 13.6, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{30}N_3O_8BrSiNa$ $[M + Na]^+$: 690.0883, Found: 690.0880.

*10.3.26. Ethyl (1'S,3S,3'S)-1-benzyl-6-bromo-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4h'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-6-bromo-2-oxoindolin-3-ylidene)acetate (**2h**, 115.9 mg, 0.3 mmol),

3a (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4h′** as a white solid in 59% yield (118.5 mg, 0.18 mmol) for two steps after flash chromatography. The dr was calculated to be 91:9 by crude ^{1}H-NMR analysis and the ee was determined to be 80% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 10.69 min, t_{major} = 13.53 min, $[\alpha]_D^{25}$ = +45.44 (*c* 1.00 in CH_2Cl_2), m.p. 89–91 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 8.53 (s, 1H), 7.35−7.28 (m, 5H), 7.20 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 5.13 (s, 1H), 4.85 (s, 2H), 3.95 (dd, *J* = 16.0, 3.6 Hz, 1H), 3.74 (q, *J* = 7.2 Hz, 2H), 3.31−3.19 (m, 2H), 0.71 (t, *J* = 7.2 Hz, 3H), −0.16 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.2, 170.6, 146.7, 146.0, 143.7, 137.2, 135.1, 129.0, 128.5, 128.2, 127.7, 125.5, 124.7, 123.8, 123.1, 118.9, 112.6, 74.3, 61.4, 54.5, 46.4, 44.4, 25.7, 13.6, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{30}N_3O_8BrSiNa$ [M + Na]$^+$: 690.0883, Found: 690.0884.

*10.3.27. Ethyl (1'S,3S,3'S)-1-benzyl-5,5',7'-trinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4i'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-5-nitro-2-oxoindolin-3-ylidene)acetate (**2i**, 105.7 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4i′** as a white solid in 53% yield (100.6 mg, 0.16 mmol) for two steps after flash chromatography. The dr was calculated to be 90:10 by crude ^{1}H-NMR analysis and the ee was determined to be 92% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 7.75 min, t_{minor} = 12.00 min, $[\alpha]_D^{25}$ = –20.85 (*c* 1.00 in CH_2Cl_2), m.p. 111–113 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.89 (s, 1H), 8.44 (s, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 7.41−7.30 (m, 5H), 6.80 (d, *J* = 8.4 Hz, 1H), 6.69 (s, 1H), 5.42 (d, *J* = 15.6 Hz, 1H), 5.31 (s, 1H), 4.68 (d, *J* = 16.0 Hz, 1H), 3.99 (dd, *J* = 18.4, 7.6 Hz, 1H), 3.89 (t, *J* = 7.6 Hz, 1H), 3.82−3.72 (m, 2H), 3.61 (dd, *J* = 18.4, 7.6 Hz, 1H), 0.80 (t, *J* = 7.2 Hz, 3H), 0.17 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 177.4, 169.1, 149.7, 148.3, 146.2, 142.7, 142.5, 136.0, 133.7, 128.6, 127.8, 127.1, 126.8, 125.6, 124.2, 119.2, 118.9, 108.3, 73.9, 61.3, 54.5, 44.4, 44.3, 25.2, 13.2, −0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{30}N_4O_{10}SiNa$ [M + Na]$^+$: 657.1629, Found: 657.1628.

*10.3.28. Ethyl (1'S,3S,3'S)-1-benzyl-5-methyl-5',7'-dinitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro -1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4j'**)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-5-methyl-2-oxoindolin-3-ylidene)acetate (**2j**, 96.4 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4j'** as a white solid in 47% yield (86.5 mg, 0.14 mmol) for two steps after flash chromatography. The dr was calculated to be 89:11 by crude ^{1}H-NMR analysis and the ee was determined to be 77% by HPLC on Chiralpak OD column (10% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 12.81 min, t_{major} = 16.61 min, $[\alpha]_D^{25}$ = +50.99 (*c* 1.00 in CH_2Cl_2), m.p. 90–92 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.76 (s, 1H), 8.56 (s, 1H), 7.36−7.25 (m, 5H), 7.08 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 5.16 (s, 1H), 4.86 (dd, *J* = 23.6, 15.6 Hz, 2H), 3.96 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.75−3.66 (m, 2H), 3.32−3.18 (m, 2H), 2.31 (s, 3H), 0.62 (t, *J* = 7.2 Hz, 3H), −0.20 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 176.4, 170.9, 148.4, 146.7, 144.4, 142.2, 137.5, 135.9, 132.5, 129.7, 129.7, 129.0, 128.0, 128.0, 124.4, 123.8, 118.8, 109.3, 74.6, 61.2, 54.8, 46.7, 44.4, 25.9, 21.3, 13.5, −0.3; HRMS (ESI): *m*/*z* Calcd. for $C_{31}H_{33}N_3O_8SiNa$ $[M + Na]^+$: 626.1935, Found: 626.1931.

*10.3.29. (1'S,3S,3'S)-3'-Benzoyl-1-benzyl-5',7'-dinitro-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H -spiro[indoline-3,2'-naphthalen]-2-one (**int-4k'**)*

Prepared according to the general procedure using (*E*)-1-benzyl-3-(2-oxo-2-phenylethylidene)indolin-2-one (**2k**, 101.8 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4k'** as a white solid in 58% yield (108.1 mg, 0.17 mmol) for two steps after flash chromatography. The dr was calculated to be 91:9 by crude ^{1}H-NMR analysis and the ee was determined to be 95% by HPLC on Chiralpak OD column (25% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 11.24 min, t_{major} = 18.78 min, $[\alpha]_D^{25}$ = +36.34 (*c* 1.00 in CH_2Cl_2), m.p. 146–148 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.81 (s, 1H), 8.59 (s, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.32−7.12 (m, 10H), 7.04−6.96 (m, 2H), 6.32 (d, *J* = 7.2 Hz, 1H), 5.17 (s, 1H), 5.03 (d, *J* = 15.2 Hz, 1H), 4.10−3.95 (m,

3H), 3.47 (dd, J = 16.8, 11.6 Hz, 1H), −0.27 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 199.3, 177.1, 148.7, 146.9, 144.6, 144.4, 138.4, 137.0, 135.7, 133.4, 129.5, 129.2, 128.7, 128.6, 128.3, 128.2, 128.1, 125.1, 123.9, 123.3, 119.1, 109.3, 75.2, 55.3, 49.2, 44.7, 26.0, −0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{34}H_{31}N_3O_7SiNa$ $[M + Na]^+$: 644.1829, Found: 644.1832.

10.3.30.

*(1'S,3S,3'S)-1-Benzyl-3'-(2-fluorobenzoyl)-5',7'-dinitro-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**int-4l'**)*

Prepared according to the general procedure using (*E*)-1-benzyl-3-(2-(2-fluorophenyl)-2-oxoethylidene)indolin-2-one (**2l**, 107.2 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4l'** as a white solid in 56% yield (107.8 mg, 0.17 mmol) for two steps after flash chromatography. The dr was calculated to be 86:14 by crude ^{1}H-NMR analysis and the ee was determined to be 99% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 7.98 min, t_{major} = 19.94 min, $[\alpha]_D^{25}$ = +261.51 (*c* 2.00 in CH_2Cl_2), m.p. 102–104 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.81 (s, 1H), 8.58 (s, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.30 (d, J = 7.2 Hz, 2H), 7.25 (d, J = 7.2 Hz, 2H), 7.19 (d, J = 7.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.01 (t, J = 7.8 Hz, 1H), 6.92 (t, J = 7.8 Hz, 1H), 6.82 (dd, J = 10.8, 8.4 Hz, 1H), 6.42 (d, J = 7.8 Hz, 1H), 5.25 (s, 1H), 4.98 (d, J = 15.6 Hz, 1H), 4.14−4.10 (m, 3H), 4.05 (dd, J = 16.8, 4.8 Hz, 1H), 3.43 (dd, J = 16.8, 10.8 Hz, 1H), −0.26 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 197.3, 176.4, 147.7 (d, J_{CF} = 276.2 Hz), 144.5, 137.9, 135.7, 134.7 (d, J_{CF} = 9.3 Hz), 130.7, 129.5, 129.1, 129.0, 128.7, 128.1, 128.0, 128.0, 127.9, 124.8, 124.4, 124.1, 123.2, 122.5, 119.1, 116.5 (d, J_{CF} = 22.8 Hz), 109.3, 74.8, 60.8, 54.6, 51.7, −0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{34}H_{30}N_3O_7FSiNa$ $[M + Na]^+$: 662.1735, Found: 662.1732.

10.3.31.

*(1'S,3S,3'S)-1-Benzyl-3'-(4-fluorobenzoyl)-5',7'-dinitro-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**int-4m'**)*

Prepared according to the general procedure using (*E*)-1-benzyl-3-(2-(4-fluorophenyl)-2-oxoethylidene)indolin-2-one (**2m**, 107.2 mg,

0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4m′** as a white solid in 59% yield (113.9 mg, 0.18 mmol) for two steps after flash chromatography. The dr was calculated to be 90:10 by crude ^{1}H-NMR analysis and the ee was determined to be 98% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 6.49 min, t_{major} = 18.86 min, $[\alpha]_D^{25}$ = +209.32 (*c* 2.00 in CH_2Cl_2), m.p. 99–101 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.39 (s, 1H), 7.40 (dd, *J* = 9.0, 5.4 Hz, 2H), 7.27 (dd, *J* = 6.6, 3.0 Hz, 3H), 7.15 (dd, *J* = 6.6, 2.4 Hz, 2H), 6.99 (t, *J* = 7.8 Hz, 1H), 6.77 (t, *J* = 9.0 Hz, 2H), 6.66 (t, *J* = 7.8 Hz, 1H), 6.45 (d, *J* = 7.8 Hz, 1H), 5.54 (d, *J* = 7.2 Hz, 1H), 5.39 (s, 1H), 4.78−4.74 (m, 2H), 4.70 (d, *J* = 15.6 Hz, 1H), 4.10 (dd, *J* = 17.4, 4.8 Hz, 1H), 3.32 (dd, *J* = 17.4, 7.8 Hz, 1H), 0.12 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 196.6, 177.6, 165.7 (d, J_{CF} = 254.3 Hz), 148.8, 146.3, 144.2, 143.9, 138.6, 135.0, 132.7, 130.8 (d, J_{CF} = 9.0 Hz), 128.9, 128.8, 127.9, 127.6, 125.5, 125.1, 124.1, 122.6, 119.1, 115.6 (d, J_{CF} = 21.8 Hz), 109.0, 73.9, 55.9, 47.1, 44.5, 25.8, 0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{34}H_{30}N_3O_7FSiNa$ $[M + Na]^+$: 662.1735, Found: 662.1730.

10.3.32.

*(1'S,3S,3'S)-1-Benzyl-3'-(3,4-dichlorobenzoyl)-5',7'-dinitro-1'-((trimethylsilyl)oxy)-3', 4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**int-4n'**)*

Prepared according to the general procedure using (*E*)-1-benzyl-3-(2-(3,4-dichlorophenyl)-2-oxoethylidene)indolin-2-one (**2n**, 122.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4n′** as a white solid in 56% yield (114.3 mg, 0.17 mmol) for two steps after flash chromatography. The dr was calculated to be 93:7 by crude ^{1}H-NMR analysis and the ee was determined to be 97% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 6.52 min, t_{major} = 21.28 min, $[\alpha]_D^{25}$ = +129.38 (*c* 2.00 in CH_2Cl_2), m.p. 109–111 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.82 (s, 1H), 8.58 (s, 1H), 7.34−7.29 (m, 4H), 7.28−7.26 (m, 2H), 7.14 (d, *J* = 7.8 Hz, 1H), 7.10 (dd, *J* = 18.0, 8.4 Hz, 2H), 7.05−7.01 (m, 2H), 6.43 (d, *J* = 7.8 Hz, 1H), 5.11 (s, 1H), 5.08 (d, *J* = 15.0 Hz, 1H), 4.13 (d, *J* = 15.6 Hz, 1H), 3.98−3.94 (m, 2H), 3.45 (dd, *J* = 16.8, 13.2 Hz, 1H), −0.27 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 197.1, 176.9, 148.6, 147.0, 144.4, 144.3, 138.0, 137.9, 136.4, 135.5, 133.4, 130.6, 130.1, 129.8, 129.2, 128.4, 128.3, 128.2, 127.0, 125.0, 123.8, 123.5, 119.2, 109.4,

75.2, 55.2, 49.5, 44.8, 25.7, −0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{34}H_{29}N_3O_7Cl_2SiNa$ $[M + Na]^+$: 712.1050, Found: 712.1049.

10.3.33.

*(1'S,3S,3'S)-1-Benzyl-3'-(4-bromobenzoyl)-5',7'-dinitro-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**int-4o'**)*

Prepared according to the general procedure using (*E*)-1-benzyl-3-(2-(4-bromophenyl)-2-oxoethylidene)indolin-2-one (**2o**, 125.5 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4o'** as a white solid in 61% yield (125.7 mg, 0.18 mmol) for two steps after flash chromatography. The dr was calculated to be 92:8 by crude ^{1}H-NMR analysis and the ee was determined to be 93% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 6.86 min, t_{major} = 23.91 min, $[\alpha]_D^{25}$ = +207.72 (*c* 2.00 in CH_2Cl_2), m.p. 108–110 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.81 (s, 1H), 8.58 (s, 1H), 7.32 (d, *J* = 6.6 Hz, 3H), 7.26−7.21 (m, 5H), 7.16 (d, *J* = 6.6 Hz, 1H), 7.08 (dd, *J* = 15.6, 7.8 Hz, 3H), 7.00 (t, *J* = 7.2 Hz, 1H), 6.42 (d, *J* = 7.8 Hz, 1H), 5.12 (s, 1H), 4.96 (d, *J* = 15.0 Hz, 1H), 4.19 (d, *J* = 15.6 Hz, 1H), 4.01 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.95 (d, *J* = 16.8 Hz, 1H), 3.46 (dd, *J* = 15.6, 12.0 Hz, 1H), −0.27 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 198.2, 177.0, 148.6, 146.9, 144.4, 144.3, 138.2, 135.6, 135.5, 131.9, 129.6, 129.6, 129.2, 128.7, 128.4, 128.3, 128.2, 125.1, 123.8, 123.3, 119.1, 109.4, 75.2, 55.3, 49.1, 44.7, 25.8, −0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{34}H_{30}N_3O_7BrSiNa$ $[M + Na]^+$: 722.0934, Found: 722.0932.

10.3.34.

*(1'S,3S,3'S)-1-Benzyl-3'-(4-methoxybenzoyl)-5',7'-dinitro-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**int-4p'**)*

Prepared according to the general procedure using (*E*)-1-benzyl-3-(2-(4-methoxyphenyl)-2-oxoethylidene)indolin-2-one (**2p**, 110.8 mg, 0.3 mmol), **3a** (75.7 mg, 0.36 mmol) and **C7** (24.8 mg, 0.06 mol). Purification of the crude product obtained **int-4p'** as a white solid in 54% yield (106.2 mg, 0.16 mmol) for two steps after flash chromatography. The dr was calculated to be 91:9 by crude ^{1}H-NMR analysis and the ee was determined to be 96% by HPLC on Chiralpak OD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 7.77 min, t_{major} =

16.34 min, $[\alpha]_D^{25}$ = +138.38 (*c* 1.00 in CH_2Cl_2), m.p. 103–105 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.86 (s, 1H), 8.41 (s, 1H), 7.48 (d, *J* = 9.0 Hz, 2H), 7.25 (dd, *J* = 6.6, 4.2 Hz, 3H), 7.10 (dd, *J* = 6.6, 2.4 Hz, 2H), 6.99 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.68−6.66 (m, 3H), 6.44 (d, *J* = 7.8 Hz, 1H), 5.66 (d, *J* = 7.8 Hz, 1H), 5.41 (s, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.75 (dd, *J* = 7.2, 6.0 Hz, 1H), 4.66 (d, *J* = 15.6 Hz, 1H), 4.05 (dd, *J* = 18.0, 6.0 Hz, 1H), 3.78 (s, 3H), 3.35 (dd, *J* = 17.4, 7.2 Hz, 1H), 0.13 (s, 9H); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 196.1, 177.6, 163.7, 148.7, 146.2, 144.2, 143.8, 138.8, 135.1, 130.6, 129.1, 128.8, 128.5, 127.7, 127.4, 125.7, 125.0, 124.2, 122.5, 119.0, 113.7, 109.0, 74.1, 55.9, 55.6, 46.4, 44.4, 26.3, 0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{35}H_{33}N_3O_8SiNa$ $[M + Na]^+$: 674.1935, Found: 674.1934.

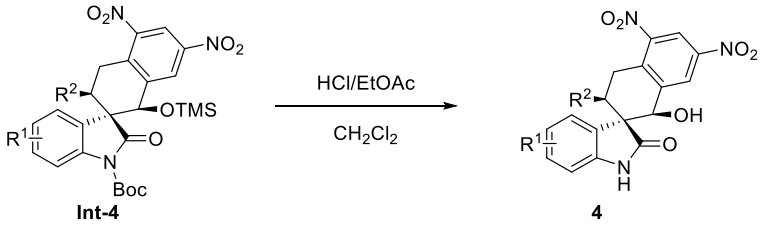
*10.3.35. Ethyl 1-benzyl-5'-nitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4q'** racemate)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-2-oxoindolin-3-ylidene)acetate (**2a**, 92.2 mg, 0.3 mmol), 2-methyl-3-nitrobenzaldehydes **3b** (59.5 mg, 0.36 mmol) and DBU (9.13 mg, 0.06 mmol). Purification of the crude product obtained **int-4q′** racemate as a semisolid in 52% yield (84.7 mg, 0.16 mmol) for two steps after flash chromatography. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 8.08 (d, *J* = 2.4 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.36−7.25 (m, 5H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 4.79 (d, *J* = 15.6 Hz, 1H), 4.70 (s, 1H), 3.99−3.91 (m, 1H), 3.86−3.78 (m, 2H), 3.71 (dd, *J* = 17.2, 12.0 Hz, 1H), 3.35 (dd, *J* = 16.8, 6.0 Hz, 1H), 0.86 (t, *J* = 7.2 Hz, 3H), −0.03 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 174.9, 171.6, 145.9, 143.2, 142.5, 137.0, 135.4, 128.9, 128.8, 128.3, 128.2, 127.2, 127.0, 125.2, 123.9, 122.5, 121.5, 108.5, 72.2, 60.5, 52.4, 43.3, 41.9, 28.8, 13.2, −0.1; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{32}N_2O_6Si^+Na$ $[M + Na]^+$: 567.1927, Found: 567.1929.

*10.3.36. Ethyl 1-benzyl-7'-nitro-2-oxo-1'-((trimethylsilyl)oxy)-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**int-4r'** racemate)*

Prepared according to the general procedure using ethyl (*E*)-2-(1-benzyl-2-oxoindolin-3-ylidene)acetate (**2a**, 92.2 mg, 0.3 mmol), 2-methyl-5-nitrobenzaldehydes **3c** (59.5 mg, 0.36 mmol) and DBU (9.13 mg, 0.06 mmol). Purification of the crude product obtained **int-4r′** racemate as a semisolid in 58% yield (94.7 mg, 0.17 mmol) for two steps after flash chromatography. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.21 (dd, J = 8.4, 2.4 Hz, 1H), 8.14 (d, J = 1.2 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 7.2 Hz, 2H), 7.35−7.27 (m, 3H), 7.06 (t, J = 8.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.61 (t, J = 7.6 Hz, 1H), 5.63 (d, J = 7.6 Hz, 1H), 5.25 (d, J = 4.8 Hz, 2H), 4.69 (d, J = 15.6 Hz, 1H), 3.88 (dd, J = 9.2, 5.6 Hz, 1H), 3.63−3.54 (m, 3H), 3.26 (dd, J = 17.2, 9.2 Hz, 1H), 0.52 (t, J = 7.2 Hz, 3H), 0.15 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 178.1, 170.1, 147.1, 144.5, 142.8, 140.5, 135.7, 128.6, 128.6, 128.3, 127.7, 127.6, 126.8, 124.1, 122.6, 122.0, 120.8, 108.7, 74.2, 60.9, 56.1, 44.9, 44.3, 28.1, 13.2, 0.2; HRMS (ESI): *m*/*z* Calcd. for $C_{30}H_{32}N_2O_6Si^{+}Na$ $[M + Na]^{+}$: 567.1927, Found: 567.1931.

*10.4. General procedure for the synthesis of **4** (Scheme S2)*



Scheme S2 General procedure for the synthesis of **4**.

To a solution of **int-4** (50 mg) in CH_2Cl_2 was added HCl/EtOAc (5−10 mL) at room temperature until the reaction was completed based on TLC. The reaction was quenched by EtOAc and water. The organic layer was dry by Na_2SO_4 and concentrated, which was purified by chromatography on silica gel to give the deprotected spiro-oxindole derivative **4** which was further analyzed by ^{1}H-NMR, ^{13}C-NMR, HPLC and HRMS.

*10.4.1. Ethyl (1'R,3R,3'S)-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4a**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4a**, 50 mg) and HCl/EtOAc (5–10 mL).

Purification of the crude product obtained **4a** as a white solid in 84% yield (30.1 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +58.26 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.43 (s, 1H, NH), 8.68 (s, 1H, ArH), 8.46 (s, 1H, ArH), 7.31 (d, *J*=7.6 Hz, 1H, ArH), 7.22 (t, *J*=7.6 Hz, 1H, ArH), 6.95 (t, *J*=7.6 Hz, 1H, ArH), 6.84 (d, *J*=7.6 Hz, 1H, ArH), 6.40 (d, *J*=6.4 Hz, 1H, CHOH), 5.11 (d, *J*=6.0 Hz, 1H, CHOH), 3.64−3.55 (m, 3H, CH_3CH_2, COCH), 3.40 (dd, *J*=16.4, 12.0 Hz, 1H, H of CH_2), 3.06 (dd, *J*=11.6, 4.4 Hz, 1H, H of CH_2), 0.66 (t, *J*=7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 178.4, 171.2, 148.3, 146.0, 145.5, 144.1, 138.9, 131.3, 128.9, 124.2, 123.2, 121.6, 118.3, 109.5, 71.6, 60.5, 55.0, 46.4, 25.7, 13.7; HRMS (ESI): *m*/*z* Calcd. for $C_{20}H_{17}N_3O_8Na$ $[M+Na]^+$: 450.0913, Found 450.0916. HPLC analysis: MeOH-H_2O (60:40), 11.27 min, HPLC purity 99.7%.

*10.4.2. Ethyl (1'R,3R,3'S)-5-fluoro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4b**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-5-fluoro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4b**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4b** as a white solid in 85% yield (30.8 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = –18.61 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.60 (s, 1H, NH), 8.72 (s, 1H, ArH), 8.43 (s, 1H, ArH), 7.07 (td, *J* = 9.6, 2.4 Hz, 1H, ArH), 6.94 (dd, *J* = 9.0, 3.0 Hz, 1H, ArH), 6.83 (dd, *J* = 8.4, 4.2 Hz, 1H, ArH), 6.54 (d, *J* = 6.6 Hz, 1H, CHOH), 4.78 (d, *J* = 6.6 Hz, 1H, CHOH), 3.91−3.84 (m, 2H, CH_3CH_2), 3.61−3.56 (m, 2H, COCH, H of CH_2), 3.48−3.42 (m, 1H, H of CH_2), 0.87 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 176.4, 171.3, 157.3 (d, J_{CF} = 234.2 Hz), 148.0, 145.4, 142.1, 138.6, 137.3, 131.2 (d, J_{CF} = 8.3 Hz), 127.6, 118.7, 114.6 (d, J_{CF} = 23.0 Hz), 113.7 (d, J_{CF} = 24.8 Hz), 109.6 (d, J_{CF} = 7.7 Hz), 68.7, 60.3, 52.2, 41.2, 25.5, 13.3; HRMS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8FNa$ $[M + Na]^+$: 468.0819, Found 468.0821. HPLC analysis: MeOH-H_2O (60:40), 12.80 min, HPLC purity 97.5%.

*10.4.3. Ethyl (1'R,3R,3'S)-7-fluoro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4c**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-7-fluoro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4c**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4c** as a white solid in 82% yield (29.5 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +18.87 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 11.23 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.38 (s, 1H, ArH), 8.19 (s, 1H, CHOH), 7.09 (t, *J* = 7.8 Hz, 1H, ArH), 6.87 (d, *J* = 6.6 Hz, 1H, ArH), 6.67 (td, *J* = 7.8, 4.8 Hz, 1H, ArH), 6.25 (d, *J* = 7.8 Hz, 1H, CHOH), 5.35 (d, *J* = 7.2 Hz, 1H, COCH), 4.15−4.10 (m, 2H, CH_3CH_2), 3.40−3.30 (m, 2H, CH_2), 1.16 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.8, 163.8, 147.6, 146.7, 146.3 (d, J_{CF} = 240.8 Hz), 143.1, 136.8, 130.3, 129.9 (d, J_{CF} = 12.3 Hz), 129.7, 128.5 (d, J_{CF} = 2.1 Hz), 123.4, 121.7 (d, J_{CF} = 5.1 Hz), 119.5, 119.2, 116.0 (d, J_{CF} = 17.1 Hz), 72.0, 61.5, 56.1, 13.5; HRMS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8FNa$ $[M + Na]^+$: 468.0819, Found 468.0822. HPLC analysis: MeOH-H_2O (60:40), 14.20 min, HPLC purity 99.3%.

*10.4.4. Ethyl (1'R,3R,3'S)-5-chloro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4d**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-5-chloro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4d**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4d** as a white solid in 87% yield (31.6 mg, 0.07 mmol) after flash chromatography, the ee was determined to be 99% by HPLC on Chiralpak IE column (20% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 33.30 min, t_{major} = 36.78 min, $[\alpha]_D^{25}$ = −75.99 (*c* 0.10 in CH_2Cl_2), ***ent*-4d**: +67.89, m.p. >220 °C. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.48 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.53 (s, 1H, ArH), 7.60 (d, *J* = 2.0 Hz, 1H, ArH), 7.26 (dd, *J* = 8.4, 2.0 Hz, 1H, ArH), 6.79 (d, *J* = 8.0 Hz, 1H, ArH), 6.62 (d, *J* = 6.8 Hz, 1H, CHOH), 5.25 (d, *J* = 6.8 Hz, 1H, CHOH), 3.90−3.72 (m, 4H, CH_3CH_2, COCH, H of CH_2),

3.33 (dd, J = 15.2, 2.4 Hz, 1H, H of CH_2), 0.83 (t, J = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 176.3, 171.1, 148.3, 146.2, 144.3, 142.9, 137.4, 133.2, 128.6, 125.7, 125.4, 124.2, 118.6, 110.7, 72.1, 60.8, 52.8, 44.6, 26.3, 13.9; HRMS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8ClNa$ $[M + Na]^+$: 484.0524, Found 484.0526. HPLC analysis: MeOH/H_2O (60:40), 9.80 min, HPLC purity 99.7%. (***ent*-4d**, 9.67 min, HPLC purity 98.3%).

*10.4.5. Ethyl (1'R,3R,3'S)-6-chloro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4e**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-6-chloro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4e**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4e** as a white solid in 86% yield (31.2 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = −76.28 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.73 (s, 1H, NH), 8.72 (s, 1H, ArH), 8.42 (s, 1H, ArH), 7.08 (d, J = 7.8 Hz, 1H, ArH), 6.99 (dd, J = 7.8, 1.8 Hz, 1H, ArH), 6.85 (d, J = 1.8 Hz, 1H, ArH), 6.52 (d, J = 6.6 Hz, 1H, CHOH), 4.78 (d, J = 6.6 Hz, 1H, CHOH), 3.92−3.85 (m, 2H, CH_3CH_2), 3.60−3.53 (m, 2H, COCH, H of CH_2), 3.45 (dd, J = 15.0, 3.0 Hz, 1H, H of CH_2), 0.90 (t, J = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 176.7, 171.4, 148.1, 145.5, 144.0, 142.3, 137.4, 132.8, 128.6, 127.6, 127.4, 120.7, 118.9, 109.1, 68.8, 60.5, 51.7, 41.5, 25.7, 13.5; HRMS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8ClNa$ $[M + Na]^+$: 484.0524, Found 484.0523. HPLC analysis: MeOH/H_2O (60:40), 14.07 min, HPLC purity 99.4%.

*10.4.6. Ethyl (1'R,3R,3'S)-4-bromo-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4f**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-4-bromo-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4f**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4f** as a white solid in 89% yield (33.2 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +42.31 (*c* 0.10 in CH_2Cl_2),

m.p. >220 ºC. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.65 (s, 1H, NH), 8.66 (s, 1H, ArH), 8.54 (s, 1H, ArH), 7.20−7.15 (m, 2H, ArH), 6.81 (t, J = 6.6 Hz, 2H, ArH, CHOH), 5.61 (d, J = 6.6 Hz, 1H, CHOH), 4.13 (dd, J = 11.4, 6.0 Hz, 1H, COCH), 3.87−3.76 (m, 3H, CH_3CH_2, H of CH_2), 3.31 (dd, J = 18.0, 6.0 Hz, 1H, H of CH_2), 0.83 (t, J = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 174.9, 170.4, 147.6, 145.8, 145.5, 143.4, 137.2, 130.6, 127.0, 125.3, 124.9, 118.0, 117.9, 108.5, 67.9, 60.3, 54.3, 41.6, 25.3, 13.2; HRMS (ESI): m/z Calcd. for $C_{20}H_{16}N_3O_8BrNa$ [M + Na]$^+$: 528.0018, Found 528.0020. HPLC analysis: MeOH/H_2O (60:40), 16.87 min, HPLC purity 98.6%.

*10.4.7. Ethyl (1'R,3R,3'S)-5-bromo-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4g**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-5-bromo-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′H-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4g**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4g** as a white solid in 88% yield (32.8 mg, 0.06 mmol) after flash chromatography, the ee was determined to be 95% by HPLC on Chiralpak IE column (20% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{minor} = 32.86 min, t_{major} = 35.72 min, $[\alpha]_D^{25}$ = −99.97 (c 0.10 in CH_2Cl_2), ***ent*-4g**: +109.98, m.p. >220 °C. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 10.48 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.52 (s, 1H, ArH), 7.72 (d, J = 2.0 Hz, 1H, ArH), 7.39 (dd, J = 8.4, 2.0 Hz, 1H, ArH), 6.75 (d, J = 8.4 Hz, 1H, ArH), 6.63 (d, J = 6.8 Hz, 1H, CHOH), 5.25 (d, J = 6.8 Hz, 1H, CHOH), 3.90−3.71 (m, 4H, CH_3CH_2, COCH, H of CH_2), 3.32 (dd, J = 16.0, 3.2 Hz, 1H, H of CH_2), 0.83 (t, J = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 176.2, 171.1, 148.3, 146.2, 144.3, 143.2, 137.4, 133.5, 131.4, 126.9, 125.4, 118.5, 113.3, 111.2, 72.1, 60.8, 52.8, 44.6, 26.2, 13.9; HRMS (ESI): m/z Calcd. for $C_{20}H_{16}N_3O_8BrNa$ [M + Na]$^+$: 528.0018, Found 528.0019. HPLC analysis: MeOH/H_2O (60:40), 10.73 min, HPLC purity 98.5%. (***ent*-4g**, 10.73, HPLC purity 98.4%).

*10.4.8. Ethyl (1'R,3R,3'S)-6-bromo-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4h**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-6-bromo-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4h**, 50 mg) and HCl/EtOAc (5-10 mL). Purification of the crude product obtained **4h** as a white solid in 86% yield (32.1 mg, 0.06 mmol) after flash chromatography, $[\alpha]_D^{25}$ = −50.22 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.87 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.38 (s, 1H, ArH), 8.20 (s, 1H, CHOH), 6.98 (d, *J* = 1.8 Hz, 1H, ArH), 6.84−6.82 (m, 2H, ArH), 6.34 (d, *J* = 7.8 Hz, 1H, CHOH), 5.33 (d, *J* = 7.2 Hz, 1H, COCH), 4.16−4.09 (m, 2H, CH_3CH_2), 3.41−3.31 (m, 2H, CH_2), 1.17 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.8, 163.8, 147.5, 146.8, 144.7, 143.0, 136.7, 130.3, 129.8, 124.9, 123.4, 121.6, 119.5, 112.3, 71.8, 61.5, 55.6, 30.9, 22.0, 13.6; HRMS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8BrNa$ $[M + Na]^+$: 528.0018, Found 528.0020. HPLC analysis: MeOH/H_2O (60:40), 32.13 min, HPLC purity 98.9%.

*10.4.9. Ethyl (1'R,3R,3'S)-1'-hydroxy-5,5',7'-trinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4i**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-5-nitro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4i**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4i** as a white solid in 84% yield (30.8 mg, 0.06 mmol) after flash chromatography, $[\alpha]_D^{25}$ = −24.57 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 11.15 (s, 1H, NH), 8.69 (s, 1H, ArH), 8.55 (d, *J* = 2.4 Hz, 1H, ArH), 8.53 (s, 1H, ArH), 8.24 (dd, *J* = 8.4, 2.4 Hz, 1H, ArH), 7.00 (d, *J* = 8.4 Hz, 1H, ArH), 6.72 (d, *J* = 6.6 Hz, 1H, CHOH), 5.40 (d, *J* = 6.6 Hz, 1H, CHOH), 4.03 (dd, *J* = 12.0, 6.0 Hz, 1H, COCH), 3.87−3.82 (m, 2H, CH_3CH_2), 3.74 (dd, *J* = 18.0, 12.0 Hz, 1H, H of CH_2), 3.42 (dd, *J* = 18.6, 6.0 Hz, 1H, H of CH_2), 0.82 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 176.5, 170.5, 150.0, 147.6, 145.6, 143.1, 141.7, 136.5, 131.6, 125.8, 124.7, 119.3, 118.1, 108.8,

71.3, 60.4, 52.1, 43.5, 25.5, 13.2; HRMS (ESI): *m/z* Calcd. for $C_{20}H_{16}N_4O_{10}Na$ [M + Na]$^+$: 495.0764, Found 495.0763. HPLC analysis: MeOH/H_2O (60:40), 6.80 min, HPLC purity 97.9%.

*10.4.10. Ethyl (1'R,3R,3'S)-1'-hydroxy-5-methyl-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4j**)*

Prepared according to the general procedure using 1-(*tert*-butyl) 3′-ethyl (1′*R*,3*R*,3′*S*)-5-methyl-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1,3′-dicarboxylate (**int-4j**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4j** as a white solid in 83% yield (29.8 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = −62.96 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.25 (s, 1H, NH), 8.66 (s, 1H, ArH), 8.52 (s, 1H, ArH), 7.24 (s, 1H, ArH), 7.01 (d, *J* = 7.8 Hz, 1H, ArH), 6.67 (d, *J* = 7.8 Hz, 1H, ArH), 6.53 (d, *J* = 7.2 Hz, 1H, CHOH), 5.18 (d, *J* = 7.2 Hz, 1H, CHOH), 3.82−3.75 (m, 3H, CH_3CH_2, COCH), 3.70 (dd, *J* = 11.4, 4.8 Hz, 1H, H of CH_2), 3.27 (dd, *J* = 17.4, 4.8 Hz, 1H, H of CH_2), 2.28 (s, 3H, CH_3), 0.78 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 179.1, 164.0, 147.5, 146.7, 143.5, 140.6, 137.7, 130.0, 129.9, 129.7, 129.3, 125.7, 123.7, 123.5, 119.6, 109.4, 72.0, 61.4, 56.0, 20.5, 13.6; HRMS (ESI): *m/z* Calcd. for $C_{21}H_{19}N_3O_8Na$ [M + Na]$^+$: 464.1070, Found 464.1071. HPLC analysis: MeOH/H_2O (60:40), 8.73 min, HPLC purity 98.1%.

*10.4.11. (1'R,3R,3'S)-3'-Benzoyl-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4k**)*

Prepared according to the general procedure using *tert*-butyl (1′*R*,3*R*,3′*S*)-3′-benzoyl-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1-carboxylate (**int-4k**, 50 mg) and HCl/EtOAc (5-10 mL). Purification of the crude product obtained **4k** as a white solid in 87% yield (31.2 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +35.53 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.52 (s, 1H, NH), 8.72 (s, 1H, ArH), 8.48 (s, 1H, ArH), 7.86 (d, *J* = 7.2 Hz, 2H, ArH), 7.63 (t, *J* = 7.2 Hz, 1H, ArH), 7.49 (t, *J* = 7.2 Hz, 2H, ArH), 7.14−7.11 (m, 1H, ArH), 7.09 (d, *J* = 7.2 Hz, 1H, ArH),

6.79 (d, *J* = 7.8 Hz, 1H, ArH), 6.76 (t, *J* = 7.2 Hz, 1H, ArH), 6.49 (s, 1H, CHOH), 4.90 (dd, *J* = 11.4, 6.0 Hz, 1H, COCH), 4.71 (s, 1H, CHOH), 3.55 (dd, *J* = 18.0, 12.0 Hz, 1H, H of CH_2), 3.48 (dd, *J* = 18.0, 5.4 Hz, 1H, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 199.7, 177.1, 147.9, 145.4, 142.5, 142.4, 137.8, 135.6, 133.7, 129.7, 128.8 (2C), 128.2 (2C), 128.0, 125.5, 120.6, 118.6, 108.9, 69.2, 51.3, 41.8, 26.7; HRMS (ESI): *m*/*z* Calcd. for $C_{24}H_{17}N_3O_7Na$ $[M + Na]^+$: 482.0964, Found 482.0966. HPLC analysis: MeOH/H_2O (60:40), 13.53 min, HPLC purity 98.7%.

10.4.12.

*(1'R,3R,3'S)-3'-(2-Fluorobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4l**)*

Prepared according to the general procedure using *tert*-butyl (1′*R*,3*R*,3′*S*)-3′-(2-fluorobenzoyl)-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1-carboxylate (**int-4l**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4l** as a white solid in 83% yield (30.5 mg, 0.06 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +40.28 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.39 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.57 (s, 1H, ArH), 7.61−7.57 (m, 1H, ArH), 7.53 (td, *J* = 7.8, 1.2 Hz, 1H, ArH), 7.29−7.21 (m, 3H, ArH), 7.10 (td, *J* = 7.8, 1.2 Hz, 1H, ArH), 6.78−6.73 (m, 2H, ArH), 6.54 (d, *J* = 7.2 Hz, 1H, CHOH), 5.33 (d, *J* = 7.2 Hz, 1H, CHOH), 4.78 (dd, *J* = 12.0, 5.4 Hz, 1H, COCH), 3.77 (dd, *J* = 18.6, 12.2 Hz, 1H, H of CH_2), 3.36 (dd, *J* = 18.0, 5.4 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 197.8, 176.5, 160.1 (d, J_{CF} = 253.1 Hz), 147.9, 145.7, 144.5, 143.5, 137.3, 135.1 (d, J_{CF} = 8.7 Hz), 130.4, 130.2, 128.1, 125.7 (d, J_{CF} = 11.1 Hz), 125.1, 124.7, 122.6, 120.8, 118.0, 116.7 (d, J_{CF} = 21.9 Hz), 108.8, 72.1, 51.9, 48.9, 26.0; HRMS (ESI): *m*/*z* Calcd. for $C_{24}H_{16}N_3O_7FNa$ $[M + Na]^+$: 500.0870, Found 500.0868. HPLC analysis: MeOH/H_2O (60:40), 10.07 min, HPLC purity 99.7%.

10.4.13.

*(1'R,3R,3'S)-3'-(4-Fluorobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4m**)*

Prepared according to the general procedure using *tert*-butyl (1′*R*,3*R*,3′*S*)-3′-(4-fluorobenzoyl)-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dih

ydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1-carboxylate (**int-4m**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4m** as a white solid in 85% yield (31.4 mg, 0.07 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +29.87 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.36 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.60 (s, 1H, ArH), 8.04−8.01 (m, 2H, ArH), 7.37 (d, *J* = 7.2 Hz, 1H, ArH), 7.31 (t, *J* = 8.4 Hz, 2H, ArH), 7.07 (t, *J* = 7.8 Hz, 1H, ArH), 6.78 (t, *J* = 7.8 Hz, 1H, ArH), 6.73 (d, *J* = 7.2 Hz, 1H, ArH), 5.34 (s, 1H, CHOH), 5.09 (dd, *J* = 12.0, 4.8 Hz, 1H, COCH), 3.69 (dd, *J* = 17.4, 12.6 Hz, 1H, H of CH_2), 3.51 (s, 1H, CHOH), 3.33 (dd, *J* = 18.0, 4.8 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 197.6, 176.9, 165.4 (d, J_{CF} = 251.4 Hz), 147.8, 145.7, 144.6, 143.7, 137.7, 132.3, 131.7 (d, J_{CF} = 9.3 Hz, 2C), 131.0, 128.0, 125.2, 122.4, 120.8, 118.0, 115.9 (d, J_{CF} = 21.6 Hz, 2C), 108.8, 72.3, 51.6, 45.0, 26.9; HRMS (ESI): *m*/*z* Calcd. for $C_{24}H_{16}N_3O_7FNa$ [M + Na]$^+$: 500.0870, Found 500.0869. HPLC analysis: MeOH/H_2O (60:40), 8.40 min, HPLC purity 99.2%.

10.4.14.

*(1'R,3R,3'S)-3'-(3,4-Dichlorobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4n**)*

Prepared according to the general procedure using *tert*-butyl (1′*R*,3*R*,3′*S*)-3′-(3,4-dichlorobenzoyl)-5′,7′-dinitro-2-oxo-1′-((trimethyl-silyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1-carboxylate (**int-4n**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4n** as a white solid in 87% yield (32.8 mg, 0.06 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +21.42 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.39 (s, 1H, NH), 8.67 (s, 1H, , ArH), 8.59 (s, 1H, ArH), 8.15 (d, *J* = 1.8 Hz, 1H, ArH), 7.79 (dd, *J* = 8.4, 1.8 Hz, 1H, ArH), 7.74 (d, *J* = 8.4 Hz, 1H, ArH), 7.38 (d, *J* = 7.2 Hz, 1H, ArH), 7.08 (t, *J* = 7.2 Hz, 1H, ArH), 6.79 (t, *J* = 7.8 Hz, 1H, ArH), 6.73 (d, *J* = 7.8 Hz, 1H, ArH), 6.55 (d, *J* = 6.6 Hz, 1H, CHOH), 5.34 (d, *J* = 7.2 Hz, 1H, CHOH), 5.07 (dd, *J* = 12.0, 4.8 Hz, 1H, COCH), 3.70 (dd, *J* = 18.0, 12.0 Hz, 1H, H of CH_2), 3.38 (dd, *J* = 18.0, 6.0 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 197.4, 176.6, 147.8, 145.7, 144.5, 143.5, 137.6, 136.7, 135.9, 132.0, 131.1, 130.6, 130.5, 128.3, 128.2, 125.1, 122.6, 120.9, 118.0, 108.8, 72.1, 51.7, 45.2, 26.5; HRMS (ESI): *m*/*z* Calcd. for

$C_{24}H_{15}N_3O_7Cl_2Na$ $[M + Na]^+$: 550.0185, Found 550.0186. HPLC analysis: MeOH/H_2O (60:40), 26.93 min, HPLC purity 99.1%.

10.4.15.

*(1'R,3R,3'S)-3'-(4-Bromobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4o**)*

Prepared according to the general procedure using *tert*-butyl (1′*R*,3*R*,3′*S*)-3′-(4-bromobenzoyl)-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)-oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1-carboxylate (**int-4o**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4o** as a white solid in 88% yield (33.2 mg, 0.06 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +27.73 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.37 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.59 (s, 1H, ArH), 7.85 (d, *J* = 8.4 Hz, 2H, ArH), 7.69 (d, *J* = 8.4 Hz, 2H, ArH), 7.36 (d, *J* = 7.2 Hz, 1H, ArH), 7.08 (t, *J* = 7.8 Hz, 1H, ArH), 6.78 (t, *J* = 7.8 Hz, 1H, ArH), 6.73 (d, *J* = 7.2 Hz, 1H, ArH), 6.54 (d, *J* = 7.2 Hz, 1H, CHOH), 5.33 (d, *J* = 7.2 Hz, 1H, CHOH), 5.07 (dd, *J* = 12.0, 4.8 Hz, 1H, COCH), 3.69 (dd, *J* = 18.0, 12.0 Hz, 1H, H of CH_2), 3.34 (dd, *J* = 18.0, 5.4 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 198.2, 176.6, 147.6, 145.3, 144.4, 143.5, 137.5, 134.4, 131.8, 130.7, 130.4, 128.0, 127.9, 125.0, 122.2, 120.7, 117.8, 108.6, 72.1, 51.4, 44.9, 26.6; HRMS (ESI): *m*/*z* Calcd. for $C_{24}H_{16}N_3O_7BrNa$ $[M + Na]^+$: 560.0069, Found 560.0067. HPLC analysis: MeOH/H_2O (60:40), 15.60 min, HPLC purity 99.9%.

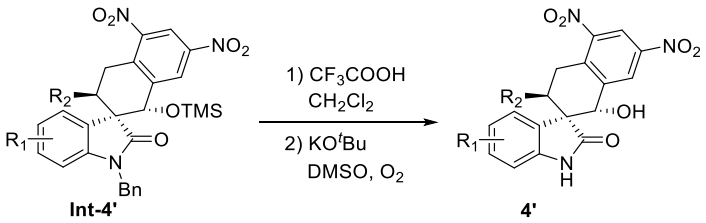
10.4.16.

*(1'R,3R,3'S)-1'-Hydroxy-3'-(4-methoxybenzoyl)-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4p**)*

Prepared according to the general procedure using *tert*-butyl (1′*R*,3*R*,3′*S*)-3′-(4-methoxybenzoyl)-5′,7′-dinitro-2-oxo-1′-((trimethyl-silyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-1-carboxylate (**int-4p**, 50 mg) and HCl/EtOAc (5–10 mL). Purification of the crude product obtained **4p** as a white solid in 86% yield (31.8 mg, 0.06 mmol) after flash chromatography, $[\alpha]_D^{25}$ = +30.99 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.32 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.59 (s, 1H, ArH), 7.94 (d, *J* = 9.0 Hz, 2H, ArH), 7.34 (d, *J* = 7.2 Hz, 1H, ArH), 7.07 (t, *J* = 7.8 Hz, 1H, ArH), 6.99 (d, *J* = 9.0 Hz, 2H, ArH), 6.79 (t, *J* =

7.8 Hz, 1H, ArH), 6.72 (d, *J* = 7.8 Hz, 1H, ArH), 6.51 (d, *J* = 6.6 Hz, 1H, CHOH), 5.32 (d, *J* = 7.2 Hz, 1H, CHOH), 5.03 (dd, *J* = 12.0, 5.4 Hz, 1H, COCH), 3.82 (s, 3H, OCH_3), 3.67 (dd, *J* = 18.0, 12.6 Hz, 1H, H of CH_2), 3.28 (dd, *J* = 18.0, 5.4 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 197.1, 177.1, 163.7, 147.8, 145.7, 144.7, 143.8, 137.9, 131.3, 131.1 (2C), 128.3, 127.9, 125.1, 122.2, 120.7, 118.0, 114.1 (2C), 108.7, 72.4, 55.7, 51.5, 44.7, 27.3; HR-MS (ESI): *m*/*z* Calcd. for $C_{25}H_{19}N_3O_8Na$ [M + Na]$^+$: 512.1070, Found 512.1068. HPLC analysis: MeOH/H_2O (60:40), 7.67 min, HPLC purity 99.0%.

*10.5. General procedure for the synthesis of **4′** (Scheme S3)*



Scheme S3 General procedure for the synthesis of **4′**.

To a solution of **int-4′** (50 mg) in CH_2Cl_2 was added CF_3COOH (5 eq.) at room temperature until the reaction was completed based on TLC. The reaction was quenched by EtOAc and water. The organic layer was dry by Na_2SO_4 and concentrated, which was purified by chromatography on silica gel to give the deprotection TMS intermediate product.

Further, potassium *tert*-butoxide (1.03 mL of a 1 mol/L solution in THF) was added to an aerated solution of the Bn-protecting THN-fused spirooxindole derivatives intermediate product, in DMSO (3.0 mL) at room temperature. After 20 min, 1mol/L HCl was added and further followed by sodium hydrogen carbonate solution to give a pH neutral solution. The solution was then diluted with brine, extracted with ethyl acetate (4 × 20 mL) and evaporated under reduced pressure[2]. The residue was purified by flash chromatography to give the deprotected spiro-oxindole derivative **4′** which was further analyzed by ^{1}H-NMR, ^{13}C-NMR, HPLC and HR-MS.

*10.5.1. Ethyl (1'S,3S,3'S)-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4a′**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4a′**, 50 mg), CF_3COOH (5 eq.) and KO^{t}Bu. Purification of the crude product obtained **4a′** as a white solid in 76% yield (27.7 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +70.25 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.60 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.44 (s, 1H, ArH), 7.11 (t, *J* = 8.4 Hz, 1H, ArH), 6.81 (d, *J* = 7.8 Hz, 1H, ArH), 6.65−6.62 (m, 2H, ArH), 6.06 (d, *J* = 7.2 Hz, 1H, CHOH), 5.06 (d, *J* = 6.6 Hz, 1H, CHOH), 3.77 (q, *J* = 7.2 Hz, 2H, CH_3CH_2), 3.70−3.62 (m, 2H, COCH, H of CH_2), 3.55 (dd, *J* = 18.8, 7.2 Hz, 1H, H of CH_2), 0.85 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.6, 170.3, 148.2, 145.8, 144.5, 143.9, 136.6, 128.2, 126.7, 124.2, 124.0, 120.8, 118.6, 109.2, 71.3, 60.5, 53.9, 43.1, 25.3, 13.4; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{17}N_3O_8Na$ $[M + Na]^+$: 450.0913, Found 450.0914. HPLC analysis: MeOH/H_2O (60:40), 11.80 min, HPLC purity 99.0%.

*10.5.2. Ethyl (1'S,3S,3'S)-5-fluoro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4b′**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-5-fluoro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4b′**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4b′** as a white solid in 74% yield (27.2 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +104.87 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.38 (s, 1H, NH), 8.67 (s, 1H, ArH), 8.53 (s, 1H, ArH), 7.42 (dd, *J* = 9.0, 3.0 Hz, 1H, ArH), 7.06−7.01 (m, 1H, ArH), 6.76 (dd, *J* = 8.4, 4.8 Hz, 1H, ArH), 6.60 (d, *J* = 6.6 Hz, 1H, CHOH), 5.24 (d, *J* = 7.2 Hz, 1H, CHOH), 3.86−3.81 (m, 2H, CH_3CH_2), 3.79−3.74 (m, 2H, COCH, H of CH_2), 3.33−3.30 (m, 1H, H of CH_2), 0.82 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 176.0, 170.6, 157.9 (d, J_{CF} = 234.3 Hz), 147.8, 145.7, 143.9, 139.7, 137.0, 132.4 (d, J_{CF} = 8.4 Hz), 124.9, 118.1, 114.4 (d, J_{CF} = 23.0 Hz), 111.4 (d, J_{CF} = 24.6 Hz), 109.5 (d, J_{CF} = 7.8 Hz), 71.7, 60.3, 52.5, 44.2, 25.8, 13.4; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8FNa$ $[M + Na]^+$: 468.0819, Found 468.0822. HPLC analysis: MeOH/H_2O (60:40), 8.40 min, HPLC purity 99.8%.

*10.5.3. Ethyl (1'S,3S,3'S)-7-fluoro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4c'**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-7-fluoro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4c'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4c'** as a white solid in 72% yield (26.4 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +68.26 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 11.14 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.44 (s, 1H, ArH), 7.06 (t, *J* = 9.6 Hz, 1H, ArH), 6.75 (d, *J* = 6.6 Hz, 1H, ArH), 6.69−6.66 (m, 1H, ArH), 5.97 (d, *J* = 7.8 Hz, 1H, CHOH), 5.08 (d, *J* = 6.6 Hz, 1H, CHOH), 3.86−3.78 (m, 2H, CH_3CH_2), 3.73 (t, *J* = 8.4 Hz, 1H, COCH), 3.62 (d, *J* = 8.4 Hz, 2H, CH_2), 0.88 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.4, 170.0, 148.1, 146.3 (d, J_{CF} = 240.0 Hz), 145.7, 144.1, 136.3, 130.9 (d, J_{CF} = 12.3 Hz), 129.8 (d, J_{CF} = 3.5 Hz), 124.2, 121.6 (d, J_{CF} = 5.6 Hz), 120.0, 118.6, 115.3 (d, J_{CF} = 16.8 Hz), 71.3, 60.5, 54.2, 42.9, 25.2, 13.3; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8FNa$ $[M + Na]^+$: 468.0819, Found 468.0820. HPLC analysis: MeOH/H_2O (60:40), 10.27 min, HPLC purity 98.8%.

*10.5.4. Ethyl (1'S,3S,3'S)-5-chloro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4d'**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-5-chloro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4d'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4d'** as a white solid in 76% yield (28.1 mg, 0.06 mmol) for two steps after flash chromatography, the ee was determined to be 95% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 9.74 min, t_{minor} = 17.08 min, $[\alpha]_D^{25}$ = +48.72 (*c* 0.10 in CH_2Cl_2), ***ent*-4d'**: −37.99, m.p. > 220 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.05 (s, 1H, NH), 8.82 (s, 1H, ArH), 8.67 (s, 1H, ArH), 7.15 (dd, *J* = 8.4, 2.0 Hz, 1H, ArH), 6.84 (d, *J* = 8.4 Hz, 1H, ArH), 6.33 (d, *J* = 2.0 Hz, 1H, ArH), 5.14 (d, *J* = 7.6 Hz, 1H,

CHOH), 4.79 (d, *J* = 7.6 Hz, 1H, CHOH), 4.09−3.97 (m, 2H, CH_3CH_2), 3.79−3.77 (m, 2H, COCH, H of CH_2), 3.61 (dd, *J* = 10.4, 8.0 Hz, 1H, H of CH_2), 1.12 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (100 MHz, DMSO-d_6): δ 178.4, 170.1, 148.3, 145.9, 143.9, 143.0, 136.2, 128.9, 128.3, 124.8, 124.5, 123.9, 118.8, 110.6, 71.3, 60.7, 54.1, 42.9, 25.3, 13.5; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8ClNa$ $[M + Na]^+$: 484.0524, Found 484.0523. HPLC analysis: MeOH/H_2O (60:40), 16.33 min, HPLC purity 98.8%. (***ent*-4d′**, 16.27 min, HPLC purity 99.2%).

*10.5.5. Ethyl (1'S,3S,3'S)-6-chloro-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4e′**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-6-chloro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4e′**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4e′** as a white solid in 75% yield (27.9 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +71.44 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.78 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.44 (s, 1H, ArH), 6.83 (d, *J* = 1.8 Hz, 1H, ArH), 6.71−6.69 (m, 2H, ArH), 6.11 (d, *J* = 7.8 Hz, 1H, CHOH), 5.06 (d, *J* = 6.6 Hz, 1H, CHOH), 3.85−3.80 (m, 2H, CH_3CH_2), 3.71 (dd, *J* = 9.6, 7.8 Hz, 1H, COCH), 3.64−3.58 (m, 2H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.7, 170.2, 148.2, 145.9, 145.6, 144.1, 136.5, 132.7, 125.8, 125.4, 124.4, 120.5, 118.8, 109.3, 71.3, 60.7, 53.7, 42.9, 25.4, 13.5; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8ClNa$ $[M + Na]^+$: 484.0524, Found 484.0522. HPLC analysis: MeOH/H_2O (60:40), 18.53 min, HPLC purity 99.9%.

*10.5.6. Ethyl (1'S,3S,3'S)-4-bromo-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4f′**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-4-bromo-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4f′**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4f′** as a white solid in 79%

yield (30.0 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = −69.97 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.65 (s, 1H, NH), 8.66 (s, 1H, ArH), 8.54 (s, 1H, ArH), 7.20−7.16 (m, 2H, ArH), 6.82−6.80 (m, 2H, ArH, CHOH), 5.61 (d, *J* = 6.6 Hz, 1H, CHOH), 4.13 (q, *J* = 5.4 Hz, 1H, COCH), 3.87−3.76 (m, 3H, CH_3CH_2, H of CH_2), 3.31 (dd, *J* = 18.0, 5.4 Hz, 1H, H of CH_2), 0.83 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 174.9, 170.4, 147.6, 145.8, 145.5, 143.3, 137.2, 130.6, 127.0, 125.3, 124.9, 118.0, 117.9, 108.5, 67.9, 60.3, 54.2, 41.6, 25.3, 13.2; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8BrNa$ [M + Na]$^+$: 528.0018, Found 528.0020. HPLC analysis: MeOH/H_2O (60:40), 16.40 min, HPLC purity 99.1%.

*10.5.7. Ethyl (1'S,3S,3'S)-5-bromo-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4g'**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-5-bromo-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4g'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4g'** as a white solid in 78% yield (29.5 mg, 0.06 mmol) for two steps after flash chromatography, the ee 95% was determined to be 85% by HPLC on Chiralpak AD column (30% 2-propanol/*n*-hexane, 1 mL/min), UV 254 nm, t_{major} = 10.67 min, t_{minor} = 16.83 min, $[\alpha]_D^{25}$ = +38.53 (*c* 0.10 in CH_2Cl_2), ***ent*-4g'**: −31.00, m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.78 (s, 1H, NH), 8.78 (s, 1H, ArH), 8.46 (s, 1H, ArH), 7.33 (dd, *J* = 8.4, 1.8 Hz, 1H, ArH), 6.79 (d, *J* = 8.4 Hz, 1H, ArH), 6.74 (d, *J* = 7.2 Hz, 1H, CHOH), 6.21 (d, *J* = 1.8 Hz, 1H, ArH), 5.06 (d, *J* = 6.6 Hz, 1H, CHOH), 3.87−3.81 (m, 2H, CH_3CH_2), 3.69 (dd, *J* = 9.6, 7.8 Hz, 1H, COCH), 3.61−3.59 (m, 2H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.2, 170.1, 148.3, 145.9, 143.9, 143.4, 136.1, 131.2, 129.4, 126.5, 124.5, 118.8, 112.5, 111.2, 71.3, 60.7, 54.2, 42.9, 25.2, 13.5; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8BrNa$ [M + Na]$^+$: 528.0018, Found 528.0019. HPLC analysis: MeOH/H_2O (60:40), 18.03 min, HPLC purity 99.7%. (***ent*-4g'**, 18.07 min, HPLC purity 98.1%).

*10.5.8. Ethyl (1'S,3S,3'S)-6-bromo-1'-hydroxy-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4h'**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-6-bromo-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4h'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4h'** as a white solid in 77% yield (29.1 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +50.85 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.77 (s, 1H, NH), 8.78 (s, 1H, ArH), 8.44 (s, 1H, ArH), 6.95 (d, *J* = 1.8 Hz, 1H, ArH), 6.83 (dd, *J* = 8.4, 1.8 Hz, 1H, ArH), 6.70 (d, *J* = 6.6 Hz, 1H, CHOH), 6.06 (d, *J* = 7.8 Hz, 1H, ArH), 5.05 (d, *J* = 6.6 Hz, 1H, CHOH), 3.86−3.80 (m, 2H,CH_3CH_2), 3.71 (dd, *J* = 9.6, 7.8 Hz, 1H, COCH), 3.61−3.59 (m, 2H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.6, 170.2, 148.2, 145.9, 145.7, 144.1, 136.5, 126.2, 125.8, 124.3, 123.5, 121.1, 118.8, 112.0, 71.2, 60.7, 53.7, 42.9, 25.4, 13.5; HR-MS (ESI): *m*/*z* Calcd. for $C_{20}H_{16}N_3O_8BrNa$ $[M + Na]^+$: 528.0018, Found 528.0016. HPLC analysis: MeOH/H_2O (60:40), 21.53 min, HPLC purity 99.8%.

*10.5.9. Ethyl (1'S,3S,3'S)-1'-hydroxy-5,5',7'-trinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4i'**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-5-nitro-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4i'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4i'** as a white solid in 73% yield (27.2 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = −35.26 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 11.43 (s, 1H, NH), 8.83 (s, 1H, ArH), 8.46 (s, 1H, ArH), 8.14 (dd, *J* = 9.0, 2.4 Hz, 1H, ArH), 7.05 (d, *J* = 9.0 Hz, 1H, ArH), 6.86−6.85 (m, 2H, ArH, CHOH), 5.14 (d, *J* = 6.6 Hz, 1H, CHOH), 3.87−3.81 (m, 2H, CH_3CH_2), 3.80 (d, *J* = 9.0 Hz, 1H, COCH), 3.64 (d, *J* = 8.4 Hz, 2H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 179.3, 170.0, 150.8, 148.5, 146.1, 143.7, 141.4, 135.7, 127.9, 126.1, 124.5, 119.2, 118.8, 109.4, 71.4, 61.0, 54.1, 43.0, 25.2, 13.5; HR-MS (ESI): *m*/*z* Calcd. for

$C_{20}H_{16}N_4O_{10}Na$ $[M + Na]^+$: 495.0764, Found 495.0766. HPLC analysis: MeOH/H_2O (60:40), 9.33 min, HPLC purity 99.2%.

*10.5.10. Ethyl (1'S,3S,3'S)-1'-hydroxy-5-methyl-5',7'-dinitro-2-oxo-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalene]-3'-carboxylate (**4j'**)*

Prepared according to the general procedure using ethyl (1′*S*,3*S*,3′*S*)-1-benzyl-5-methyl-5′,7′-dinitro-2-oxo-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalene]-3′-carboxylate (**int-4j'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4j'** as a white solid in 70% yield (25.7 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +68.52 (*c* 0.10 in CH_2Cl_2), m.p. >220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.47 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.46 (s, 1H, ArH), 6.92 (d, *J* = 7.8 Hz, 1H, ArH), 6.70 (d, *J* = 7.8 Hz, 1H, ArH), 6.58 (d, *J* = 6.6 Hz, 1H, CHOH), 5.90 (s, 1H, ArH), 5.04 (d, *J* = 6.6 Hz, 1H, CHOH), 3.81−3.76 (m, 2H, CH_3CH_2), 3.66−3.61 (m, 2H, COCH, H of CH_2), 3.57−3.52 (m, 1H, H of CH_2), 1.98 (s, 3H, CH_3), 0.87 (t, *J* = 7.2 Hz, 3H, CH_3CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.5, 170.2, 148.2, 145.8, 144.5, 141.5, 136.5, 129.3, 128.5, 126.8, 124.7, 124.3, 118.5, 108.9, 71.3, 60.4, 53.9, 43.0, 25.3, 20.7, 13.4; HR-MS (ESI): *m*/*z* Calcd. for $C_{21}H_{19}N_3O_8Na$ $[M + Na]^+$: 464.1070, Found 464.1071. HPLC analysis: MeOH/H_2O (60:40), 12.67 min, HPLC purity 98.5%.

*10.5.11. (1'S,3S,3'S)-3'-Benzoyl-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4k'**)*

Prepared according to the general procedure using (1′*S*,3*S*,3′*S*)-3′-benzoyl-1-benzyl-5′,7′-dinitro-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalen]-2-one (**int-4k'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4k'** as a white solid in 77% yield (28.4 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +101.84 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.51 (s, 1H, NH), 8.77 (s, 1H, ArH), 8.48 (s, 1H, ArH), 7.77 (d, *J* = 7.8 Hz, 2H, ArH), 7.60 (t, *J* = 7.8 Hz, 1H, ArH), 7.44 (t, *J* = 7.8 Hz, 2H, ArH), 7.05 (dd, *J* = 8.4, 7.2 Hz, 1H, ArH), 6.69 (d, *J* = 7.8 Hz, 1H, ArH), 6.63 (dd, *J* = 15.6, 7.2 Hz, 2H, ArH), 6.06 (d, *J* = 7.2 Hz,

1H, CHOH), 5.21 (d, *J* = 6.6 Hz, 1H, CHOH), 4.77 (dd, *J* = 9.0, 7.2 Hz, 1H, COCH), 3.60−3.52 (m, 2H, CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 198.6, 178.8, 148.2, 145.9, 145.1, 143.7, 137.5, 135.8, 133.5, 128.7 (2C), 128.4 (2C), 127.8, 127.5, 124.6, 124.2, 121.0, 118.7, 109.3, 71.8, 54.1, 45.8, 27.0; HR-MS (ESI): *m*/*z* Calcd. for $C_{24}H_{17}N_3O_7Na$ $[M + Na]^+$: 482.0964, Found 482.0967. HPLC analysis: MeOH/H_2O (60:40), 18.00 min, HPLC purity 99.8%.

10.5.12.

*(1'S,3S,3'S)-3'-(2-Fluorobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4l'**)*

Prepared according to the general procedure using (1′*S*,3*S*,3′*S*)-1-benzyl-3′-(2-fluorobenzoyl)-5′,7′-dinitro-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalen]-2-one (**int-4l′**, 50 mg), CF_3COOH (5 equiv) and KO′Bu. Purification of the crude product obtained **4l′** as a white solid in 71% yield (26.5 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = +87.99 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.57 (s, 1H, NH), 8.73 (s, 1H, ArH), 8.47 (s, 1H, ArH), 7.61 (dd, *J* = 13.8, 7.2 Hz, 1H, ArH), 7.50 (t, *J* = 7.8 Hz, 1H, ArH), 7.28 (dd, *J* = 11.4, 8.4 Hz, 1H, ArH), 7.23 (t, *J* = 7.8 Hz, 1H, ArH), 7.14 (t, *J* = 7.8 Hz, 1H, ArH), 7.05 (d, *J* = 7.8 Hz, 1H, ArH), 6.80 (d, *J* = 7.8 Hz, 1H, ArH), 6.75 (t, *J* = 7.8 Hz, 1H, ArH), 6.55 (d, *J* = 6.0 Hz, 1H, CHOH), 4.75 (d, *J* = 6.6 Hz, 1H, CHOH), 4.69 (dd, *J* = 10.8, 6.0 Hz, 1H, COCH), 3.60 (dd, *J* = 18.6, 11.4 Hz, 1H, H of CH_2), 3.47 (dd, *J* = 18.6, 5.4 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 198.7, 176.8, 160.4 (d, *J* = 252.6 Hz), 148.2, 145.5, 142.7, 142.5, 137.7, 135.3 (d, J_{CF} = 9.3 Hz), 130.3, 129.3, 128.3, 128.1, 125.8, 125.7 (d, J_{CF} = 11.3 Hz), 124.8 (d, J_{CF} = 2.0 Hz), 120.8, 118.8, 116.8 (d, J_{CF} = 22.5 Hz), 109.2, 69.1, 51.8, 45.9, 25.9; HR-MS (ESI): *m*/*z* Calcd. for $C_{24}H_{16}N_3O_7FNa$ $[M + Na]^+$: 500.0870, Found 500.0872. HPLC analysis: MeOH/H_2O (60:40), 13.80 min, HPLC purity 99.3%.

10.5.13.

*(1'S,3S,3'S)-3'-(4-Fluorobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4m'**)*

Prepared according to the general procedure using (1′*S*,3*S*,3′*S*)-1-benzyl-3′-(4-fluorobenzoyl)-5′,7′-dinitro-1′-((trimethylsilyl)oxy)-3′,4′-d

ihydro-1′*H*-spiro[indoline-3,2′-naphthalen]-2-one (**int-4m′**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4m′** as a white solid in 75% yield (27.8 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = −129.98 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.53 (s, 1H, NH), 8.72 (s, 1H, ArH), 8.48 (s, 1H, ArH), 7.94 (dd, *J* = 9.0, 6.0 Hz, 2H, ArH), 7. 31 (t, *J* = 9.0 Hz, 2H, ArH), 7.13 (t, *J* = 7.8 Hz, 1H, ArH), 7.08 (d, *J* = 7.2 Hz, 1H, ArH), 6.79 (d, *J* = 7.2 Hz, 1H, ArH), 6.76 (t, *J* = 7.8 Hz, 1H, ArH), 6.50 (d, *J* = 6.6 Hz, 1H, CHOH), 4.87 (dd, *J* = 12.0, 6.0 Hz, 1H, COCH), 4.72 (d, *J* = 6.6 Hz, 1H, CHOH), 3.55 (dd, *J* = 18.0, 11.4 Hz, 1H, H of CH_2), 3.47 (dd, *J* = 18.0, 6.0 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 198.2, 176.9, 165.1 (d, J_{CF} = 251.3 Hz), 147.9, 145.3, 142.4, 142.3, 137.7, 132.4, 131.2 (d, J_{CF} = 9.5 Hz, 2C), 129.5, 128.1, 128.0, 125.4, 120.5, 118.5, 115.7 (d, J_{CF} = 21.8 Hz, 2C), 108.8, 69.0, 51.3, 41.8, 26.5; HR-MS (ESI): *m*/*z* Calcd. for $C_{24}H_{16}N_3O_7FNa$ $[M + Na]^+$: 500.0870, Found 500.0868. HPLC analysis: MeOH/H_2O (60:40), 12.60 min, HPLC purity 99.3%.

10.5.14.

*(1'S,3S,3'S)-3'-(3,4-Dichlorobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4n′**)*

Prepared according to the general procedure using (1′*S*,3*S*,3′*S*)-1-benzyl-3′-(3,4-dichlorobenzoyl)-5′,7′-dinitro-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalen]-2-one (**int-4n′**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4n′** as a white solid in 77% yield (29.3 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = −157.34 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.55 (s, 1H, NH), 8.74 (s, 1H, ArH), 8.48 (s, 1H, ArH), 7.96 (s, 1H, ArH), 7.74 (br s, 2H, ArH), 7.14 (t, *J* = 7.8 Hz, 1H, ArH), 7.00 (d, *J* = 7.2 Hz, 1H, ArH), 6.77 (dd, *J* = 13.8, 7.8 Hz, 2H, ArH), 6.52 (d, *J* = 7.2 Hz, 1H, CHOH), 4.80−4.76 (m, 2H, CHOH, COCH), 3.54−3.49 (m, 2H, CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 198.0, 176.8, 147.9, 145.3, 142.6, 142.3, 137.6, 136.4, 136.0, 131.7, 131.0, 129.9, 129.3, 128.1, 128.0, 127.6, 125.4, 120.7, 118.5, 108.9, 69.0, 51.8, 42.6, 26.1; HR-MS (ESI): *m*/*z* Calcd. for $C_{24}H_{15}N_3O_7Cl_2Na$ $[M + Na]^+$: 550.0185, Found 550.0187. HPLC analysis: MeOH/H_2O (60:40), 14.87 min, HPLC purity 99.8%.

10.5.15.

*(1'S,3S,3'S)-3'-(4-Bromobenzoyl)-1'-hydroxy-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4o'**)*

Prepared according to the general procedure using (1′*S*,3*S*,3′*S*)-1-benzyl-3′-(4-bromobenzoyl)-5′,7′-dinitro-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalen]-2-one (**int-4o'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4o'** as a white solid in 78% yield (29.9 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = −139.98 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.53 (s, 1H, NH), 8.78 (s, 1H, ArH), 8.47 (s, 1H, ArH), 7.66 (br s, 4H, ArH), 7.06 (t, *J* = 7.8 Hz, 1H, ArH), 6.69 (d, *J* = 7.8 Hz, 1H, ArH), 6.64 (t, *J* = 7.8 Hz, 2H, ArH), 6.02 (d, *J* = 7.8 Hz, 1H, CHOH), 5.21 (d, *J* = 6.6 Hz, 1H, CHOH), 4.76 (dd, *J* = 9.0, 6.6 Hz, 1H, COCH), 3.59 (dd, *J* = 18.6, 9.0 Hz, 1H, H of CH_2), 3.53 (dd, *J* = 18.6, 6.6 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz, DMSO-d_6): δ 197.6, 178.3, 148.0, 145.6, 144.7, 143.3, 137.1, 134.6, 131.4 (2C), 130.1 (2C), 127.6, 127.4, 127.0, 124.2, 124.0, 120.7, 118.4, 109.0, 71.4, 53.9, 45.5, 26.3; HR-MS (ESI): *m*/*z* Calcd. for $C_{24}H_{16}N_3O_7BrNa$ $[M + Na]^+$: 560.0069, Found 560.0070. HPLC analysis: MeOH/H_2O (60:40), 30.73 min, HPLC purity 99.5%.

10.5.16.

*(1'S,3S,3'S)-1'-Hydroxy-3'-(4-methoxybenzoyl)-5',7'-dinitro-3',4'-dihydro-1'H-spiro[indoline-3,2'-naphthalen]-2-one (**4p'**)*

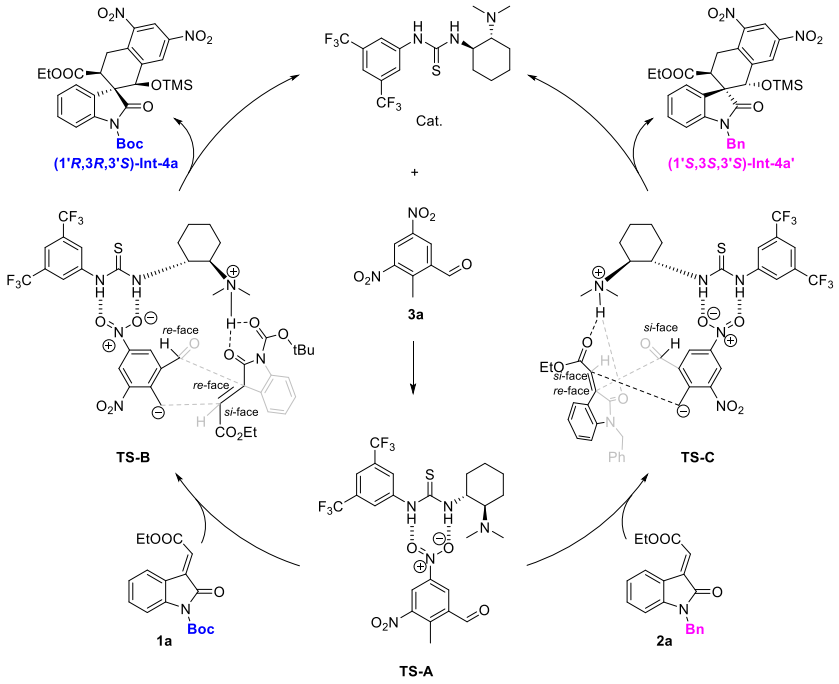
Prepared according to the general procedure using (1′*S*,3*S*,3′*S*)-1-benzyl-3′-(4-methoxybenzoyl)-5′,7′-dinitro-1′-((trimethylsilyl)oxy)-3′,4′-dihydro-1′*H*-spiro[indoline-3,2′-naphthalen]-2-one (**int-4p'**, 50 mg), CF_3COOH (5 equiv) and KO^{t}Bu. Purification of the crude product obtained **4p'** as a white solid in 75% yield (28.2 mg, 0.06 mmol) for two steps after flash chromatography, $[\alpha]_D^{25}$ = –108.68 (*c* 0.10 in CH_2Cl_2), m.p. > 220 °C. ^{1}H-NMR (600 MHz, DMSO-d_6): δ 10.55 (s, 1H, NH), 8.78 (s, 1H, ArH), 8.54 (s, 1H, ArH), 7.93 (d, *J* = 9.0 Hz, 2H, ArH), 7.17 (dd, *J* = 7.8, 3.6 Hz, 2H, ArH), 7.05 (d, *J* = 9.0 Hz, 2H, ArH), 6.83 (dd, *J* = 18.0, 7.8 Hz, 2H, ArH), 6.53 (d, *J* = 7.2 Hz, 1H, CHOH), 4.92 (dd, *J* = 12.0, 6.0 Hz, 1H, COCH), 4.73 (d, *J* = 7.2 Hz, 1H, CHOH), 3.88 (s, 3H, OCH_3), 3.59 (dd, *J* = 18.0, 12.0 Hz, 1H, H of CH_2), 3.48 (dd, *J* = 18.6, 6.0 Hz, 1H, H of CH_2); ^{13}C-NMR (150 MHz,

DMSO-d_6): δ 197.6, 177.1, 163.4, 147.8, 145.2, 142.4, 142.4, 137.9, 130.6 (2C), 129.8, 128.3, 128.3, 127.8, 125.3, 120.4, 118.5, 113.9 (2C), 108.8, 69.1, 55.4, 51.1, 41.2, 26.9; HR-MS (ESI): *m/z* Calcd. for $C_{25}H_{19}N_3O_8Na$ [M + Na]$^+$: 512.1070, Found 512.1069. HPLC analysis: MeOH/H_2O (60:40), 14.20 min, HPLC purity 97.9%.

11. Plausible mechanism of the protecting group-controlled the stereoselectivity

We hypothesized a plausible mechanism for this cyclization (Scheme S4). These transition states and the associated catalytic modes are consistent with the mechanistic models proposed by Takemoto and others[3–5]. In our proposal, as exemplified by the reaction of the Boc-protected 3-ylideneoxindole (**1a**) with 2-methyl-3,5-dinitrobenzaldehyde (**3a**), two hydrogen bonds form between the nitro group of the substrate **3a** and the two N–H groups of the thiourea catalyst and generating the transition state (**TS**)-**A**.

Next, the protonated tertiary amine group may form another two hydrogen-bonding interactions with the two carbonyls of **1a** and generating the **TS-B**. Finally, this affords the major isomer **int-4a** with a (1′*R*,3*R*,3′*S*)-configuration undergoing the process of Michael-aldol tandem reaction.



Scheme S4 Proposed mechanism for the synthesis of chiral THN-fused spirooxindole derivatives.

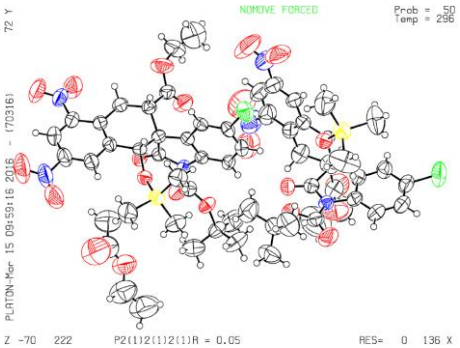
While with the presence of Bn-protected 3-ylideneoxindole (**2a**) as substrate, the protonated tertiary amine group may form the hydrogen-bonds with the C2 carbonyl

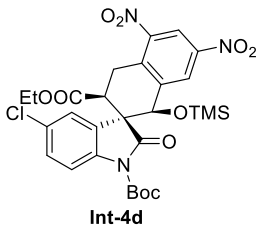
and ethyl ester groups on the substrate **2a** and generating the **TS-C**. This furnishes the major isomer **int-4a′** with a (1′*S*,3*S*,3′*S*)-configuration undergoing the process of Michael-aldol tandem reaction.

References

1. Onufriev A, Bashford D, Case DA. Modification of the generalized born model suitable for macromolecules. *J Phys Chem B* 2000;**104**:3712–20.
2. Arnott G, Brice H, Clayden J, Blaney E. Electrophile-induced dearomatizing spirocyclization of *N*-arylisonicotinamides: a route to spirocyclic piperidines. *Org Lett* 2008;**10**:3089–92.
3. Tian X, Jiang K, Peng J, Du W, Chen YC. Organocatalytic stereoselective Mannich reaction of 3-substituted oxindoles. *Org Lett* 2008;**10**:3583–6.
4. Okino T, Nakamura S, Furukawa T, Takemoto Y. Enantioselective Aza-Henry reaction catalyzed by a bifunctional organocatalyst. *Org Lett* 2004;**6**:625–7.
5. Xu X, Furukawa T, Okino T, Miyabe H, Takemoto Y. Bifunctional-thiourea-catalyzed diastereo- and enantioselective Aza-Henry reaction. *Chem Eur J* 2006;**12**:466–76.

12. Crystal data

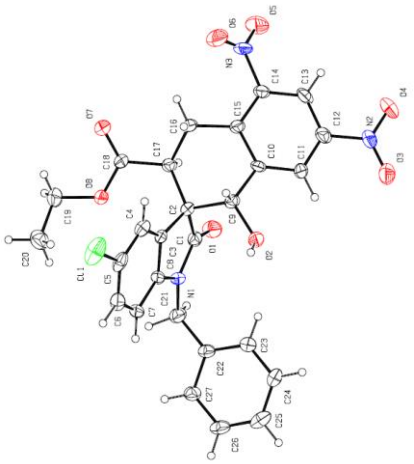


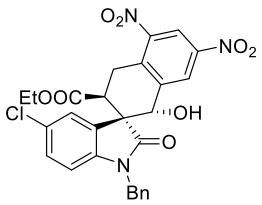


Int-4d

Identification code	**Int-4d**
Empirical formula	$C_{60}H_{72}Cl_2N_6O_{22}Si_2$
Formula weight	1356.31
Temperature/K	296.15
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a/Å	13.8238(10)
b/Å	16.1894(12)

c/Å	31.377(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	7022.2(9)
Z	4
ρ_{calc}g/cm^3	1.283
μ/mm	0.202
F(000)	2848.0
Crystal size/mm^3	0.298 × 0.217 × 0.2
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.976 to 55.17
Index ranges	$-18 \le h \le 17$, $-19 \le k \le 21$, $-40 \le l \le 40$
Reflections collected	109326
Independent reflections	16190 [R_{int} = 0.0982, R_{sigma} = 0.1084]
Data/restraints/parameters	16190/618/896
Goodness-of-fit on F^2	0.886
Final R indexes [I>=2σ (I)]	R_1 = 0.0456, wR_2 = 0.0985
Final R indexes [all data]	R_1 = 0.1613, wR_2 = 0.1229
Largest diff. peak/hole / e Å^{-3}	0.31/−0.17
Flack parameter	0.02(2)

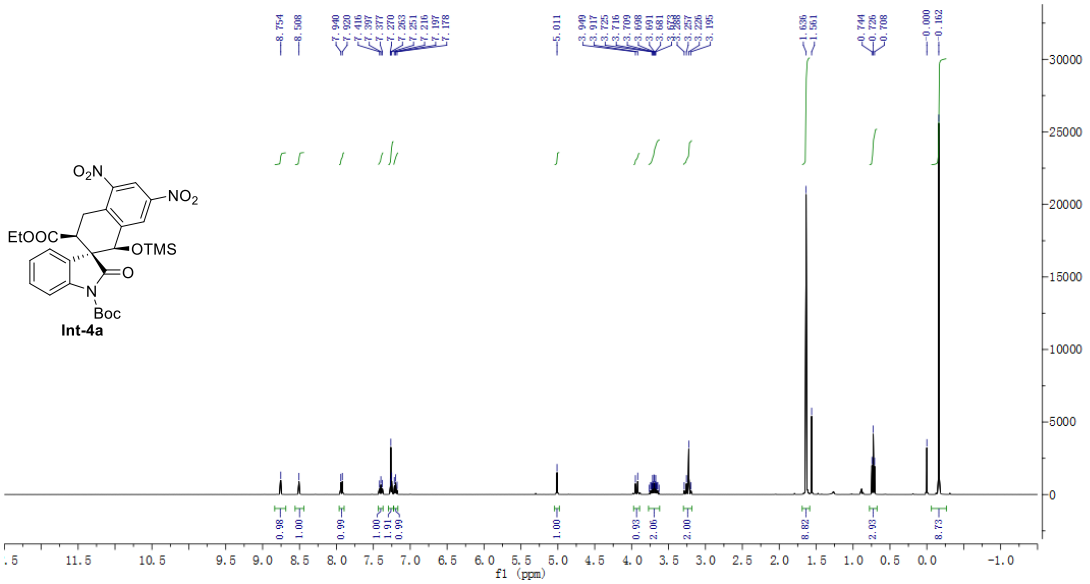


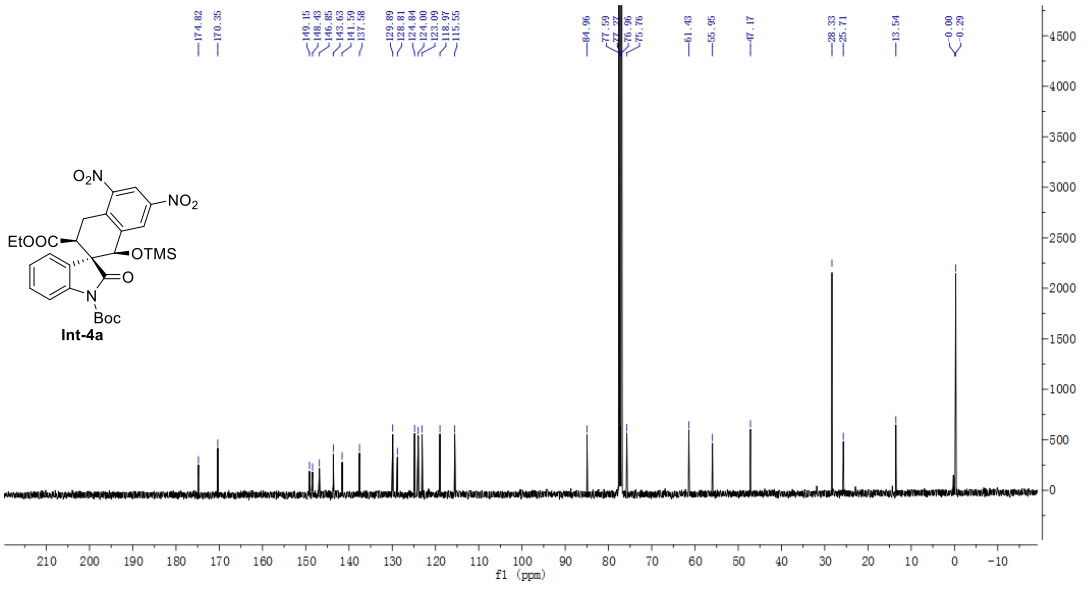


Identification code	The TMS protecting group of **int-4d′** was removed
Empirical formula	$C_{27}H_{22}ClN_3O_8$
Formula weight	551.92
Temperature/K	150
Crystal system	Triclinic

Space group	P1
a/Å	7.5537(7)
b/Å	12.8817(11)
c/Å	13.5102(13)
α/°	107.124(8)
β/°	94.728(8)
γ/°	90.025(7)
Volume/Å^3	1251.6(2)
Z	2
ρ_{calc}g/cm^3	1.464
μ/mm^{-1}	0.211
F(000)	572.0
Crystal size/mm^3	0.4 × 0.3 × 0.3
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.032 to 58.466
Index ranges	$-10 \le h \le 10$, $-15 \le k \le 16$, $-18 \le l \le 18$
Reflections collected	7683
Independent reflections	7683 [R_{int} = ?, R_{sigma} = 0.0594]
Data/restraints/parameters	7683/3/708
Goodness-of-fit on F^2	0.913
Final R indexes [I ≥ 2σ (I)]	R_1 = 0.0465, wR_2 = 0.1021
Final R indexes [all data]	R_1 = 0.0745, wR_2 = 0.1093
Largest diff. peak/hole / e Å^{-3}	0.26/−0.21
Flack parameter	0.26(5)

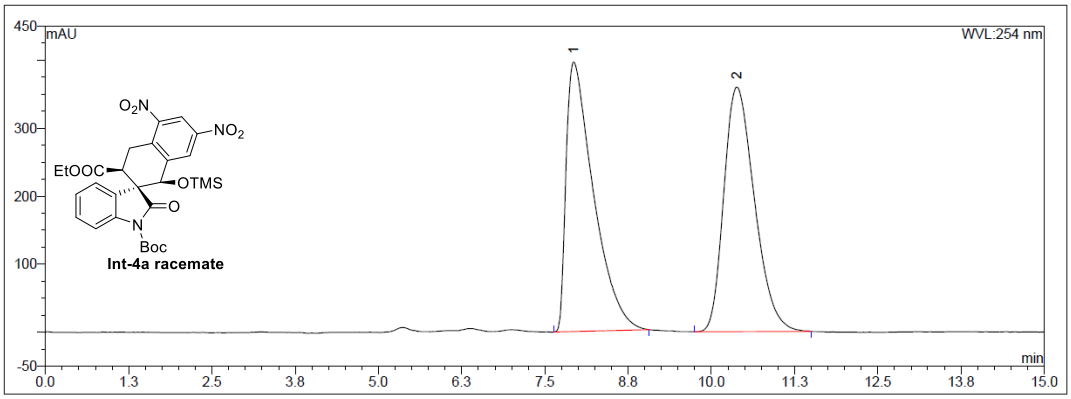
13. NMR spectra and HPLC of THN-fused spirooindole derivatives int-4 and int-4′





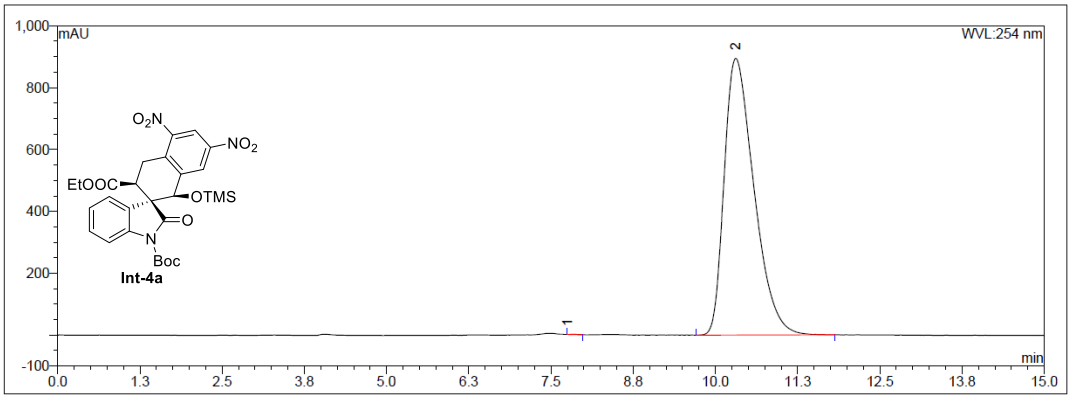
Peak Analysis Report

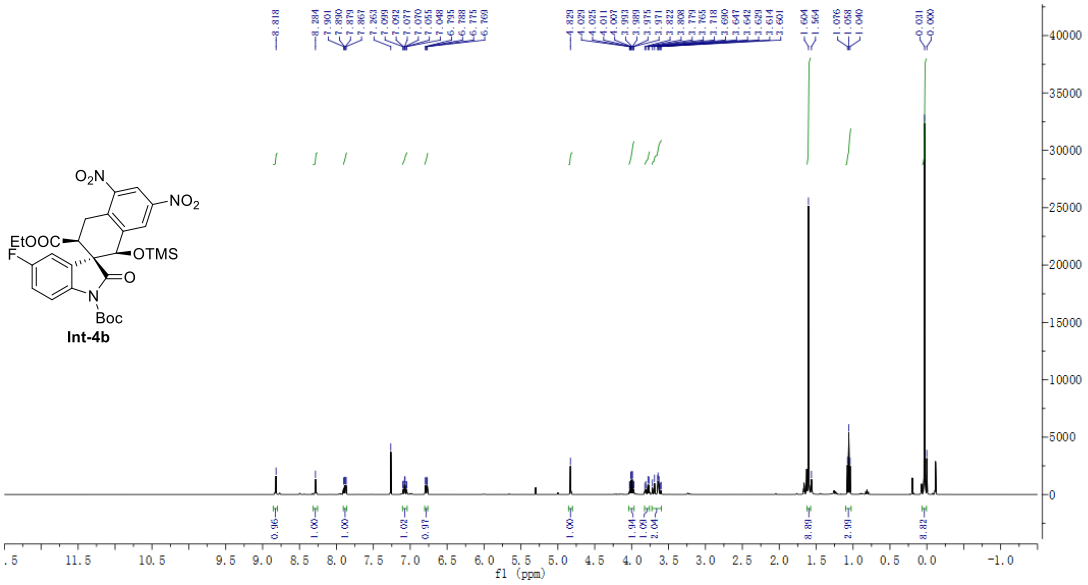
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.93	188.920	49.62	396.118	n.a.
2	n.a.	10.38	191.835	50.38	359.560	n.a.

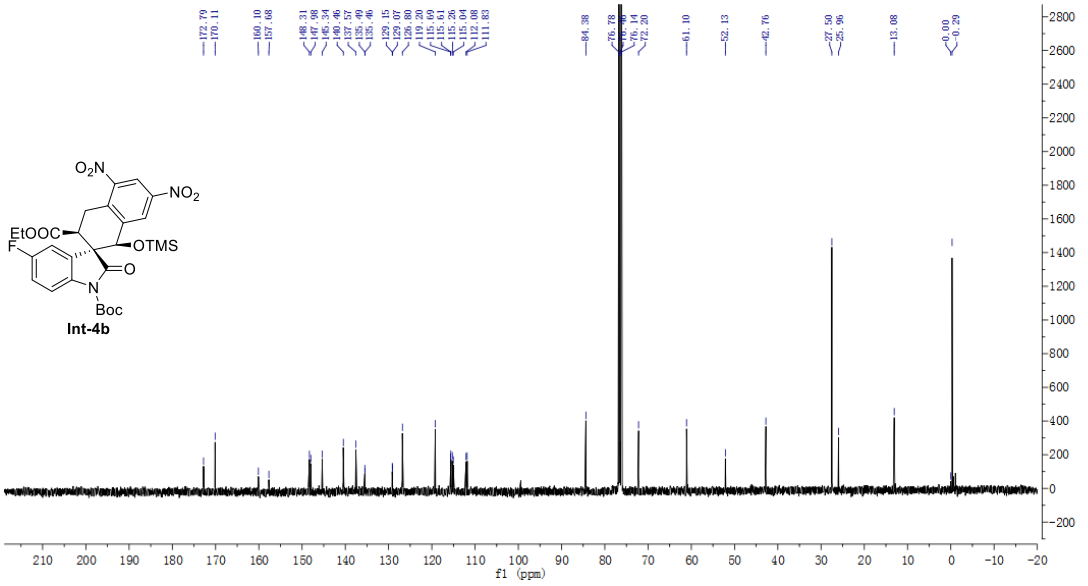


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.75	0.079	0.02	0.063	n.a.
2	n.a.	10.31	470.025	99.98	894.892	n.a.

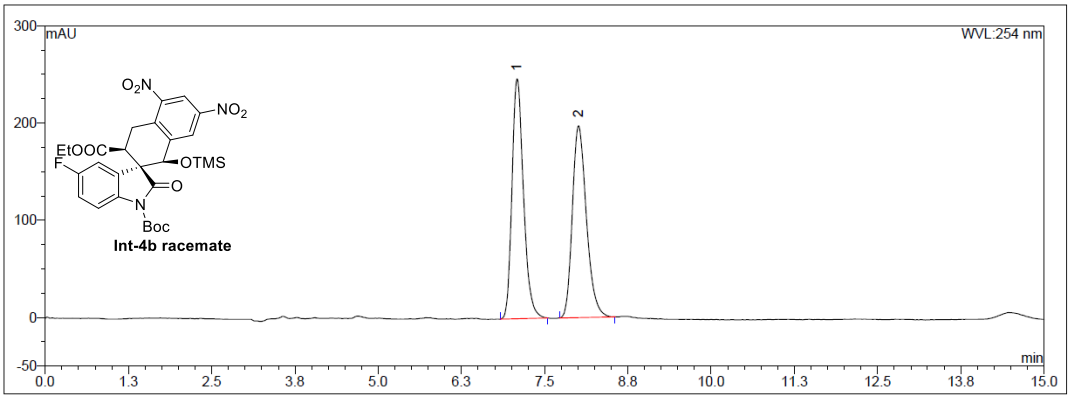



O2N
NO2
EtOOC
F
OTMS
O
N
Boc
Int-4b
f1 (ppm)


O2N
NO2
EtOOC
F
OTMS
O
N
Boc
Int-4b
f1 (ppm)

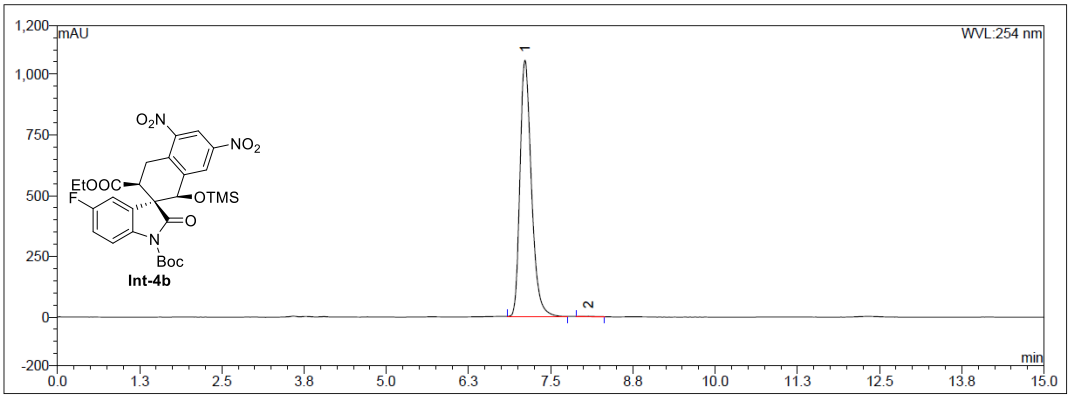
Peak Analysis Report

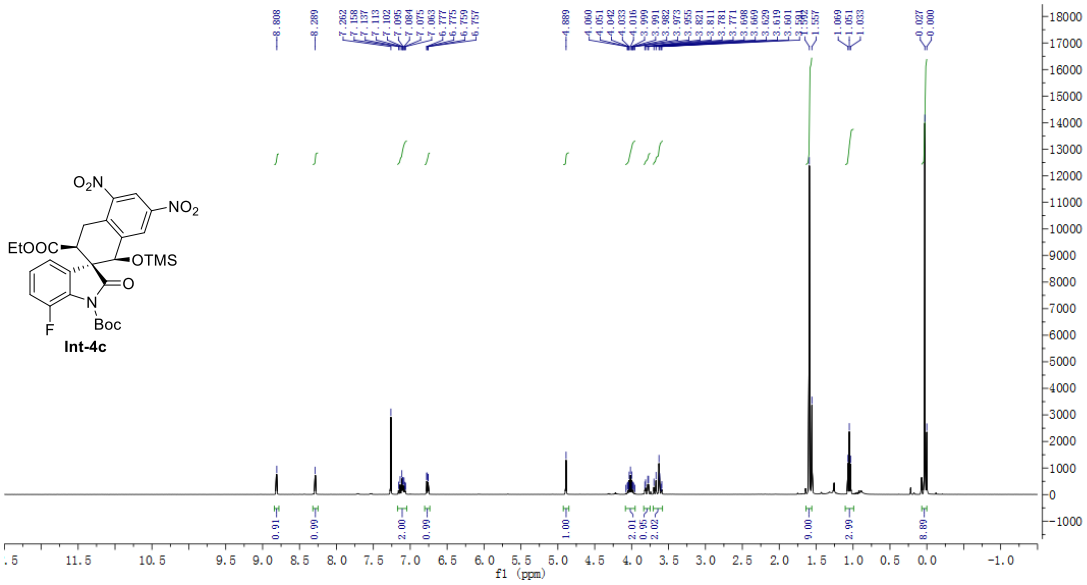
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.08	49.414	50.61	246.796	n.a.
2	n.a.	8.01	48.229	49.39	197.520	n.a.

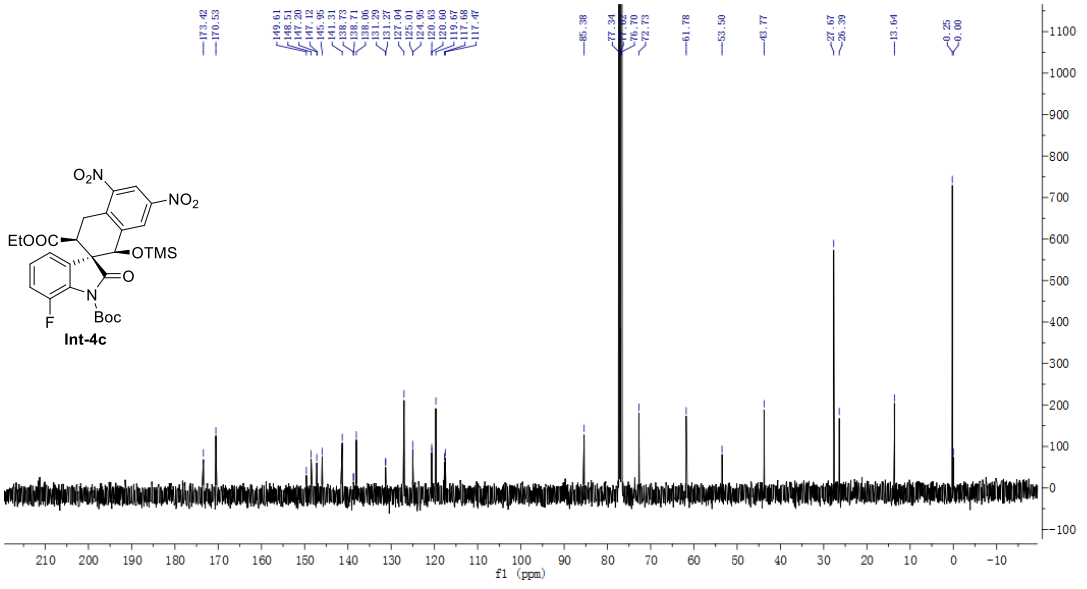


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.11	212.380	99.90	1054.584	n.a.
2	n.a.	8.08	0.217	0.10	1.098	n.a.

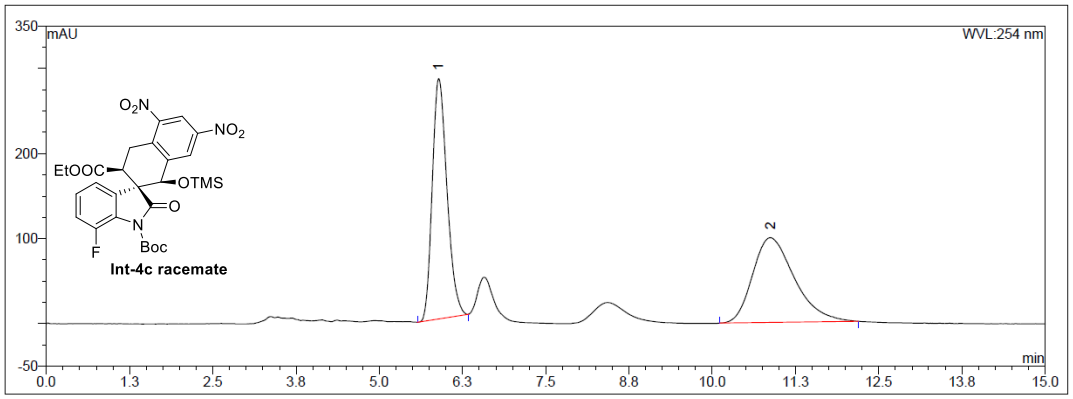



O2N
NO2
EtOOC
OTMS
O
N
Boc
F
Int-4c
f1 (ppm)


O2N
NO2
EtOOC
OTMS
O
N
Boc
F
Int-4c
f1 (ppm)

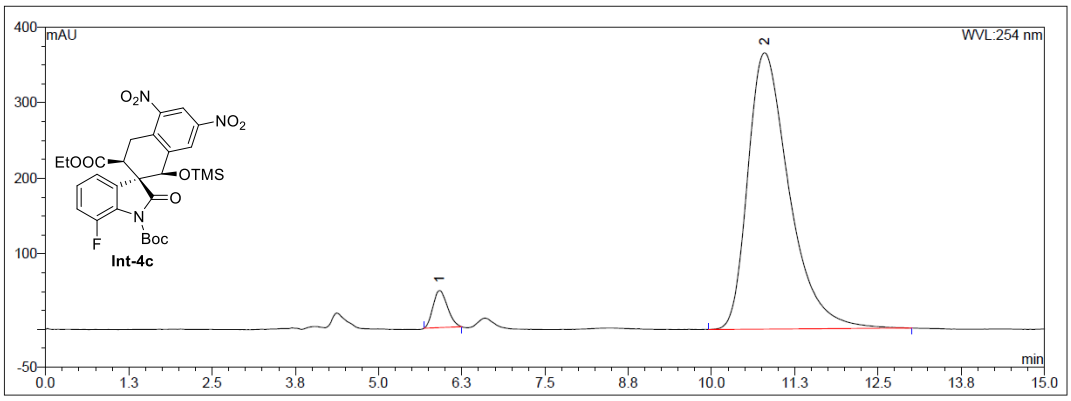
Peak Analysis Report

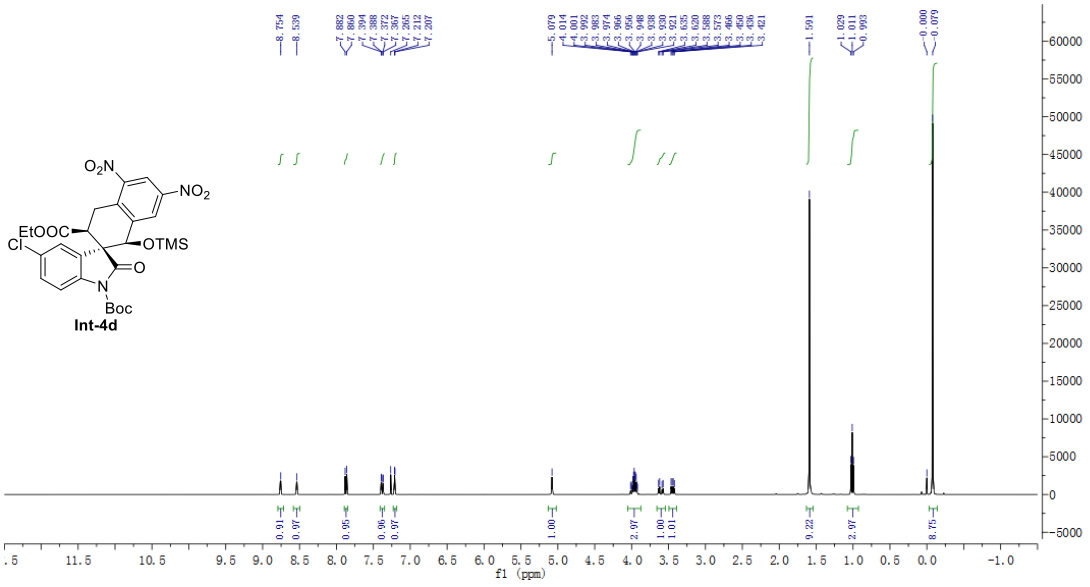
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.89	72.554	49.99	282.716	n.a.
2	n.a.	10.88	72.588	50.01	99.644	n.a.

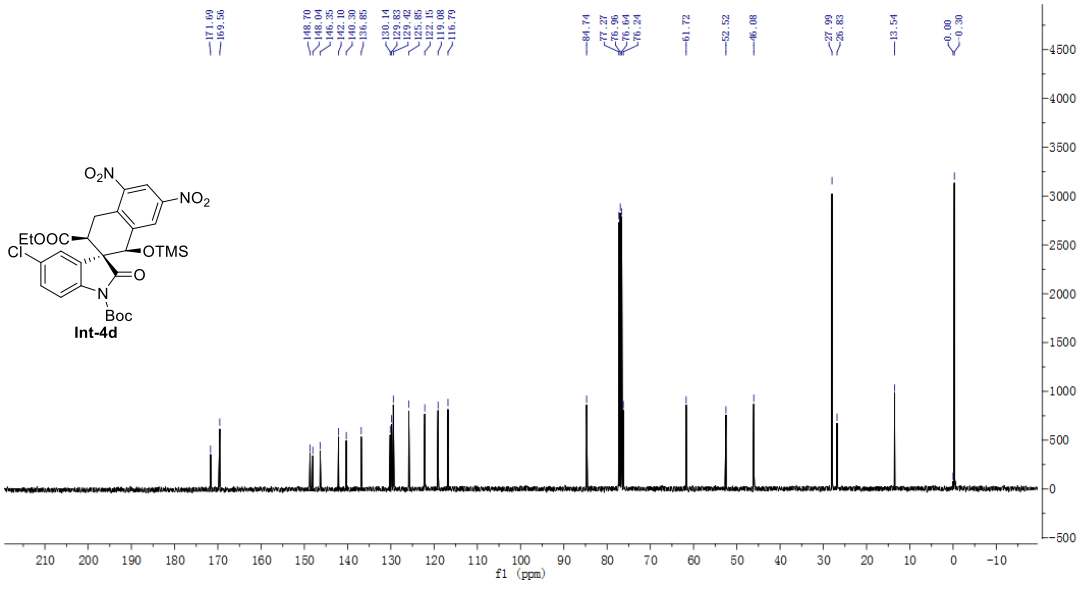


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.92	12.338	4.47	49.097	n.a.
2	n.a.	10.80	263.450	95.53	365.673	n.a.

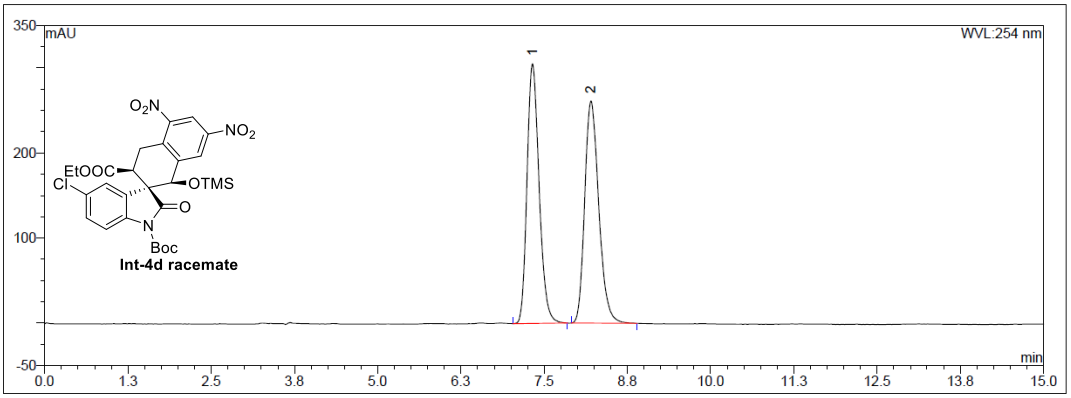



Int-4d


Int-4d

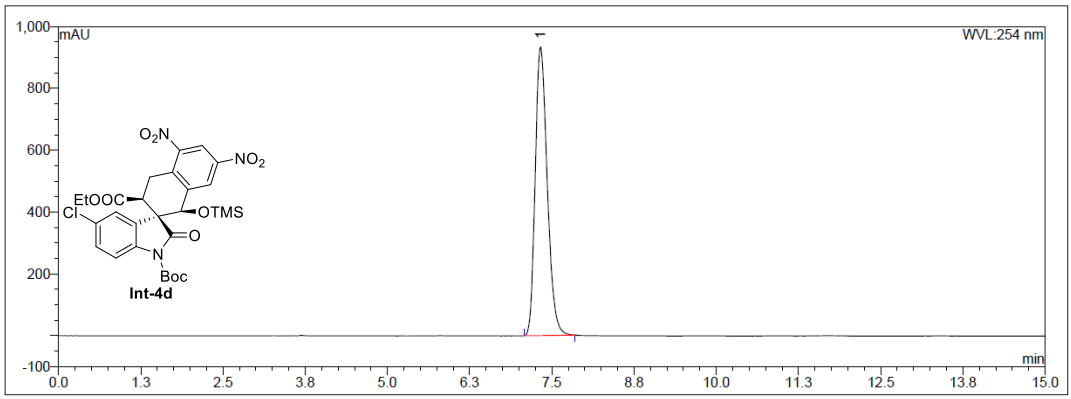
Peak Analysis Report

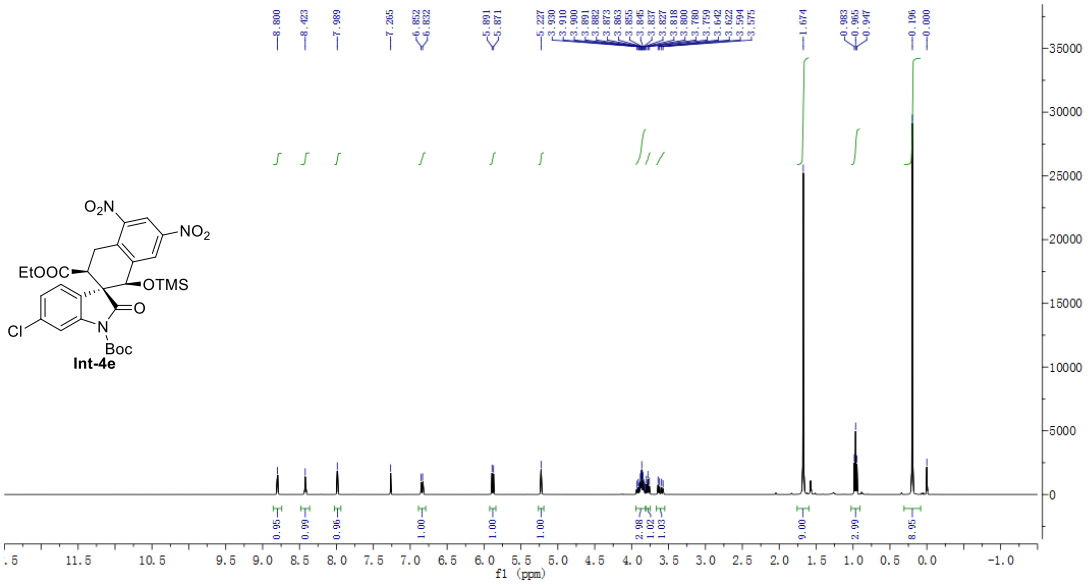
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.33	64.167	50.05	305.463	n.a.
2	n.a.	8.20	64.036	49.95	261.098	n.a.

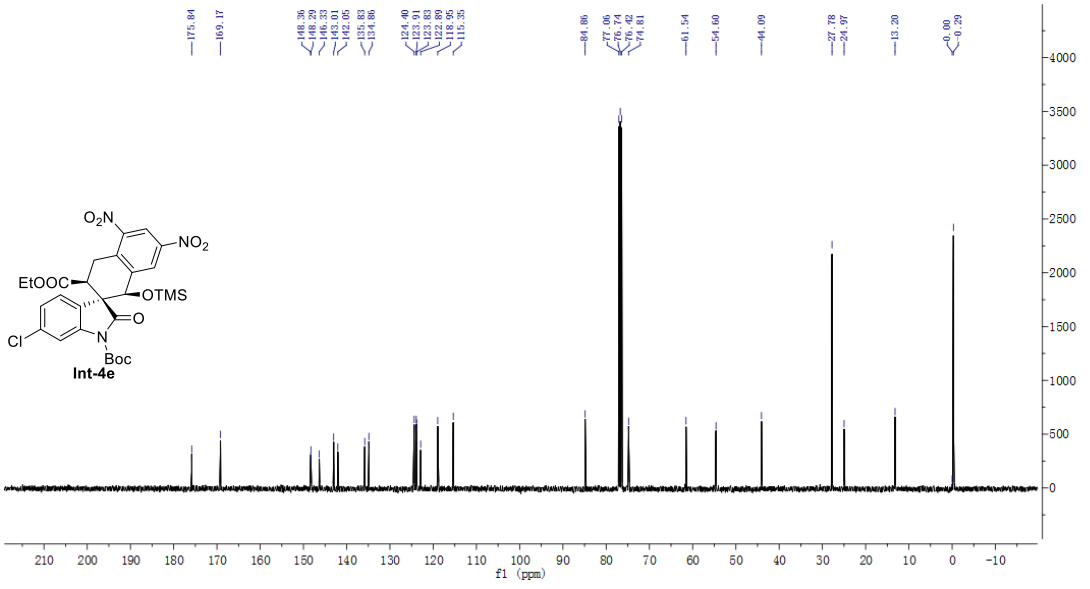


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.33	197.871	100.00	933.311	n.a.

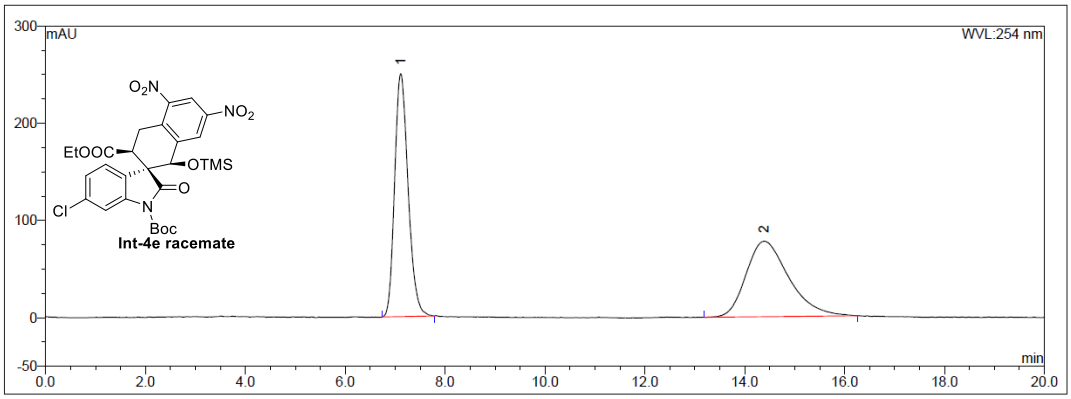



8.800
8.423
7.989
7.285
6.852
6.832
5.891
5.871
5.227
1.074
0.983
0.966
0.947
0.196
0.000
O2N
NO2
EtOOC
OTMS
O
Cl
N
Boc
Int-4e
f1 (ppm)


175.84
169.17
148.36
148.29
146.33
143.01
142.05
135.83
134.86
124.40
123.91
123.83
122.89
118.95
115.35
84.86
77.06
76.74
76.42
74.81
61.54
54.60
44.09
27.78
24.97
13.20
0.00
0.29
O2N
NO2
EtOOC
OTMS
O
Cl
N
Boc
Int-4e
f1 (ppm)

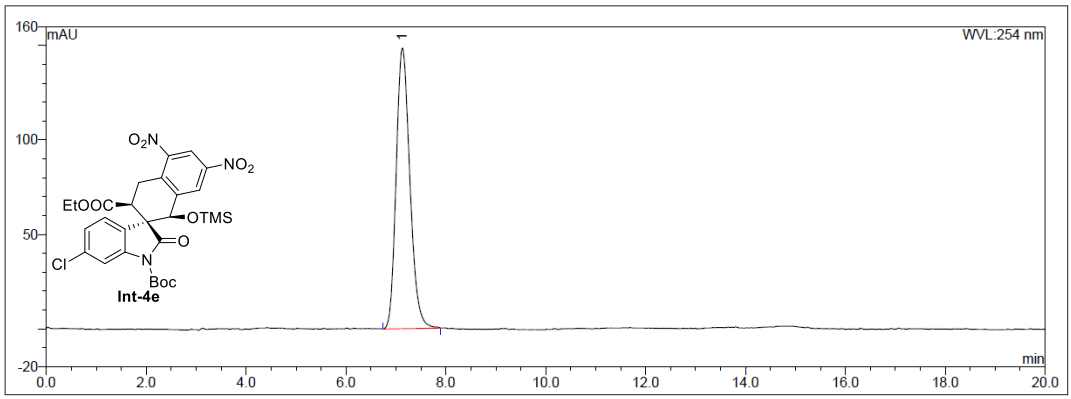
Peak Analysis Report

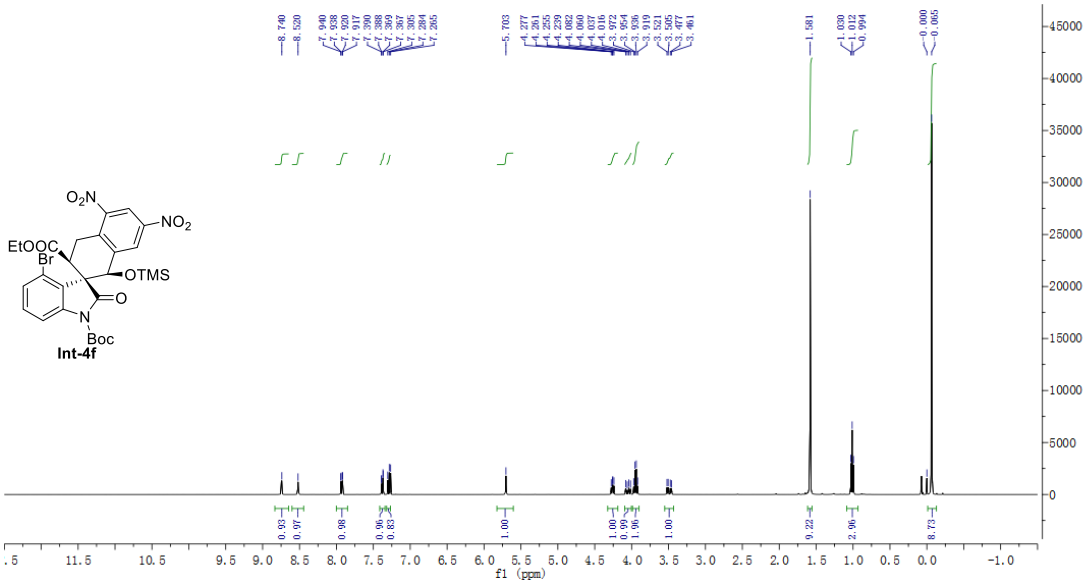
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.11	78.290	50.36	250.015	n.a.
2	n.a.	14.38	77.183	49.64	77.709	n.a.

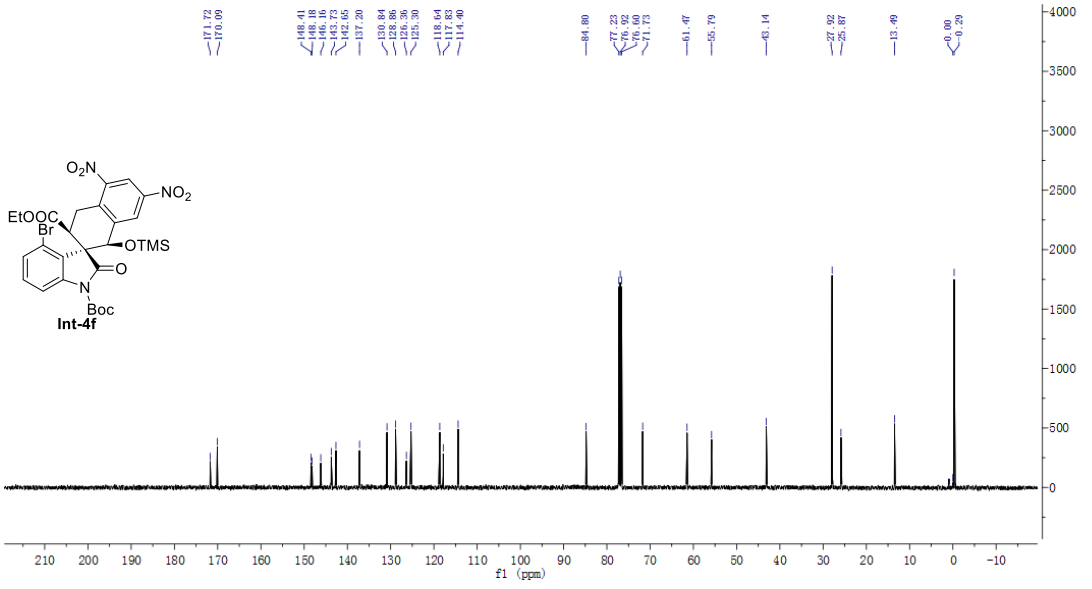


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.13	47.295	100.00	148.462	n.a.

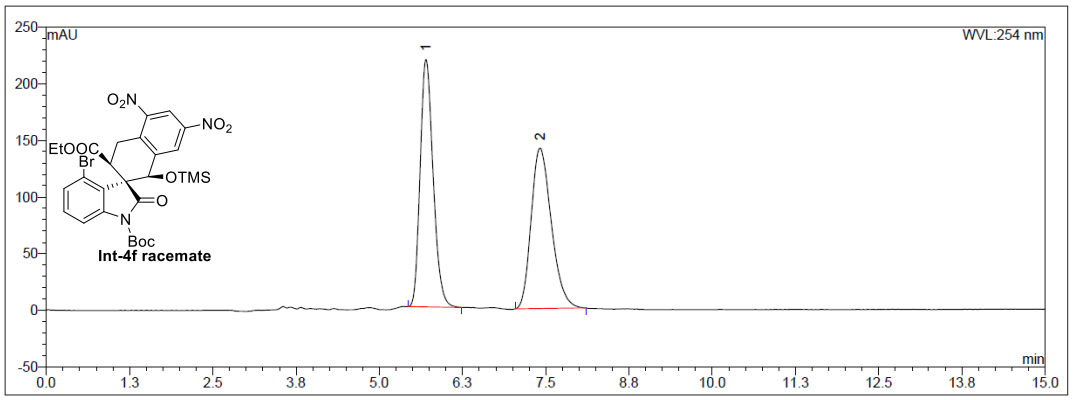



Int-4f


Int-4f

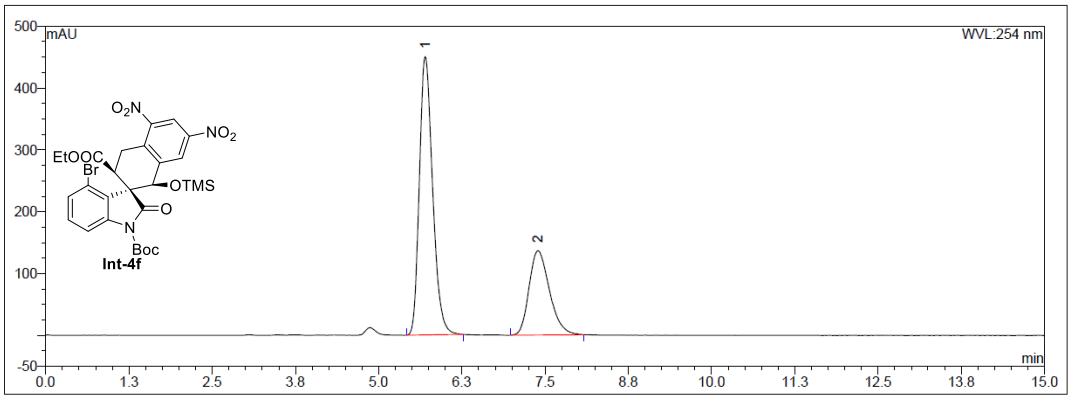
Peak Analysis Report

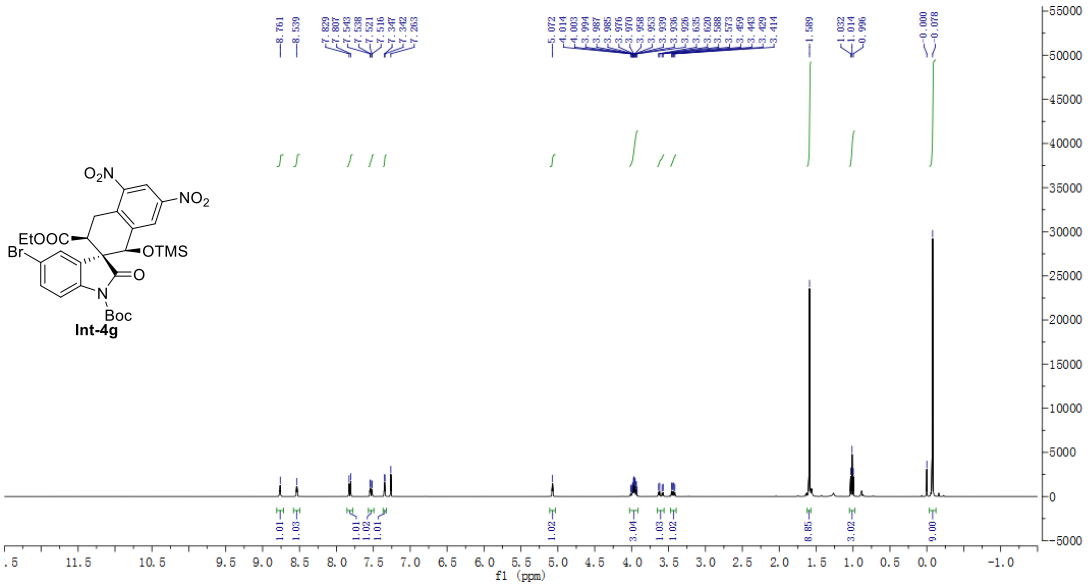
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.70	49.297	49.80	218.184	n.a.
2	n.a.	7.42	49.689	50.20	141.507	n.a.

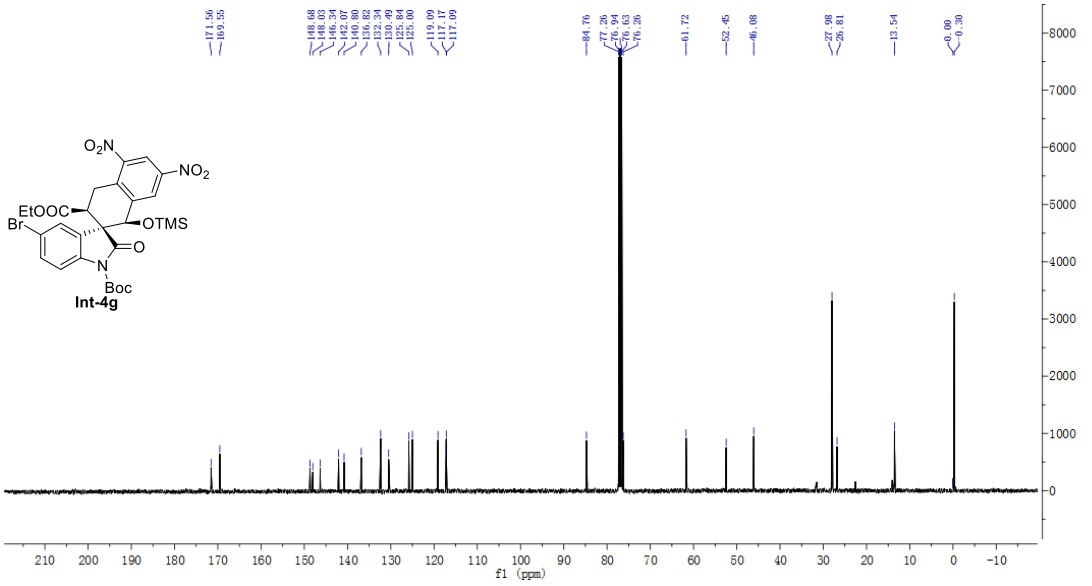


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.70	103.613	68.22	449.998	n.a.
2	n.a.	7.39	48.270	31.78	136.178	n.a.

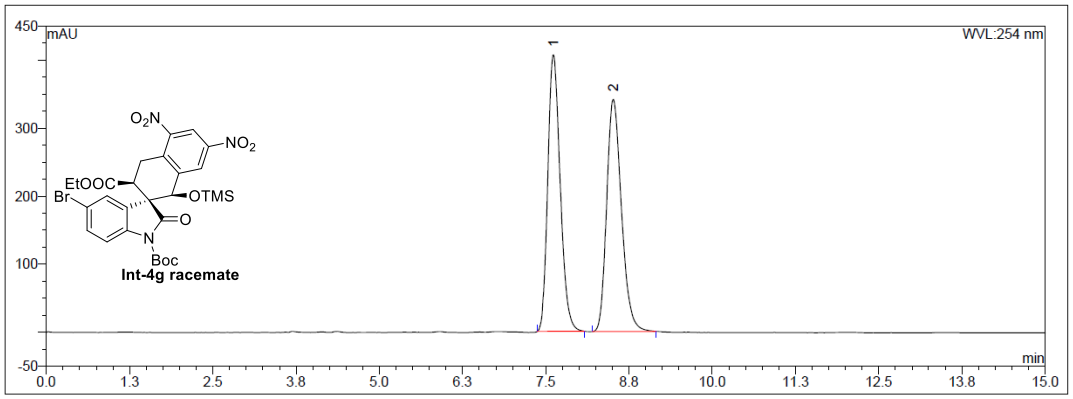



O2N
NO2
EtOOC
Br
OTMS
O
N
Boc
Int-4g
f1 (ppm)


O2N
NO2
EtOOC
Br
OTMS
O
N
Boc
Int-4g
f1 (ppm)

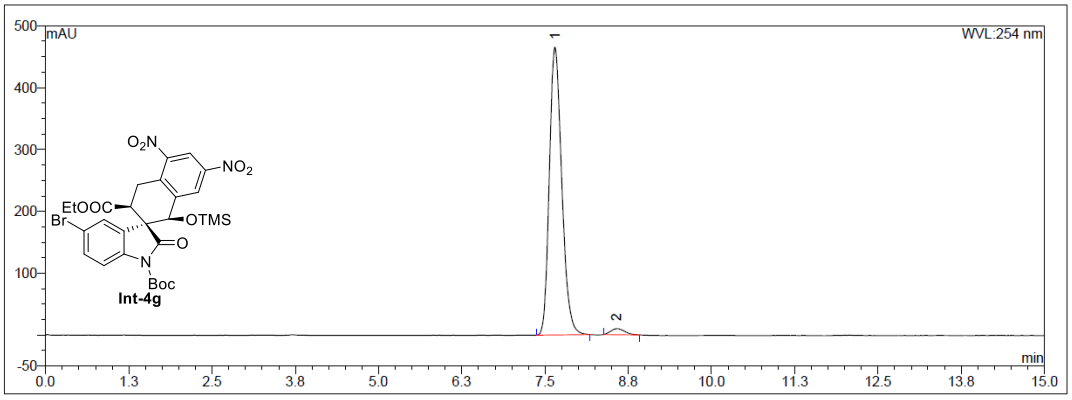
Peak Analysis Report

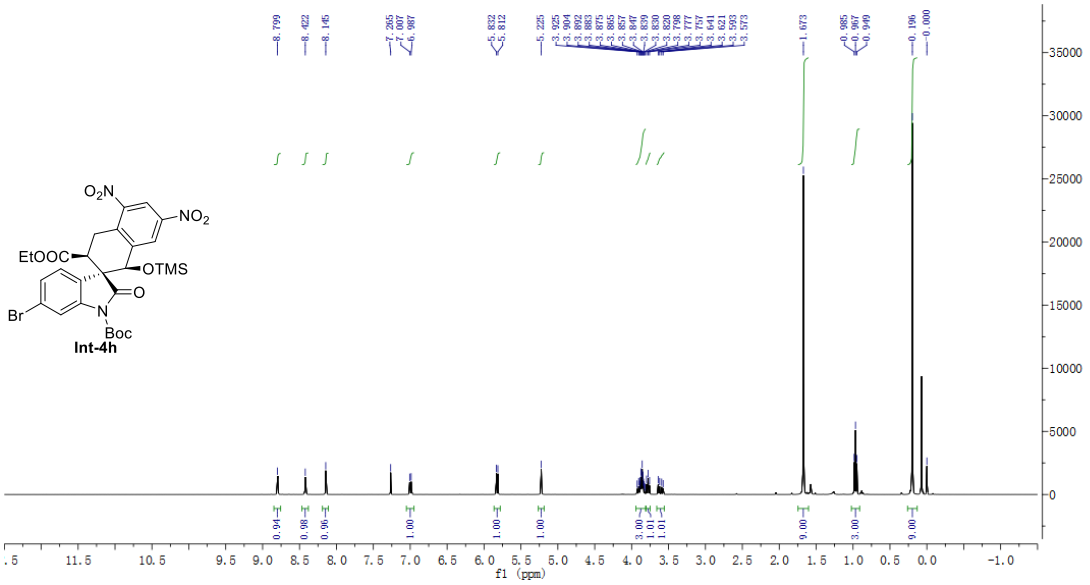
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.62	87.854	49.96	406.161	n.a.
2	n.a.	8.52	87.996	50.04	341.379	n.a.

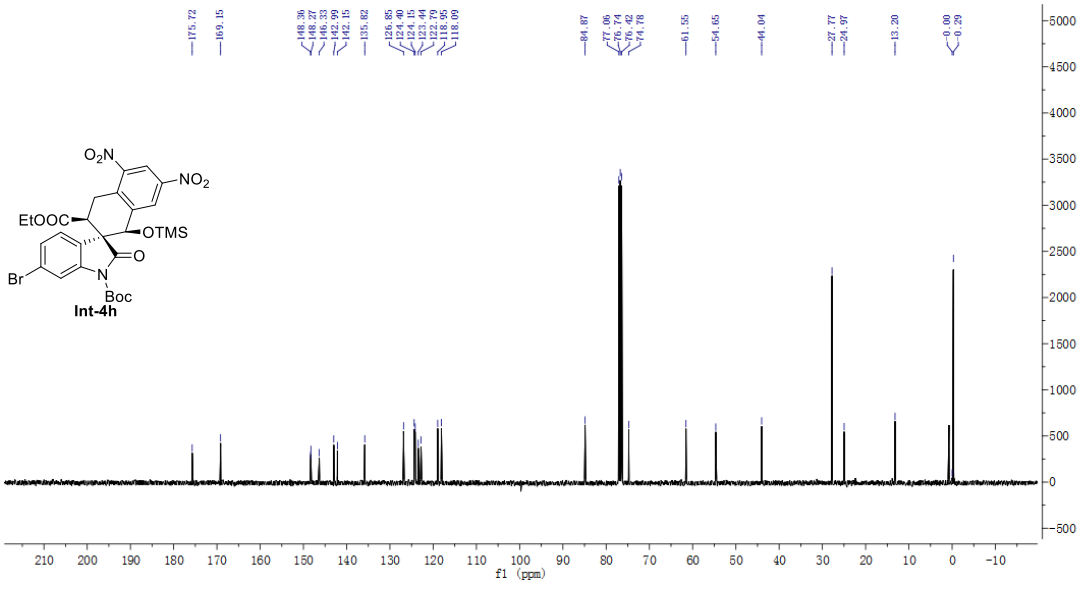


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.65	100.783	97.69	465.416	n.a.
2	n.a.	8.58	2.381	2.31	9.810	n.a.

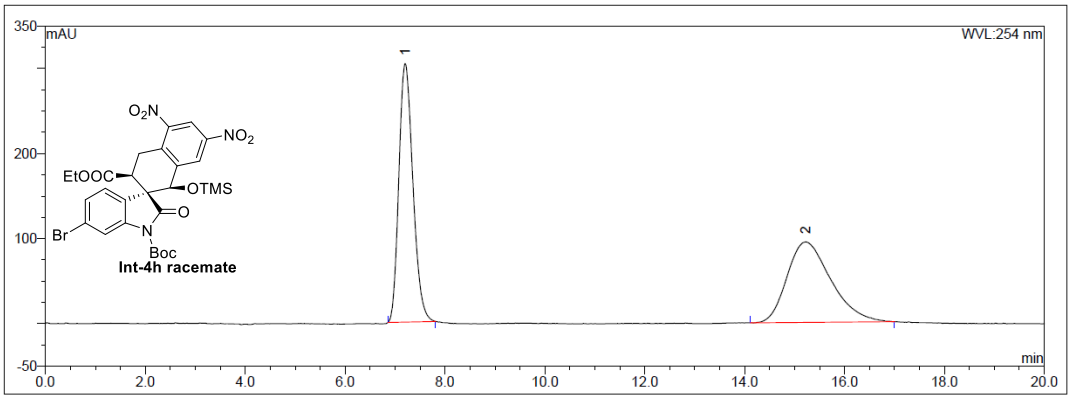



Int-4h


Int-4h

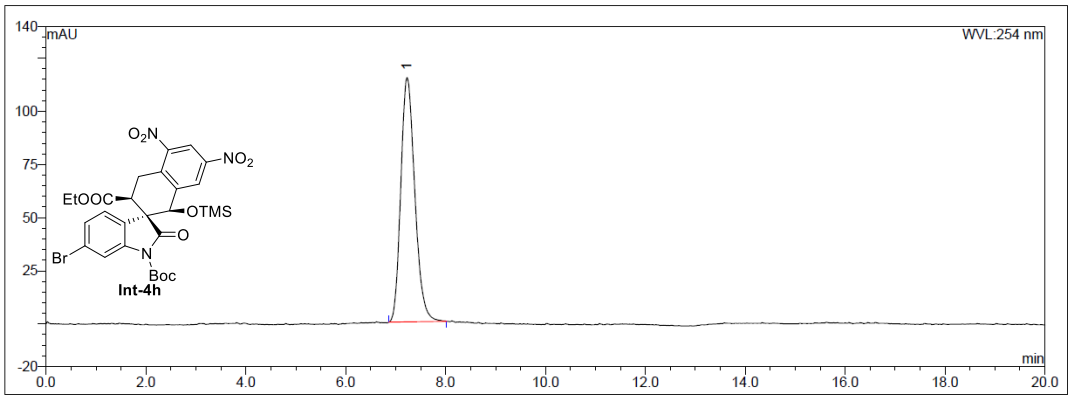
Peak Analysis Report

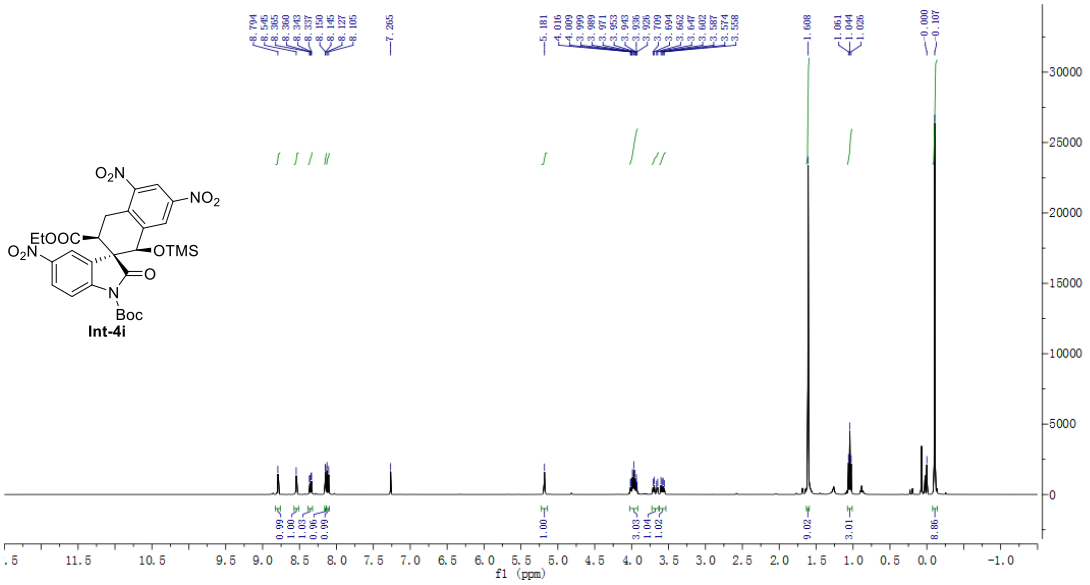
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.20	99.219	50.78	303.877	n.a.
2	n.a.	15.23	96.181	49.22	94.637	n.a.

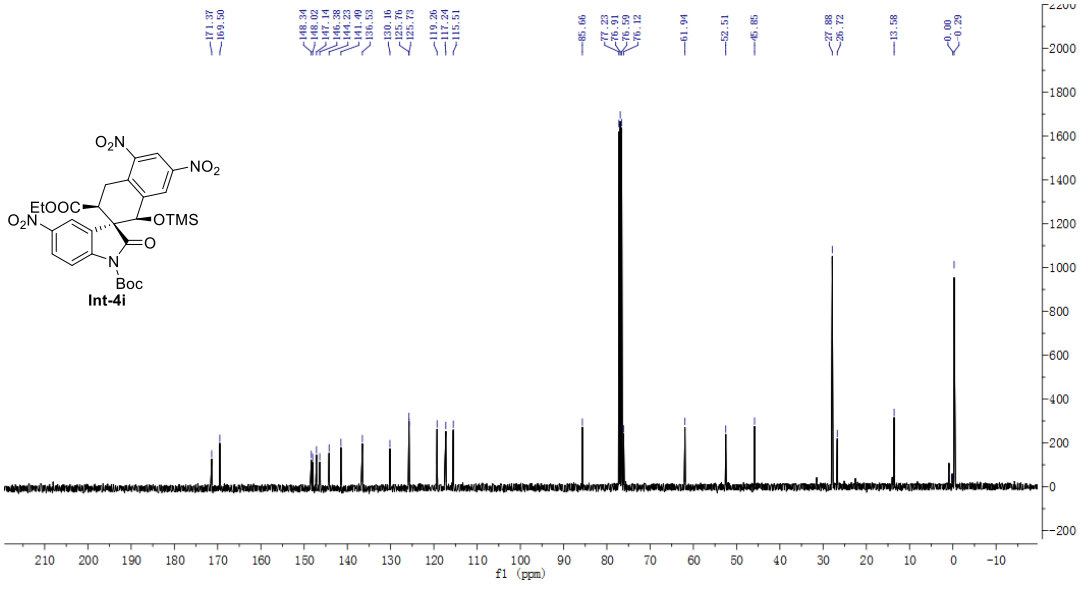


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.23	37.412	100.00	114.890	n.a.

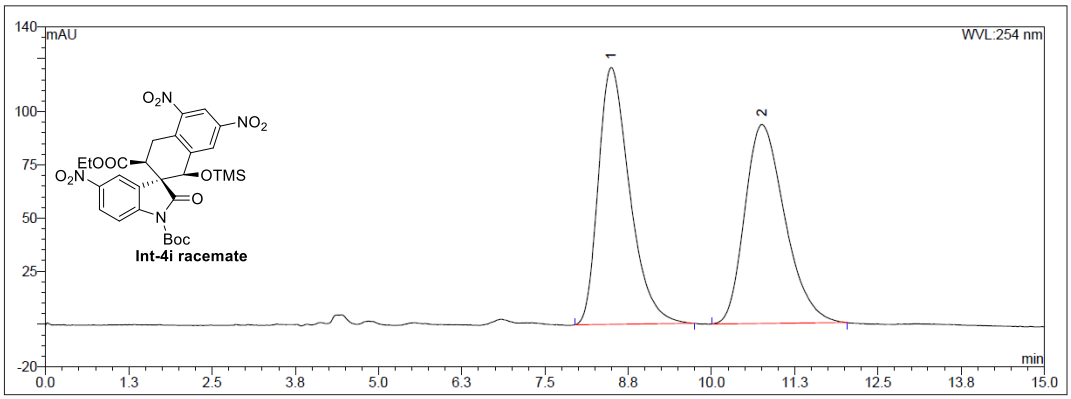



Int-4i


Int-4i

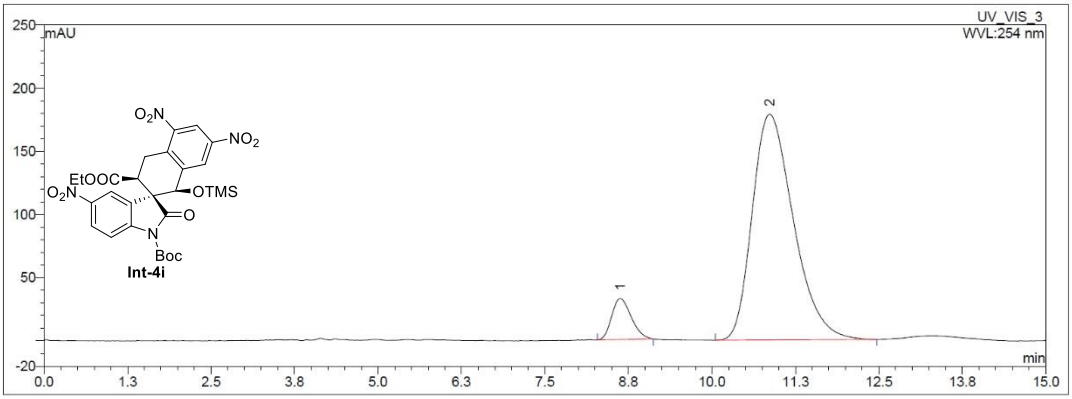
Peak Analysis Report

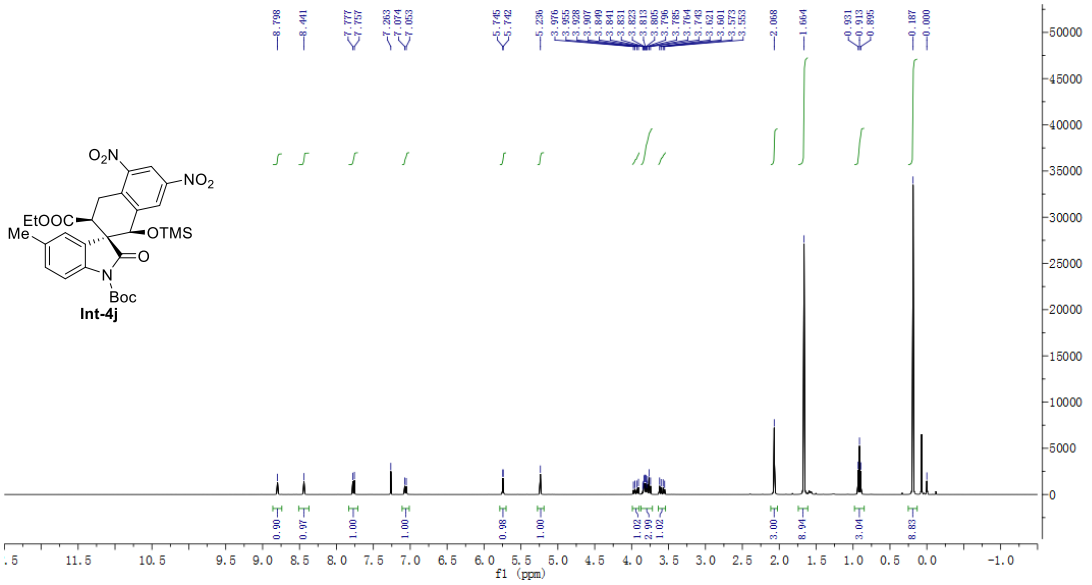
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.49	66.112	50.31	120.740	n.a.
2	n.a.	10.76	65.301	49.69	93.562	n.a.

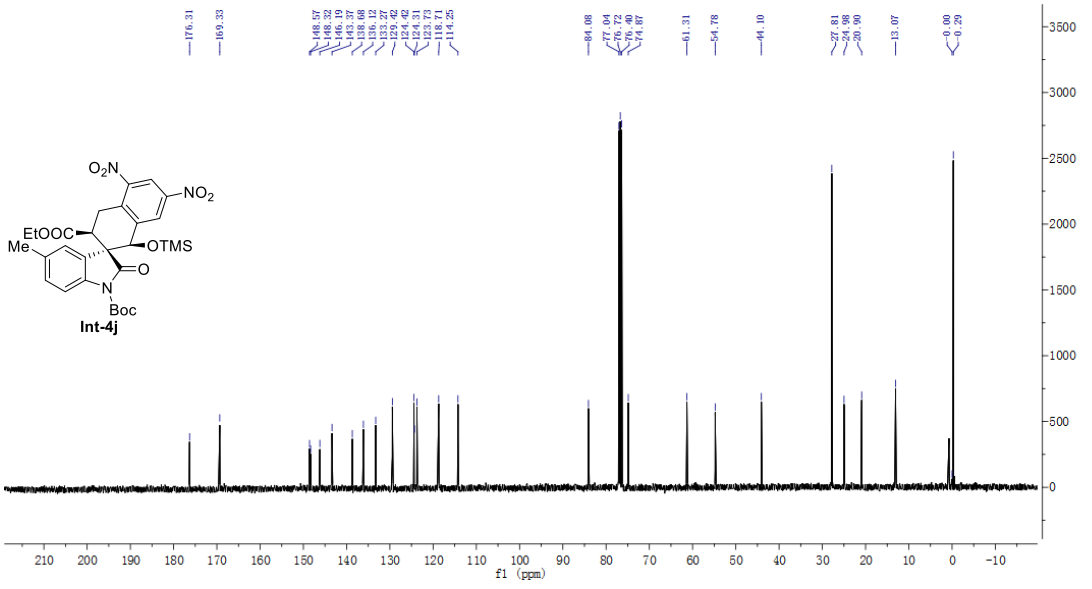


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.63	14.765	10.35	34.260	n.a.
2	n.a.	10.87	127.962	89.65	178.784	n.a.

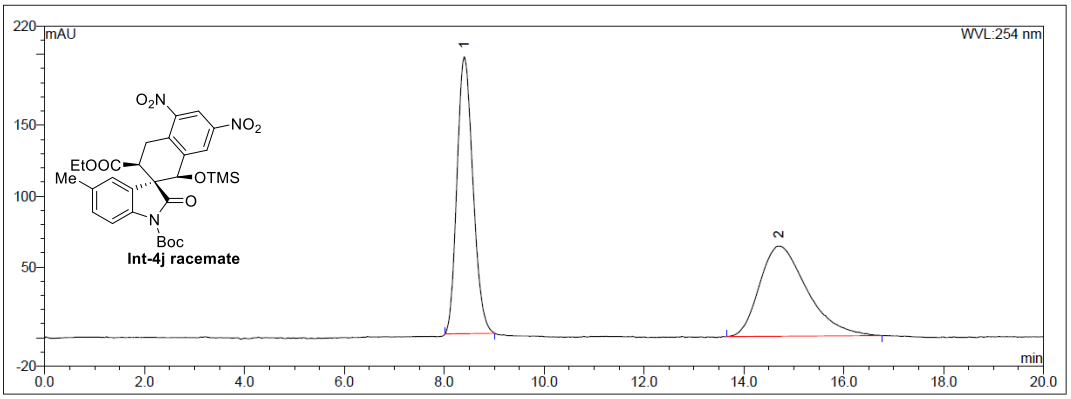



Int-4j


Int-4j

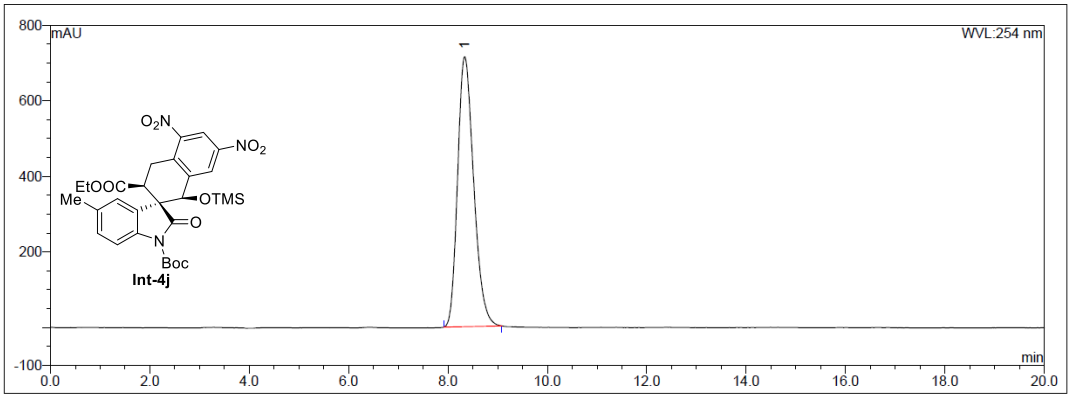
Peak Analysis Report

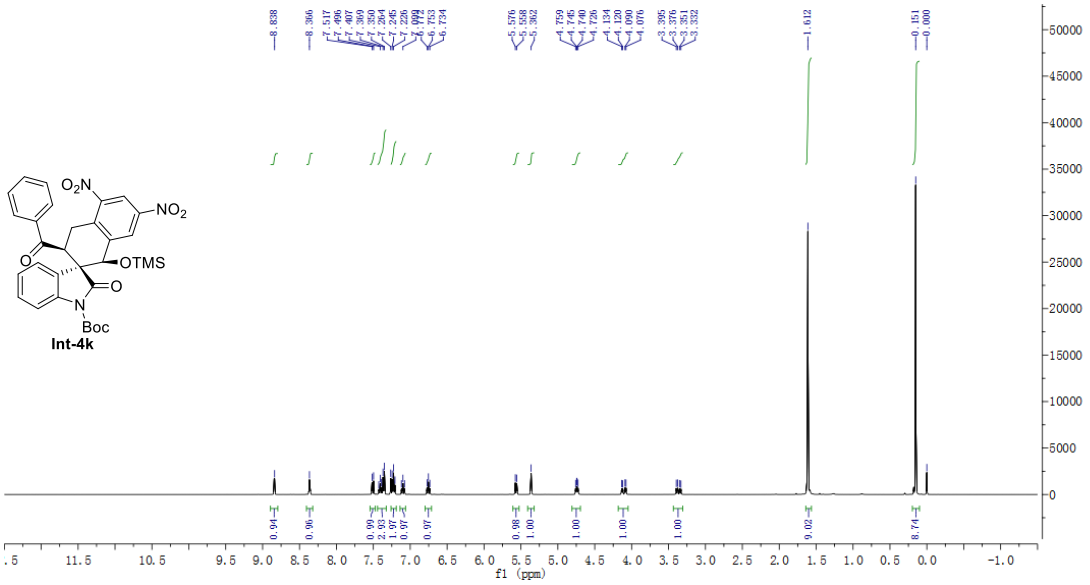
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.40	72.315	50.86	195.213	n.a.
2	n.a.	14.70	69.859	49.14	63.617	n.a.

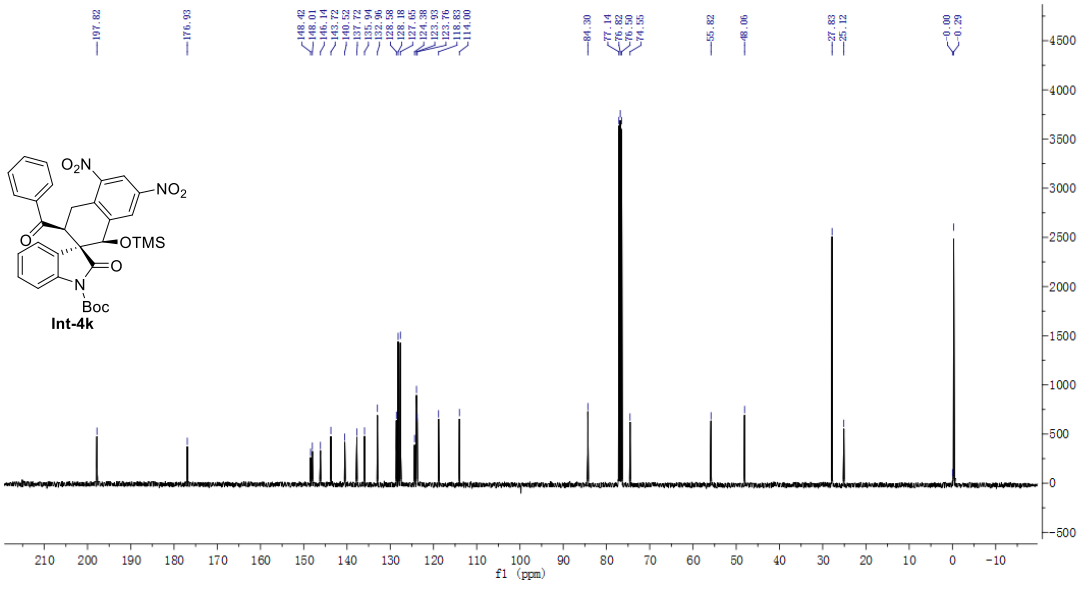


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.33	267.685	100.00	714.265	n.a.

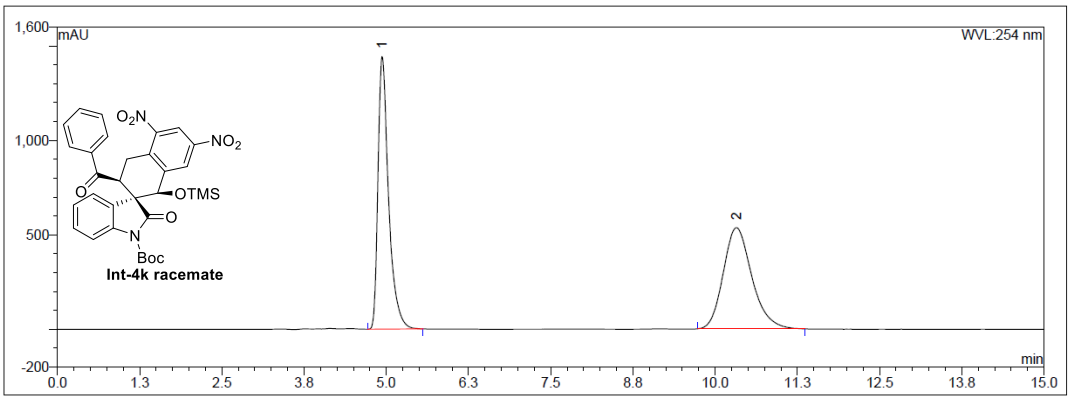



8.838
8.366
7.517
7.496
7.407
7.369
7.350
7.284
7.245
7.226
7.099
7.078
6.753
6.734
5.576
5.558
5.392
4.759
4.745
4.740
4.726
4.154
4.139
4.080
4.076
3.396
3.376
3.351
3.332
1.612
0.151
0.000
O2N
NO2
OTMS
O
O
N
Boc
Int-4k
0.94
0.96
0.99
2.93
1.97
0.97
0.97
0.98
1.00
1.00
1.00
1.00
9.02
8.74
f1 (ppm)


197.82
176.93
148.42
148.01
146.14
143.72
140.52
137.72
135.94
132.96
128.58
128.18
127.65
124.38
123.93
123.76
118.83
114.00
84.30
77.14
75.82
76.50
74.55
55.82
48.06
27.83
25.12
0.00
-0.29
O2N
NO2
OTMS
O
O
N
Boc
Int-4k
f1 (ppm)

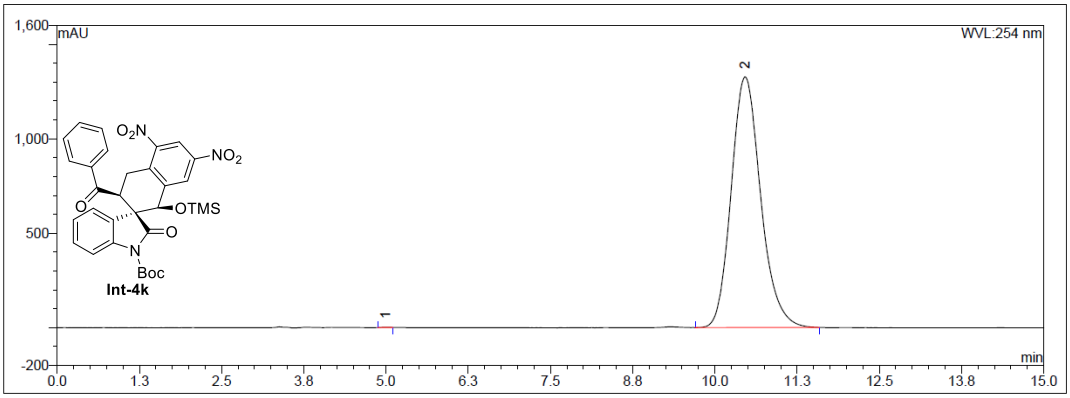
Peak Analysis Report

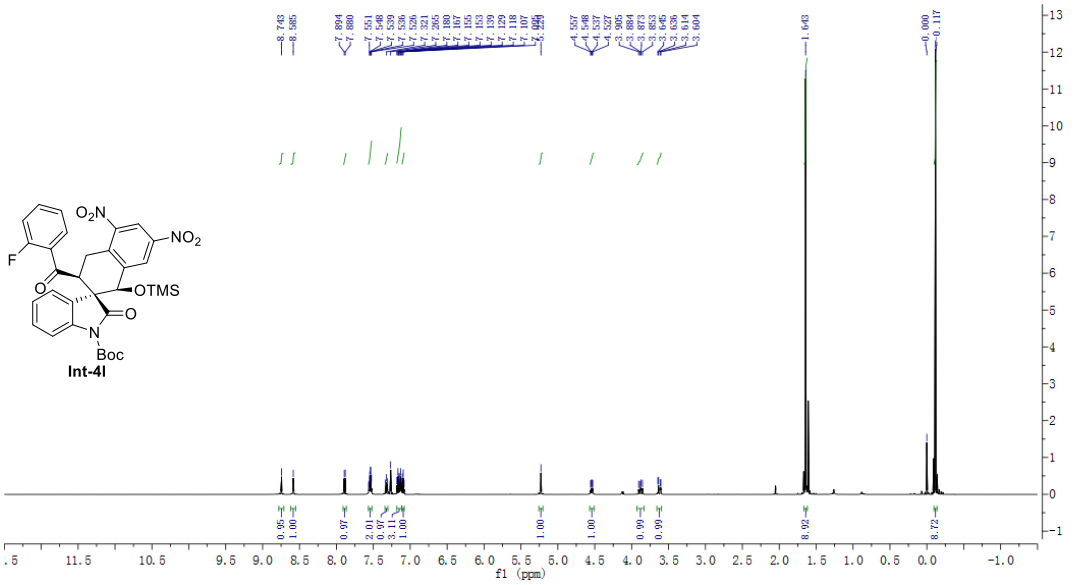
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.93	269.403	49.99	1441.705	n.a.
2	n.a.	10.33	269.493	50.01	535.329	n.a.

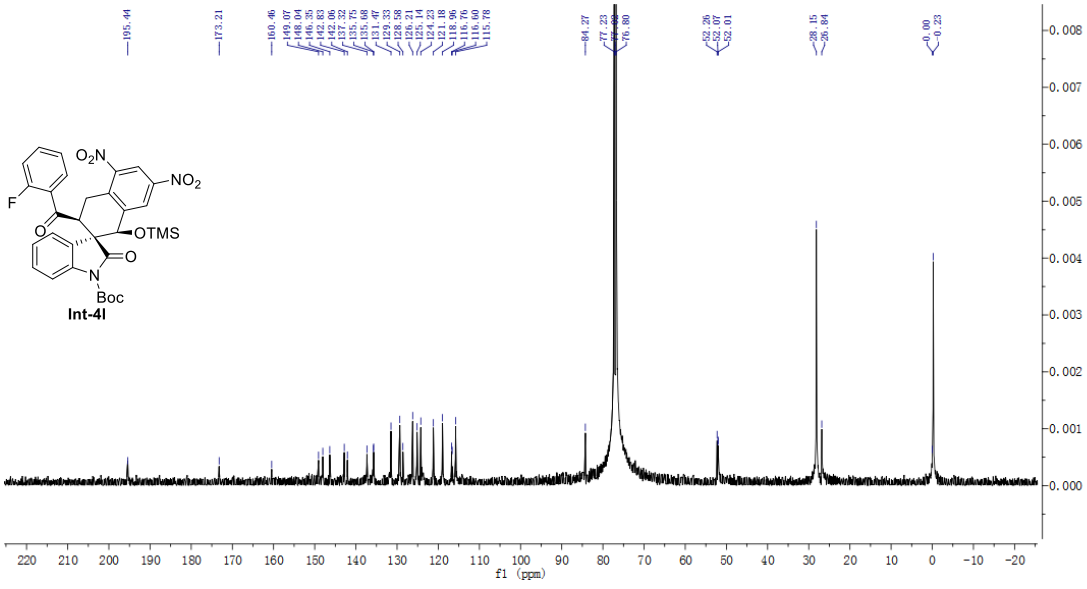


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.99	0.188	0.03	1.408	n.a.
2	n.a.	10.46	688.656	99.97	1325.707	n.a.



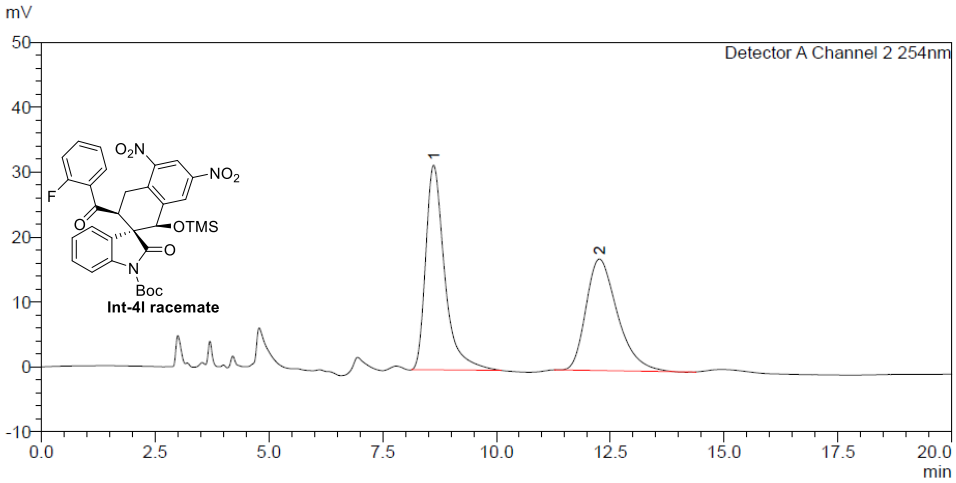

O2N
NO2
F
O
OTMS
O
N
Boc
Int-4l
f1 (ppm)


O2N
NO2
F
O
OTMS
O
N
Boc
Int-4l
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

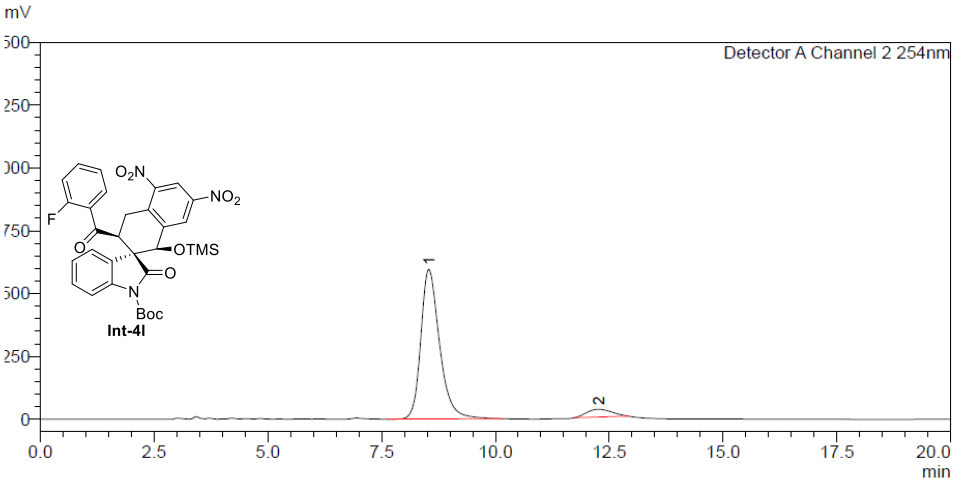
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.619	31534	914259	52.615
2	12.259	17165	823368	47.385
Total		48699	1737627	100.000

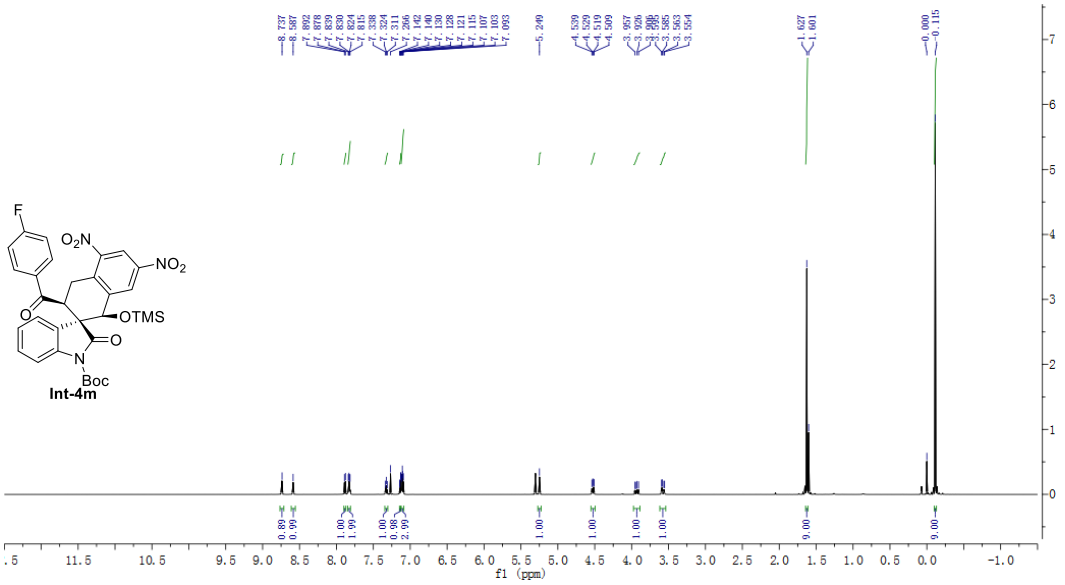


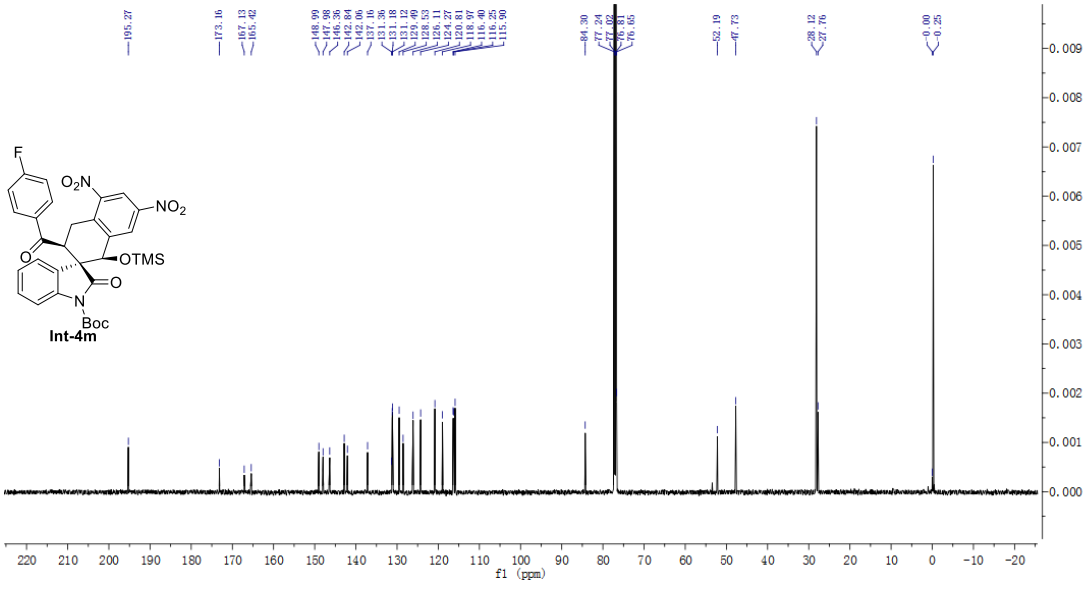
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.535	595457	17072653	93.458
2	12.266	31014	1195063	6.542
Total		626471	18267716	100.000



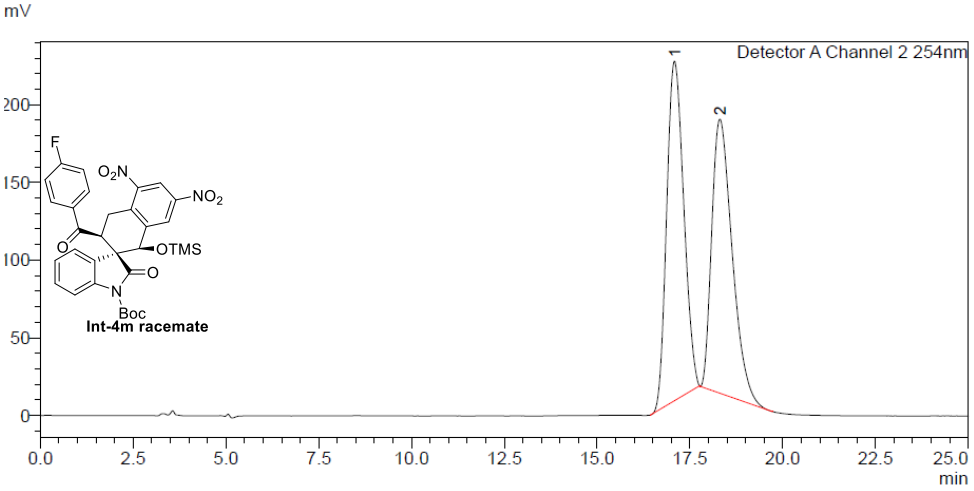

F
O2N
NO2
OTMS
O
O
N
Boc
Int-4m
f1 (ppm)


F
O2N
NO2
OTMS
O
O
N
Boc
Int-4m
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

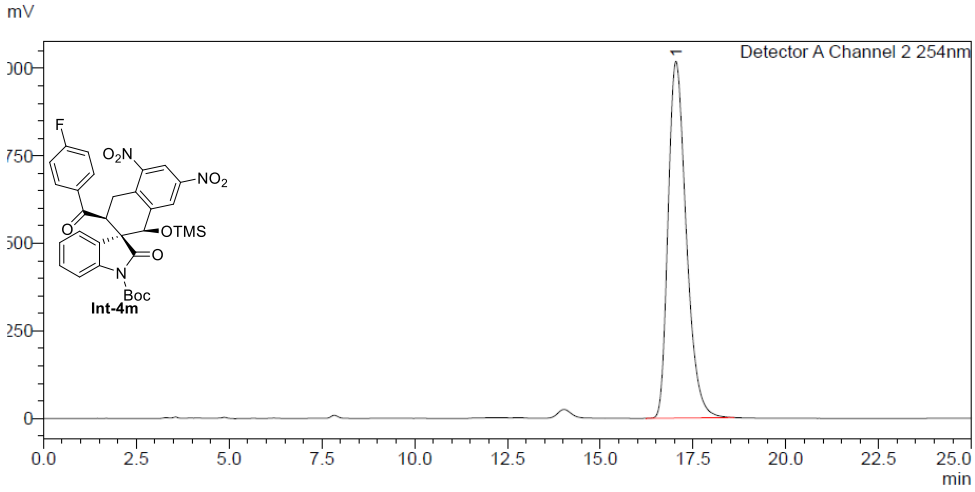
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	17.085	218372	6971526	50.853
2	18.308	176354	6737765	49.147
Total		394726	13709291	100.000

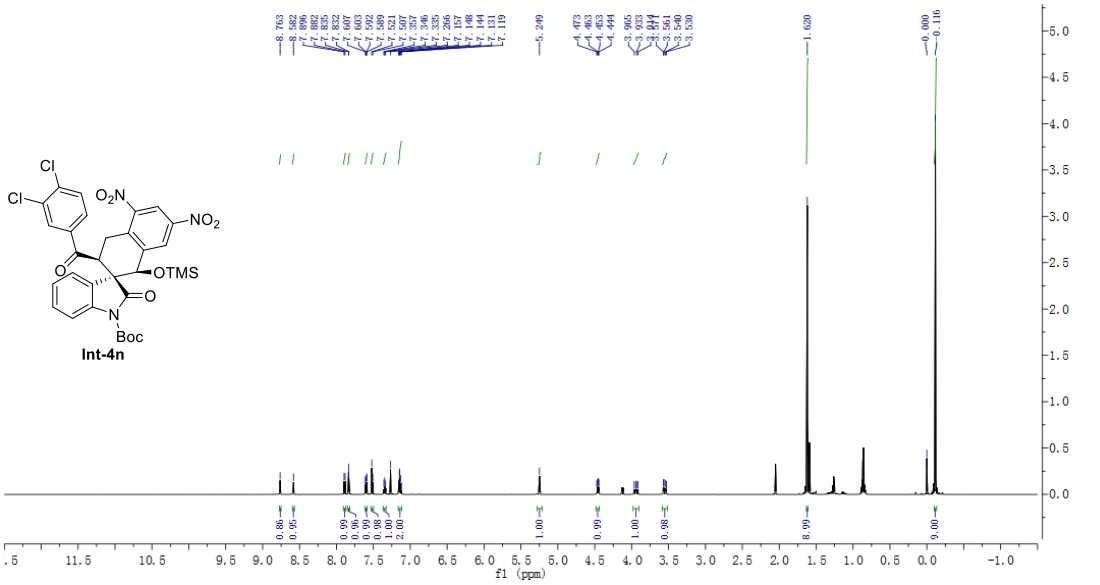


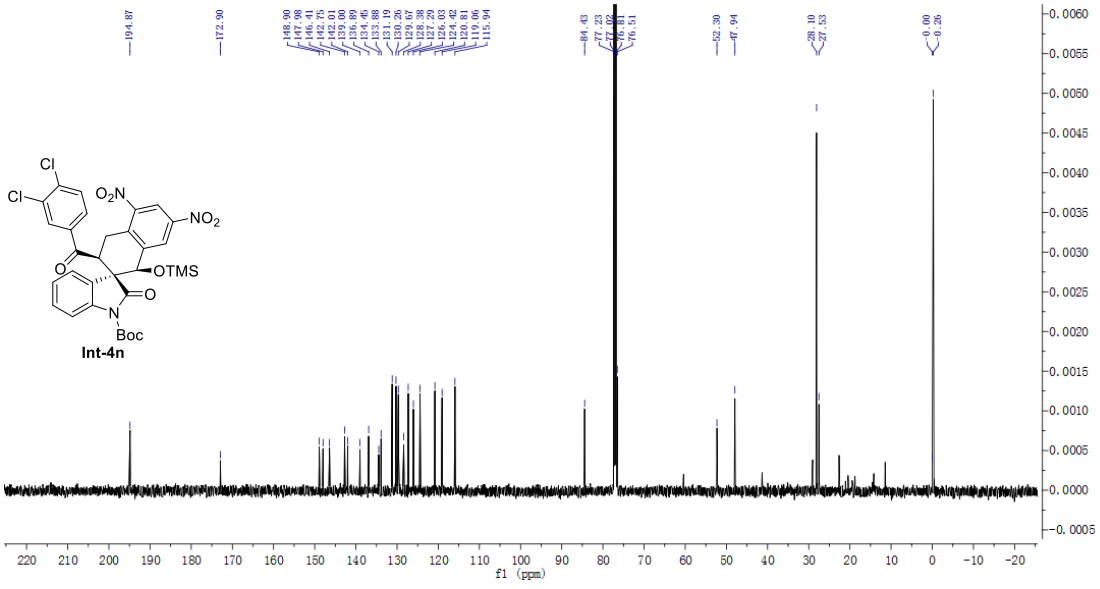
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	17.039	1019082	34697796	100.000
Total		1019082	34697796	100.000



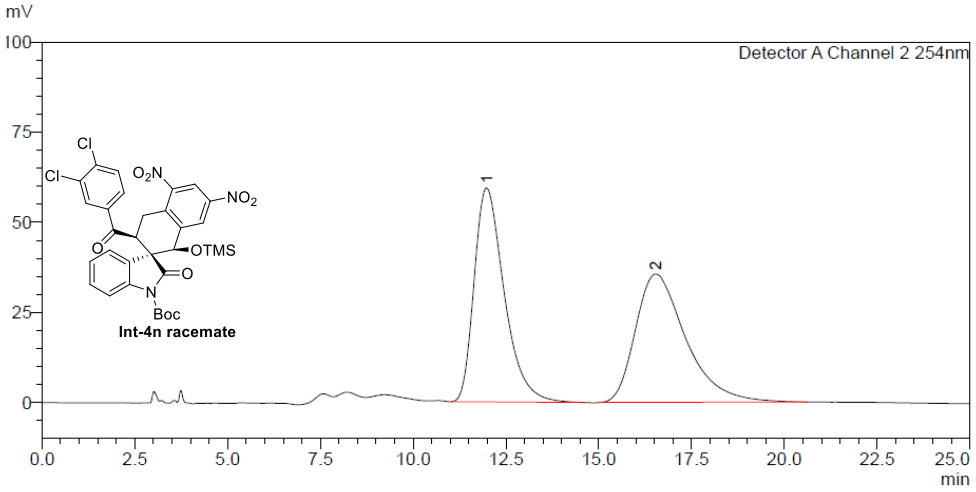

Cl
Cl
O2N
NO2
O
OTMS
O
N
Boc
Int-4n
f1 (ppm)


Cl
Cl
O2N
NO2
O
OTMS
O
N
Boc
Int-4n
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

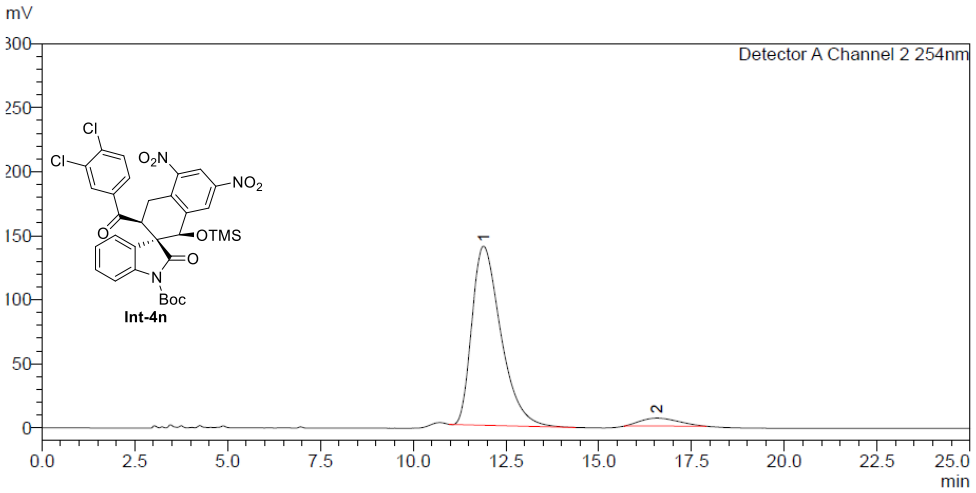
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	11.976	59348	3347605	49.987
2	16.533	35591	3349350	50.013
Total		94939	6696955	100.000

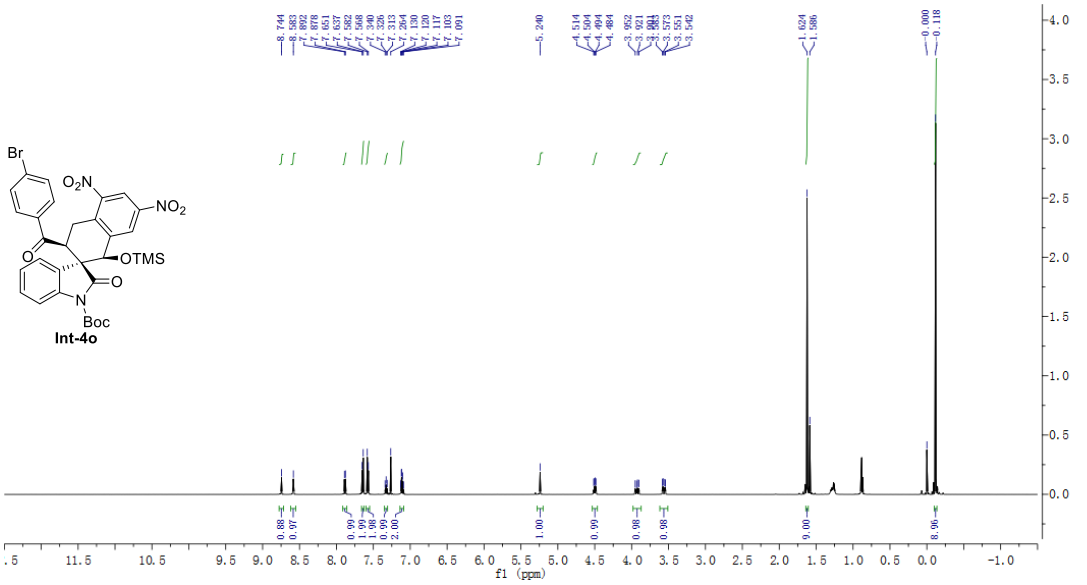


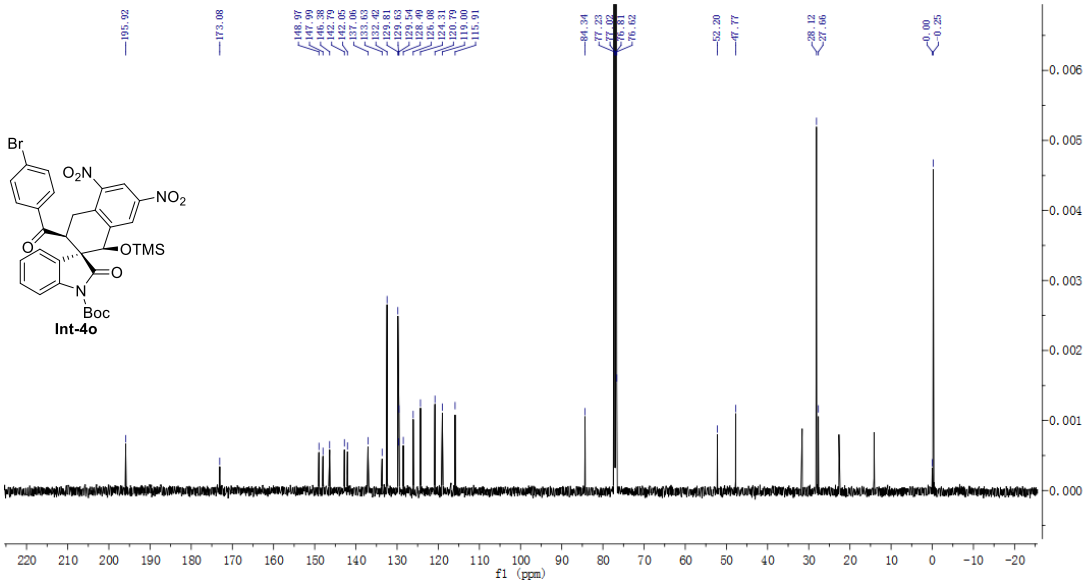
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	11.895	139832	7598902	94.529
2	16.560	6187	439798	5.471
Total		146019	8038700	100.000



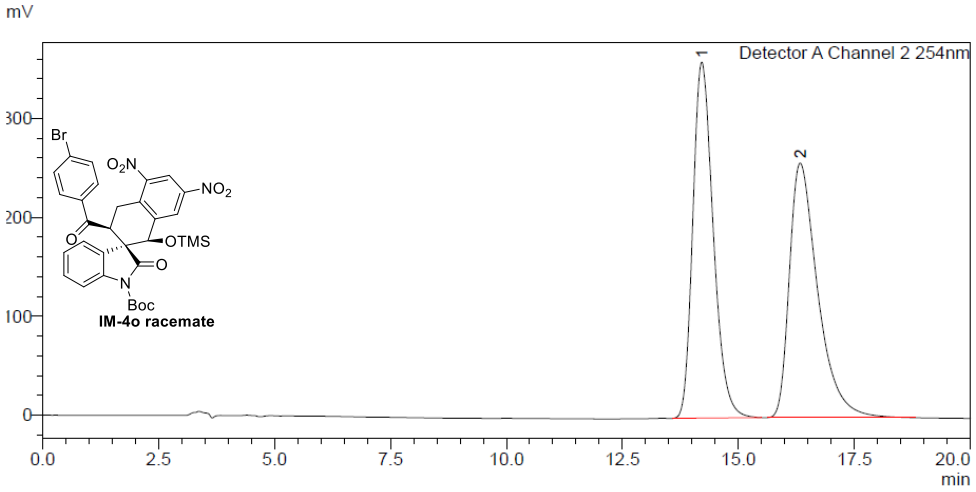

Br
O2N
NO2
O
OTMS
O
N
Boc
Int-4o
f1 (ppm)


Br
O2N
NO2
O
OTMS
O
N
Boc
Int-4o
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

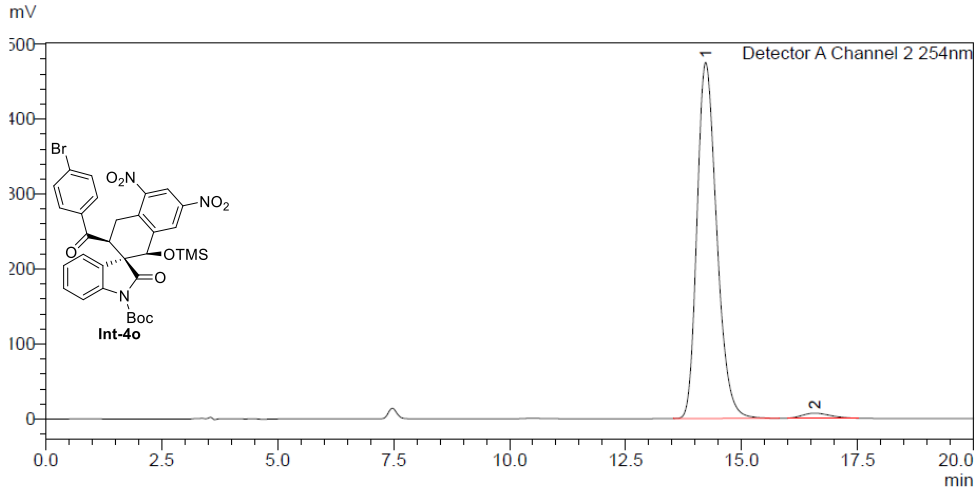
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	14.210	359913	11028835	50.186
2	16.331	257404	10946911	49.814
Total		617317	21975745	100.000

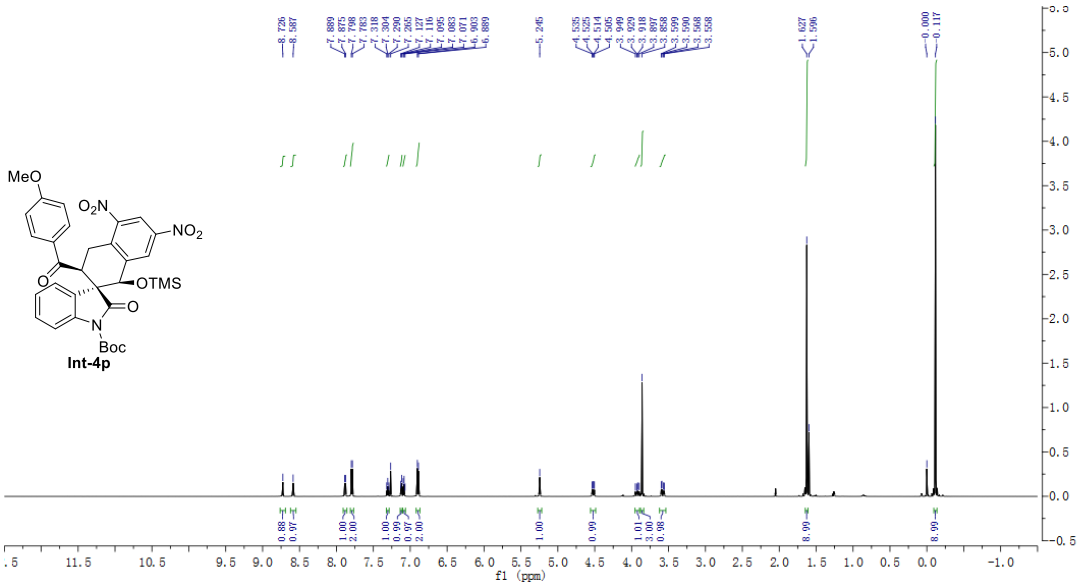


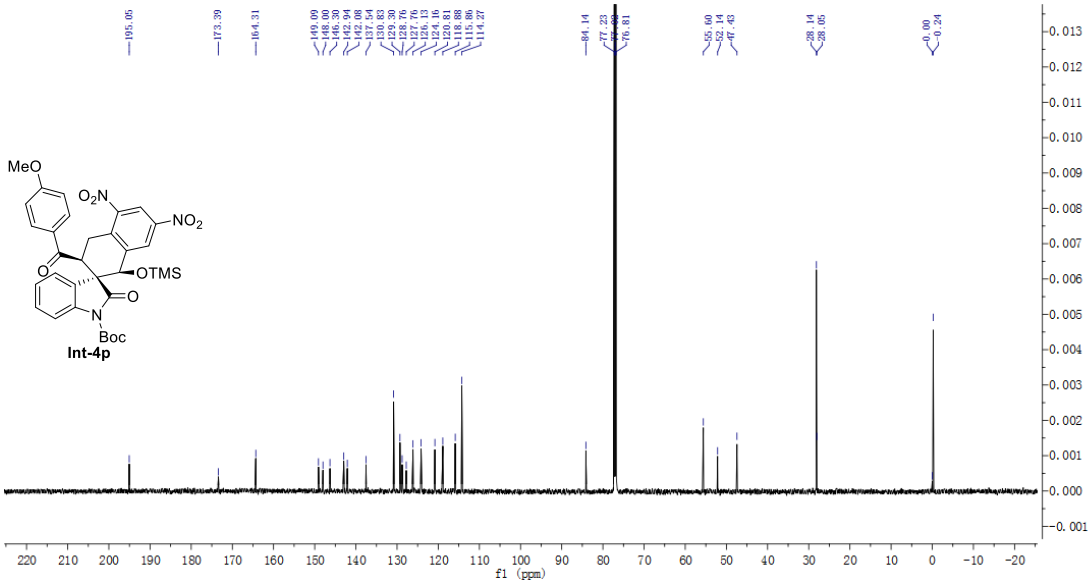
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	14.226	474763	14010859	98.060
2	16.575	6722	277218	1.940
Total		481485	14288078	100.000



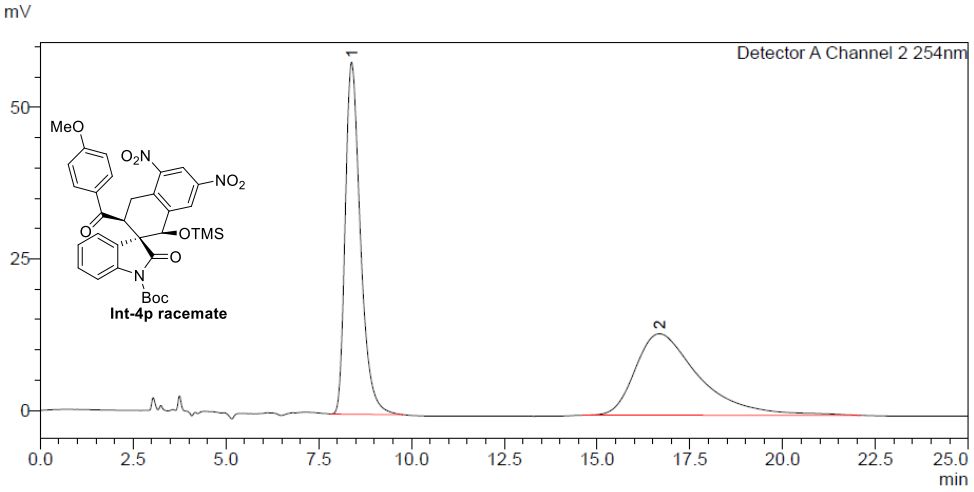

MeO
O2N
NO2
OTMS
O
N
Boc
Int-4p
f1 (ppm)


MeO
O2N
NO2
OTMS
O
N
Boc
Int-4p
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

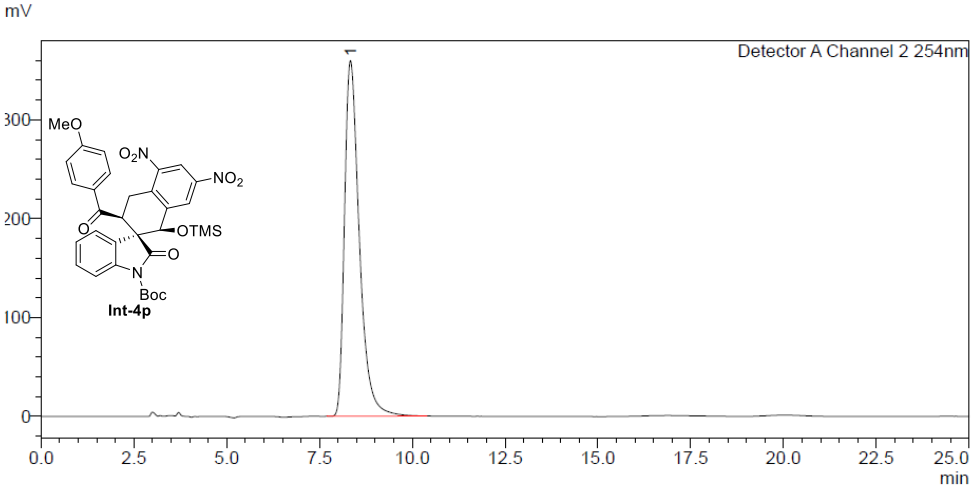
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.385	58074	1654071	50.742
2	16.682	13442	1605691	49.258
Total		71516	3259762	100.000

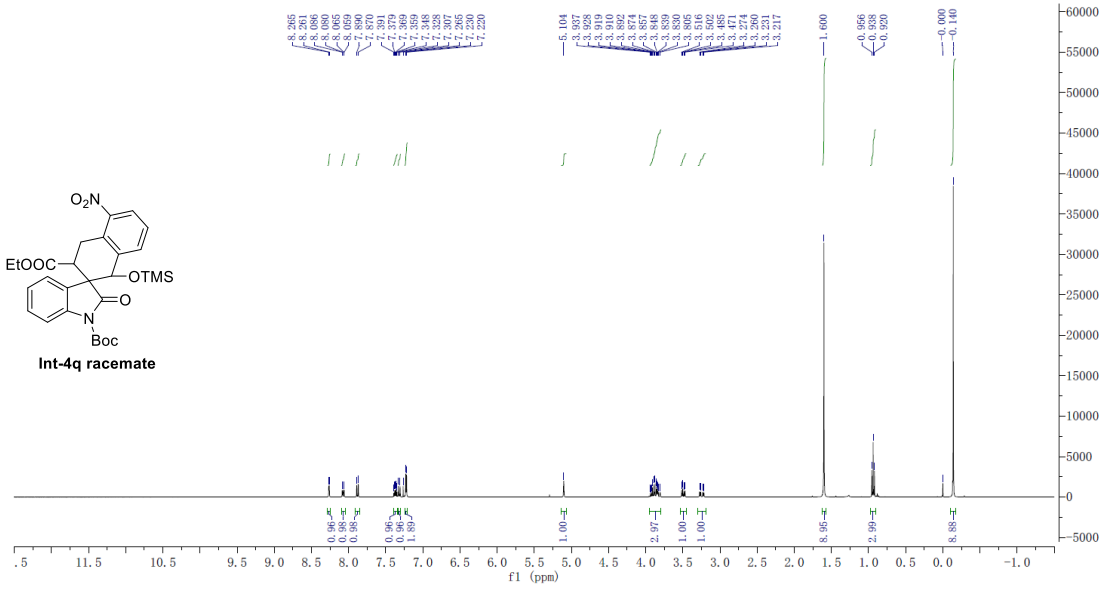


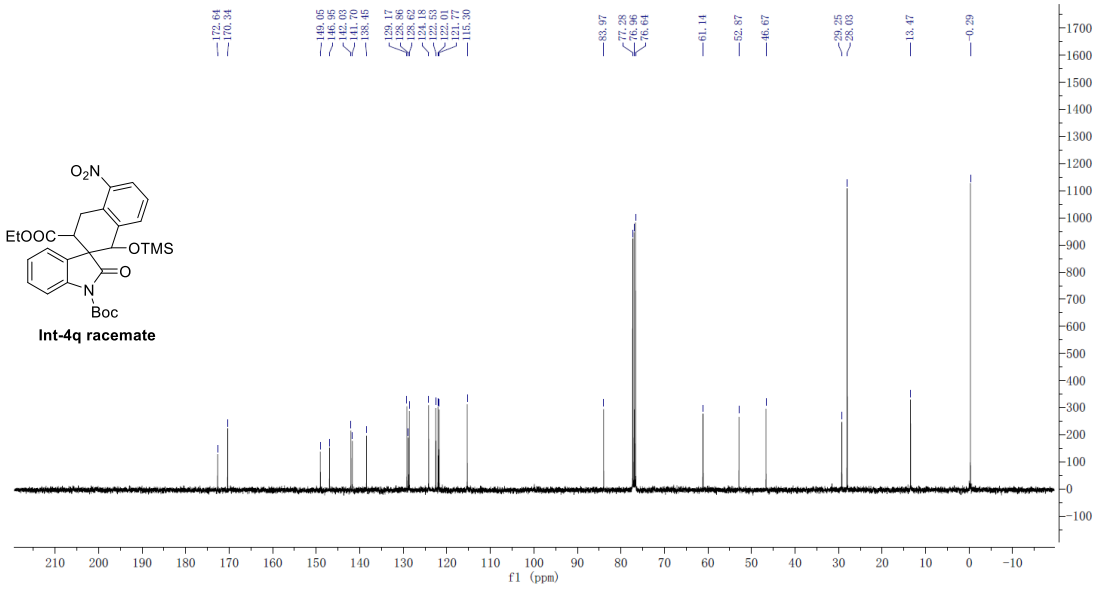
Peak Analysis Report

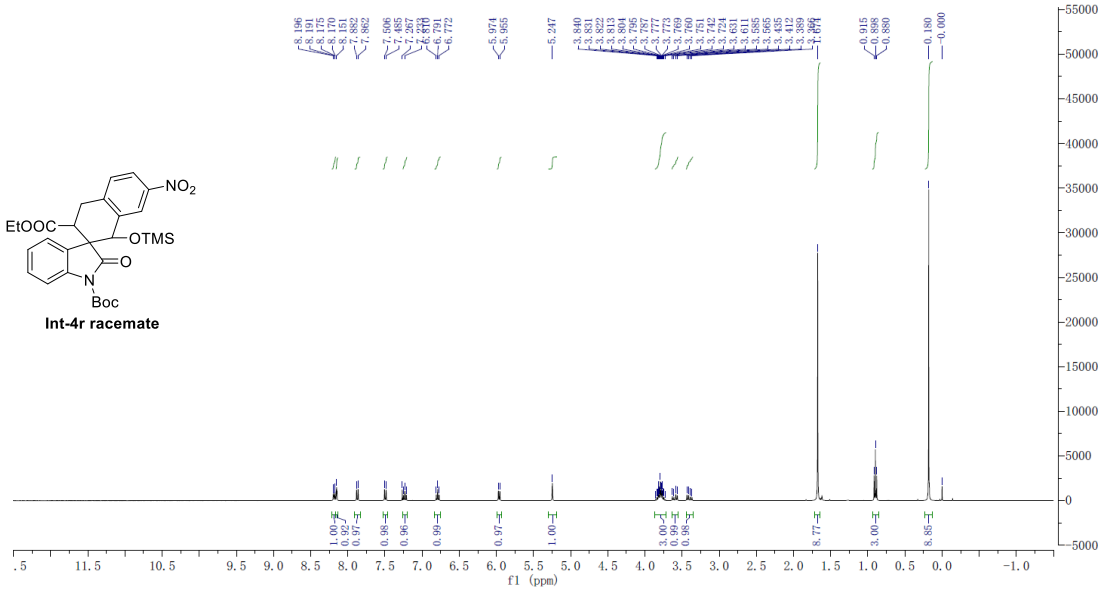
Detector A Channel 2 254nm

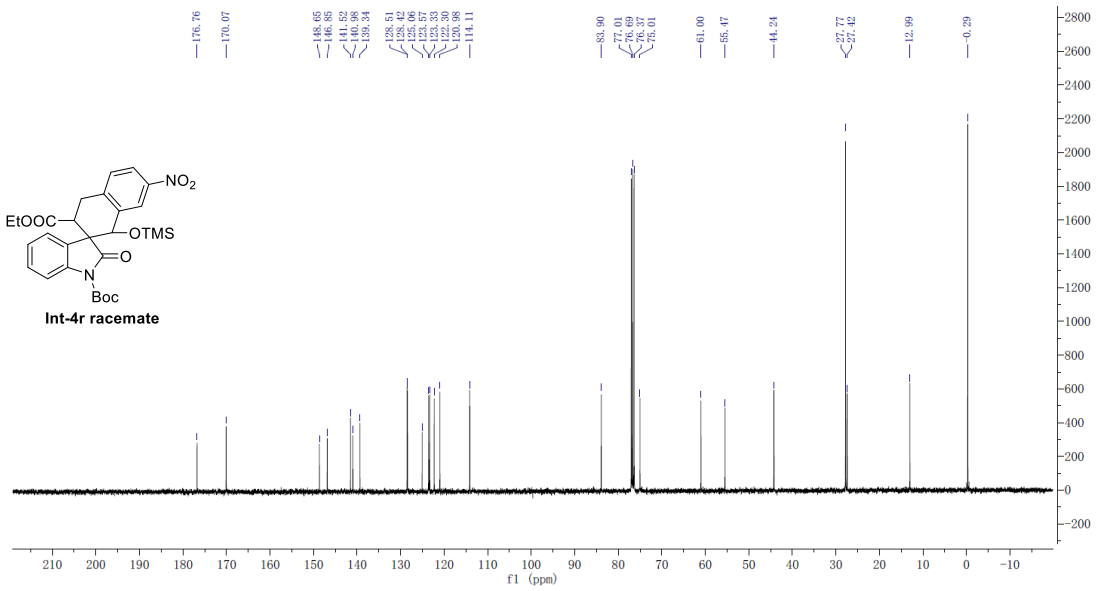
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	8.334	359550	10005451	100.000
Total		359550	10005451	100.000

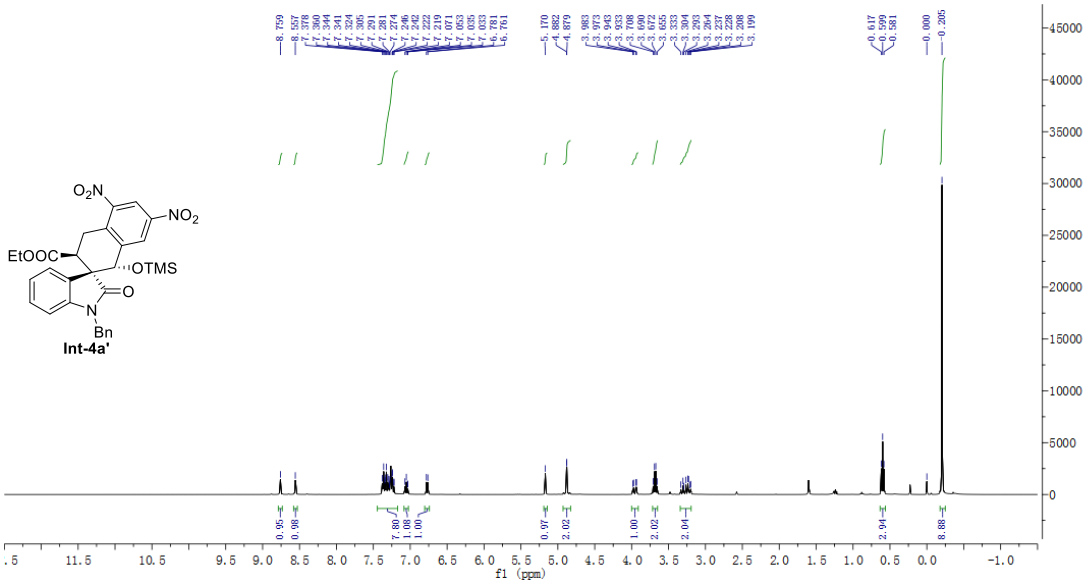


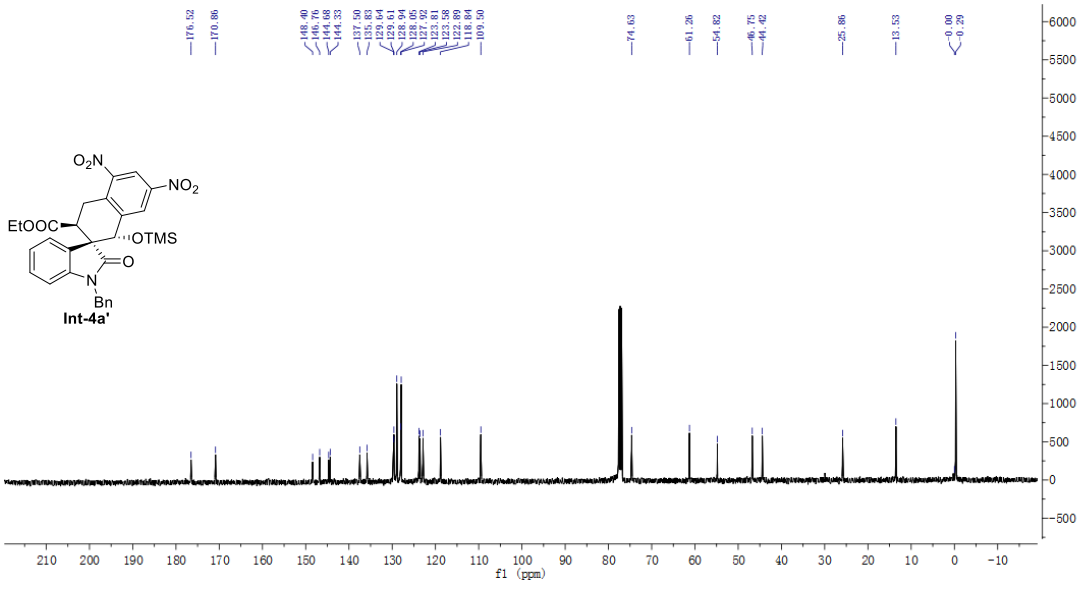

EtOOC
OTMS
O
N
Boc
O2N
Int-4q racemate
f1 (ppm)


EtOOC
OTMS
O
N
Boc
O2N
Int-4q racemate
f1 (ppm)


NO2
EtOOC
OTMS
O
N
Boc
Int-4r racemate
f1 (ppm)

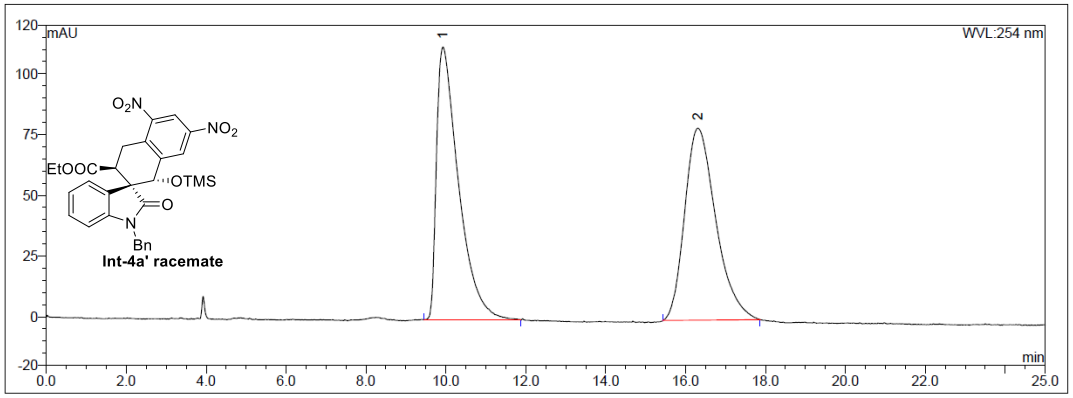

NO2
EtOOC
OTMS
O
N
Boc
Int-4r racemate
f1 (ppm)


O2N
NO2
EtOOC
OTMS
O
N
Bn
Int-4a'
f1 (ppm)


O2N
NO2
EtOOC
OTMS
O
N
Bn
Int-4a'
f1 (ppm)

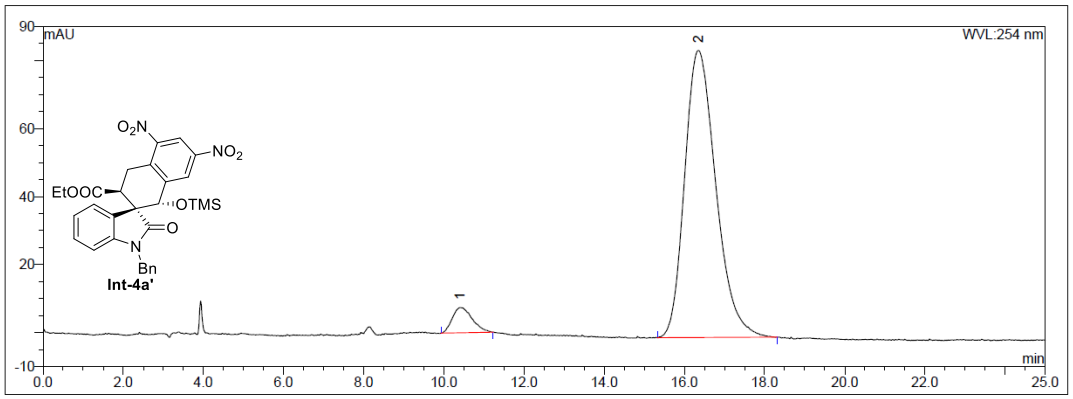
Peak Analysis Report

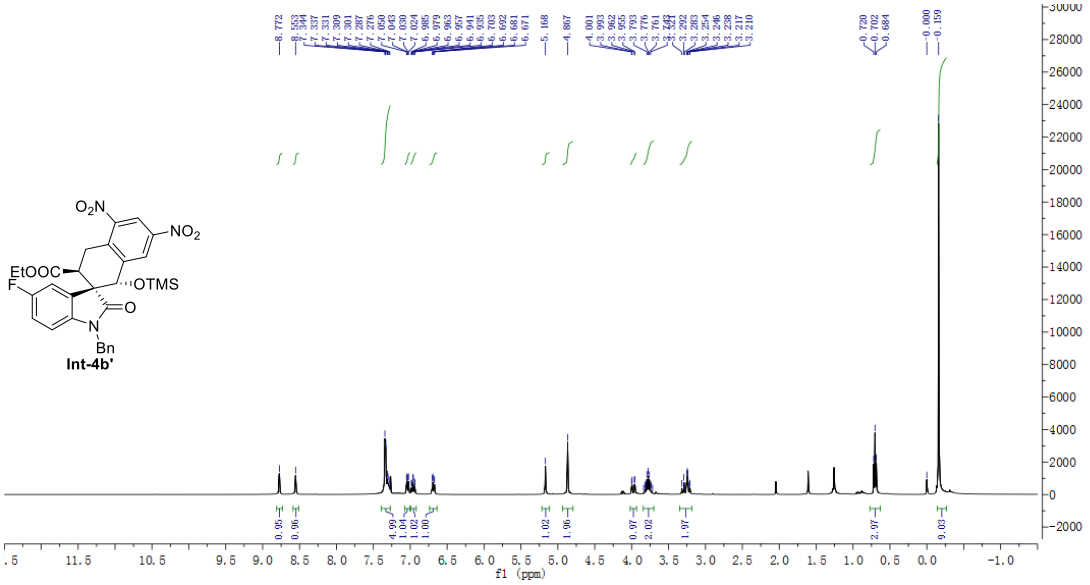
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.93	71.709	50.13	112.288	n.a.
2	n.a.	16.31	71.346	49.87	79.022	n.a.

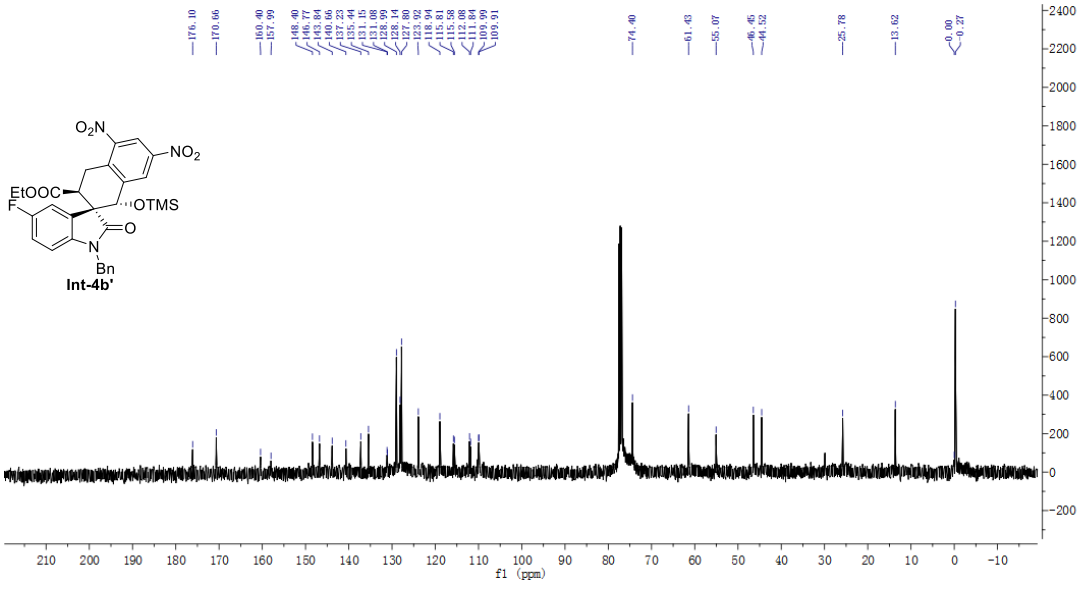


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.40	4.239	5.27	7.395	n.a.
2	n.a.	16.35	76.213	94.73	84.419	n.a.

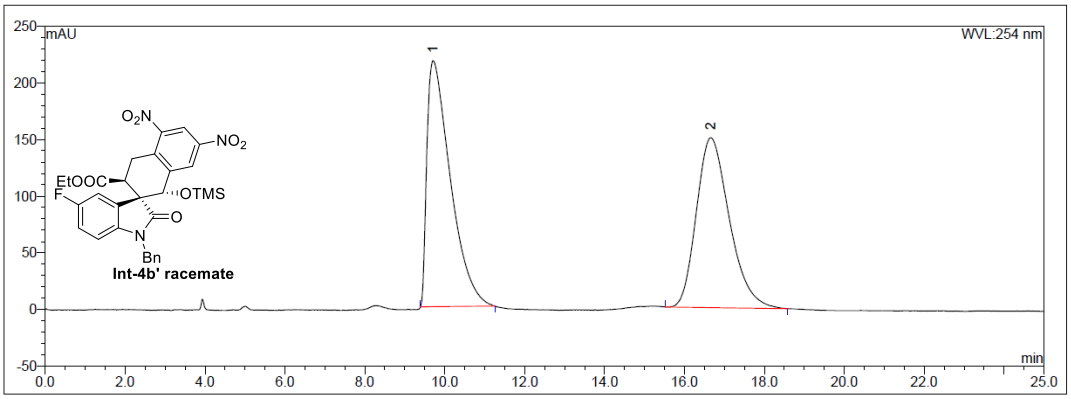



Int-4b'


Int-4b'

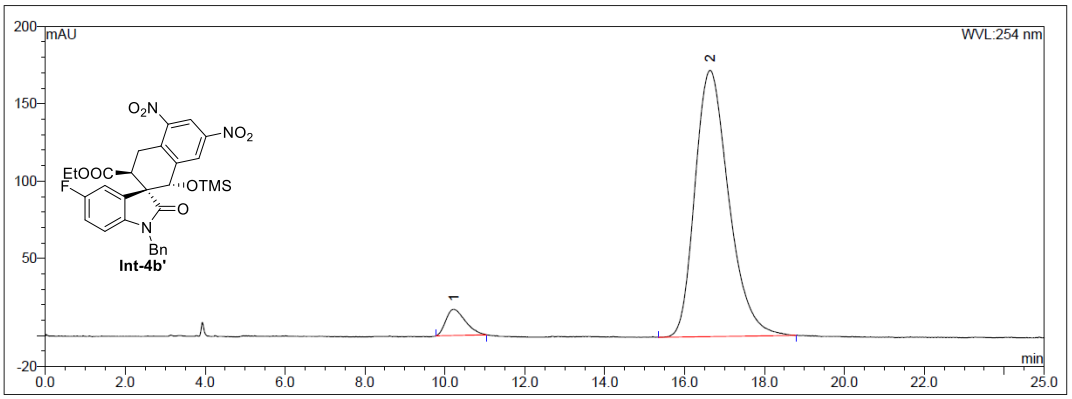
Peak Analysis Report

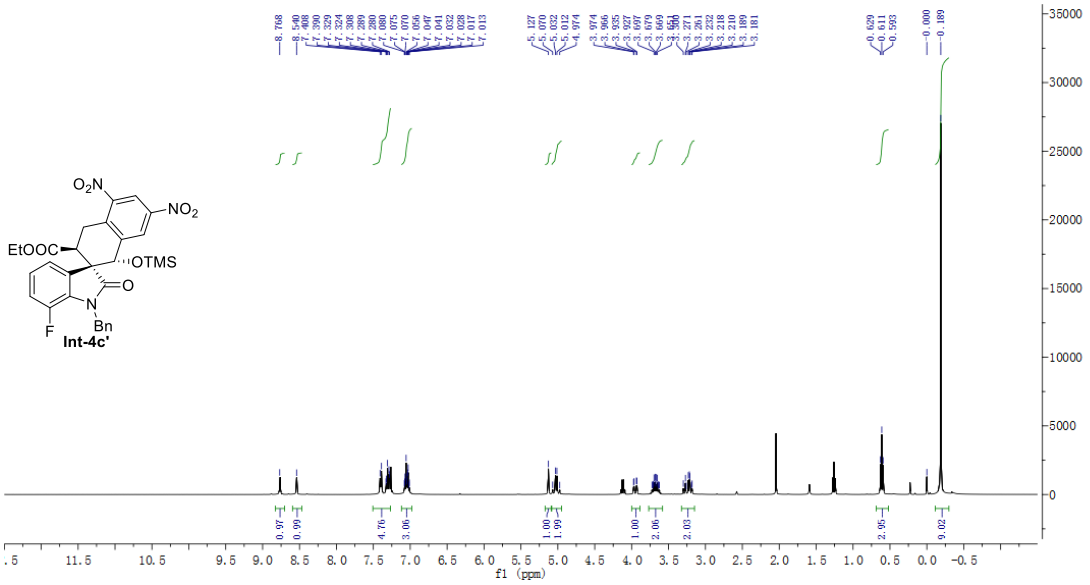
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.71	147.472	50.75	217.009	n.a.
2	n.a.	16.66	143.140	49.25	149.812	n.a.

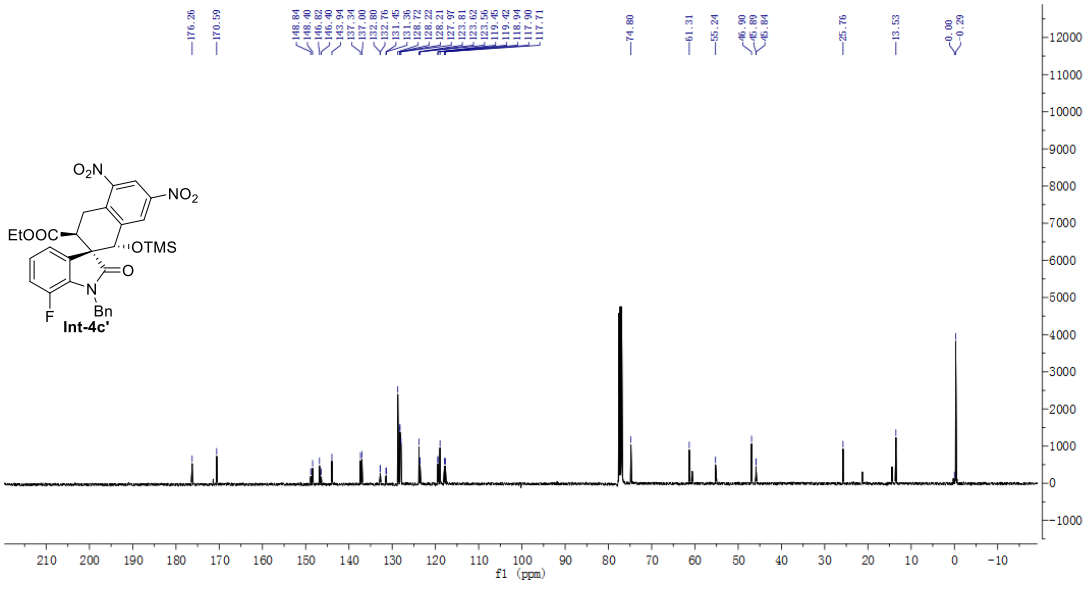


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.23	9.480	5.32	16.820	n.a.
2	n.a.	16.64	168.716	94.68	172.212	n.a.

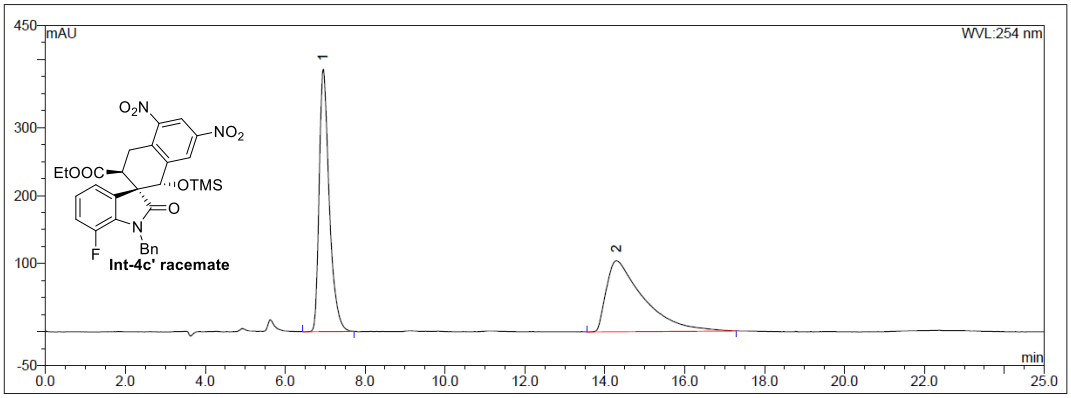



O2N
NO2
EtOOC
OTMS
O
N
Bn
F
Int-4c'
f1 (ppm)


O2N
NO2
EtOOC
OTMS
O
N
Bn
F
Int-4c'
f1 (ppm)

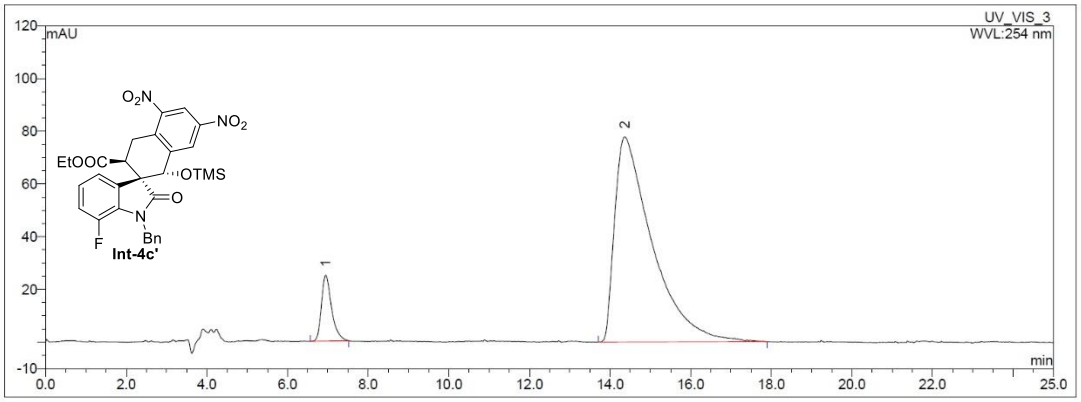
Peak Analysis Report

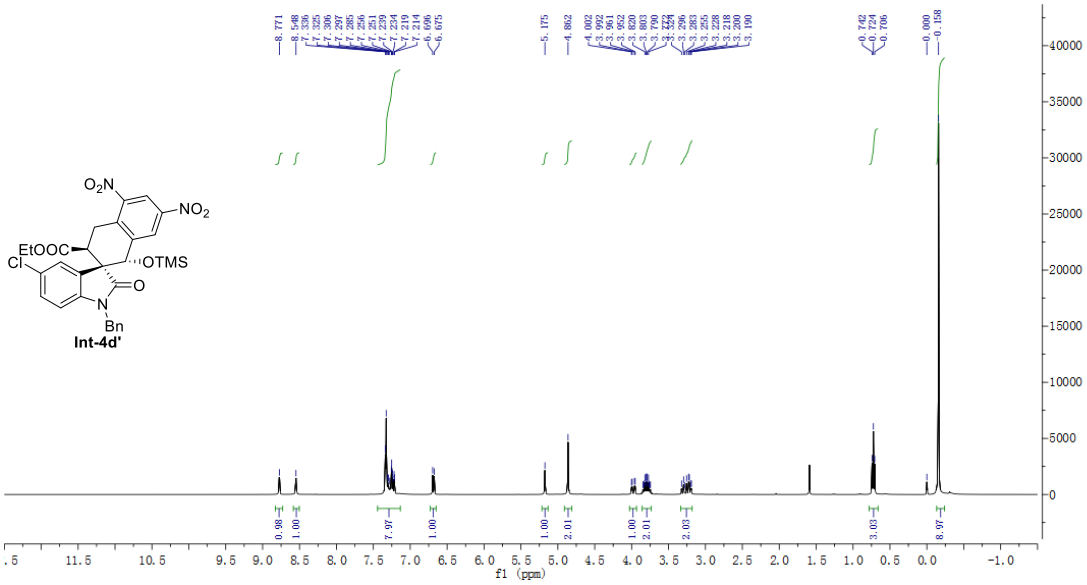
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	6.95	112.837	50.20	385.652	n.a.
2	n.a.	14.29	111.953	49.80	104.298	n.a.

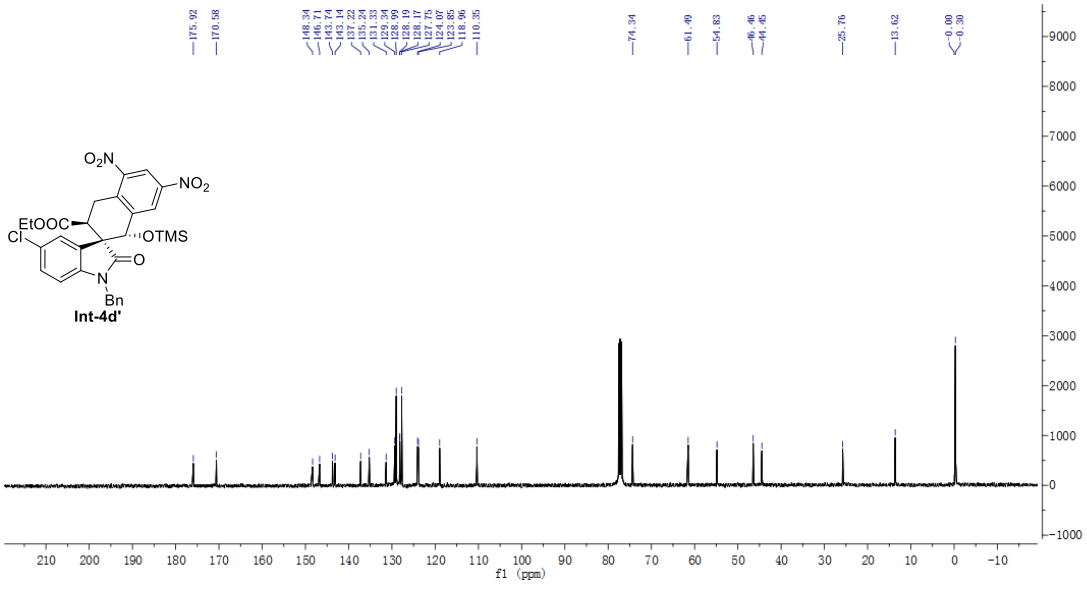


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.00	13.267	13.68	48.223	n.a.
2	n.a.	14.37	83.684	86.32	77.751	n.a.

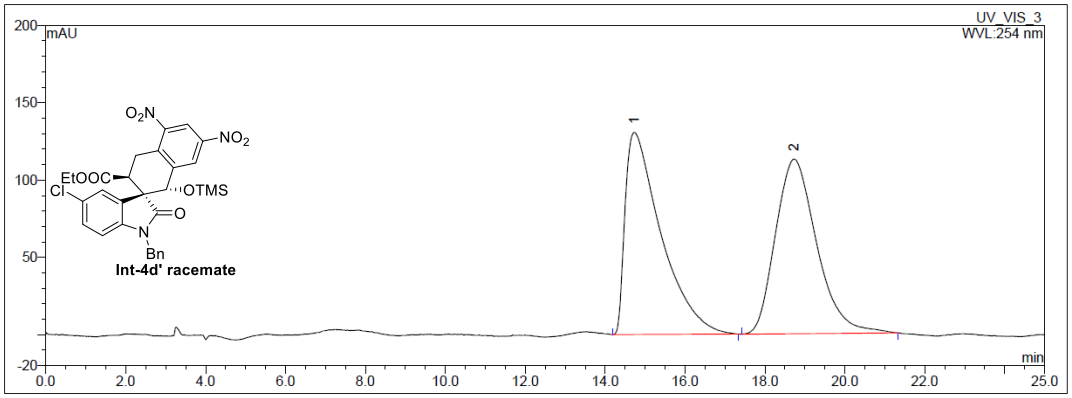



O2N
NO2
EtOOC
Cl
OTMS
O
N
Bn
Int-4d'
f1 (ppm)


O2N
NO2
EtOOC
Cl
OTMS
O
N
Bn
Int-4d'
f1 (ppm)

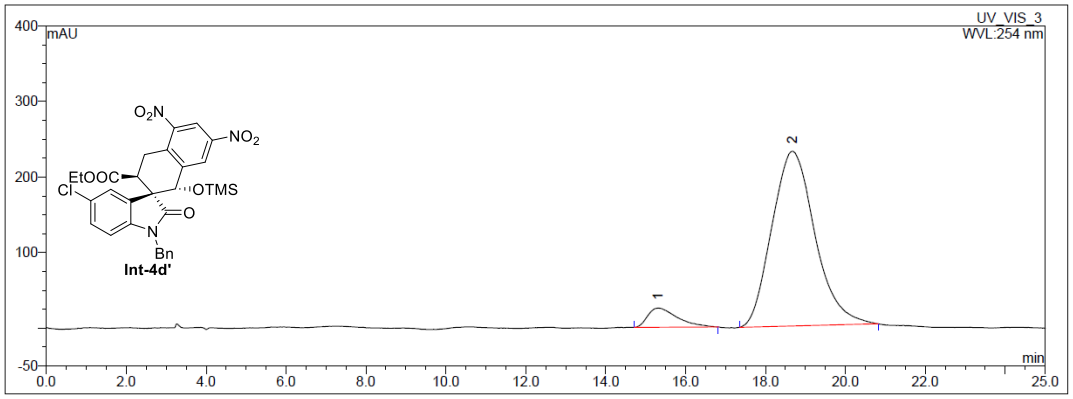
Peak Analysis Report

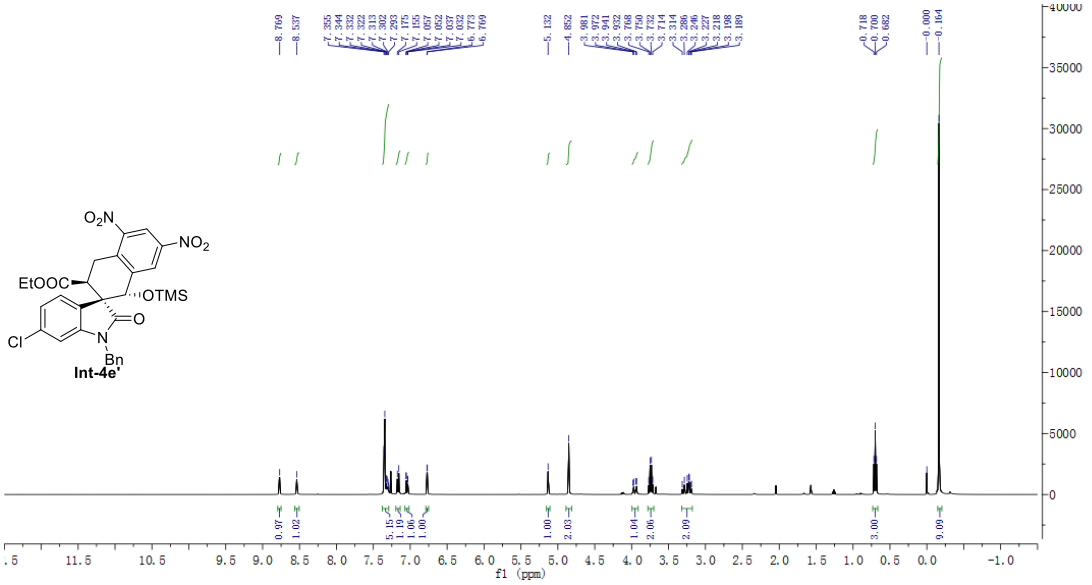
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.73	135.935	50.17	130.774	n.a.
2	n.a.	18.73	135.028	49.83	112.960	n.a.

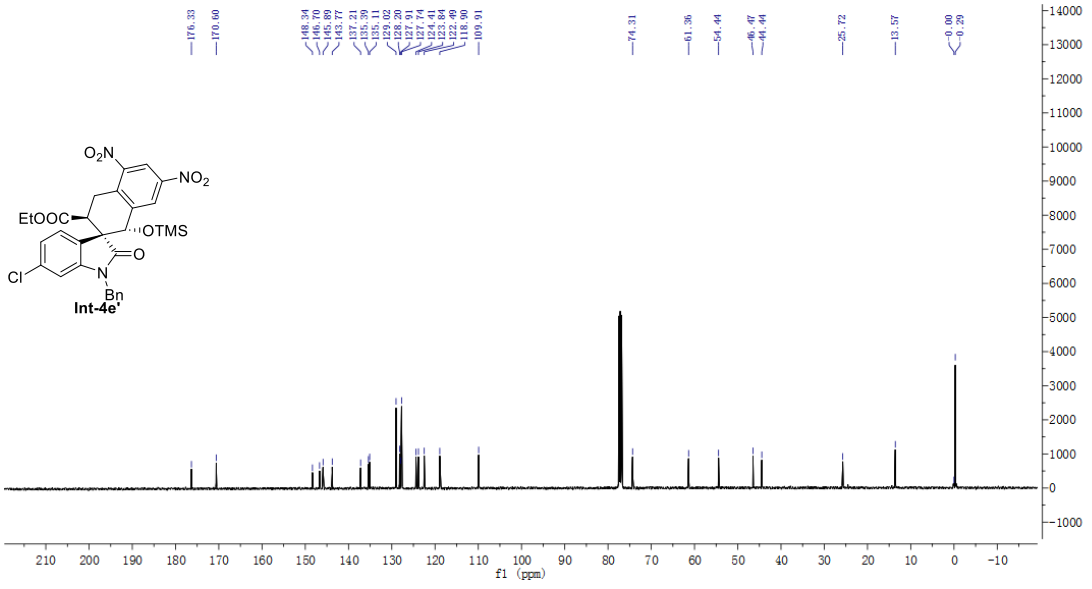


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	15.31	21.742	7.01	25.349	n.a.
2	n.a.	18.68	288.539	92.99	231.043	n.a.

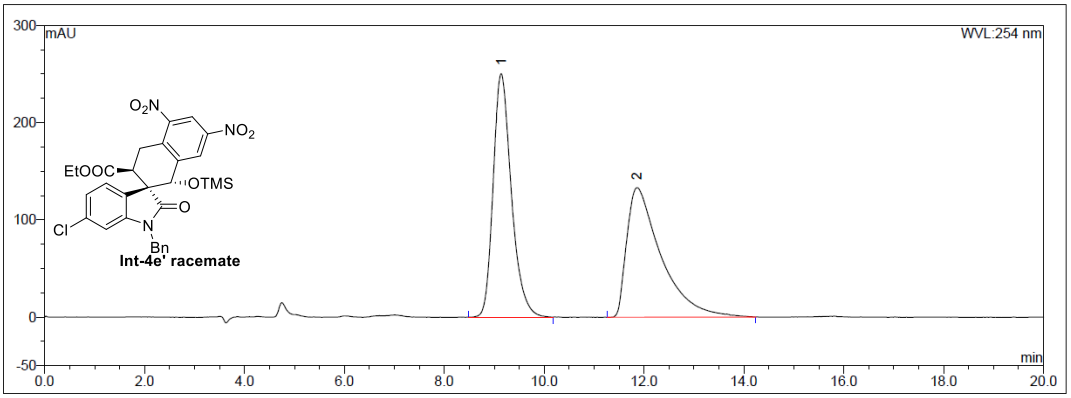



O2N
NO2
EtOOC
OTMS
O
Cl
N
Bn
Int-4e'
f1 (ppm)


O2N
NO2
EtOOC
OTMS
O
Cl
N
Bn
Int-4e'
f1 (ppm)

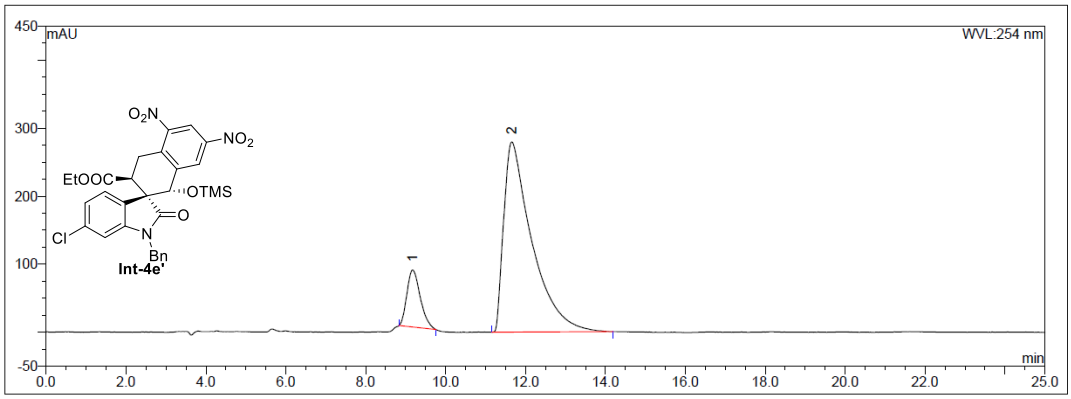
Peak Analysis Report

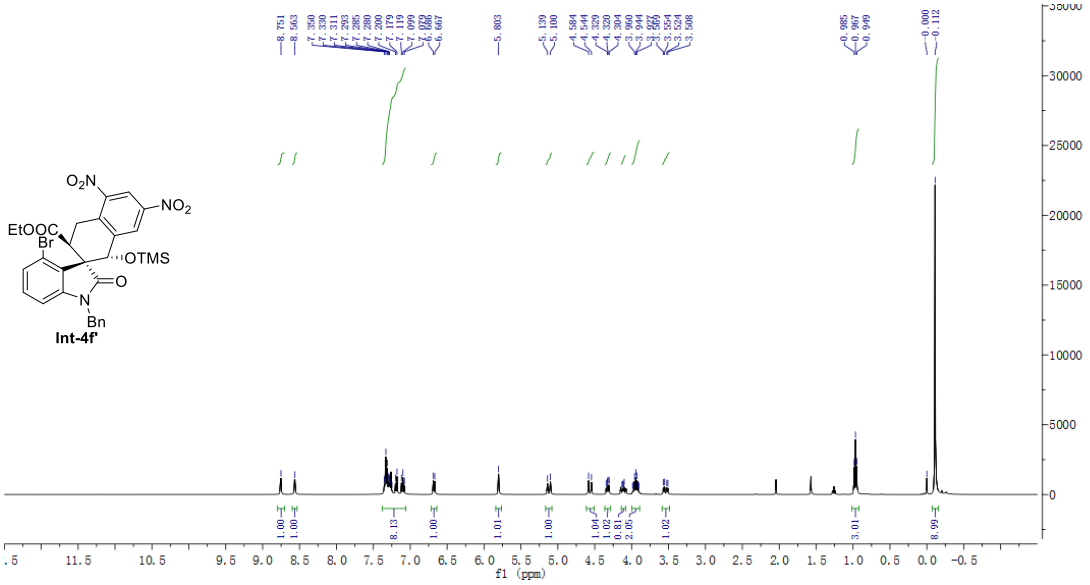
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.14	105.921	50.03	250.518	n.a.
2	n.a.	11.86	105.795	49.97	133.298	n.a.

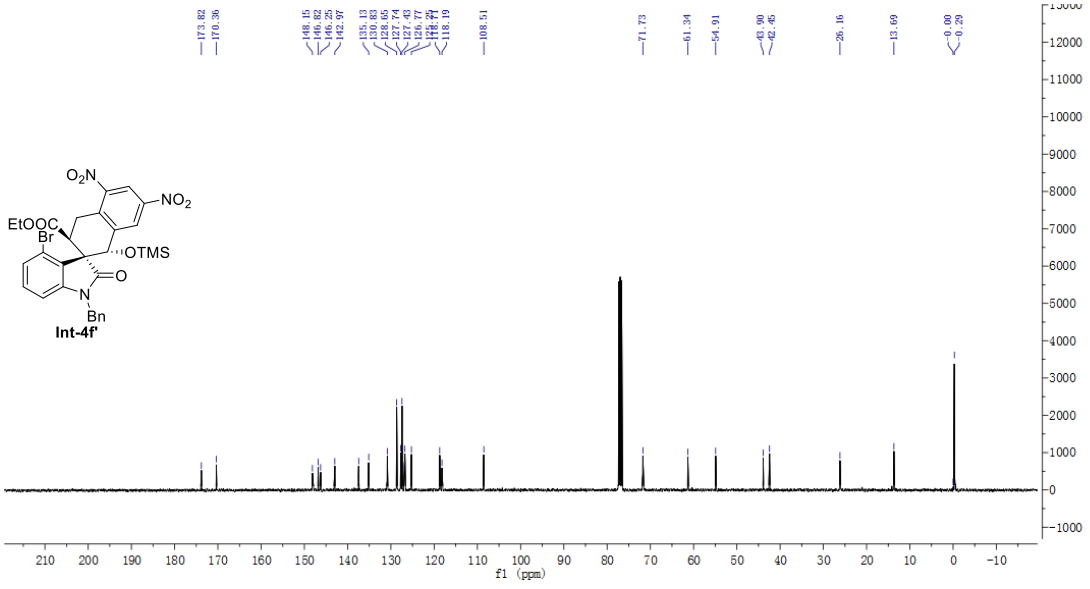


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.18	32.522	12.50	83.814	n.a.
2	n.a.	11.66	227.741	87.50	279.610	n.a.

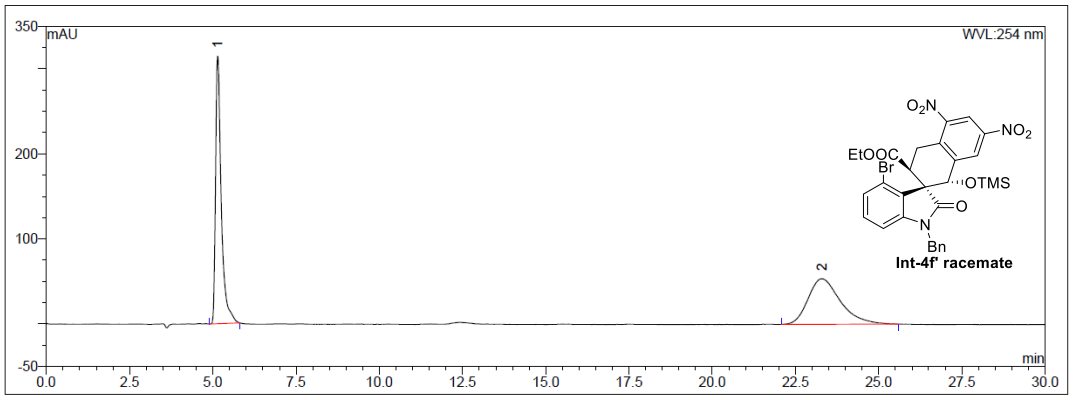



Int-4f'


Int-4f'

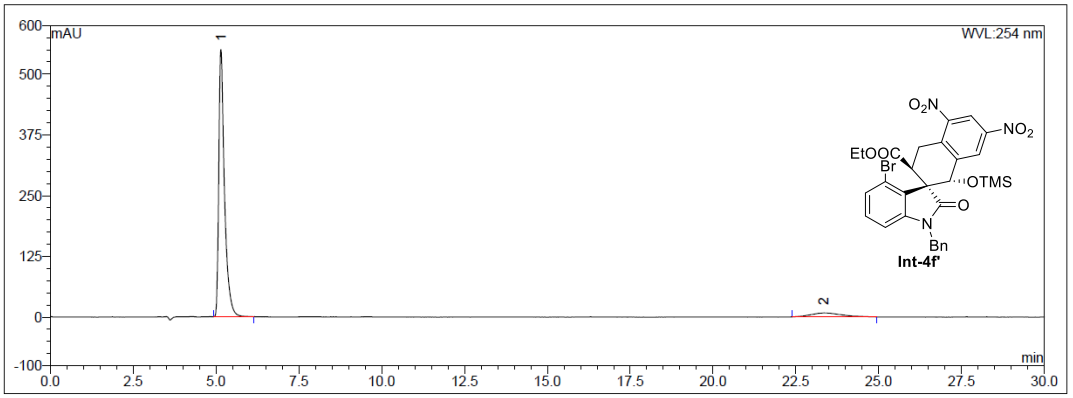
Peak Analysis Report

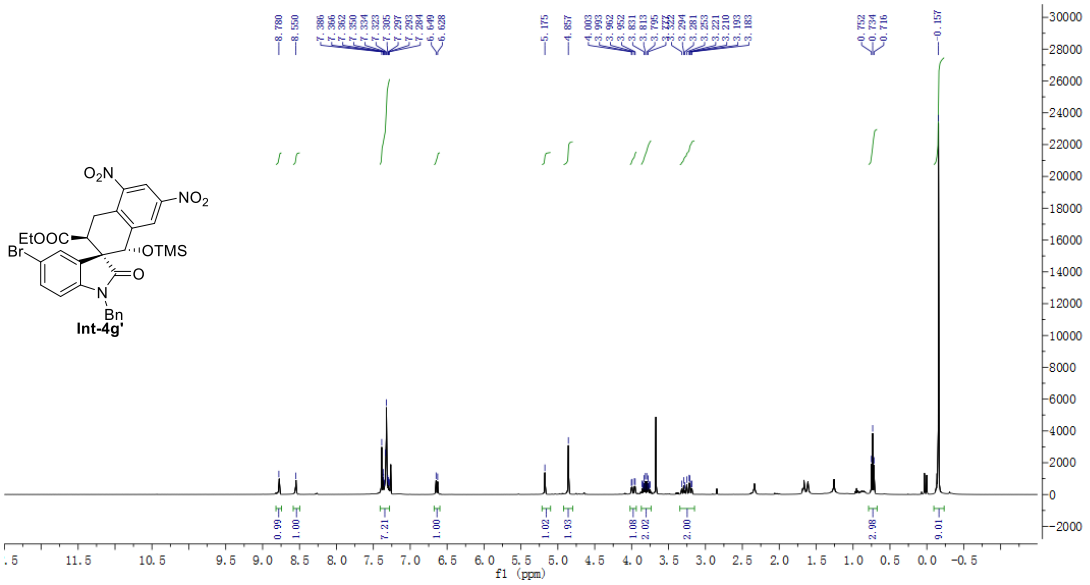
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.14	62.289	50.84	314.515	n.a.
2	n.a.	23.29	60.219	49.16	53.532	n.a.

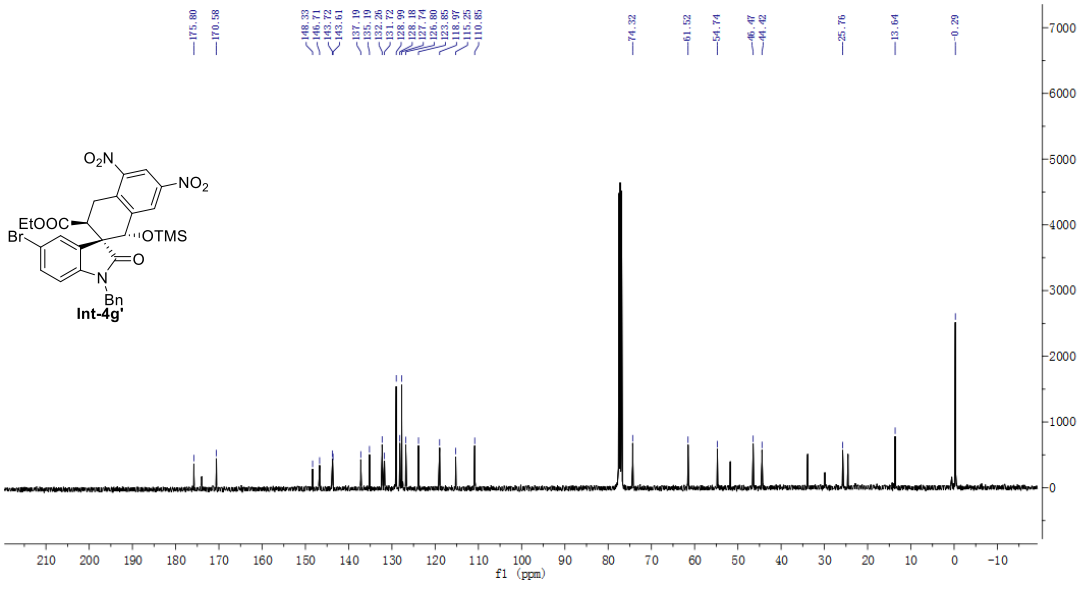


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.15	110.372	92.71	550.155	n.a.
2	n.a.	23.35	8.673	7.29	8.323	n.a.

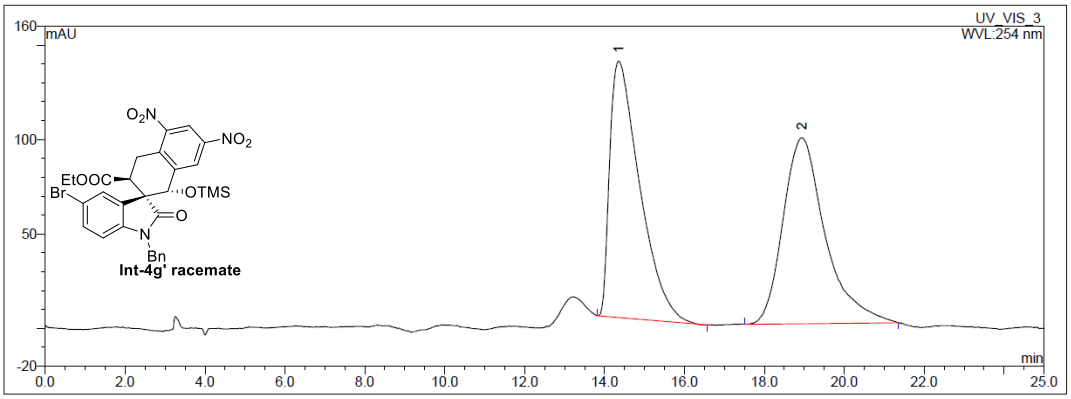



Int-4g'


Int-4g'

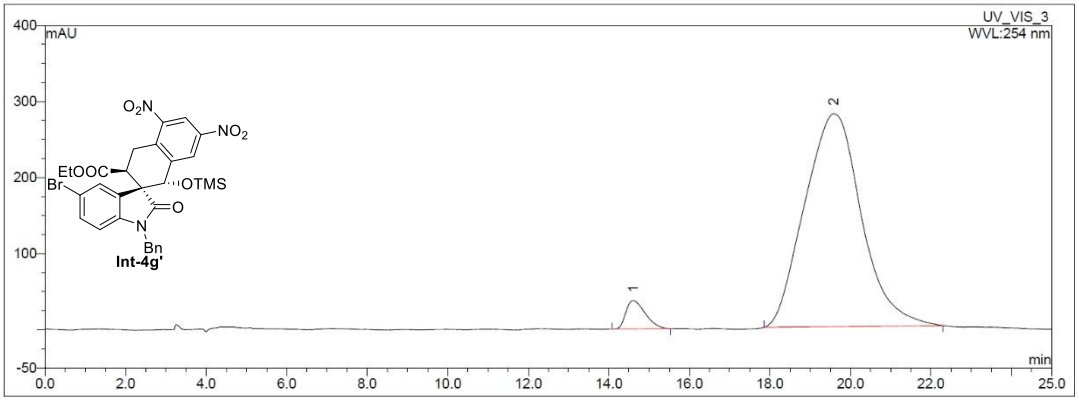
Peak Analysis Report

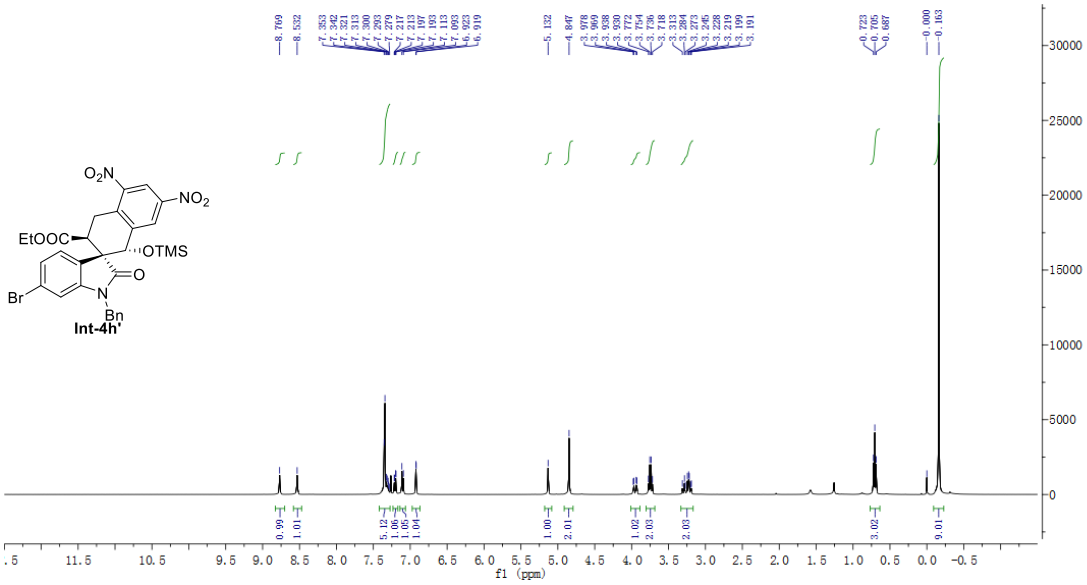
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.35	118.081	49.52	135.665	n.a.
2	n.a.	18.94	120.357	50.48	98.320	n.a.

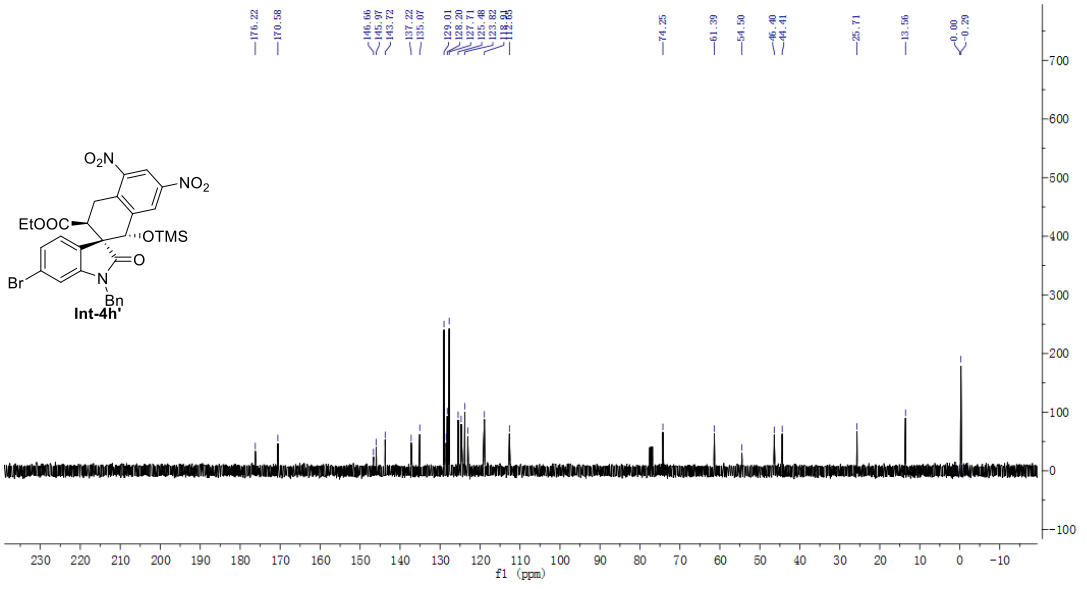


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.65	37.105	7.53	60.395	n.a.
2	n.a.	19.58	455.613	92.47	279.910	n.a.

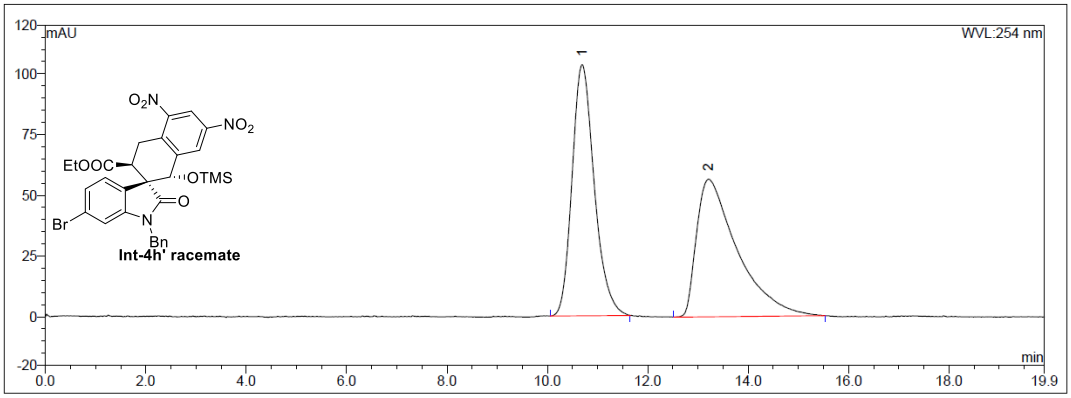



Int-4h'
fl (ppm)


Int-4h'
fl (ppm)

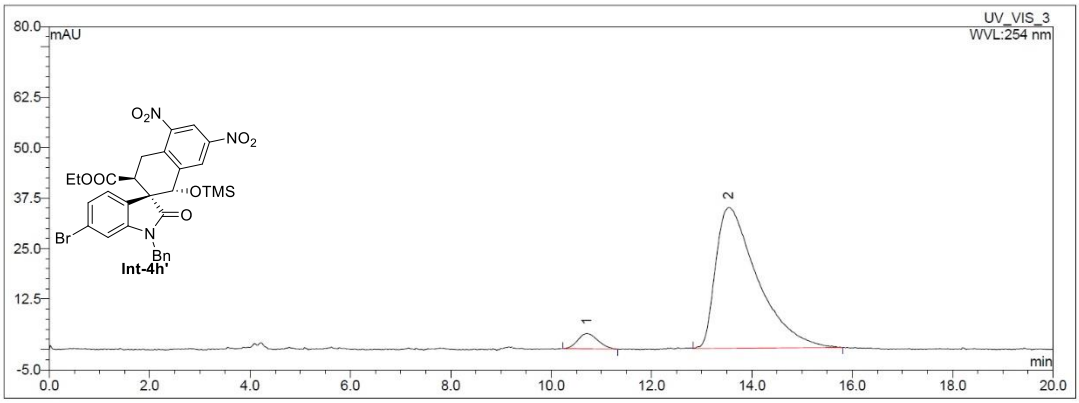
Peak Analysis Report

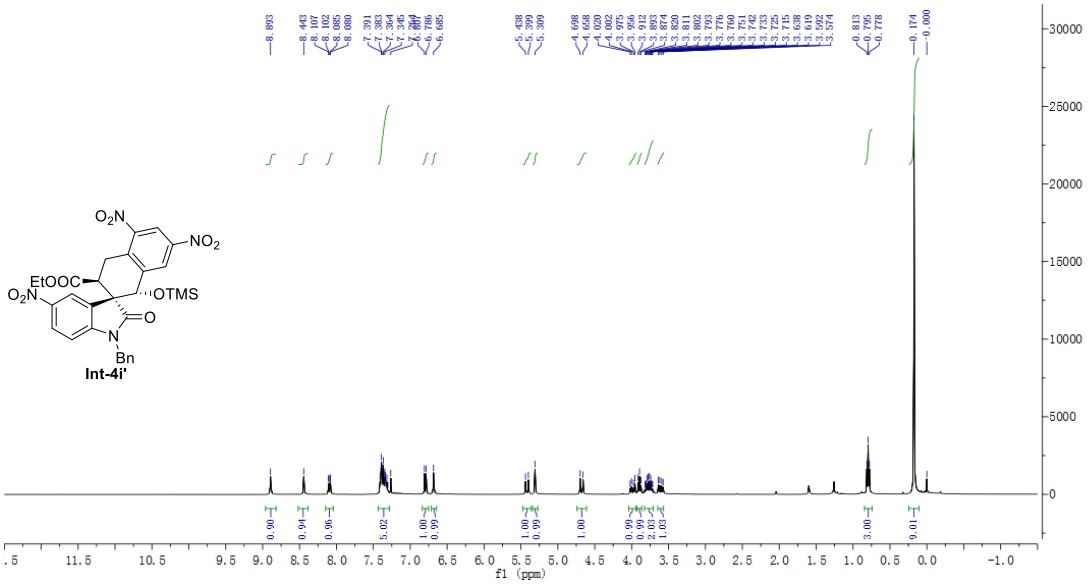
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.69	53.150	49.98	103.387	n.a.
2	n.a.	13.21	53.185	50.02	56.626	n.a.

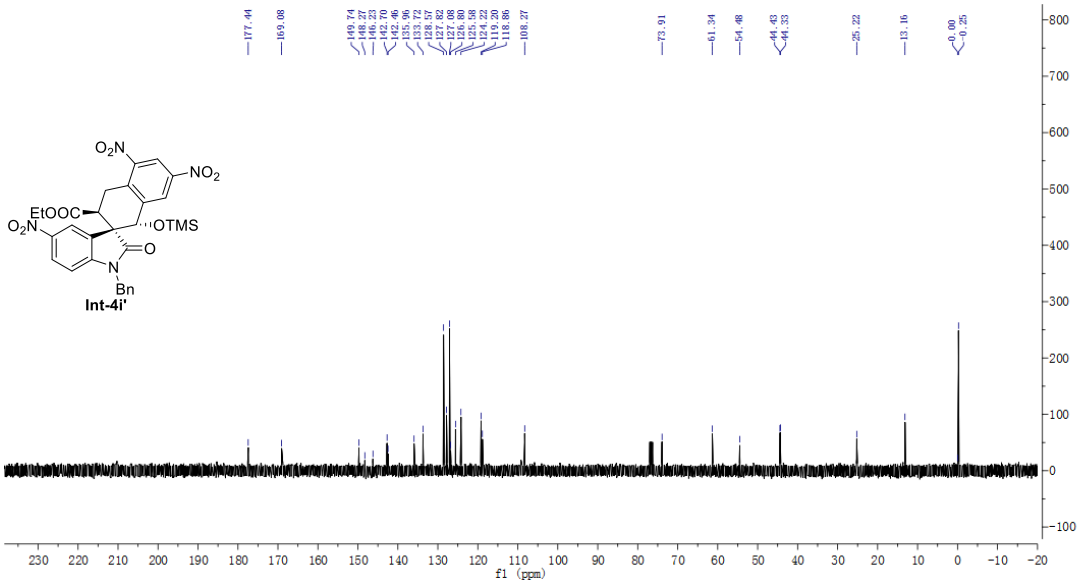


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.69	3.756	10.02	8.601	n.a.
2	n.a.	13.53	33.729	89.98	34.889	n.a.

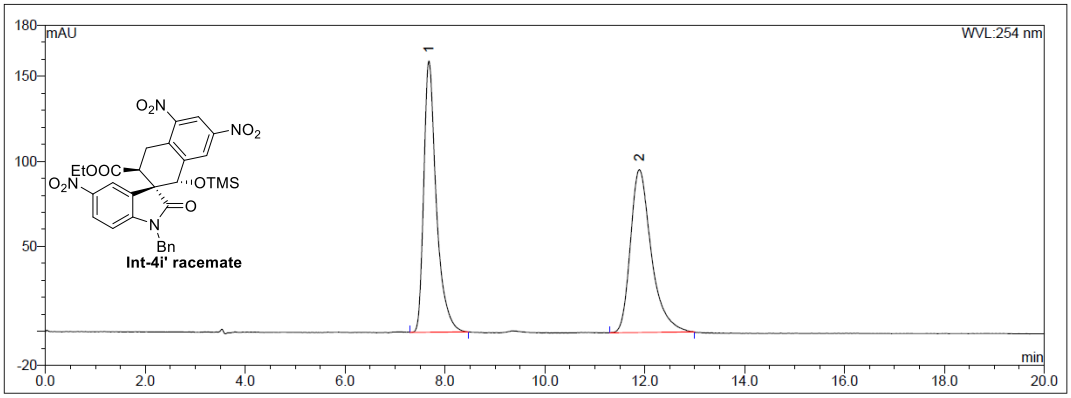



Int-4i'


Int-4i'

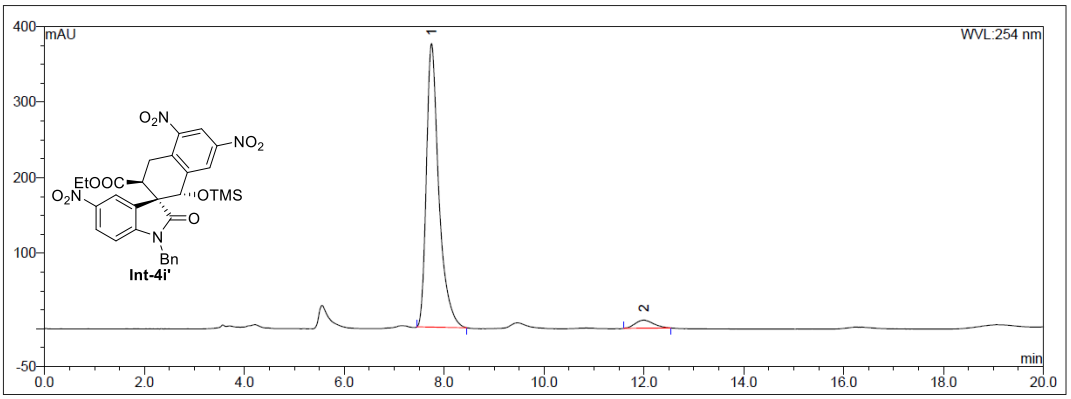
Peak Analysis Report

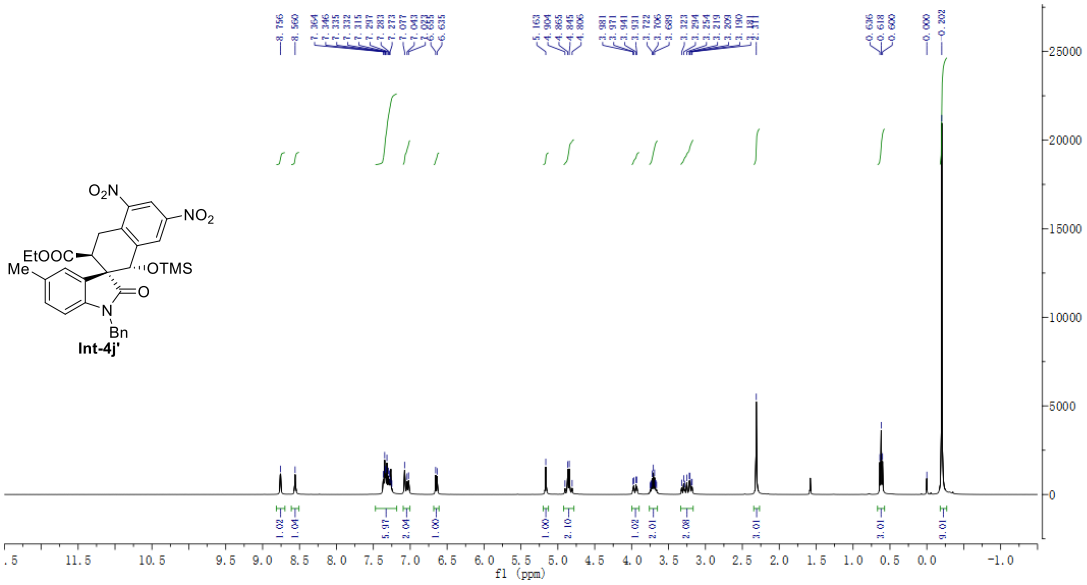
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.68	46.426	50.05	159.466	n.a.
2	n.a.	11.89	46.327	49.95	95.790	n.a.

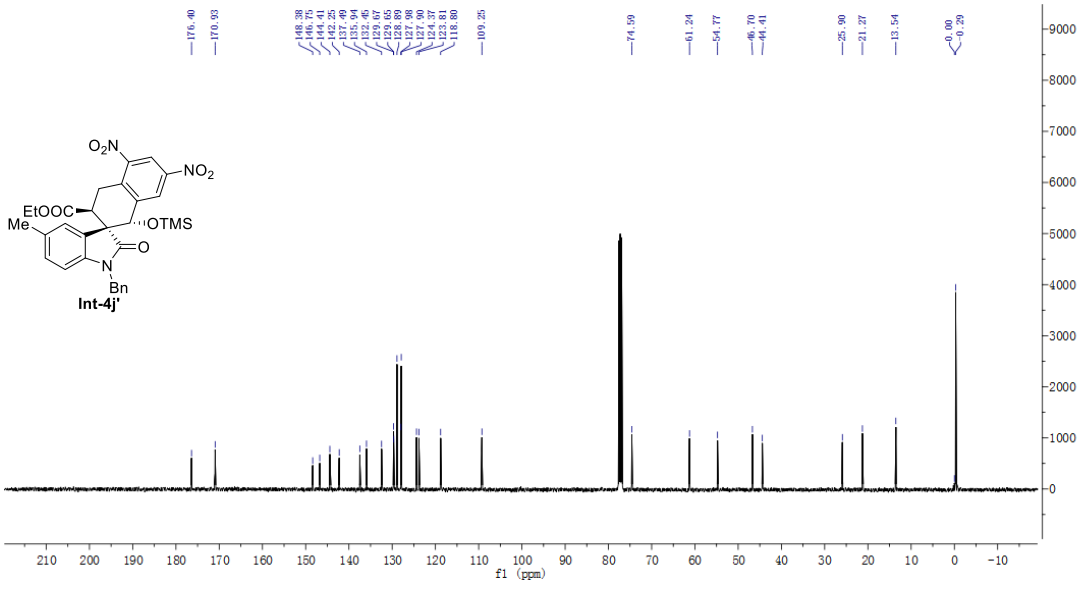


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.75	107.969	96.03	375.042	n.a.
2	n.a.	12.00	4.463	3.97	10.586	n.a.

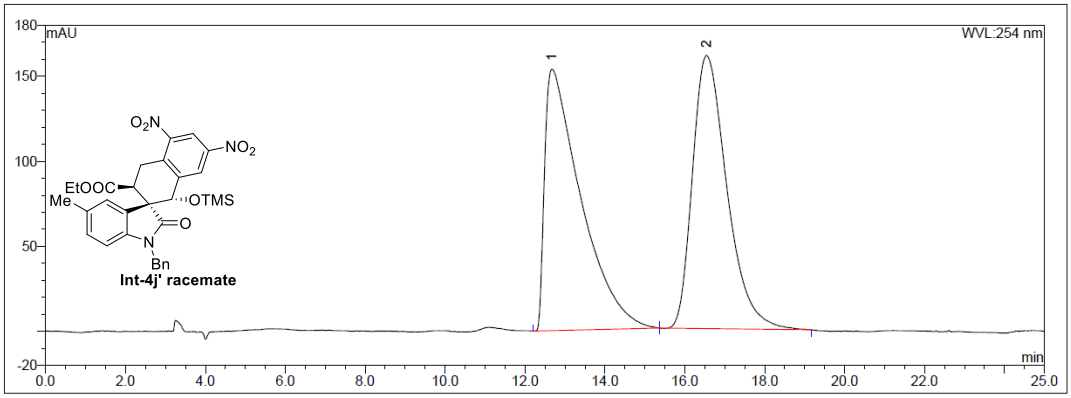



O2N
NO2
EtOOC
Me
OTMS
O
N
Bn
Int-4j'
f1 (ppm)


O2N
NO2
EtOOC
Me
OTMS
O
N
Bn
Int-4j'
f1 (ppm)

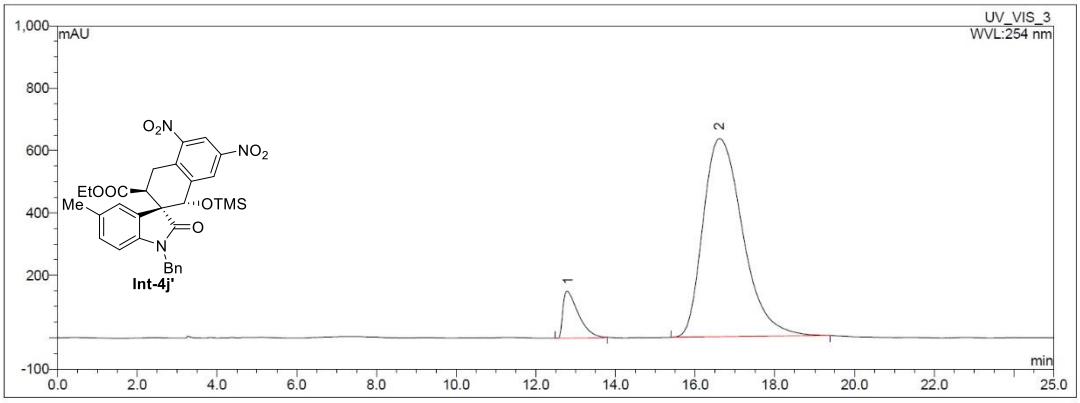
Peak Analysis Report

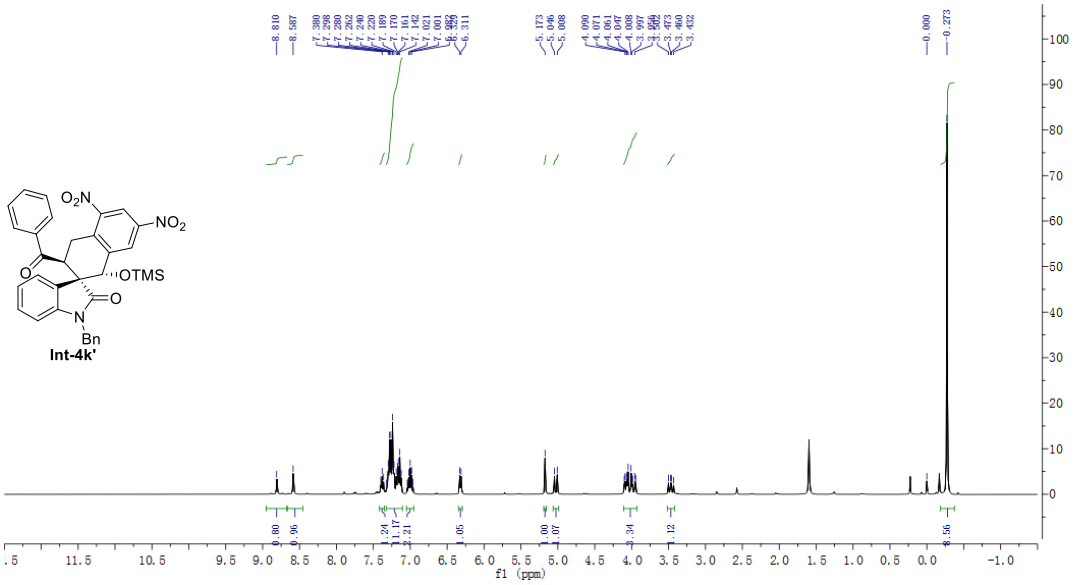
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	12.67	161.107	50.07	153.755	n.a.
2	n.a.	16.54	160.649	49.93	160.613	n.a.

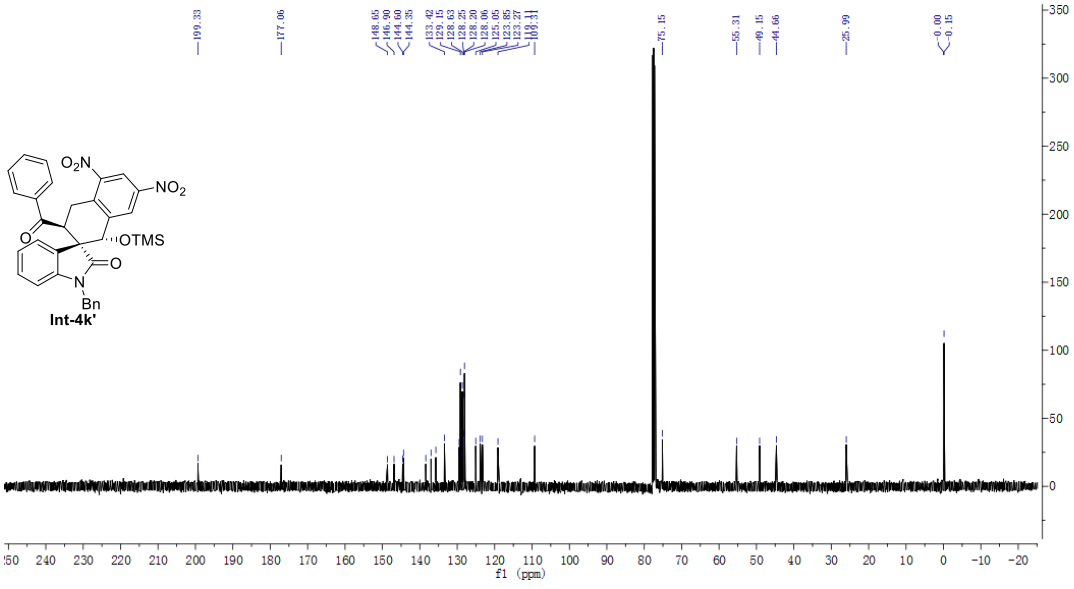


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	12.81	94.046	11.36	110.640	n.a.
2	n.a.	16.61	733.488	88.64	635.379	n.a.

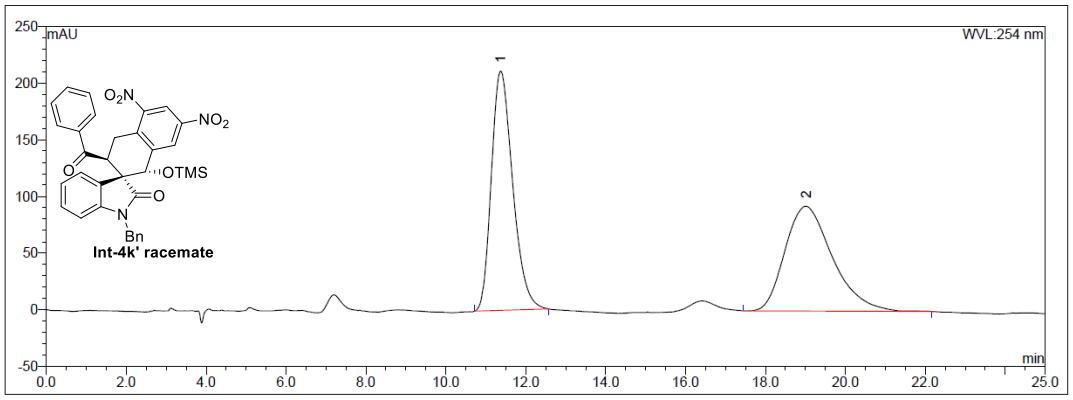



O2N
NO2
OTMS
O
O
N
Bn
Int-4k'
f1 (ppm)


O2N
NO2
OTMS
O
O
N
Bn
Int-4k'
f1 (ppm)

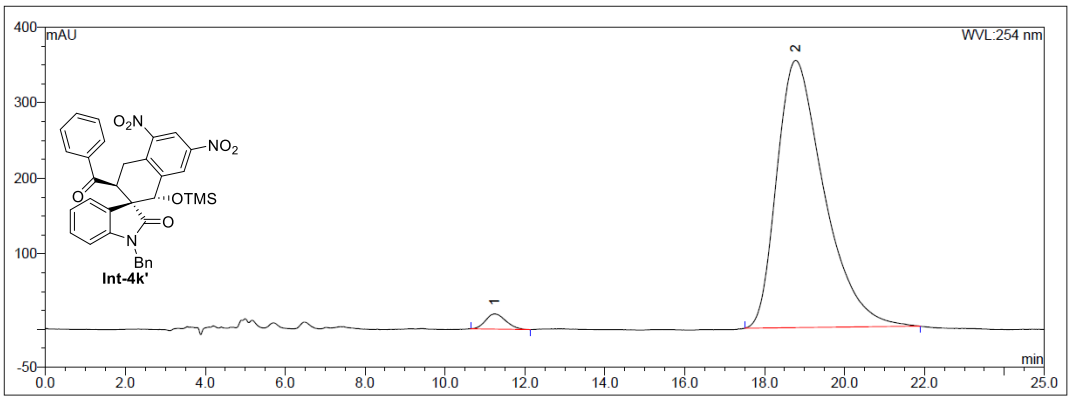
Peak Analysis Report

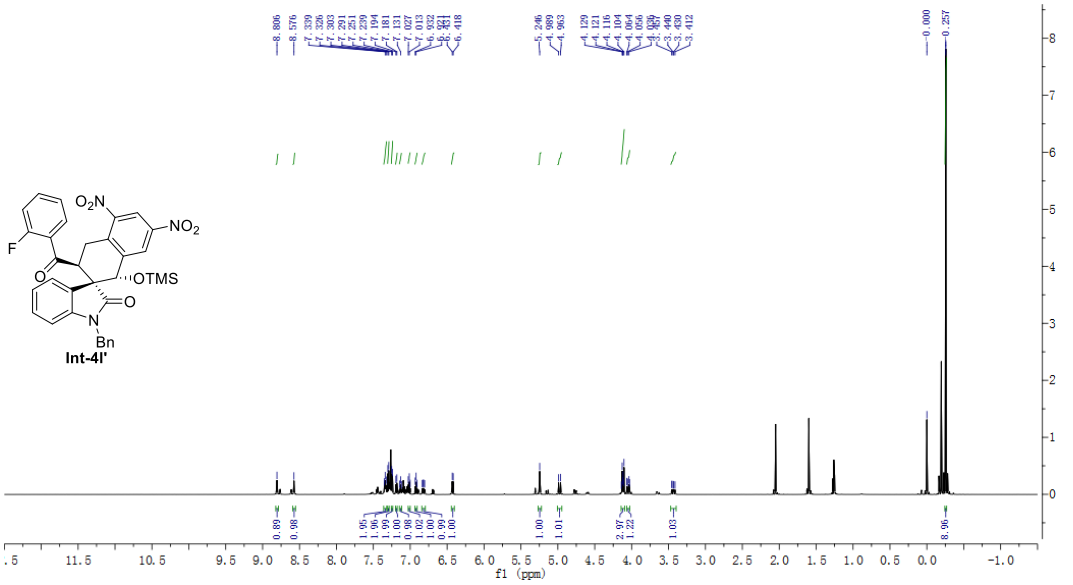
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.38	130.421	50.66	211.025	n.a.
2	n.a.	19.03	127.009	49.34	92.431	n.a.

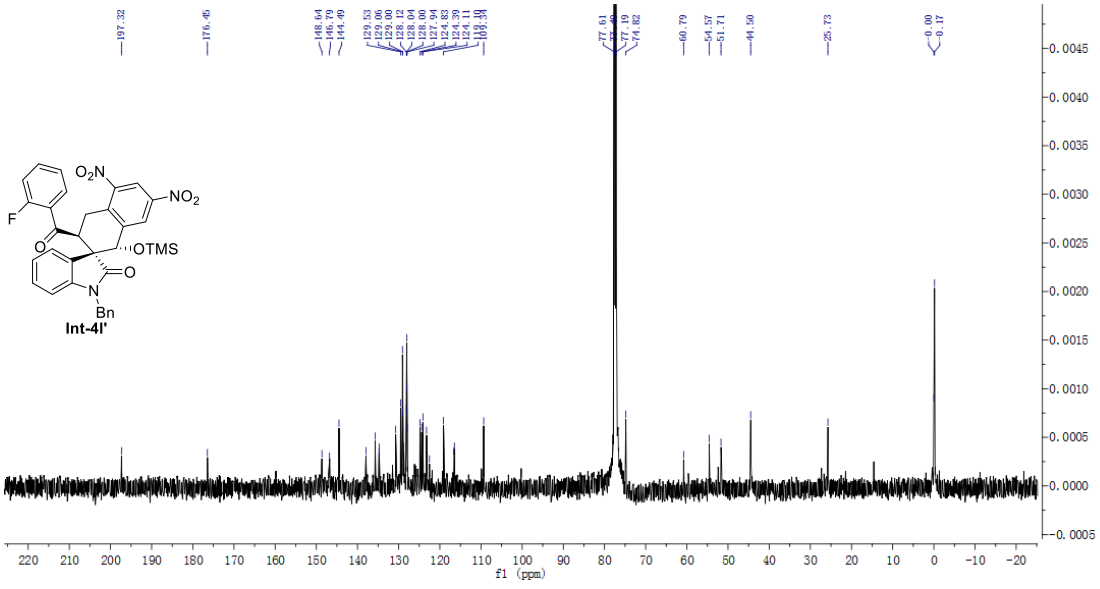


Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.24	11.767	2.37	20.102	n.a.
2	n.a.	18.78	485.023	97.63	353.469	n.a.



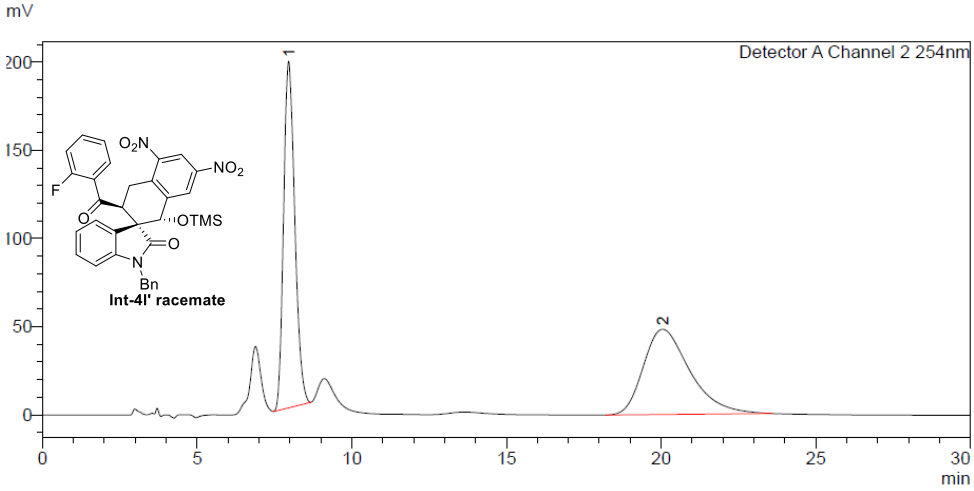

O2N
NO2
F
O
OTMS
O
N
Bn
Int-4l'
f1 (ppm)


O2N
NO2
F
O
OTMS
O
N
Bn
Int-4l'
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

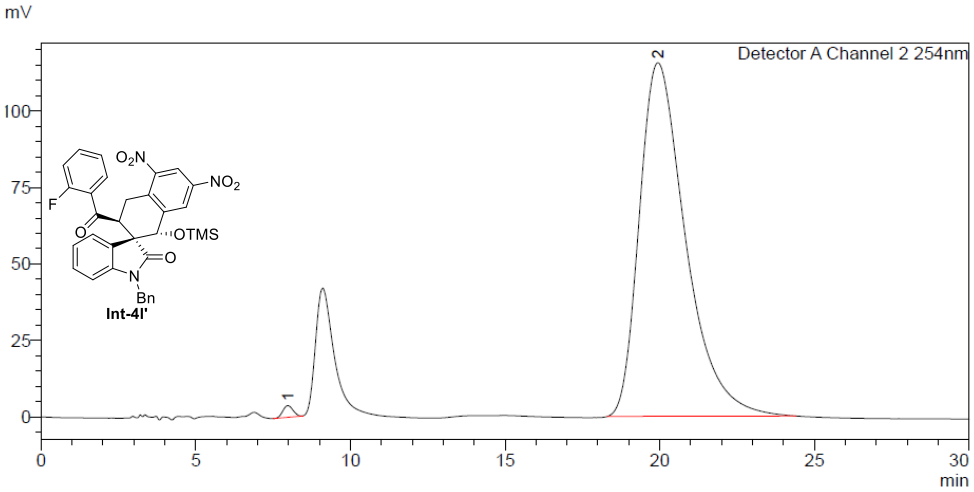
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.957	196450	4950901	49.508
2	20.049	48335	5049202	50.492
Total		244785	10000103	100.000

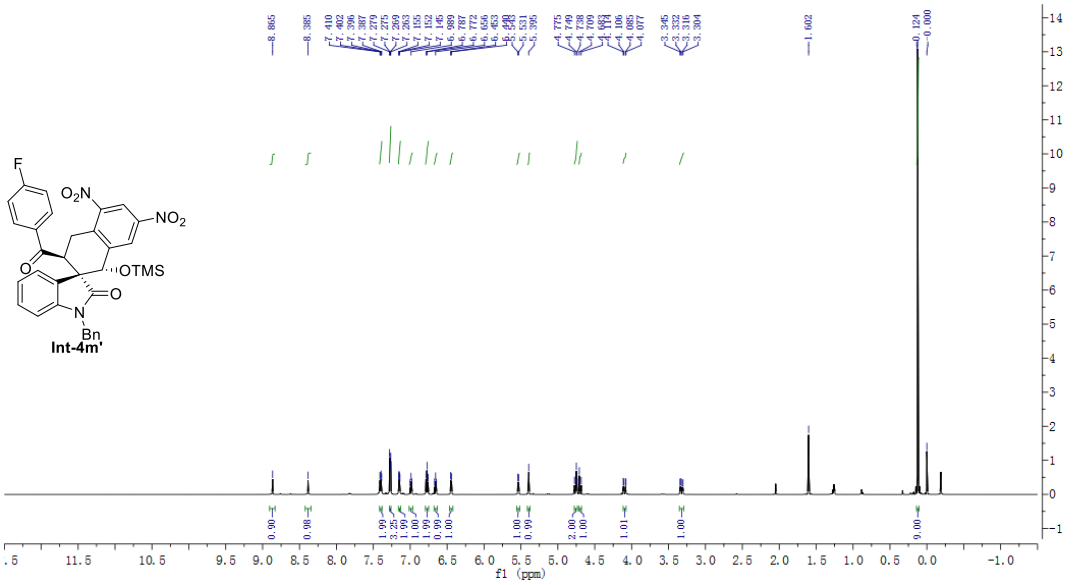


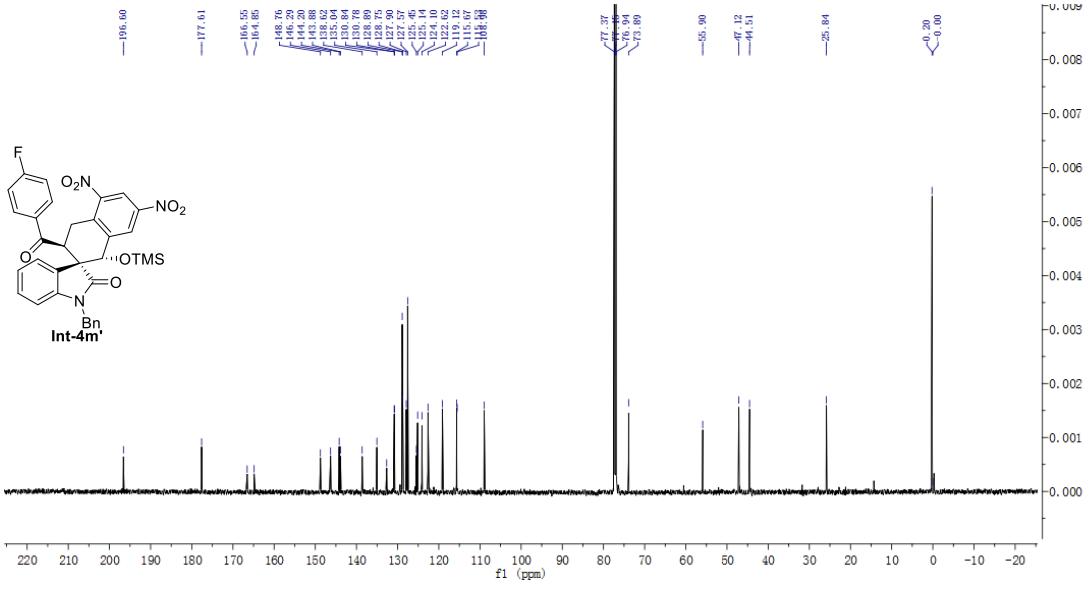
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.975	3812	87104	0.720
2	19.941	115633	12017766	99.280
Total		119445	12104870	100.000



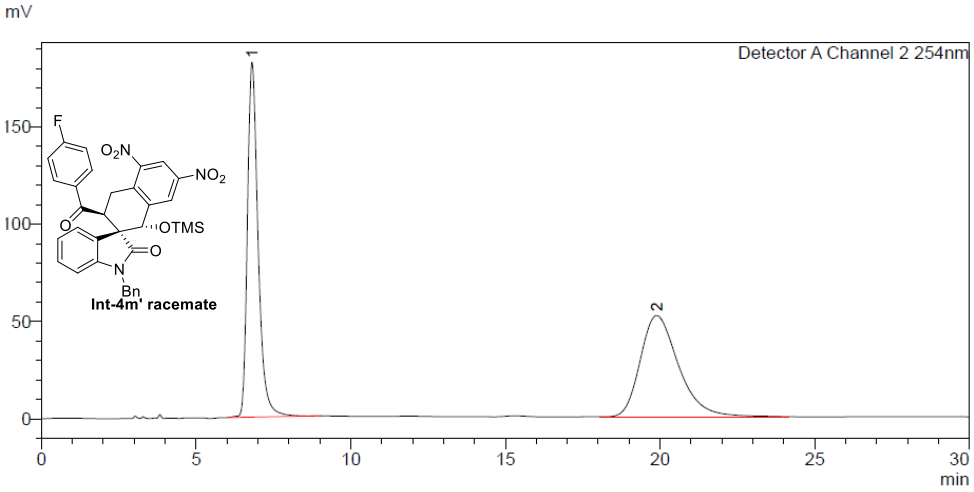

F
O2N
NO2
O
OTMS
O
N
Bn
Int-4m'
8.865
8.385
7.410
7.402
7.396
7.387
7.279
7.275
7.269
7.263
7.155
7.152
7.145
6.989
6.977
6.772
6.656
6.453
5.548
5.531
5.395
4.775
4.749
4.738
4.709
4.689
4.196
4.185
4.077
3.345
3.332
3.316
3.304
1.602
0.124
0.000
f1 (ppm)


F
O2N
NO2
O
OTMS
O
N
Bn
Int-4m'
196.60
177.61
166.55
164.65
148.76
146.29
144.20
143.88
138.52
135.04
130.84
130.78
128.89
128.75
127.90
127.57
125.45
124.14
122.62
119.12
115.67
77.37
77.16
76.94
73.80
55.90
47.12
44.51
25.84
0.20
0.00
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

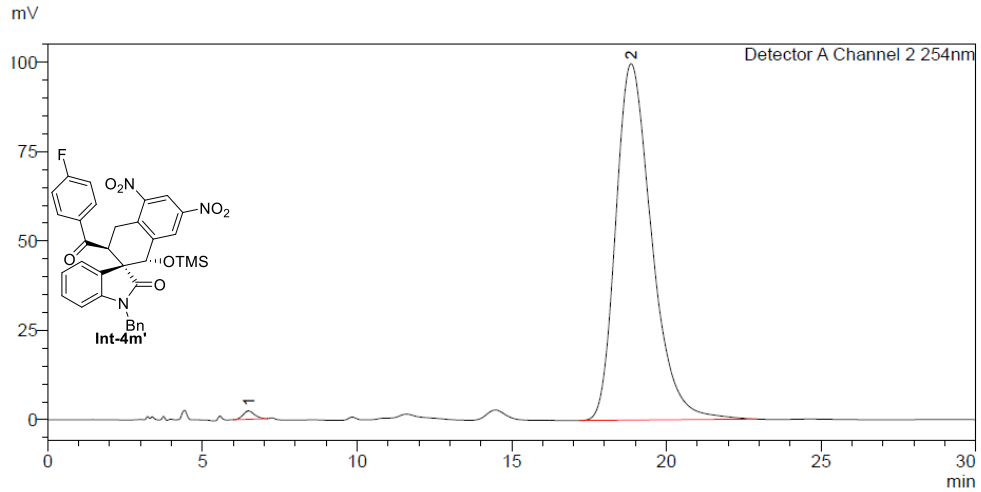
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.806	182416	4380411	49.481
2	19.891	52029	4472232	50.519
Total		234445	8852644	100.000

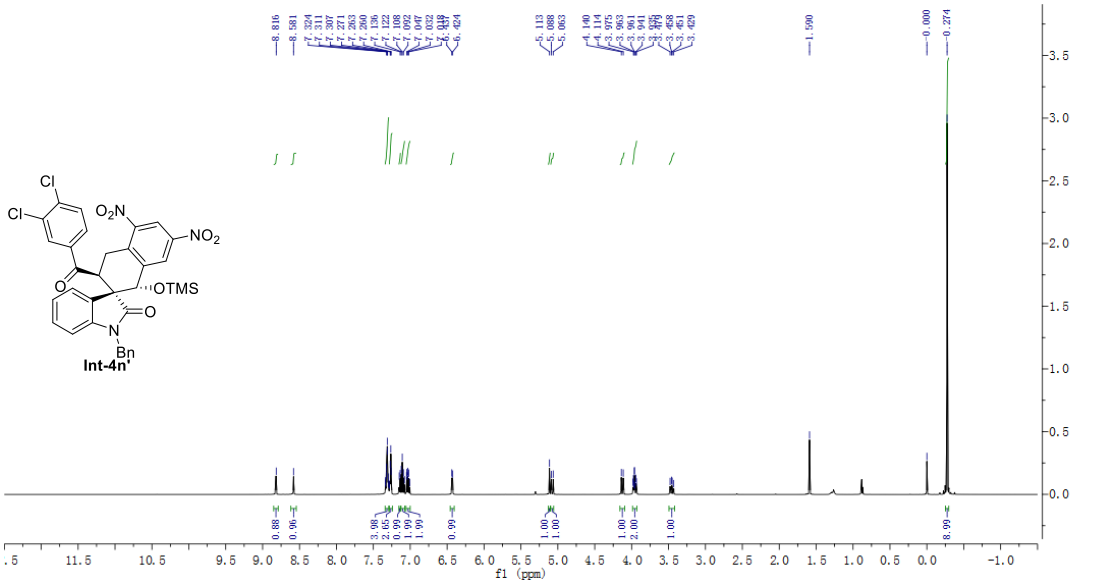


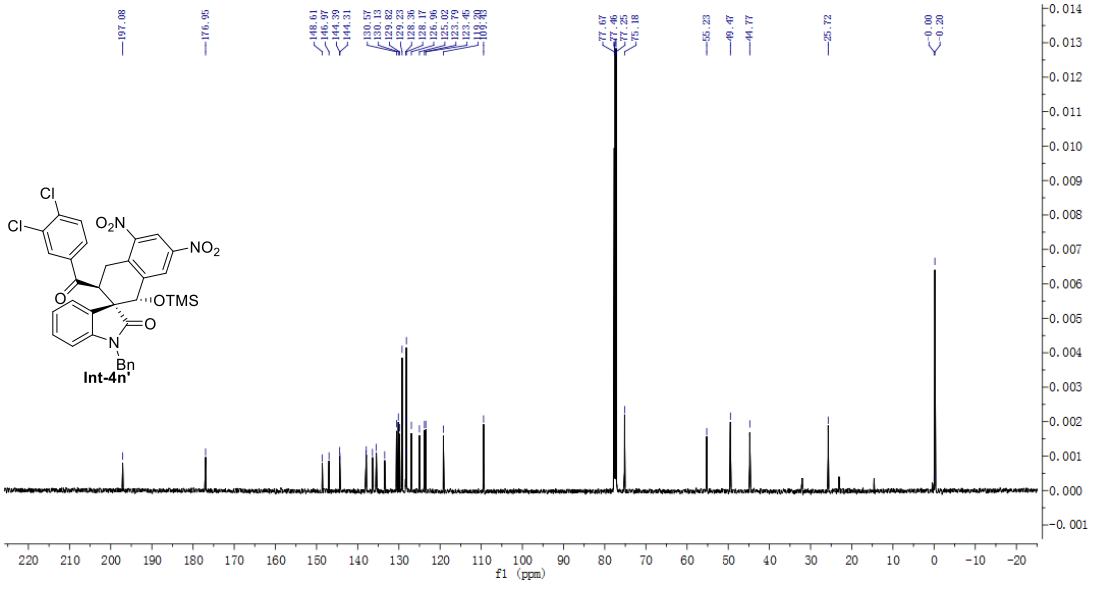
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.492	2399	61124	0.754
2	18.859	99689	8045397	99.246
Total		102088	8106521	100.000



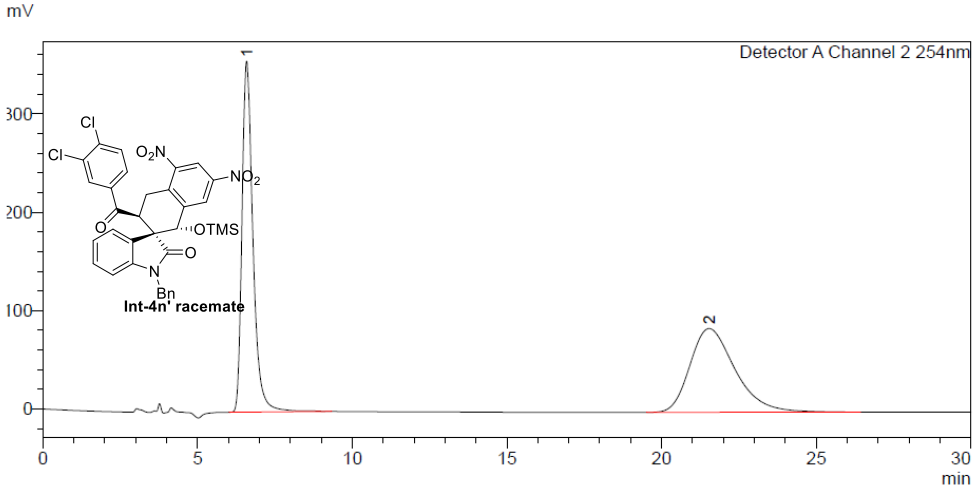

Cl
Cl
O2N
NO2
O
OTMS
O
N
Bn
Int-4n'


Cl
Cl
O2N
NO2
O
OTMS
O
N
Bn
Int-4n'

Peak Analysis Report

Detector A Channel 2 254nm

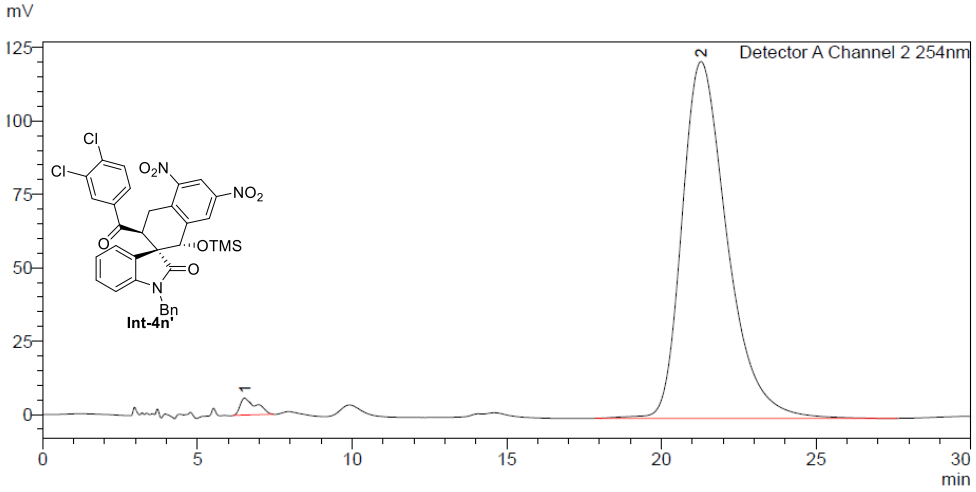
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.584	356641	8819990	50.528
2	21.537	85155	8635783	49.472
Total		441796	17455772	100.000

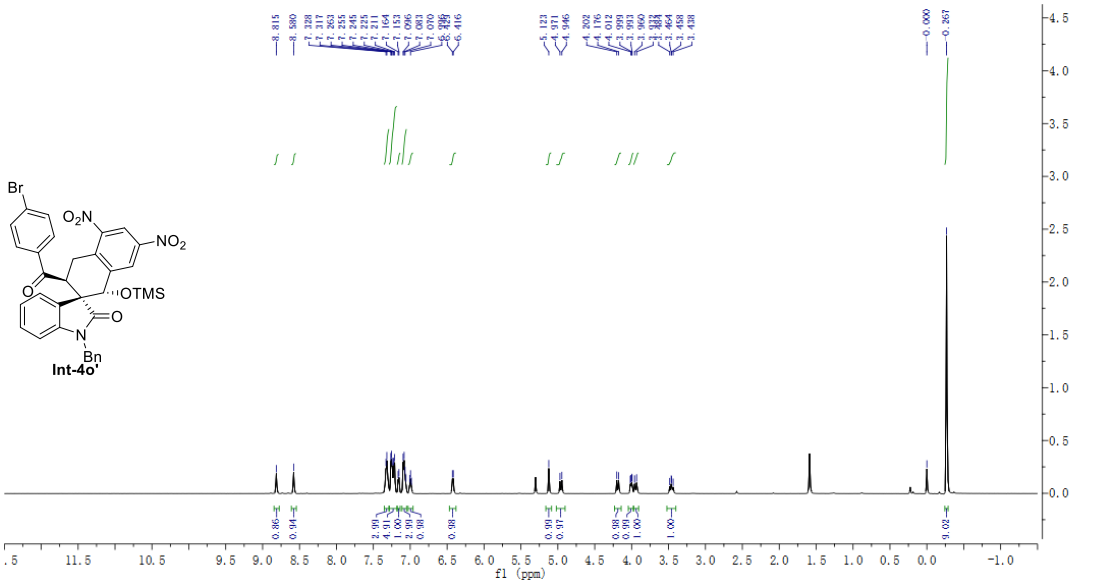


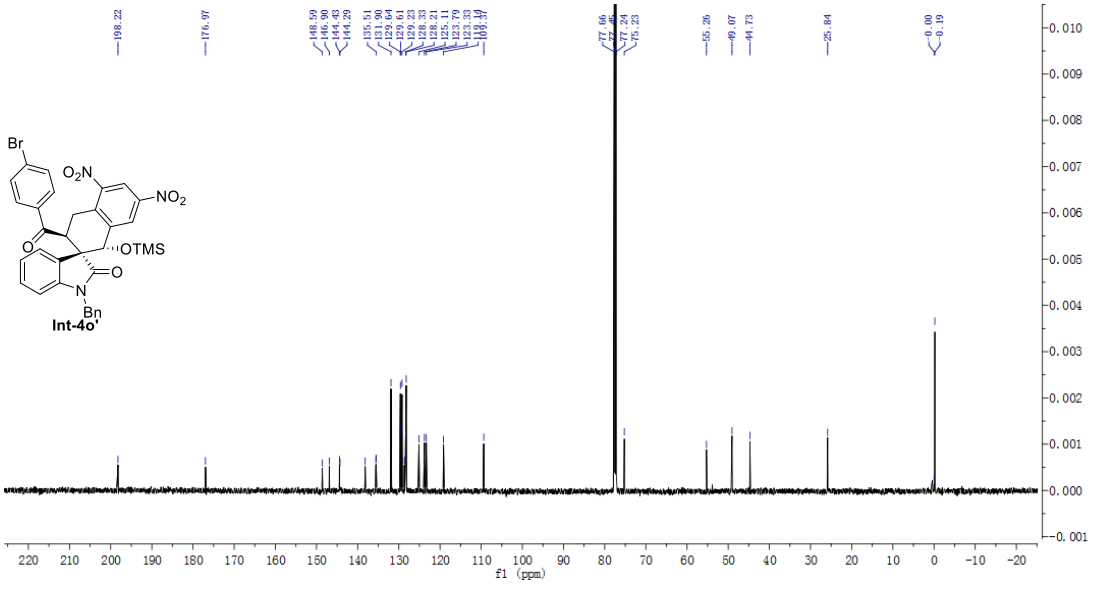
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.521	5769	209495	1.665
2	21.280	121527	12376296	98.335
Total		127295	12585791	100.000



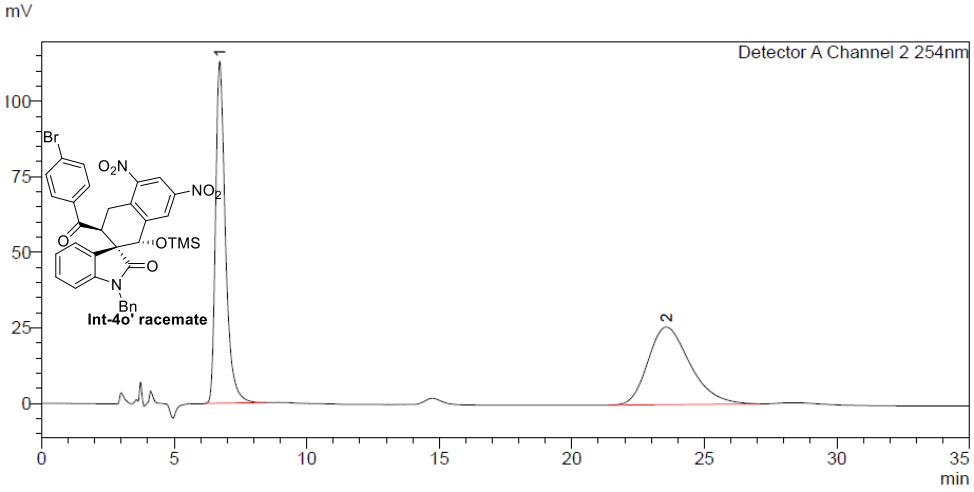

Br
O2N
NO2
OTMS
O
O
N
Bn
Int-4o'
f1 (ppm)


Br
O2N
NO2
OTMS
O
O
N
Bn
Int-4o'
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

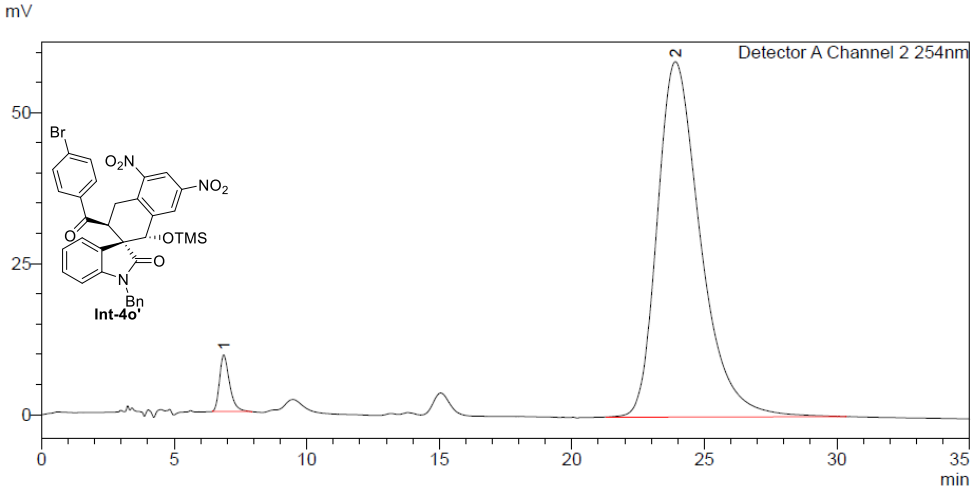
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.718	113116	2944475	50.987
2	23.570	25686	2830424	49.013
Total		138802	5774899	100.000

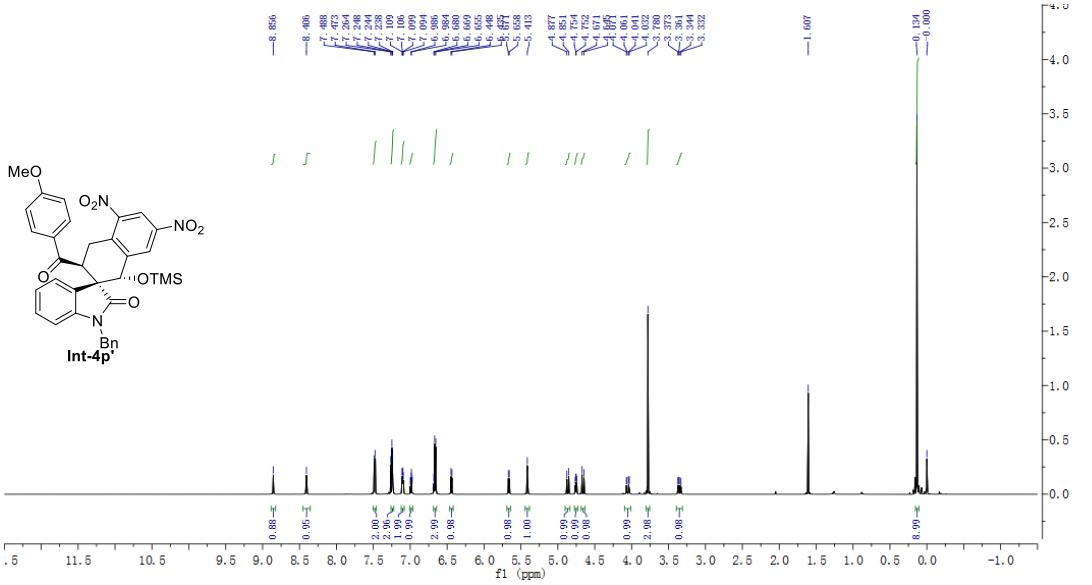


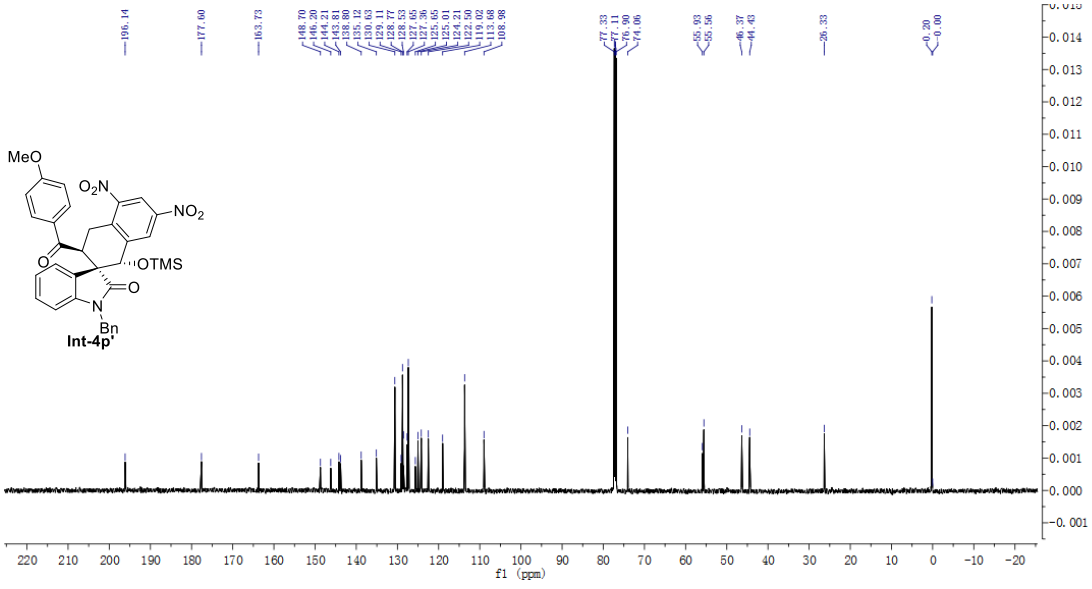
Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	6.869	9363	245796	3.556
2	23.905	58838	6666310	96.444
Total		68201	6912105	100.000



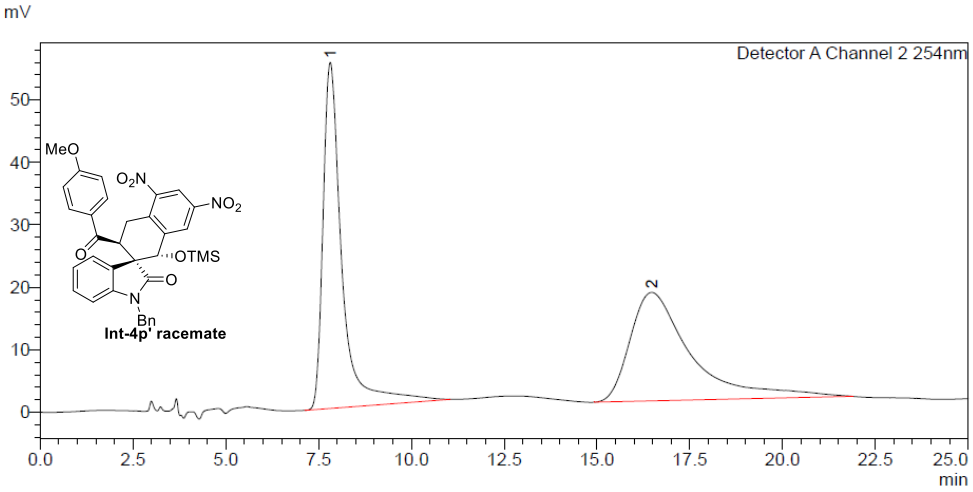

MeO
O2N
NO2
OTMS
O
O
N
Bn
Int-4p'
f1 (ppm)


MeO
O2N
NO2
OTMS
O
O
N
Bn
Int-4p'
f1 (ppm)

Peak Analysis Report

Detector A Channel 2 254nm

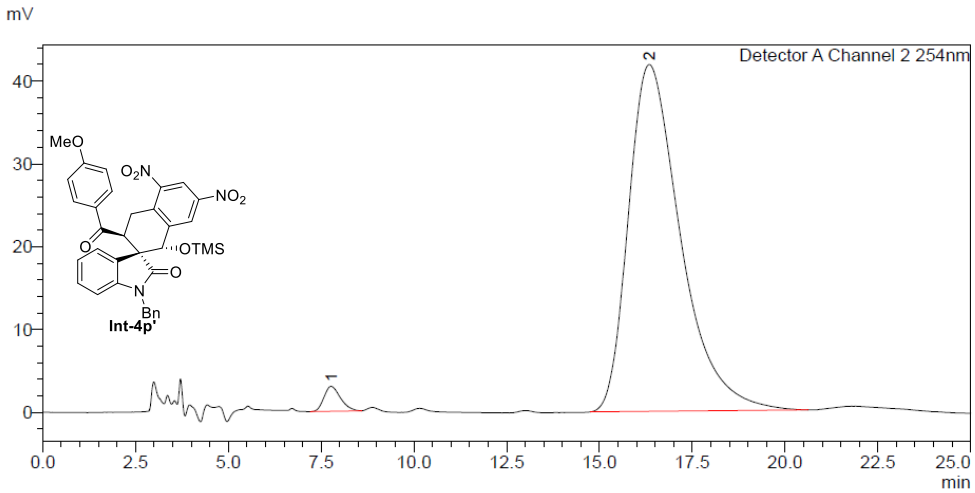
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.813	55395	1969613	49.868
2	16.473	17364	1980021	50.132
Total		72760	3949634	100.000

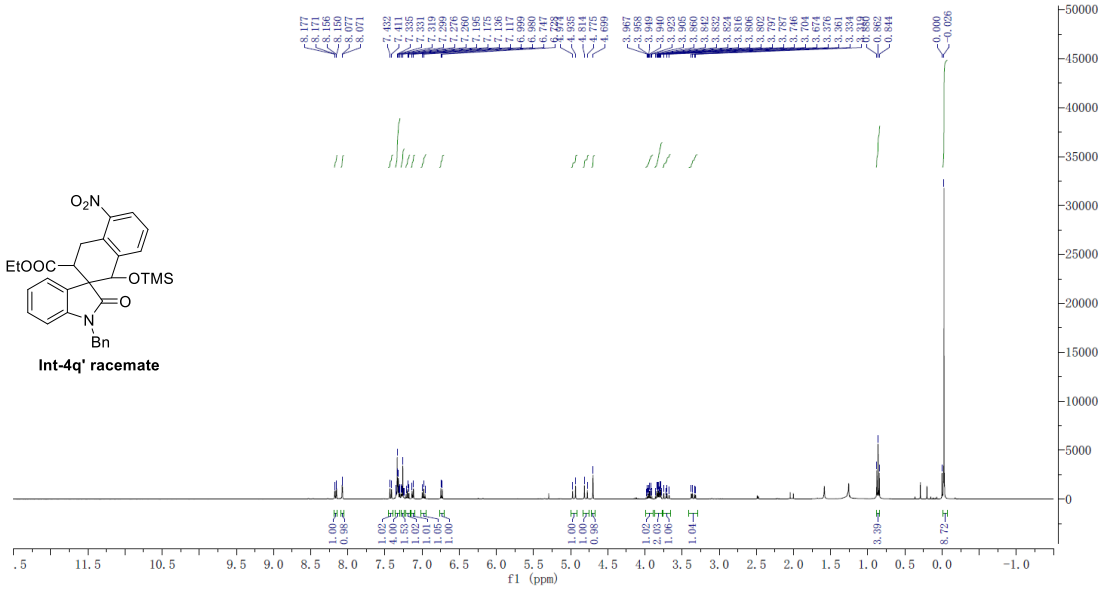


Peak Analysis Report

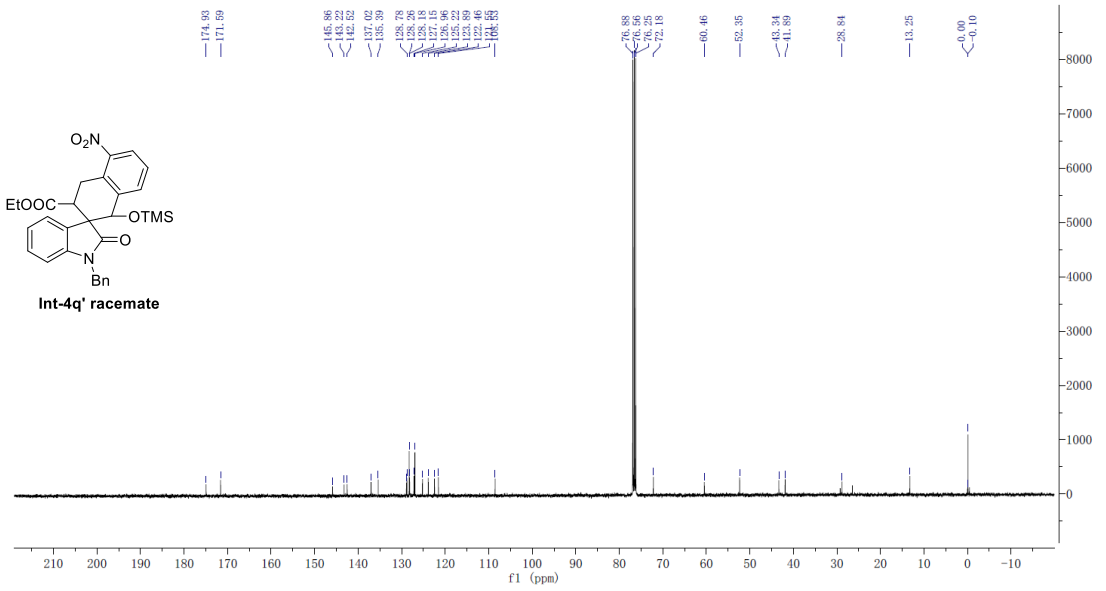
Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	7.774	3008	92784	2.218
2	16.343	41874	4089772	97.782
Total		44882	4182557	100.000

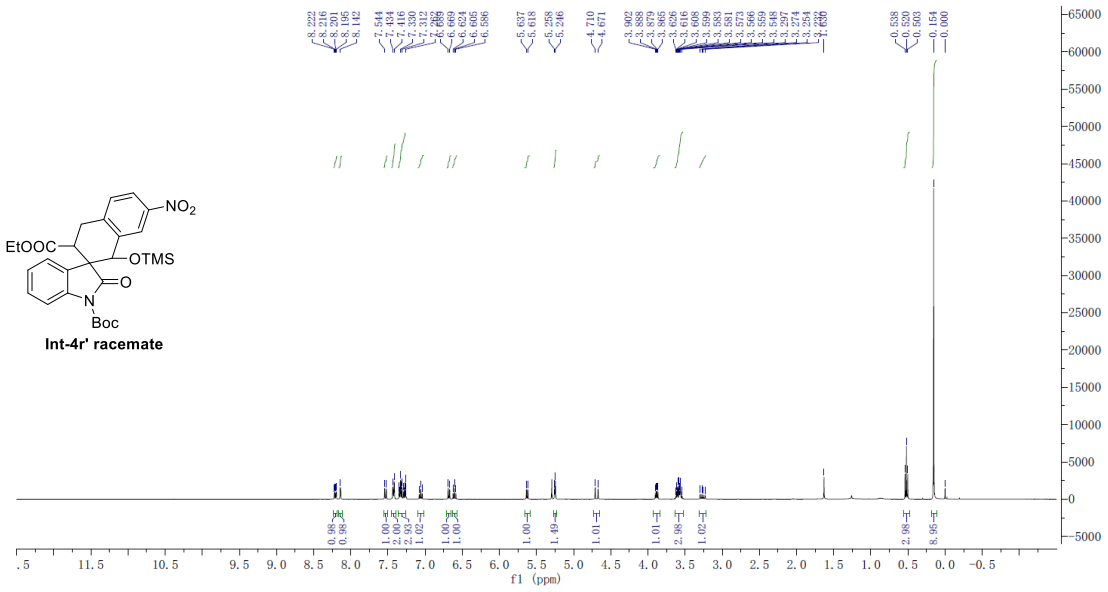


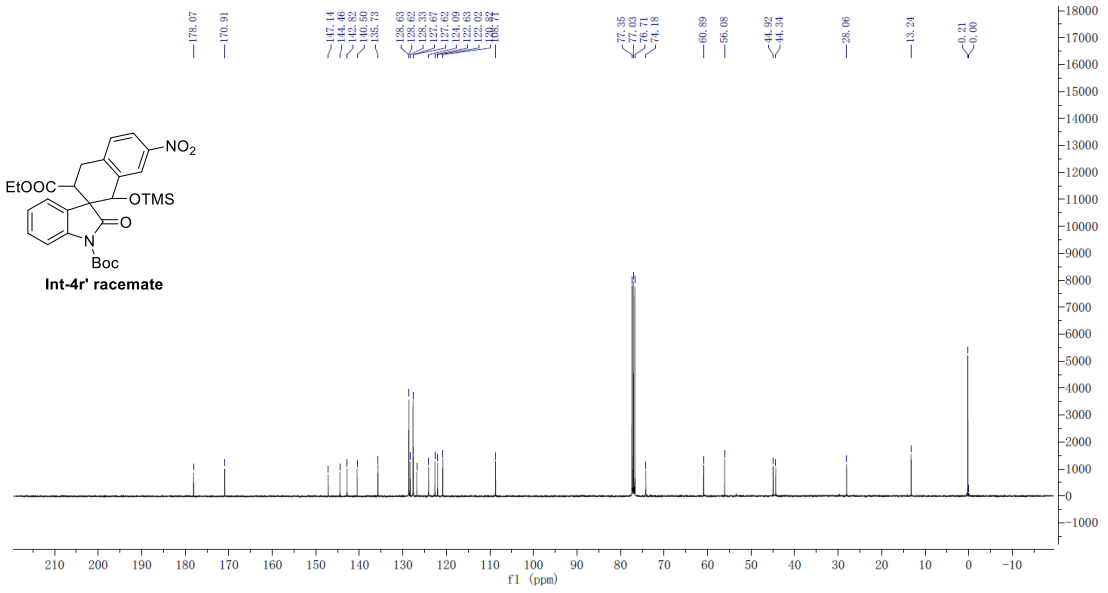


Int-4q' racemate

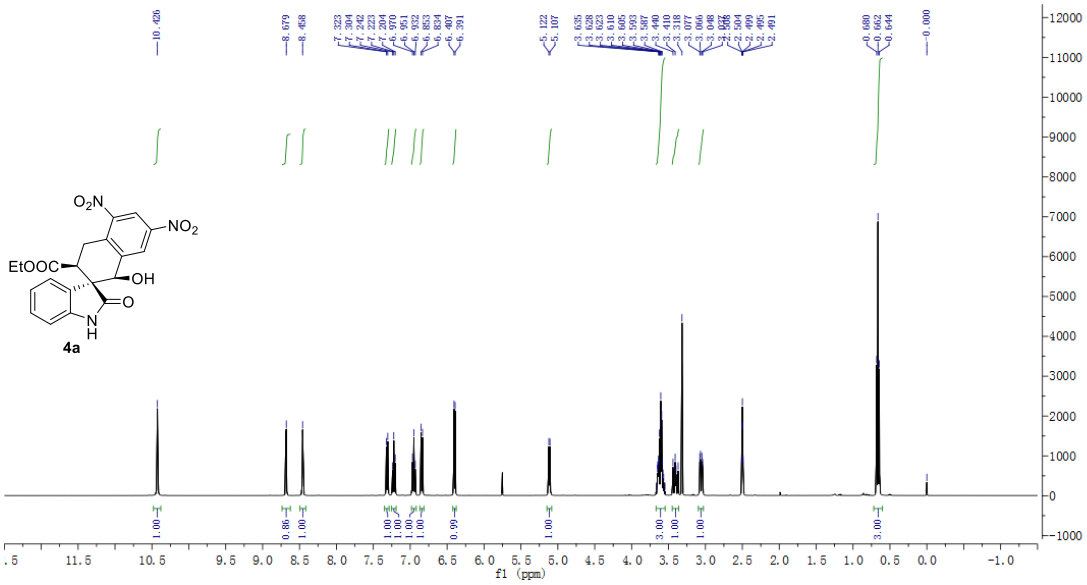


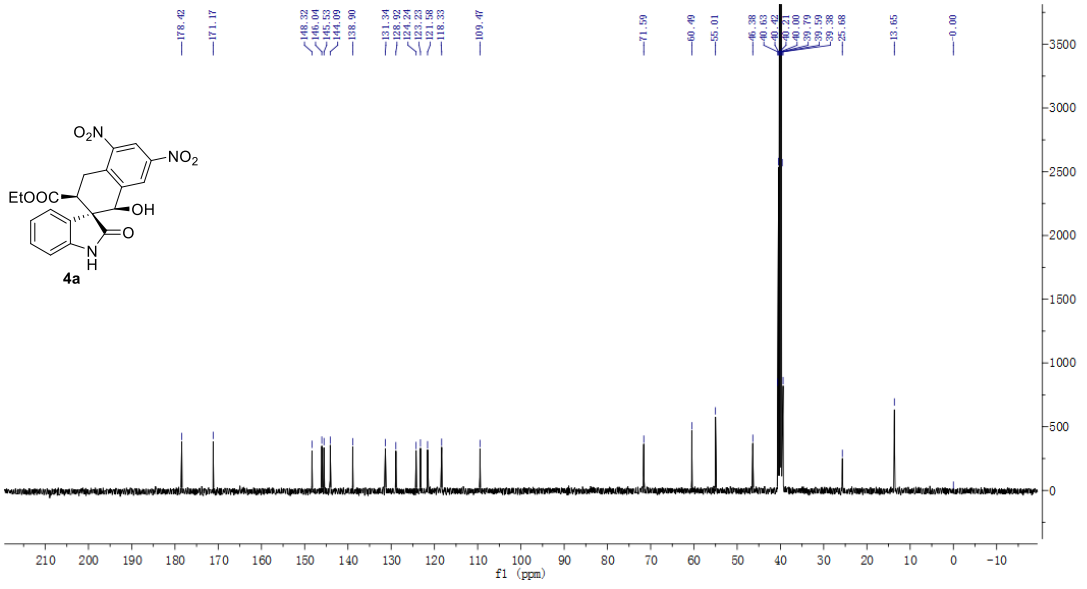
Int-4q' racemate

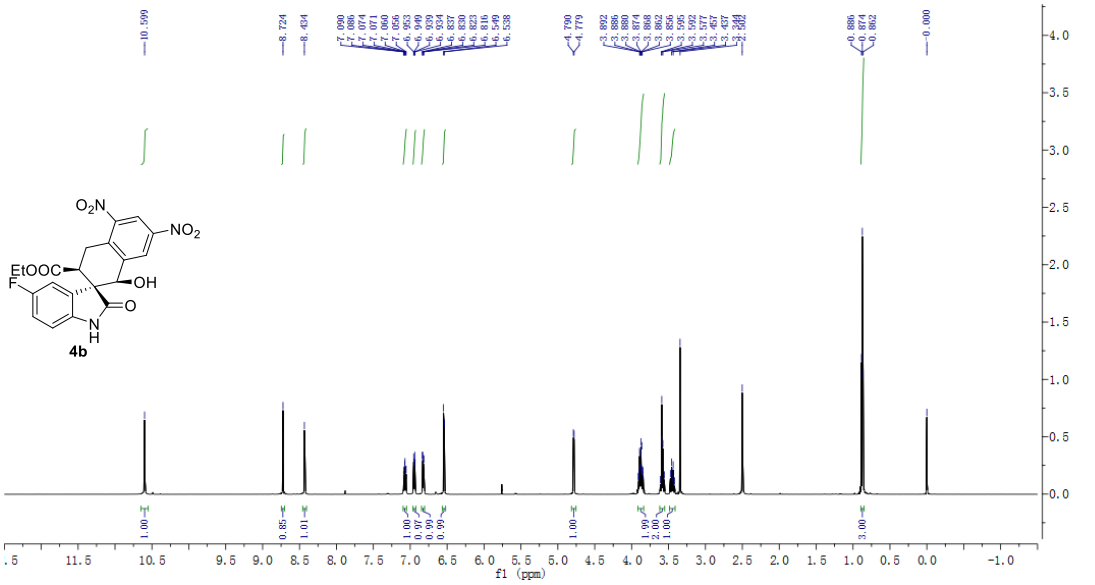


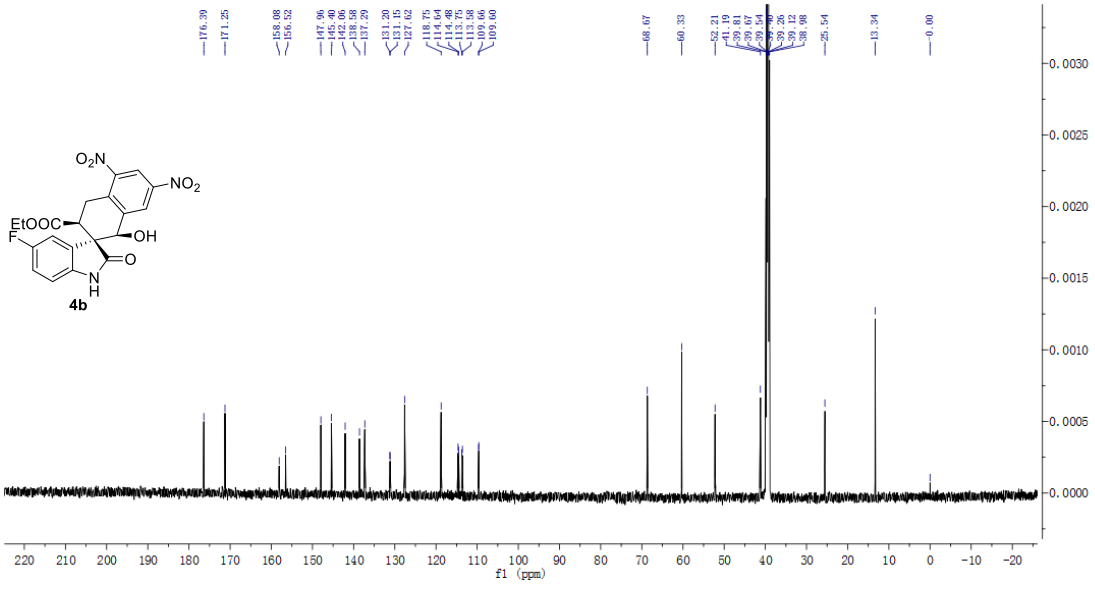


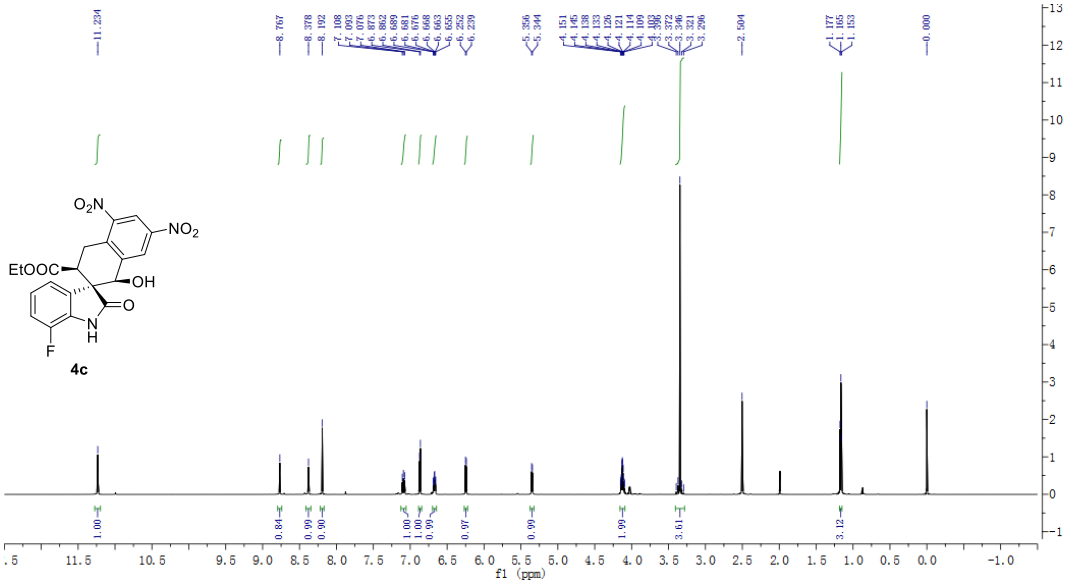
14. NMR spectra of compounds 4 and 4’

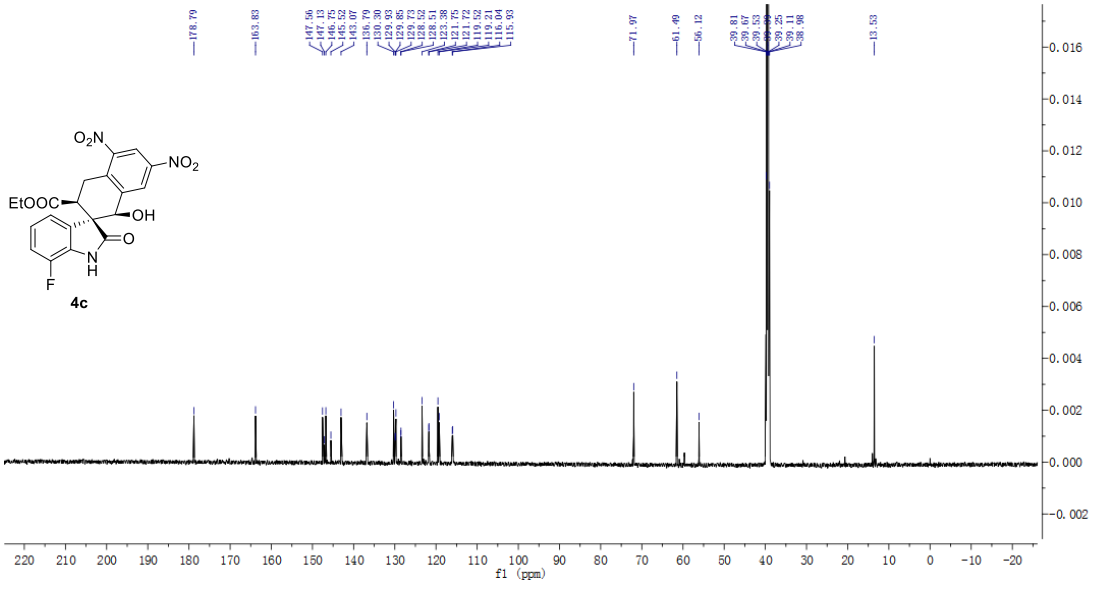

10.426
8.679
8.458
7.323
7.304
7.242
7.223
7.204
7.070
6.951
6.932
6.853
6.834
6.407
6.391
5.122
5.107
3.635
3.628
3.623
3.610
3.605
3.593
3.587
3.440
3.410
3.318
3.077
3.066
3.048
2.504
2.499
2.495
2.491
0.680
0.662
0.644
0.000
O2N
NO2
EtOOC
OH
O
N
H
4a
f1 (ppm)

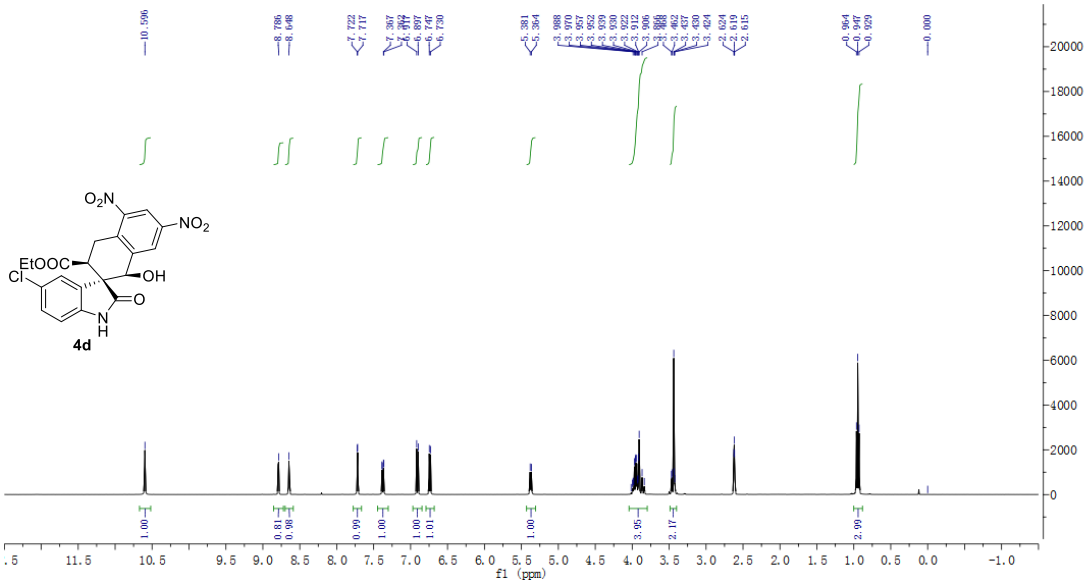

178.42
171.17
148.32
146.04
145.53
144.49
138.90
131.34
128.92
127.54
123.23
121.58
118.33
109.47
71.59
60.49
55.01
46.38
40.63
40.42
40.21
40.00
39.79
39.59
39.38
25.66
13.65
0.00
O2N
NO2
EtOOC
OH
O
N
H
4a
f1 (ppm)

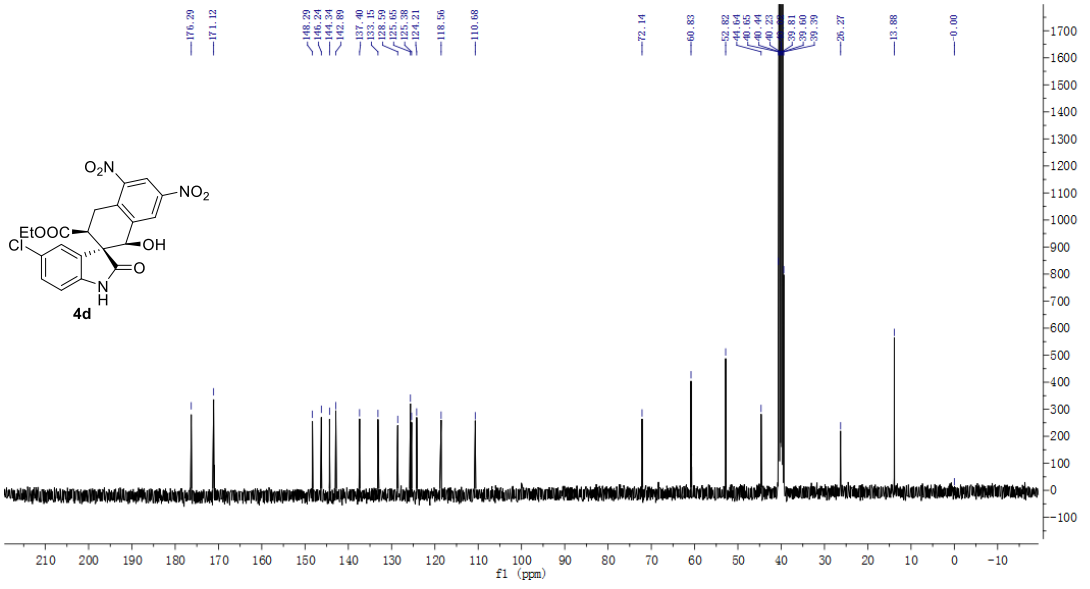

10.599
8.724
8.494
7.090
7.086
7.074
7.071
7.060
7.056
6.955
6.949
6.939
6.934
6.837
6.830
6.823
6.816
6.549
6.538
4.790
4.779
3.892
3.886
3.880
3.874
3.868
3.862
3.856
3.595
3.592
3.577
3.567
3.437
3.431
0.886
0.874
0.862
0.000
O2N
NO2
EtOOC
F
OH
O
N
H
4b
1.00
0.85
1.01
1.00
0.97
0.99
0.99
1.00
1.09
2.00
1.00
3.00
f1 (ppm)

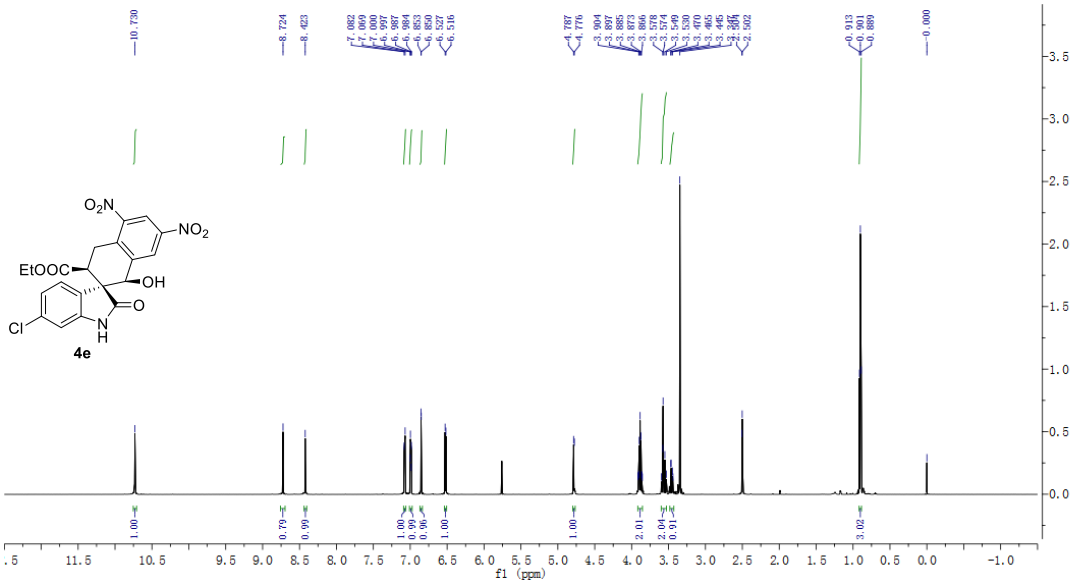

176.39
171.25
158.08
156.52
147.96
145.40
142.06
138.58
137.39
131.20
131.15
127.62
118.75
114.64
114.48
113.75
113.58
109.66
109.60
68.67
60.33
52.21
41.19
39.81
39.67
39.54
39.40
39.26
39.12
38.98
25.54
13.34
0.00
O2N
NO2
EtOOC
F
OH
O
N
H
4b
f1 (ppm)

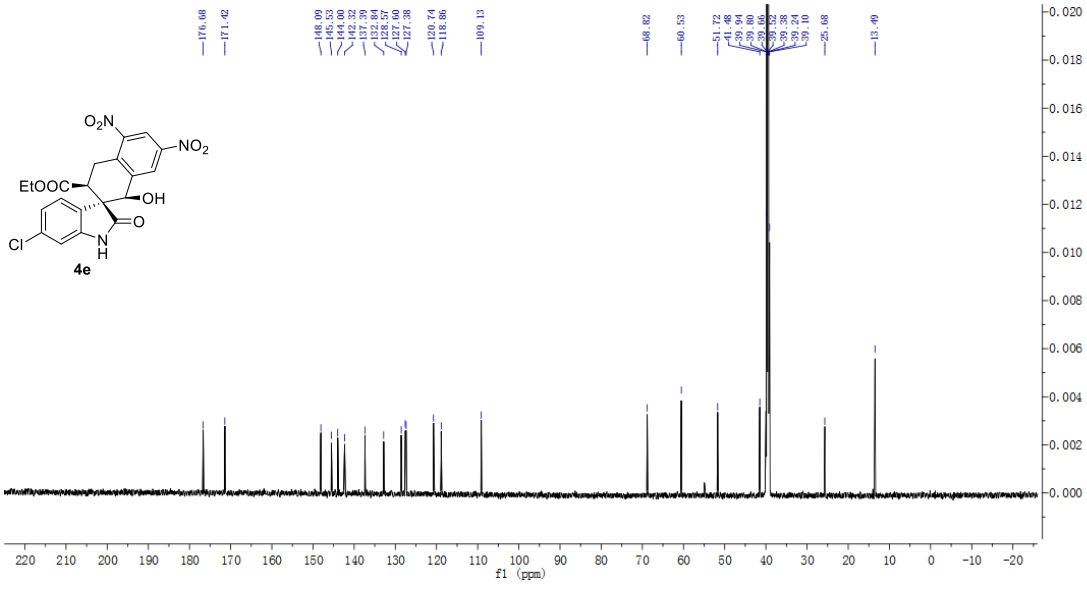

11.234
8.767
8.378
8.192
7.108
7.093
7.076
6.873
6.862
6.699
6.681
6.676
6.668
6.663
6.655
6.252
6.239
5.356
5.344
4.151
4.146
4.138
4.133
4.126
4.121
4.114
4.109
3.372
3.346
3.321
3.296
2.504
1.177
1.165
1.153
0.000
O2N
NO2
EtOOC
OH
O
N
H
F
4c
1.00
0.84
0.99
0.90
1.00
1.00
0.99
0.97
0.99
1.99
3.01
3.12
f1 (ppm)

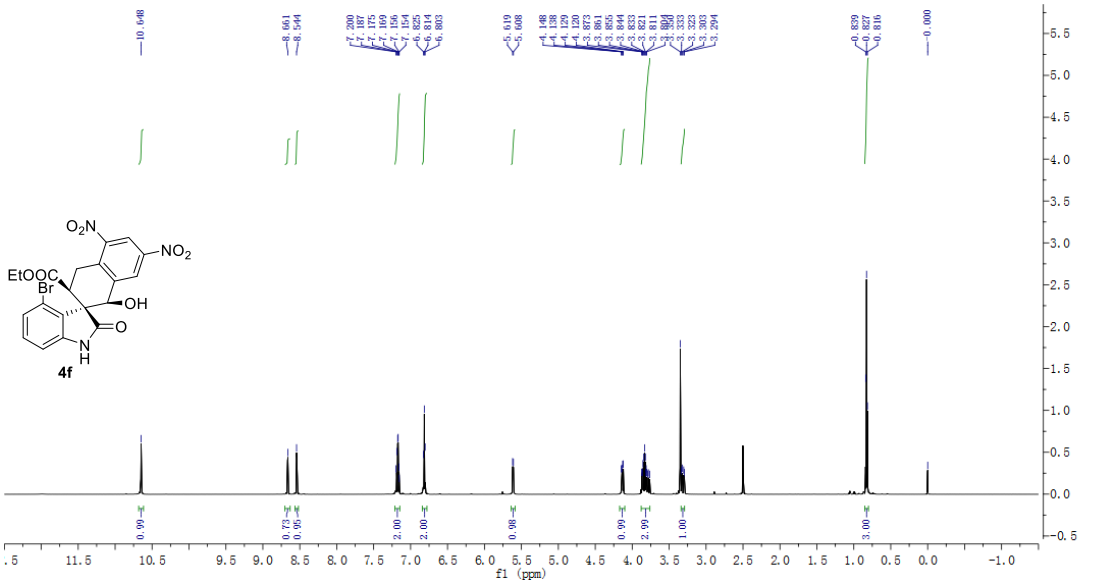

178.79
163.83
147.56
147.13
146.75
145.52
143.07
130.79
130.39
129.93
129.85
129.73
129.62
128.51
123.38
121.75
121.72
119.52
119.21
116.04
115.93
71.97
61.49
56.12
39.81
39.67
39.53
39.39
39.25
39.11
38.98
13.53
O2N
NO2
EtOOC
OH
O
N
H
F
4c
f1 (ppm)


4d


4d


10.730
8.724
8.423
7.082
7.069
7.000
6.997
6.984
6.853
6.527
6.516
4.787
4.776
3.904
3.897
3.885
3.873
3.866
3.578
3.574
3.549
3.539
3.470
3.465
3.445
2.502
0.913
0.901
0.889
0.000
1.00
0.79
0.99
1.00
0.99
0.96
1.00
1.00
2.01
2.04
0.91
3.02
f1 (ppm)
4e


176.68
171.42
148.09
145.53
144.00
143.32
137.39
132.84
128.57
127.60
127.38
120.74
118.86
109.13
68.82
60.53
51.72
41.46
39.94
39.80
39.66
39.52
39.38
39.24
39.10
25.68
13.49
f1 (ppm)
4e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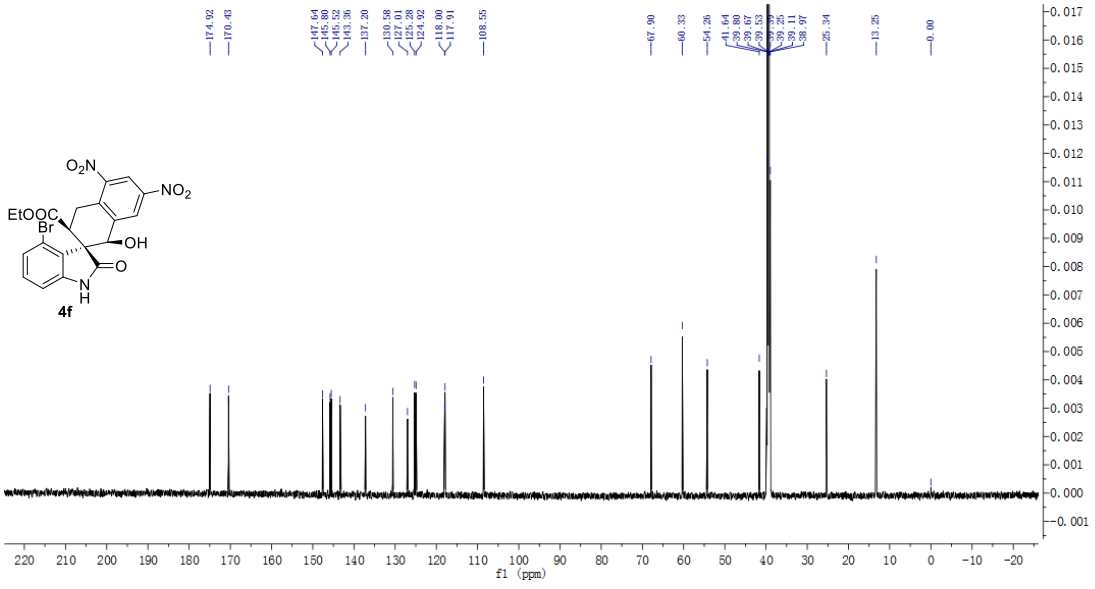
8.544
7.200
7.187
7.175
7.169
7.156
7.154
6.825
6.814
6.803
5.619
5.608
4.148
4.138
4.129
4.120
3.873
3.861
3.855
3.844
3.833
3.821
3.811
3.333
3.323
3.303
3.294
0.839
0.827
0.816
0.000
O2N
NO2
EtOOC
Br
OH
O
N
H
4f
0.99
0.73
0.95
2.00
2.00
0.98
0.99
2.99
1.00
3.00
f1 (ppm)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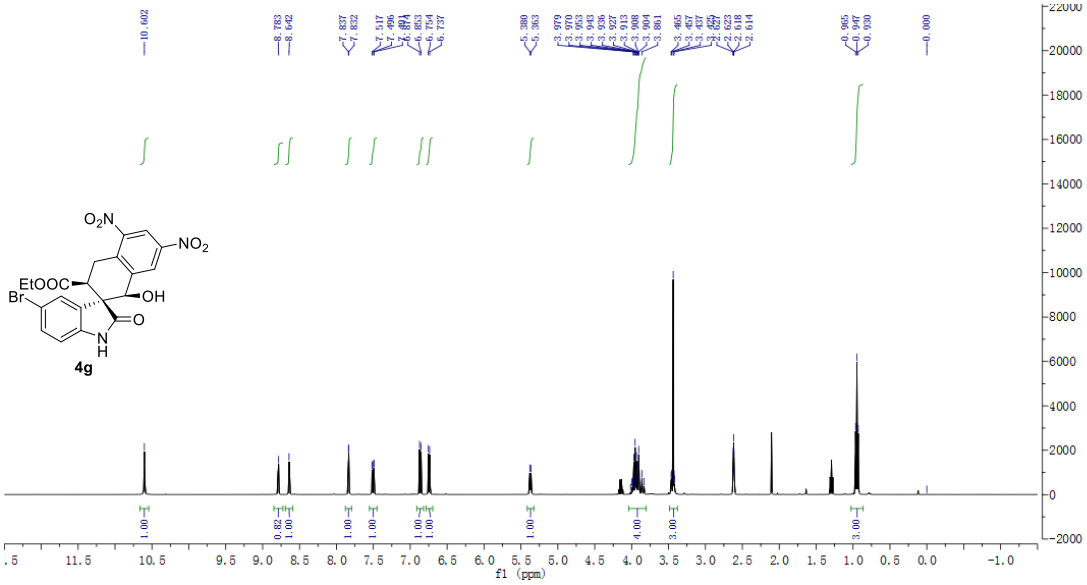
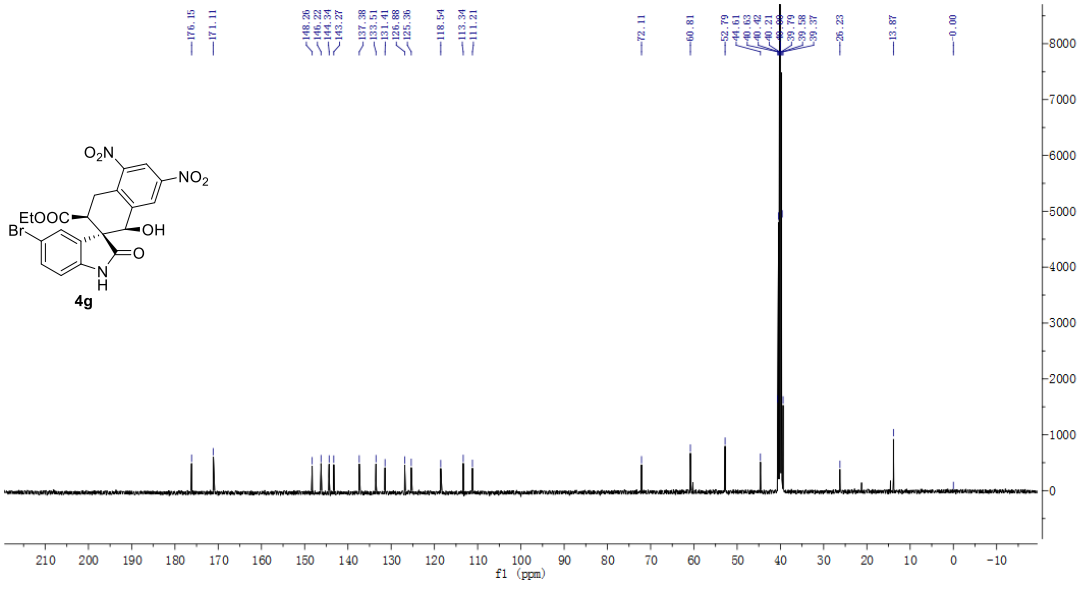
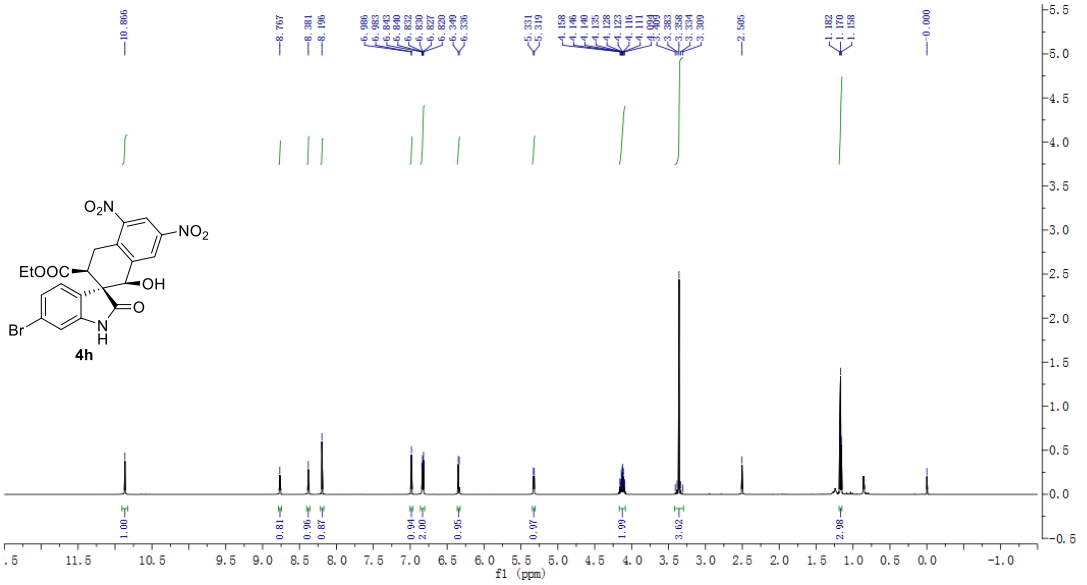
147.64
145.89
145.52
143.36
137.20
130.58
127.01
125.28
124.92
118.00
117.91
108.55
67.90
60.33
54.26
41.64
39.80
39.67
39.53
39.39
39.25
39.11
38.97
25.34
13.25
0.00
O2N
NO2
EtOOC
Br
OH
O
N
H
4f
f1 (ppm)


4g
fl (ppm)


4g
fl (ppm)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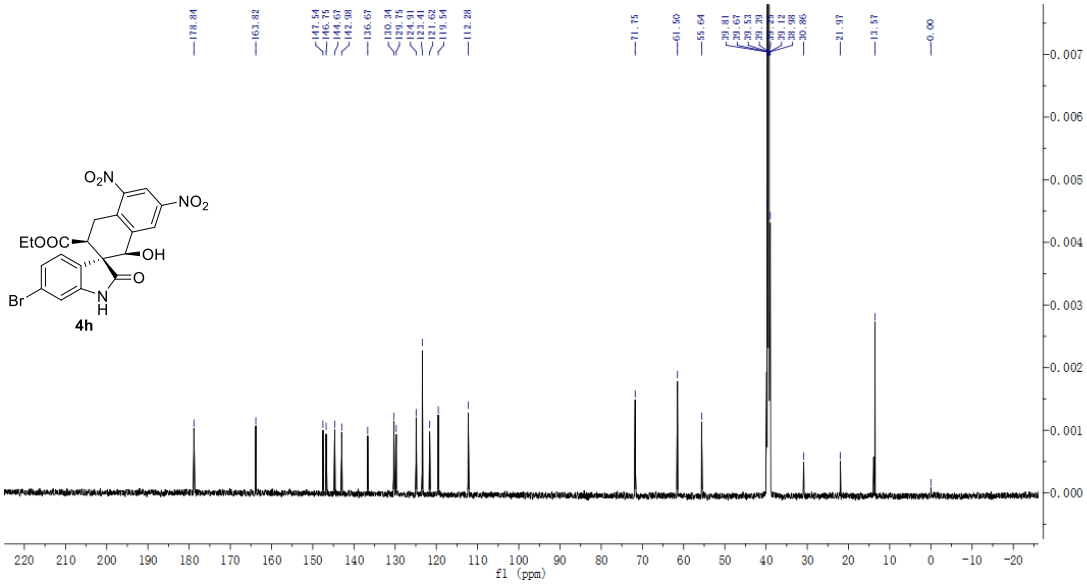
6.843
6.840
6.832
6.830
6.827
6.820
6.349
6.336
5.331
5.319
4.158
4.146
4.140
4.135
4.128
4.123
4.115
4.111
3.383
3.358
3.354
3.309
2.505
1.182
1.170
1.158
0.000
O2N
NO2
EtOOC
OH
O
Br
N
H
4h
1.00
0.81
0.90
0.87
0.94
2.00
0.95
0.97
1.99
3.02
2.98
f1 (ppm)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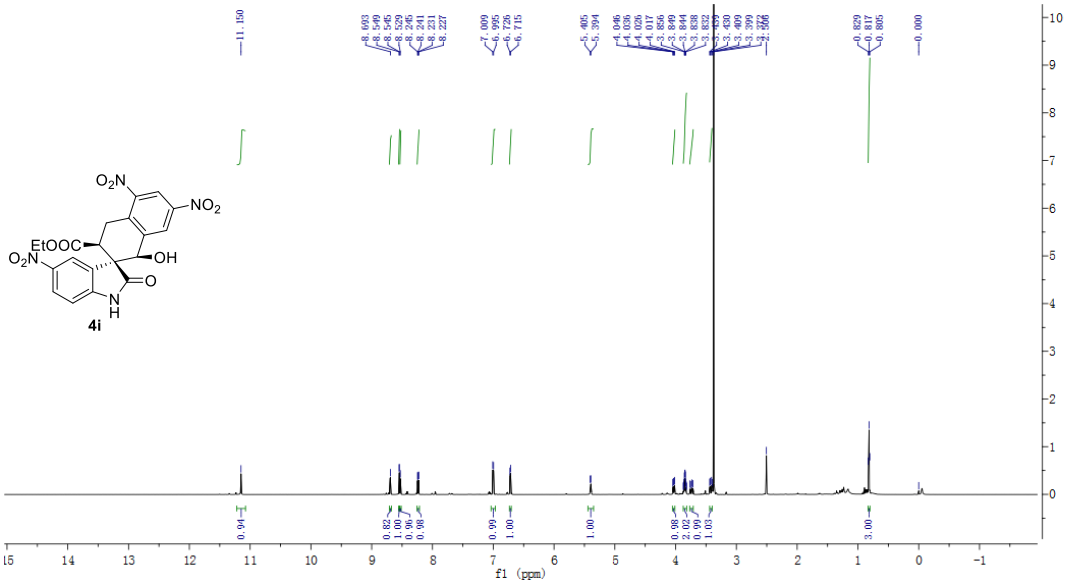
163.82
147.54
146.75
144.67
142.98
136.67
130.34
129.75
124.91
123.44
121.62
119.54
112.28
71.75
61.50
55.64
29.81
29.67
29.53
29.39
29.12
28.98
20.86
21.97
13.57
0.00
O2N
NO2
EtOOC
OH
O
Br
N
H
4h
f1 (ppm)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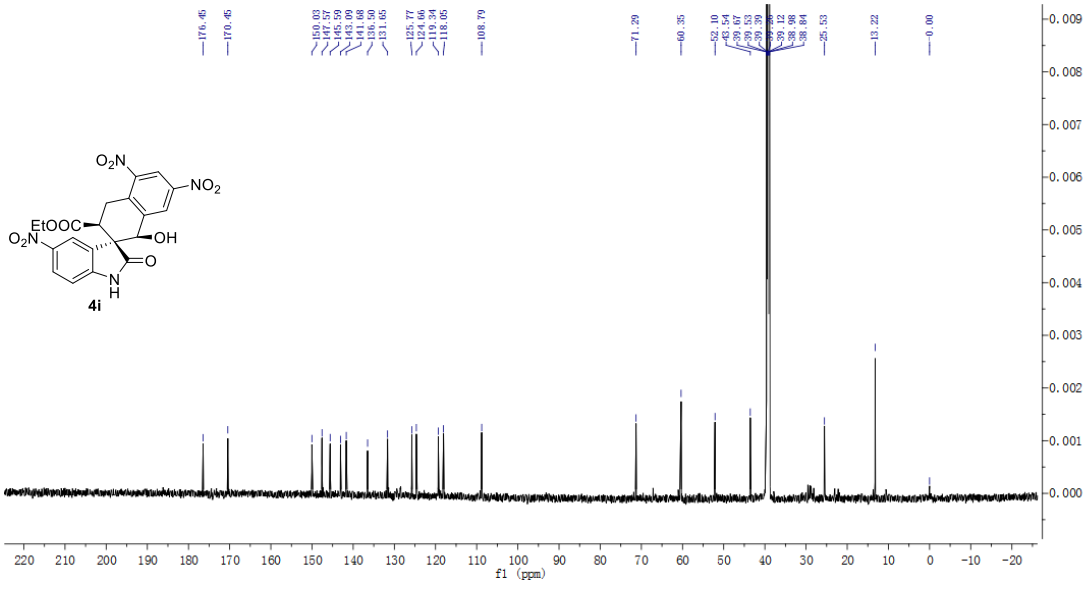
8.241
8.231
8.227
7.009
6.995
6.725
6.715
5.405
5.394
4.046
4.036
4.026
4.017
3.856
3.849
3.844
3.838
3.832
3.430
3.409
3.399
3.388
1.566
0.829
0.817
0.805
0.000
0.94
0.82
1.00
0.98
0.98
1.00
0.99
1.00
1.00
0.98
2.02
0.99
1.03
3.00
f1 (ppm)
O2N
NO2
EtOOC
O2N
OH
O
N
H
4i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170.45
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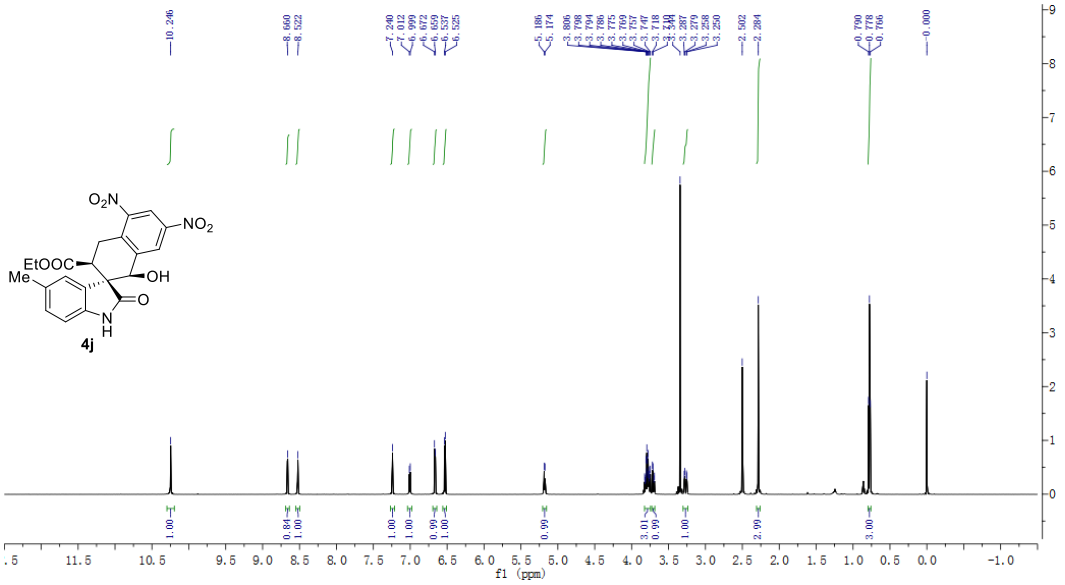
145.59
143.09
141.68
136.50
131.65
125.77
124.46
119.34
118.05
108.79
71.29
60.35
52.10
43.54
39.67
39.53
39.39
39.25
39.12
38.98
38.84
25.53
13.22
0.00
f1 (ppm)
O2N
NO2
EtOOC
O2N
OH
O
N
H
4i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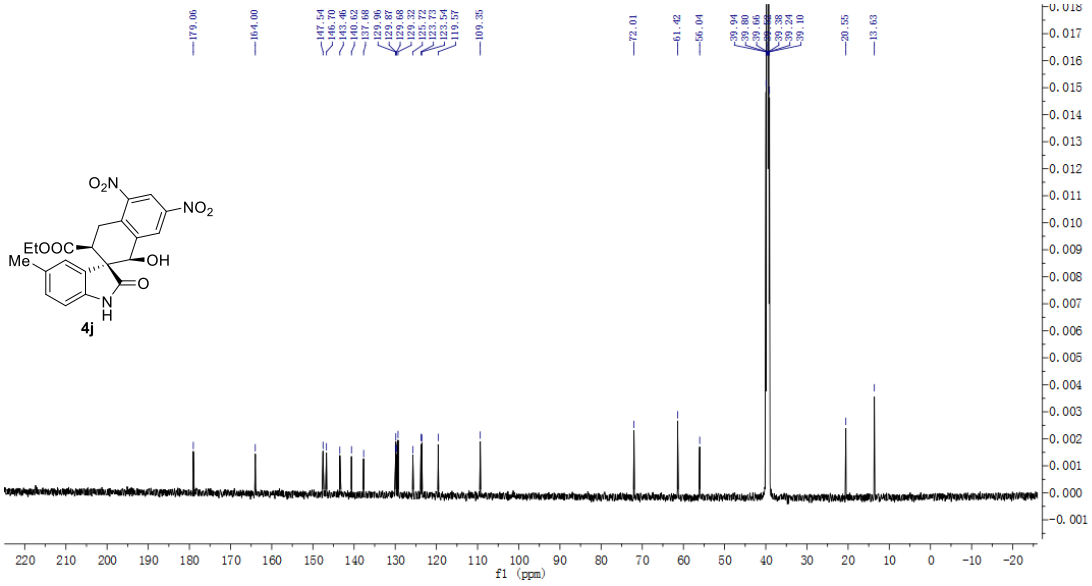
8.522
7.240
7.012
6.999
6.672
6.659
6.537
6.525
5.186
5.174
3.806
3.798
3.794
3.786
3.775
3.769
3.757
3.747
3.718
3.279
3.258
3.250
2.502
2.284
0.790
0.778
0.766
0.000
1.00
0.84
1.00
1.00
1.00
0.99
1.00
0.99
3.01
0.99
1.00
2.99
3.00
f1 (ppm)
O2N
NO2
EtOOC
Me
OH
O
N
H
4j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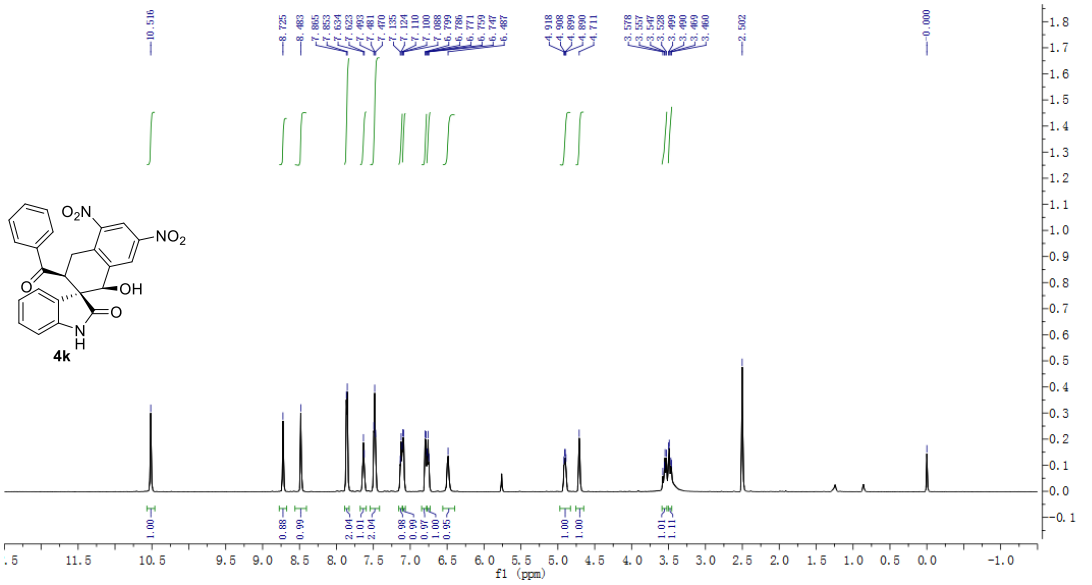
164.00
147.54
146.70
143.46
140.62
137.68
129.96
129.87
129.68
129.32
125.72
123.73
123.54
119.57
109.35
72.01
61.42
56.04
39.94
39.80
39.66
39.52
39.38
39.24
39.10
20.55
13.63
f1 (ppm)
O2N
NO2
EtOOC
Me
OH
O
N
H
4j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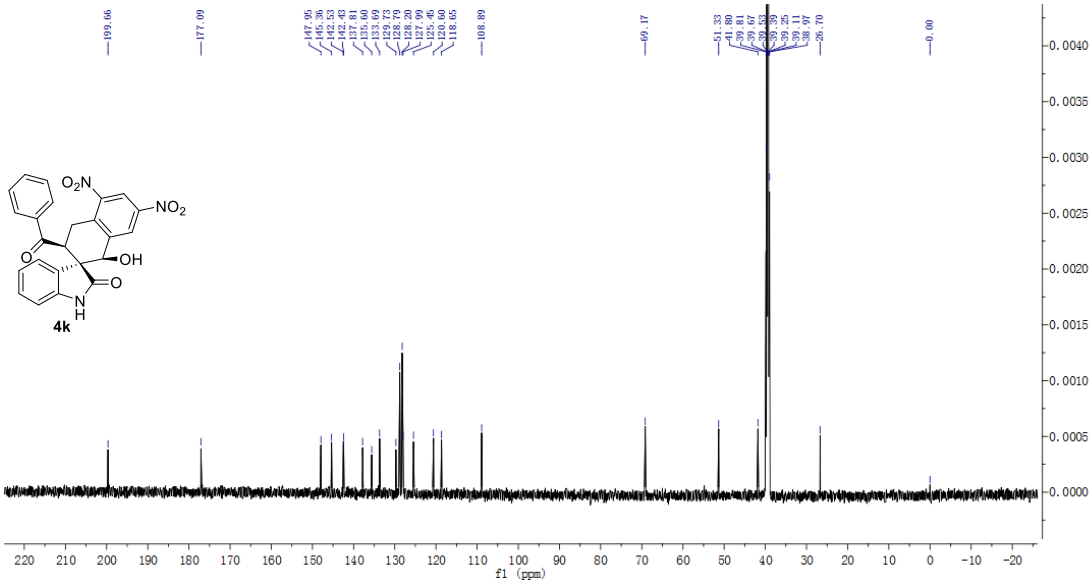
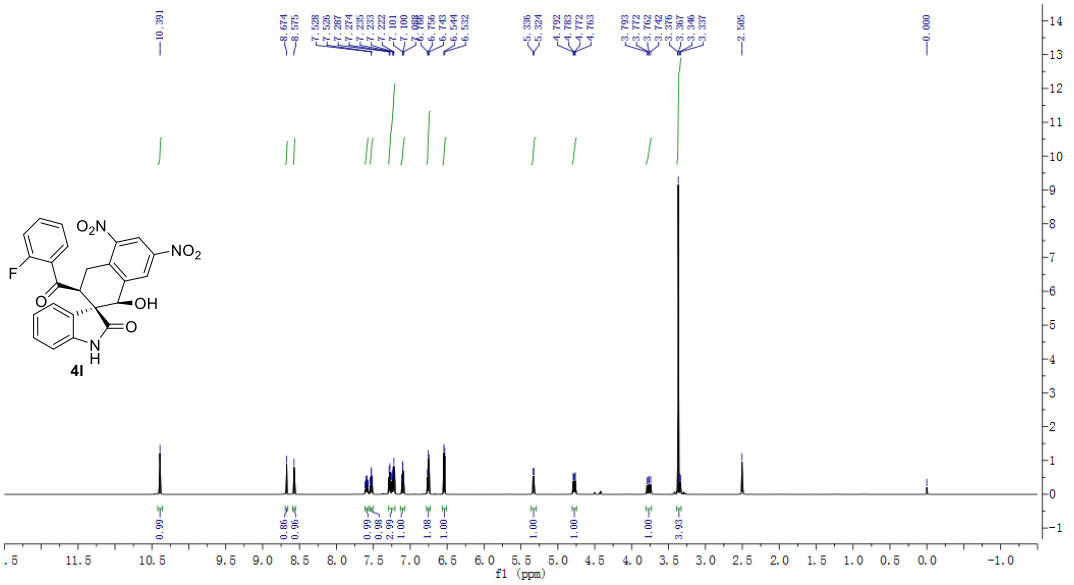
8.483
7.865
7.853
7.654
7.624
7.493
7.481
7.470
7.135
7.124
7.110
7.100
6.788
6.786
6.771
6.759
6.747
6.487
4.918
4.908
4.899
4.890
4.711
3.578
3.557
3.547
3.538
3.490
3.469
3.460
2.502
0.000
O2N
NO2
O
OH
O
N
H
4k
1.00
0.88
0.99
2.04
1.01
2.04
0.98
0.99
0.97
1.00
0.95
1.00
1.00
1.01
1.11
f1 (ppm)


199.66
177.09
147.95
145.36
142.53
142.43
137.61
135.60
133.69
129.73
128.79
128.39
127.99
125.45
120.60
118.65
108.89
69.17
51.33
41.80
39.81
39.67
39.53
39.39
39.25
39.11
38.97
26.70
0.00
O2N
NO2
O
OH
O
N
H
4k
f1 (ppm)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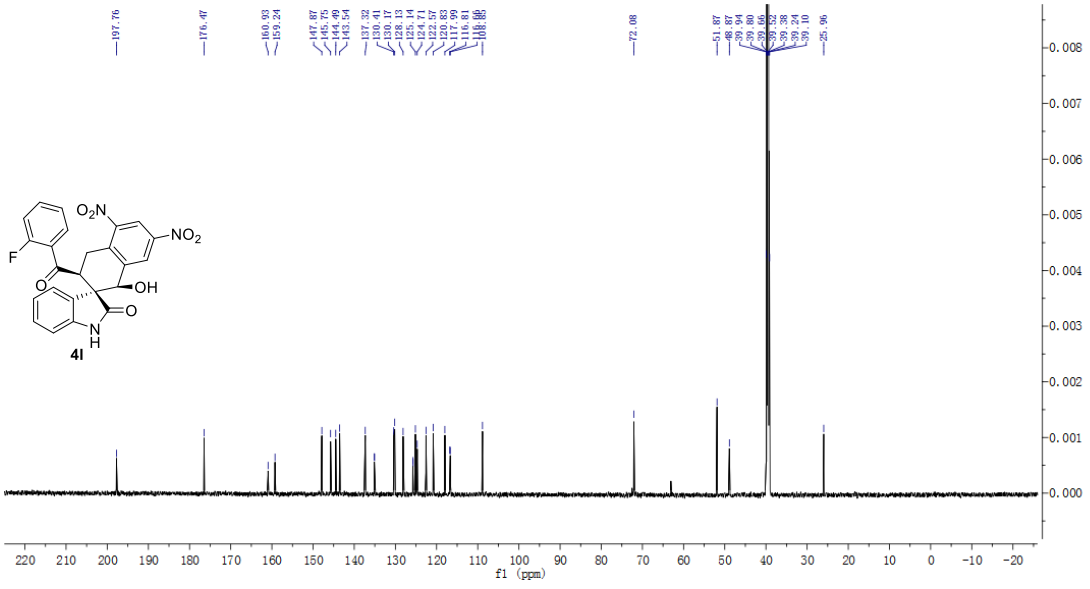
7.526
7.297
7.294
7.274
7.235
7.233
7.222
7.101
7.100
6.998
6.996
6.756
6.743
6.544
6.532
5.336
5.324
4.792
4.783
4.772
4.763
3.793
3.772
3.762
3.752
3.376
3.367
3.346
3.337
2.505
0.000
O2N
NO2
F
O
OH
O
N
H
4l
0.99
0.86
0.96
0.99
0.98
2.99
1.00
1.98
1.00
1.00
1.00
1.00
3.03
f1 (ppm)


197.76
176.47
160.93
159.24
147.87
145.75
144.49
143.54
137.32
130.41
130.17
128.13
125.14
124.71
122.57
120.83
117.99
116.61
72.08
51.87
48.87
39.94
39.80
39.66
39.52
39.38
39.24
39.10
25.96
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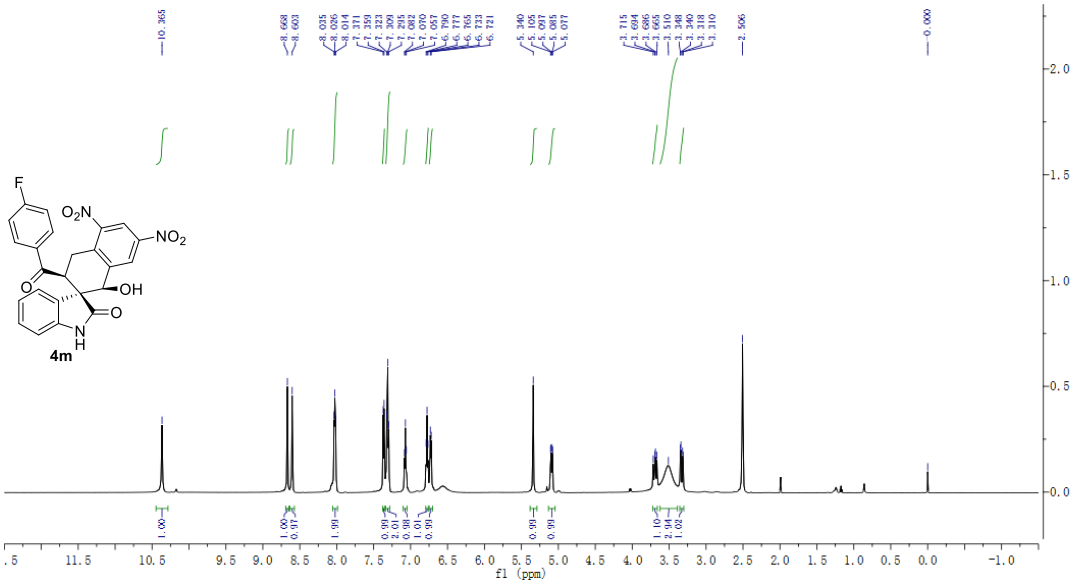
NO2
F
O
OH
O
N
H
4l
f1 (ppm)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8.014
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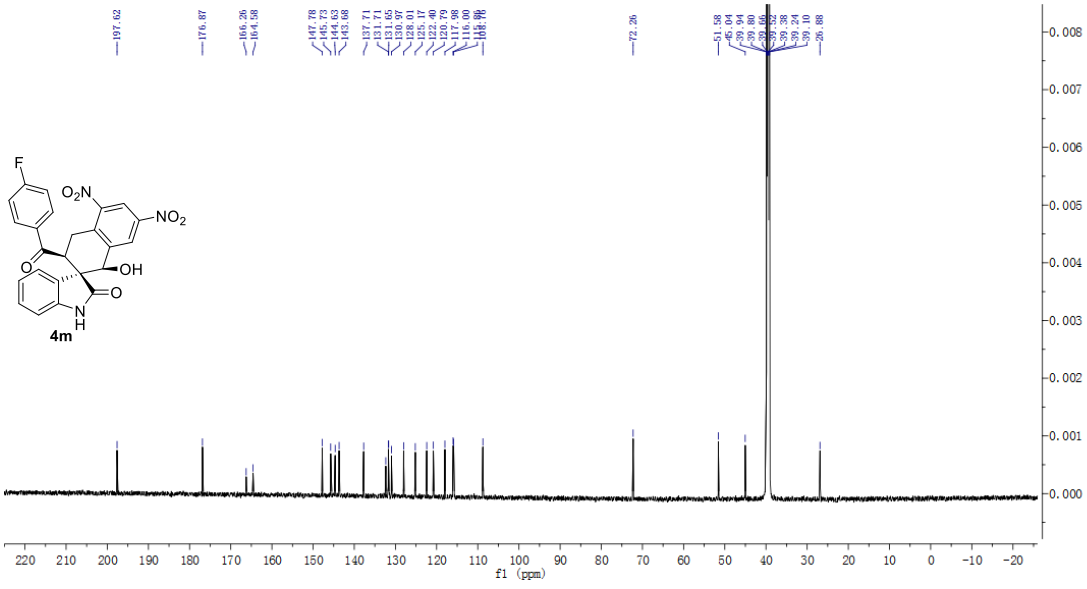
7.359
7.331
7.309
7.295
7.082
7.070
7.057
6.790
6.777
6.765
6.733
6.721
5.340
5.105
5.097
5.085
5.077
3.715
3.694
3.686
3.665
3.510
3.348
3.340
3.318
3.310
2.506
0.000
F
O2N
NO2
O
OH
O
N
H
4m
1.00
1.00
0.97
1.99
0.99
2.00
0.98
1.01
0.99
0.99
0.99
1.10
2.04
1.02
f1 (ppm)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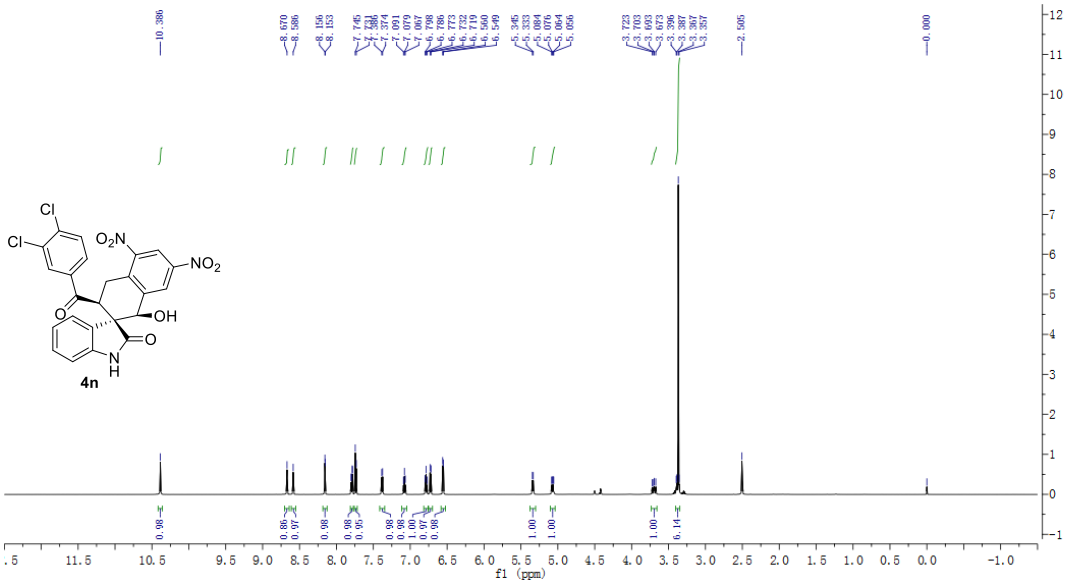
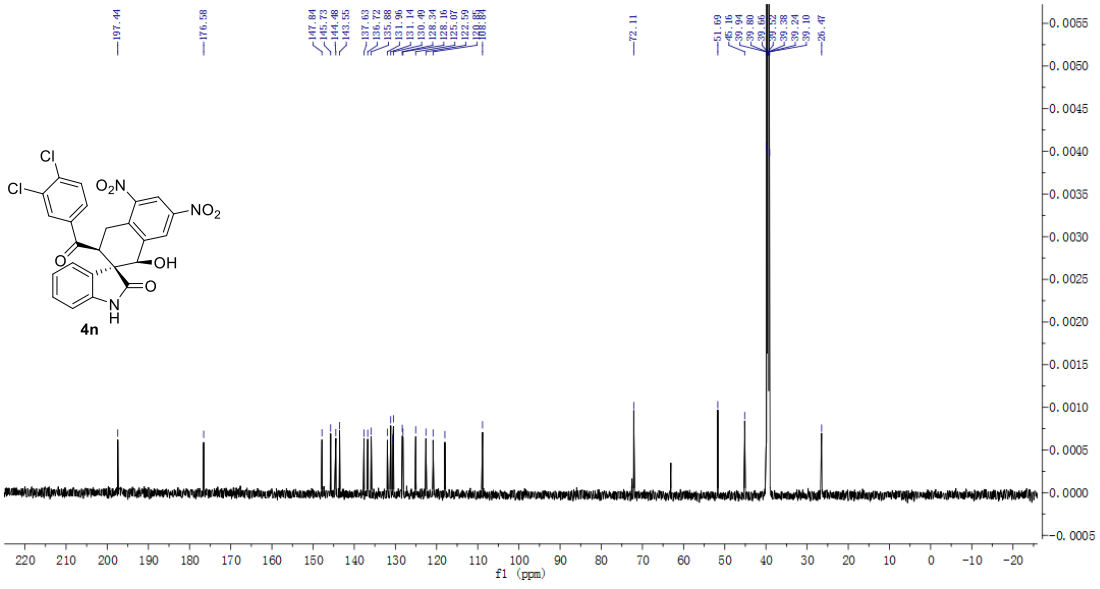
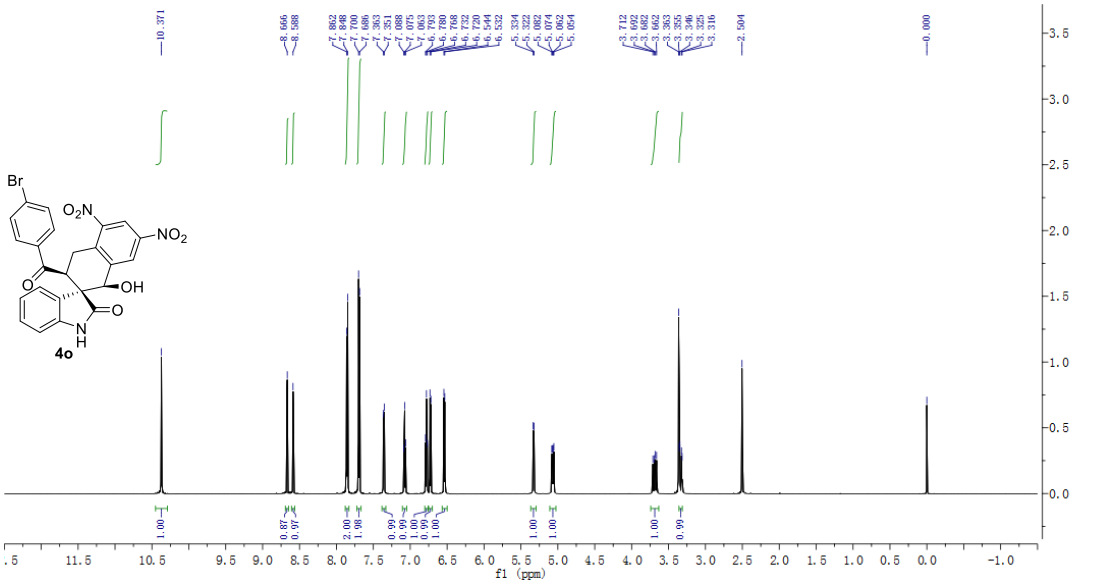
176.87
166.26
164.58
147.78
145.73
144.63
143.68
137.71
131.71
131.65
130.97
128.01
125.17
122.40
120.79
117.98
116.60
72.26
51.58
45.04
39.94
39.80
39.66
39.52
39.38
39.24
39.10
26.88
F
O2N
NO2
O
OH
O
N
H
4m
f1 (ppm)


Cl
Cl
O2N
NO2
O
OH
O
N
H
4n
f1 (ppm)


Cl
Cl
O2N
NO2
O
OH
O
N
H
4n
f1 (ppm)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7.363
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7.088
7.075
6.963
6.793
6.780
6.768
6.732
6.720
6.544
6.532
5.334
5.322
5.082
5.074
5.062
5.054
3.712
3.692
3.682
3.662
3.363
3.355
3.346
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2.504
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Br
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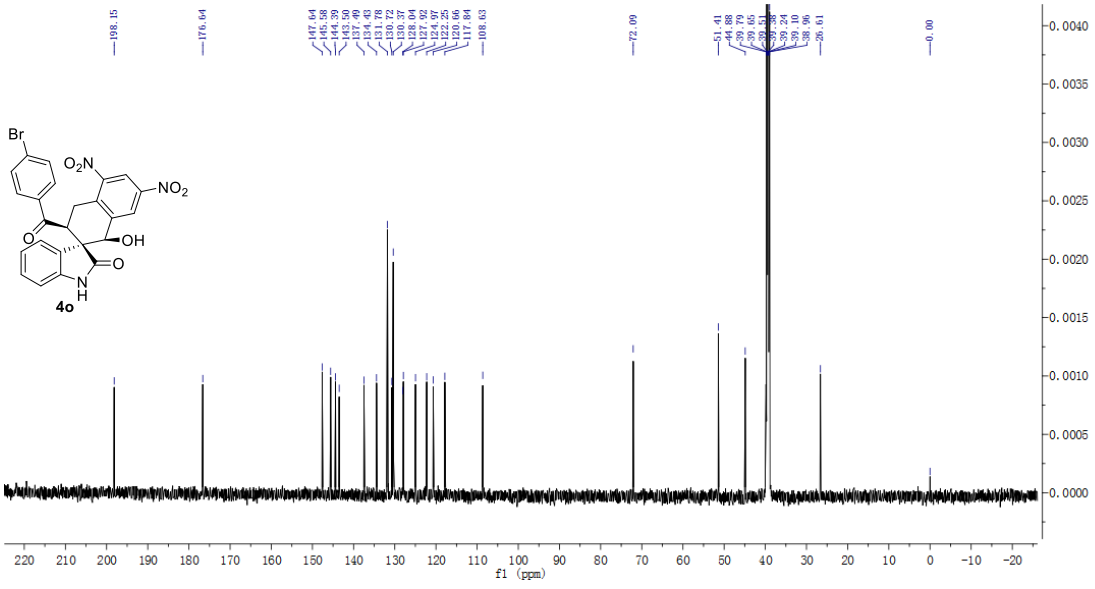
NO2
O
OH
O
N
H
4o
f1 (ppm)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145.98
144.39
143.50
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134.43
131.78
130.72
130.37
128.04
127.92
124.97
122.25
120.66
117.84
108.63
72.09
51.41
44.88
39.79
39.65
39.51
39.38
39.24
39.10
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26.61
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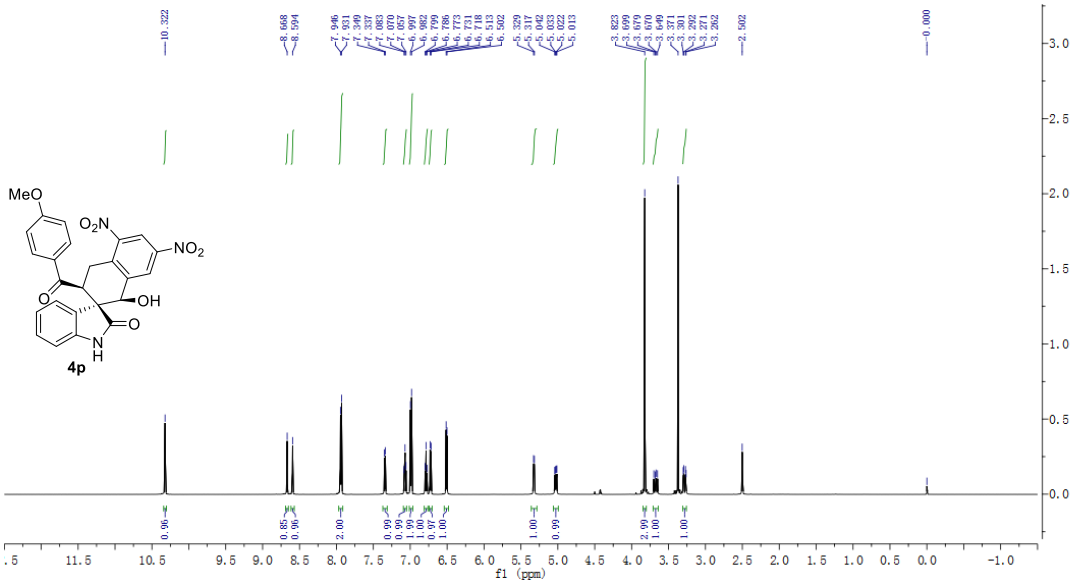
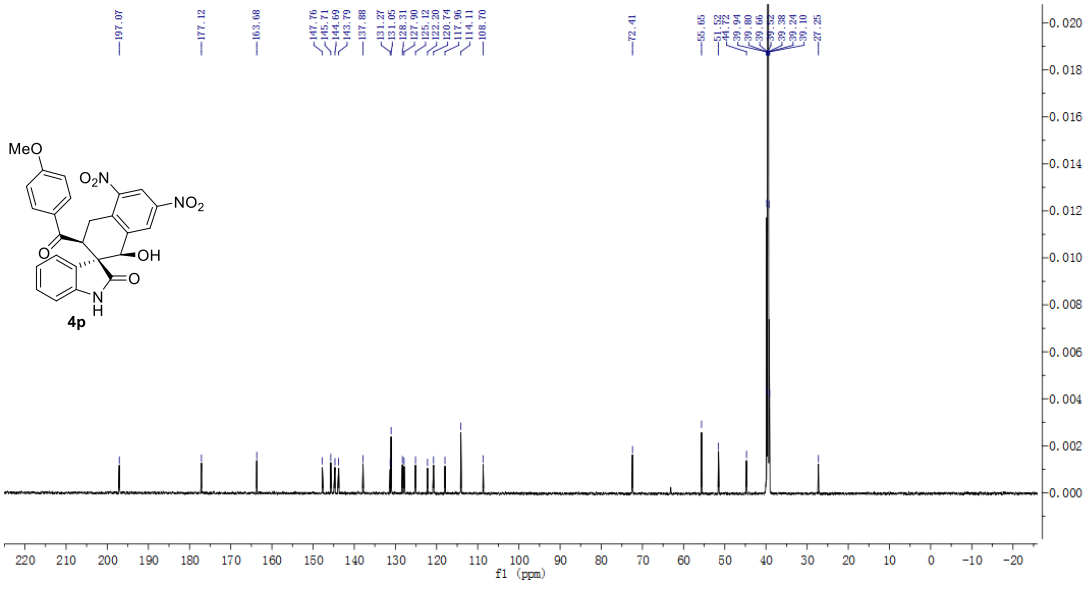
NO2
O
OH
O
N
H
4o
f1 (ppm)


MeO
O2N
NO2
O
OH
O
N
H
4p
f1 (ppm)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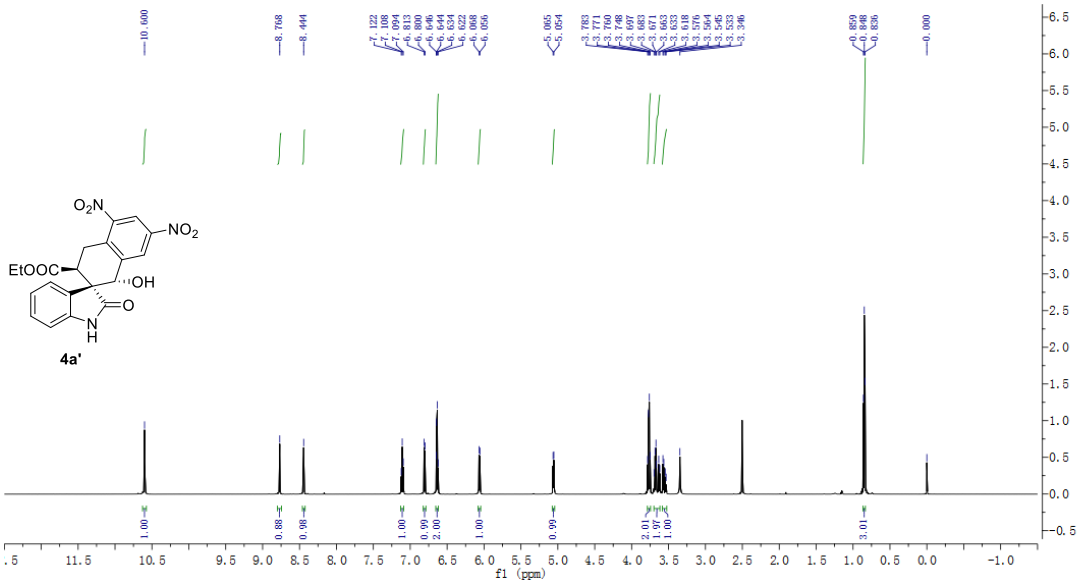
O2N
NO2
O
OH
O
N
H
4p
f1 (ppm)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8.444
7.122
7.108
7.094
6.833
6.800
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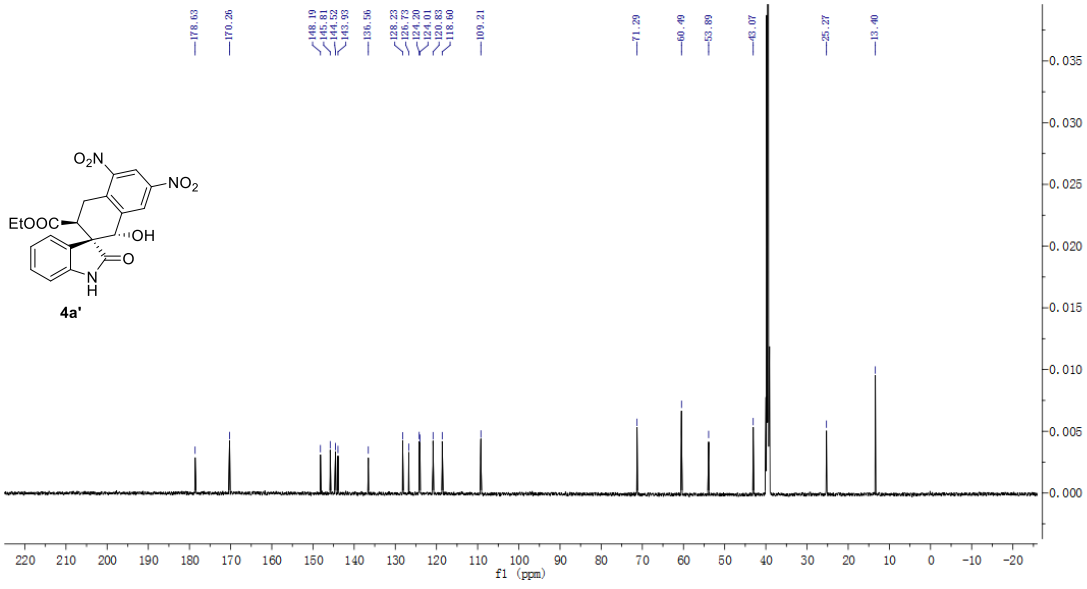
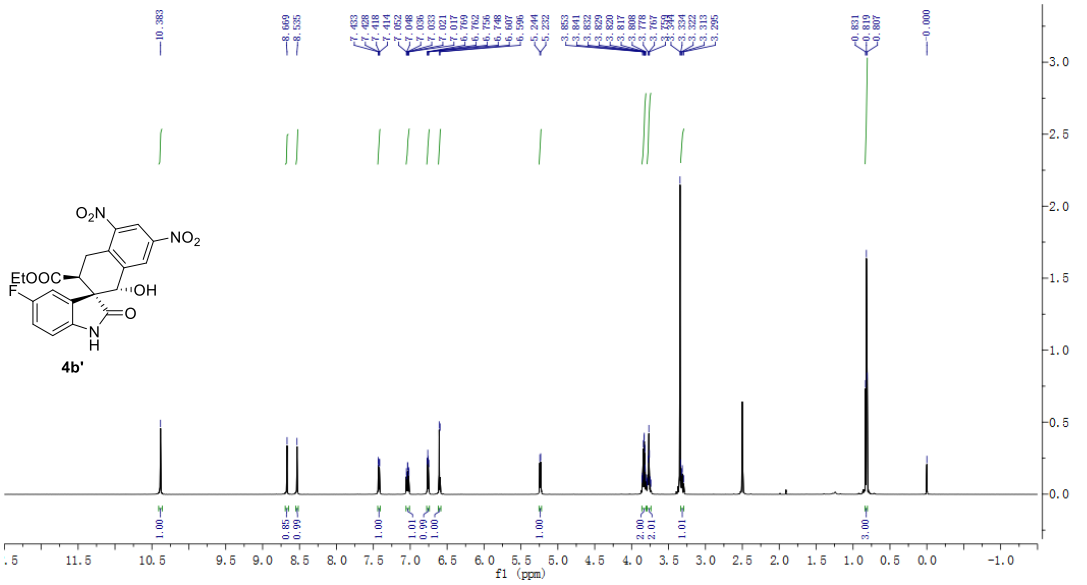
6.644
6.634
6.632
6.068
6.056
5.065
5.054
3.783
3.771
3.760
3.748
3.697
3.683
3.671
3.663
3.653
3.618
3.576
3.564
3.545
3.533
3.346
0.859
0.848
0.836
0.000
O2N
NO2
EtOOC
OH
O
N
H
4a'
1.00
0.88
0.98
1.00
0.99
2.00
1.00
0.99
2.01
1.97
1.00
3.01
f1 (ppm)


178.63
170.26
148.19
145.81
144.52
143.93
136.56
128.23
126.73
124.20
124.01
120.83
118.60
109.21
71.29
60.49
53.89
43.07
25.27
13.40
O2N
NO2
EtOOC
OH
O
N
H
4a'
f1 (ppm)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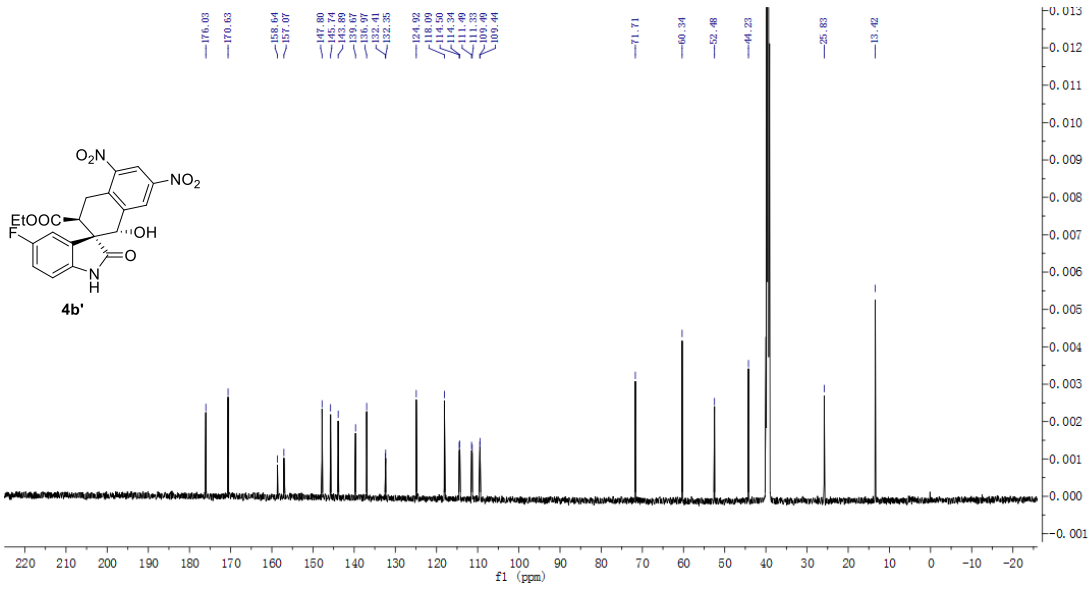
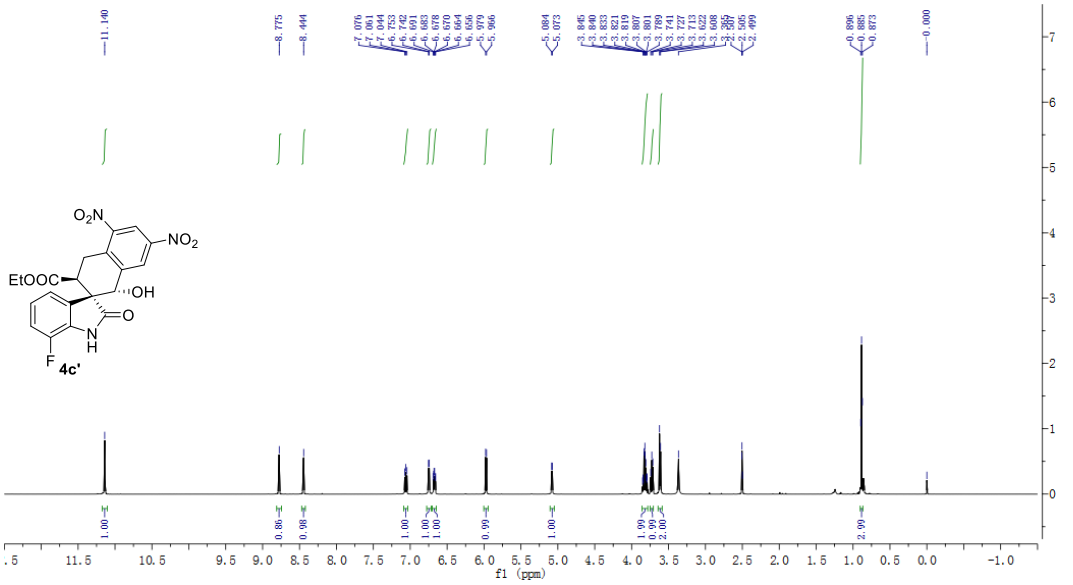
8.535
7.453
7.438
7.418
7.414
7.052
7.048
7.036
7.033
7.021
7.017
6.769
6.762
6.756
6.748
6.607
6.596
5.244
5.232
3.853
3.841
3.832
3.829
3.820
3.817
3.808
3.798
3.767
3.334
3.322
3.313
3.295
0.831
0.819
0.807
0.000
O2N
NO2
EtOOC
F
OH
O
N
H
4b'
f1 (ppm)


176.03
170.63
158.64
157.07
147.80
145.74
143.89
139.67
136.97
132.41
132.35
124.92
118.09
114.50
114.34
111.46
111.33
109.40
109.44
71.71
60.34
52.48
44.23
25.83
13.42
O2N
NO2
EtOOC
F
OH
O
N
H
4b'
f1 (ppm)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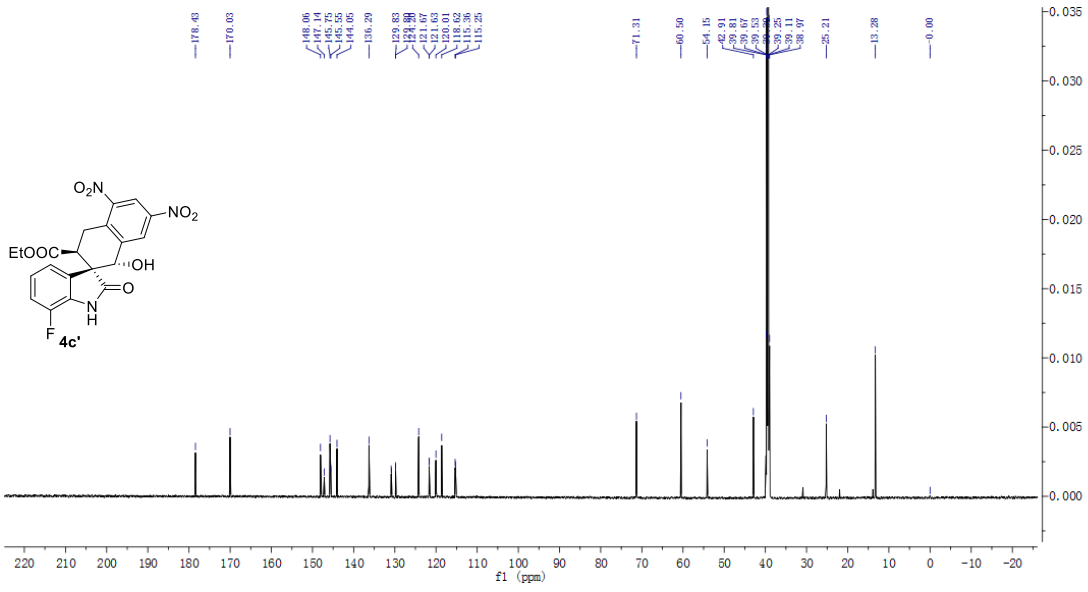
7.061
7.044
6.753
6.742
6.691
6.683
6.678
6.670
6.664
6.656
5.979
5.966
5.084
5.073
3.845
3.840
3.833
3.821
3.819
3.807
3.801
3.799
3.741
3.727
3.713
3.698
3.688
3.265
2.505
2.499
0.896
0.885
0.873
0.000
O2N
NO2
EtOOC
OH
O
N
H
F
4c'
1.00
0.86
0.98
1.00
1.00
1.00
0.99
1.00
1.99
0.99
2.00
2.99
f1 (ppm)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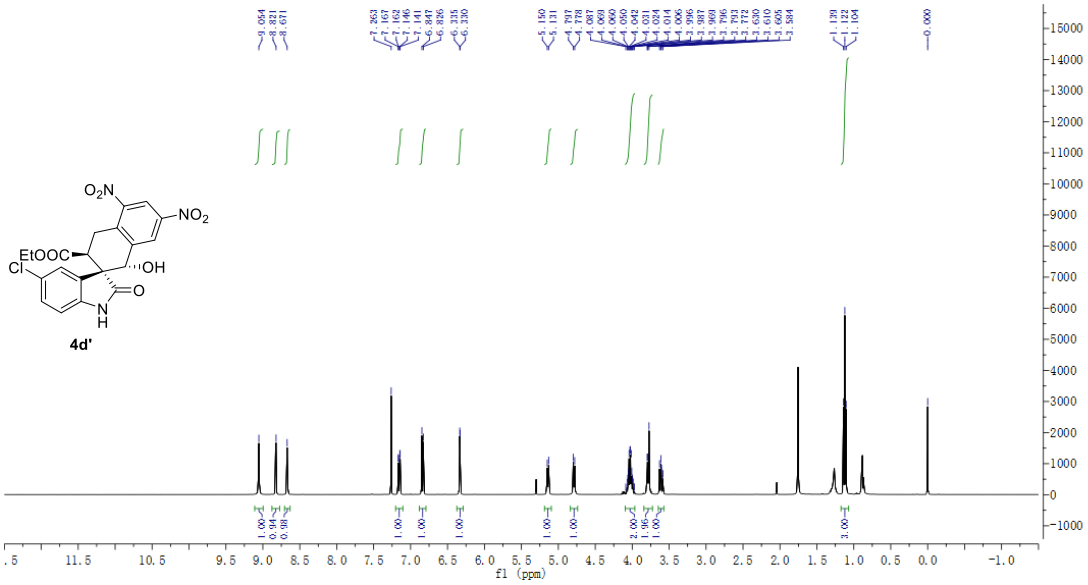
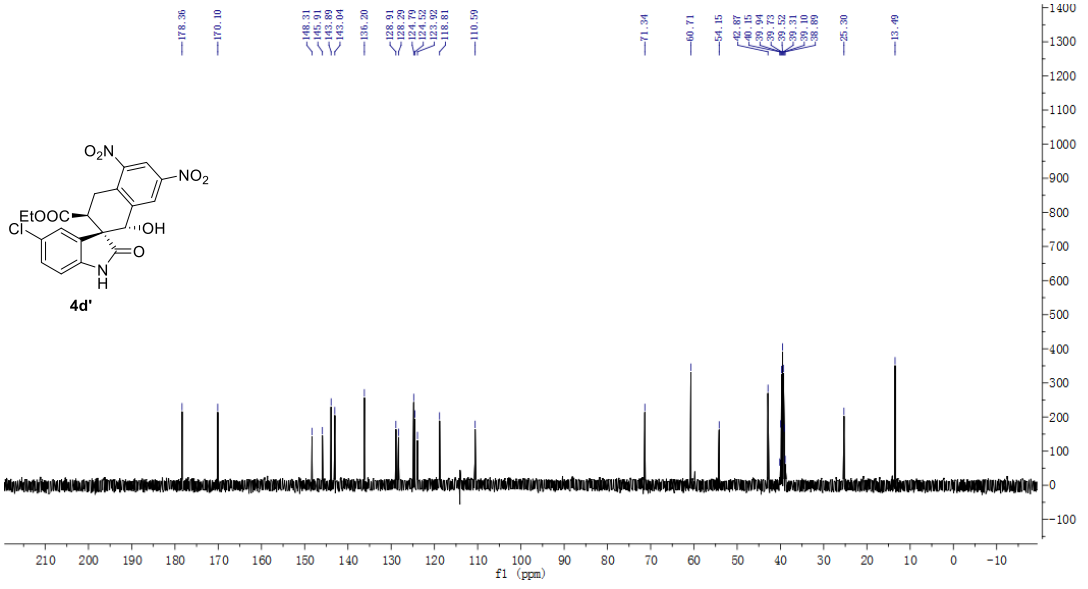
170.03
148.06
147.14
145.75
145.55
144.65
136.29
129.83
124.80
124.59
121.67
121.55
120.01
118.62
115.36
115.25
71.31
60.50
54.15
42.91
39.81
39.67
39.53
39.25
39.11
38.97
25.21
13.28
0.00
O2N
NO2
EtOOC
OH
O
N
H
F
4c'
f1 (ppm)


9.054
8.821
8.671
7.563
7.167
7.162
7.146
7.141
6.847
6.826
6.335
6.330
5.150
5.131
4.797
4.778
4.697
4.060
4.050
4.042
4.031
4.024
4.014
4.006
3.996
3.987
3.969
3.796
3.793
3.772
3.630
3.610
3.605
3.584
1.139
1.122
1.104
0.000
O2N
NO2
EtOOC
Cl
OH
O
N
H
4d'
1.00
0.94
0.98
1.00
1.00
1.00
1.00
1.00
2.00
1.95
1.00
3.00
f1 (ppm)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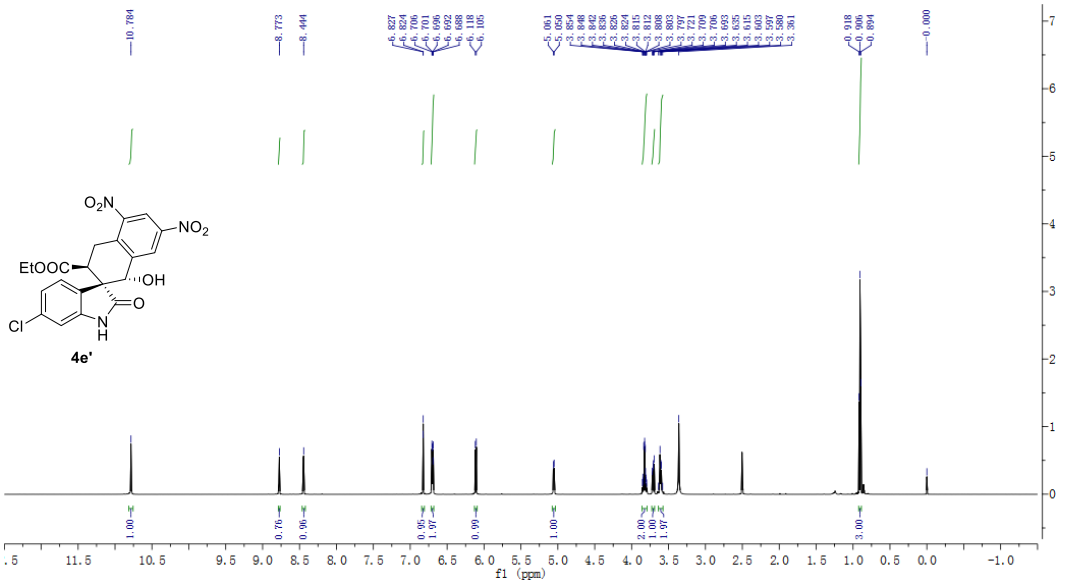
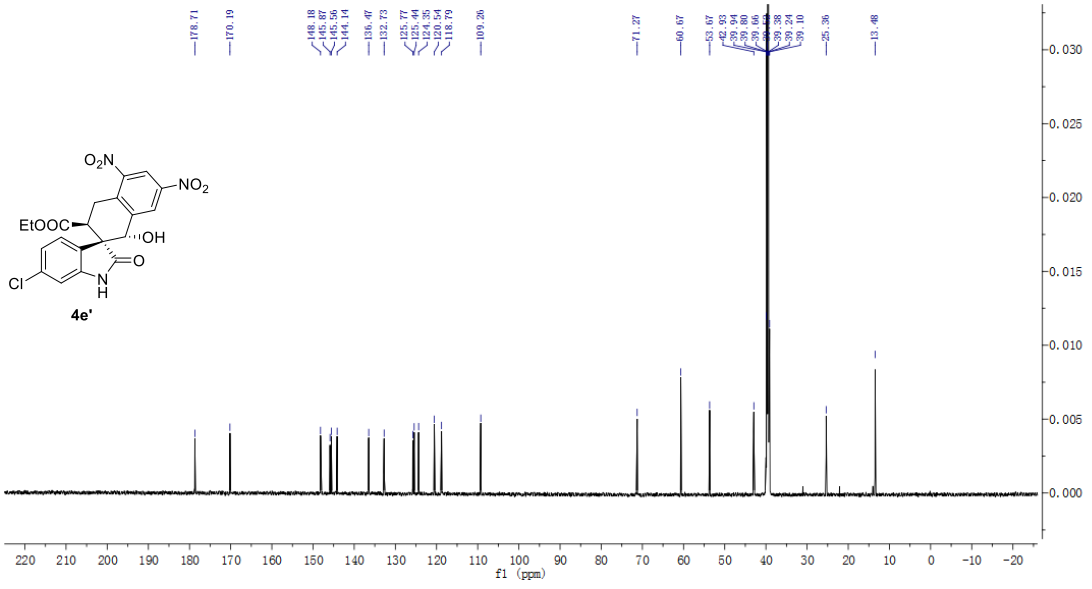
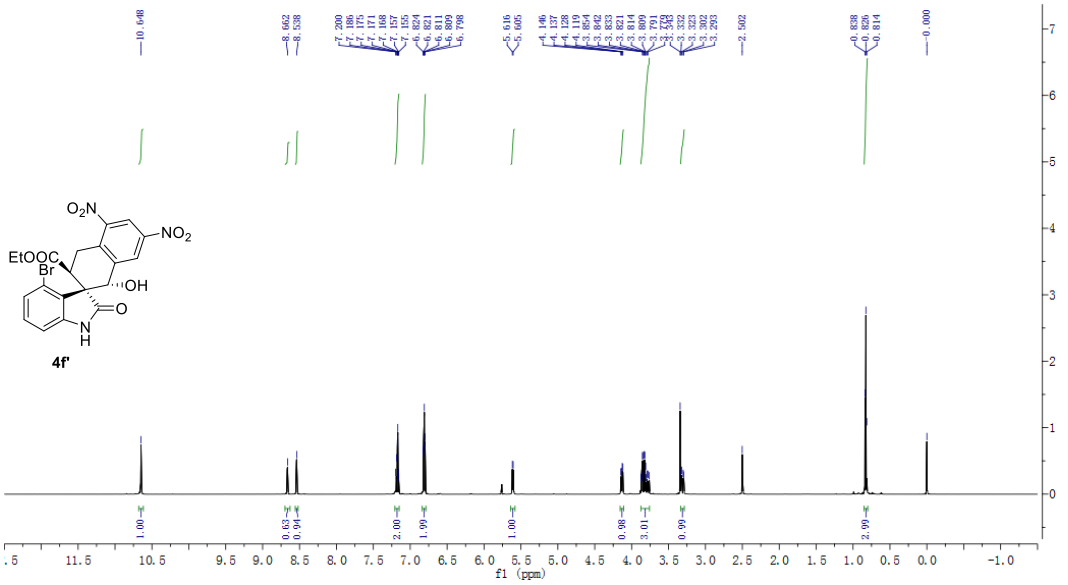
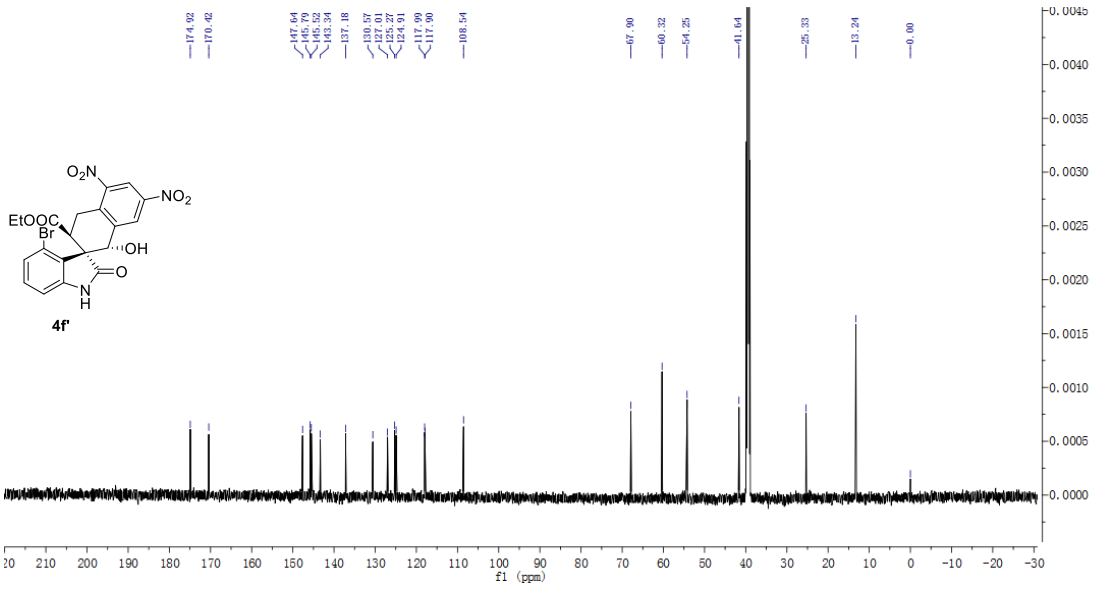
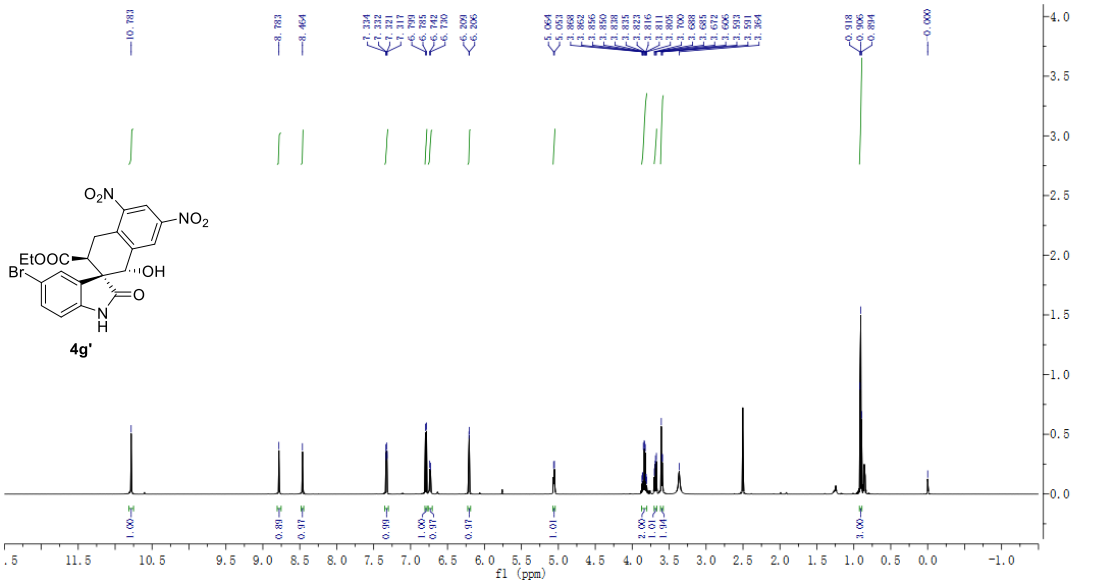
170.10
148.31
145.91
143.89
143.04
136.20
128.91
128.29
124.73
124.49
123.92
118.81
110.59
71.34
60.71
54.15
42.87
40.15
39.94
39.73
39.52
39.31
39.10
38.89
25.30
13.49
O2N
NO2
EtOOC
Cl
OH
O
N
H
4d'
f1 (ppm)

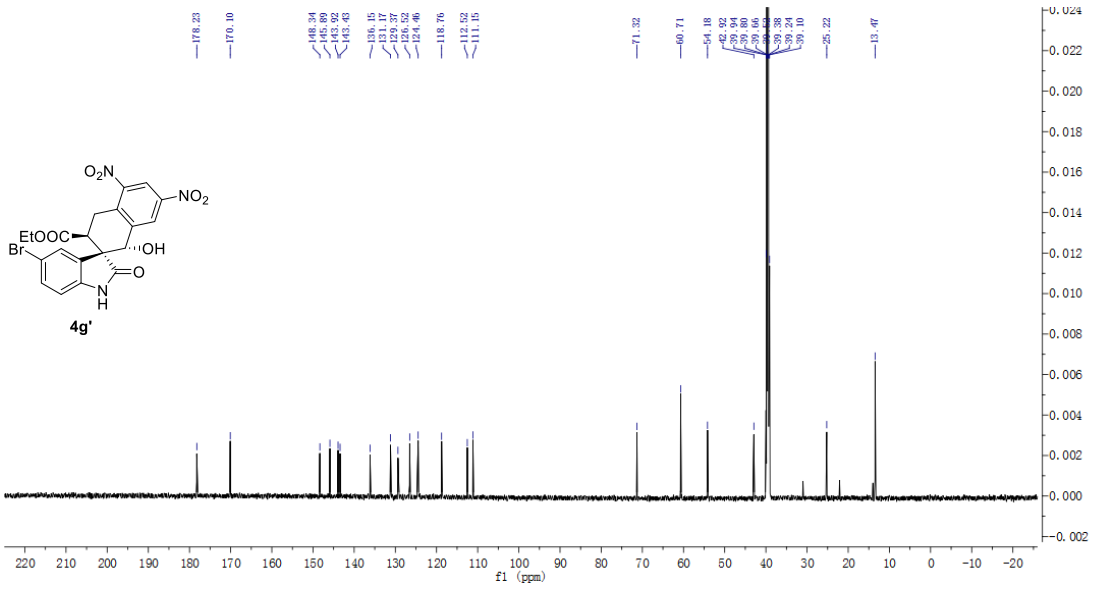

10.784
8.773
8.444
6.827
6.824
6.706
6.701
6.696
6.692
6.688
6.118
6.105
5.061
5.050
3.854
3.848
3.842
3.836
3.826
3.824
3.815
3.812
3.808
3.803
3.797
3.721
3.709
3.706
3.693
3.635
3.615
3.607
3.597
3.580
3.361
0.918
0.906
0.894
0.000
O2N
NO2
EtOOC
OH
O
Cl
N
H
4e'
f1 (ppm)

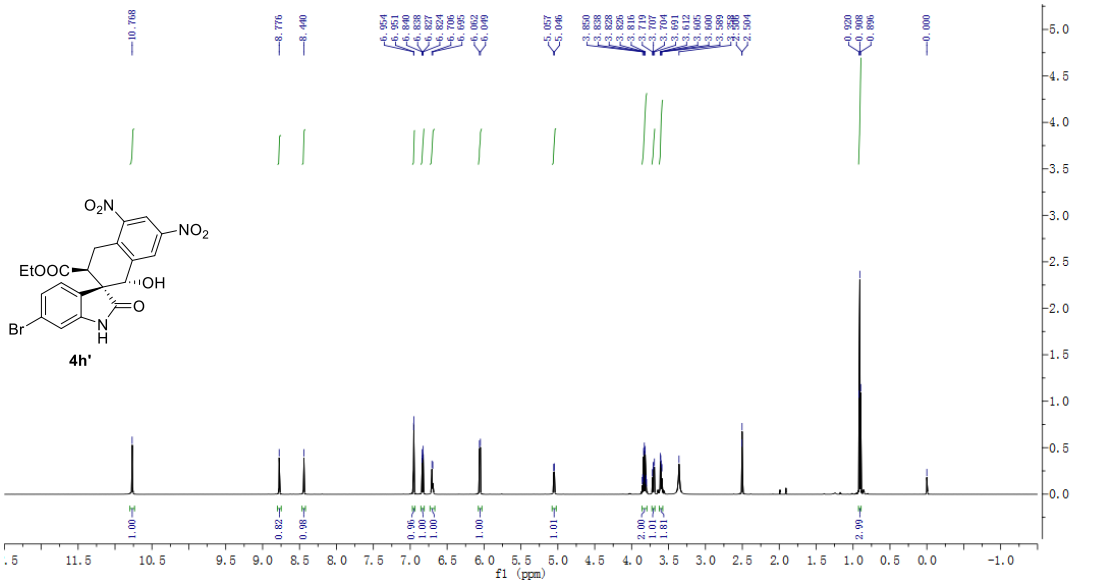

178.71
170.19
148.18
145.87
145.56
144.14
136.47
132.73
125.77
125.44
124.35
120.54
118.79
109.26
71.27
60.67
53.67
42.93
39.94
39.80
39.66
39.52
39.38
39.24
39.10
25.36
13.48
O2N
NO2
EtOOC
OH
O
Cl
N
H
4e'
f1 (ppm)

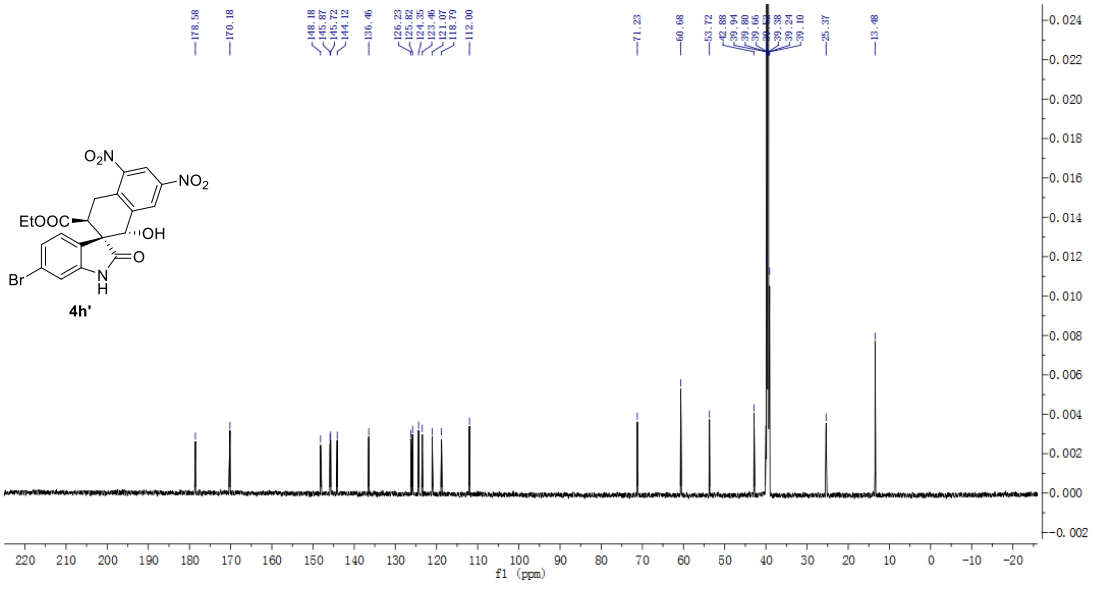

10.648
8.662
8.538
7.200
7.186
7.175
7.171
7.168
7.157
7.155
6.824
6.821
6.811
6.809
6.798
5.616
5.605
4.146
4.137
4.128
4.119
3.854
3.842
3.833
3.821
3.814
3.809
3.791
3.543
3.538
3.332
3.323
3.302
3.293
2.502
0.838
0.826
0.814
0.000
O2N
NO2
EtOOC
Br
OH
O
N
H
4f'
1.00
0.63
0.94
2.00
1.99
1.00
0.98
3.01
0.99
2.99
f1 (ppm)

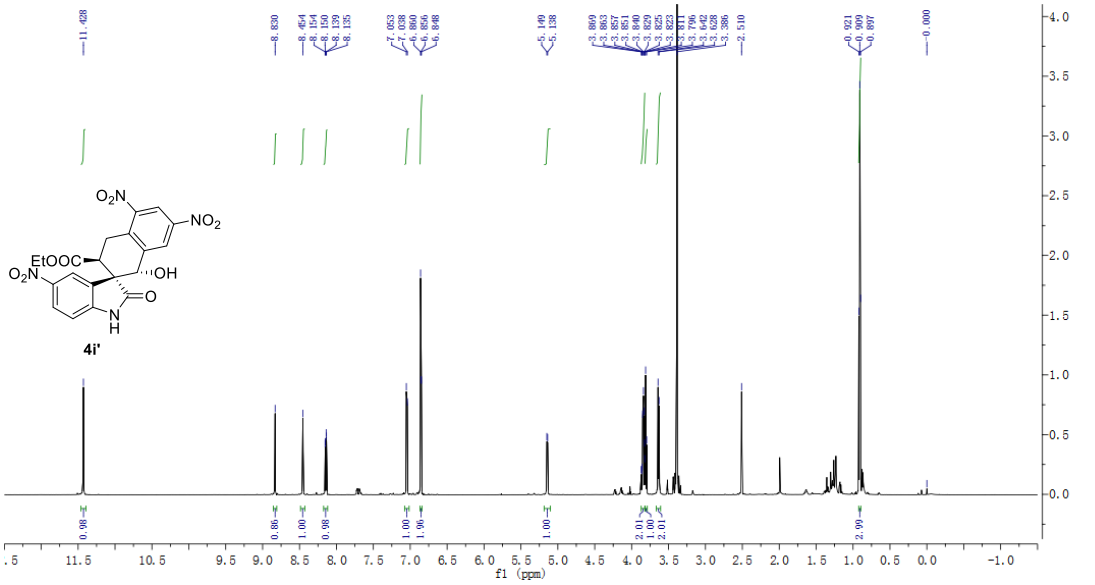

174.92
170.42
147.64
145.79
145.52
143.34
137.18
130.57
127.01
125.27
124.91
117.99
117.90
108.54
67.90
60.32
54.25
41.64
25.33
13.24
0.00
O2N
NO2
EtOOC
Br
OH
O
N
H
4f'
f1 (ppm)

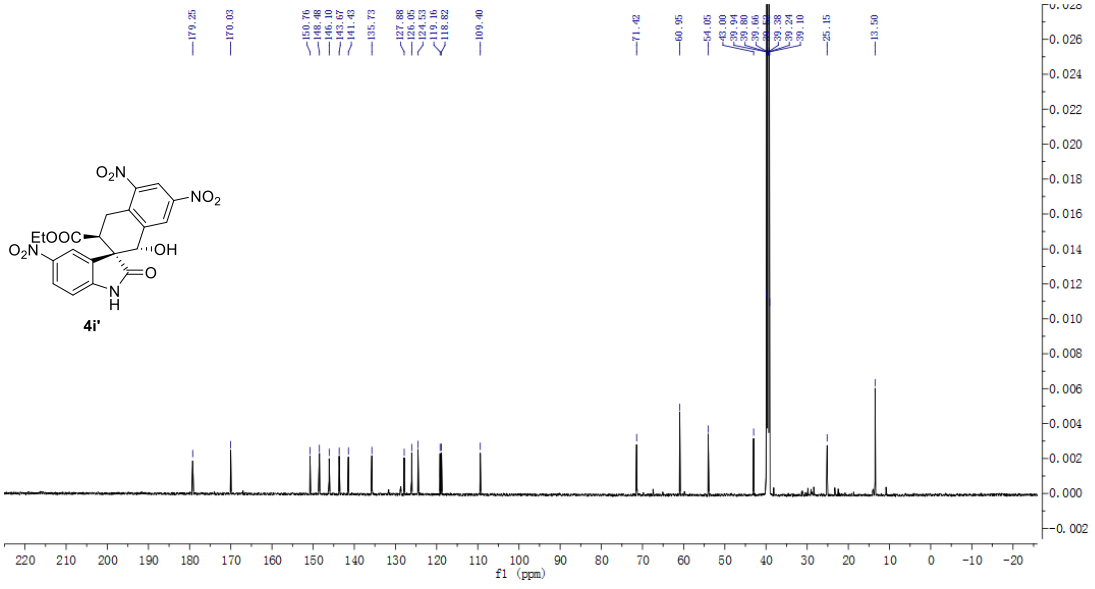

10.783
8.783
8.464
7.324
7.322
7.321
7.317
6.799
6.795
6.792
6.730
6.209
6.205
5.064
5.053
3.868
3.862
3.835
3.823
3.816
3.811
3.805
3.700
3.688
3.681
3.672
3.606
3.593
3.591
3.364
0.918
0.906
0.894
0.000
O2N
NO2
EtOOC
Br
OH
O
N
H
4g'
f1 (ppm)

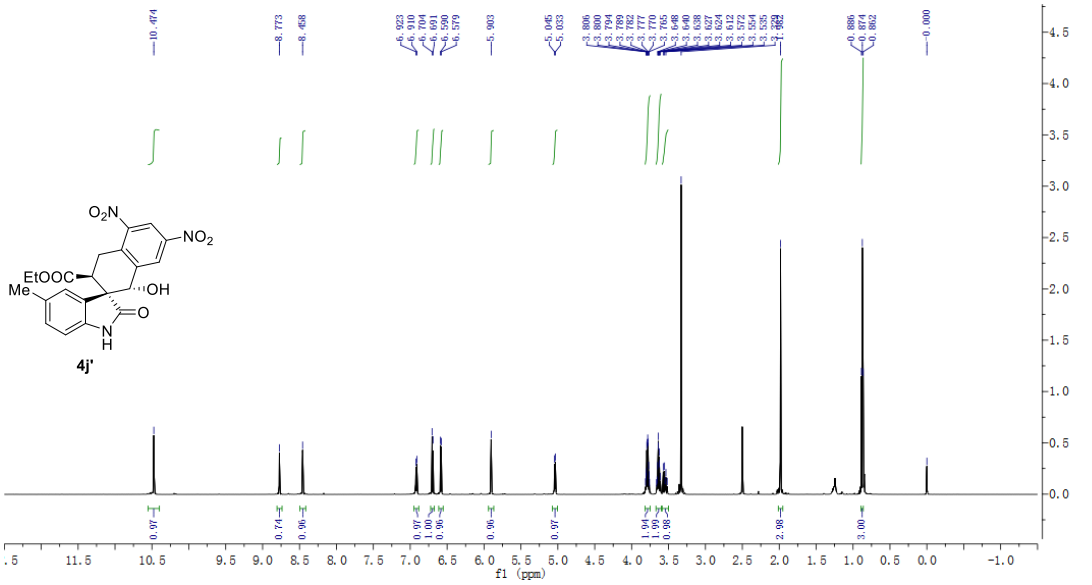

178.23
170.10
148.34
145.89
143.92
143.43
136.15
131.17
129.37
126.52
124.46
118.76
112.52
111.15
71.32
60.71
54.18
42.92
39.94
39.80
39.66
39.52
39.38
39.24
39.10
25.22
13.47
O2N
NO2
EtOOC
Br
OH
O
N
H
4g'
f1 (ppm)

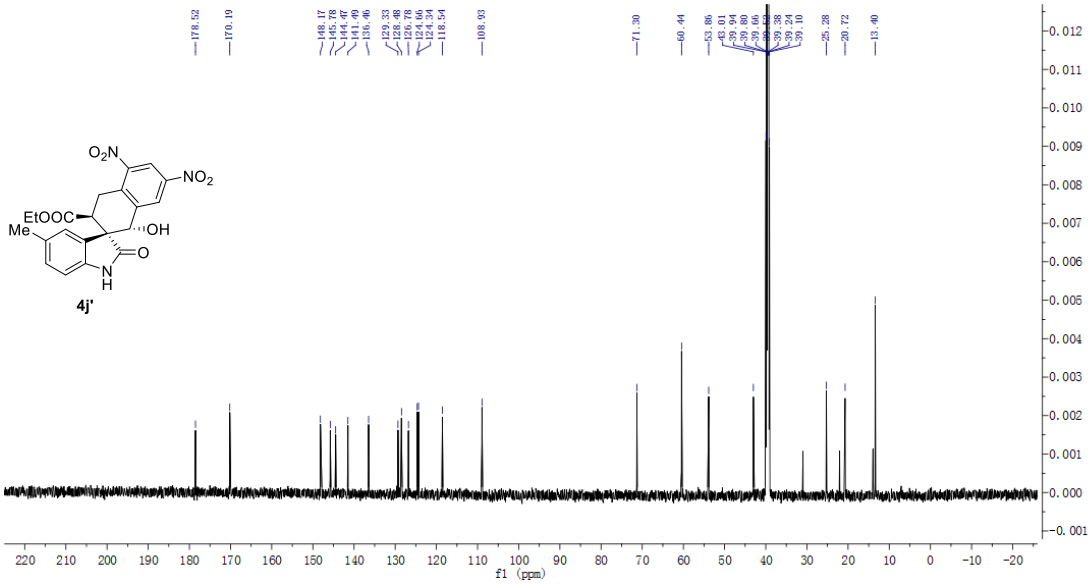

10.768
8.776
8.440
6.954
6.951
6.838
6.827
6.824
6.705
6.695
6.062
6.049
5.057
5.046
3.850
3.838
3.828
3.826
3.816
3.719
3.707
3.704
3.691
3.612
3.605
3.600
3.589
2.504
0.920
0.908
0.896
0.000
1.00
0.82
0.98
0.96
1.00
1.00
1.00
1.01
2.00
1.01
1.81
2.99
f1 (ppm)
O2N
NO2
EtOOC
OH
O
Br
N
H
4h'

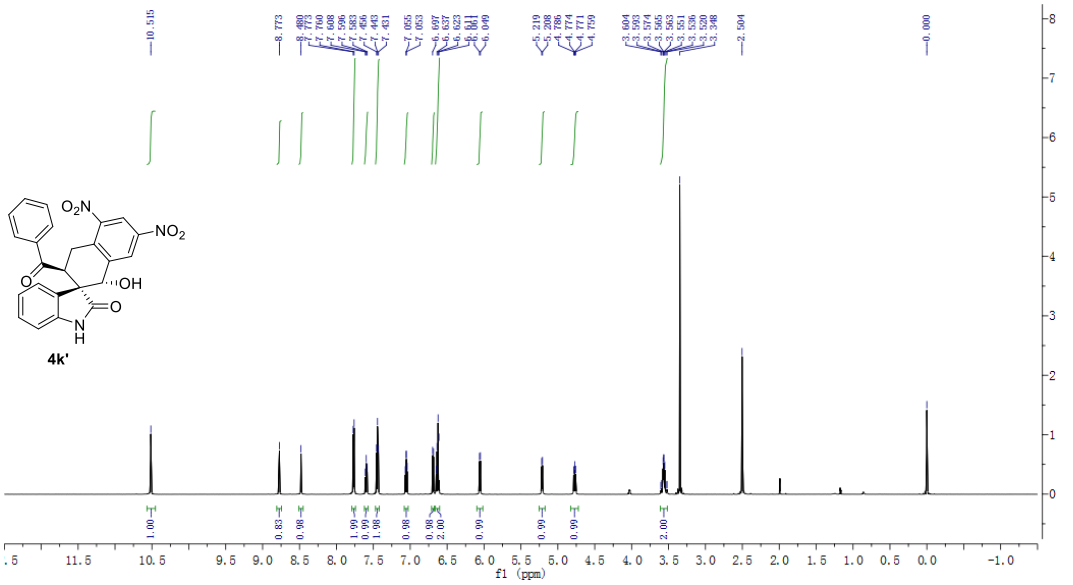

178.58
170.18
148.18
145.87
145.72
144.12
136.46
126.23
125.82
124.35
123.46
121.07
118.79
112.00
71.23
60.68
53.72
42.88
39.94
39.80
39.66
39.52
39.38
39.24
39.10
25.37
13.48
f1 (ppm)
O2N
NO2
EtOOC
OH
O
Br
N
H
4h'

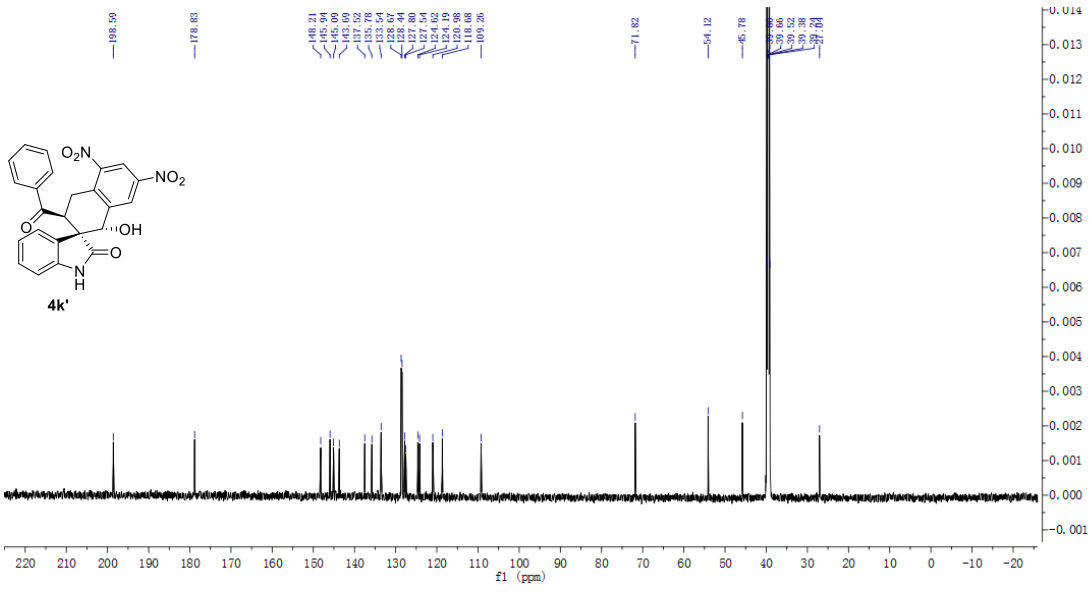

11.428
8.830
8.454
8.154
8.150
8.135
7.053
7.038
6.860
6.856
6.846
5.149
5.138
3.869
3.853
3.857
3.851
3.840
3.829
3.825
3.823
3.811
3.796
3.642
3.638
3.386
2.510
0.921
0.909
0.897
0.000
O2N
NO2
EtOOC
O2N
OH
O
N
H
4i'
f1 (ppm)

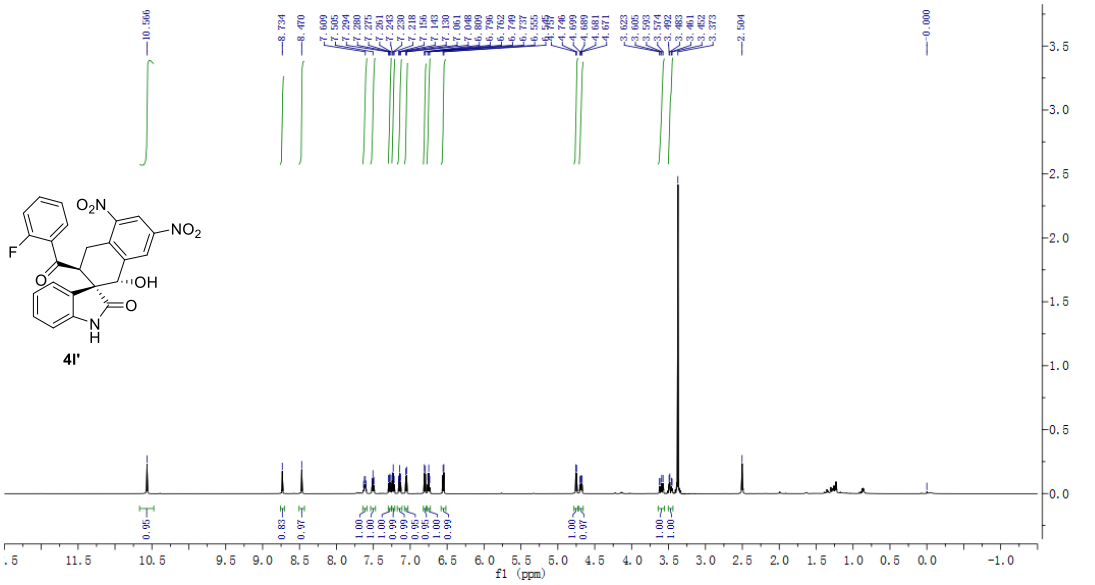

179.25
170.03
150.76
148.48
146.10
143.67
141.45
135.73
127.88
126.05
124.53
119.15
118.82
109.40
71.42
60.95
54.05
43.00
39.94
39.80
39.66
39.38
39.24
39.10
25.15
13.50
O2N
NO2
EtOOC
O2N
OH
O
N
H
4i'
f1 (ppm)

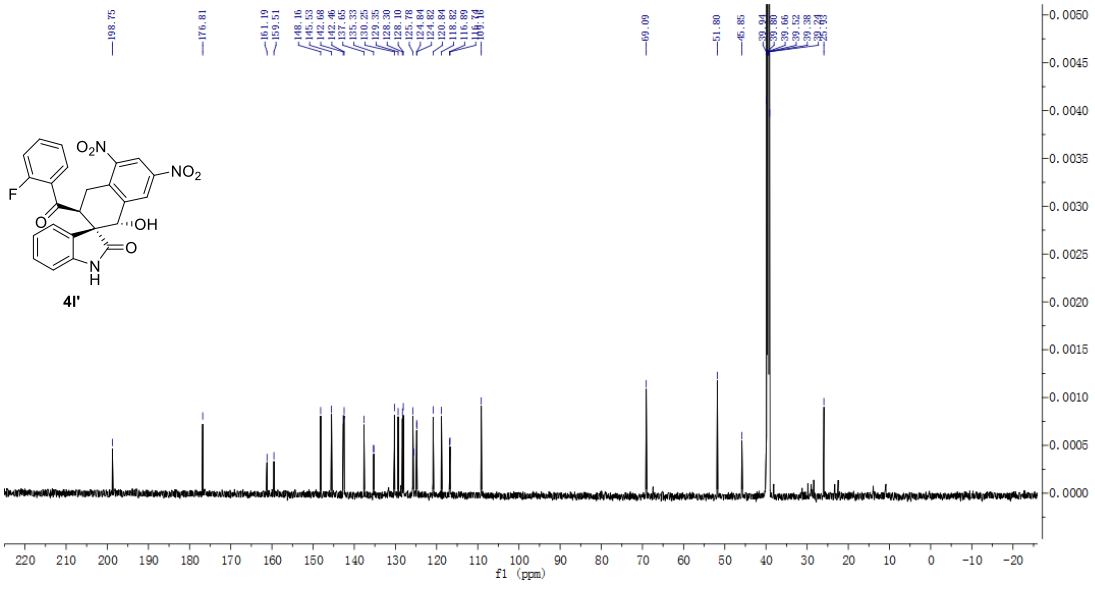

10.474
8.773
8.458
6.923
6.910
6.904
6.601
6.590
6.579
5.903
5.045
5.033
3.806
3.800
3.794
3.789
3.782
3.777
3.770
3.765
3.648
3.638
3.627
3.624
3.572
3.564
3.535
0.886
0.874
0.862
0.000
O2N
NO2
EtOOC
Me
OH
O
N
H
4j'
f1 (ppm)

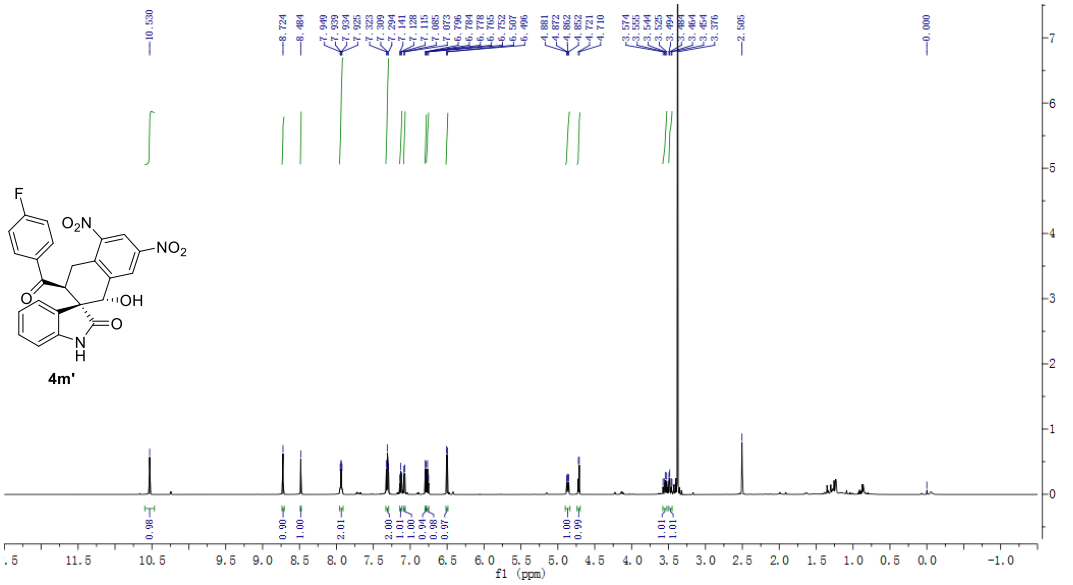

178.52
170.19
148.17
145.78
144.47
141.49
136.46
129.33
128.48
125.78
124.66
124.34
118.54
108.93
71.30
60.44
53.86
43.01
39.94
39.80
39.66
39.52
39.38
39.24
39.10
25.28
20.72
13.40
O2N
NO2
EtOOC
Me
OH
O
N
H
4j'
f1 (ppm)

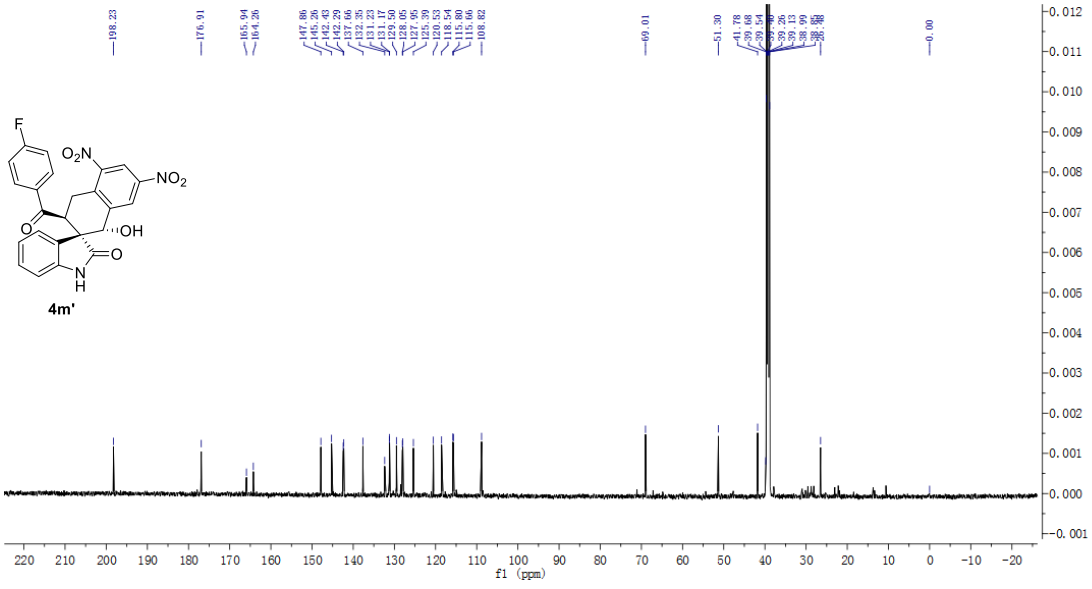

10.515
8.773
8.490
8.475
7.760
7.608
7.596
7.483
7.466
7.451
7.055
7.053
6.697
6.637
6.623
6.611
6.601
6.049
5.219
5.208
4.786
4.774
4.771
4.759
3.604
3.593
3.574
3.565
3.563
3.551
3.536
3.530
3.498
2.504
0.000
1.00
0.83
0.98
1.99
1.00
1.98
0.98
0.98
2.00
0.99
0.99
0.99
2.00
f1 (ppm)
4k'

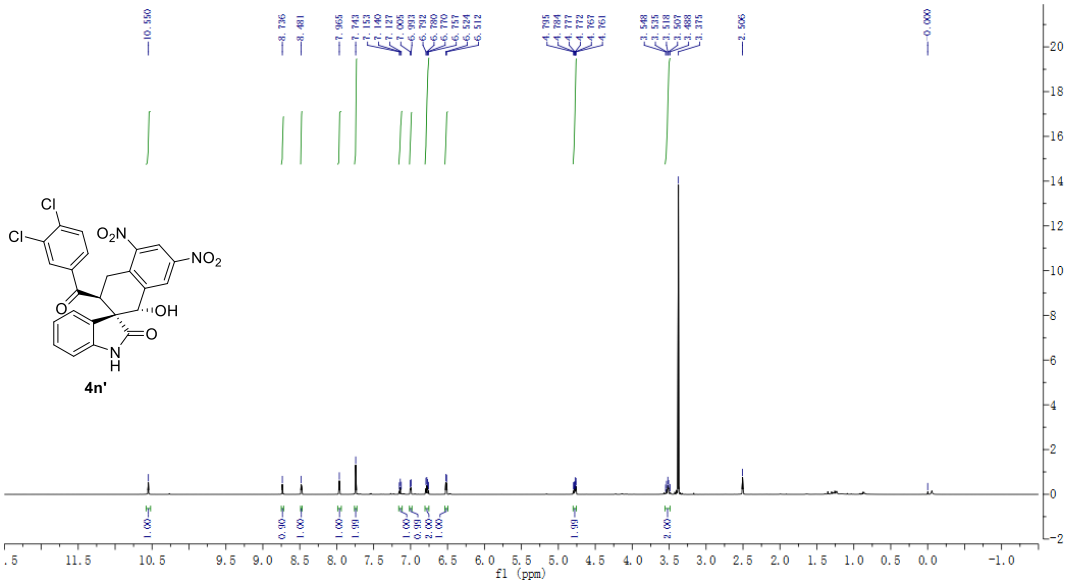

198.59
178.83
148.21
145.64
145.09
143.69
137.52
135.78
133.54
128.67
128.44
127.80
127.54
124.62
124.19
120.98
118.68
109.26
71.82
54.12
45.78
39.66
39.52
39.38
39.24
f1 (ppm)
4k'

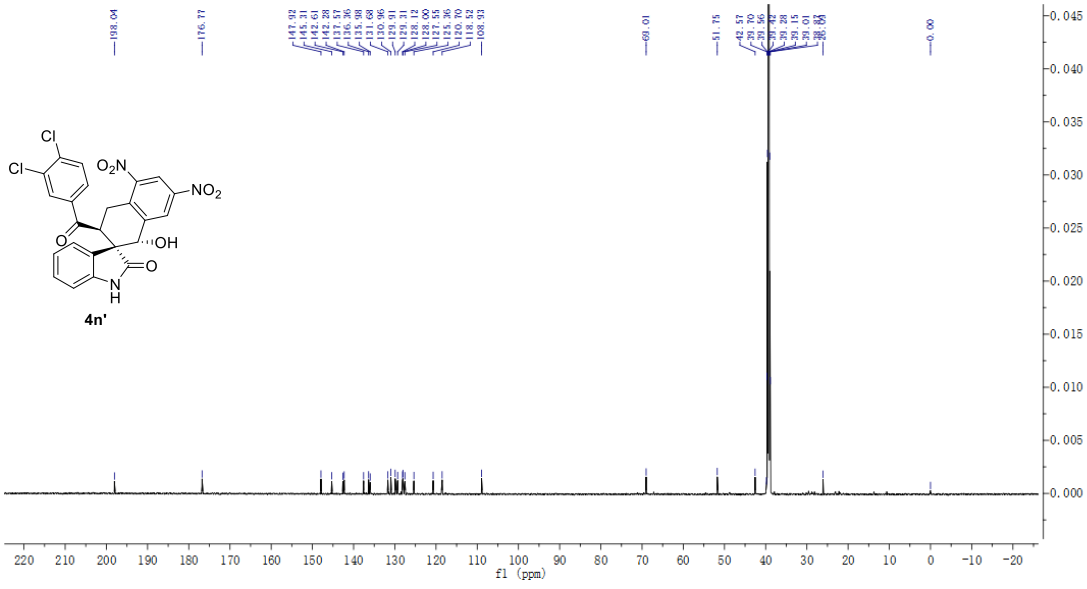

10.566
8.734
8.470
7.609
7.505
7.294
7.280
7.275
7.251
7.243
7.230
7.218
7.156
7.145
7.130
7.061
7.048
6.809
6.796
6.762
6.749
6.737
6.555
6.545
4.706
4.699
4.689
4.681
4.671
3.623
3.605
3.593
3.574
3.492
3.483
3.461
3.452
3.373
2.504
0.000
O2N
NO2
F
O
OH
O
N
H
4l'
fl (ppm)

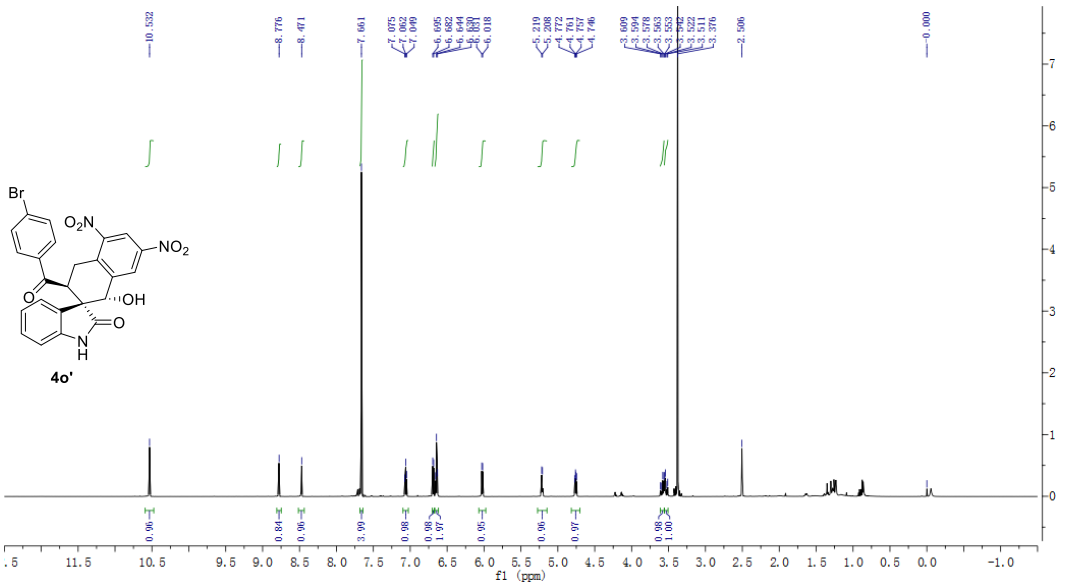

198.75
176.81
161.19
159.51
148.16
145.53
142.68
142.46
137.65
135.33
130.25
129.35
128.30
128.10
125.78
124.84
124.82
120.84
118.82
116.99
69.09
51.80
45.85
O2N
NO2
F
O
OH
O
N
H
4l'
fl (ppm)

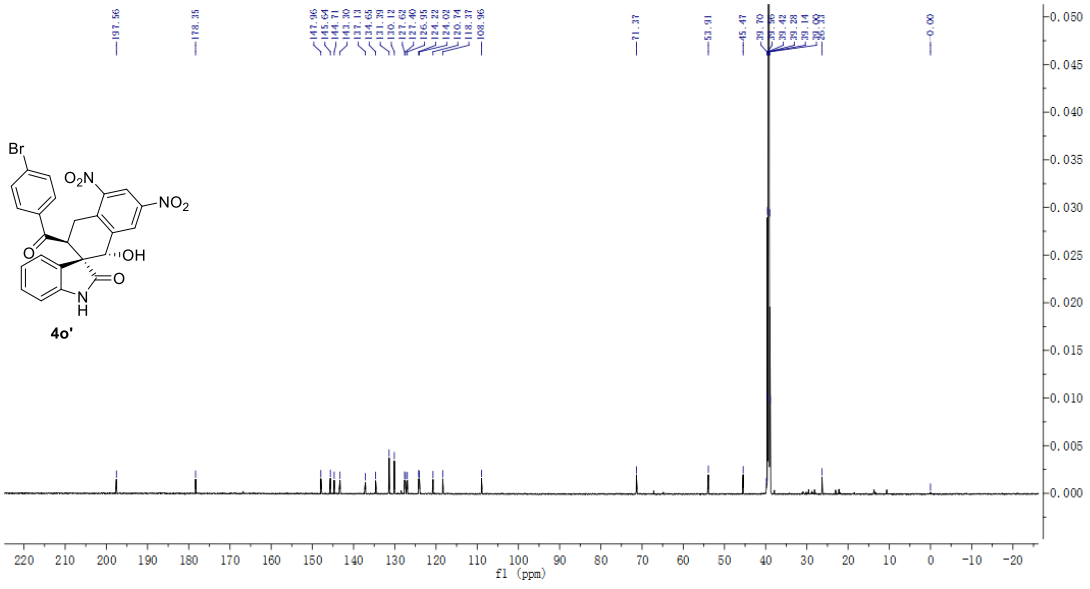

4m'

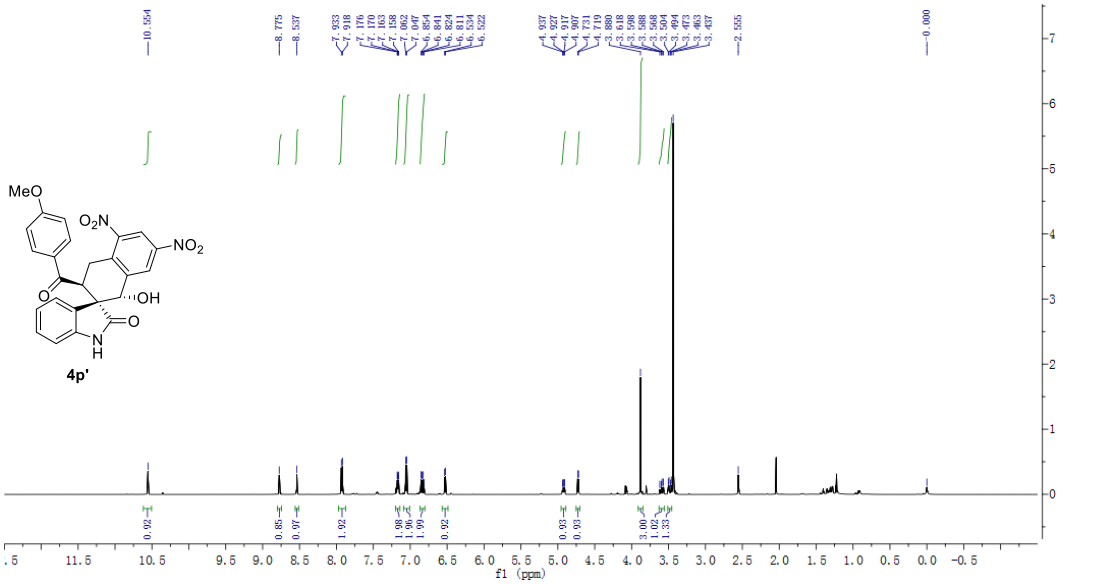

4m'

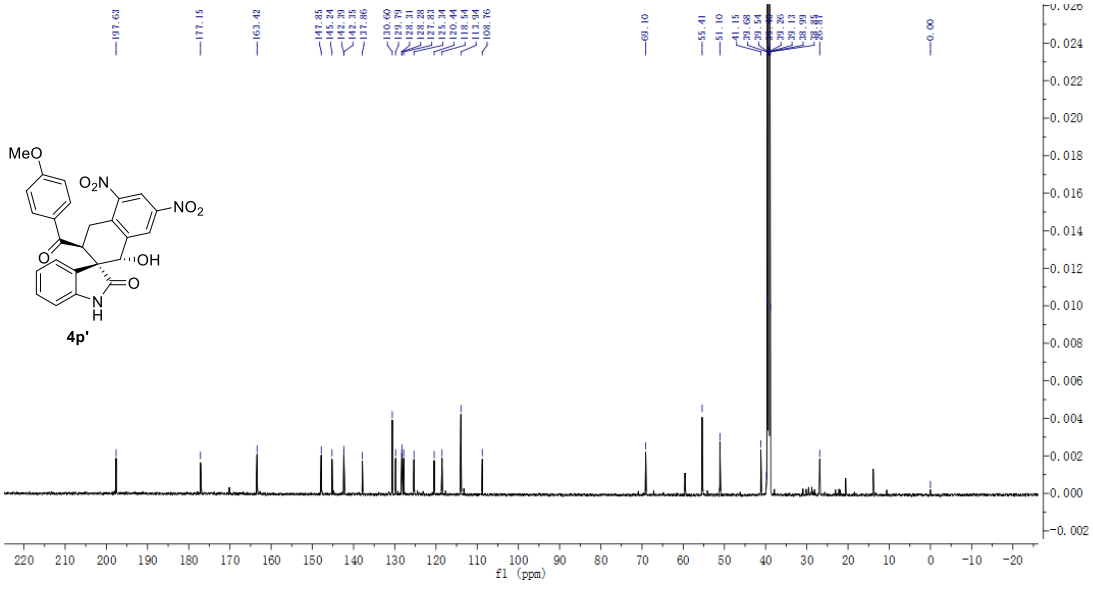

10.550
8.736
8.481
7.965
7.743
7.153
7.140
7.127
7.005
6.993
6.792
6.780
6.770
6.757
6.524
6.512
4.795
4.784
4.777
4.772
4.767
4.761
3.548
3.535
3.518
3.507
3.498
3.375
2.505
0.000
Cl
Cl
O2N
NO2
O
OH
O
N
H
4n'
fl (ppm)


193.04
176.17
147.92
145.31
142.61
142.28
137.57
136.36
135.98
131.68
130.95
130.01
129.31
128.12
128.00
127.55
125.36
120.70
118.52
108.93
69.01
51.75
42.57
39.70
39.66
39.28
39.15
39.01
0.00
Cl
Cl
O2N
NO2
O
OH
O
N
H
4n'
fl (ppm)


Br
O2N
NO2
O
OH
O
N
H
4o'
f1 (ppm)

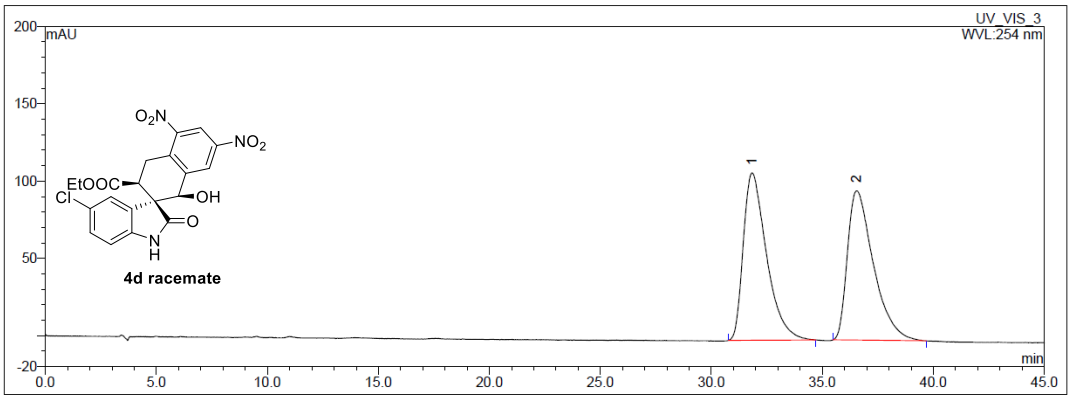

Br
O2N
NO2
O
OH
O
N
H
4o'
f1 (ppm)


MeO
O2N
NO2
O
OH
O
N
H
4p'
f1 (ppm)


MeO
O2N
NO2
O
OH
O
N
H
4p'
f1 (ppm)

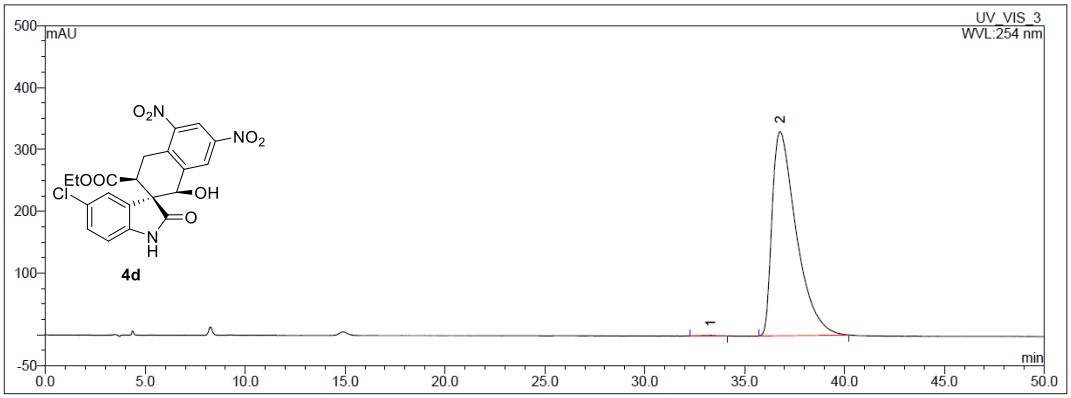
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	31.83	131.471	50.08	108.328	n.a.
2	n.a.	36.54	131.033	49.92	96.527	n.a.



Peak Analysis Report

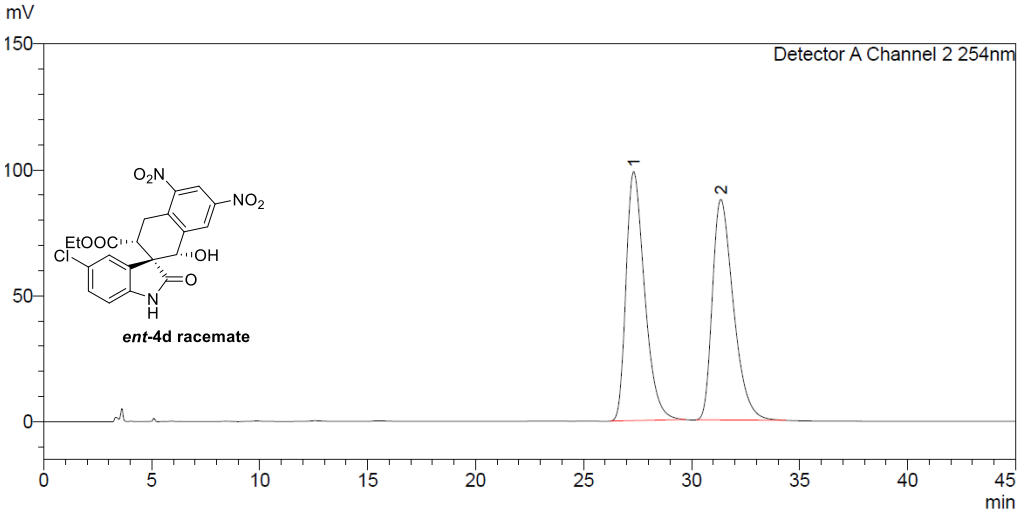
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	33.30	0.960	0.21	1.060	n.a.
2	n.a.	36.78	463.785	99.79	330.087	n.a.



Peak Analysis Report

Detector A Channel 2 254nm

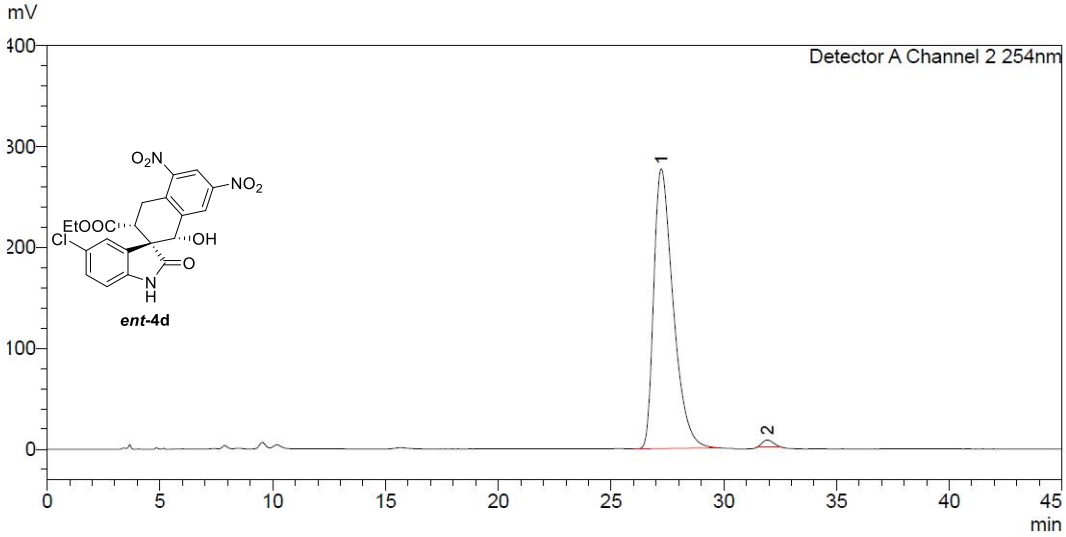
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	27.314	98898	5902777	49.909
2	31.350	87575	5924299	50.091
Total		186473	11827076	100.000



Peak Analysis Report

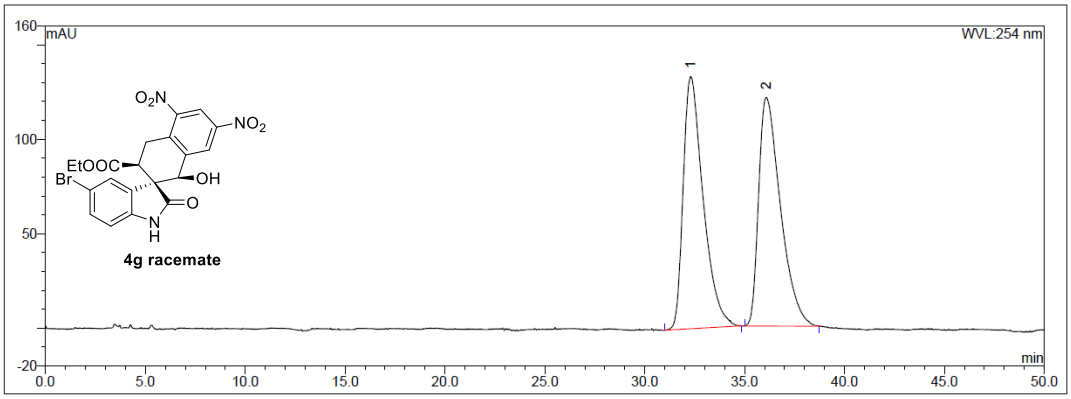
Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	27.228	277235	16584890	97.929
2	31.880	7484	350763	2.071
Total		284719	16935653	100.000



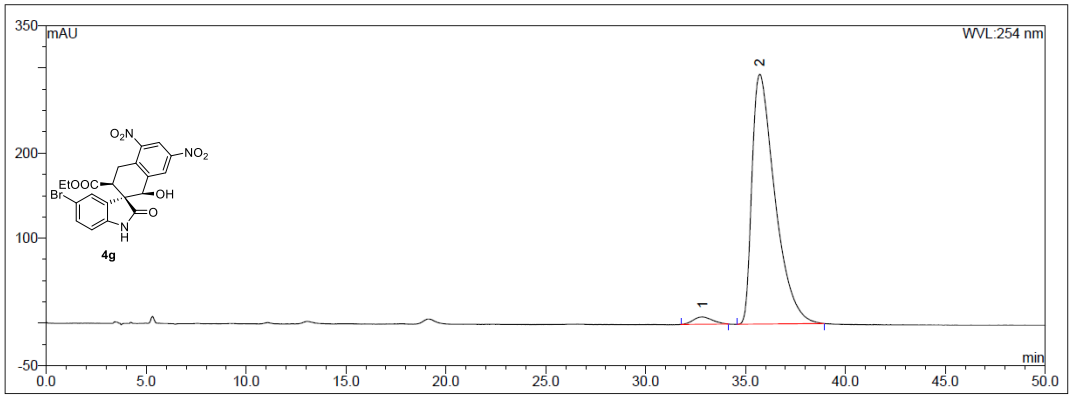
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	32.29	154.639	50.25	133.538	n.a.
2	n.a.	36.08	153.115	49.75	120.956	n.a.



Peak Analysis Report

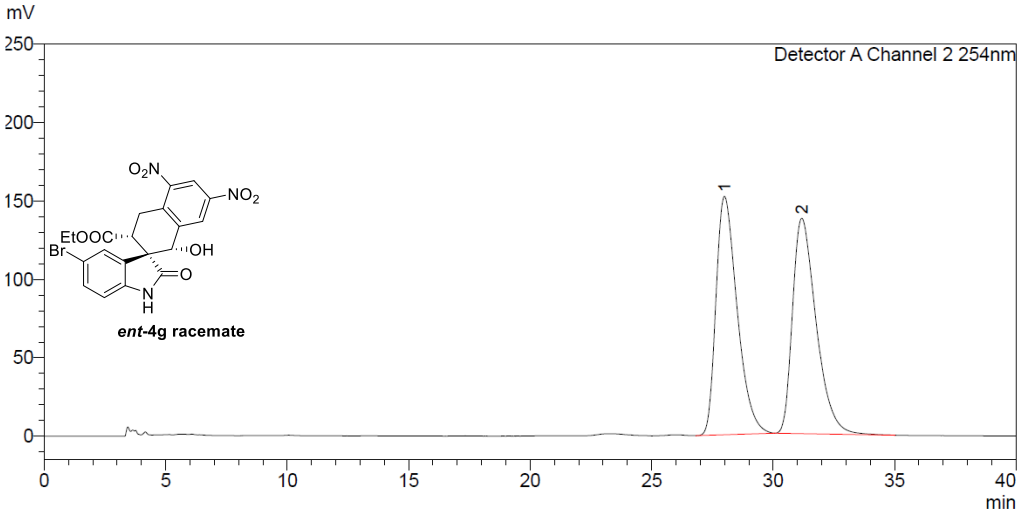
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	32.86	9.572	2.39	8.736	n.a.
2	n.a.	35.72	390.992	97.61	293.834	n.a.



Peak Analysis Report

Detector A Channel 2 254nm

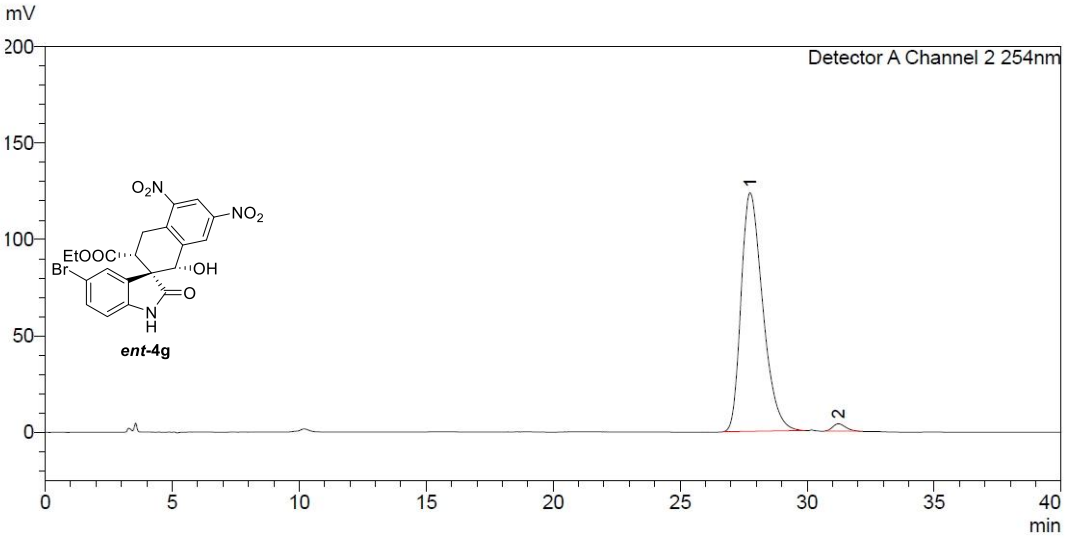
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	27.997	152043	9230522	49.870
2	31.179	137370	9278663	50.130
Total		289413	18509185	100.000



Peak Analysis Report

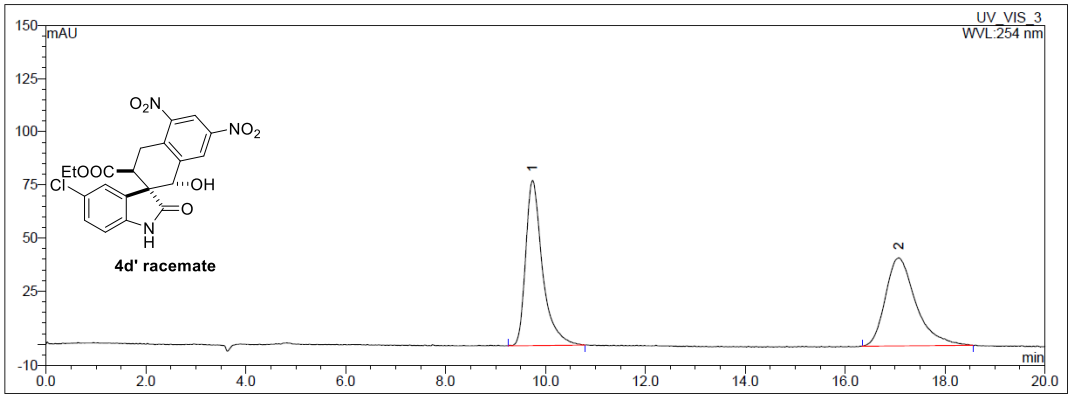
Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	27.753	123680	7327410	97.634
2	31.135	5510	177536	2.366
Total		129191	7504946	100.000



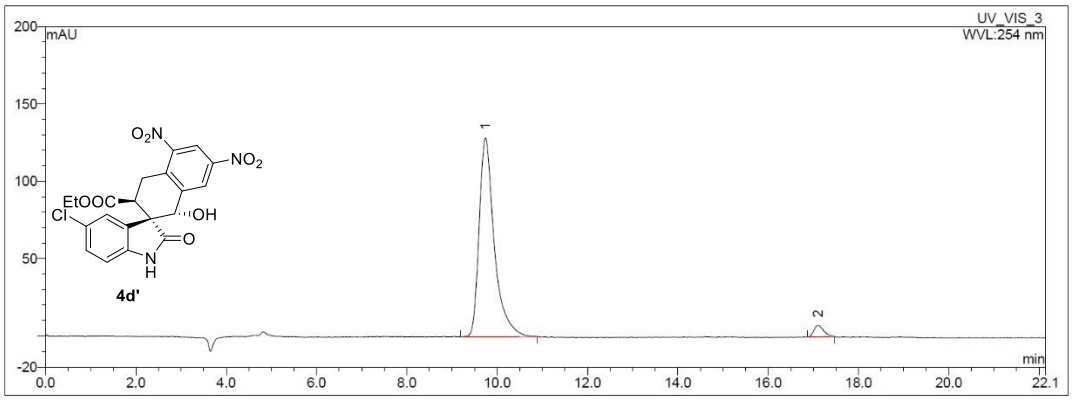
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.74	30.152	50.74	77.696	n.a.
2	n.a.	17.08	29.269	49.26	41.460	n.a.



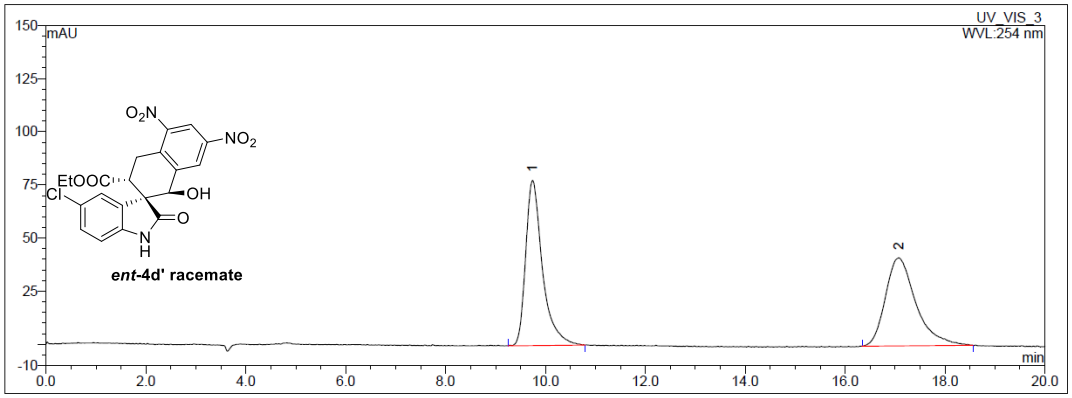
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.74	49.780	92.87	128.314	n.a.
2	n.a.	17.08	3.821	7.13	8.338	n.a.



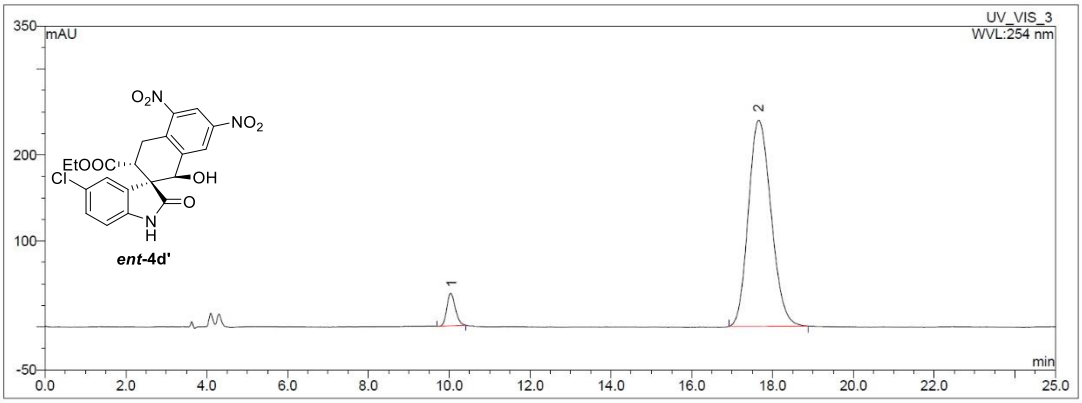
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.74	30.152	50.74	77.696	n.a.
2	n.a.	17.08	29.269	49.26	41.460	n.a.



Peak Analysis Report

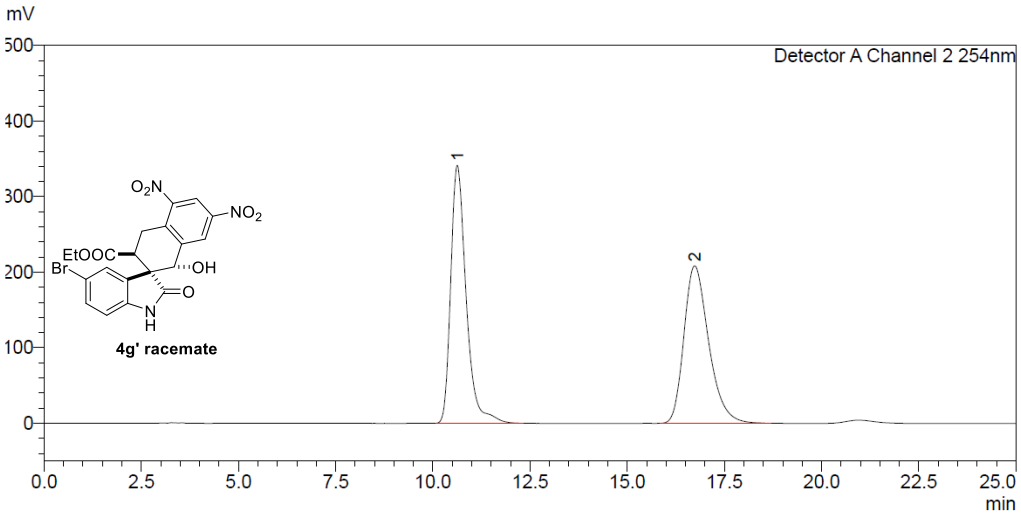
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.09	12.327	7.32	49.346	n.a.
2	n.a.	17.66	156.161	92.68	239.785	n.a.



Peak Analysis Report

Detector A Channel 2 254nm

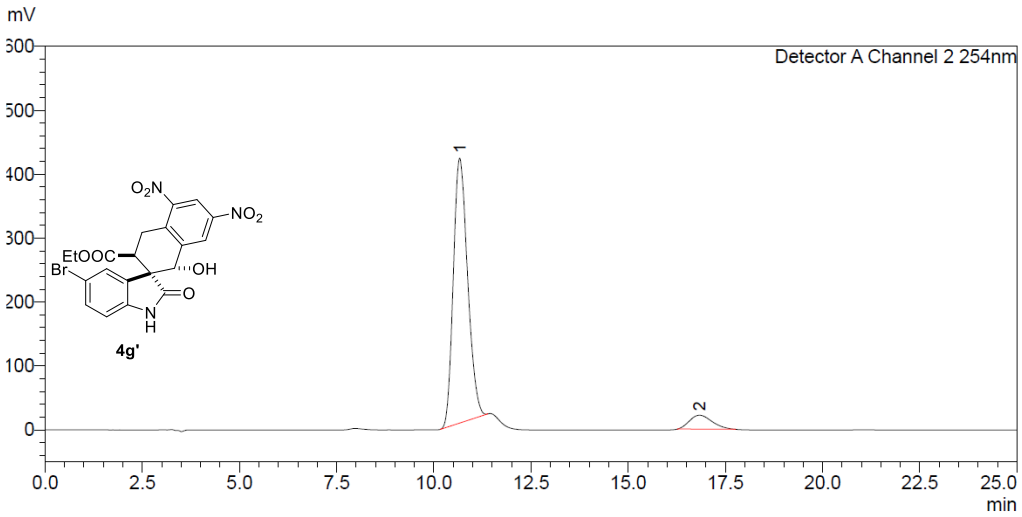
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	10.627	341407	9442988	50.565
2	16.734	208473	9231857	49.435
Total		549880	18674845	100.000



Peak Analysis Report

Detector A Channel 2 254nm

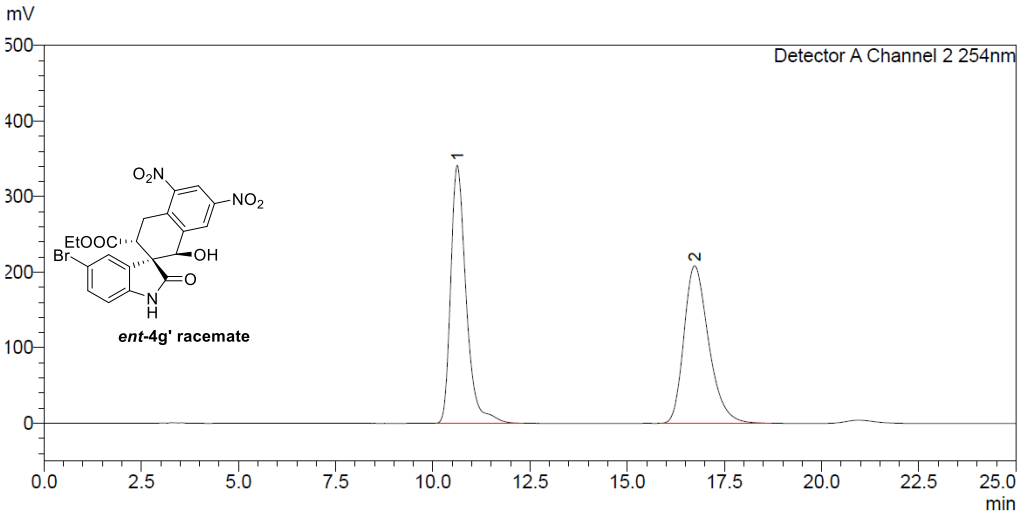
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	10.665	414312	10601279	92.324
2	16.832	21835	881457	7.676
Total		436146	11482737	100.000



Peak Analysis Report

Detector A Channel 2 254nm

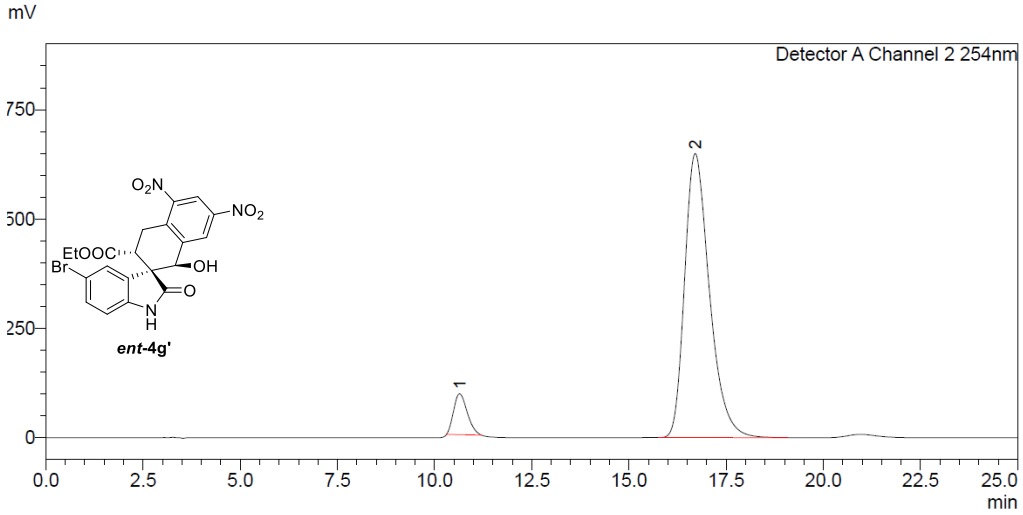
No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	10.627	341407	9442988	50.565
2	16.734	208473	9231857	49.435
Total		549880	18674845	100.000



Peak Analysis Report

Detector A Channel 2 254nm

No.	Ret. Time	Height (mAu)	Area (mAu*min)	Rel. Area (%)
1	10.642	93359	2275633	7.309
2	16.703	649527	28858011	92.691
Total		742886	31133644	100.000

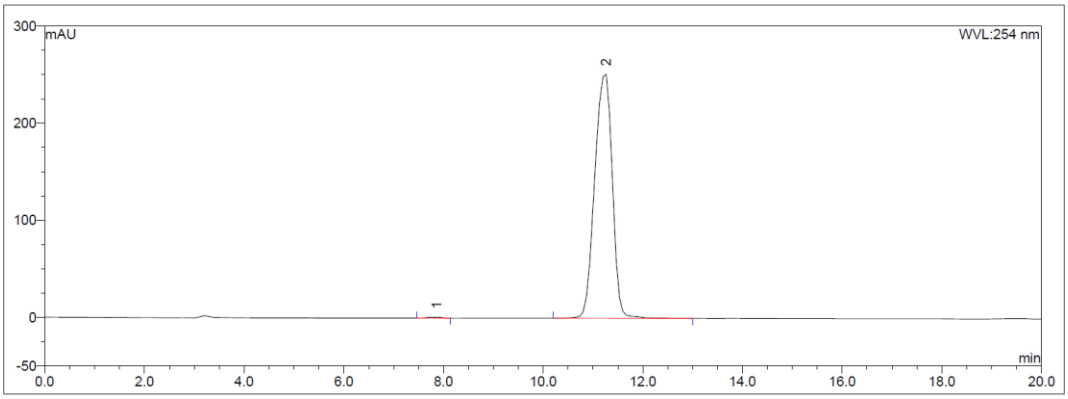


15. The purity of compounds 4 and 4'.

Compound **4a**

Peak Analysis Report

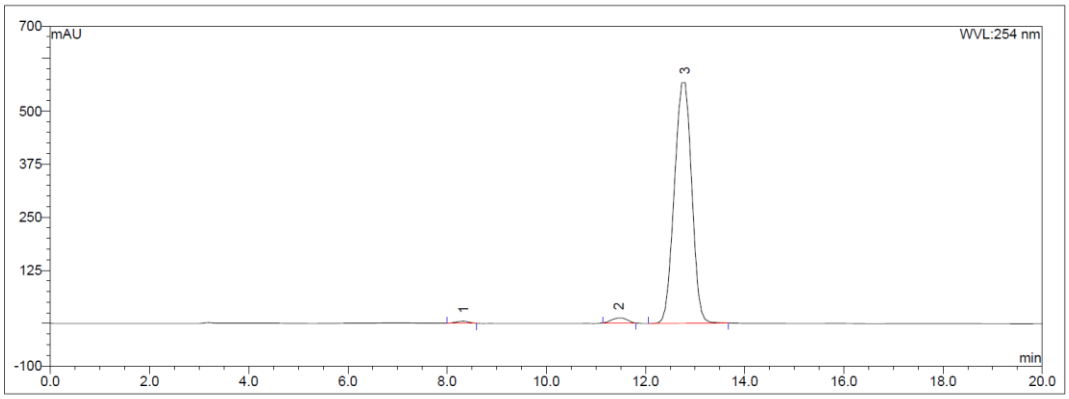
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.87	0.328	0.32	0.999	n.a.
2	n.a.	11.27	103.700	99.68	251.513	n.a.



Compound **4b**

Peak Analysis Report

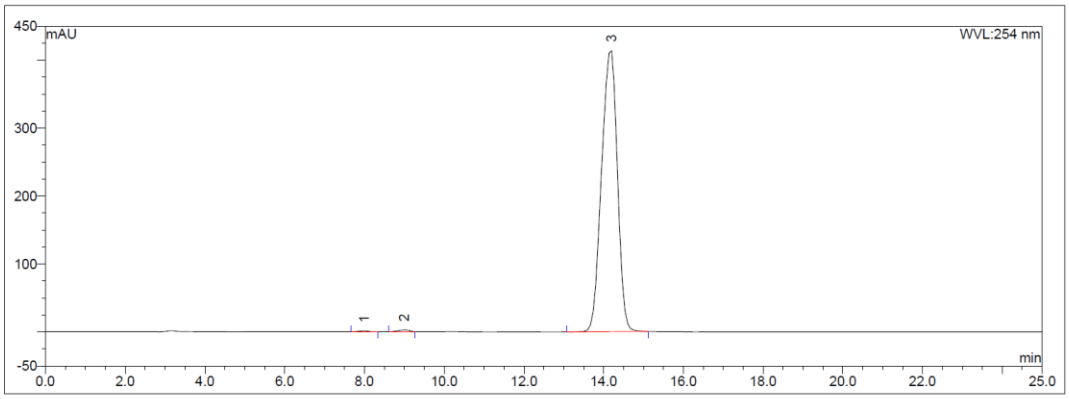
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.33	1.552	0.66	5.008	n.a.
2	n.a.	11.47	4.425	1.87	12.121	n.a.
3	n.a.	12.80	230.519	97.47	567.623	n.a.



Compound **4c**

Peak Analysis Report

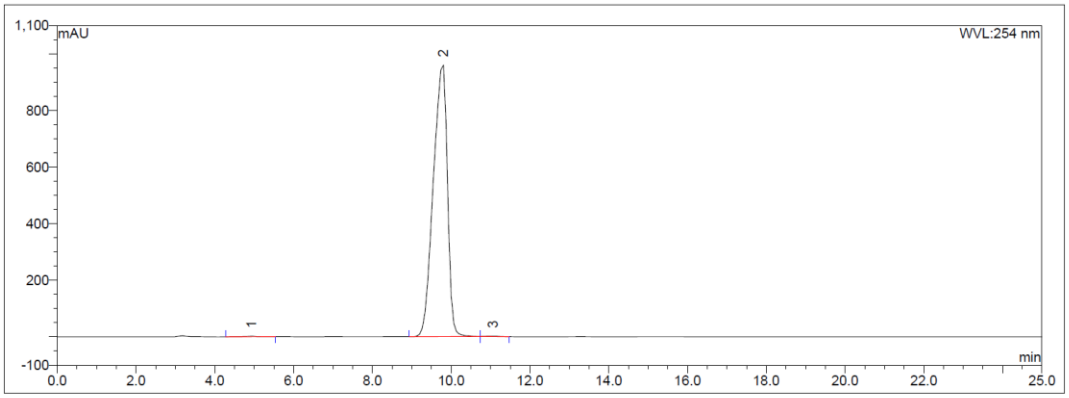
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.00	0.404	0.21	1.347	n.a.
2	n.a.	9.00	0.939	0.49	2.835	n.a.
3	n.a.	14.20	191.271	99.30	413.759	n.a.



Compound **4d**

Peak Analysis Report

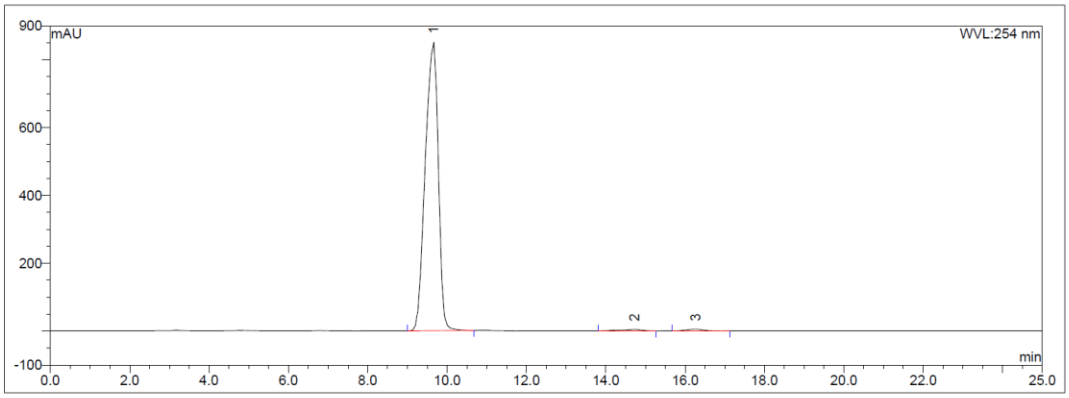
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.93	0.778	0.19	2.441	n.a.
2	n.a.	9.80	398.513	99.66	959.378	n.a.
3	n.a.	11.07	0.598	0.15	1.617	n.a.



Compound ***Ent*-4d**

Peak Analysis Report

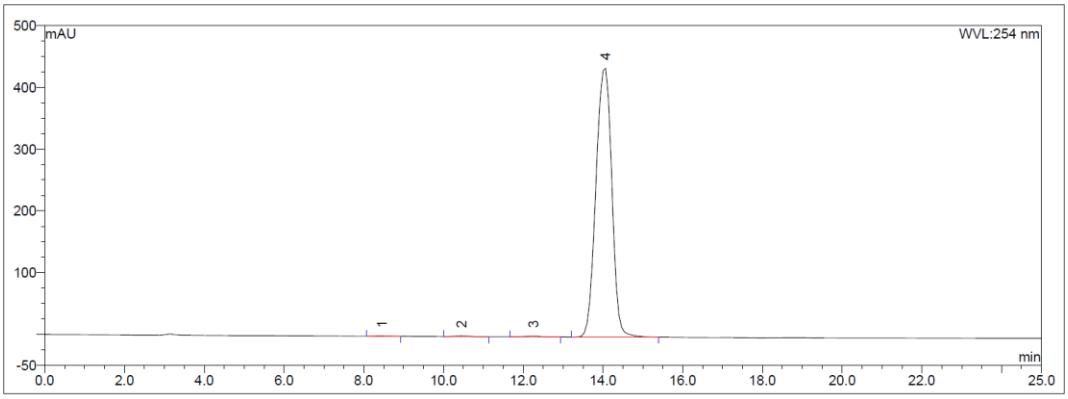
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.67	323.162	98.28	851.975	n.a.
2	n.a.	14.73	2.965	0.90	4.299	n.a.
3	n.a.	16.27	2.702	0.82	5.525	n.a.



Compound **4e**

Peak Analysis Report

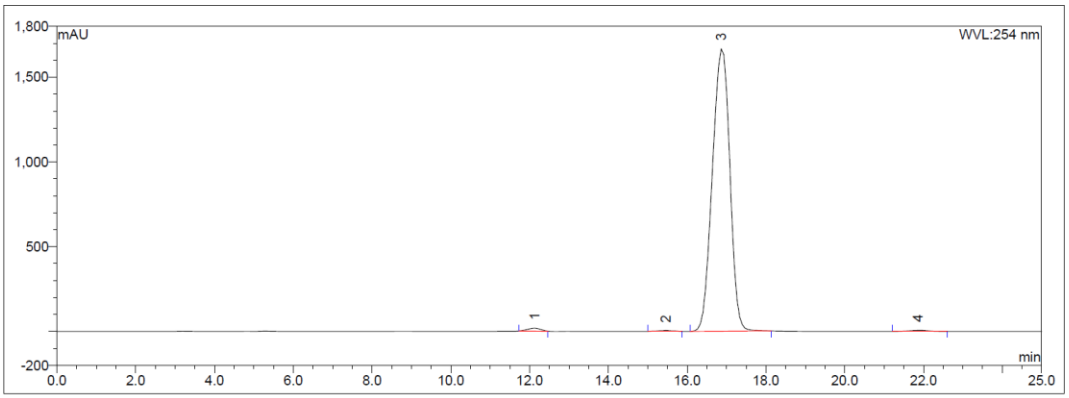
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.47	0.130	0.06	0.362	n.a.
2	n.a.	10.47	0.497	0.25	1.195	n.a.
3	n.a.	12.27	0.588	0.29	1.321	n.a.
4	n.a.	14.07	201.151	99.40	435.583	n.a.



Compound **4f**

Peak Analysis Report

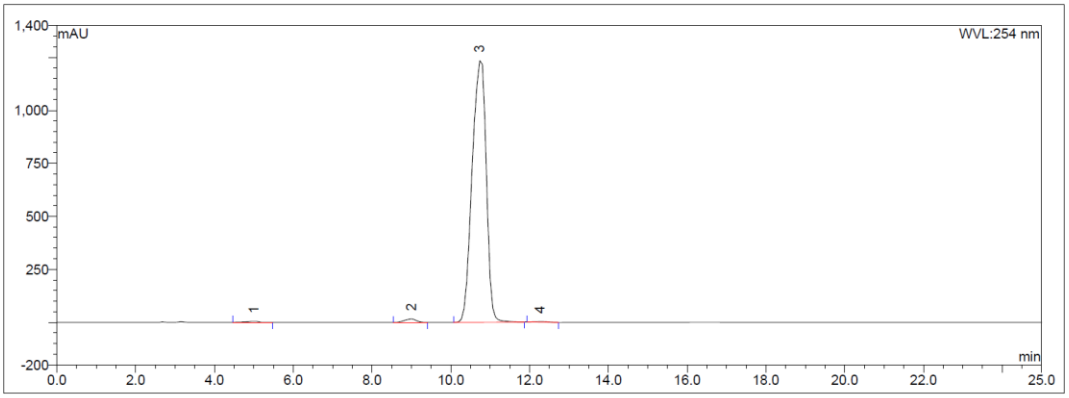
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	12.13	6.457	0.74	16.961	n.a.
2	n.a.	15.47	2.219	0.25	4.888	n.a.
3	n.a.	16.87	857.948	98.60	1665.501	n.a.
4	n.a.	21.87	3.528	0.41	6.062	n.a.



Compound **4g**

Peak Analysis Report

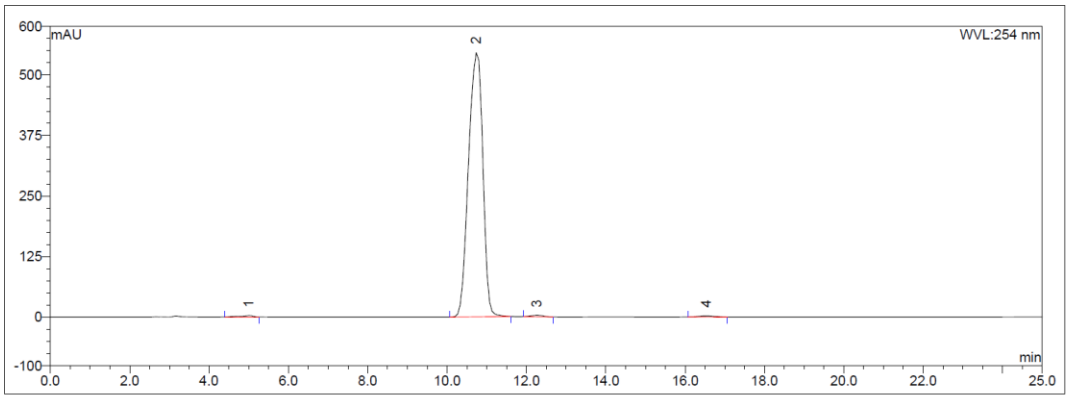
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.00	1.526	0.29	4.542	n.a.
2	n.a.	9.00	5.385	1.03	15.794	n.a.
3	n.a.	10.73	514.079	98.50	1233.653	n.a.
4	n.a.	12.27	0.894	0.17	2.314	n.a.



Compound ***Ent*-4g**

Peak Analysis Report

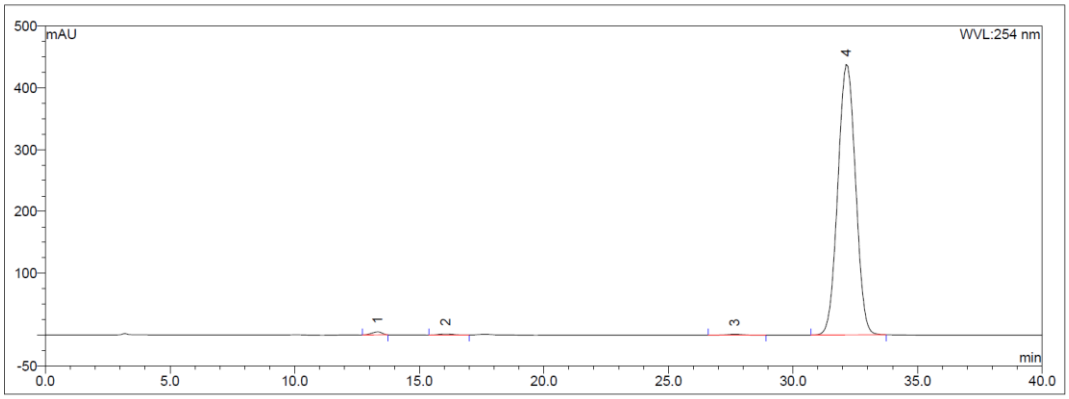
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.00	1.308	0.57	3.003	n.a.
2	n.a.	10.73	226.680	98.41	545.607	n.a.
3	n.a.	12.27	1.136	0.49	2.928	n.a.
4	n.a.	16.53	1.215	0.53	2.510	n.a.



Compound **4h**

Peak Analysis Report

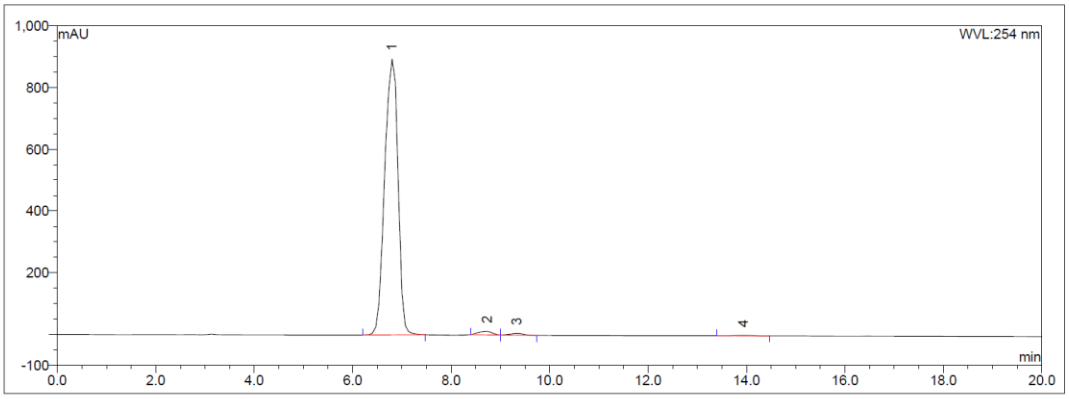
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	13.33	2.235	0.61	4.758	n.a.
2	n.a.	16.07	0.962	0.26	1.506	n.a.
3	n.a.	27.67	0.753	0.21	1.023	n.a.
4	n.a.	32.13	360.776	98.92	437.936	n.a.



Compound **4i**

Peak Analysis Report

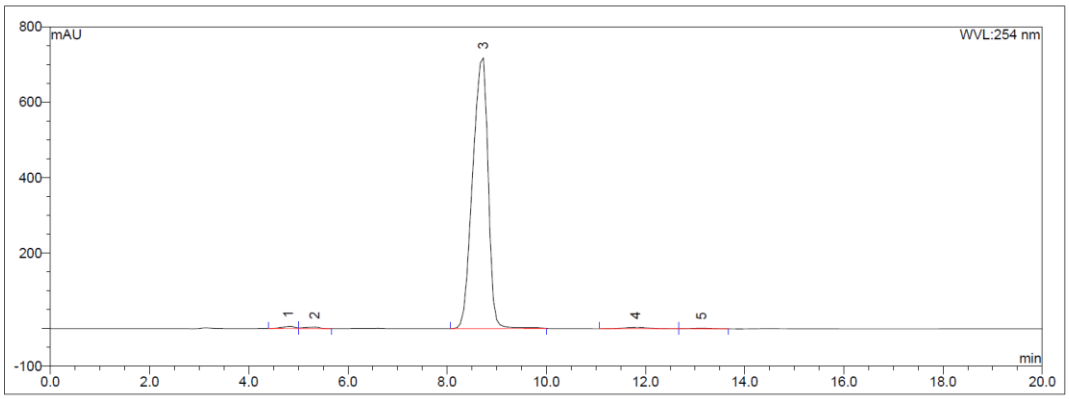
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	6.80	280.067	97.89	893.790	n.a.
2	n.a.	8.73	3.589	1.25	11.083	n.a.
3	n.a.	9.33	1.705	0.60	5.181	n.a.
4	n.a.	13.93	0.751	0.26	1.666	n.a.



Compound **4j**

Peak Analysis Report

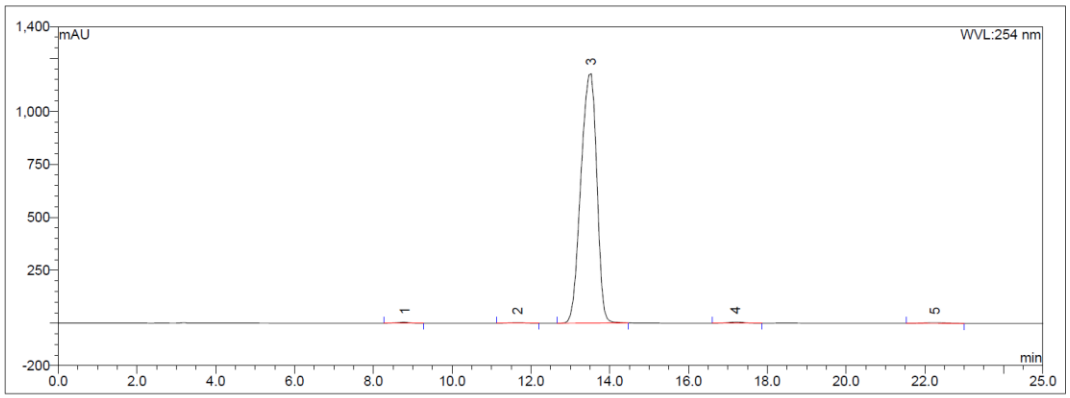
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.80	1.609	0.61	5.959	n.a.
2	n.a.	5.33	1.169	0.44	3.725	n.a.
3	n.a.	8.73	258.795	98.11	717.706	n.a.
4	n.a.	11.80	1.723	0.65	3.056	n.a.
5	n.a.	13.13	0.475	0.18	1.161	n.a.



Compound **4k**

Peak Analysis Report

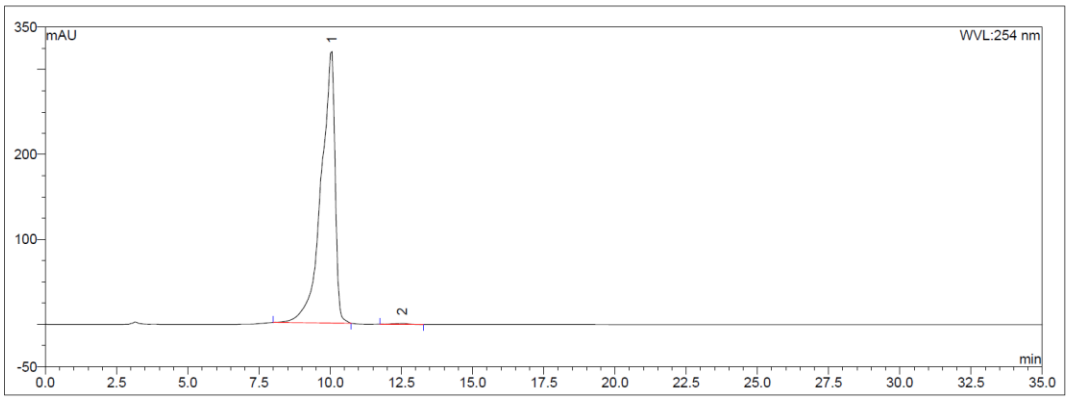
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.80	1.541	0.28	4.121	n.a.
2	n.a.	11.67	1.160	0.21	2.620	n.a.
3	n.a.	13.53	551.810	98.69	1177.635	n.a.
4	n.a.	17.20	2.573	0.46	5.111	n.a.
5	n.a.	22.27	2.048	0.37	3.314	n.a.



Compound **4l**

Peak Analysis Report

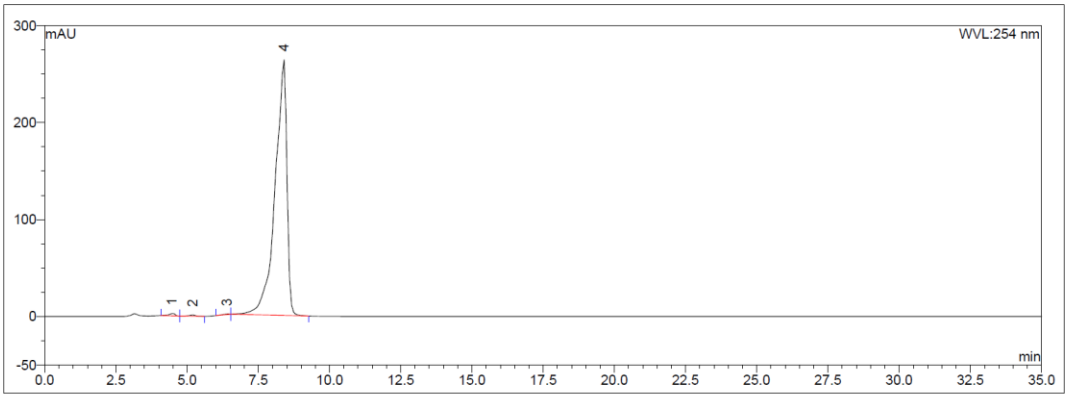
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	10.07	182.560	99.66	319.988	n.a.
2	n.a.	12.53	0.624	0.34	1.070	n.a.



Compound **4m**

Peak Analysis Report

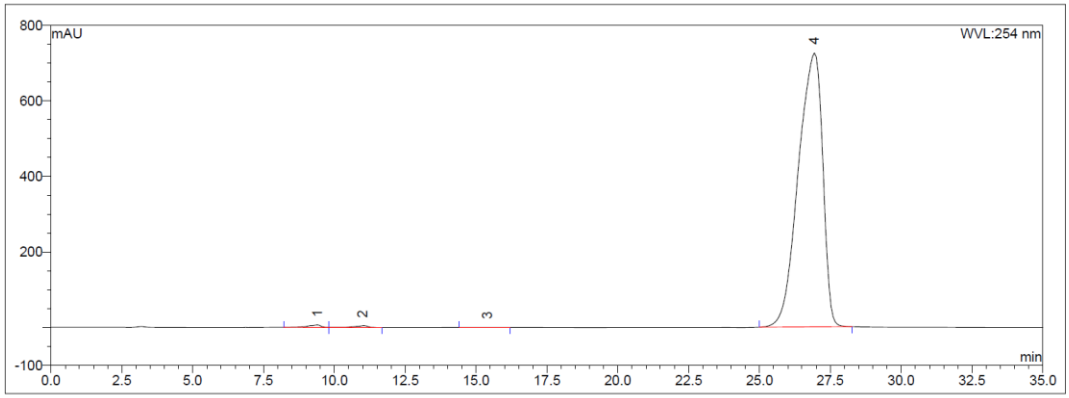
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.47	0.560	0.44	2.339	n.a.
2	n.a.	5.20	0.328	0.26	1.206	n.a.
3	n.a.	6.40	0.121	0.09	0.526	n.a.
4	n.a.	8.40	127.345	99.21	263.982	n.a.



Compound **4n**

Peak Analysis Report

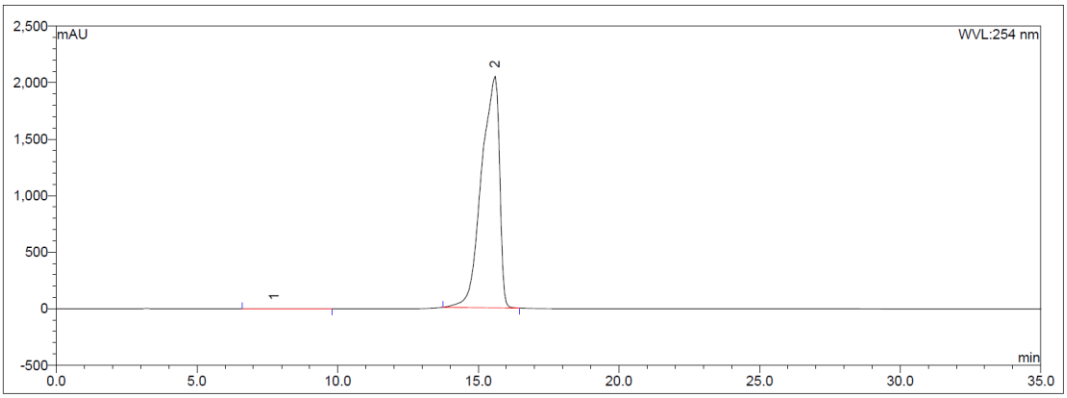
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.40	3.561	0.49	6.522	n.a.
2	n.a.	11.00	2.539	0.35	4.502	n.a.
3	n.a.	15.40	0.344	0.05	0.513	n.a.
4	n.a.	26.93	721.801	99.12	725.824	n.a.



Compound **4o**

Peak Analysis Report

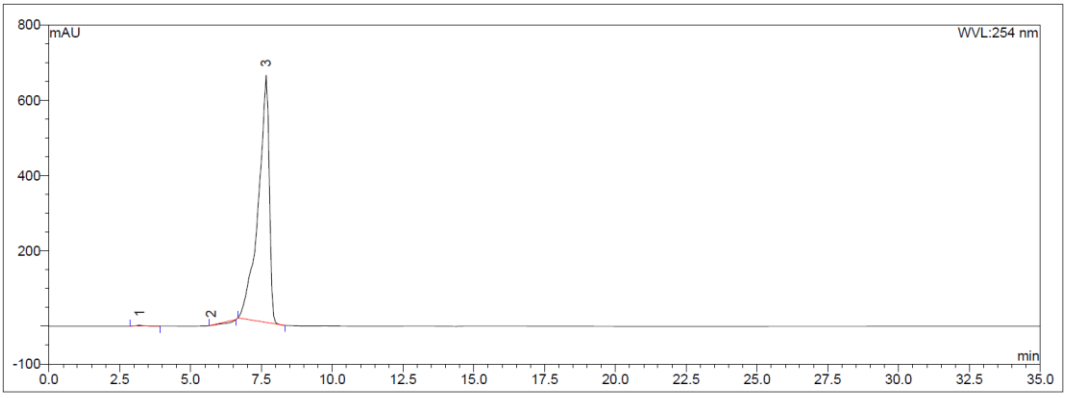
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	7.73	1.359	0.09	1.026	n.a.
2	n.a.	15.60	1518.351	99.91	2050.933	n.a.



Compound **4p**

Peak Analysis Report

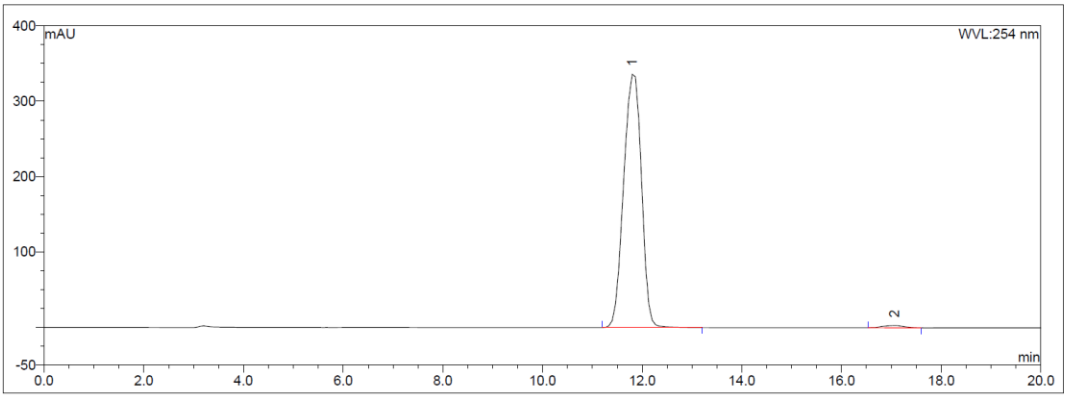
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	3.20	0.738	0.25	2.942	n.a.
2	n.a.	5.73	2.188	0.74	0.421	n.a.
3	n.a.	7.67	294.145	99.02	656.082	n.a.



Compound **4a′**

Peak Analysis Report

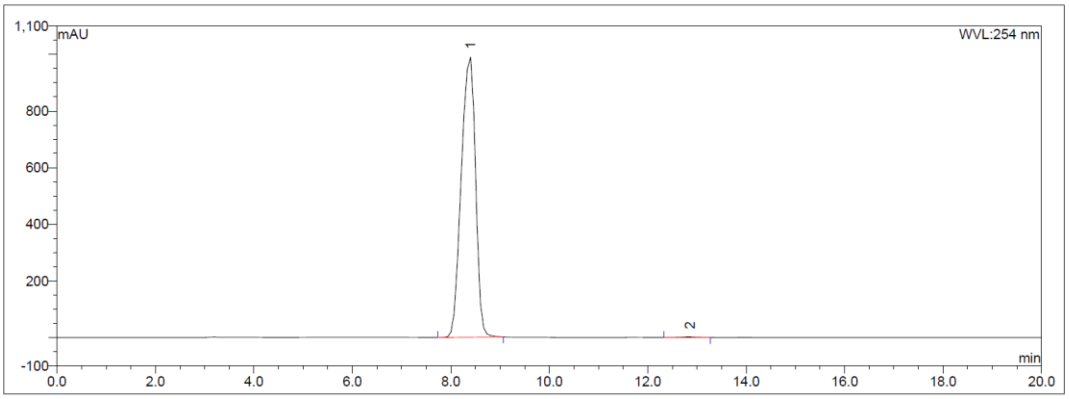
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.80	138.377	98.96	336.155	n.a.
2	n.a.	17.07	1.451	1.04	2.989	n.a.



Compound **4b′**

Peak Analysis Report

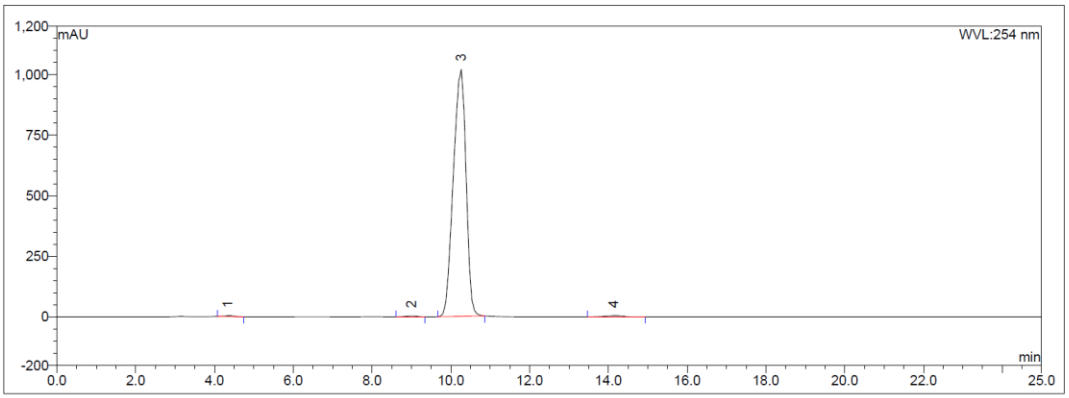
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.40	332.428	99.76	989.773	n.a.
2	n.a.	12.87	0.796	0.24	1.918	n.a.



Compound **4c′**

Peak Analysis Report

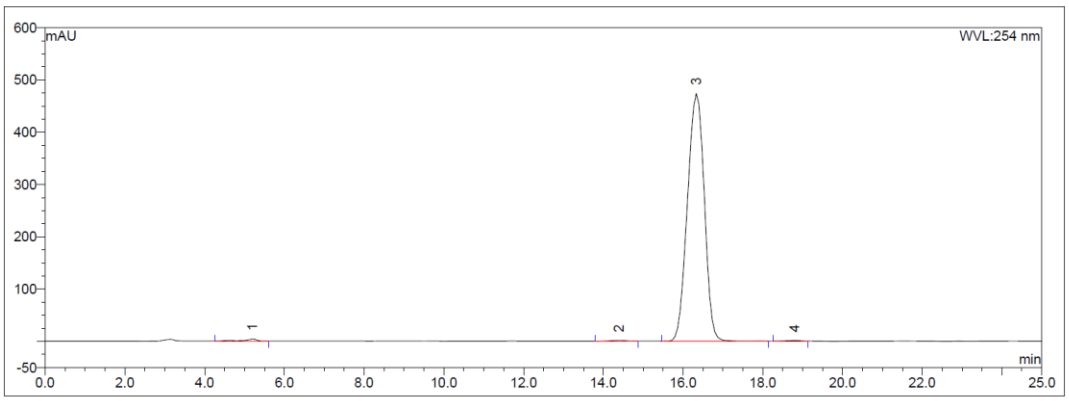
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.33	1.064	0.28	4.036	n.a.
2	n.a.	9.00	1.150	0.30	3.390	n.a.
3	n.a.	10.27	381.633	98.80	1020.051	n.a.
4	n.a.	14.13	2.430	0.63	5.183	n.a.



Compound **4d′**

Peak Analysis Report

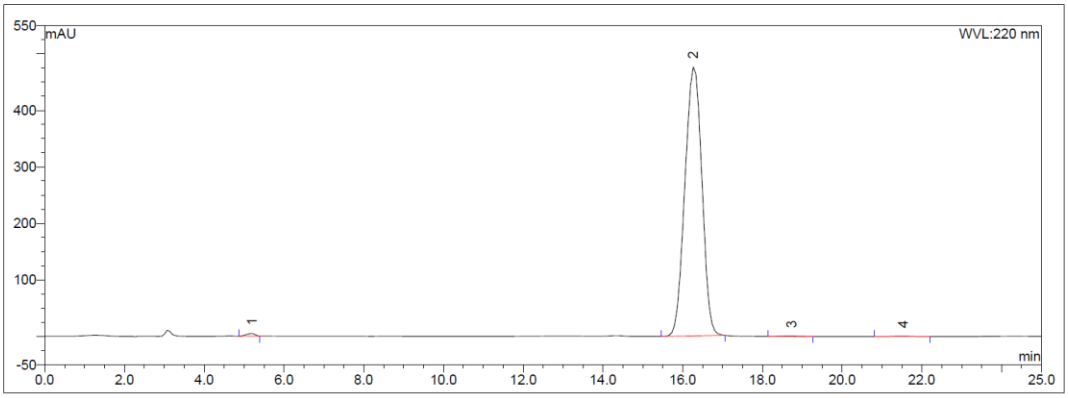
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.20	1.494	0.63	3.773	n.a.
2	n.a.	14.40	0.841	0.36	1.863	n.a.
3	n.a.	16.33	232.463	98.78	474.204	n.a.
4	n.a.	18.80	0.534	0.23	1.157	n.a.



Compound ***Ent*-4d′**

Peak Analysis Report

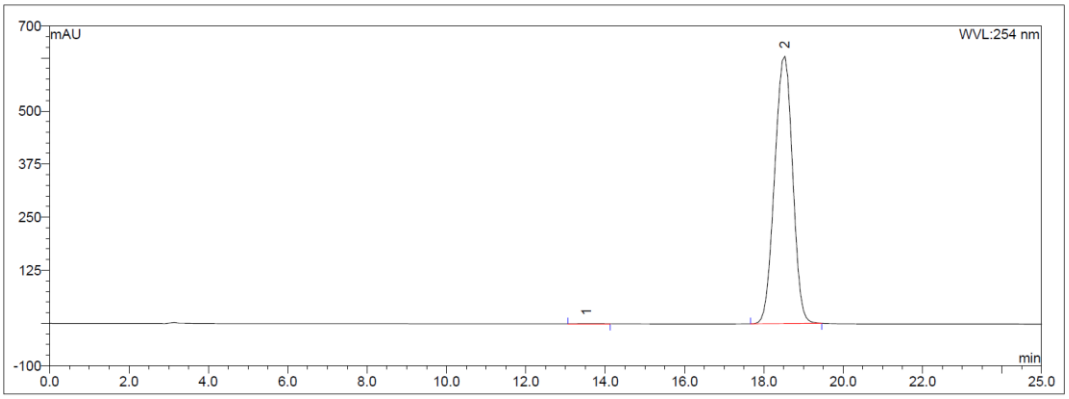
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.20	1.147	0.48	4.652	n.a.
2	n.a.	16.27	234.876	99.17	475.899	n.a.
3	n.a.	18.73	0.486	0.21	0.959	n.a.
4	n.a.	21.53	0.343	0.14	0.592	n.a.



Compound **4e′**

Peak Analysis Report

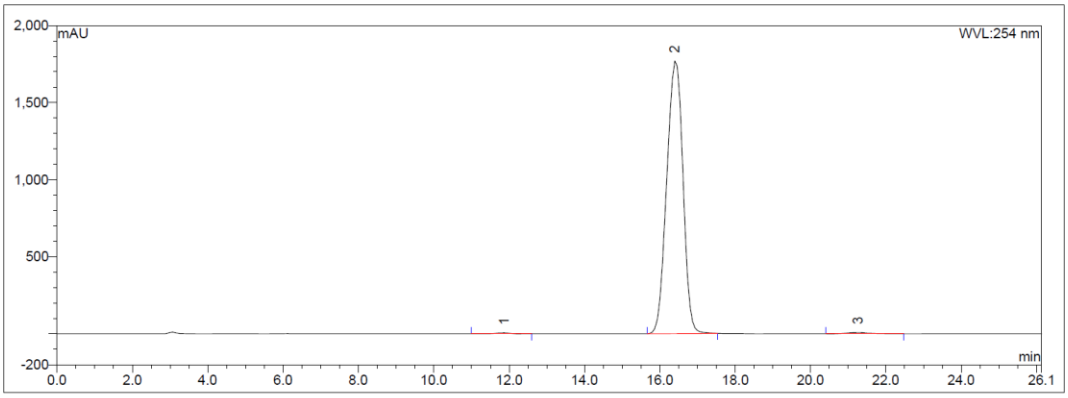
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	13.53	0.249	0.07	0.535	n.a.
2	n.a.	18.53	331.983	99.93	629.990	n.a.



Compound **4f′**

Peak Analysis Report

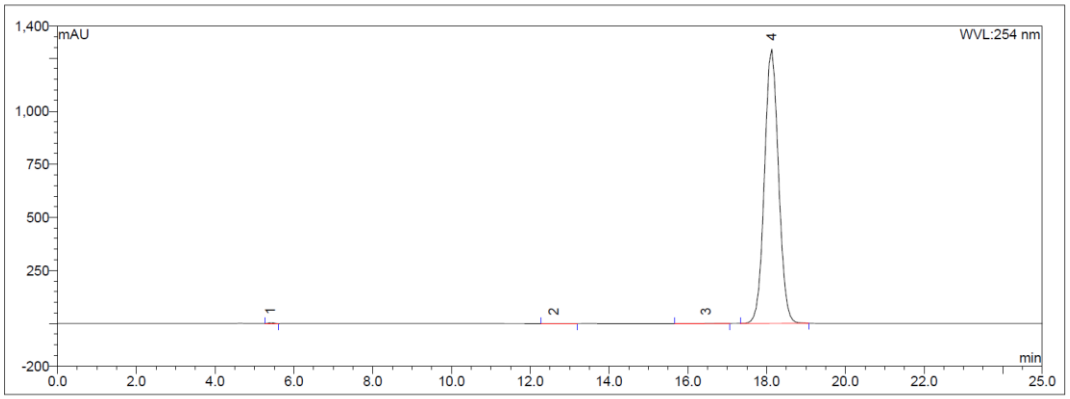
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	11.87	2.570	0.29	6.107	n.a.
2	n.a.	16.40	882.871	99.08	1769.665	n.a.
3	n.a.	21.27	5.590	0.63	8.011	n.a.



Compound **4g′**

Peak Analysis Report

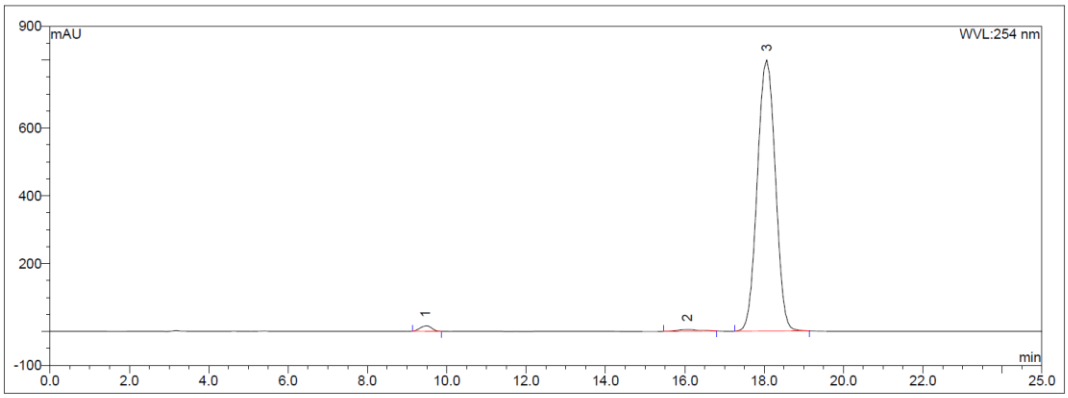
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.40	0.515	0.10	3.151	n.a.
2	n.a.	12.60	0.261	0.05	0.798	n.a.
3	n.a.	16.47	0.614	0.11	0.994	n.a.
4	n.a.	18.13	533.332	99.74	1292.093	n.a.



Compound ***Ent*-4g′**

Peak Analysis Report

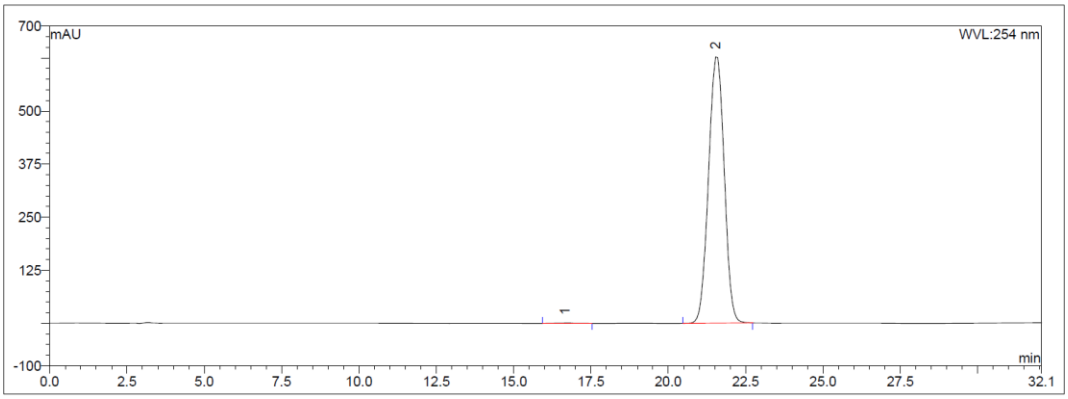
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.47	5.397	1.25	15.791	n.a.
2	n.a.	16.07	2.839	0.66	4.602	n.a.
3	n.a.	18.07	421.854	98.09	800.512	n.a.



Compound **4h′**

Peak Analysis Report

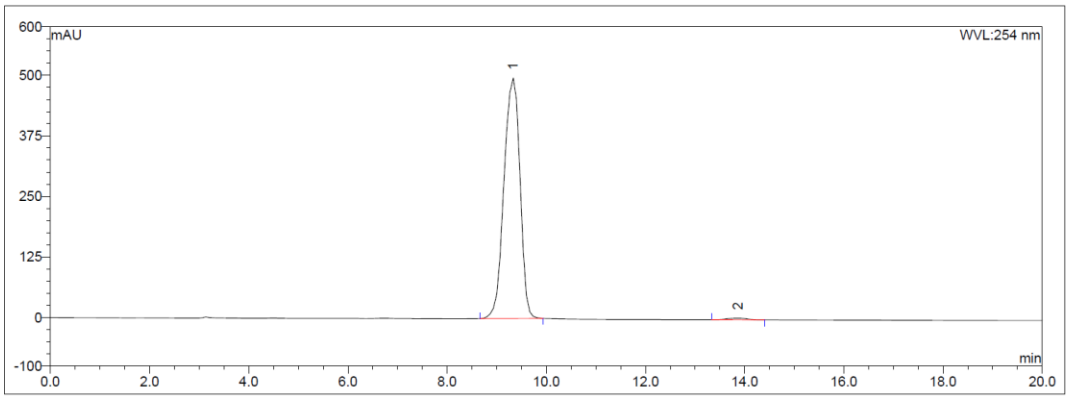
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	16.67	0.656	0.18	0.971	n.a.
2	n.a.	21.53	369.233	99.82	627.093	n.a.



Compound **4i′**

Peak Analysis Report

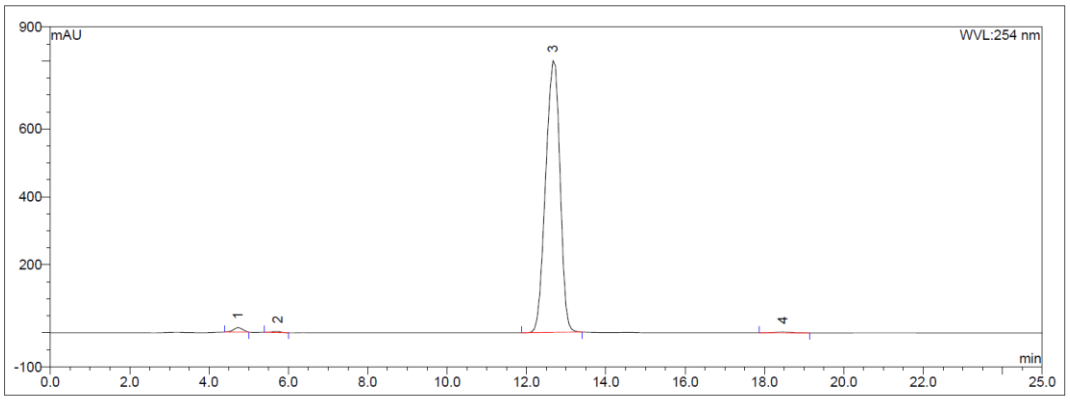
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	9.33	185.757	99.22	496.674	n.a.
2	n.a.	13.87	1.458	0.78	3.299	n.a.



Compound **4j′**

Peak Analysis Report

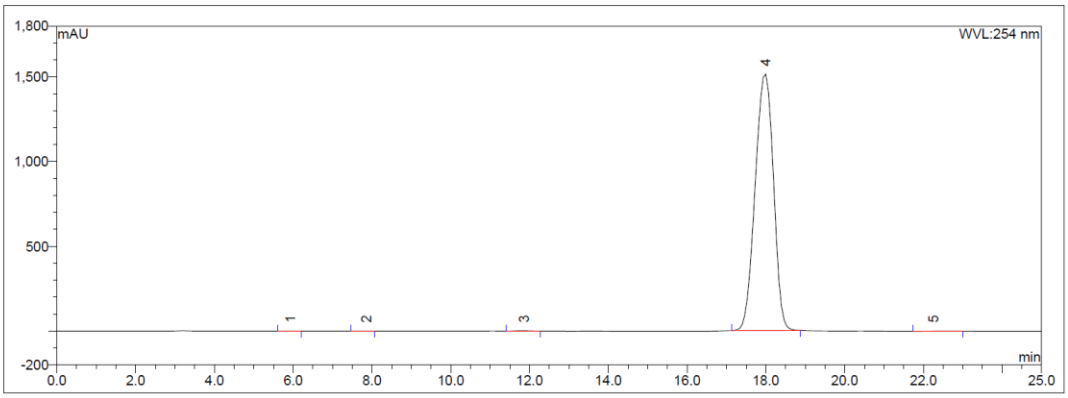
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.73	3.458	1.01	13.090	n.a.
2	n.a.	5.73	0.683	0.20	2.897	n.a.
3	n.a.	12.67	337.282	98.52	799.806	n.a.
4	n.a.	18.47	0.936	0.27	1.860	n.a.



Compound **4k′**

Peak Analysis Report

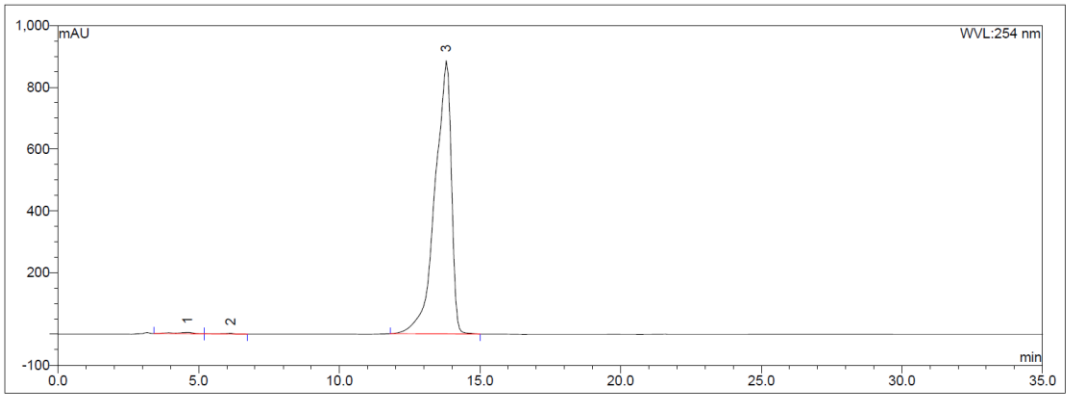
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	5.93	0.126	0.02	0.458	n.a.
2	n.a.	7.87	0.095	0.01	0.313	n.a.
3	n.a.	11.87	0.930	0.11	2.387	n.a.
4	n.a.	18.00	815.623	99.81	1513.856	n.a.
5	n.a.	22.27	0.428	0.05	0.710	n.a.



Compound **4l′**

Peak Analysis Report

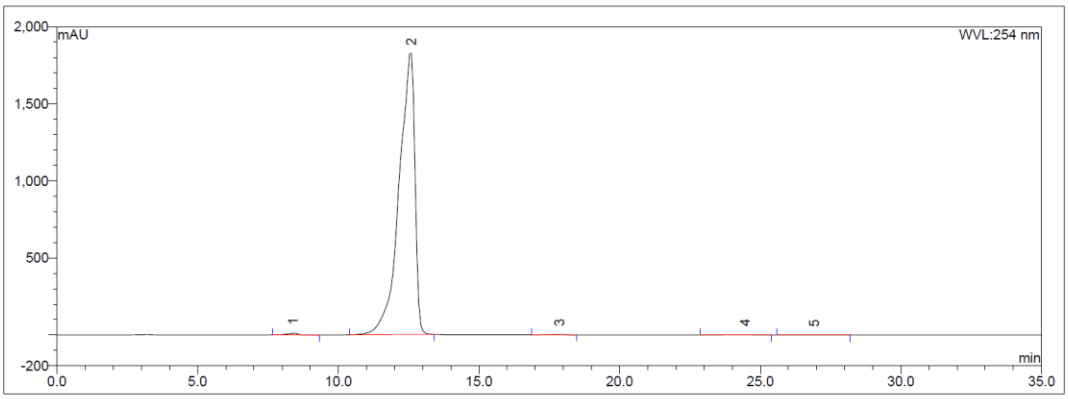
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	4.60	3.294	0.55	4.292	n.a.
2	n.a.	6.13	0.902	0.15	2.369	n.a.
3	n.a.	13.80	594.802	99.30	885.194	n.a.



Compound **4m′**

Peak Analysis Report

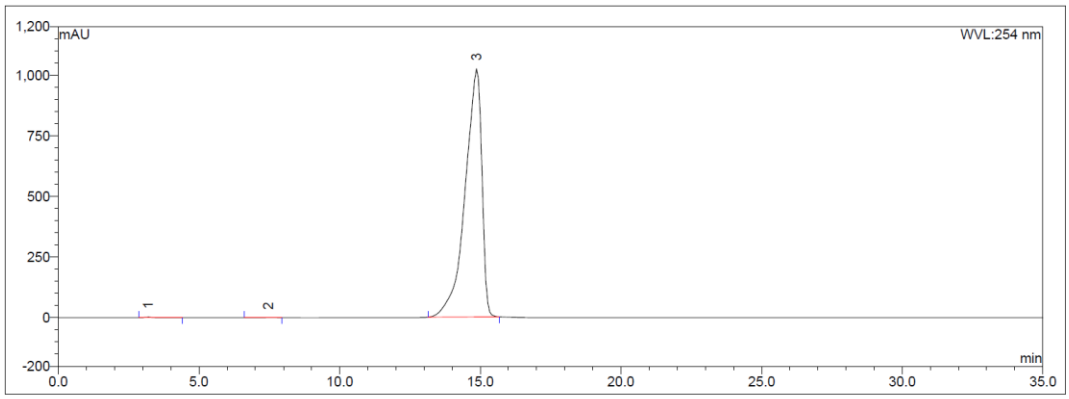
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	8.40	5.173	0.43	11.932	n.a.
2	n.a.	12.60	1194.181	99.25	1822.572	n.a.
3	n.a.	17.87	1.892	0.16	2.628	n.a.
4	n.a.	24.47	1.508	0.13	1.569	n.a.
5	n.a.	26.93	0.512	0.04	0.420	n.a.



Compound **4n′**

Peak Analysis Report

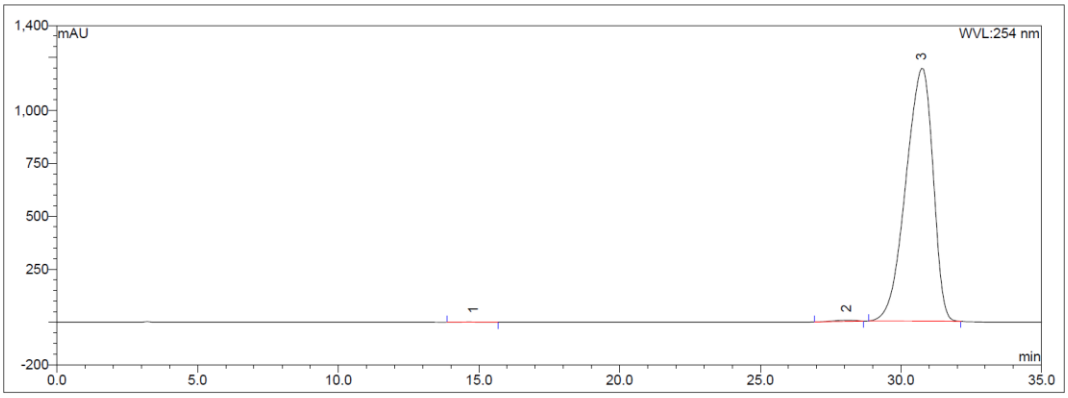
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	3.20	1.010	0.14	3.189	n.a.
2	n.a.	7.47	0.376	0.05	0.855	n.a.
3	n.a.	14.87	703.895	99.80	1023.025	n.a.



Compound **4o′**

Peak Analysis Report

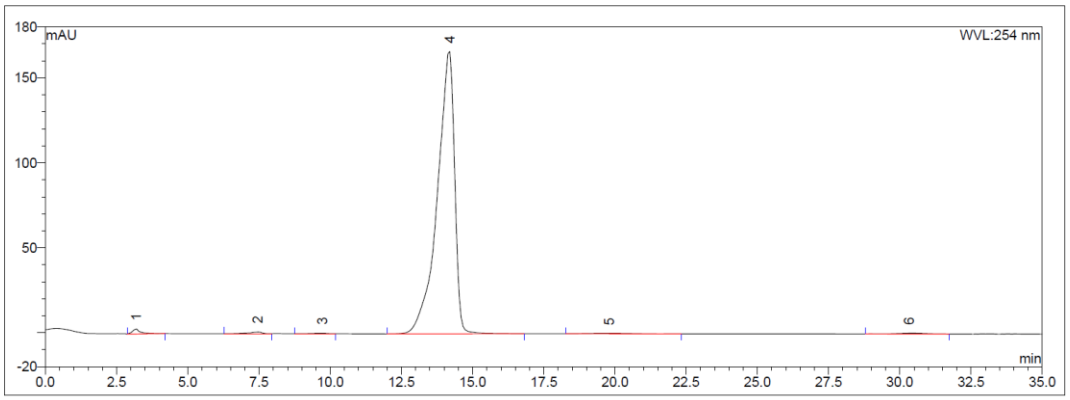
No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	14.80	1.152	0.09	1.655	n.a.
2	n.a.	28.07	5.437	0.41	6.550	n.a.
3	n.a.	30.73	1333.325	99.51	1193.340	n.a.



Compound **4p′**

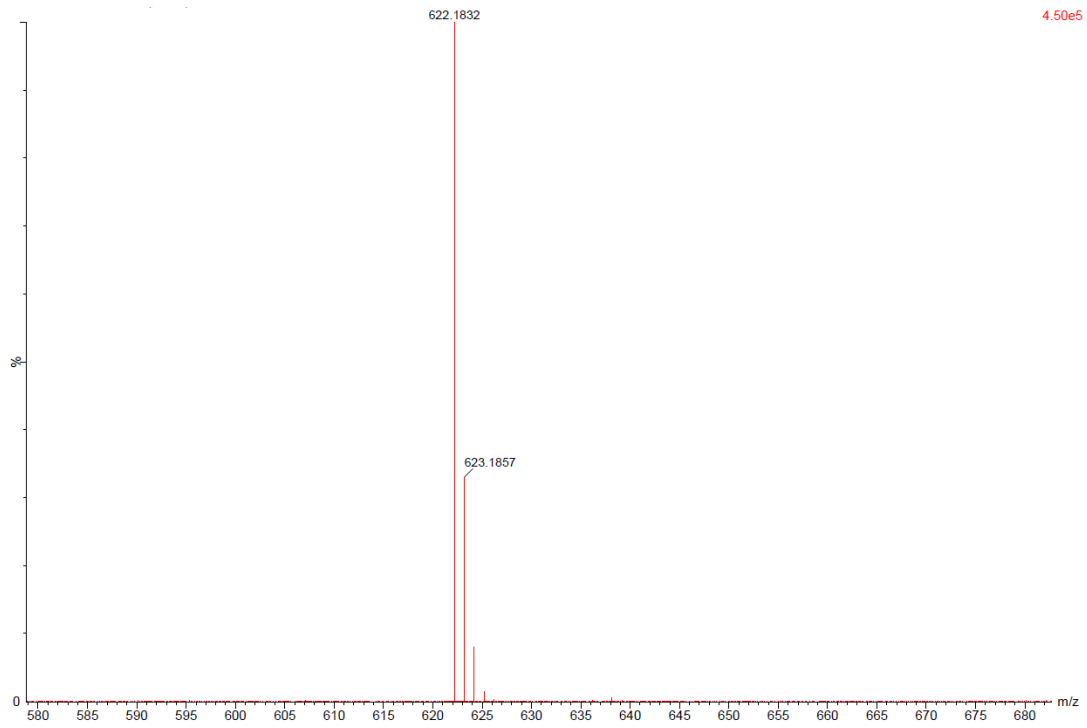
Peak Analysis Report

No.	Peak Name	Ret.Time (detected)	Area	Rel.Area	Height	Amount
		min	mAU*min	%	mAU	
1	n.a.	3.20	0.955	0.80	2.965	n.a.
2	n.a.	7.47	0.467	0.39	0.990	n.a.
3	n.a.	9.73	0.173	0.15	0.314	n.a.
4	n.a.	14.20	116.739	97.85	166.089	n.a.
5	n.a.	19.80	0.443	0.37	0.275	n.a.
6	n.a.	30.33	0.531	0.45	0.467	n.a.

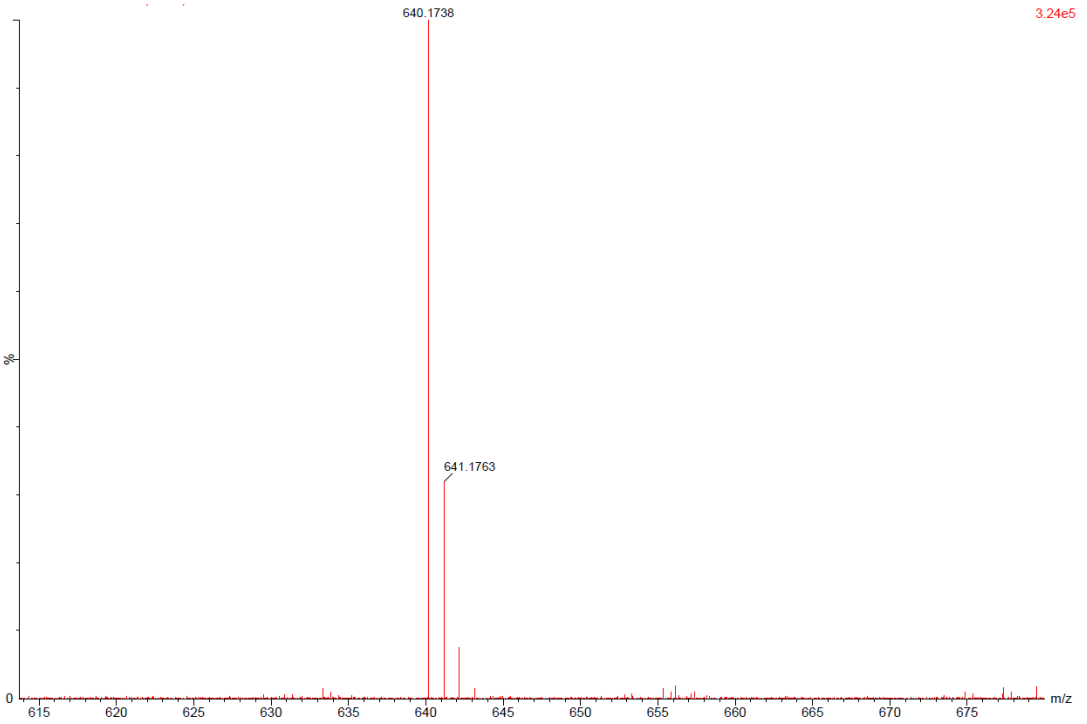


16. The HR-MS chromatography of the THN-fused spirooxindole derivatives

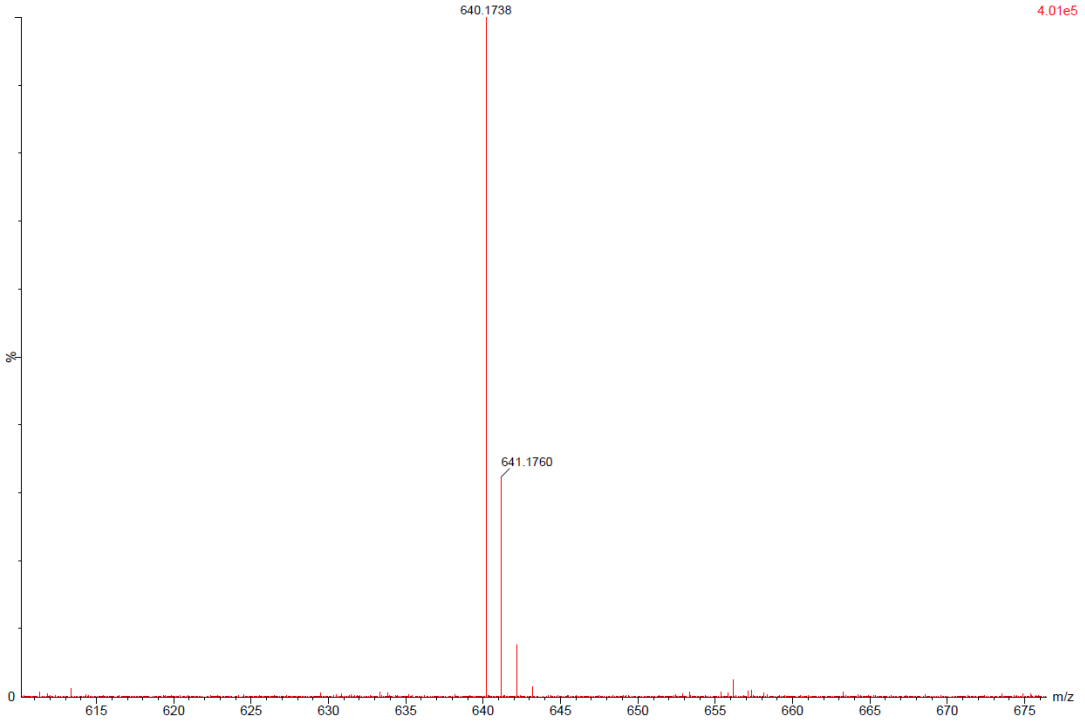
Compound **int-4a**



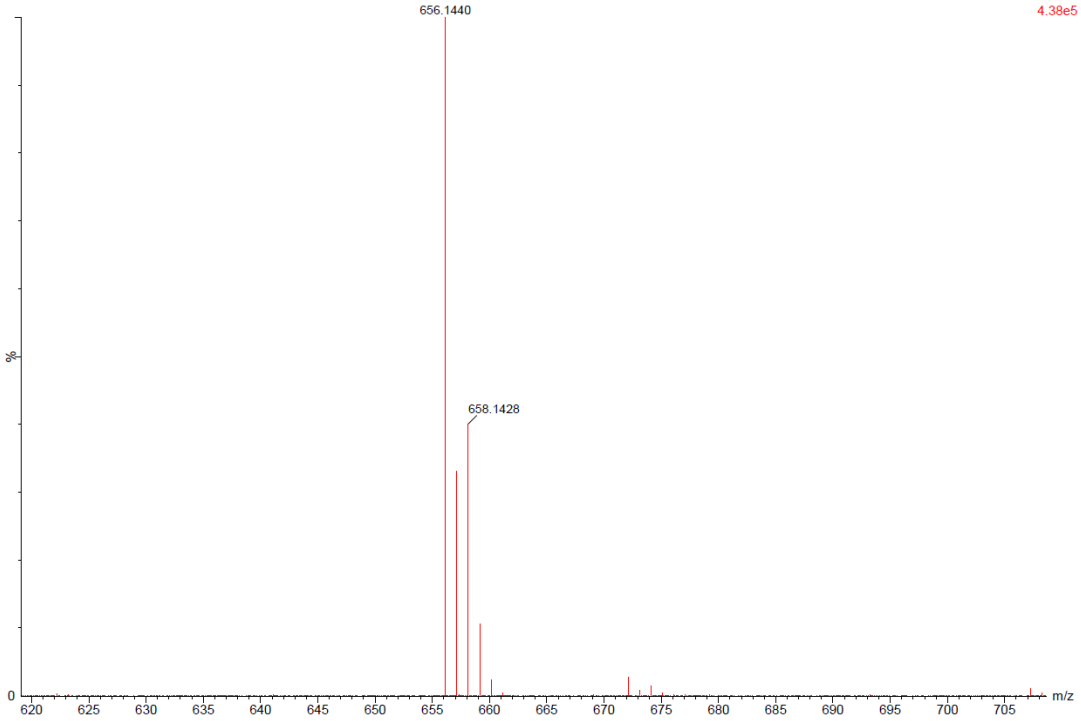
Compound **int-4b**



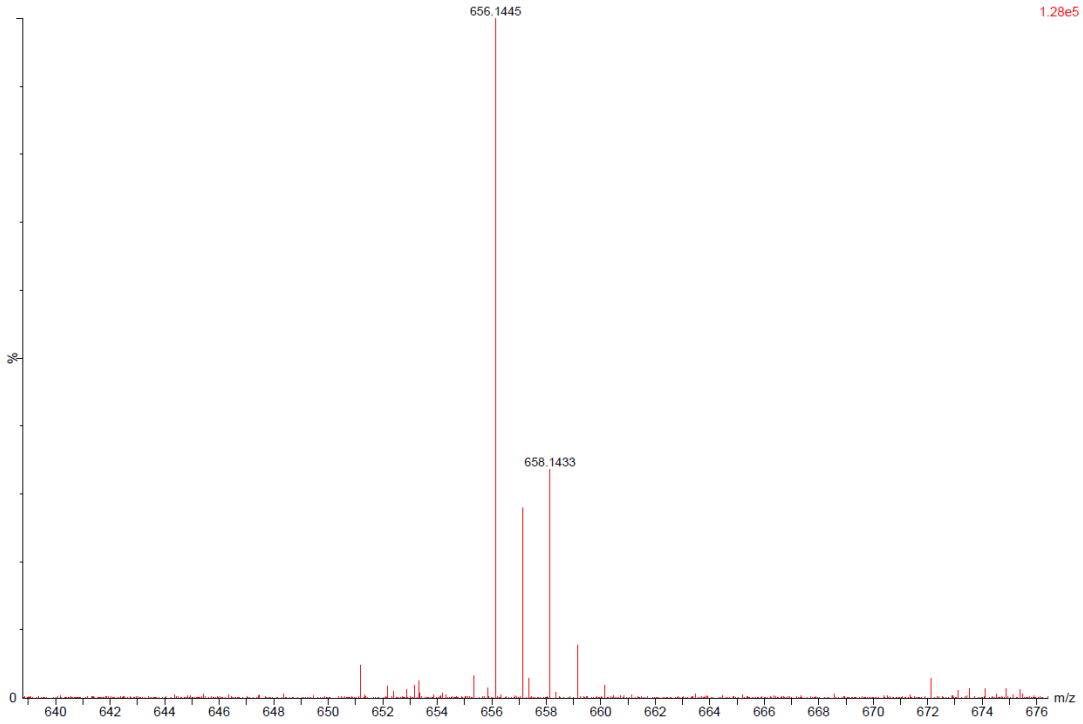
Compound **int-4c**



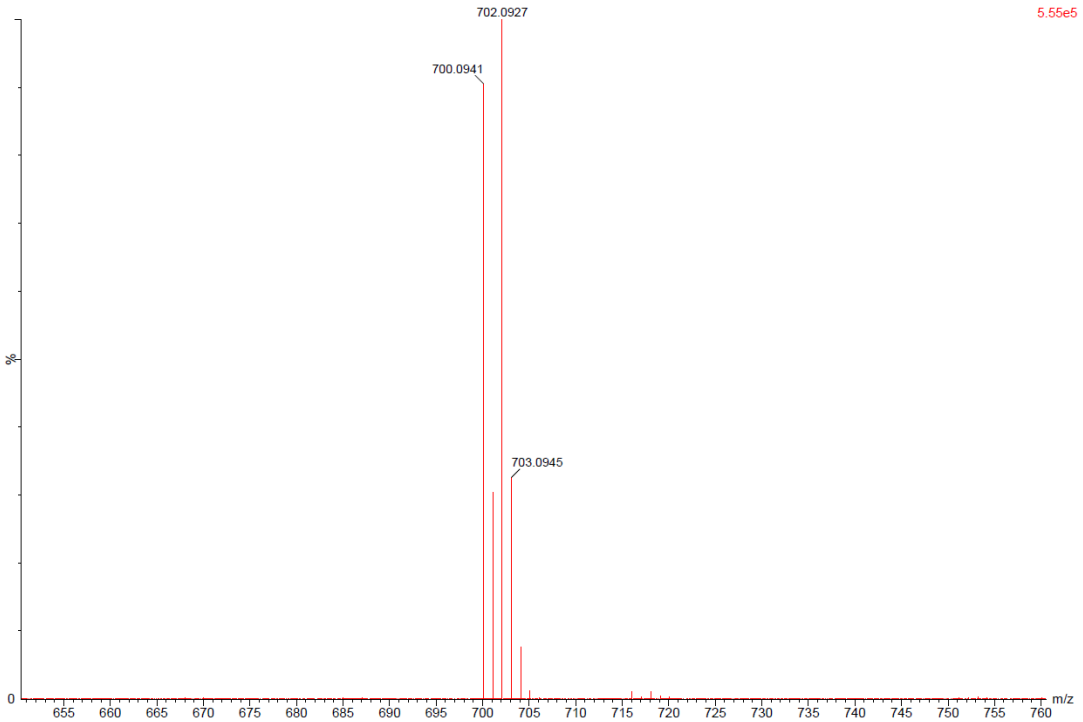
Compound **int-4d**



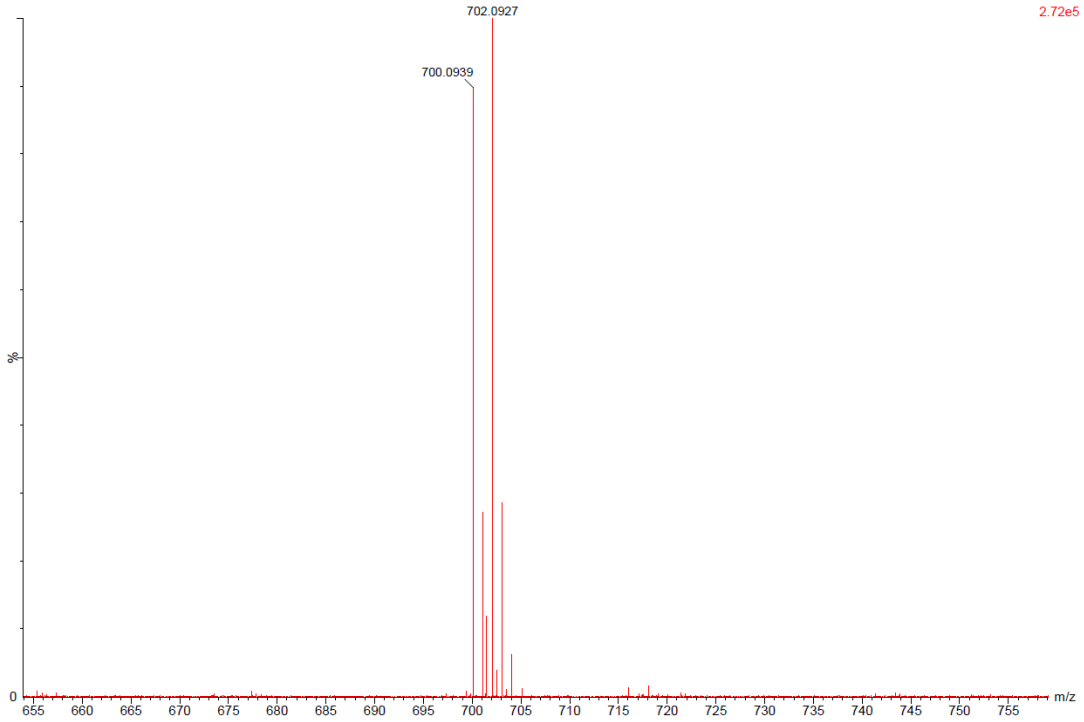
Compound **int-4e**



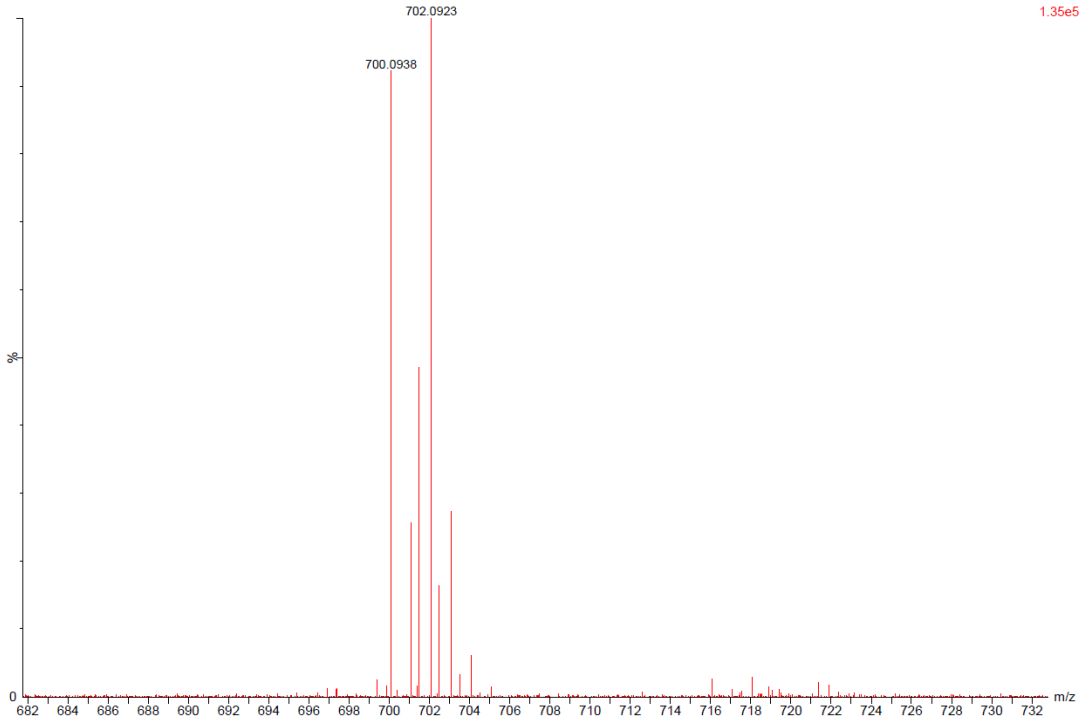
Compound **int-4f**



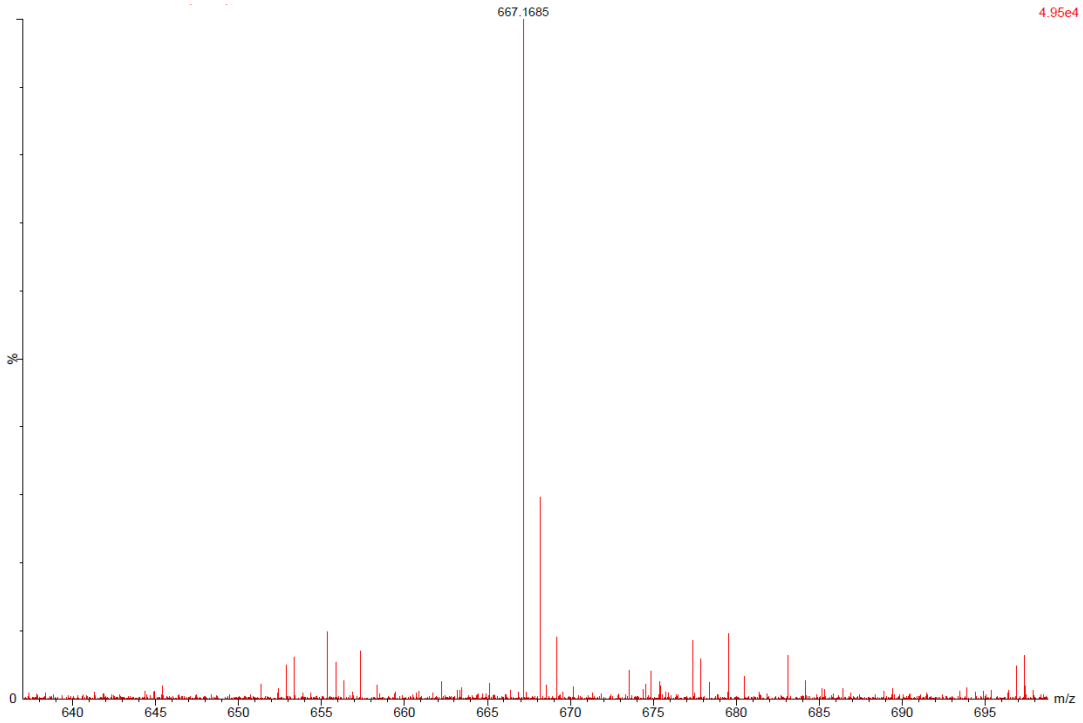
Compound **int-4g**



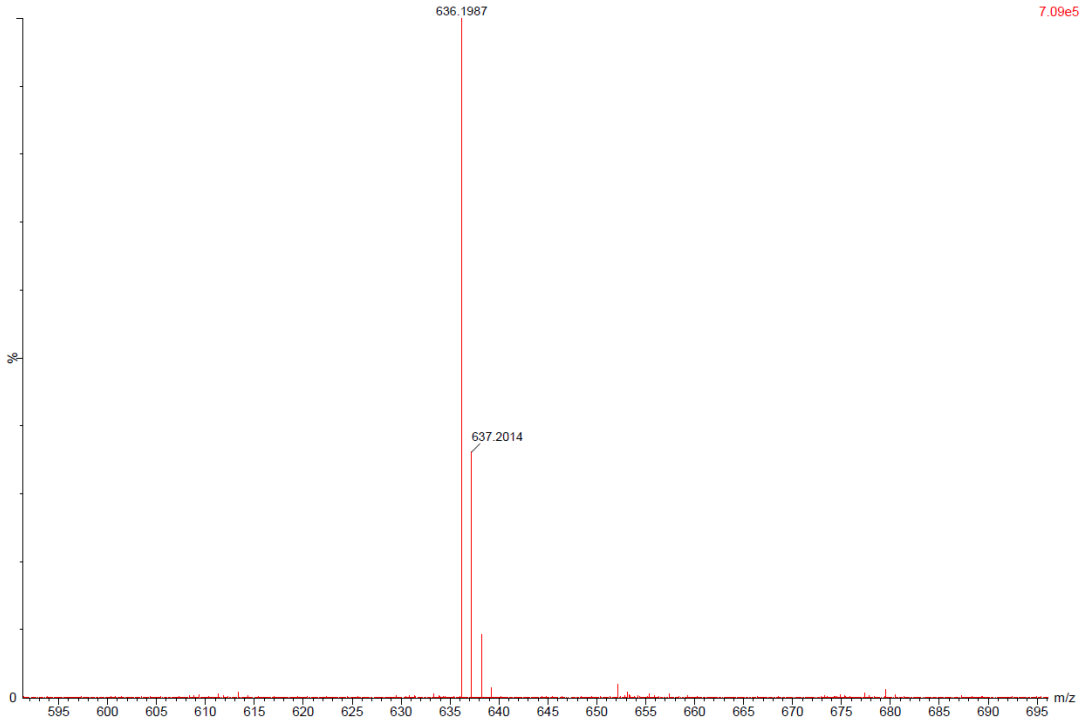
Compound **int-4h**



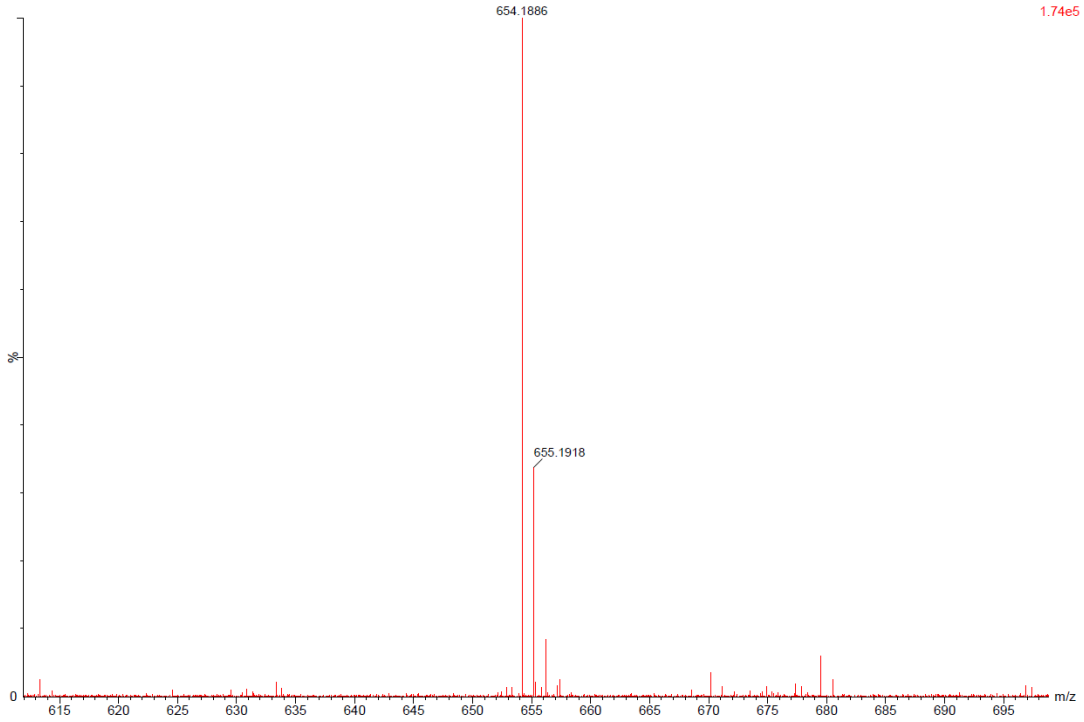
Compound **int-4i**



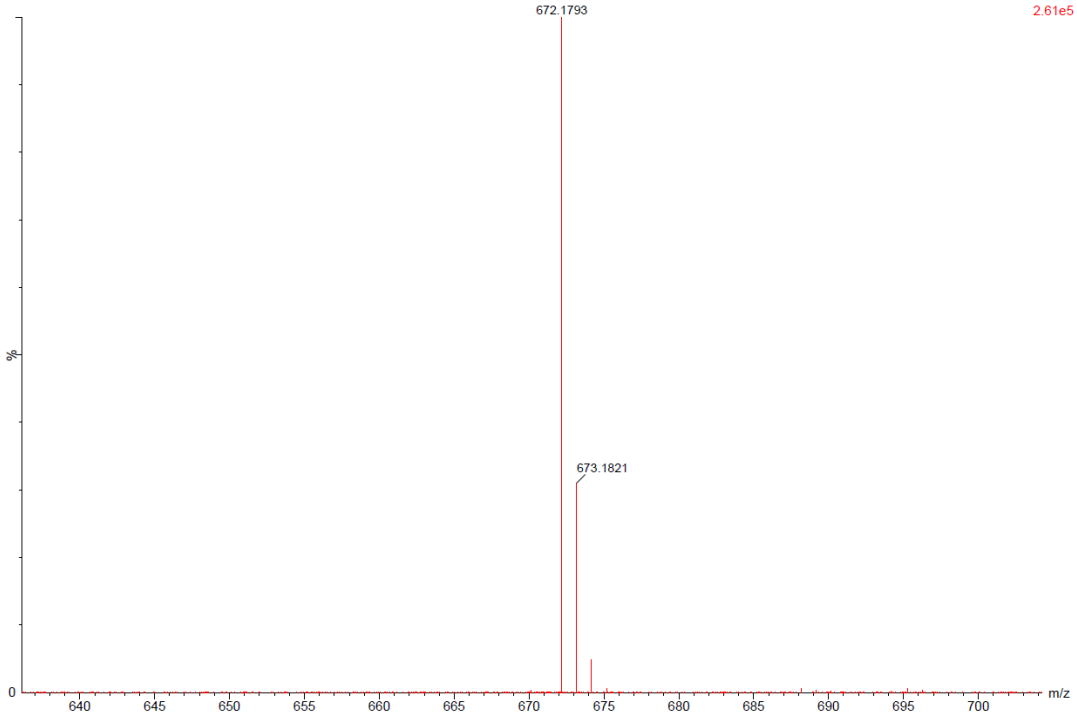
Compound **int-4j**



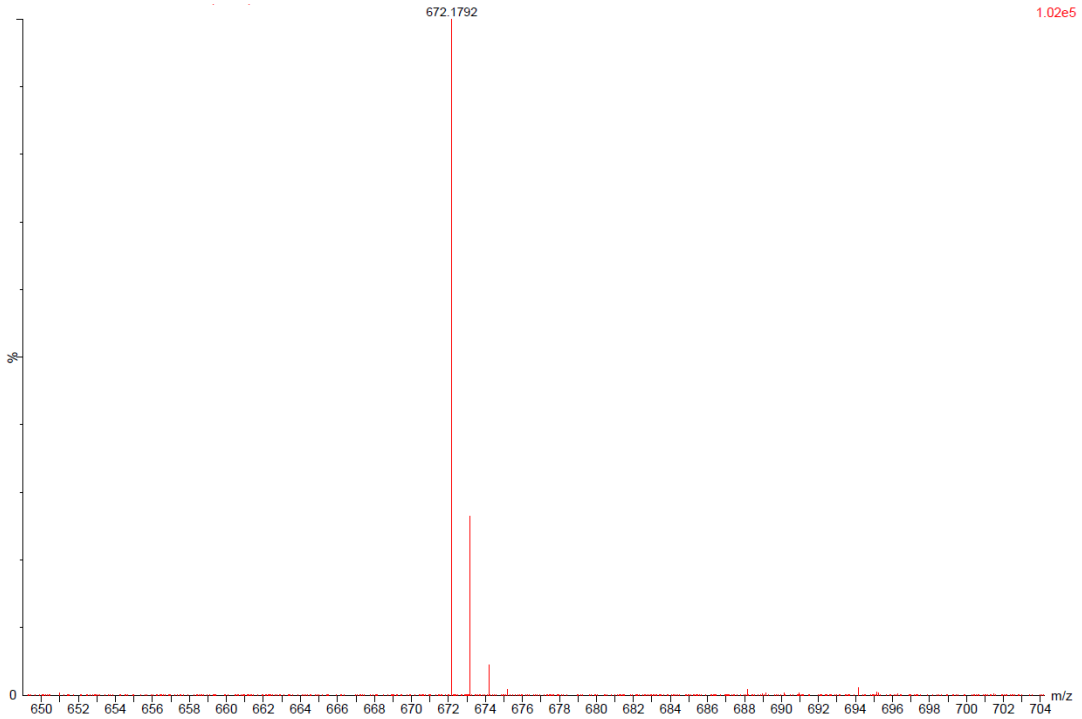
Compound **int-4k**



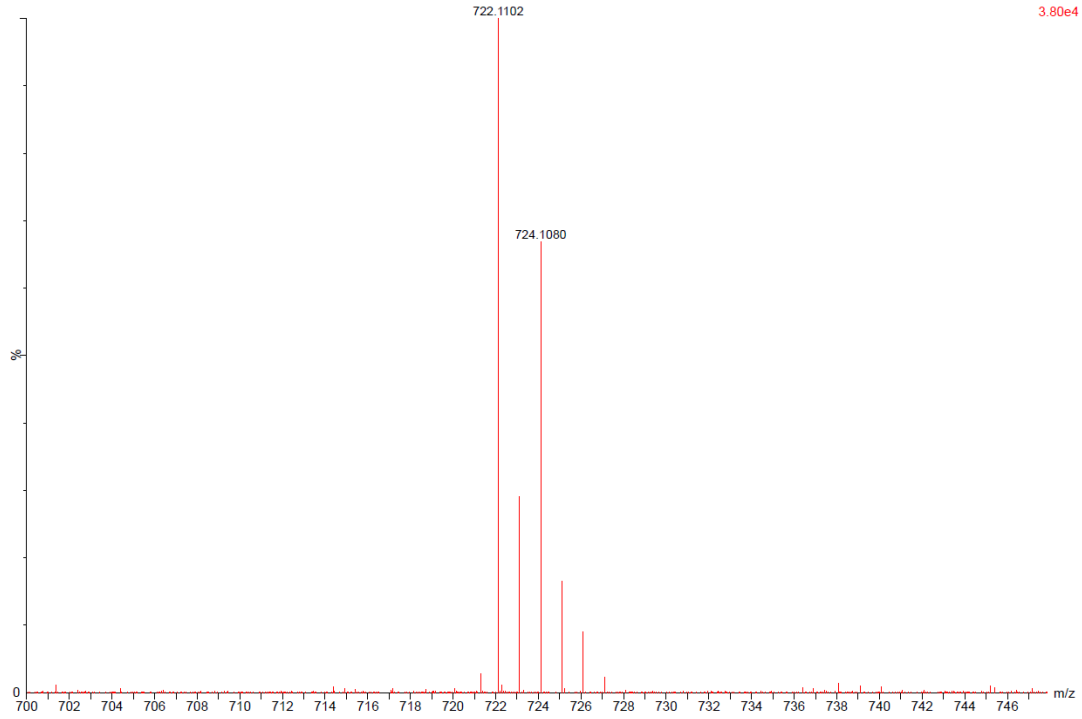
Compound **int-4l**



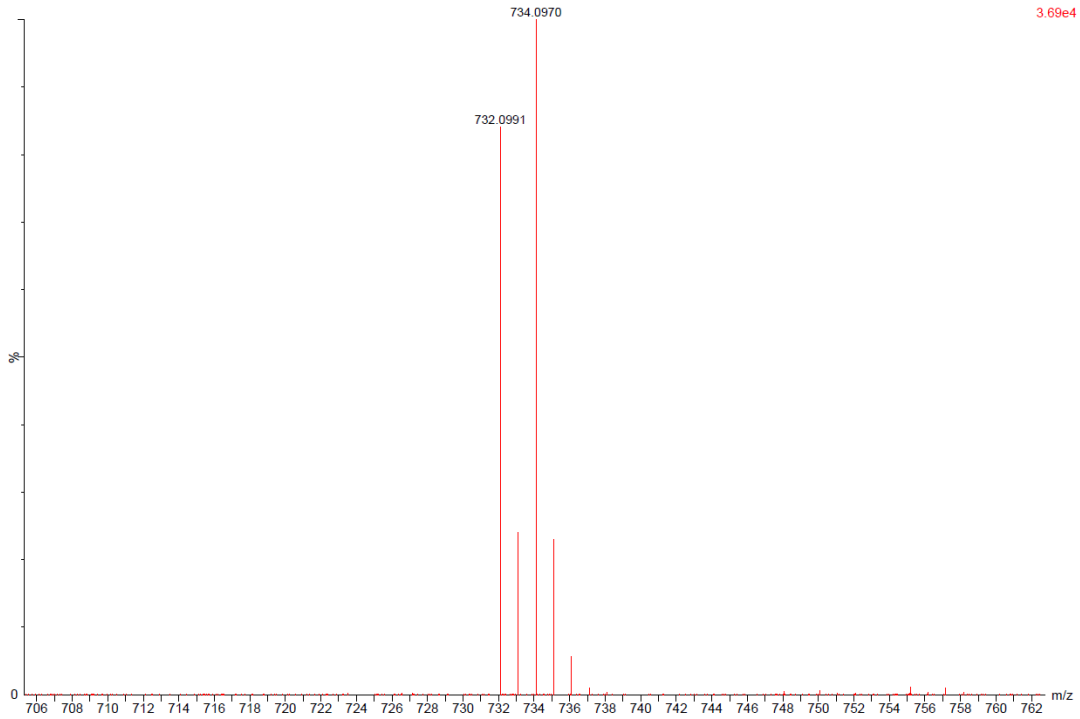
Compound **int-4m**



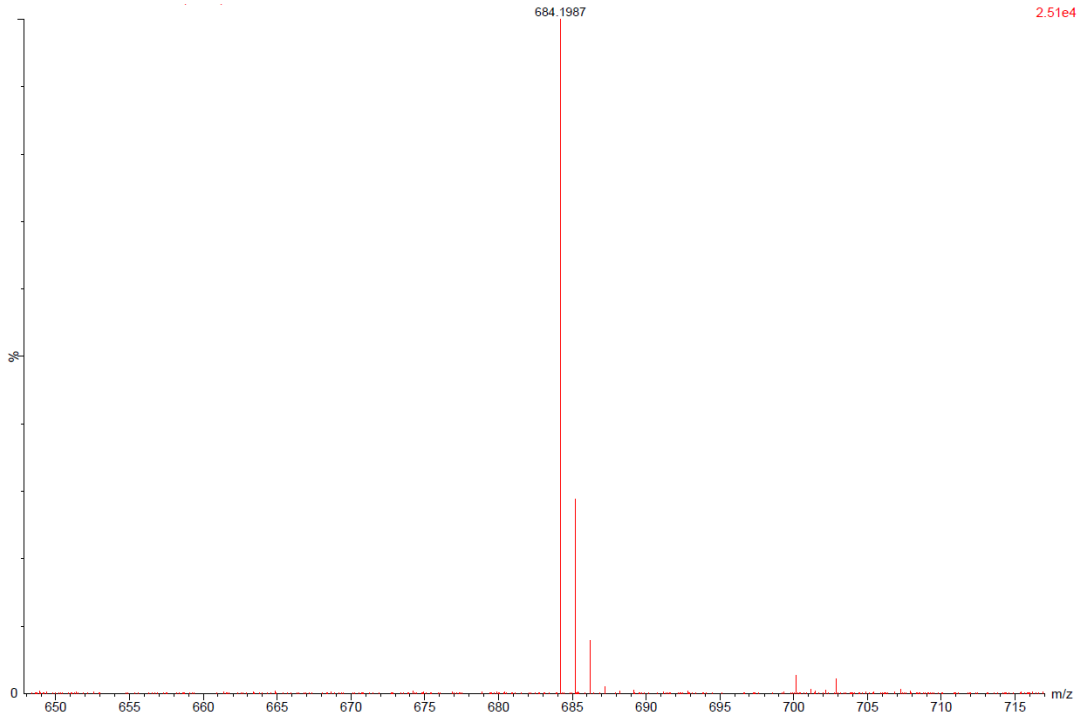
Compound **int-4n**



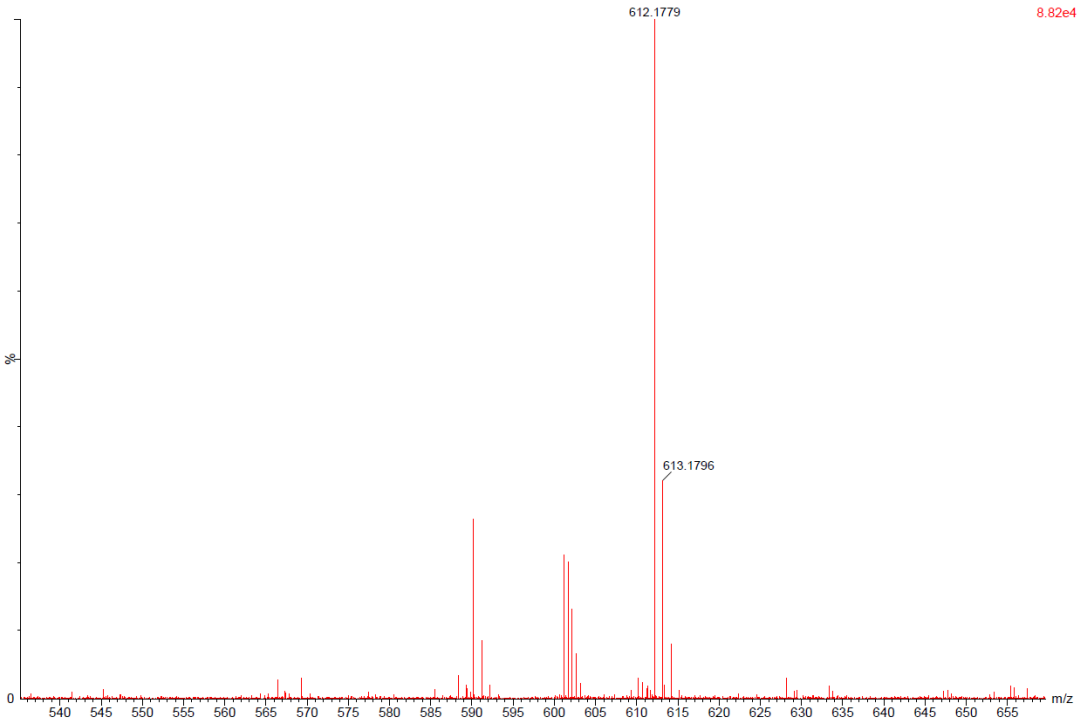
Compound **int-4o**



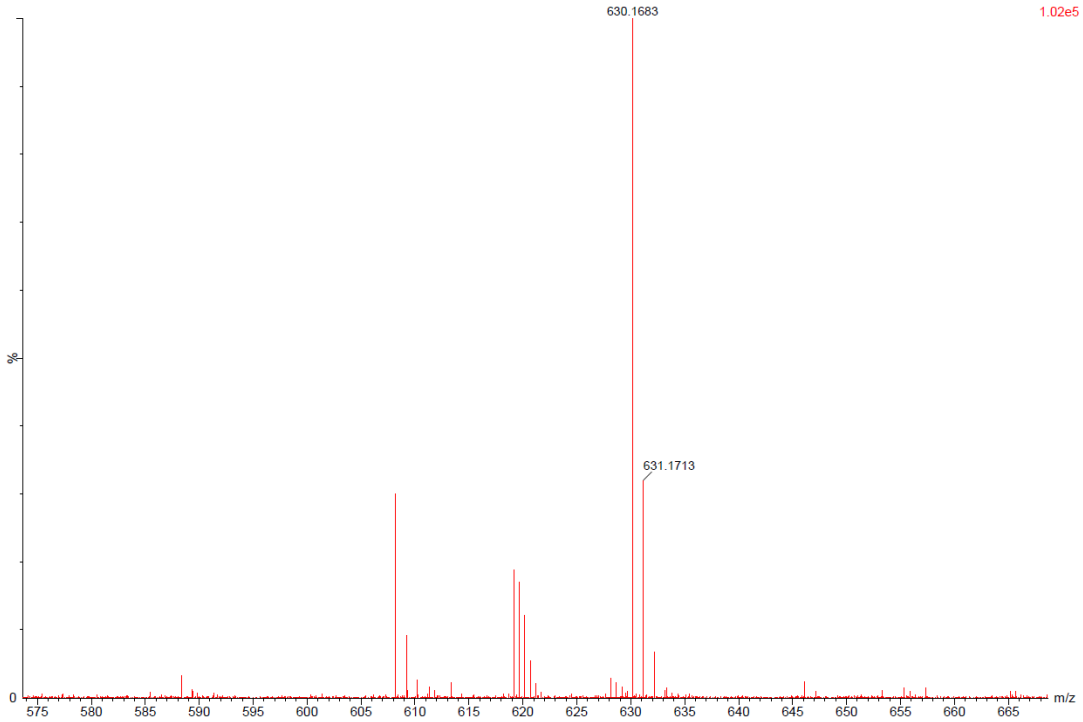
Compound **int-4p**



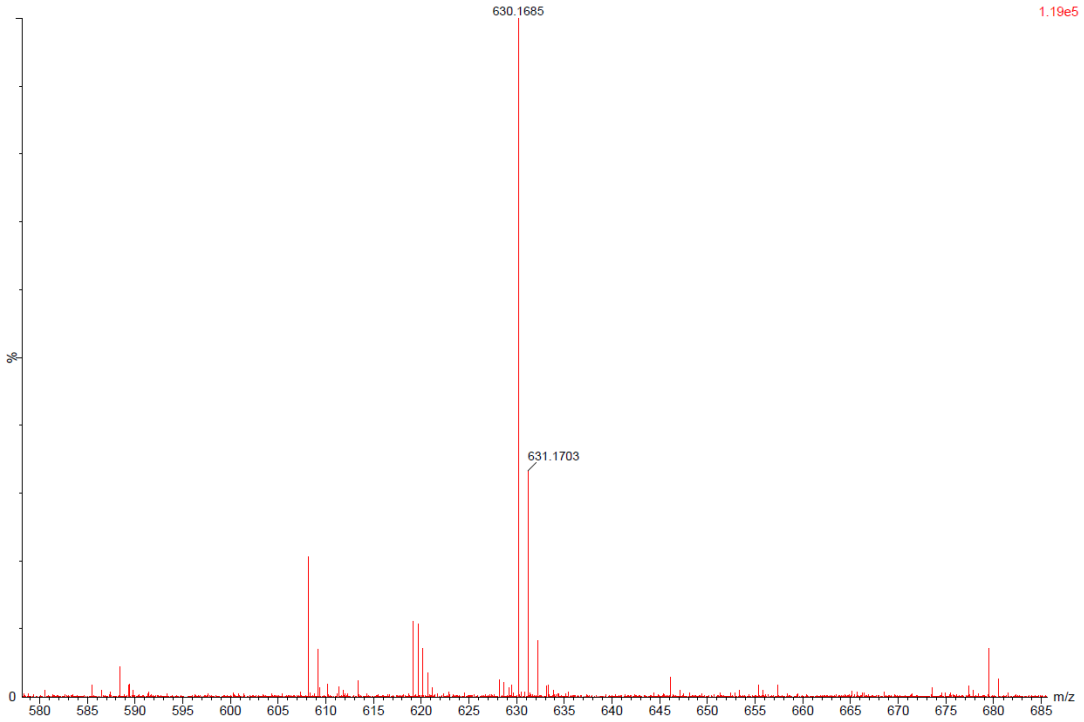
Compound **int-4a′**



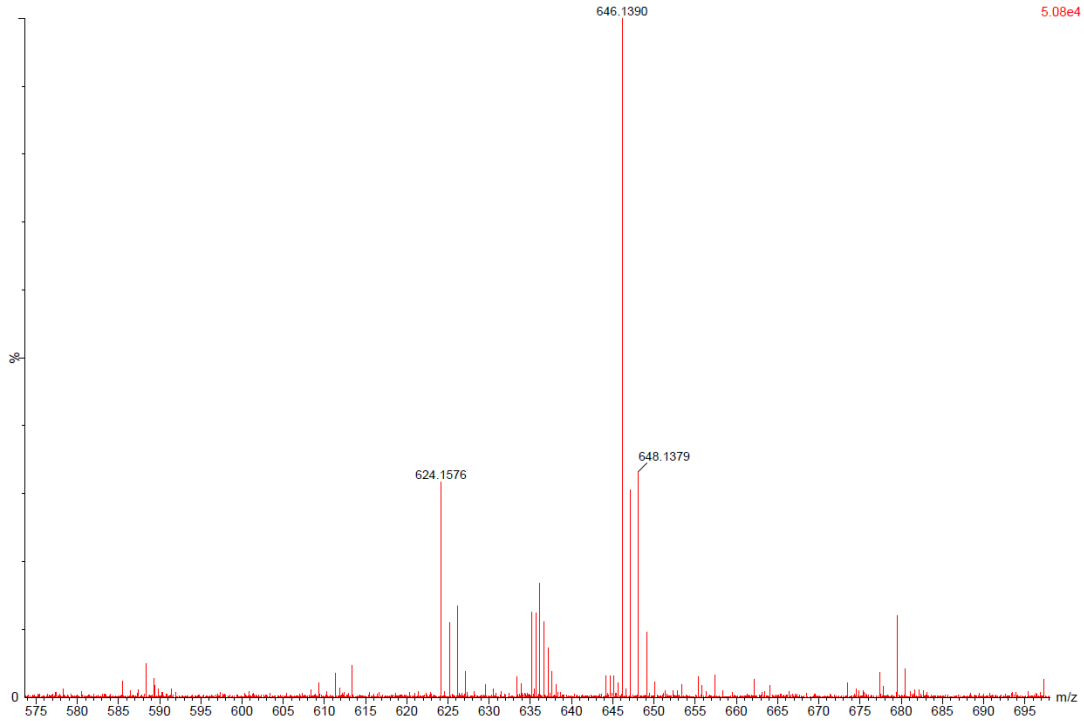
Compound **int-4b′**



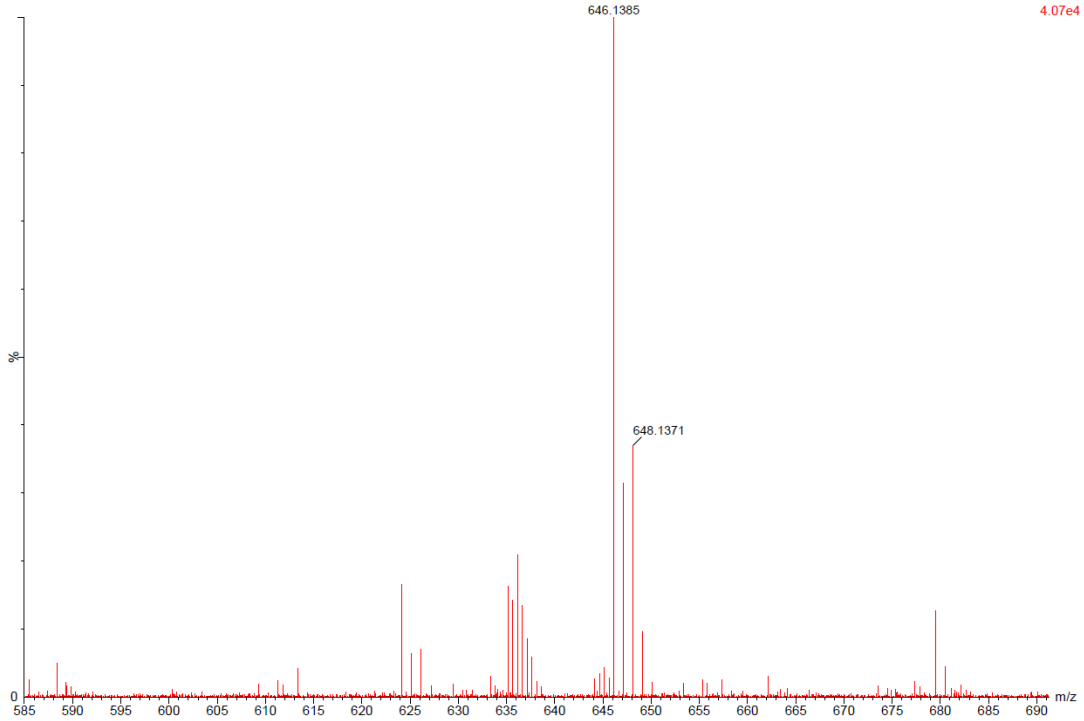
Compound **int-4c′**



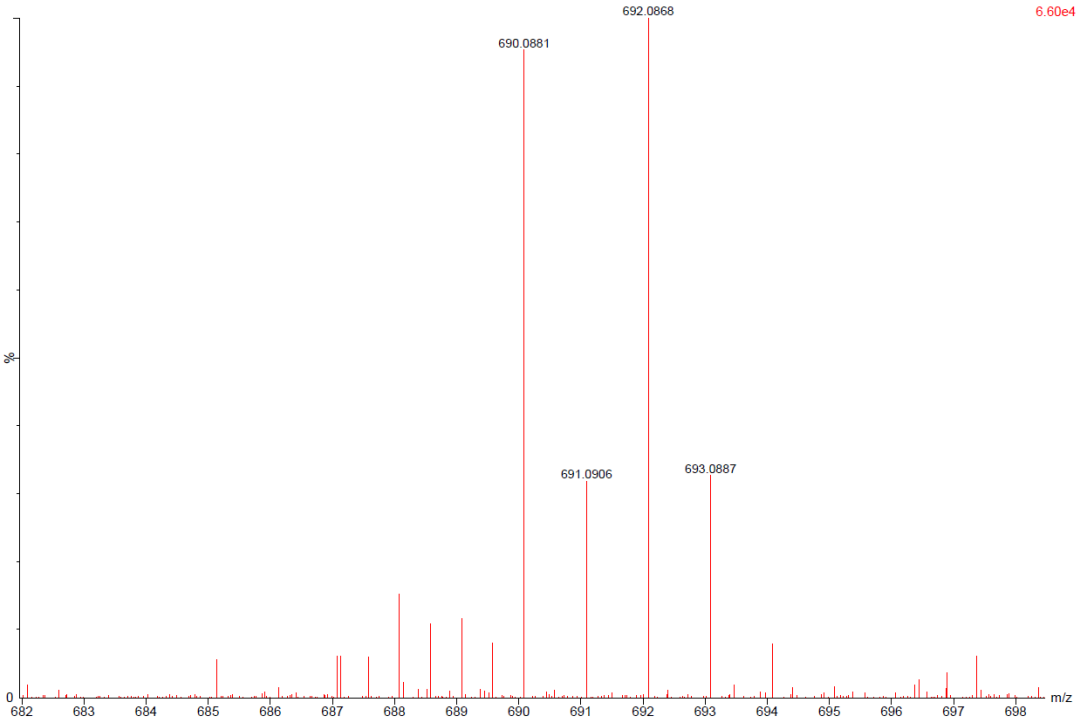
Compound **int-4d′**



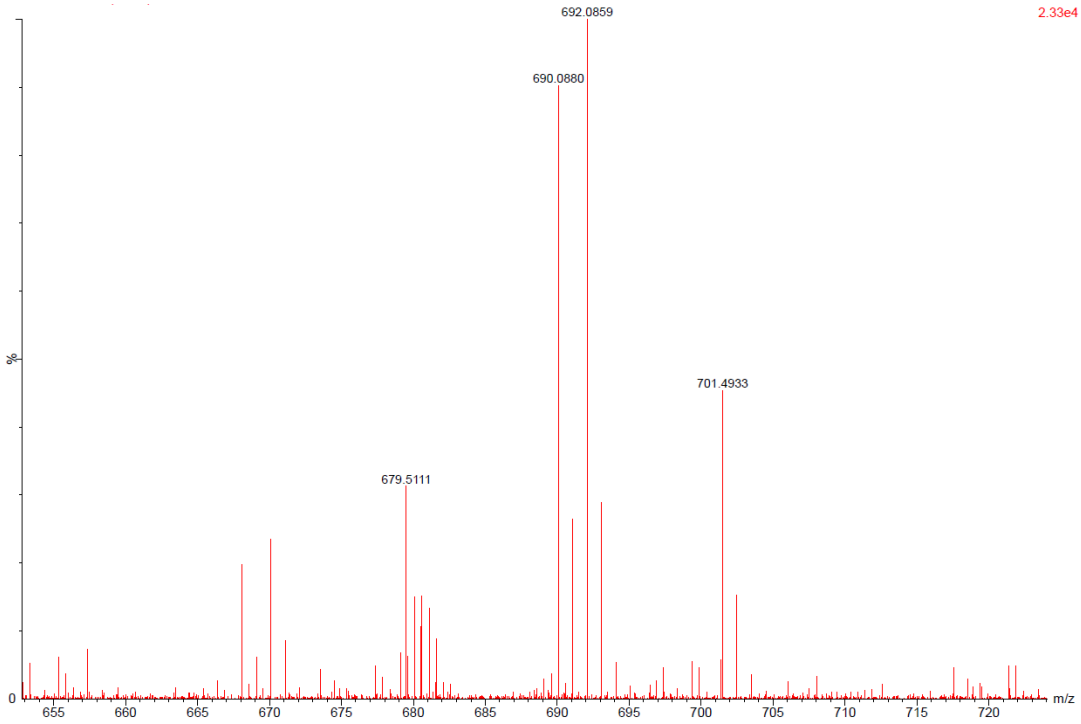
Compound **int-4e′**



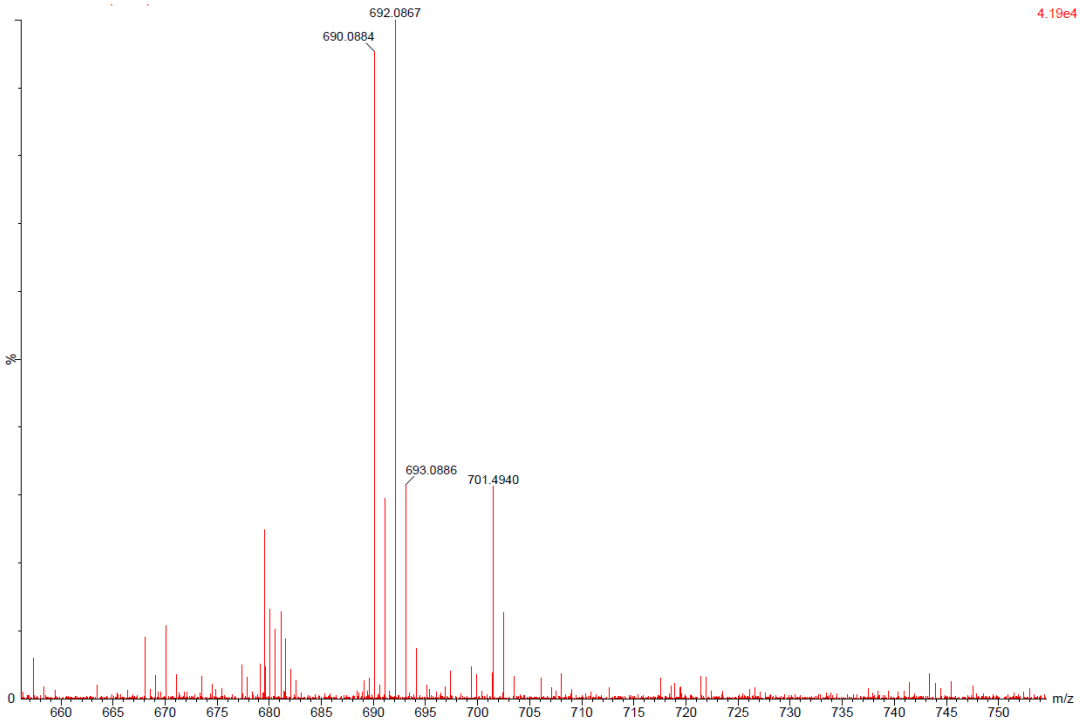
Compound **int-4f′**



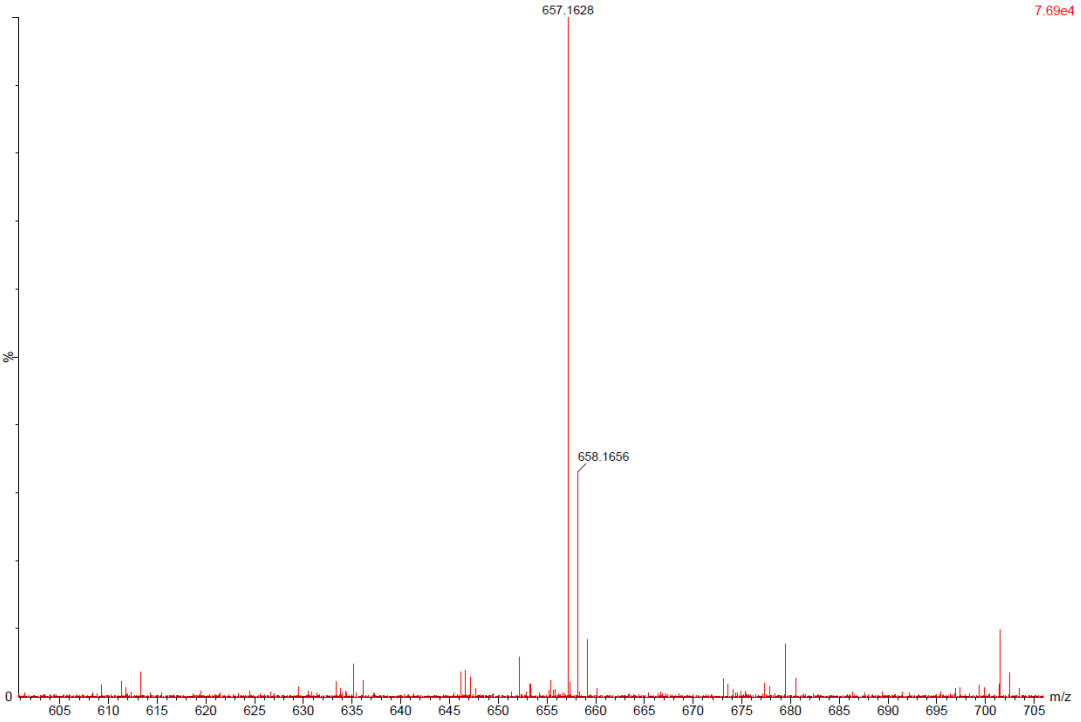
Compound **int-4g′**



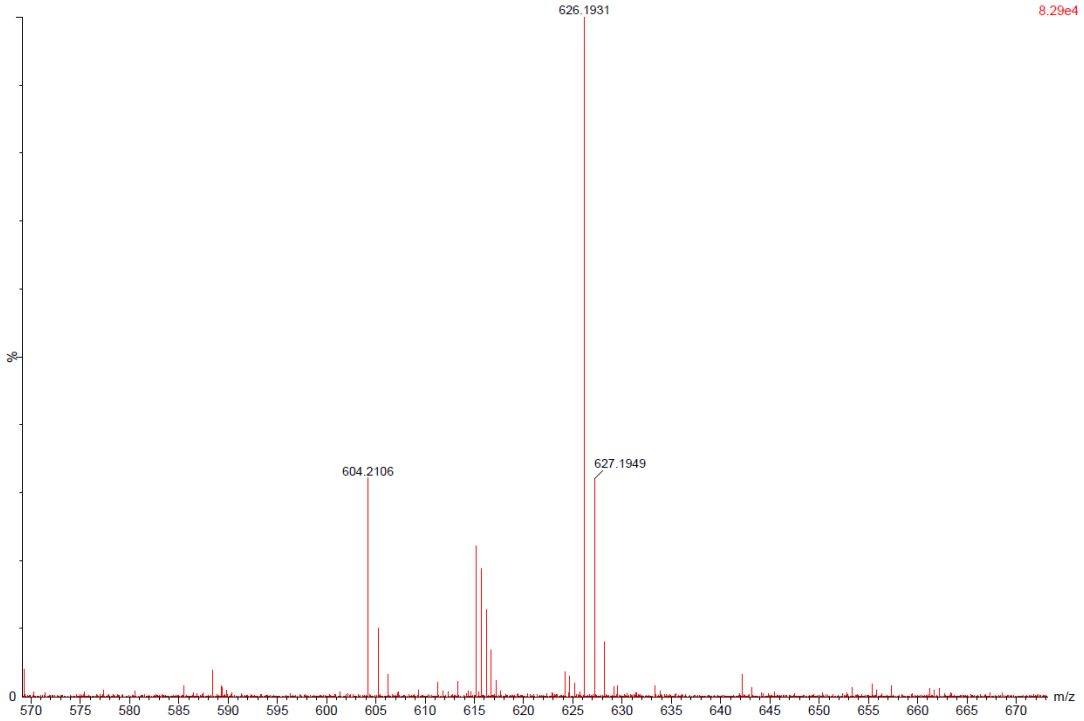
Compound **int-4h′**



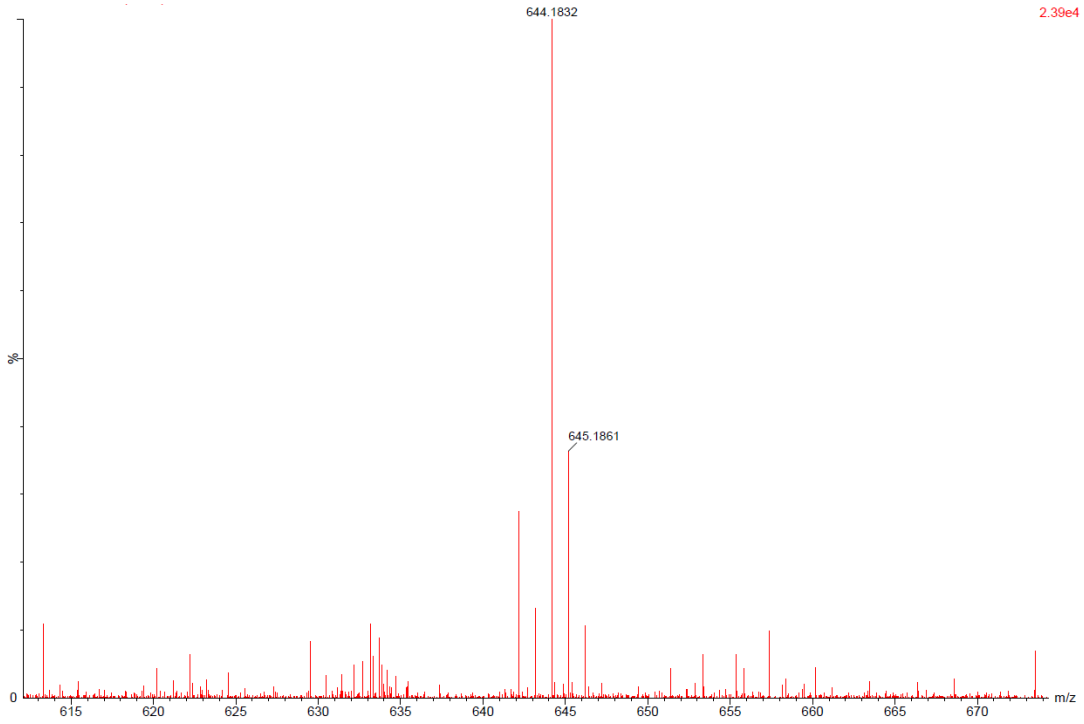
Compound **int-4i′**



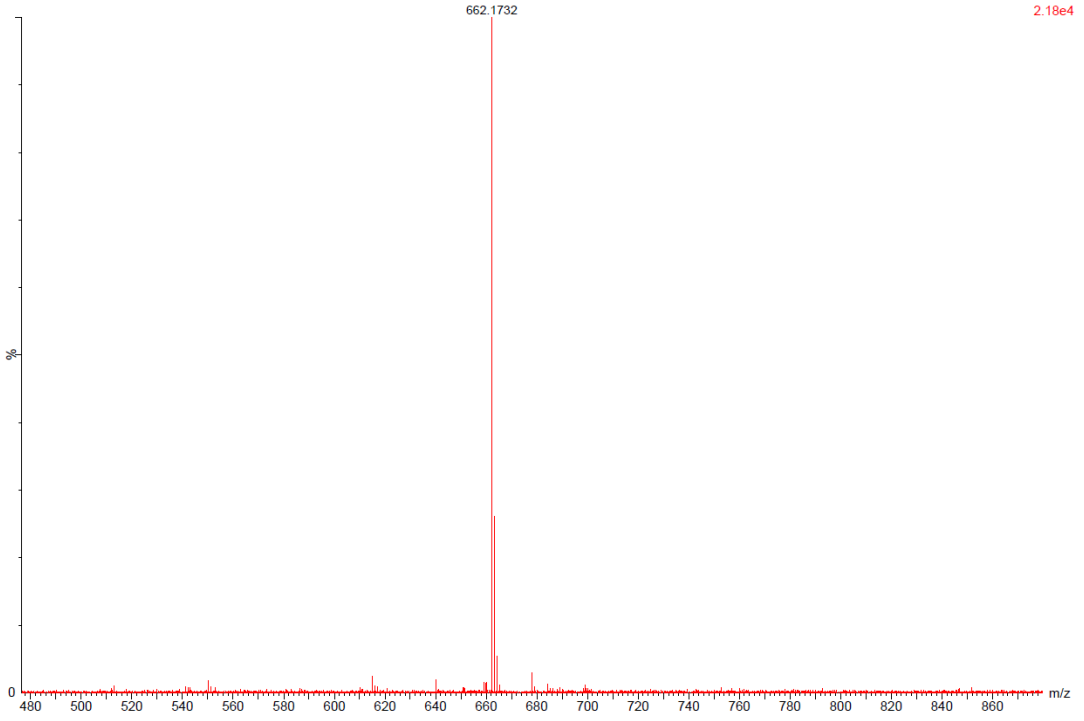
Compound **int-4j′**



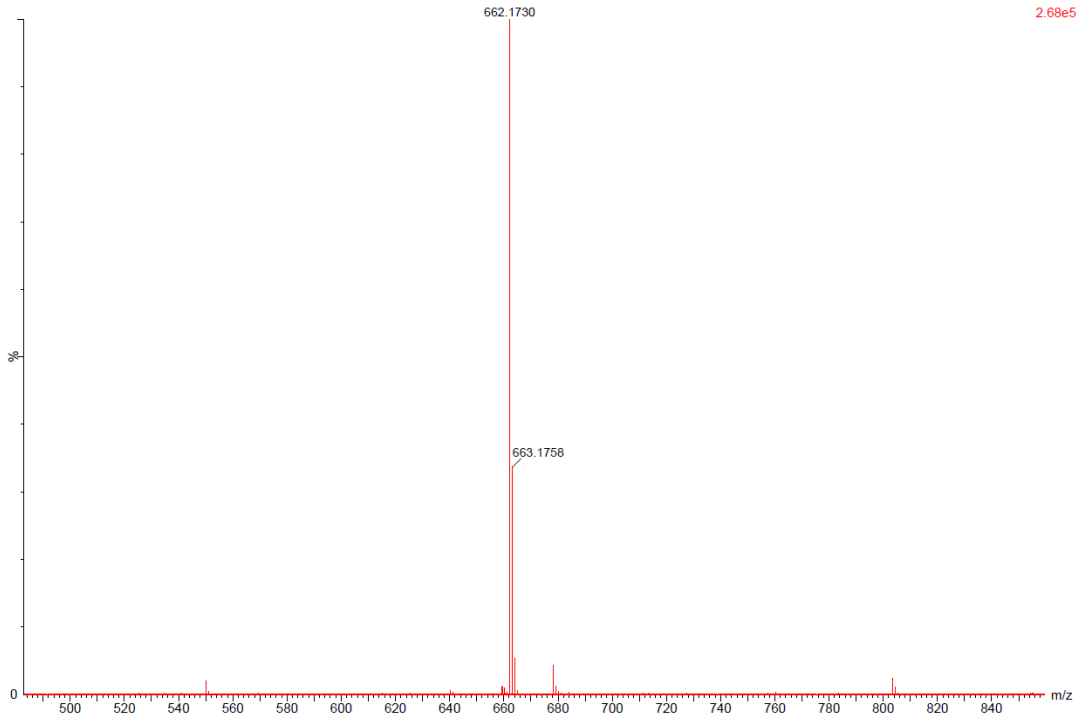
Compound **int-4k′**



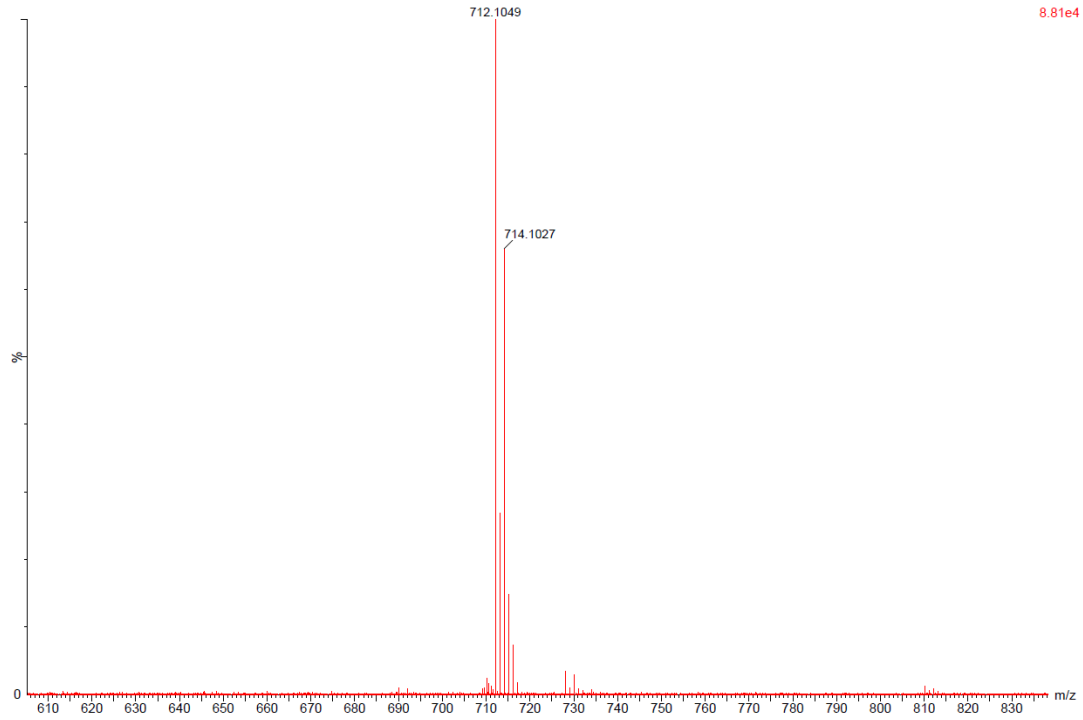
Compound **int-4l′**



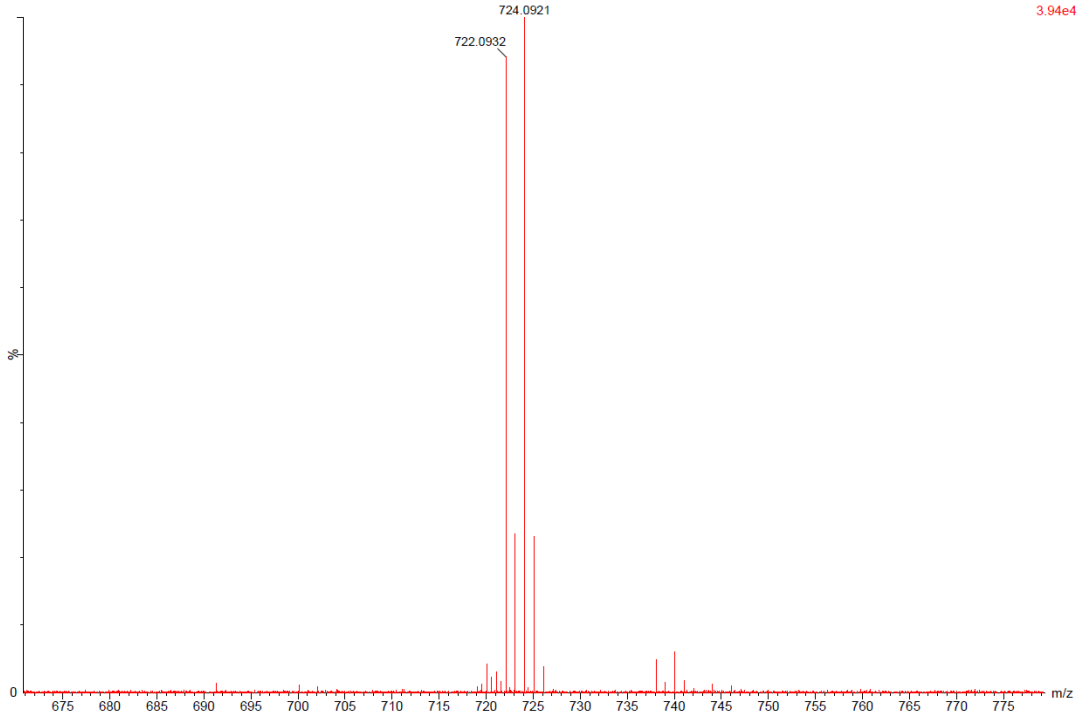
Compound **int-4m′**



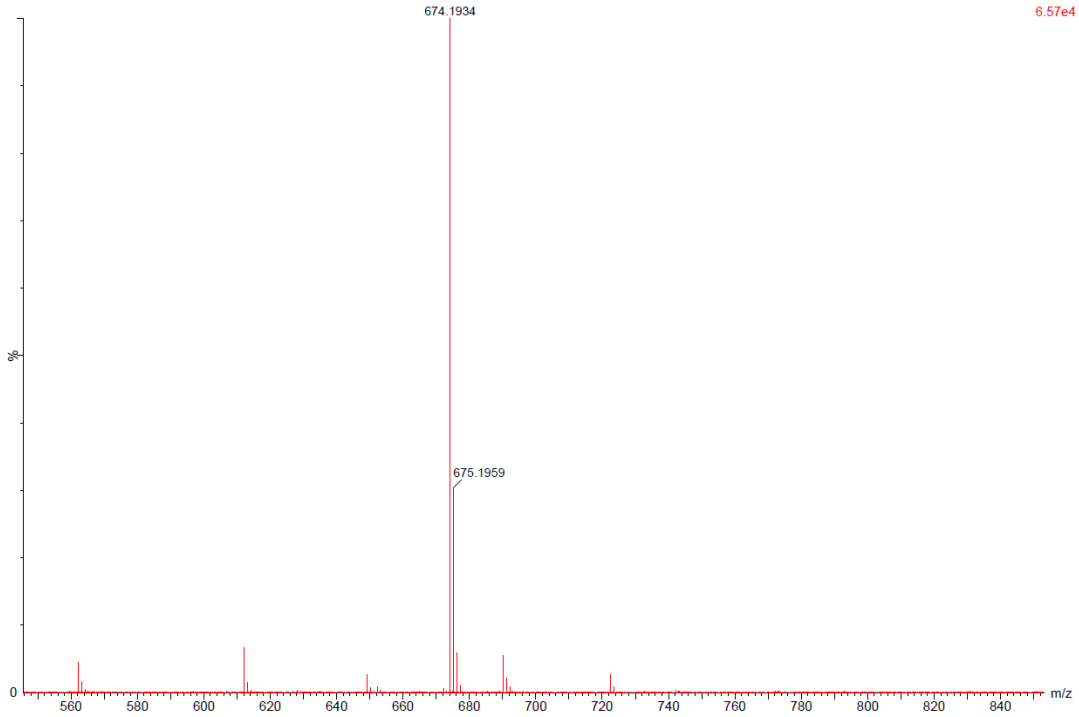
Compound **int-4n′**



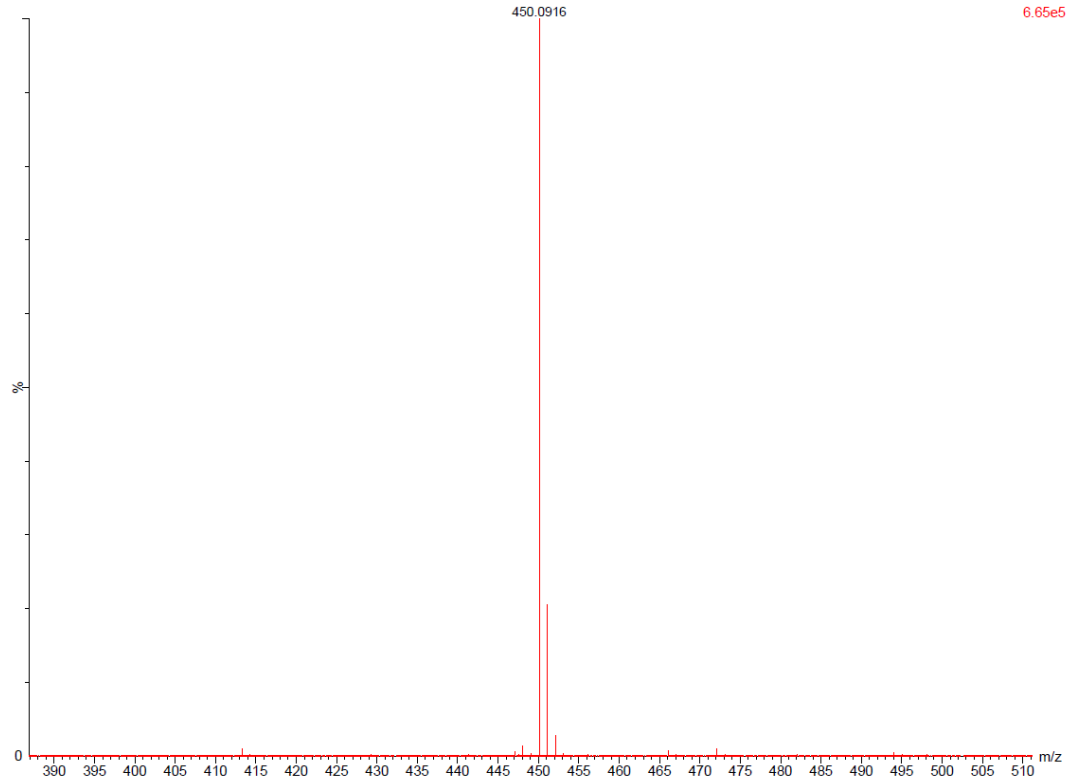
Compound **int-4o′**



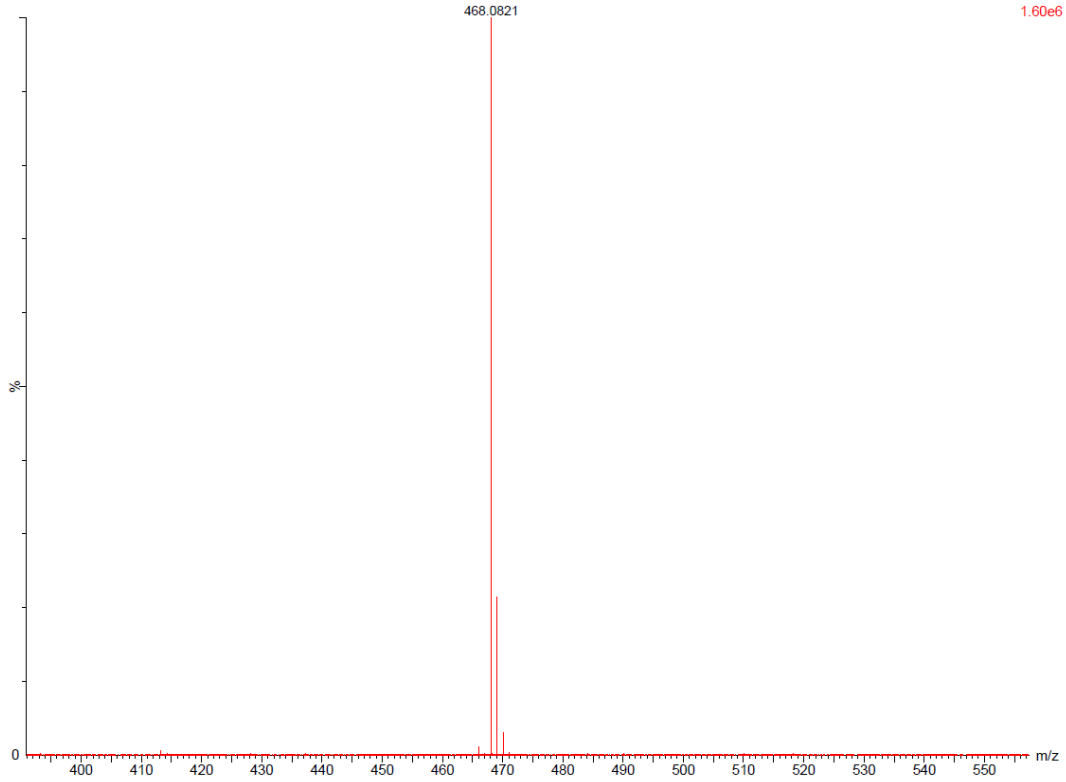
Compound **int-4p′**


674.1934
6.57e4
675.1959
%
0
560 580 600 620 640 660 680 700 720 740 760 780 800 820 840
m/z

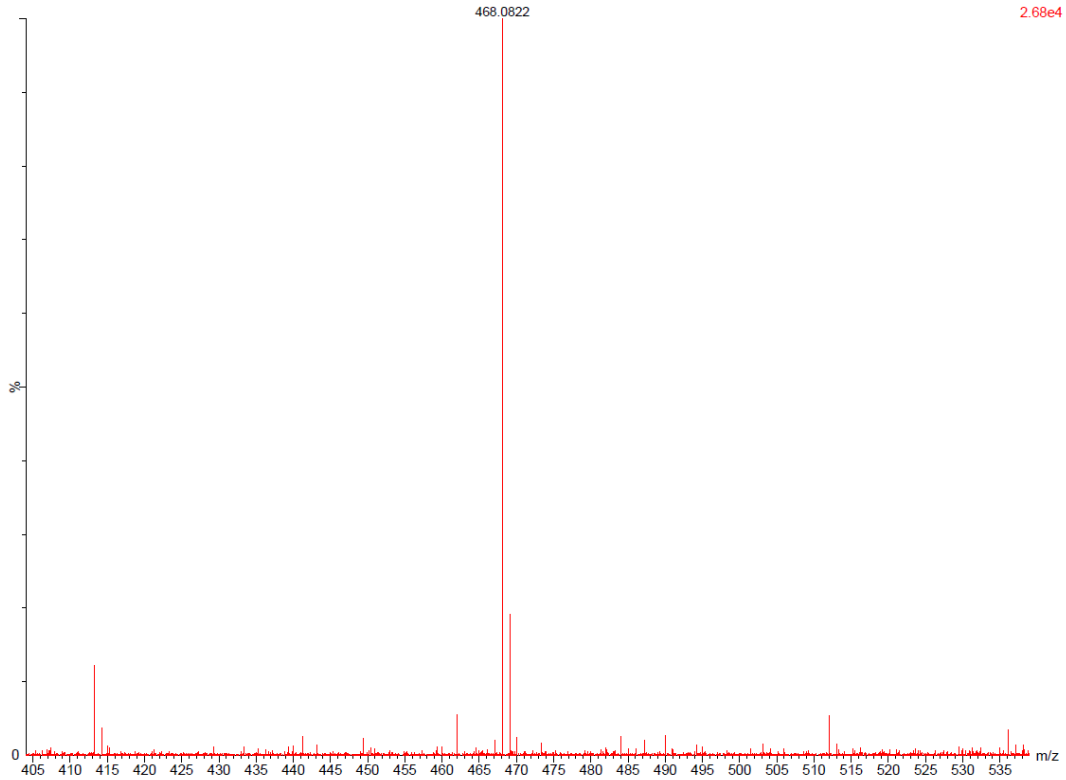
Compound **4a**


450.0916
6.65e5
%
0
390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510
m/z

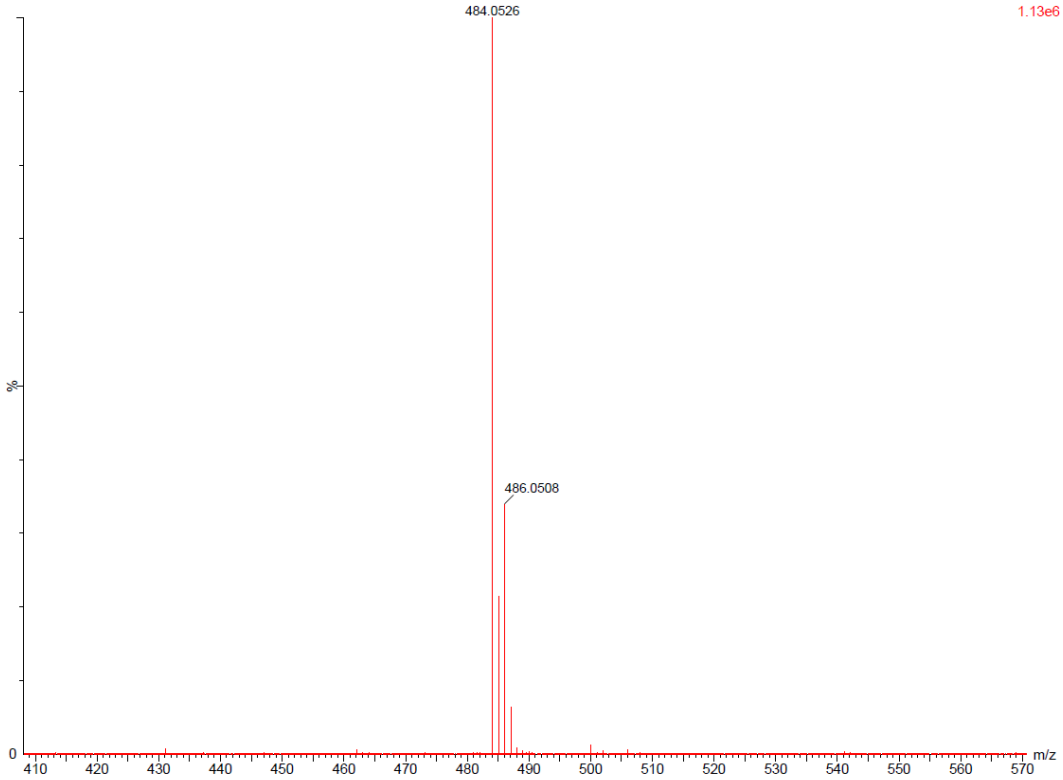
Compound **4b**



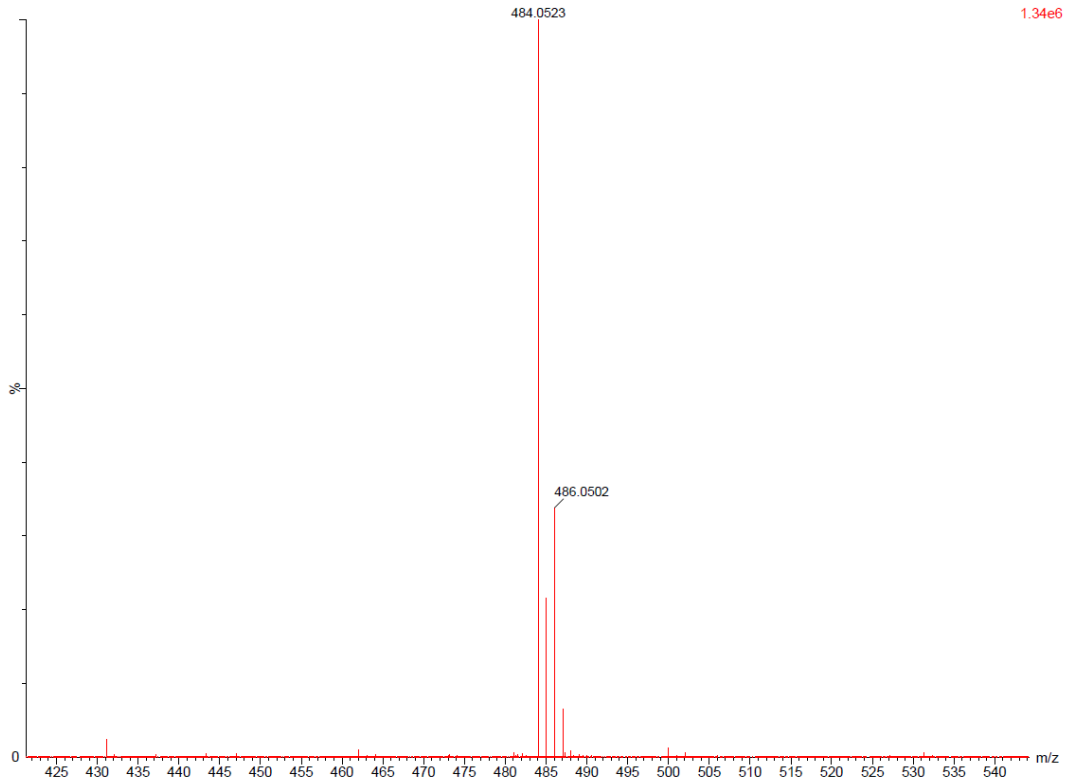
Compound **4c**


468.0822
2.68e4
%
0
405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535
m/z

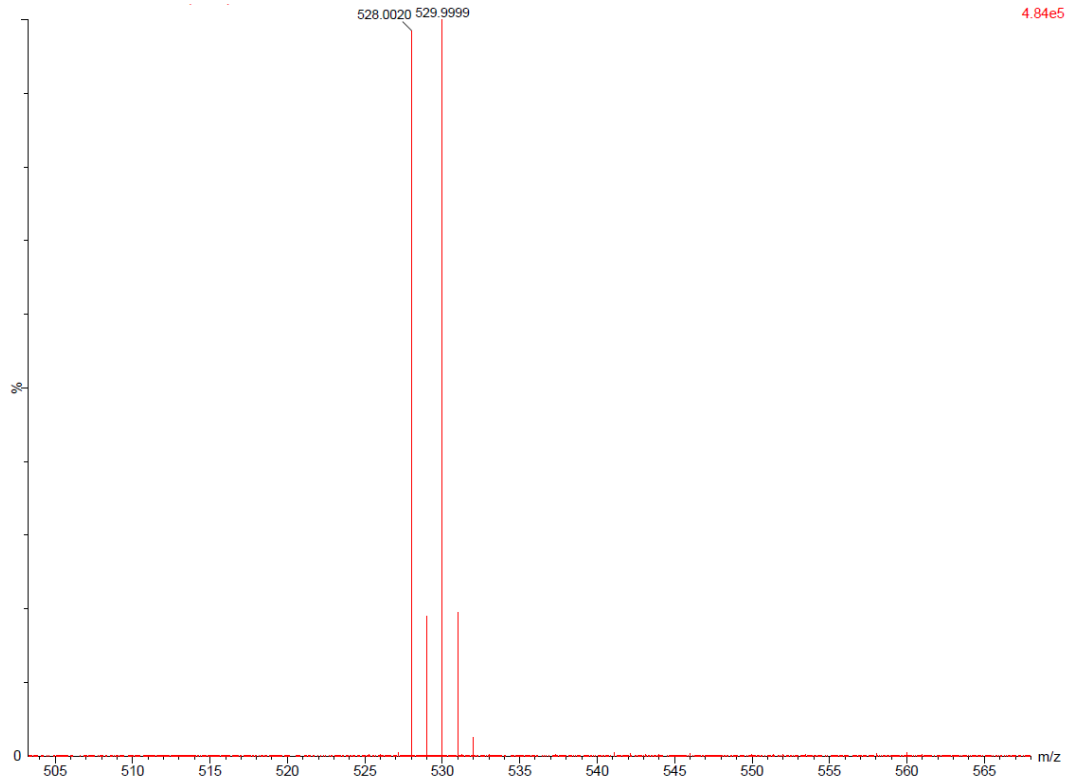
Compound **4d**


484.0526
1.13e6
%
486.0508
0
410 420 430 440 450 460 470 480 490 500 510 520 530 540 550 560 570
m/z

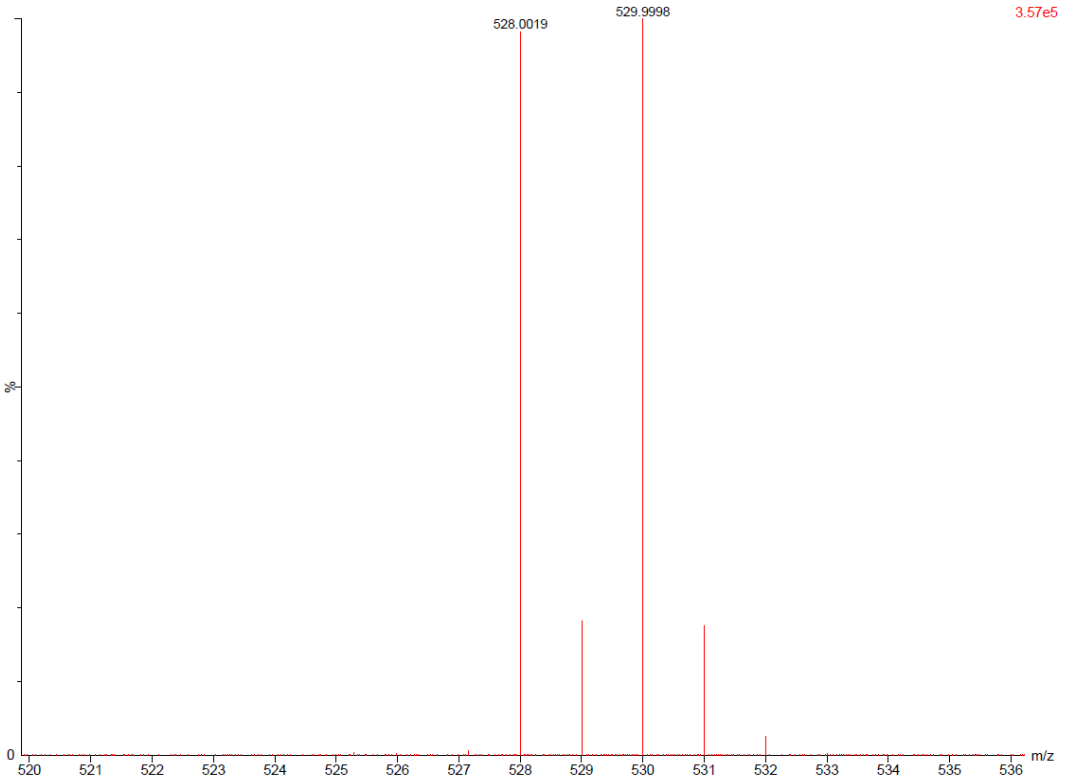
Compound **4e**



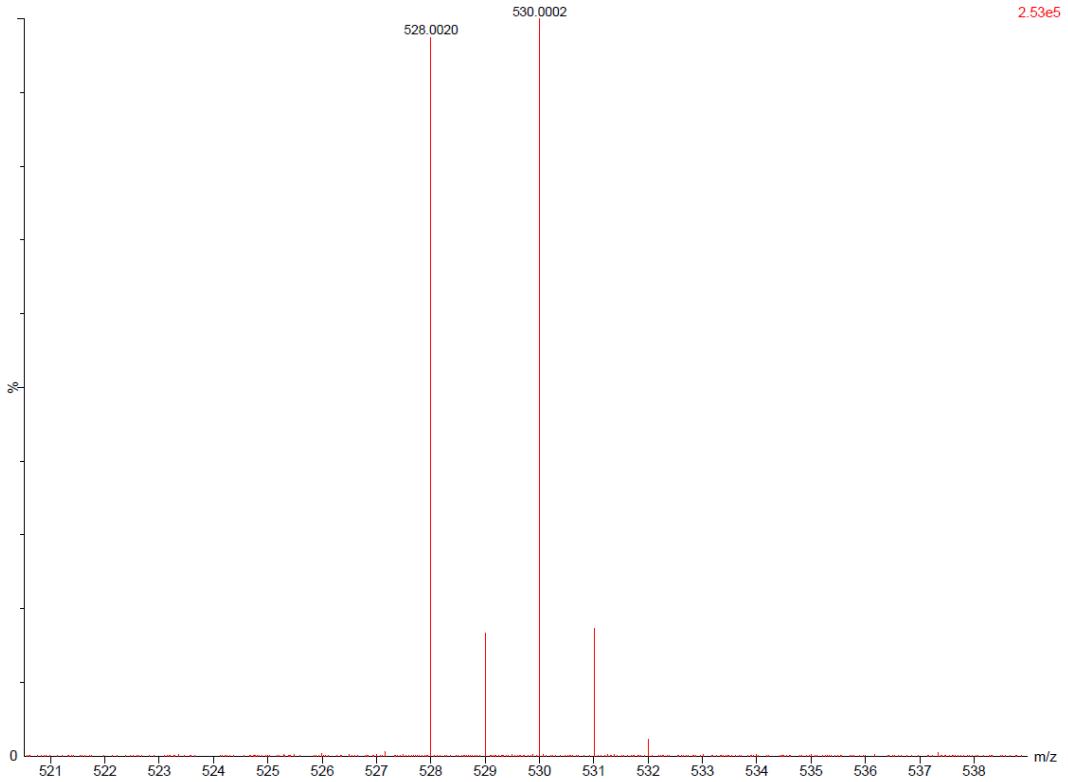
Compound **4f**


528.0020
529.9999
4.84e5
%
0
505
510
515
520
525
530
535
540
545
550
555
560
565
m/z

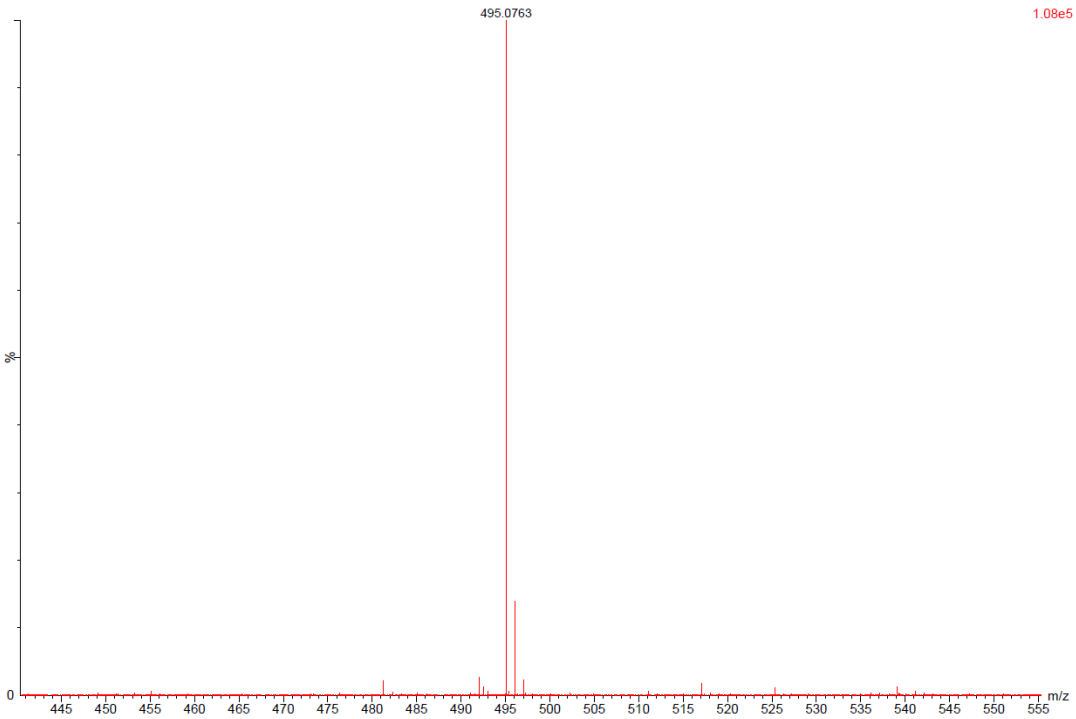
Compound **4g**


528.0019
529.9998
3.57e5
%
0
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
m/z

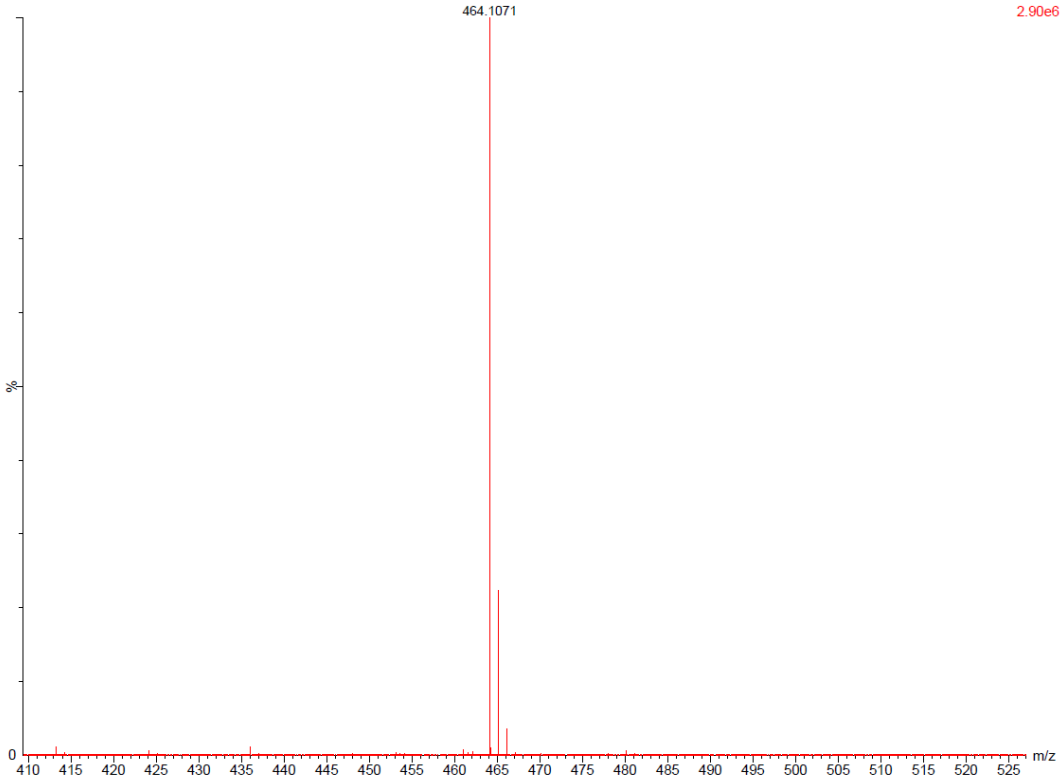
Compound **4h**



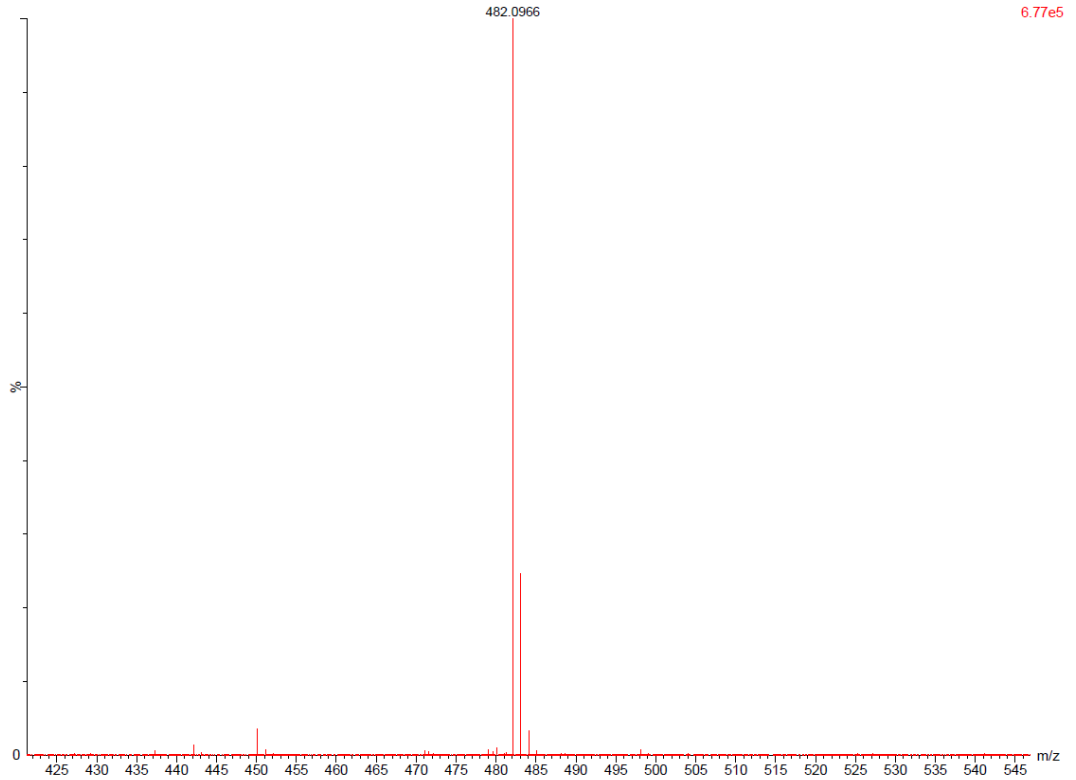
Compound **4i**



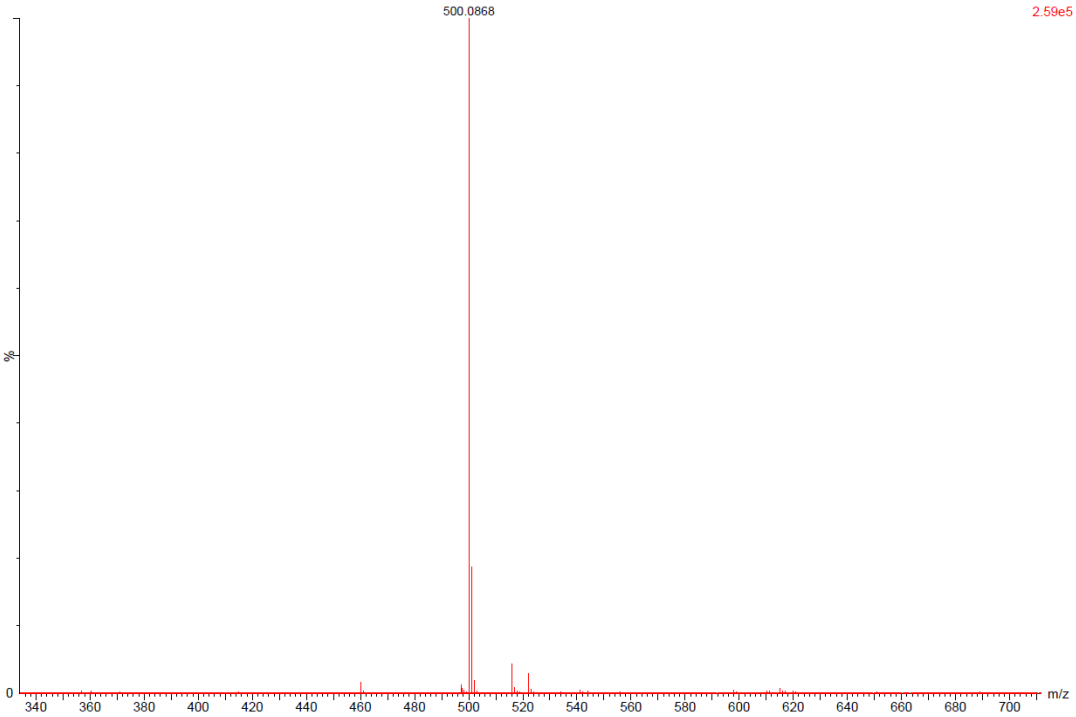
Compound **4j**



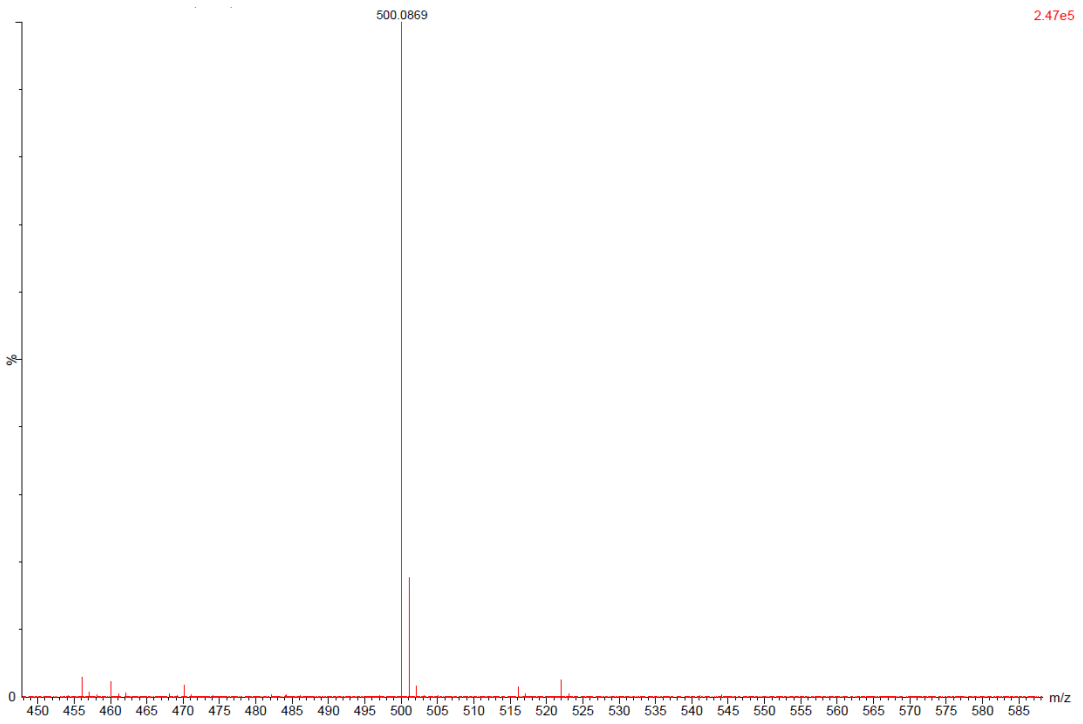
Compound **4k**



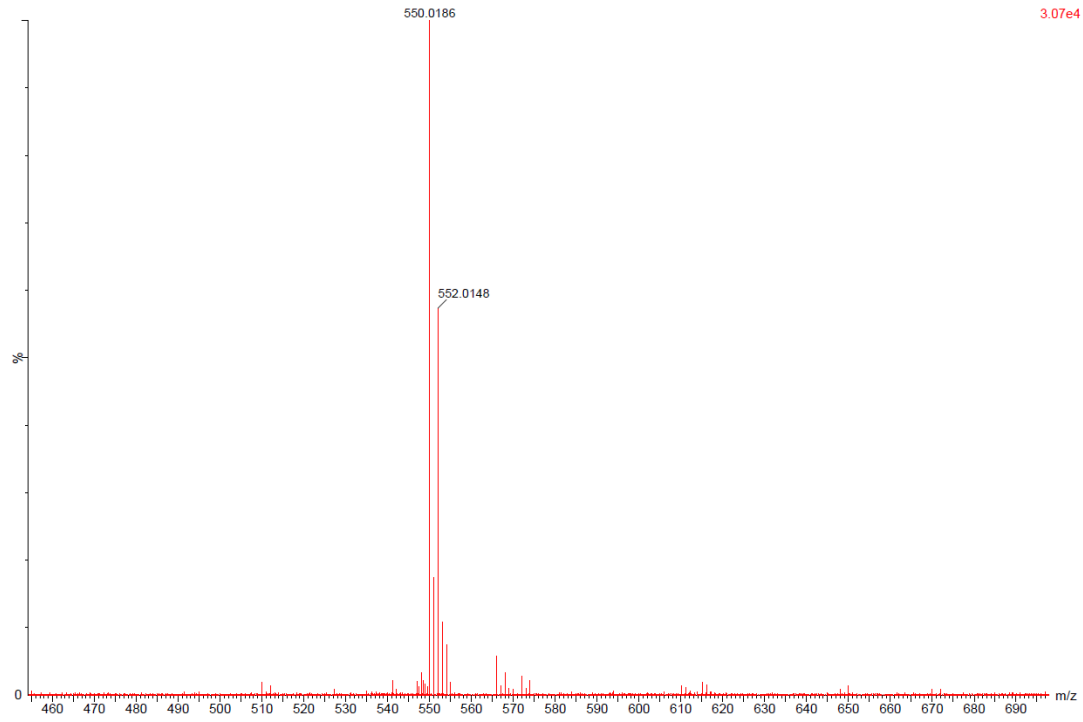
Compound **4l**



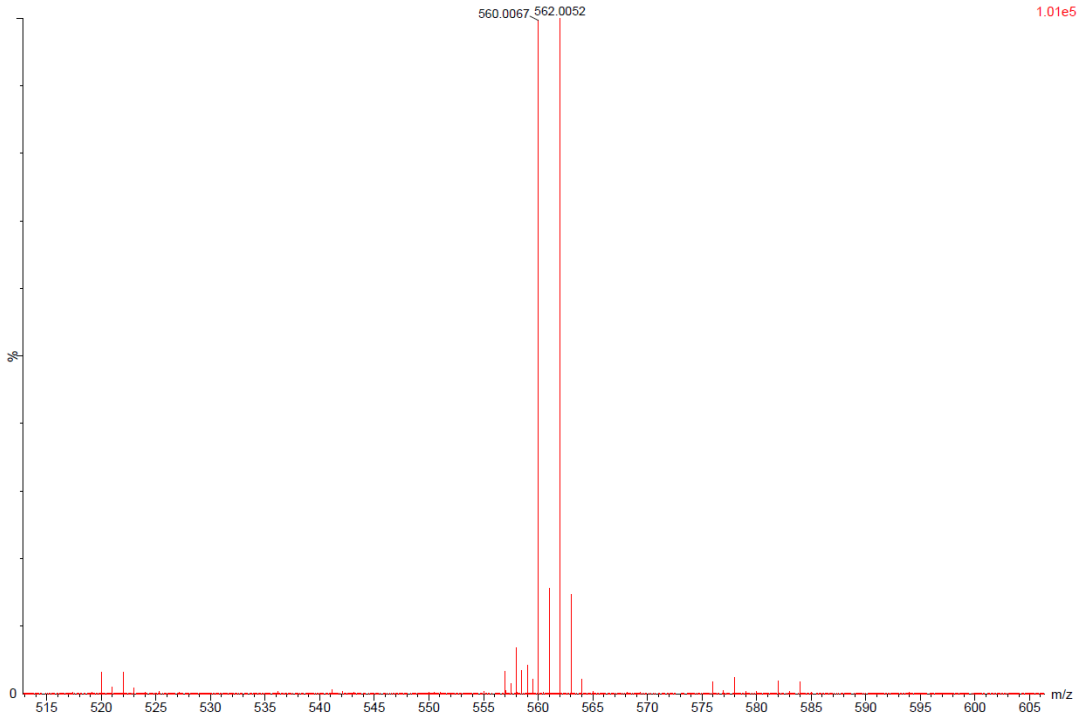
Compound **4m**


500.0869
2.47e5
%
0
450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585
m/z

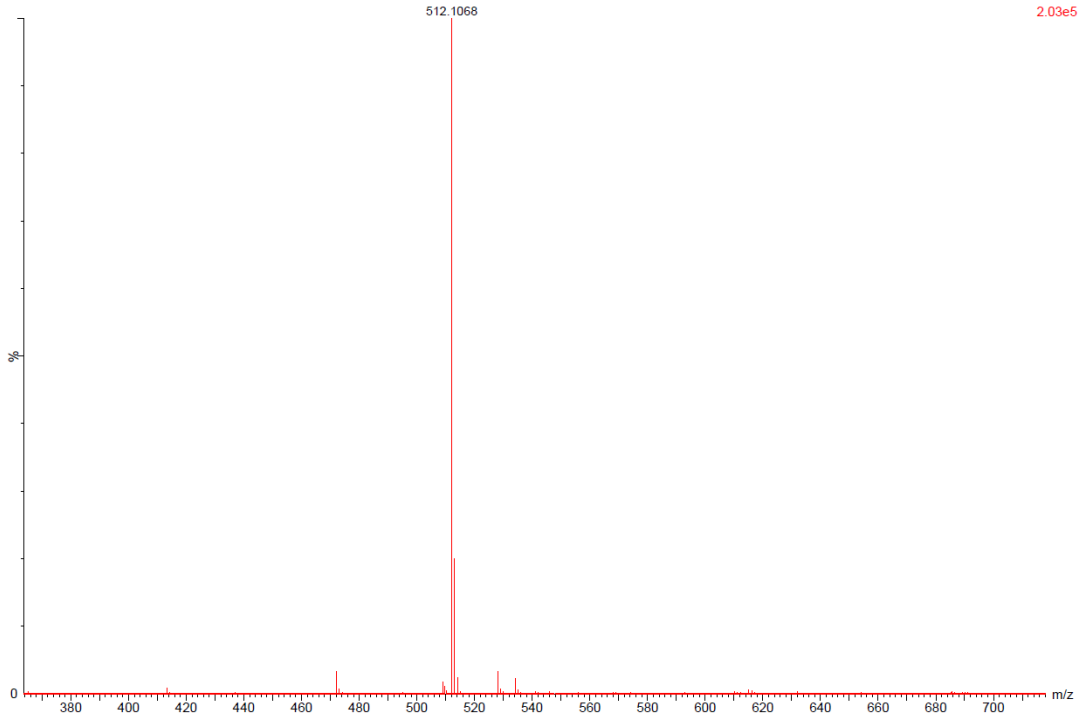
Compound **4n**


550.0186
3.07e4
552.0148
%
0
460 470 480 490 500 510 520 530 540 550 560 570 580 590 600 610 620 630 640 650 660 670 680 690
m/z

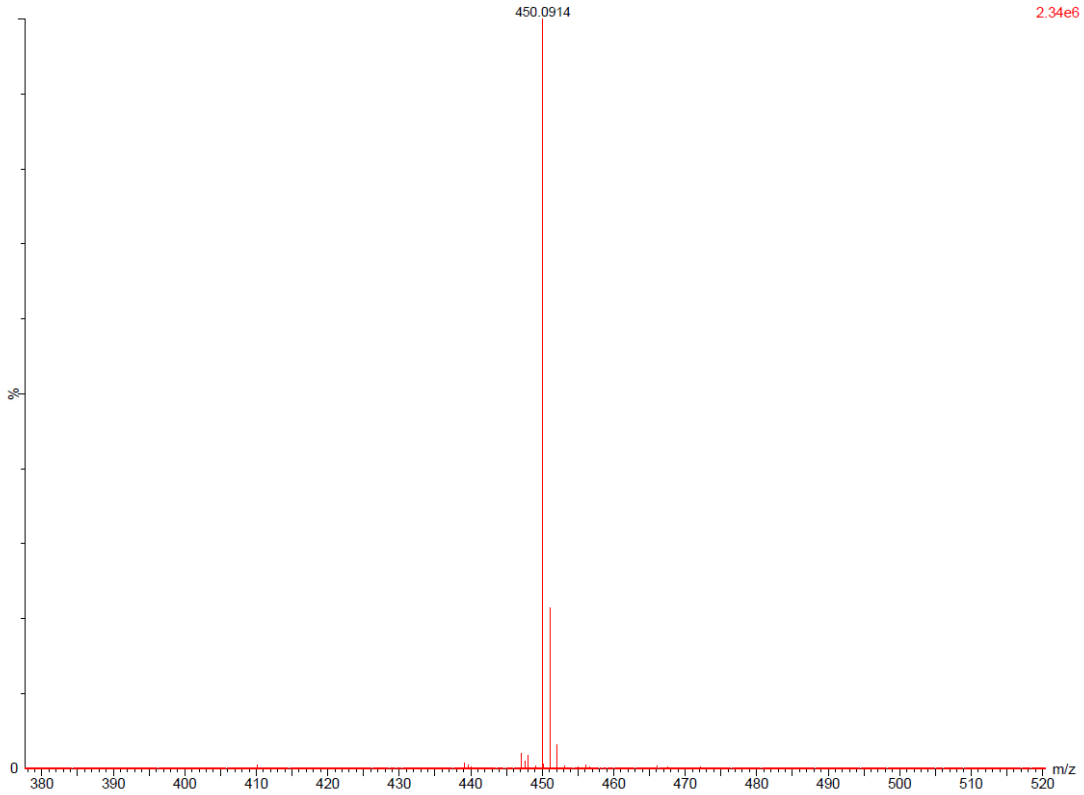
Compound **4o**



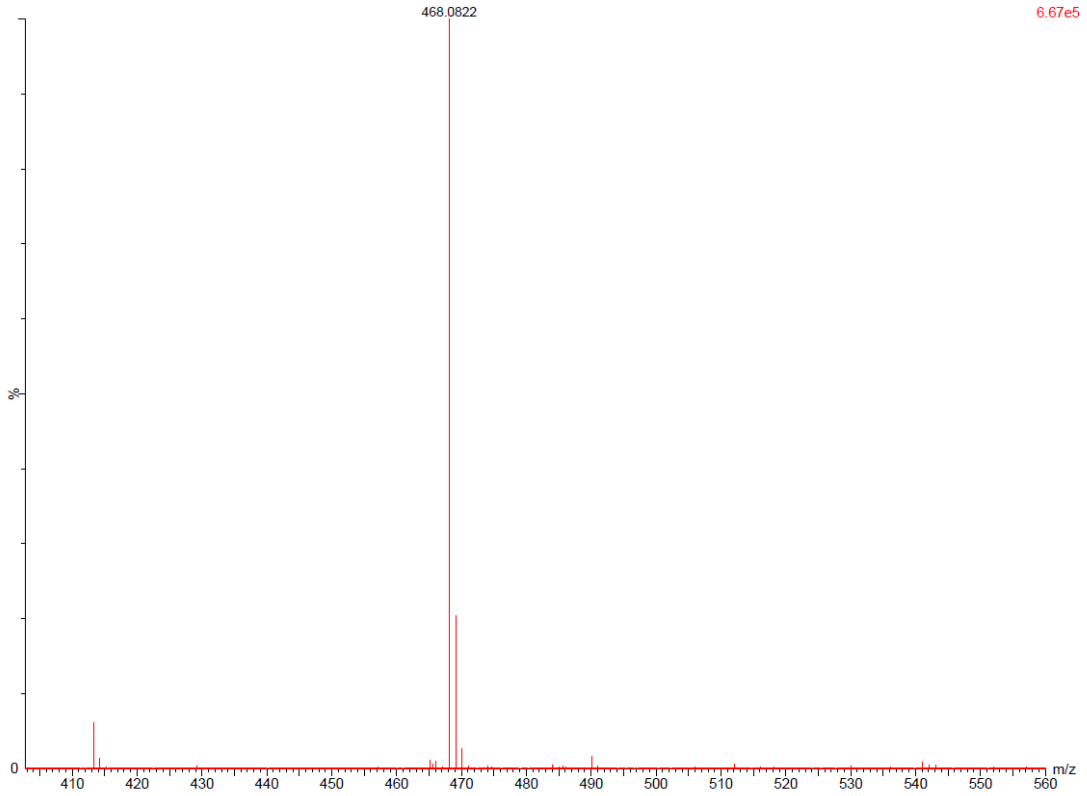
Compound **4p**



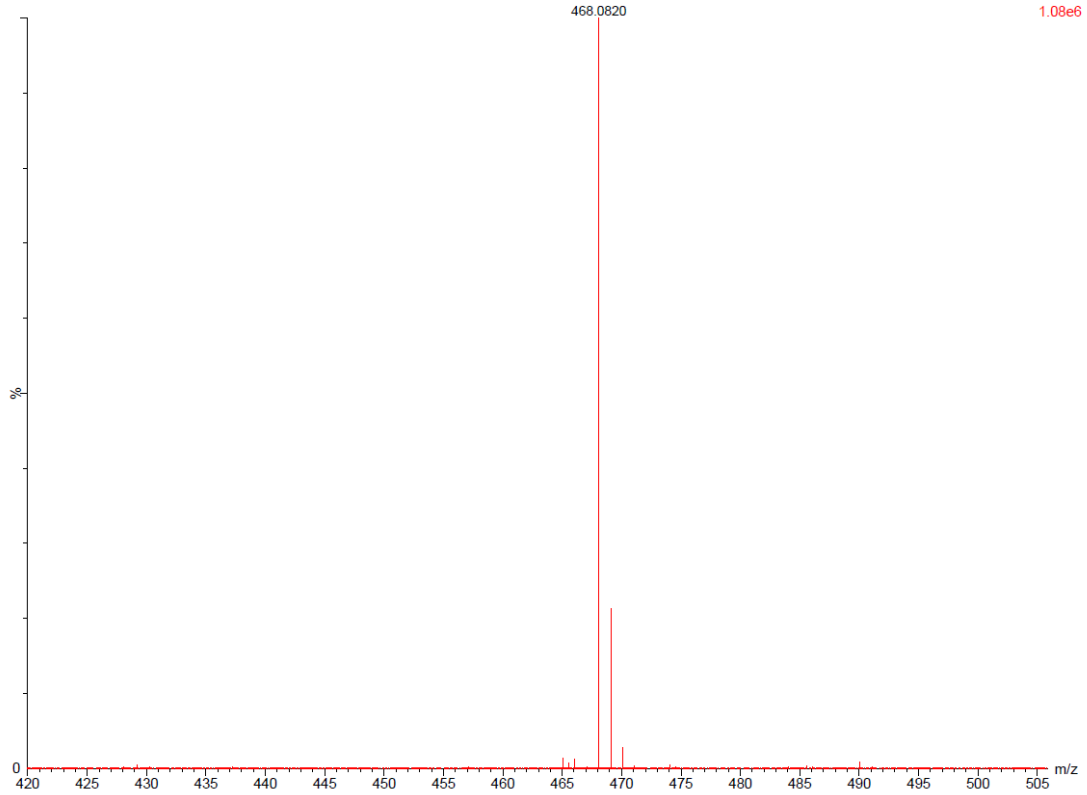
Compound **4a′**



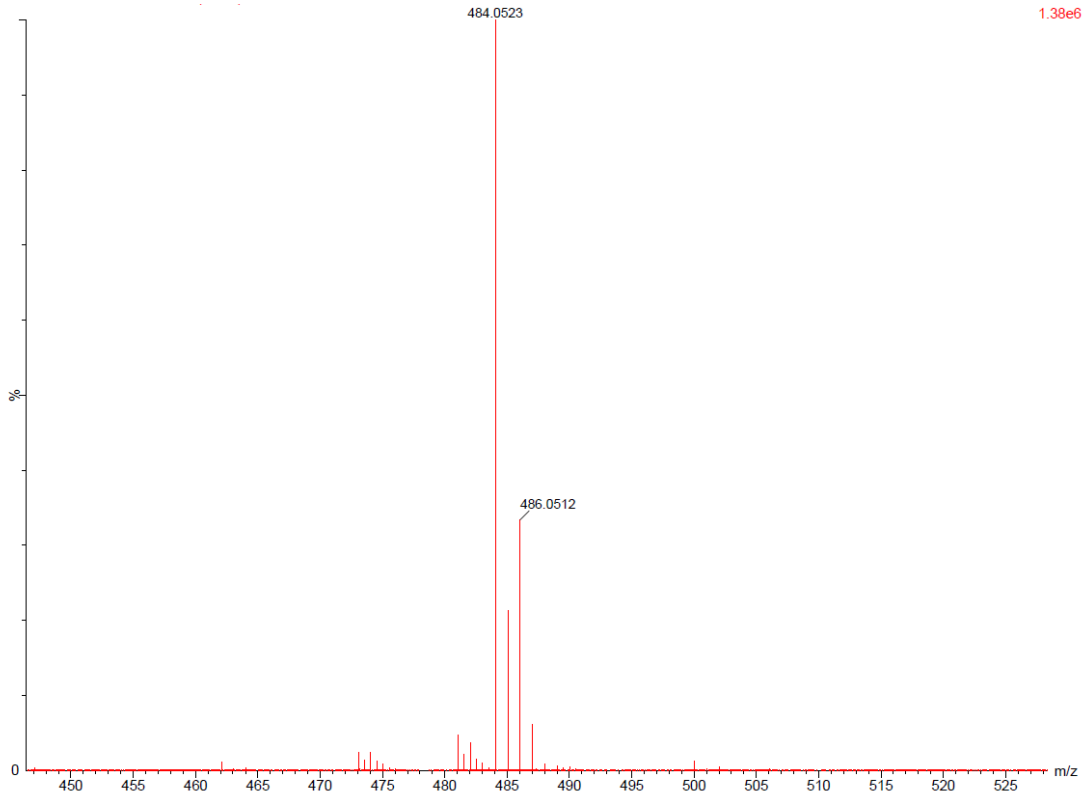
Compound **4b′**



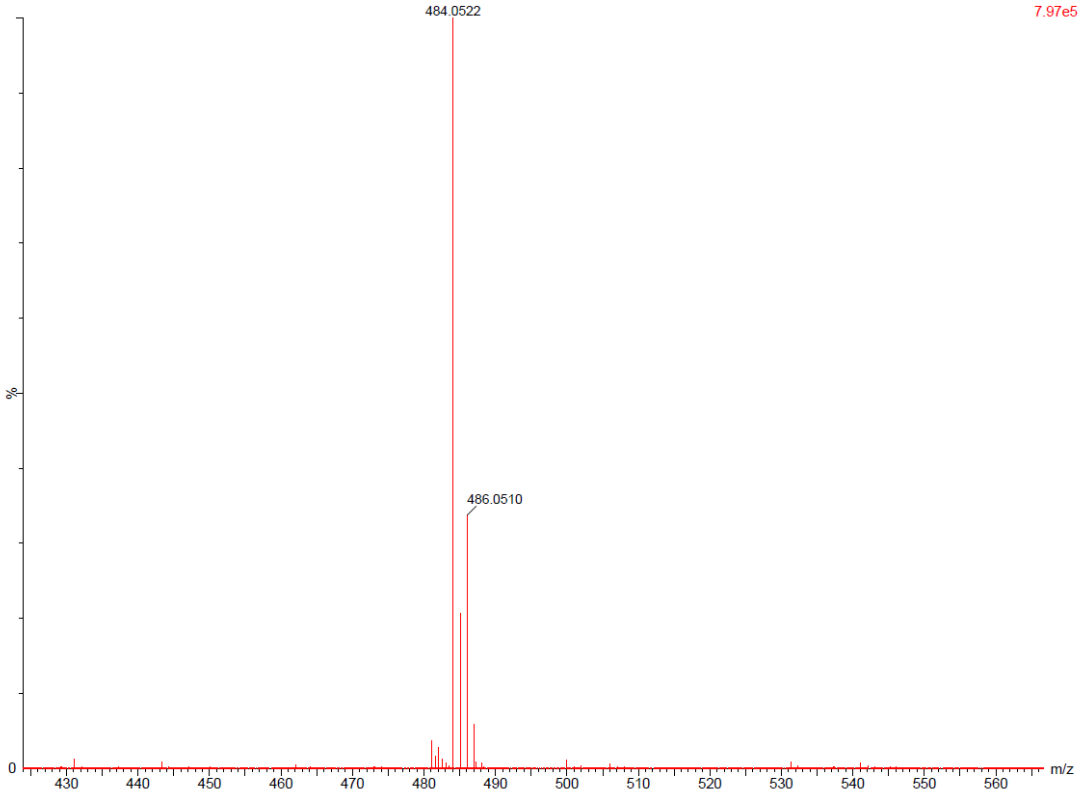
Compound **4c′**



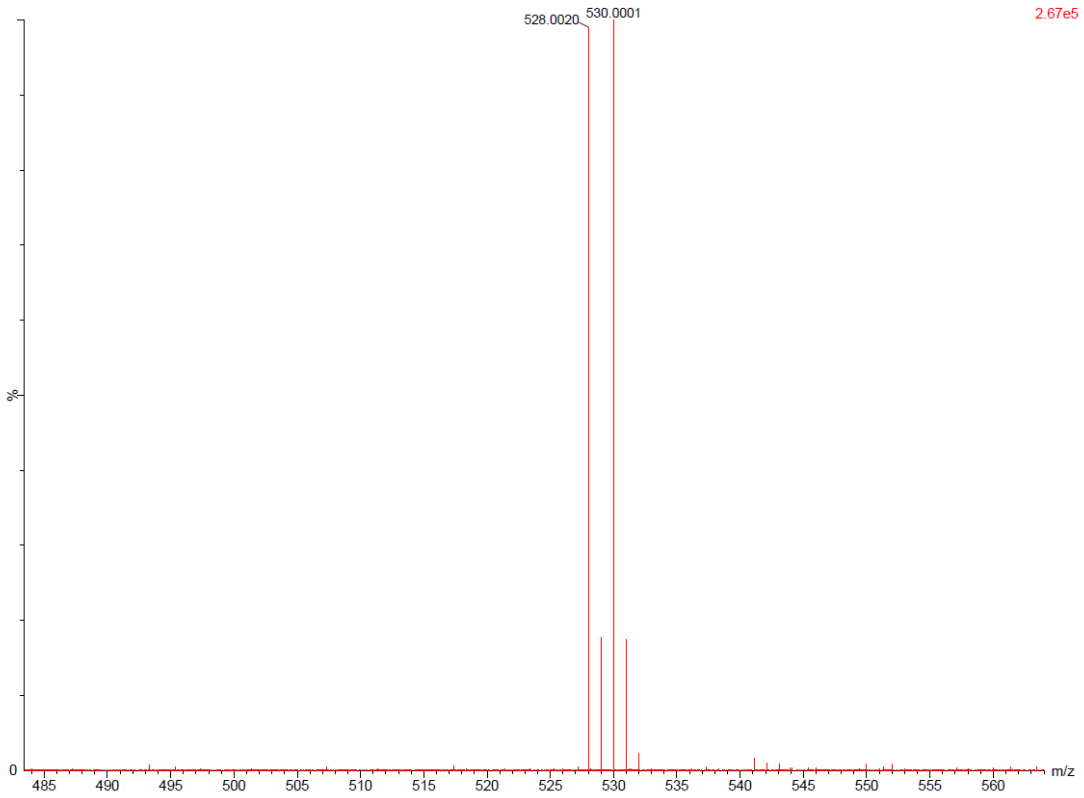
Compound **4d′**


484.0523
1.38e6
%
486.0512
0
450
455
460
465
470
475
480
485
490
495
500
505
510
515
520
525
m/z

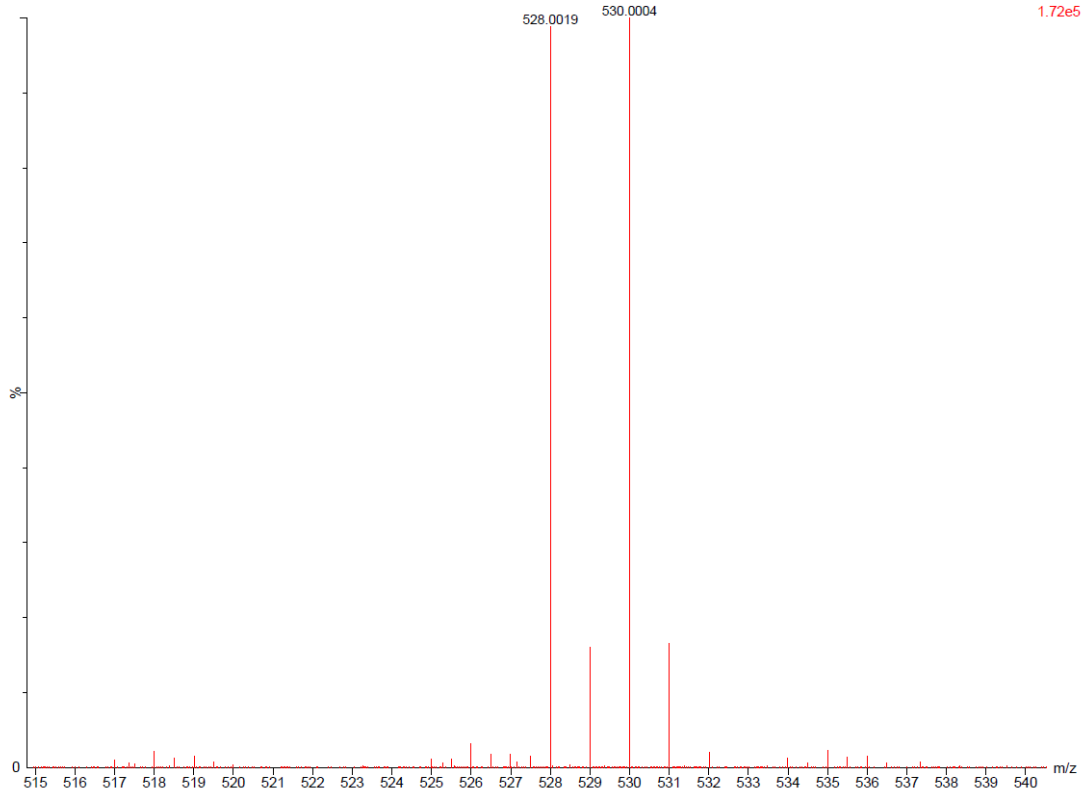
Compound **4e′**


484.0522
7.97e5
%
486.0510
0
430
440
450
460
470
480
490
500
510
520
530
540
550
560
m/z

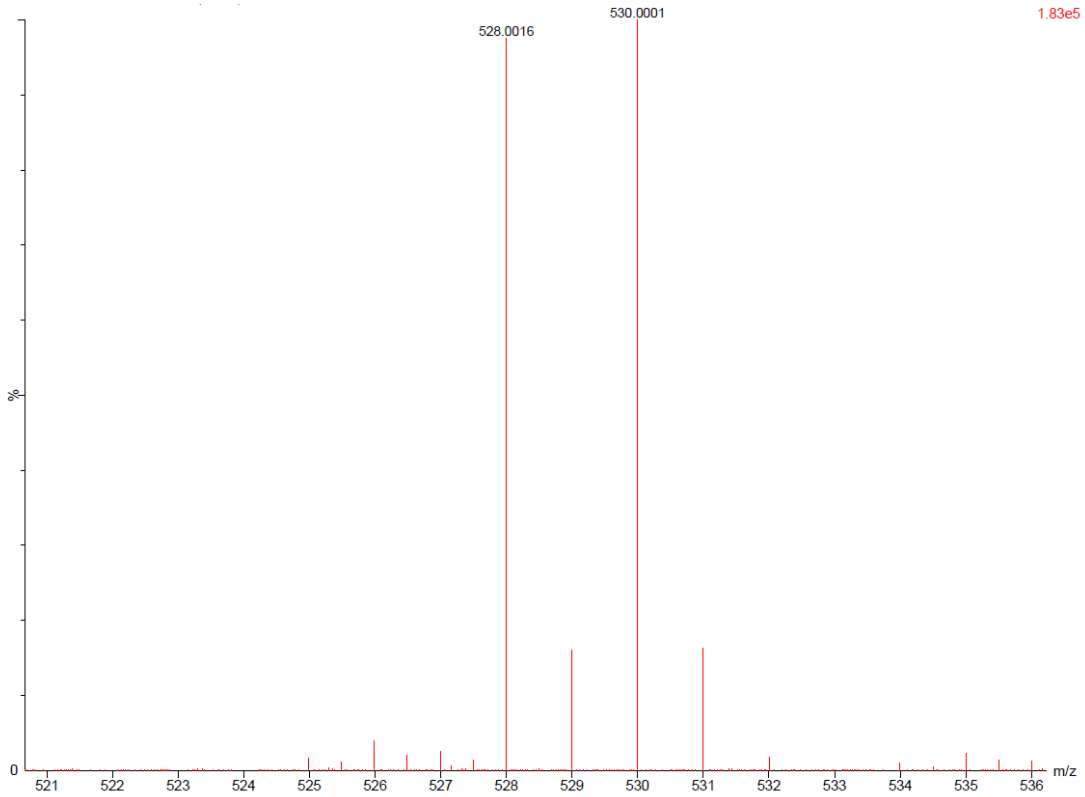
Compound **4f′**



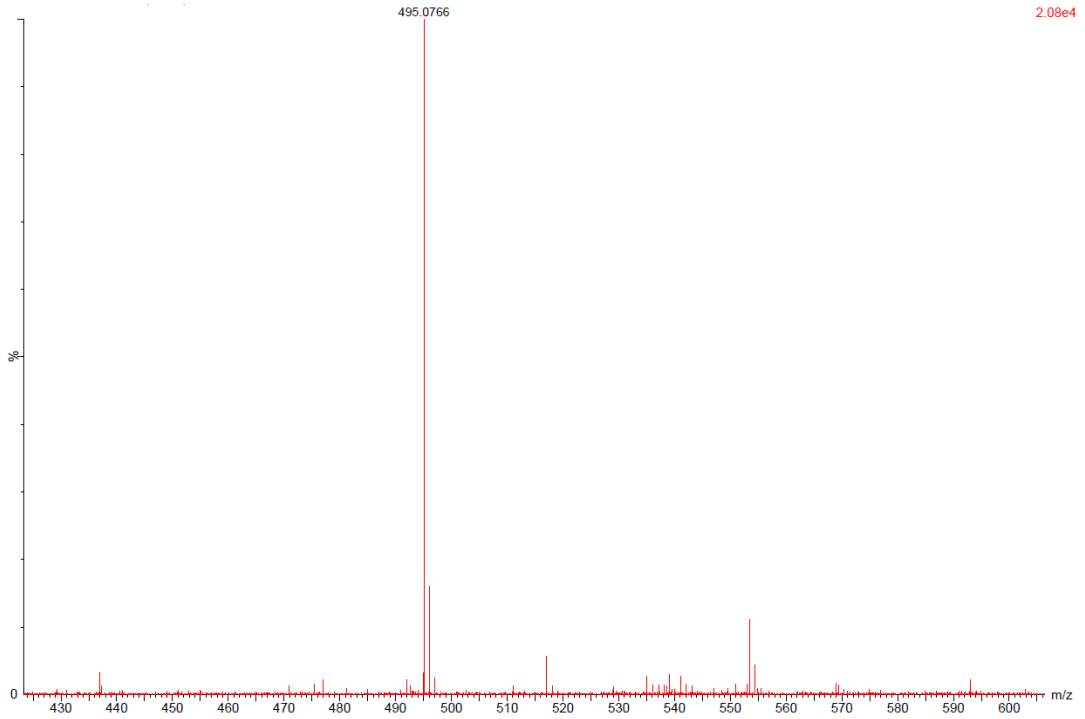
Compound **4g′**



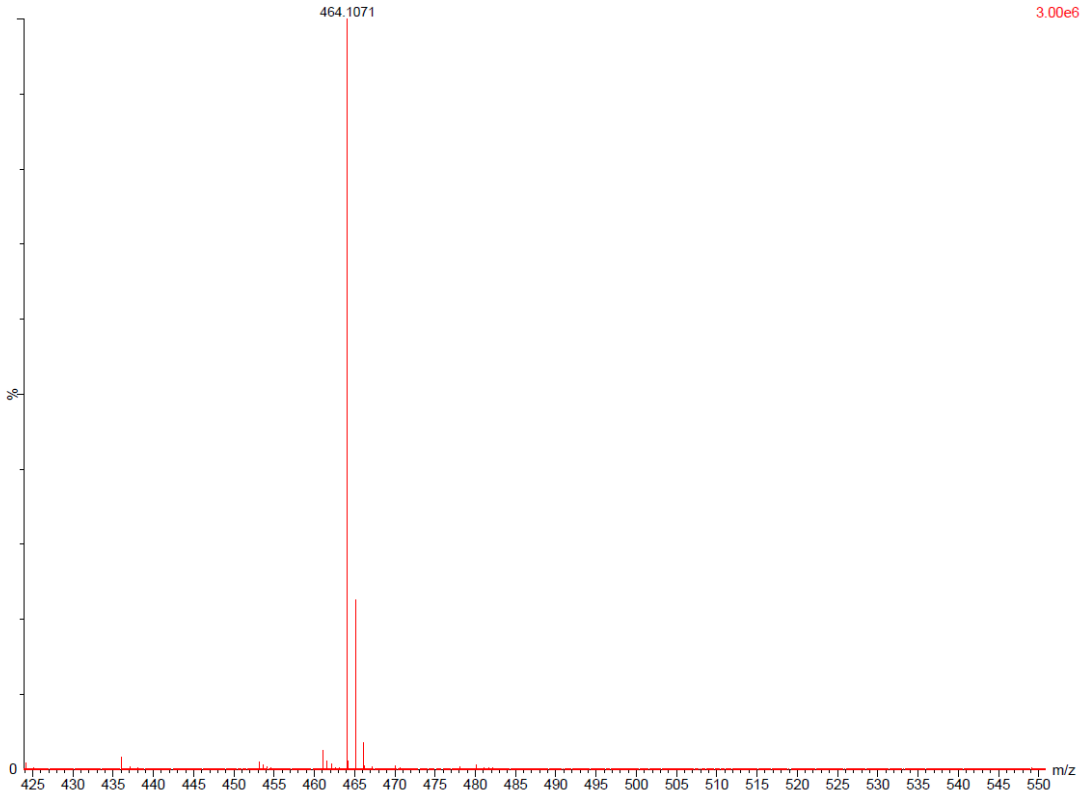
Compound **4h′**



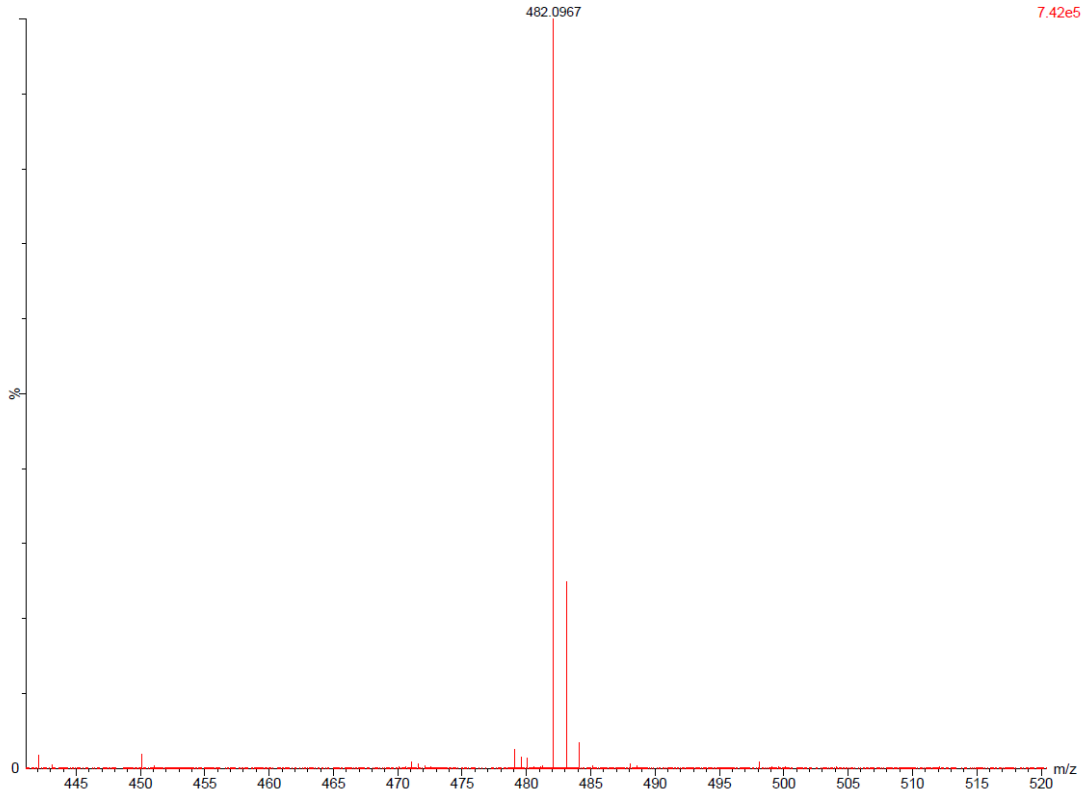
Compound **4i′**



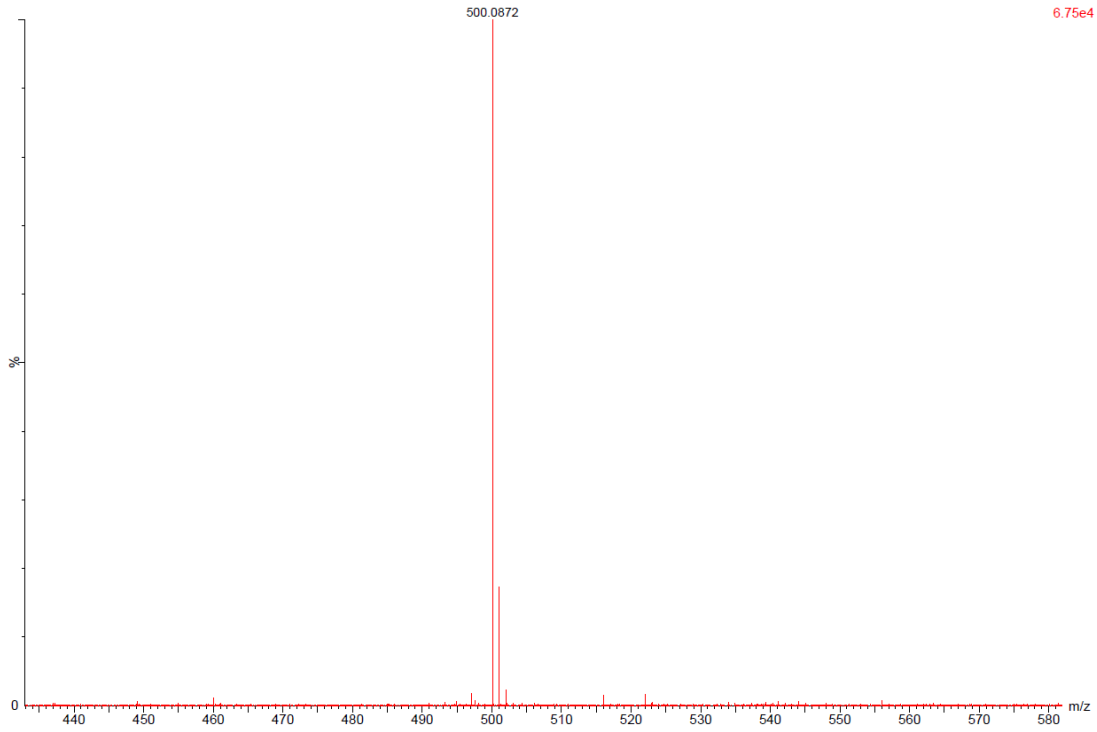
Compound **4j′**



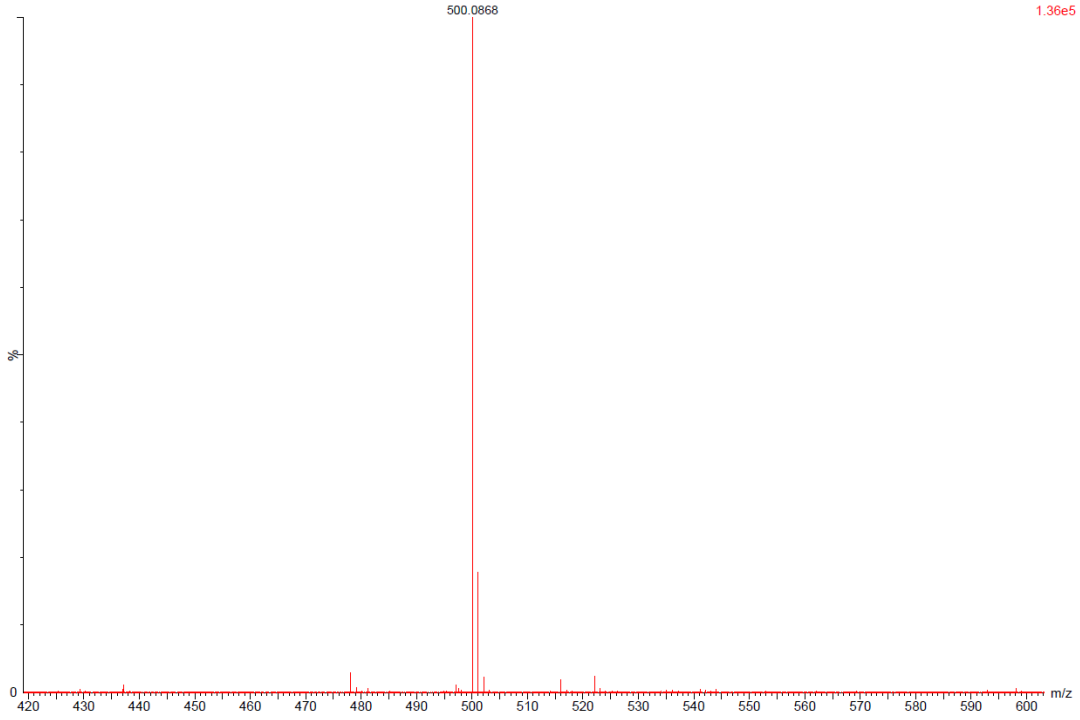
Compound **4k′**



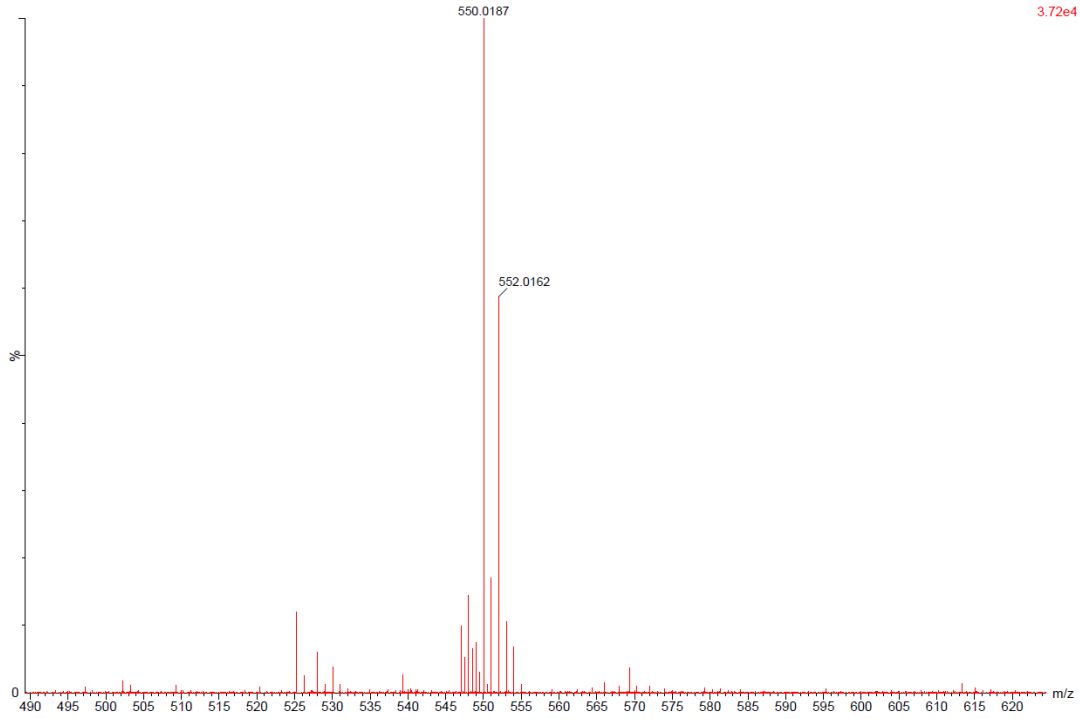
Compound **4l′**



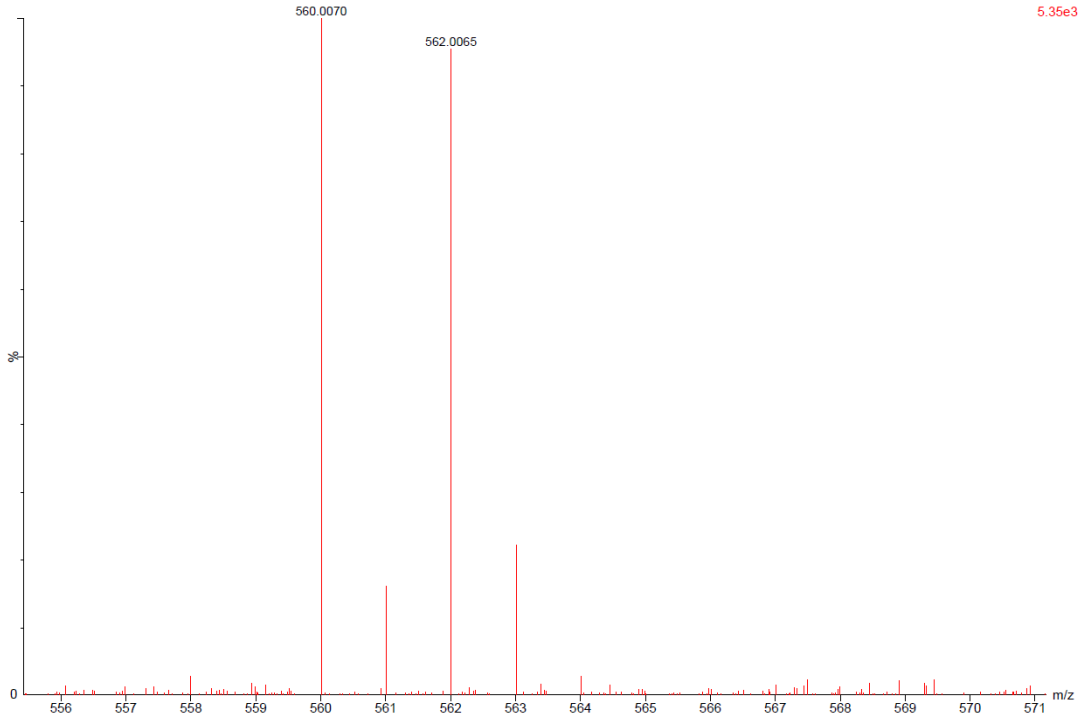
Compound **4m′**


500.0868
1.36e5
%
0
420 430 440 450 460 470 480 490 500 510 520 530 540 550 560 570 580 590 600
m/z

Compound **4n′**


550.0187
3.72e4
552.0162
%
0
490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620
m/z

Compound **4o′**



Compound **4p′**