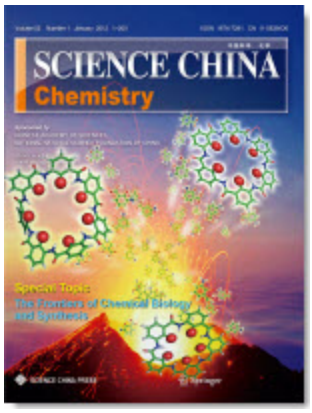

Rhodium-Catalyzed Enantio- and Diastereoselective Carboami-dation of Bicyclic Olefins toward Construction of Remote Chiral Centers and Axis

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Rhodium-Catalyzed Enantio- and Diastereoselective Carboamidation of Bicyclic Olefins toward Construction of Remote Chiral Centers and Axis

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The precise control of multiple chiral elements through a single step catalytic process remains a significant challenge in asymmetric catalysis. Reported herein is rhodium-catalyzed three-component asymmetric carboamidation between aryl boronic acid, achiral strain-activated symmetric bicyclic olefins bearing a prochiral C-N or N-N axis, and dioxazolones. The reaction proceeded effectively in excellent enantio- and diastereoselectivity under mild conditions to produce the bicyclic framework with six contiguous chiral centers as well as a N-N or C-N chiral axis. The reaction featured excellent functional group tolerance, chemoselectivity, and stereoselectivity. Mechanistic studies indicated that the coupling system proceeded *via* initial transmetalation, followed by stereo-determining migratory insertion into the olefin and electrophilic amidation.

carboamidation, axial chirality, desymmetrization,, bicyclic olefin, transmetalation

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1 Introduction

The π-bonds in olefins can be easily reshaped from achiral to chiral platforms *via* a single synthetic operation, which is attractive in synthetic chemistry due to abundance of the olefin materials. Consequently, various potential difunctionalization reactions of olefins through sequential installation of two different functional groups have been developed as efficient ways to rapidly increasing molecular complexity in a single reaction [1]. Many transformation systems have been well studied to date. Among the various

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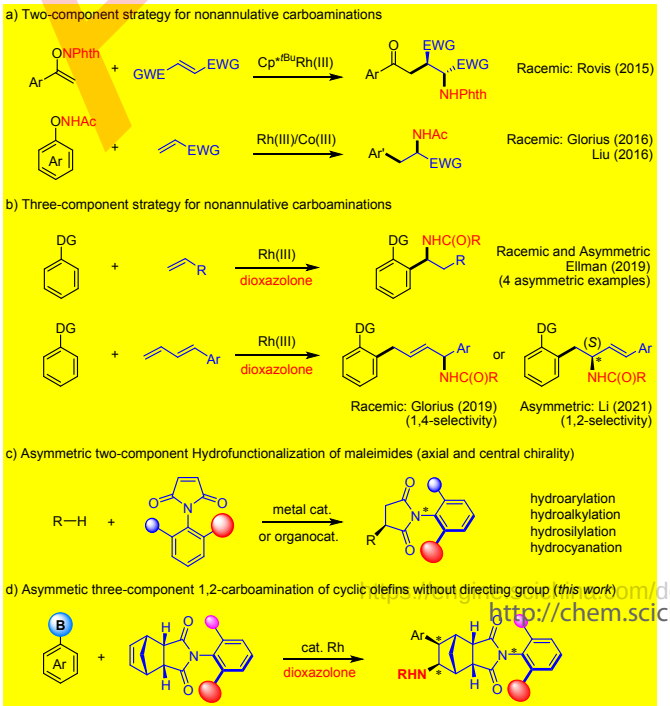
difunctionalization systems, carboamination [2], which simultaneously installs both C−C and C−N bonds in one shot, has attracted increasing attention for the prevalence of nitrogen-containing scaffolds in drug candidates and bioactive molecules [3]. In this context, a handful systems have been developed to access useful nitrogen-containing compounds through annulative coupling of olefins [4] or intramolecular carboaminations [2b, 5]. These transformations mainly focused on synthesis of heterocyclic compounds.

In the field of carboamination of olefin, group IX metal catalysts [6], especial Rh(III) complexes [7] stabilized by a cyclopentadienyl ligand, have demonstrated unique power owing to their reactivity. Two strategies have been developed to give diverse non-annulated molecules. In the two-component carboamination systems, the nitrogen moieties worked as both directing groups as well as aminating reagents (Scheme 1a), where the oxidizing directing groups based on *N*-enoxy imides and *N*-phenoxy amides were well studied, as disclosed by Rovis [8], Glorius [9], Liu [10], and others [11]. Inspired by these advances, the asymmetric version of these carboamination transformations was independently achieved by Cramer [12] and by Yi [13].

In recent years, three-component carboamination of olefins has been emerged as another attractive alternative to create both C−N and C−C bonds in a single transformation for the increasingly desirable availability of carbon and nitrogen sources [14]. In this regard, Ellman reported novel 1,1-carboamination reactions for synthesis of α-branched amines (Scheme 1b). Of note, the use of Cramer's second-generation chiral catalysts also enables the enantioselective transformation (up to 84% ee) [15]. More recently, Glorius reported highly selective intermolecular racemic 1,4-carboamination of conjugated dienes, with high levels of *E*-selectivity and regioselectivity [16]. Subsequently, our group developed an enantioselective three-component carboamination of dienes with excellent enantioselectivity and high 1,2- regioselectivity (Scheme 1b), which complements that in Glorius' study [17]. Despite the advances in the field, the majority of the investigations has been mainly restricted to racemic systems. Overall, only several asymmetric examples have been realized for the synthesis of central chirality, and axial chirality remains rarely touched [18].



Scheme 1. Access to enantio-enriched products via C-H activation using a chiral substrate.

To address these limitations, we envisioned a challenging solution to these problems by developing a three-component carboamination with axially prochiral olefins. From the perspective of construction of axial chirality, symmetric *N*-arylmaleimide [19] with a prochiral C-N axis appeared as a versatile substrate. Ideally, the achiral alkene could be easily reshaped to chiral products, and the C−N axis were also achieved in the same step *via* desymmetrization. Our group has recently applied this substrate as a coupling partner to stereoselective C-H activation of benzamides [20], affording hydroarylation products with axial and central chirality in a distal fashion (Scheme 1c). However, the asymmetric reaction pattern of *N*-arylmaleimides has been predominantly limited to hydrofunctionalization in the context of axial chirality [19-21].

To achieve the construction of central and axial chirality *via* three-component carboamination of olefins, the following challenges should be addressed: 1) the efficient access to the organometallic species (C-M bonds) that could smoothly undergo stereo-determining migratory insertion, followed by effective trapping by an electrophile terminating reagent; 2) the effective control of both chiral centers and axis in a remote fashion; 3) the suppress of undesired side reaction such as two-component coupling. While C-H activation events have allowed facile access to M-C bonds and development of carboamination systems in two- or three-component reactions, this strategy heavily depends on the use of a directing group [8-13, 15-17]. To address this limitation and tackle the rarity of axially chiral systems with multiple chiral elements, we resort to transmetaltion-derived Rh-C bonds to create the first organometallic species [14d-e] (**Scheme 1d**). In our system, the challenges of two-component side reaction and the remote disposition of the chiral centers and the axis have been successfully addressed using proper chiral catalysts and reaction conditions.

2 Experimental

General Procedure for Asymmetric Synthesis of 4

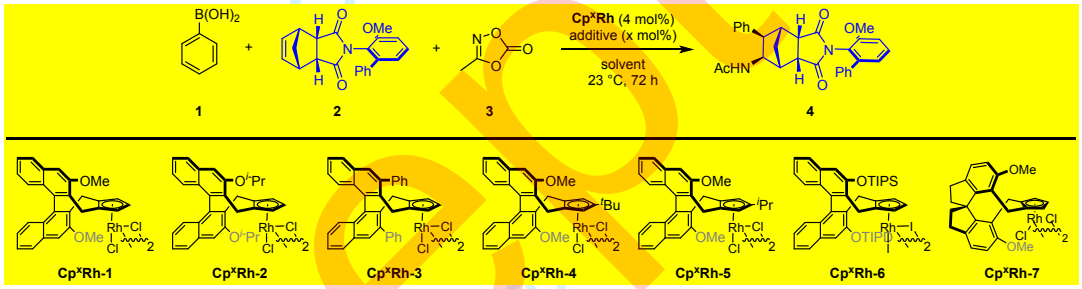
Under N_2 atmosphere, to a 8 mL tube were added arylboronic acid **1** (0.2 mmol), *N*-arylmaleimide adduct **2**

(0.1 mmol) and $KHCO_3$ (200 mol%) Then, **Cp^{x}Rh-4** (4 mol%) and dioxazolone **3** (0.3 mmol, 3 equiv) were dissolved in 0.30 mL (EtOAc/^{t}BuCN = 1:1) of the mixed solvent in a separate tube and transferred to the first one. It was rinsed with an additional 0.1 mL of the mixed solvent and transferred again to the first tube twice. After stirred at room temperature for 72 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated. The residue was purified by flash chromatography on silica gel or preparational TLC using ethyl acetate and hexane or DCM and MeOH as the eluent to afford the desired products. The details are listed in the Supporting information online.

3 Results and discussion

With this initial design in mind, we first conducted investigations by the optimization studies using commercial phenylboronic acid (**1**), a Diels-Alder reaction-derived maleimide adduct (**2**), and methyldioxazolone (**3**) [22] with the Cramer's 2nd generation **Cp^{X}Rh(III)** [23a-b] as a chiral catalyst in the presence of a $KHCO_3$ at room temperature (Table 1). Methanol was initially applied as a solvent, affording the desired carboamination product in low yield but acceptable

Table 1. Optimization of Reaction Conditions. [a]

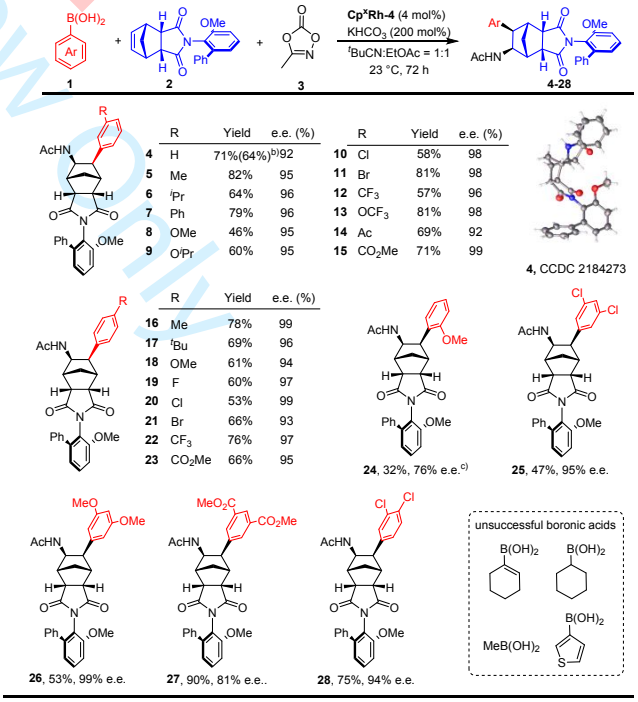


entry	[Rh]	additive (x% mol)	solvent	Yield [b] (%)	d.r. [b]	e.e. (%) [c]
1	**Rh-1**	$KHCO_3$ (200)	MeOH	43	7:1	61
2	**Rh-1**	$KHCO_3$ (200)	TFE	55	8:1	65
3	**Rh-1**	$KHCO_3$ (200)	DCM	<5	ND	ND
4	**Rh-1**	$KHCO_3$ (200)	MeCN	57	8:1	79
5	**Rh-1**	$KHCO_3$ (200)	EtOAc	67	5:1	64
6	**Rh-1**	$KHCO_3$ (200)	EtOAc/MeCN (3:1)	67	6:1	70
7	**Rh-1**	$KHCO_3$ (200)	EtOAc/MeCN (1:1)	61	8:1	87
8	**Rh-1**	$KHCO_3$ (200)	EtOAc/MeCN (1:3)	55	9:1	81
9	**Rh-1**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	71	8:1	90
10 [d]	**Rh-1**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	75	8:1	90
11 [d]	**Rh-1**	$KHCO_3$ (100)	EtOAc/^{t}BuCN (1:1)	64	8:1	90
12 [d]	**Rh-1**	$KHCO_3$ (50)	EtOAc/^{t}BuCN (1:1)	45	8:1	88
13 [d]	**Rh-1**	$NaHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	67	8:1	87
14 [d]	**Rh-1**	KH_2PO_4 (200)	EtOAc/^{t}BuCN (1:1)	43	8:1	81
15 [d]	**Rh-2**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	62	9:1	78
16 [d]	**Rh-3**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	<5	ND	ND
17 [d]	**Rh-4**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	70	>19:1	92
18 [d]	**Rh-5**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	66	11:1	89
19 [d]	**Rh-6**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	<5	ND	ND
20 [d]	**Rh-7**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	64	9:1	86
21 [e]	**Rh-4**	$KHCO_3$ (200)	EtOAc/^{t}BuCN (1:1)	80 (71) [f]	>19:1	92

a) Reaction conditions: phenylboronic acid (0.1 mmol), bicyclic olefins (0.05 mmol), dioxazolone (0.15 mol), **Cp^{x}Rh** cat. (4 mol%), additive (x mol%), solvent (1.0 mL), under N_2 for 72 h. b) The yield and dr were determined by ^{1}H NMR analysis of crude product using an internal standard. c) The ee value was determined by HPLC using a chiral stationary phase. d) 0.1 M. e) 0.2 M. f) Isolated yield. ND = Not determined.

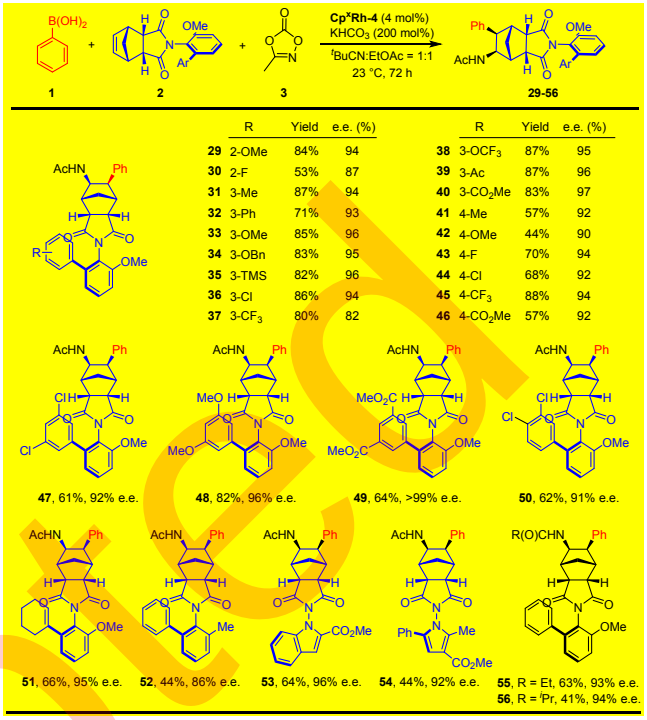
enantioselectivity when the catalyst **Cp^{x}Rh-1** was employed (entry 1). Subsequently, other commercially available organoboron reagents or readily accessible nitrene precursors were screened. Unfortunately, these alternatives were incompatible with this three-compent carboamination system (see the Supporting Information). Screening of solvents showed that EtOAc and MeCN were beneficial to the three-component carboamination transformation. Besides, coupling in MeCN generally led to higher e.e. and higher yield was realized when EtOAc was used a solvent (entries 2-5). Consequently, a mixed solvent of EtOAc:MeCN = 1:1 was applied, from which the desired product **4** was isolated in moderate yield, acceptable diastereoselectivity, and high enantioselectivity (61% yield, 8:1 dr, 87% e.e. entries 6-8). Moreover, an analogous solvent of ^{t}BuCN was found to be crucial to the improvement of both the conversion and enantioselectivity, and the reaction concentration had minimal effect on the reaction yield (entries 9 and 10). Screening of the base additive indicated that a stoichiometric amount of $KHCO_3$ was the optimal choice (entries 11-14). However, the diastereoselectivity failed to improve under the above various reaction conditions. To our delight, replacing the chiral Cp ligand with a *tert*-butyl-substituted one (**Cp^{x}Rh-4**) [23c] successfully afforded the target product with excellent enantioselectivity and diastereoselectivity (entries 15-21).

After establishment of the optimal reaction conditions, the scope of boronic acids in this three-component transformation was determined (Scheme 2). Arylboronic acids with electron-donating or -withdrawing groups at the *meta* position all reacted smoothly furnishing the products in moderate to good yield, excellent diastereoselectivity, and impressive enantioselectivity (**4-15**). The absolute configuration of the product **4** was determined by X-ray crystallographic analysis (**CCDC 2184273**), and the nascent C-C and C-N bonds were pointed *cis* to the methylene bridge of the norbornene framework, possibly due to the steric effect during the alkene coordination and the subsequent migratory insertion step. Moreover, the mmol-scale synthesis of **4** resulted in no obvious erosion of yield and stereoselectivities (64% yield, 92% e.e.). The installation of Me, OMe, and halogen groups at the *para* position of the benzene ring was also tolerated, delivering products with excellent enantioselectivity (**16-23**, 93-99% e.e.). Meanwhile, 3,5- and 3,4- disubstituted arylboronic acids also reacted well (**25-28**). In contrast, exception was found for 2-methoxyphenylboronic acid, which reacted with lower enantioselectivity (**24**, 76% e.e.), likely due to the negative steric effect. In all cases, consistently excellent diastereoselectivity was observed in call cases. These reactions all proceeded to give a small amount of the two-component amidation side product. The only fly in the ointment is that cycloalkenyl, alkyl and 3-thiophene boronic acids were not tolerable in this transformation because of this dominant two-component side reaction (See the Supporting Information for limitations).



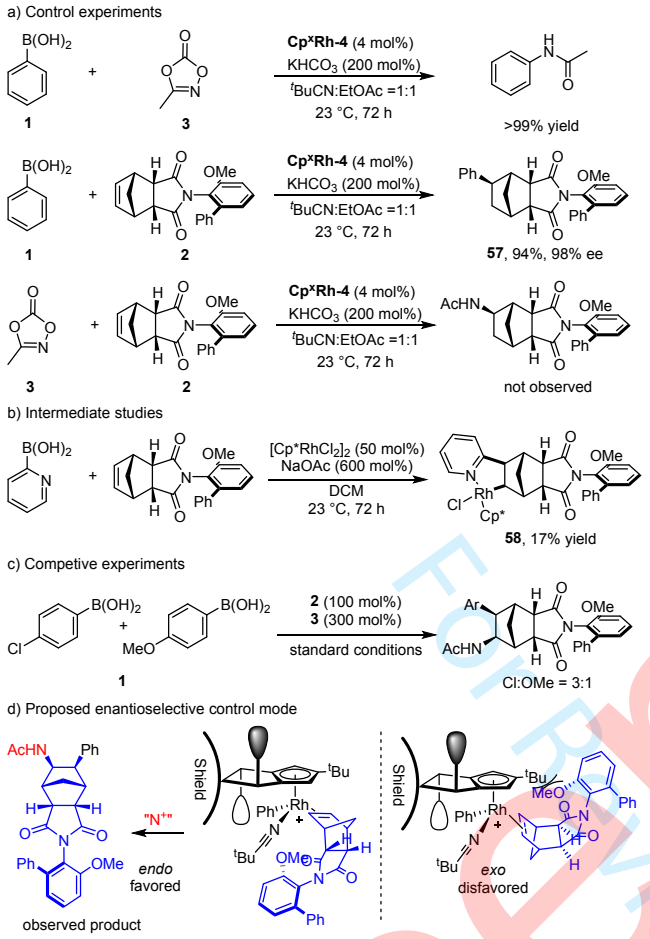
Scheme 2. Substrate Scope of boronic acid. a) Reaction conditions: arylboronic acid (0.2 mmol), bicyclic olefins (0.1 mmol), dioxazolone (0.3 mmol), Cp^{x}Rh-4 (4 mol%), $KHCO_3$ (200 mol%), Solvent (0.50 mL), under N_2 for 72 h. The ee values were determined by HPLC analysis on a chiral stationary phase. b) The reaction was on 1.0 mmol. c)The **Cp^{x}Rh-1** was used.

The scope of prochiral *N*-aryl maleimide substrate (Diels-Alder adduct) and the dioxazolone was next explored (Scheme 3). As expected, the reaction of *N*-aryl maleimide substrates bearing a 2-OMe or -F substituted *ortho* aryl ring were well-tolerated (**29-30**). Satisfyingly, substrates with 3- or 4- methoxy, alkyl, halogen and ester substituents in the *ortho* phenyl ring also reacted to give the expected products with small variations in efficiency and enantioselectivities (**31-46**). When multiple-substituted phenyl or cycloalkenyl were attached to *ortho* position of C-N bond, the corresponding carboamination products were formed with excellent enantioselectivity ranging from 91% to >99% e.e. (**47-51**). The chiral product was also accessible with a moderate yield and no obvious decrease of enatiopurity when the *ortho* methoxy group was extended to a methyl group (**52**). All these results indicated that electronic properties of the olefin substrates had limited influence on the stereoselectivity of the carboamination reaction. To further demonstrate the scope of our asymmetric catalytic system, construction of N-N atropisomers was next explored. On the basic of related works, [24] the prochiral alkenes with a N-N axis were successfully synthesized. To our delight, the N-N prochiral indole or pyrrole substrates were applicable under the optimal conditions, delivering the corresponding products with good efficiency and excellent enantioselectity (**53-54**). Unfortunately, in the case of the bicyclic olefins with N-Ph or -Bn group, the transformations were unsuccessful, presumably due to a faster nitrene migratory insertion (See the Supporting Information for limitations). Finally, extension of the dioxazolones to those with logner alkyl chains successfully produced the three-component carboamination products with a slight loss of reactivity (**55-56**).



Scheme 3. Scope of the bicyclic olefins and the amidating reagents. a) Reaction conditions: a) arylboronic acid (0.2 mmol), bicyclic olefins (0.1 mmol), dioxazolone (0.3 mmol), **Cp*Rh-4** (4 mol%), $KHCO_3$ (200 mol%), Solvent (0.50 mL), under N_2 for 72 h.

To further interrogate the mechanistic details of the reaction, a series of control experiments have been performed. Firstly, the two-component coupling of phenylboronic acid and the dioxazolone quantitatively afforded the amidation product. Meanwhile, the two-component coupling between the phenylboronic acid and the maleimide adduct also readily delivered the hydroarylation product in excellent efficiency and stereoselectivity. Whereas, treatment of dioxazolone and prochiral olefin under the standard conditions failed to give any corresponding hydroamination product (Scheme 4a). These results reveled that although the two side-reactions may occur, they were largely inhibited when all reagents were present and when proper reaction conditions were provided. Consequently, this multiple-component reaction is expected to proceed *via* transmetallation of boronic acid to give a Rh-aryl species with subsequent migratory insertion of prochiral maleimide adduct and further amidation with dioxazolone, which was in line with our initial hypothesis. In addition, stoichiometric two-component coupling between 2-pyridineboronic acid and the olefin **2** was further explored, from which the five-membered rhodacyclic complex was successfully isolated as a single isomer (Scheme 4b). This result provided direct evidence to our proposed reaction process. Subsequently, competitive studies were carried out under the standard conditions using an equimolar amount of 4-chloro and 4-methoxy phenylboronic acids (Scheme 4c). A yield ratio of 3:1 was obtained, which indicated that the electron-deficient arylboronic acids is kinetically more reactive possibly due to more favorable transmetaltion.



Scheme 4. Mechanistic Studies and Mechanistic Considerations.

The stereoselective control of this multiple-component system was next rationalized based on our experimental observations and our previous reports [20] (**Scheme 4d**). The reaction initially generates a Rh(III) aryl species via transmetalation and it is supported by a coordinating nitrile solvent molecule which is pointed frontward for minimized steric interactions. The Rh-aryl species is then saturated by the prochiral olefin in two coordination fashions, namely, *exo* and *endo* selectivity. The *exo* coordination fashion is strongly disfavored because of the strong steric repulsion between the Cp-^{t}Bu group and an *ortho* group in the olefin, as proposed and solidly supported by the studies in our previous related work. In the *endo* ligation mode, the less bulky aryl group was pointed backward to satisfy the steric demand in this intermediate. This orientation eventually accounts for the observed both enantio- and diastereoselectivity.

4 Conclusions

We have developed a novel desymmetrization approach to access *N*-aryl succinimides bearing a chiral C-N axis as well as six chiral centers. The three-component reaction of commercially available arylboronic acids, prochiral alkenes, and dioxazolones proceeded smoothly *via* Rh(III) catalysis under very mild conditions. A broad scope of arylboronic acids and prochiral alkenes has been defined, accessing the products with excellent enantioselectivity and diastereoselectivity. In addition, N-N axial chirality was also accessible in two examples under the same reaction conditions. More importantly, the induction of axial and central chirality was achieved in a single elementary step (migratory insertion into the olefin), and the axial and central chirality were constructed in a remote fashion by judicious choice of the ligand the solvent conditions. This transformation may provide new insight into asymmetric difunctionalization of unsaturated reagents for generation of diversified multiple chiral elements in complex molecules in a single operation. Future studies of asymmetric synthesis of complex molecules with multiple chiral elements are underway in our laboratories.

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Conflict of interest The authors declare that they have no conflict of interest.

Supporting information The supporting information is available online at http://chem.scichina.com and http://link.springer.com/journal/11426. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.

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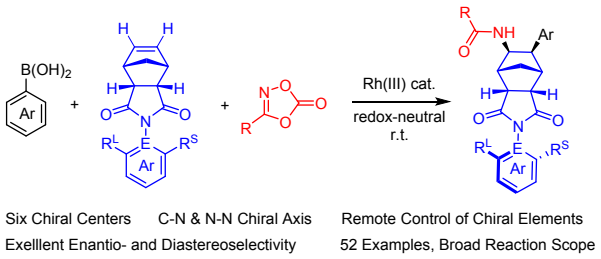

Six Chiral Centers C-N & N-N Chiral Axis Remote Control of Chiral Elements

Exelllent Enantio- and Diastereoselectivity 52 Examples, Broad Reaction Scope

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Supporting Information

Rhodium-Catalyzed Eantio- and Diastereoselective Carboamidation of Bicyclic Olefins toward Construction of Remote Multiple Chiral Centers and Axis

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http://chem.scichina.com/english

1. General Information:

All chemicals were obtained from commercial sources and were used as received unless otherwise noted. All the reactions were carried out in an argon-filled glove box. The ^{1}H NMR spectra were recorded on a 400 MHz or 600 MHz NMR spectrometer. The ^{13}C NMR spectra were recorded at 100 MHz or 150 MHz. The ^{19}F NMR spectra were recorded at 376 MHz or 565 MHz. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane (TMS), and were reported as s (singlet), d (doublet), t (triplet), dd (doublets of doublet), dt (doublets of triplet), and m (multiplet). The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ H = 7.26 ppm, δ C = 77.16 ppm). The coupling constants *J* were given in Hz. High resolution mass spectra (HRMS) were obtained via ESI mode by using a MicroTOF mass spectrometer. The conversion of starting materials was monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm). Column chromatography was performed on silica gel 200-300 mesh. The enantiomeric excess (ee) of the products were determined by high-performance liquid chromatography (HPLC) with a chiral stationary phase in comparison with the authentic racemate sample. All the chiral stationary phases including Chiralcel AD-H, IC-H, ID-H, OD-H used in this study were purchased from Daicel Chirsal Technologies. Optical rotations were reported as follows: $[\alpha]_D^T$ = (c: g/100 mL in $CDCl_3$).

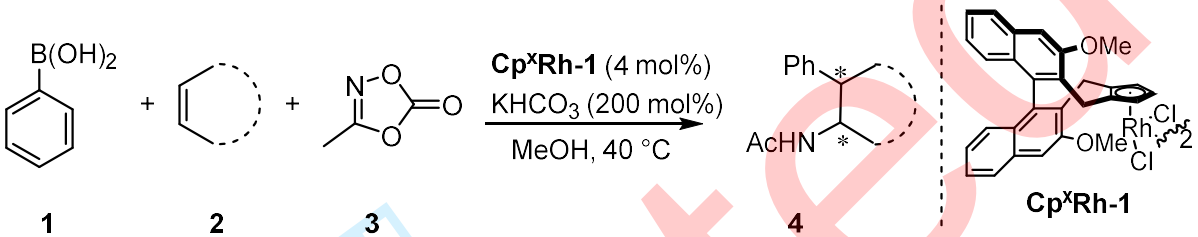
The chiral rhodium catalysts[1], *N*-aryl maleimide adducts[2] and dioxazolone[3] were

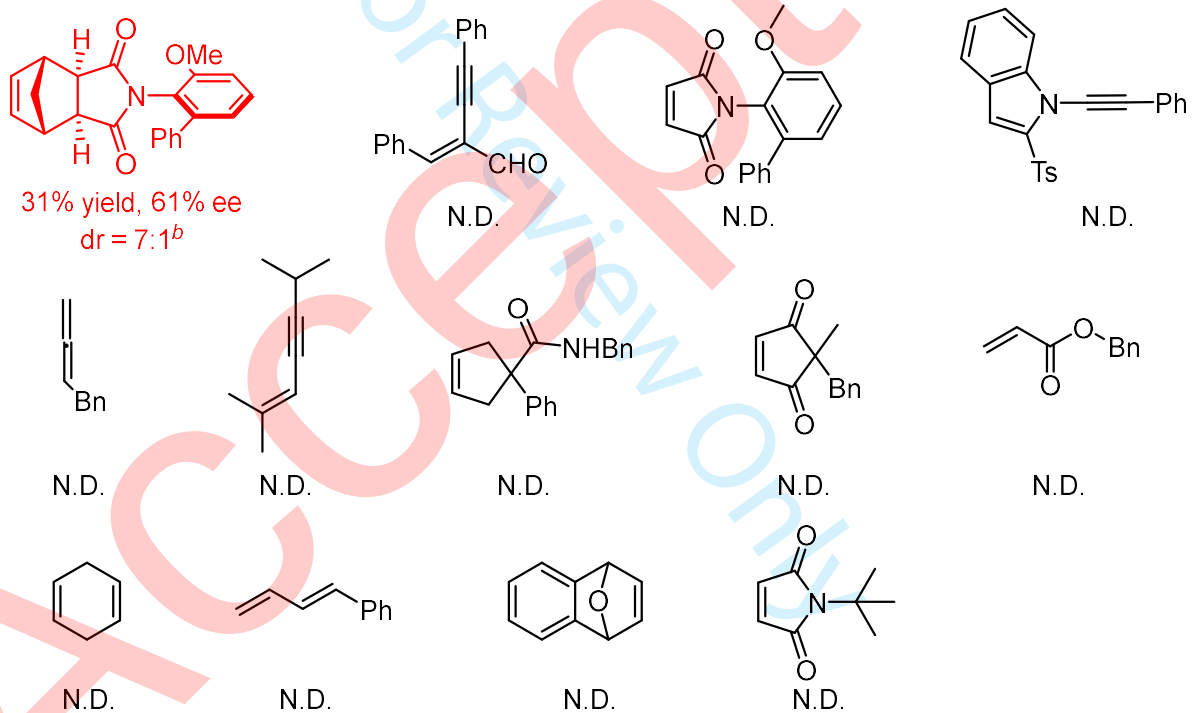
prepared according to published procedures.

2. Experimental Section

2. 1 Tables of the Optimization of Reaction Conditions

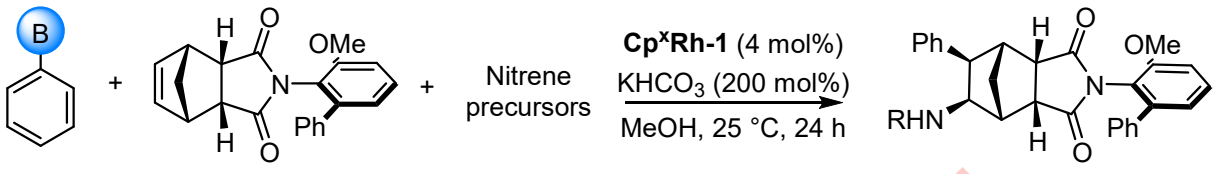
Table S1. Screening of alkene substrates [a]



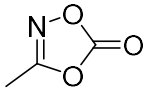


[a] Reaction Conditions: phenylboronic acid (0.1 mmol), N-aryl maleimide adduct (0.05 mmol), dioxazolone (0.15 mol), **Cp^{x}Rh1** (4 mol%), $KHCO_3$ (200 mol%), MeOH (1.0 mL), under N_2 for 24 h. [b] The yield and dr were determined by ^1H NMR analysis of crude reaction mixture using methoxybenzene as the internal standard.

Table S2. Screening of organoboron reagents and nitrene precursors [a]

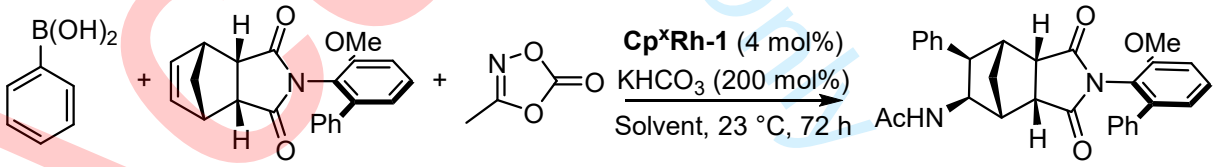


1 **2** **3** **4**

Entry	**organoboron**	**nitrene**	Yield[b] (%)	d.r.[b]	e.e. (%)
1	$PhB(OH)_2$		31	7:1	61
2	PhBpin		trace	ND	ND
3	$(PhBO)_3$		trace	ND	ND
4	$PhBF_3K$		trace	ND	ND
5	$PhB(OH)_2$	TsN_3	trace	ND	ND
6	$PhB(OH)_2$	TsNHOPiv	trace	ND	ND

[a]Reaction Conditions: organoboron reagents (0.1 mmol), N-aryl maleimide adduct (0.05 mmol), nitrene precursors (0.15 mol), **Cp^{x}Rh1** (4 mol%), $KHCO_3$ (200 mol%), solvent (1.0 mL), under N_2 for 72 h. [b] The yield and dr were determined by ^1H NMR analysis of crude reaction mixture using methoxybenzene as the internal standard. ND = Not determined.

Table S3. Screening of solvent [a]



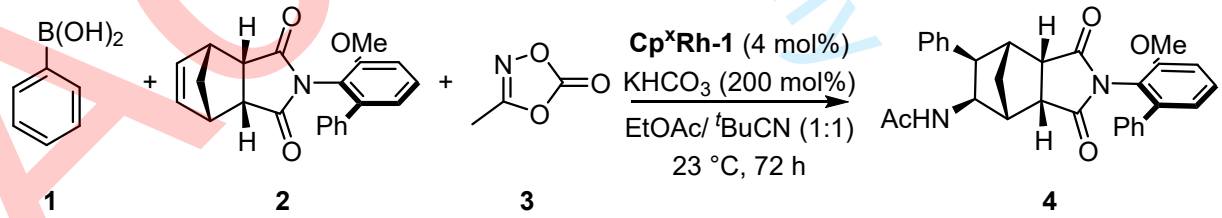
1 **2** **3** **4**

Entry	Solvent	Yield[b] (%)	d.r.[b]	e.e. (%)
1	MeOH	43	7:1	61
2	TFE	55	8:1	65
3	MeCN	57	8:1	79
4	1,4-dioxane	60	8:1	65
5	DCM	<5	ND	ND
6	EtOAc	67	5:1	64

7	EtOAc/ MeCN (3:1)	67	6:1	70
8	EtOAc/ MeCN (1:1)	61	8:1	87
9	EtOAc/ MeCN (1:3)	55	9:1	81
10	EtOAc/ PhCN (1:1)	<5	ND	ND
11	EtOAc/ BnCN (1:1)	<5	ND	ND
12	EtOAc/ ^{t}BuCN (1:1)	71	8:1	90
13	^{i}PrOAc/ MeCN (1:1)	64	8:1	79
14	^{t}BuOAc/ MeCN (1:1)	<5	ND	ND
15	EtOAc/ MeOH (1:1)	<5	ND	ND
16[c]	EtOAc/ ^{t}BuCN (1:1)	75	8:1	90
17[d]	EtOAc/ ^{t}BuCN (1:1)	80	8:1	90
18[e]	EtOAc/ ^{t}BuCN (1:1)	60	8:1	86

[a] Reaction Conditions: phenylboronic acid (0.1 mmol), N-aryl maleimide adduct (0.05 mmol), dioxazolone (0.15 mol), **Cp^{x}Rh1** (4 mol%), $KHCO_3$ (200 mol%), solvent (1.0 mL), under N_2 for 72 h. [b] The yield and dr were determined by ^1H NMR analysis of crude reaction mixture using methoxybenzene as the internal standard. [c] solvent (0.5 mL). [d] solvent (0.3 mL). [e] 40 °C. ND = Not determined.

Table S4. Screening of rato of the substrates 1 and 2 [a]



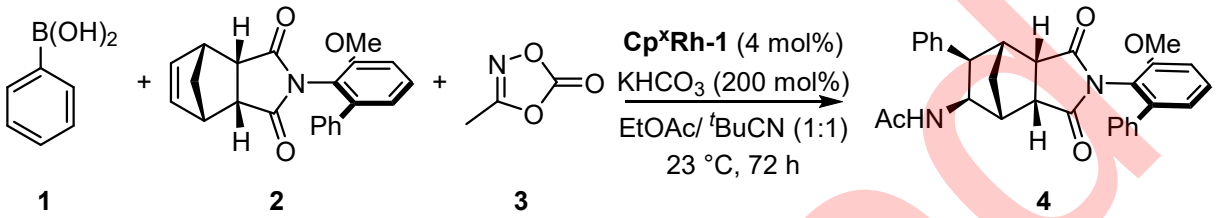
1 **2** **3** **4**

entry	rato (1:2:3)	yield [b] (%)	dr [b]	ee (%)
1	2:1:3	75	8:1	90
2	1:1.5:3	38	8:1	89
3	2:1.5:1	41	8:1	88
4	1.5:1:3	60	8:1	89

[a] Reaction Conditions: **Cp^{x}Rh1** (4 mol%), $KHCO_3$ (200 mol%), solvent (0.5 mL), under N_2 for 72 h. [b]

The yield and dr were determined by ^{1}H NMR analysis of crude reaction mixture using methoxybenzene as the internal standard.

Table S5. Screening of the additive [a]

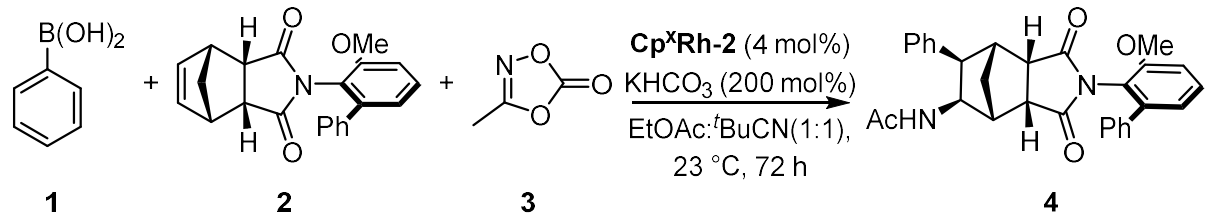


1 2 3 4

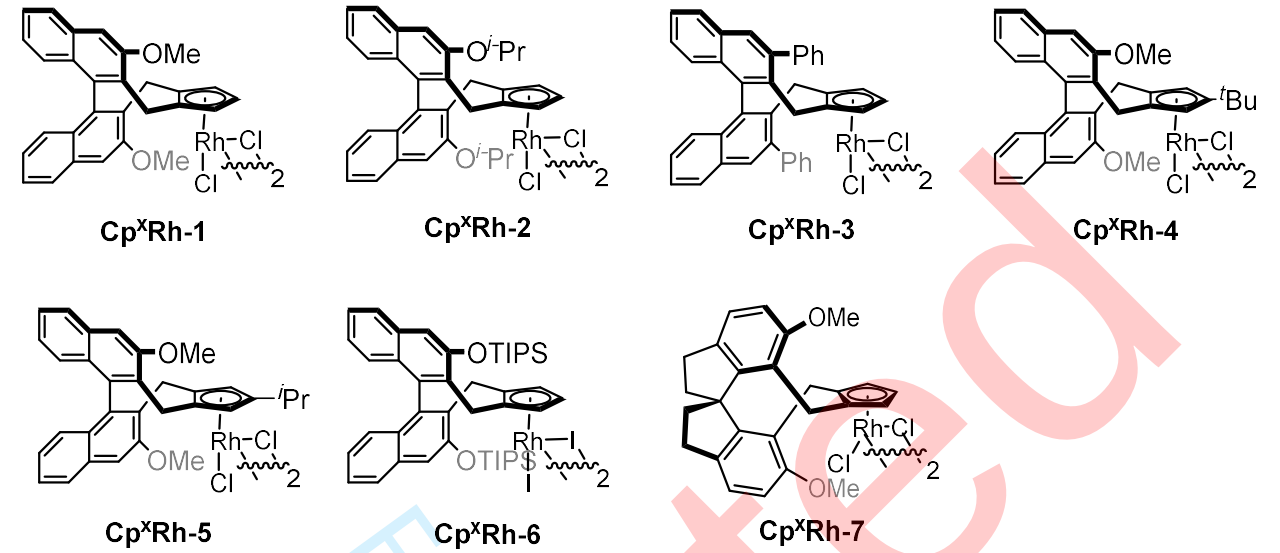
entry	Base (x mol%)	yield [b] (%)	dr [b]	ee (%)
1	$KHCO_3$ (200)	75	8:1	90
2	$NaHCO_3$ (200)	67	8:1	87
3	$Ca(HCO_3)_2$ (200)	47	8:1	88
4	KH_2PO_3 (200)	43	8:1	81
5	NaH_2PO_3 (200)	37	8:1	80
6	KOH (200)	54	9:1	81
7	$KHCO_3$ (50)	45	8:1	88
8	$KHCO_3$ (100)	64	8:1	90
9	$KHCO_3$ (300)	70	8:1	90

[a] Reaction Conditions: phenylboronic acid (0.1 mmol), N-aryl maleimide adduct (0.05 mmol), dioxazolone (0.15 mol), **Cp^{x}Rh1** (4 mol%), base (x mol%), Solvent (0.5 mL), under N_2 for 72 h. [b] The yield and dr were determined by ^{1}H NMR analysis of crude reaction mixture using methoxybenzene as the internal standard.

Table S6. Screening of catalyst [a]



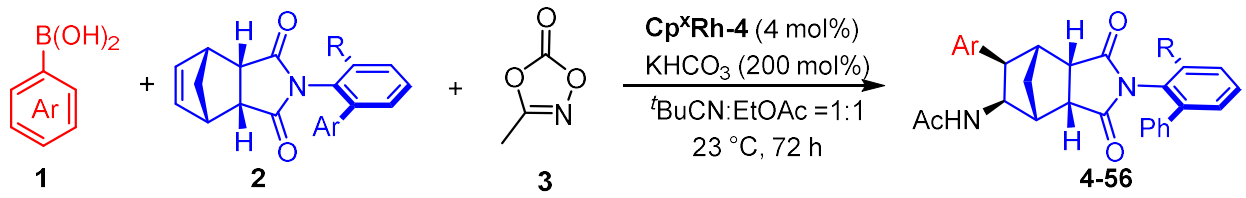
1 2 3 4



entry	catalyst	yield [b] (%)	dr [b]	ee (%)
1	**Cp^{x}Rh-1**	75	8:1	90
2	**Cp^{x}Rh-2**	62	9:1	78
3	**Cp^{x}Rh-3**	<5	ND	ND
4	**Cp^{x}Rh-4**	70	>19:1	92
5	**Cp^{x}Rh-5**	66	11:1	89
6	**Cp^{x}Rh-6**	<5	ND	ND
7	**Cp^{x}Rh-7**	64	9:1	86
8[c]	**Cp^{x}Rh-4**	80 (71)[d]	>19:1	92

[a] Reaction Conditions: phenylboronic acid (0.1 mmol), N-aryl maleimide adduct (0.05 mmol), dioxazolone (0.15 mol), **Cp^{x}Rh** (4 mol%), $KHCO_3$ (200 mol%), Solvent (0.5 mL), under N_2 for 72 h. [b] The yield and dr were determined by ^1H NMR analysis of crude reaction mixture using methoxybenzene as the internal standard. [c] N-aryl maleimide adduct (0.1 mmol), solvent (0.5 mL). [d] Isolated yield. ND = Not determined.

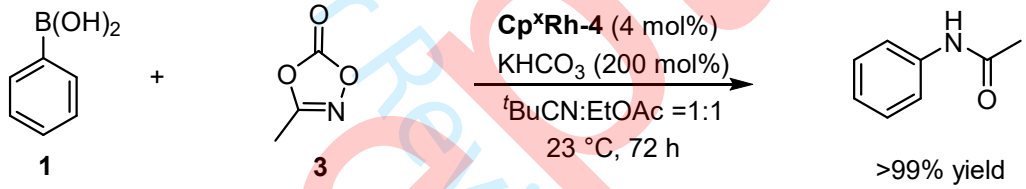
2.2. Representative Procedure for the three-component Carboamination of olefins



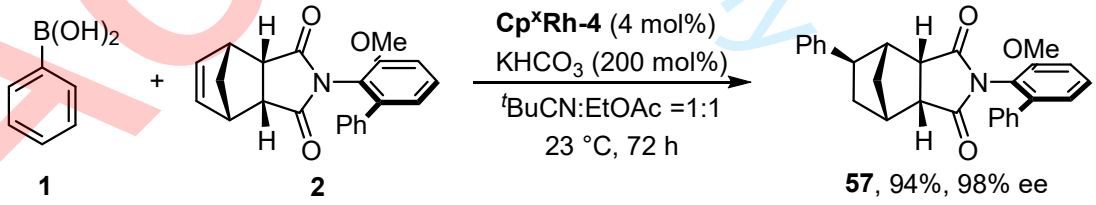
Under N_2 atmosphere, to a 8 mL tube were added arylboronic acid **1** (0.2 mmol), *N*-arylmaleimide adduct **2** (0.1 mmol) and $KHCO_3$ (200 mol%). Then, **Cp^{x}Rh-4** (4 mol%) and dioxazolone (0.3 mmol, 3 equiv) were dissolved in 0.30 mL (EtOAc/^{t}BuCN = 1:1, 0.3 mL) of the mixed solvent in a separate tube and transferred to the first one. It was rinsed with an additional 0.10 mL of the mixed solvent and transferred again to the first tube twice. After stirred at room temperature for 72 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated. The residue was purified by flash chromatography on silica gel or preparational TLC using ethyl acetate and hexane or DCM and MeOH as the eluent to afford the desired products **4-56**.

2.3 Mechanistic Studies

a) Control experiments

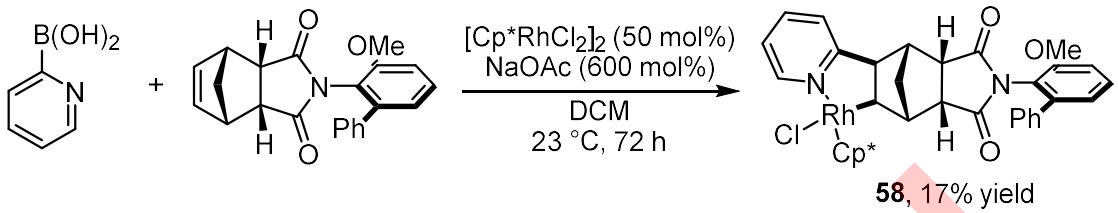


Under N_2 atmosphere, to a 8 mL tube were added arylboronic acid **1** (0.2 mmol), dioxazolone **3** (0.15 mol), $KHCO_3$ (200 mol%), **Cp^{x}Rh-4** (4 mol%) and 0.30 mL the mixed solvent (EtOAc/^{t}BuCN = 1:1, 0.5 mL). After stirred at room temperature for 72 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane as the eluent to afford the product (>99% yield).

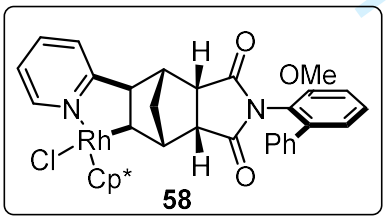


Under N_2 atmosphere, to a 8 mL tube were added arylboronic acid **1** (0.2 mmol), *N*-arylmaleimide adduct **2** (0.1 mmol), $KHCO_3$ (200 mol%), **Cp^{x}Rh-4** (4 mol%) and the mixed solvent (EtOAc/^{t}BuCN = 1:1, 0.5 mL). After stirred at room temperature for 72 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated. The residue was purified by flash chromatography on silica gel using ethyl acetate and hexane as the eluent to afford the desired hydroarylation product **57** (94%, 98% ee).

b) Intermediate studies

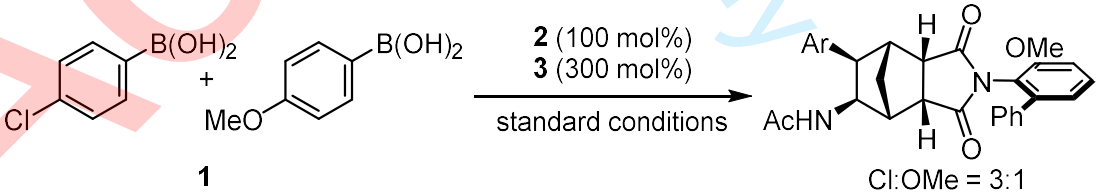


Under N_2 atmosphere, to a 8 mL tube were added 2-pyridineboronic acid (0.2 mmol), *N*-arylmaleimide adduct **2** (0.1 mmol), $KHCO_3$ (200 mol%), $[Cp^*RhCl_2]_2$ (4 mol%) and DCM (1.0 mL). After stirred at room temperature for 72 h, the reaction mixture was diluted with DCM, filtered, and concentrated. The residue was purified by preparational TLC using ethyl acetate and hexane as the eluent to afford the desired product **58** (17% yield).



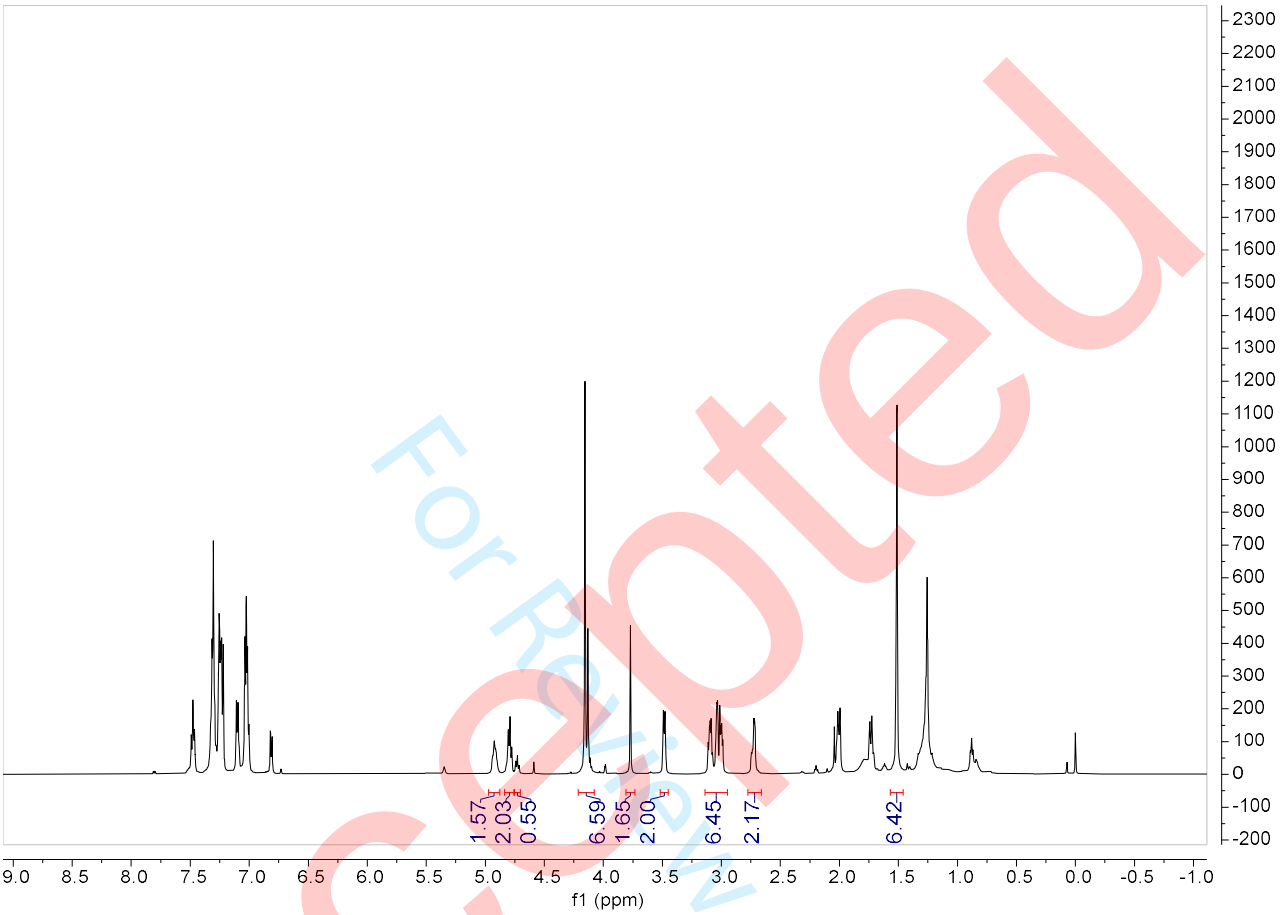
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (dd, J = 5.7, 1.6 Hz, 1H), 7.61 (td, J = 7.7, 1.6 Hz, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.36 – 7.30 (m, 3H), 7.28 – 7.27 (m, 2H), 7.26 – 7.25 (m, 1H),7.14 (t, J = 6.6 Hz, 1H), 7.08 (dd, J = 7.8, 1.2 Hz, 1H), 7.05 (dd, J = 8.4, 1.2 Hz, 1H), 3.83 – 3.81 (m, 1H), 3.77 (s, 3H), 3.62 (d, J = 8.4 Hz, 1H), 3.14 (dd, J = 9.5, 5.3 Hz, 1H), 2.80 (dd, J = 9.6, 5.1 Hz, 1H), 2.75 – 2.73 (m, 2H), 2.18 – 2.15 (m, 1H), 1.85 – 1.80 (m, 1H), 1.51 (s, 15H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 178.4, 177.6, 175.2, 155.3, 152.2, 143.0, 138.6, 136.9, 130.3, 128.2, 128.1, 127.7, 123.2, 122.9, 121.9, 119.5, 111.3, 94.7 (d, J = 6.5 Hz), 57.2, 56.5, 51.9, 49.7, 48.7, 48.1, 43.7, 43.5, 40.8, 8.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{37}H_{38}N_2NaClO_3$, ($[M\text{-}Cl]^+$): 661.1937, found: 661.1928.

c) Competive experiments



Under N_2 atmosphere, to a 8 mL tube were added 4-Chlorophenylboronic acid (0.1 mmol), 4-Methoxyphenylboronic acid (0.1 mmol), *N*-arylmaleimide adduct **2** (0.1 mmol) and $KHCO_3$ (200 mol%). Then, **Cp^{x}Rh-4** (4 mol%) and dioxazolone (0.3 mmol, 3 equiv) were dissolved in 0.30 mL (EtOAc/^{t}BuCN = 1:1, 0.30 mL) of the mixed solvent in a separate tube and transferred to the first one. It was rinsed with an additional 0.10 mL of the mixed solvent and transferred again to the first tube twice. After stirred at room temperature for 72 h, the reaction mixture was diluted with EtOAc, filtered, and concentrated. The residue was purified by flash chromatography on silica gel using ethyl acetate

and hexane as the eluent to afford the corresponding products, which were characterized by ^{1}H NMR spectroscopy.



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http://chem.scichina.com/english

3. X-Ray crystal structure of 4

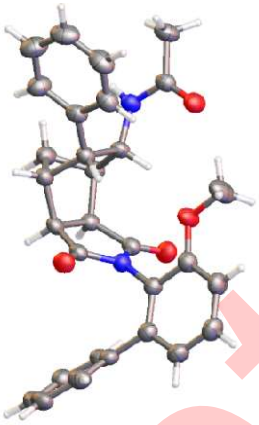


Table S7 Crystal data and structure refinement for 4.

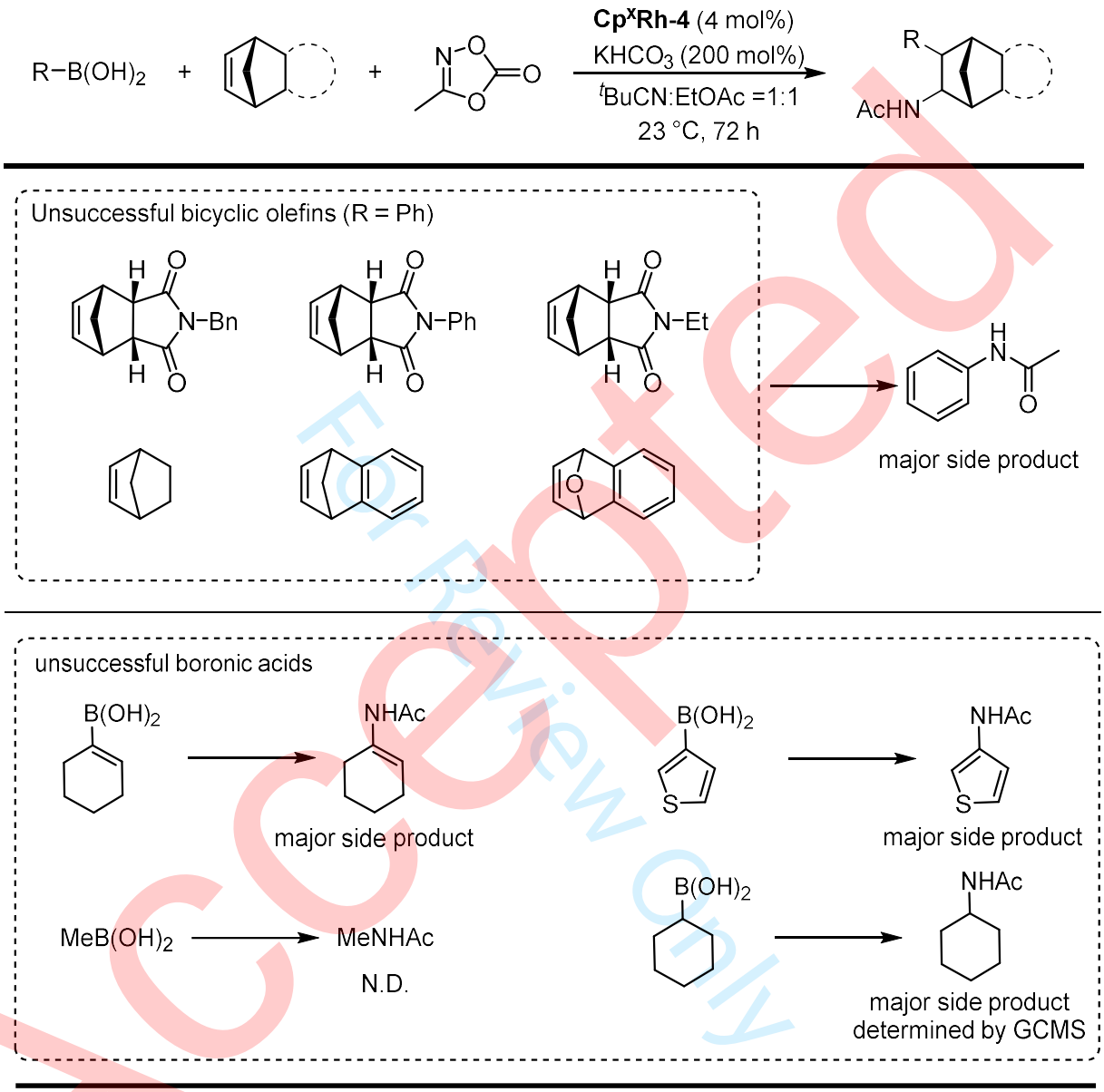
Identification code	s
Empirical formula	$C_{30}H_{28}N_2O_4$
Formula weight	480.54
Temperature/K	228.00
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.7702(13)
b/Å	12.9777(17)
c/Å	19.844(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2516.2(6)
Z	4
ρ_{calc}g/cm^3	1.269
μ/mm^{-1}	0.680
F(000)	1016.0
Crystal size/mm^3	0.5 × 0.4 × 0.3
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	11.336 to 136.996
Index ranges	-11 ≤ h ≤ 11, -15 ≤ k ≤ 15, -23 ≤ l ≤ 23
Reflections collected	34180
Independent reflections	4561 [R_{int} = 0.0531, R_{sigma} = 0.0300]
Data/restraints/parameters	4561/0/331

https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english

Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	$R_1 = 0.0316$, $wR_2 = 0.0828$
Final R indexes [all data]	$R_1 = 0.0390$, $wR_2 = 0.0907$
Largest diff. peak/hole / e $Å^{-3}$	0.25/-0.22
Flack parameter	-0.03(5)

https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english

4. Limitations



https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english

5. References

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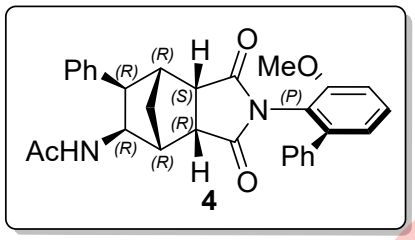
https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english

6. Characterization Data

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 4



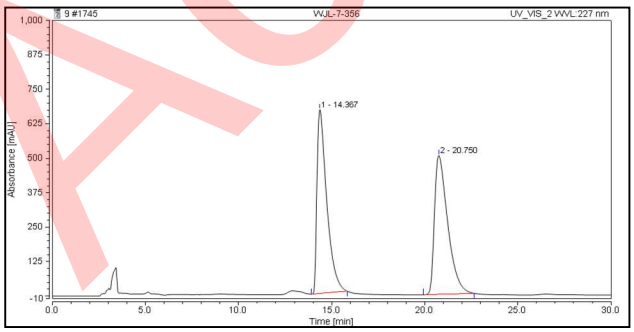
4

Prepared according to general procedure on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white solid (34.1 mg, 71% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.33 – 7.29 (m, 3H), 7.28 – 7.25 (m, 4H), 7.19 (t, J = 7.5 Hz, 1H), 7.11 – 7.09 (m, 3H), 7.02 (dd, J = 7.7, 1.2 Hz, 1H), 4.82 – 4.76 (m, 2H), 4.16 (s, 3H), 3.54 (d, J = 6.1 Hz, 1H), 3.11 – 3.09 (m, 2H), 3.01 (dd, J = 10.0, 5.2 Hz, 1H), 2.75 (d, J = 5.5 Hz, 1H), 2.04 (d, J = 11.0, 1H), 1.75 (d, J = 11.0 Hz, 1H), 1.47 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.7, 155.2, 142.9, 138.6, 138.4, 130.7, 128.3, 128.3, 128.1, 128.1, 127.6, 126.6, 122.2, 118.6, 111.0, 56.2, 52.0, 48.5, 47.6, 47.1, 45.2, 42.9, 39.7, 22.9.

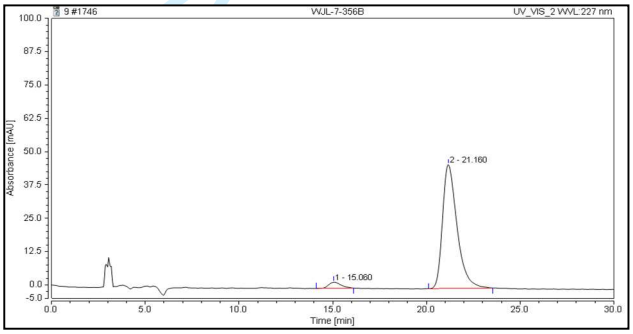
HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{28}N_2NaO_4$, ($[M + Na]^+$): 503.1941, found: 503.1934.

$[\alpha]_D^{20}$ = 88 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA-H column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 21.16 min, tr (minor) = 15.06 min, 92% ee.

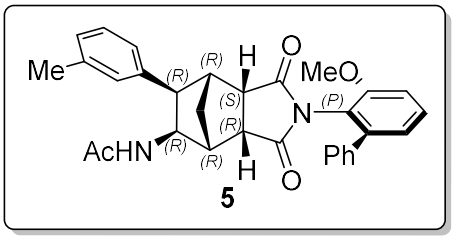


No.	Retention Time min	Area mAU*min	Relative Area %
1	14.367	407.132	49.53
2	20.750	414.872	50.47



No.	Retention Time min	Area mAU*min	Relative Area %
1	15.060	1.733	3.99
2	21.160	41.678	96.01

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-(m-tolyl)octahydro-1H-4,7-methanoisoindol-5-yl)acetamide 5



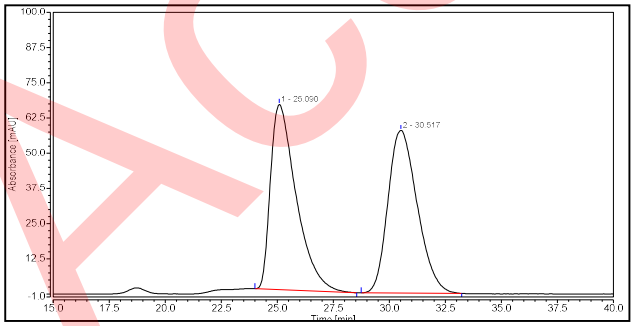
5

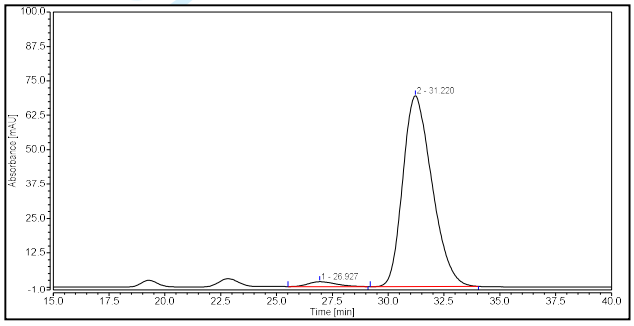
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white solid (40.5 mg, 82% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.32 – 7.29 (m, 3H), 7.26 – 7.24 (m, 2H), 7.15 (t, J = 7.7 Hz, 1H), 7.10 – 7.09 (m, 1H), 7.02 – 6.99 (m, 2H), 6.89 – 6.89 (m, 2H), 4.84 (brs, 1H), 4.78– 4.75 (m, 1H), 4.14 (s, 3H), 3.50 (d, J = 8.3 Hz, 1H), 3.09 – 3.06 (m, 2H), 2.99 (dd, J = 10.0, 5.2 Hz, 1H), 2.73 (d, J = 5.6 Hz, 1H), 2.30 (s, 3H), 2.03 (d, J = 10.4 Hz, 1H), 1.71 (d, J = 10.3 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.1, 175.9, 168.8, 155.2, 142.9, 138.5, 138.4, 137.9, 130.6, 128.9, 128.3, 128.2, 128.2, 127.6, 127.3, 125.1, 122.2, 118.6, 111.0, 56.2, 52.0, 48.5, 47.4, 47.1, 45.2, 42.9, 39.7, 22.9, 21.5.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_4$, ($[M + Na]^+$): 517.2098, found: 517.2093.

$[\alpha]_D^{20}$ = 108 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 31.22 min, tr (minor) = 26.93 min, 95% ee.

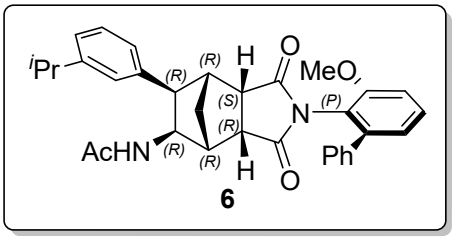




No.	Retention Time min	Area mAU*min	Relative Area %
1	25.09	87.505	50.00
2	30.52	87.507	50.00

No.	Retention Time min	Area mAU*min	Relative Area %
1	26.93	2.613	2.43
2	31.22	105.014	97.57

(P)-N-((*3aR,4R,5R,6R,7R,7aS*)-6-(3-isopropylphenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 6



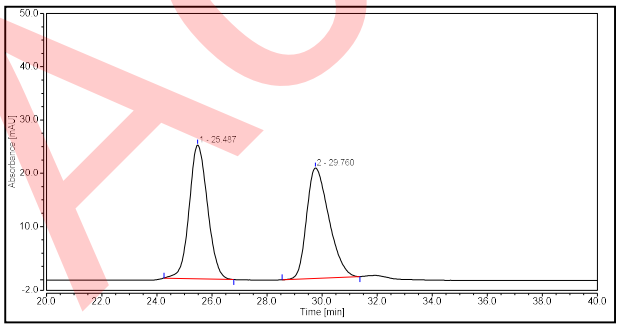
6

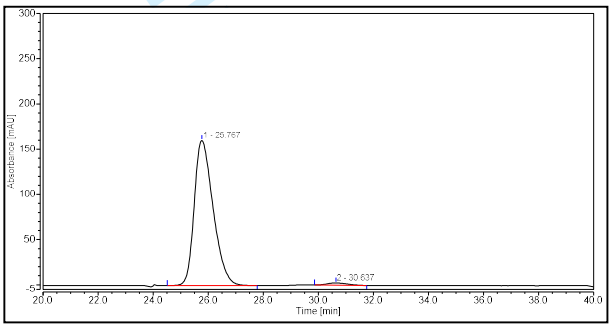
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (33.6 mg, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.33 – 7.27(m, 3H), 7.25 – 7.23 (m, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.09 (dd, J = 8.5, 1.2 Hz, 1H), 7.05 – 7.00 (m, 2H), 6.92 – 6.90 (m, 2H), 4.82 – 4.75 (m, 2H), 4.15 (s, 3H), 3.51 (d, J = 10.3 Hz, 1H), 3.09 – 3.05 (m, 2H), 2.99 (dd, J = 9.8, 5.2 Hz, 1H), 2.86 – 2.79 (m, 1H), 2.72 (d, J = 5.5 Hz, 1H), 2.03 – 2.00 (m, 1H), 1.71 (d, J = 10.9 Hz, 1H), 1.43 (s, 3H), 1.19 (dd, J = 6.9, 1.7 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.3, 176.0, 168.7, 155.2, 149.0, 143.0, 138.6, 138.5, 130.8, 128.4, 128.3, 128.2, 127.7, 127.3, 124.9, 124.4, 122.3, 118.6, 111.0, 56.2, 52.0, 48.6, 47.7, 47.2, 45.3, 42.9, 39.8, 34.1, 24.1, 24.1, 23.0.

HRMS (ESI-TOF) (m/z): Calcd for $C_{33}H_{34}N_2NaO_4$, ($[M + Na]^+$): 545.2411, found: 545.2402.

$[\alpha]_D^{20}$ = 58 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 30.64min, tr (minor) = 25.77 min, 96% ee.

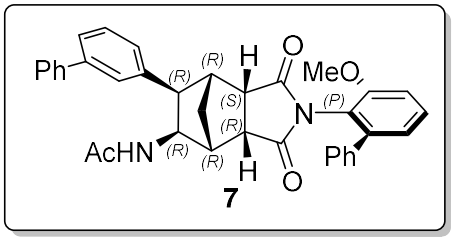




No.	Retention Time min	Area mAU*min	Relative Area %
1	25.487	19.402	49.98
2	29.760	19.414	50.02

No.	Retention Time min	Area mAU*min	Relative Area %
1	25.767	127.413	98.39
2	30.637	2.088	1.61

(*P*)- *N*- ((*3aR,4R,5R,6R,7R,7aS*)-6-([1,1'-biphenyl]-3-yl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 7



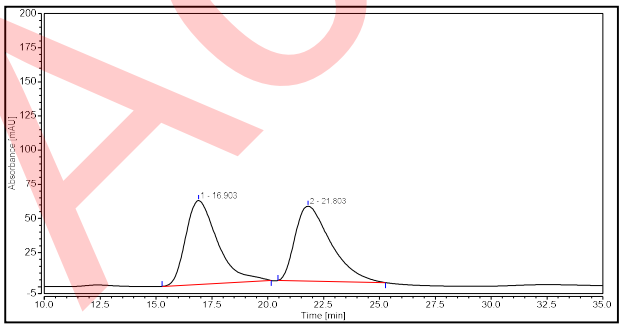
7

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (44.1 mg, 79% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 – 7.54 (m, 2H), 7.48 – 7.40 (m, 4H), 7.36 – 7.29 (m, 6H), 7.26 – 7.24 (m, 2H), 7.10 – 7.06 (m, 2H), 7.01 (dd, J = 7.7, 1.2 Hz, 1H), 4.92 – 4.83 (m, 2H), 4.17 (s, 3H), 3.60 (d, J = 7.4 Hz, 1H), 3.15 (d, J = 5.2 Hz, 1H), 3.12 – 3.07 (m, 1H), 3.01 (ddd, J = 10.0, 5.1, 1.4 Hz, 1H), 2.74 (d, J = 5.5 Hz, 1H), 2.06 (d, J = 11.0 Hz, 1H), 1.75 (d, J = 11.0 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.2, 176.0, 168.9, 155.3, 143.0, 141.2, 141.1, 139.3, 138.5, 130.8, 129.0, 128.8, 128.3, 128.2, 127.8, 127.6, 127.1, 126.5, 125.5, 122.3, 118.6, 111.0, 56.3, 52.2, 48.5, 47.9, 47.2, 45.2, 43.0, 39.9, 23.0.

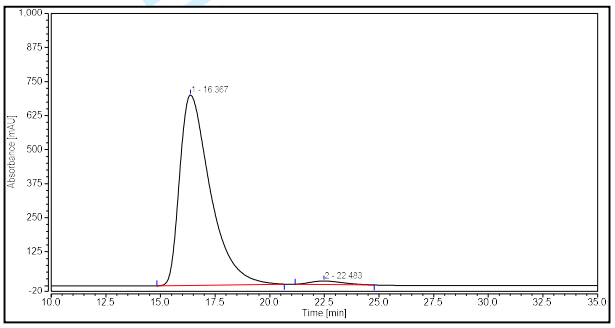
HRMS (ESI-TOF) (m/z): Calcd for $C_{36}H_{32}N_2NaO_4$, ($[M + Na]^+$): 579.2255, found: 579.2249.

$[\alpha]_D^{20}$ = 112 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 16.37 min, tr (minor) = 22.48 min, 96% ee.

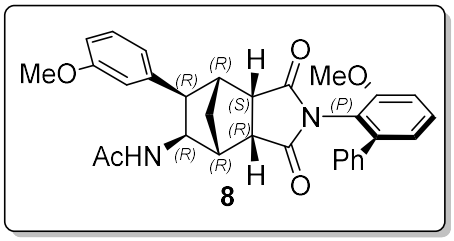


No.	Retention Time min	Area mAU*min	Relative Area %
1	16.903	101.661	49.92
2	21.803	101.996	50.08



No.	Retention Time min	Area mAU*min	Relative Area %
1	16.367	1135.894	98.05
2	22.483	22.540	1.95

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-6-(3-methoxyphenyl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 8



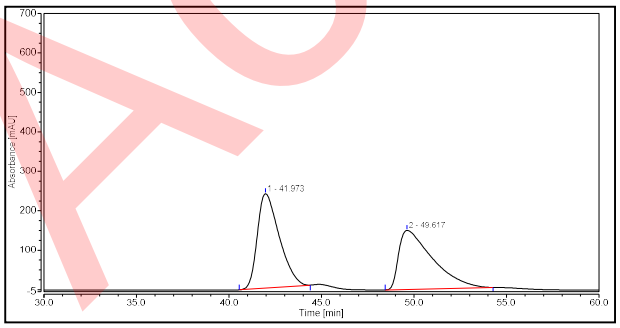
8

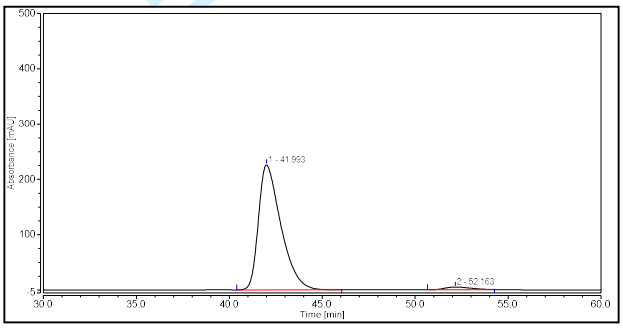
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (23.3 mg, 46% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 1H), 7.33 – 7.29 (m, 3H), 7.26 – 7.25 (m, 2H), 7.19 (t, J = 7.9 Hz, 1H), 7.09 (dd, J = 8.4, 1.2 Hz, 1H), 7.02 (dd, J = 7.7, 1.2 Hz, 1H), 6.74 – 6.72 (m, 1H), 6.69 – 6.67 (m, 1H), 6.65 – 6.64 (m, 1H), 4.80 (d, J = 4.2 Hz, 2H), 4.15 (s, 3H), 3.77 (s, 3H), 3.52 – 3.50 (m, 1H), 3.10 – 3.08 (m, 2H), 3.00 (dd, J = 9.9, 5.2 Hz, 1H), 2.75 – 2.73 (m, 1H), 2.03 – 2.00 (m, 1H), 1.73 (d, J = 11.0 Hz, 1H), 1.51 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.8, 159.5, 155.2, 142.9, 140.3, 138.4, 130.6, 129.3, 128.2, 128.1, 128.1, 127.6, 122.2, 120.2, 118.6, 114.2, 111.7, 110.9, 56.2, 55.2, 52.0, 48.4, 47.6, 47.1, 45.2, 42.9, 39.7, 23.0.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_5$, ($[M + Na]^+$): 533.2047, found: 533.2041.

$[\alpha]_D^{20}$ = 76 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 41.99 min, tr (minor) = 51.16 min, 95% ee.

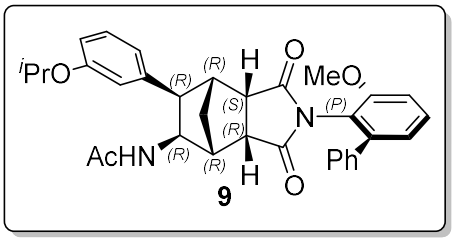




No.	Retention Time min	Area mAU*min	Relative Area %
1	41.973	330.104	51.07
2	49.617	316.209	48.93

No.	Retention Time min	Area mAU*min	Relative Area %
1	41.993	316.753	97.57
2	52.163	7.878	2.43

(*P*)- *N*-((*3aR,4R,5R,6R,7R,7aS*)-6-(3-isopropoxyphenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 9

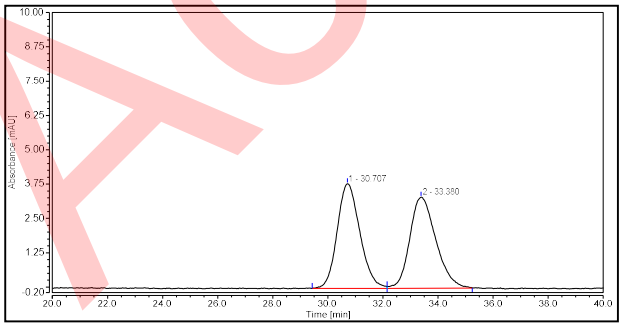


Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (32.4 mg, 60% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.31 – 7.27 (m, 3H), 7.25 – 7.23 (m, 2H), 7.15 (t, J = 7.9 Hz, 1H), 7.08 (dd, J = 8.4, 1.2 Hz, 1H), 7.00 (dd, J = 7.7, 1.2 Hz, 1H), 6.70 (dd, J = 8.1, 2.4 Hz, 1H), 6.64 – 6.60 (m, 2H), 4.84 – 4.75 (m, 2H), 4.49 (hept, J = 6.0 Hz, 1H), 4.13 (s, 3H), 3.47 (d, J = 8.7 Hz, 1H), 3.10 – 3.06 (m, 2H), 2.98 (dd, J = 9.8, 5.2 Hz, 1H), 2.72 (d, J = 5.5 Hz, 1H), 2.02 (d, J = 10.5 Hz, 1H), 1.71 (d, J = 10.9 Hz, 1H), 1.50 (s, 3H), 1.30 (t, J = 6.6 Hz, 7H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.1, 176.0, 168.9, 157.9, 155.2, 143.0, 140.4, 138.5, 130.8, 129.4, 128.3, 128.2, 127.7, 122.3, 120.4, 118.6, 116.0, 113.6, 111.0, 69.9, 56.2, 52.0, 48.5, 47.6, 47.2, 45.2, 43.0, 39.8, 23.1, 22.2, 22.1.

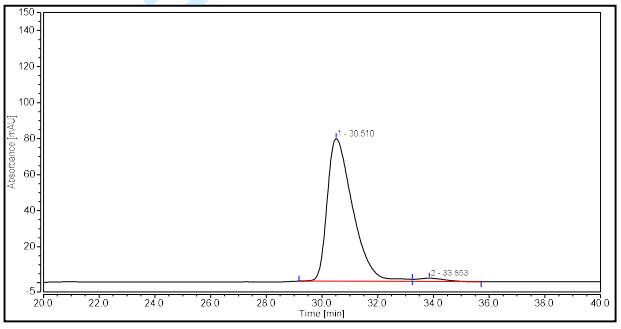
HRMS (ESI-TOF) (m/z): Calcd for $C_{33}H_{34}N_2NaO_5$, ($[M + Na]^+$): 561.2360, found: 561.2351.

$[\alpha]_D^{20}$ = 102 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 30.51 min, tr (minor) = 33.85 min, 95% ee.

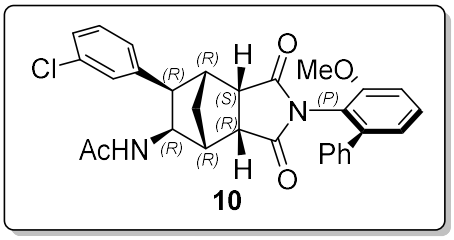


No.	Retention Time min	Area mAU*min	Relative Area %
1	30.707	3.643	50.02
2	33.380	3.640	49.98



No.	Retention Time min	Area mAU*min	Relative Area %
1	30.510	83.958	97.51
2	33.853	2.145	2.49

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-6-(3-chlorophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 10



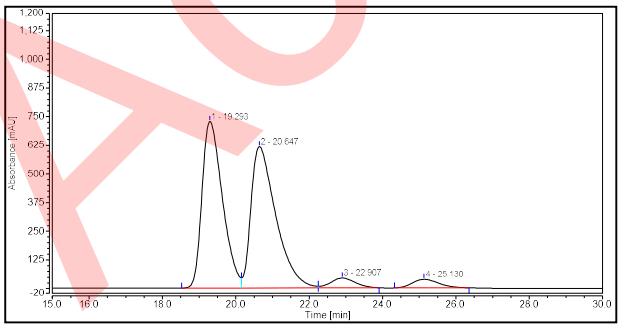
10

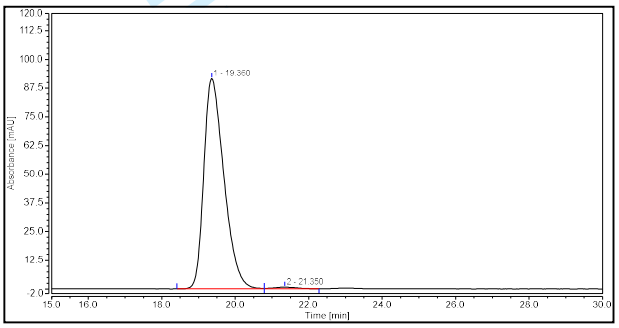
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (30.0 mg, 58% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (t, J = 8.0 Hz, 1H), 7.33 – 7.29 (m, 3H), 7.26 – 7.24 (m, 2H), 7.21 – 7.16 (m, 2H), 7.11 – 7.08 (m, 2H), 7.02 (d, J = 7.7 Hz, 1H), 6.97 (dd, J = 7.2, 1.9 Hz, 1H), 4.93 – 4.89 (m, 1H), 4.81 (d, J = 9.6 Hz, 1H), 4.17 (s, 3H), 3.50 (d, J = 8.2 Hz, 1H), 3.11 (dd, J = 9.8, 5.6 Hz, 1H), 3.06 – 3.05 (m, 1H), 3.01 (dd, J = 9.9, 5.3 Hz, 1H), 2.73 (d, J = 5.6 Hz, 1H), 2.02 (d, J = 11.1 Hz, 1H), 1.51 (m, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.4, 175.6, 169.1, 154.2, 143.8, 141.0, 138.4, 134.9, 131.8, 129.5, 128.2, 128.1, 127.7, 127.6, 127.1, 126.7, 122.2, 118.4, 111.0, 56.2, 52.1, 48.3, 47.7, 47.1, 45.1, 42.9, 39.8, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}N_2NaClO_4$, ([M + Na]$^+$): 537.1552, found: 537.1547.

$[\alpha]_D^{20}$ = 90 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 19.36 min, tr (minor) = 21.36 min, 98% ee.

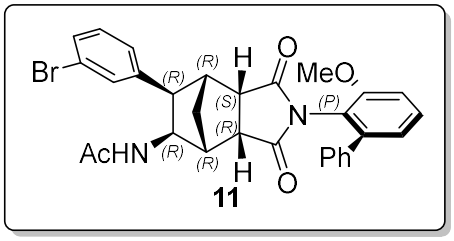




No.	Retention Time min	Area mAU*min	Relative Area %
1	19.293	468.643	46.11
2	20.647	483.614	47.58
3	22.907	33.173	3.26
4	25.130	30.966	3.05

No.	Retention Time min	Area mAU*min	Relative Area %
1	19.360	58.169	99.11
2	21.350	0.520	0.89

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-6-(3-bromophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 11

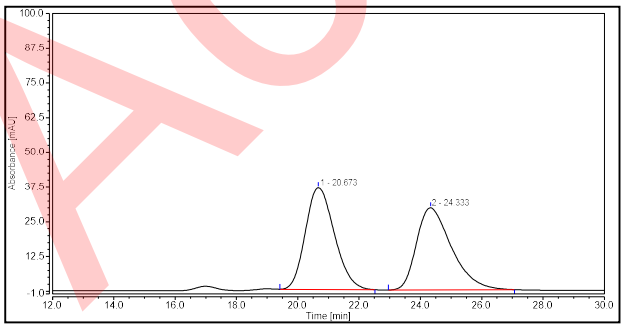


Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (45.1 mg, 81% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.33 – 7.29 (m, 4H), 7.25 – 7.22 (m, 3H), 7.13 – 7.09 (m, 2H), 7.02 (dd, J = 7.7, 1.3 Hz, 2H), 4.99 (d, J = 9.5 Hz, 1H), 4.81 – 4.78 (m, 1H), 4.16 (s, 3H), 3.49 (dd, J = 8.2, 1.8 Hz, 1H), 3.09 (dd, J = 9.8, 5.6 Hz, 1H), 3.05 – 3.04 (m, 1H), 3.00 (dd, J = 9.8, 5.3 Hz, 1H), 2.71 (d, J = 5.6 Hz, 1H), 2.01 (d, J = 11.1 Hz, 1H), 1.74 (d, J = 11.2 Hz, 1H), 1.50 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.7, 168.8, 155.2, 142.9, 141.3, 138.4, 130.7, 130.5, 129.8, 129.6, 128.2, 128.2, 128.1, 127.7, 127.6, 122.3, 122.2, 118.5, 111.0, 56.2, 52.2, 48.3, 47.8, 47.1, 45.1, 42.9, 39.7, 22.8.

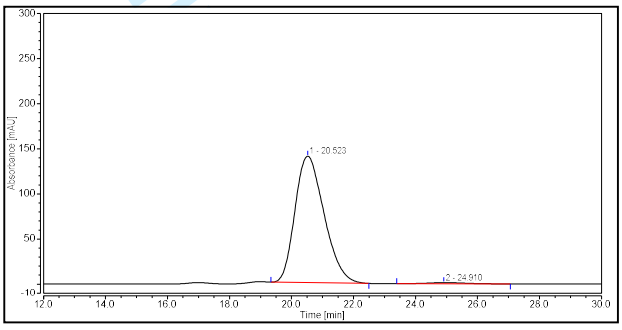
HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}BrN_2NaO_4$, ([M + Na]$^+$): 581.1046, found: 581.1045.

$[\alpha]_D^{20}$ = 68 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 20.52 min, tr (minor) =24.91 min, 98% ee.

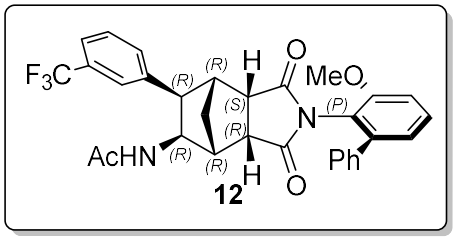


No.	Retention Time min	Area mAU*min	Relative Area %
1	20.673	40.293	50.70
2	24.333	39.184	49.30



No.	Retention Time min	Area mAU*min	Relative Area %
1	20.523	152.629	98.92
2	24.910	1.667	1.08

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-(3-(trifluoro-methyl)phenyl)octahydro-1H-4,7-methanoisoindol-5-yl)acetamide 12



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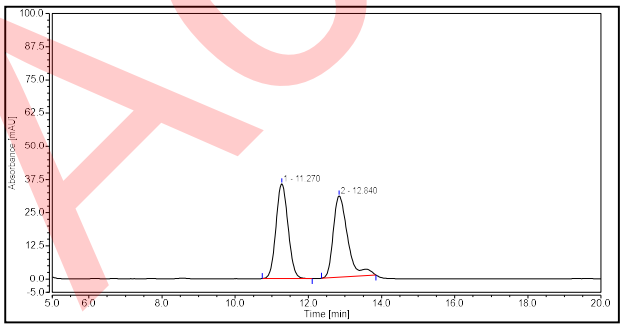
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (31.3 mg, 57% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 2H), 7.40 – 7.34 (m, 2H), 7.32 – 7.27 (m, 4H), 7.25 – 7.22 (m, 2H), 7.10 (dd, J = 8.5, 1.2 Hz, 1H), 7.01 (dd, J = 7.7, 1.2 Hz, 1H), 4.97 – 4.91 (m, 1H), 4.83 (t, J = 8.7 Hz, 1H), 4.17 (s, 3H), 3.57 (d, J = 7.3 Hz, 1H), 3.13 – 3.08 (m, 2H), 3.02 (dd, J = 9.8, 5.2 Hz, 1H), 2.72 (d, J = 5.4 Hz, 1H), 2.04 (d, J = 11.2 Hz, 1H), 1.77 (d, J = 11.1 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.0, 175.8, 168.8, 155.2, 143.0, 140.0, 138.4, 132.1, 130.9, 130.5 (q, J = 32.0 Hz), 128.7, 128.31, 128.26, 127.8, 124.5, 124.1 (q, J = 271.1 Hz), 123.5 (q, J = 3.8 Hz), 122.3, 118.4, 111.0, 56.3, 52.3, 48.4, 48.1, 47.1, 45.1, 43.1, 39.9, 22.7.

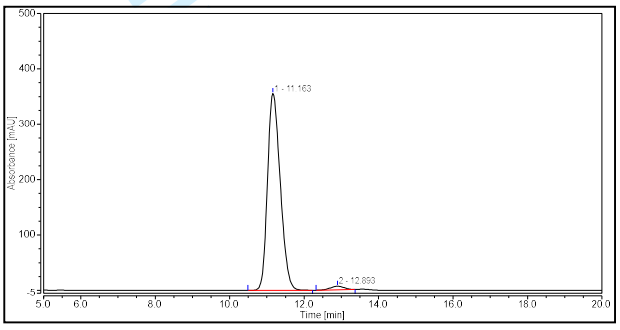
HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{27}F_3N_2NaO_4$, ([M + Na]$^+$): 571.1815, found: 571.1805.

[α]$_D^{20}$ = 72 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 11.16 min, tr (minor) =12.89 min, 96% ee.

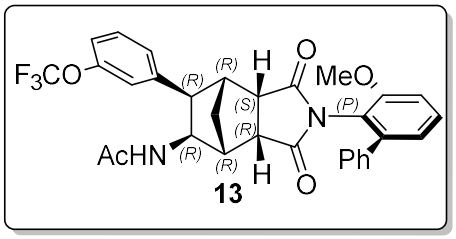


No.	Retention Time min	Area mAU*min	Relative Area %
1	11.270	13.633	49.45
2	12.840	13.937	50.55



No.	Retention Time min	Area mAU*min	Relative Area %
1	11.163	140.855	98.06
2	12.893	2.781	1.94

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-(3-(trifluoro-methoxy)phenyl)octahydro-1H-4,7-methanoisoindol-5-yl)acetamide 13

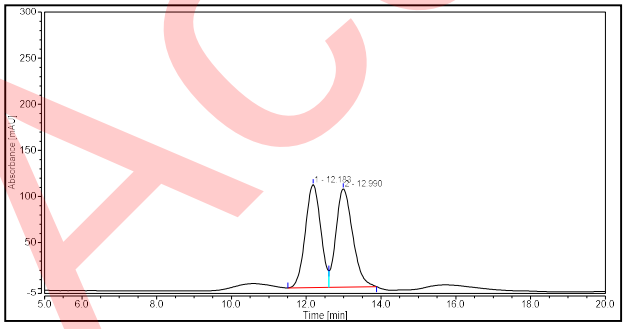


Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (45.7 mg, 81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.32 – 7.28 (m, 3H), 7.25 – 7.22 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H), 7.05 – 7.00 (m, 3H), 6.94 (s, 1H), 4.99 – 4.95 (m, 1H), 4.82 – 4.78 (m, 1H), 4.15 (s, 3H), 3.52 (d, J = 8.0 Hz, 1H), 3.11 – 3.07 (m, 1H), 3.05 – 2.98 (m, 2H), 2.71 (d, J = 5.5 Hz, 1H), 2.01 (d, J = 10.9 Hz, 1H), 1.74 (d, J = 11.1 Hz, 1H), 1.46 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.0, 175.8, 168.8, 155.2, 149.2, 142.9, 141.4, 138.4, 130.9, 129.6, 128.3, 128.2, 127.8, 126.9, 122.3, 120.6, 120.5 (q, J = 7.7 Hz), 119.1, 118.4, 111.8, 56.2, 52.2, 48.4, 47.9, 47.1, 45.1, 43.2, 39.9, 22.7.

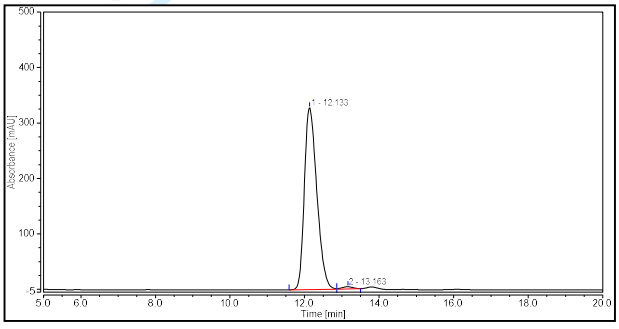
HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{27}F_3N_2NaO_5$, ([M + Na]$^+$): 587.1764, found: 587.1763.

[α]$_D^{20}$ = 74 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 12.13 min, tr (minor) =13.16 min, 98% ee.

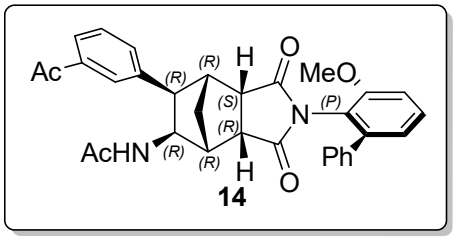


No.	Retention Time min	Area mAU*min	Relative Area %
1	12.183	53.282	49.20
2	12.990	55.006	50.80



No.	Retention Time min	Area mAU*min	Relative Area %
1	12.133	126.633	98.95
2	13.163	1.343	1.05

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-6-(3-acetylphenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 14



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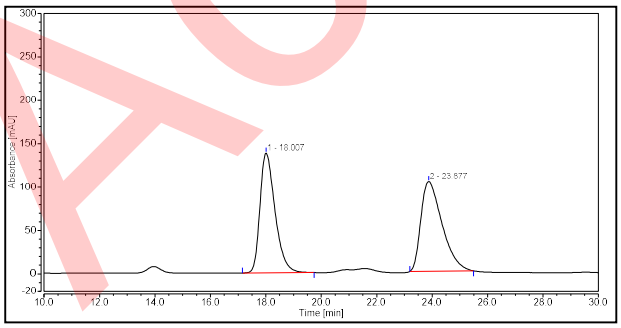
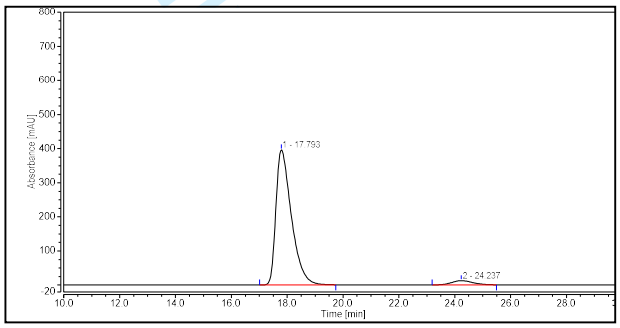
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (36.1 mg, 69% yield). **^{1}H NMR** (600 MHz, acetone-d_6) δ 7.81 – 7.78 (m, 2H), 7.55 (t, J = 8.0 Hz, 1H), 7.44 – 7.33 (m, 5H), 7.29 – 7.27 (m, 1H), 7.25 – 7.24 (m, 2H), 7.04 (dd, J = 7.7, 1.2 Hz, 1H), 6.73 (d, J = 9.4 Hz, 1H), 4.90 – 4.87 (m, 1H), 4.28 (s, 3H), 3.56 (d, J = 7.9 Hz, 1H), 3.28 (dd, J = 9.9, 5.7 Hz, 1H), 3.13 (dd, J = 10.0, 5.3 Hz, 1H), 3.03 (dd, J = 5.2, 1.6 Hz, 1H), 2.69 (dd, J = 5.6, 1.6 Hz, 1H), 2.57 (s, 3H), 2.39 (d, J = 11.0 Hz, 1H), 1.89 (d, J = 11.0, 1H), 1.36 (s, 3H). **^{13}C NMR** (150 MHz, acetone-d_6) δ 197.1, 176.0, 176.0, 168.1, 155.7, 142.8, 140.3, 138.6, 136.72 132.8, 130.5, 128.9, 128.1, 128.1, 127.9, 127.6, 125.6, 121.8, 119.4, 110.9, 55.9, 52.5, 48.6, 48.5, 47.1, 45.0, 43.2, 39.5, 25.9, 21.5.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{30}N_2NaO_5$, ([M + Na]$^+$): 545.2047, found: 545.2041.

[α]$_D^{20}$ = 64 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 70:30, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 17.79 min, tr (minor) =24.24 min, 92% ee.

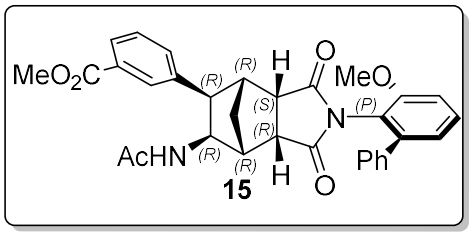




No.	Retention Time min	Area mAU*min	Relative Area %
1	18.007	87.026	48.73
2	23.877	91.552	51.27

No.	Retention Time min	Area mAU*min	Relative Area %
1	17.793	253.703	95.83
2	24.237	11.050	4.17

(*P*)-methyl-3-((*3aS,4R,5R,6R,7R,7aR*)-6-acetamido-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)benzoate 15

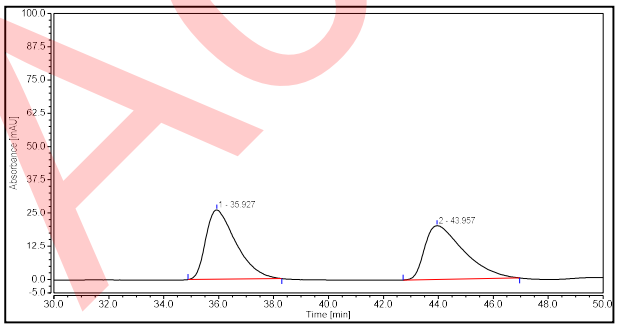


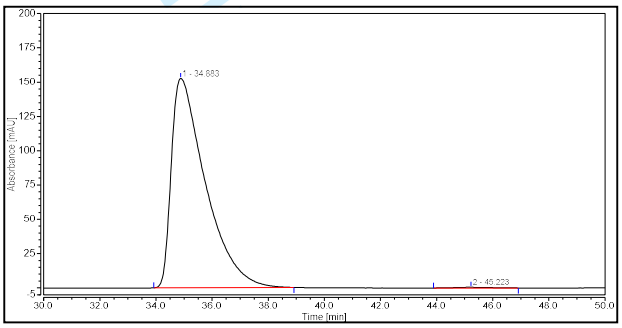
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (38.3 mg, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.5 Hz, 1H), 7.81 (s, 1H), 7.48 (t, J = 8.1 Hz, 1H), 7.36 – 7.30 (m, 5H), 7.28 – 7.24 (m, 2H), 7.12 (dd, J = 8.5, 1.2 Hz, 1H), 7.02 (dd, J = 7.8, 1.2 Hz, 1H), 4.97 – 4,94 (m, 1H), 4.82 (t, J = 8.7 Hz, 1H), 4.20 (s, 3H), 3.90 (s, 3H), 3.58 (dd, J = 8.2, 1.7 Hz, 1H), 3.15 – 3.10 (m, 2H), 3.05 – 3.01 (m, 1H), 2.75 (d, J = 5.6 Hz, 1H), 2.12 (m, J = 11.2 Hz, 1H), 1.79 (d, J = 11.3 Hz, 2H), 1.45 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.1, 175.9, 168.7, 167.1, 155.2, 143.0, 139.4, 138.4, 134.2, 130.8, 130.0, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 122.3, 118.4, 111.0, 56.3, 52.4, 52.4, 48.5, 48.0, 47.1, 45.1, 43.3, 40.0, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{30}N_2NaO_6$, ($[M + Na]^+$): 561.1996, found: 561.1989.

$[\alpha]_D^{20}$ = 74 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 34.88 min, tr (minor) =45.22 min, 99% ee.

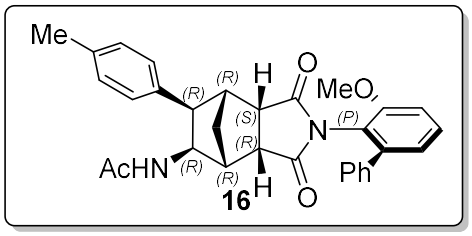




No.	Retention Time min	Area mAU*min	Relative Area %
1	35.927	33.276	49.97
2	43.957	33.312	50.03

No.	Retention Time min	Area mAU*min	Relative Area %
1	34.883	214.463	99.66
2	45.223	0.742	0.34

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-(p-tolyl)octahydro-1H-4,7-methanoisoindol-5-yl)acetamide 16

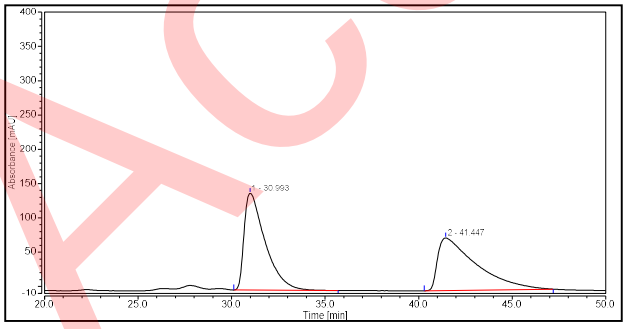


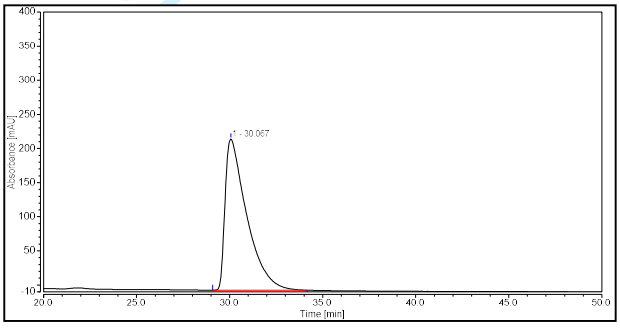
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (39.5 mg, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.32 – 7.28 (m, 3H), 7.26 – 7.24 (m, 2H), 7.10 – 7.06 (m, 3H), 7.01 (dd, J = 7.7, 1.2 Hz, 1H), 6.98 – 6.95 (m, 2H) 4.87 – 4.83(m, 1H), 4.76 – 4.71 (m, 1H), 4.13 (s, 3H), 3.49 (d, J = 8.2 Hz, 1H), 3.12 – 3.05 (m, 2H), 3.01 – 2.97 (m, 1H), 2.73 (d, J = 5.5 Hz, 1H), 2.29 (s, 3H), 2.03 – 2.00 (m, 1H), 1.72 – 1.69 (m, 1H), 1.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.2, 176.0, 168.9, 155.2, 142.9, 138.5, 136.3, 135.5, 130.8, 129.1, 128.3, 128.2, 128.0, 127.7, 122.3, 118.6, 111.0, 56.3, 52.1, 48.6, 47.2, 47.2, 45.2, 43.1, 39.8, 23.0, 21.1.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_4$, ($[M + Na]^+$): 517.2098, found: 517.2095.

$[\alpha]_D^{20}$ = 82 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak ID column (hexane: 2-propanol = 75:25, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 30.07 min, >99% ee.

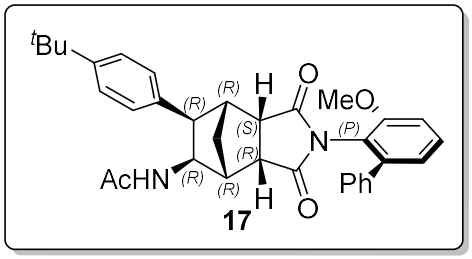




No.	Retention Time min	Area mAU*min	Relative Area %
1	30.993	184.698	50.28
2	41.447	182.617	49.72

No.	Retention Time min	Area mAU*min	Relative Area %
1	30.067	298.302	100.00
2	-	-	-

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-6-(4-(tert-butyl)phenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 17



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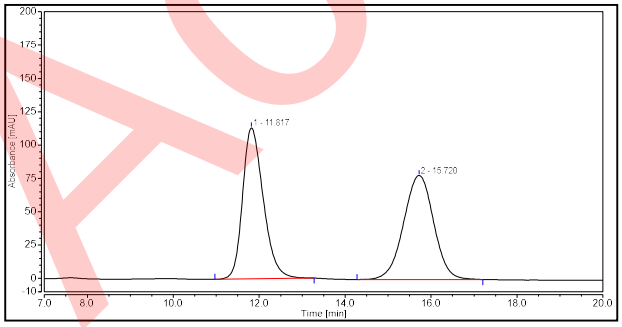
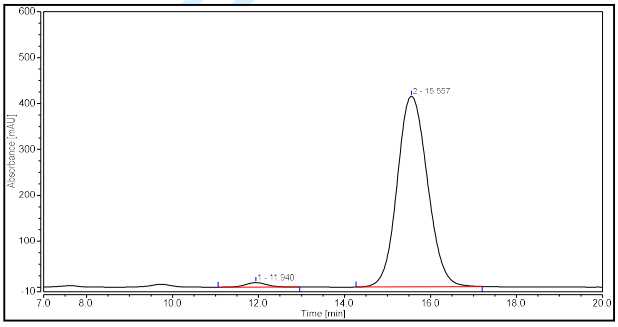
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (37.0 mg, 69% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.32 – 7.28 (m, 5H), 7.26 – 7.24 (m, 2H), 7.10 (dd, J = 8.4, 1.2 Hz, 1H), 7.03 – 7.00 (m, 3H), 4.84 (d, J = 9.5 Hz, 1H), 4.76 (t, J = 8.0 Hz, 1H), 4.15 (s, 3H), 3.51 (d, J = 8.2 Hz, 1H), 3.08 – 3.06 (m, 2H), 2.99 (dd, J = 9.9, 5.2 Hz, 1H), 2.72 (d, J = 5.6 Hz, 1H), 2.04 – 2.02 (m, 1H), 1.71 (d, J = 11.0 Hz, 1H), 1.42 (s, 3H), 1.28 (s, 9H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.1, 175.9, 168.8, 155.2, 149.6, 142.9, 138.4, 135.6, 130.6, 128.2, 128.15, 128.12, 127.8, 127.6, 125.2, 122.2, 118.6, 110.9, 56.2, 52.1, 48.5, 47.2, 47.1, 45.1, 43.0, 39.7, 34.4, 31.3, 31.6, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{34}H_{36}N_2NaO_4$, ($[M + Na]^+$): 559.2567, found: 559.2563.

$[\alpha]_D^{20}$ = 76 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 °C, 227 nm); tr (major) = 15.56 min, tr (minor) =11.94 min, 96% ee.

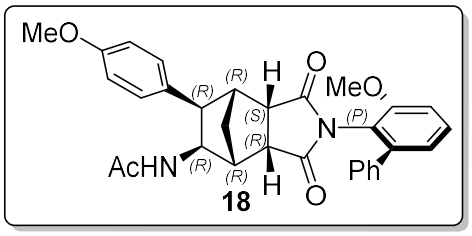




No.	Retention Time min	Area mAU*min	Relative Area %
1	11.817	63.303	50.06
2	15.720	63.145	49.94

No.	Retention Time min	Area mAU*min	Relative Area %
1	11.940	5.686	1.65
2	15.557	338.003	98.35

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-6-(4-methoxyphenyl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 18

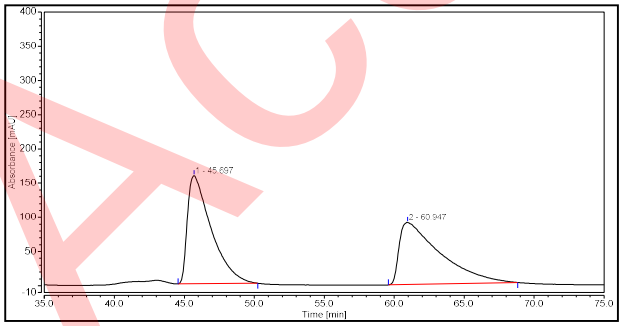


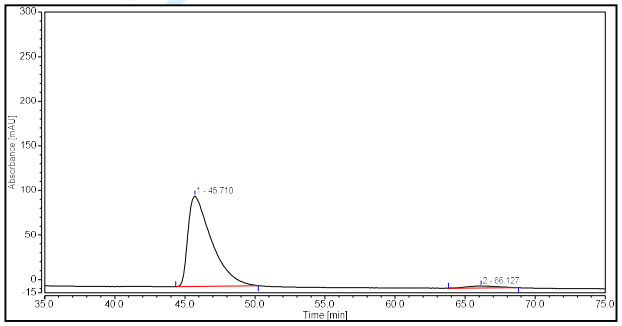
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (31.3 mg, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.35 – 7.32 (m, 3H), 7.26 – 7.24 (m, 2H), 7.11– 7.08 (m, 1H), 7.03 – 7.00 (m, 3H), 6.84 – 6.80 (m, 2H), 4.86 (d, J = 9.4 Hz, 1H), 4.72 (t, J = 8.7 Hz, 1H), 4.13 (s, 3H), 3.77 (s, 3H), 3.48 (d, J = 8.2 Hz, 1H), 3.10 – 2.98 (m, 3H), 2.74 (d, J = 5.5 Hz, 1H), 2.02 (d, J = 11.1 Hz, 1H), 1.71 (d, J = 11.0 Hz, 1H), 1.51 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.2, 176.0, 168.9, 158.2, 155.2, 142.9, 138.5, 130.8, 130.6, 129.2, 128.3, 128.2, 127.7, 122.3, 118.6, 113.8, 111.0, 56.3, 55.4, 52.2, 48.6, 47.2, 46.9, 45.2, 43.3, 39.7, 23.1.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_5$, ($[M + Na]^+$): 533.2047, found: 533.2040.

$[\alpha]_D^{20}$ = 106 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak ID column (hexane: 2-propanol = 75:25, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 45.71 min, tr (minor) =66.13 min, 94% ee.

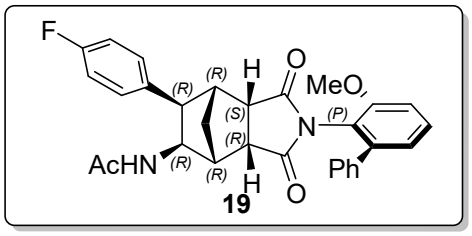




No.	Retention Time min	Area mAU*min	Relative Area %
1	45.697	312.588	50.39
2	60.947	307.782	49.61

No.	Retention Time min	Area mAU*min	Relative Area %
1	45.710	198.259	97.23
2	66.127	5.639	2.77

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-6-(4-fluorophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 19



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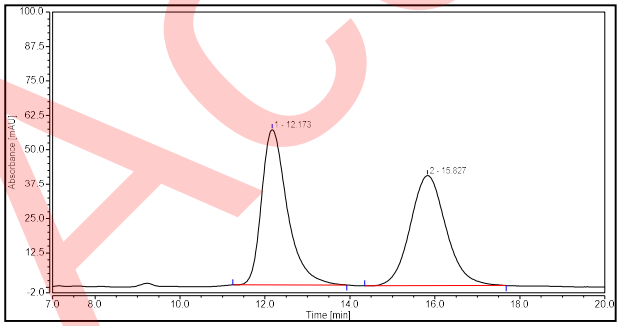
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (29.8 mg, 60% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.0 Hz, 1H), 7.34 – 7.28 (m, 3H), 7.25 – 7.22 (m, 2H), 7.10 – 7.00 (m, 4H), 6.96 – 6.91 (m, 2H), 4.92 – 4.89 (m, 1H), 4.78 – 4.73 (m, 1H), 4.14 (s, 3H), 3.48 (d, J = 8.1 Hz, 1H), 3.08 (dd, J = 9.6, 5.6 Hz, 1H), 3.03 – 2.97 (m, 2H), 2.71 (d, J = 5.5 Hz, 1H), 2.00 (d, J = 11.1 Hz, 1H), 1.71 (d, J = 11.0 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.1, 175.9, 168.9, 161.4 (d, J = 245.6 Hz), 155.2, 142.9, 138.4, 134.5 (d, J = 3.3 Hz), 130.8, 129.7 (d, J = 7.8 Hz), 128.3, 128.2, 127.8, 122.3, 118.5, 115.1 (d, J = 21.2 Hz), 111.0, 56.3, 52.2, 48.5, 47.3, 47.1, 45.2, 43.3, 39.7, 22.9.

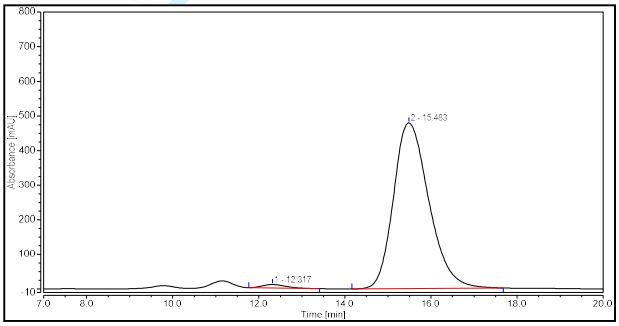
HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}FN_2NaO_4$, ([M + Na]$^+$): 521.1847, found: 521.1843.

[α]$_D^{20}$ = 66 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 15.48 min, tr (minor) =12.32 min, 97% ee.

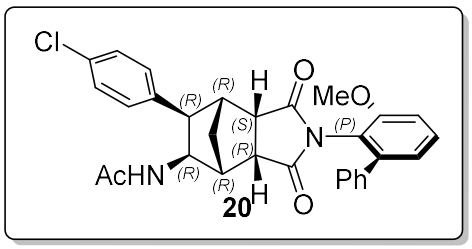


No.	Retention Time min	Area mAU*min	Relative Area %
1	12.173	39.509	50.32
2	15.827	39.013	49.68



No.	Retention Time min	Area mAU*min	Relative Area %
1	12.317	6.467	1.40
2	15.483	456.186	98.60

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-6-(4-chlorophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 20

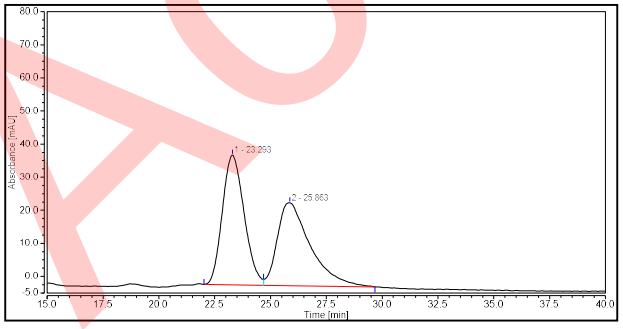


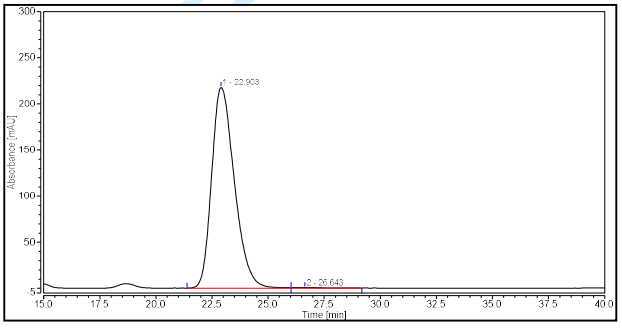
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (27.2 mg, 53% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (t, J = 8.1 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.24 – 7.21 (m, 4H), 7.09 (dd, J = 8.5, 1.2 Hz, 1H), 7.03 – 7.00 (m, 3H), 4.88 (brs, 1H), 4.80 – 4.76 (m, 1H), 4.14 (s, 3H), 3.47 (d, J = 8.9 Hz, 1H), 3.09 (dd, J = 9.5, 5.6 Hz, 1H), 3.03 – 2.97 (m, 2H), 2.71 (d, J = 5.4 Hz, 1H), 1.99 (d, J = 11.3 Hz, 1H), 1.72 (d, J = 11.0 Hz, 1H), 1.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.0, 175.8, 168.9, 155.2, 142.9, 138.4, 137.3, 132.4, 130.8, 129.6, 128.4, 128.3, 128.2, 127.8, 122.3, 118.5, 111.0, 56.3, 52.2, 48.4, 47.5, 47.1, 45.2, 43.1, 39.8, 23.0.

HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}ClN_2NaO_4$, ($[M + Na]^+$): 537.1552, found: 537.1549.

$[\alpha]_D^{20}$ = 98 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 22.90 min, tr (minor) =26.64 min, 99% ee.

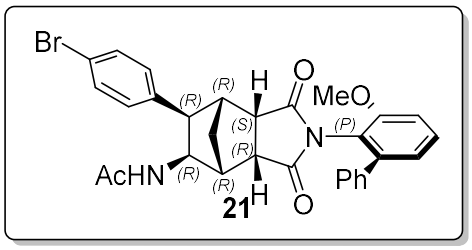




No.	Retention Time min	Area mAU*min	Relative Area %
1	23.293	44.268	50.87
2	25.863	42.757	49.13

No.	Retention Time min	Area mAU*min	Relative Area %
1	22.903	256.116	99.65
2	26.643	0.908	0.35

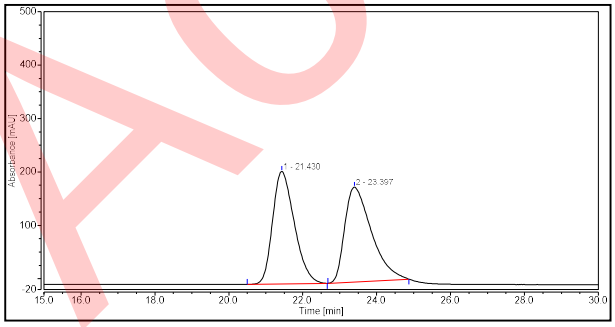
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-6-(4-bromophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 21

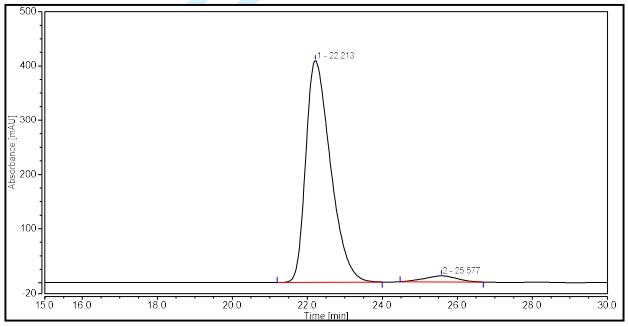


21

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (36.7 mg, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.38 – 7.35 (m, 2H), 7.32 – 7.27 (m, 3H), 7.24 – 7.21 (m, 2H), 7.08 (dd, J = 8.6, 1.2 Hz, 1H), 7.01 (dd, J = 7.8, 1.2 Hz, 1H), 6.95 (d, J = 8.5 Hz, 2H), 4.94 – 4.91 (m, 1H), 4.79 – 4.74 (m, 1H), 4.13 (s, 3H), 3.45 (d, J = 8.1 Hz, 1H), 3.08 (dd, J = 9.4, 5.6 Hz, 1H), 3.02 – 2.97 (m, 2H), 2.70 (d, J = 5.5 Hz, 1H), 1.98 (d, J = 10.6 Hz, 1H), 1.71 (d, J = 11.1 Hz, 1H), 1.50 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.0, 175.9, 169.0, 155.2, 142.9, 138.4, 137.8, 131.4, 130.9, 129.9, 128.3, 128.2, 127.8, 122.4, 120.5, 118.4, 111.1, 56.3, 52.1, 48.4, 47.5, 47.1, 45.2, 43.1, 39.8, 23.0. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}BrN_2NaO_4$, ($[M + Na]^+$): 581.1046, found: 581.1042. **$[\alpha]_D^{20}$** = 80 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 22.21 min, tr (minor) =25.58 min, 93% ee.

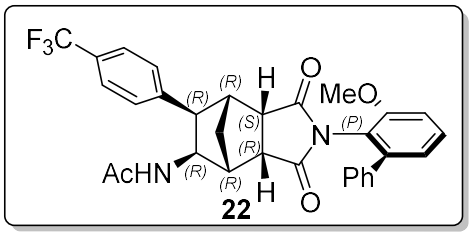




No.	Retention Time min	Area mAU*min	Relative Area %
1	21.430	143.569	49.15
2	23.397	148.529	50.85

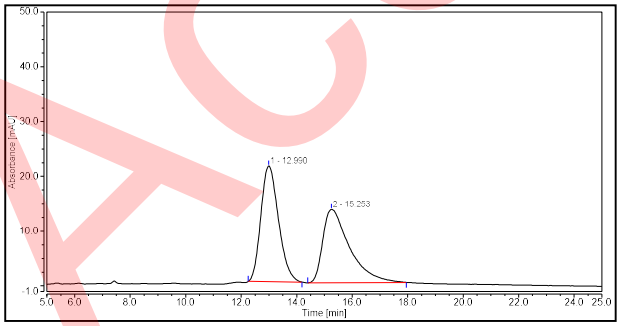
No.	Retention Time min	Area mAU*min	Relative Area %
1	22.213	312.569	96.54
2	25.577	11.211	3.46

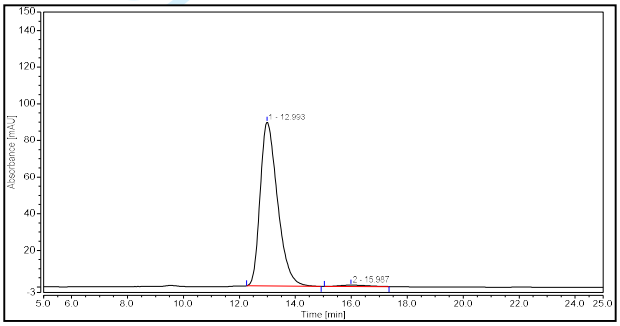
(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-(4-(trifluoro-methyl)phenyl)octahydro-1H-4,7-methanoisoindol-5-yl)acetamide 22



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (41.8 mg, 76% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 3H), 7.33 – 7.28 (m, 3H), 7.25 – 7.22 (m, 4H), 7.11 (dd, J = 8.4, 1.2 Hz, 1H), 7.03 (dd, J = 7.7, 1.2 Hz, 1H), 5.00 – 4.98 (m, 1H), 4.85 – 4.82 (m, 1H), 4.18 (s, 3H), 3.57 (d, J = 8.2 Hz, 1H), 3.12 – 3.07 (m, 2H), 3.01 (dd, J = 9.9, 5.3 Hz, 1H), 2.72 (d, J = 5.6 Hz, 1H), 2.04 (d, J = 11.1 Hz, 1H), 1.76 (d, J = 11.9 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.8, 175.6, 168.7, 155.1, 143.1, 142.9, 138.3, 130.8, 128.9 (q, J = 32.4 Hz), 128.5, 128.2, 128.1, 127.7, 125.0 (q, J = 3.7 Hz), 124.96 (q, J = 271.0 Hz), 122.3, 118.4, 111.0, 56.2, 52.3, 48.3, 48.0, 47.1, 45.1, 43.0, 39.8, 22.7. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{31}H_{27}F_3N_2NaO_4$, ($[M + Na]^+$): 571.1815, found: 571.1806. **$[\alpha]_D^{20}$** = 70 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 12.99 min, tr (minor) =15.99 min, 97% ee.

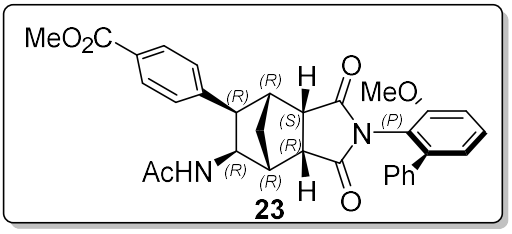




No.	Retention Time min	Area mAU*min	Relative Area %
1	12.990	15.554	50.95
2	15.253	14.972	49.05

No.	Retention Time min	Area mAU*min	Relative Area %
1	12.993	64.268	98.66
2	15.987	0.873	1.34

(*P*)-methyl 4-((*3aS,4R,5R,6R,7R,7aR*)-6-acetamido-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)benzoate 23

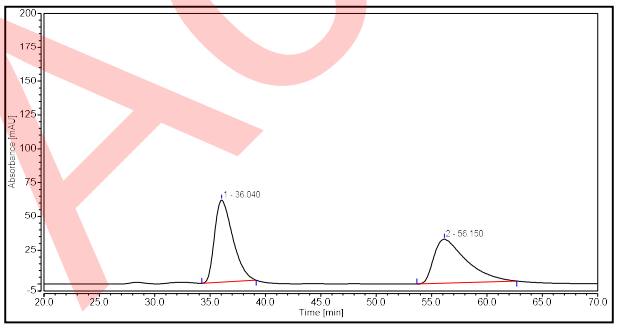


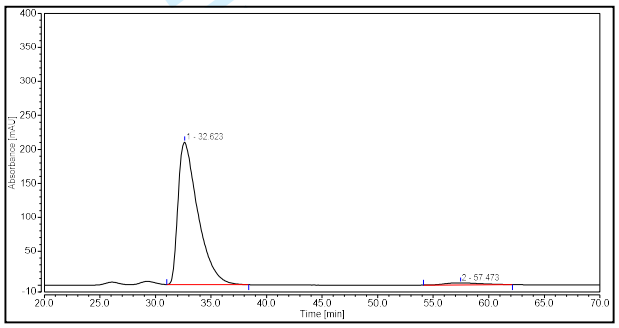
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (35.6 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.92 (d, J = 7.4 Hz, 2H), 7.48 (t, J = 8.0 Hz, 1H), 7.33 – 7.29 (m, 3H), 7.25 – 7.24 (m, 2H), 7.18 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 7.7 Hz, 1H), 5.06 – 5.01 (m, 1H), 4.83 (t, J = 9.0 Hz, 1H), 4.17 (s, 3H), 3.89 (s, 3H), 3.57 (d, J = 8.3 Hz, 1H), 3.12– 3.08 (m, 2H), 3.01 (dd, J = 9.9, 5.3 Hz, 1H), 2.72 (d, J = 5.6 Hz, 1H), 2.06 (d, J = 11.1 Hz, 1H), 1.75 (d, J = 11.1 Hz, 1H), 1.44 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.7, 168.7, 166.8, 155.6, 144.3, 142.9, 138.4, 130.7, 129.4, 128.4, 128.2, 128.1, 127.7, 122.3, 118.5, 111.0, 56.3, 52.2, 52.1, 48.3, 48.1, 47.1, 45.1, 43.0, 39.8, 22.7.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{30}N_2NaO_6$, ($[M + Na]^+$): 561.1996, found: 561.1991.

$[\alpha]_D^{20}$ = 80 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 32.62 min, tr (minor) =57.47 min, 95% ee.

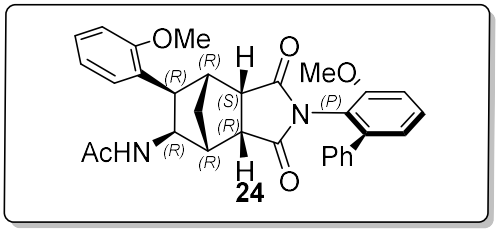




No.	Retention Time min	Area mAU*min	Relative Area %
1	36.040	115.928	51.11
2	56.150	110.895	48.89

No.	Retention Time min	Area mAU*min	Relative Area %
1	32.623	433.353	97.51
2	57.473	11.055	2.49

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-6-(2-methoxyphenyl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 24

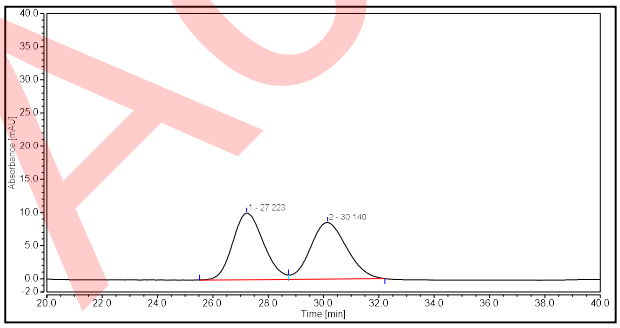


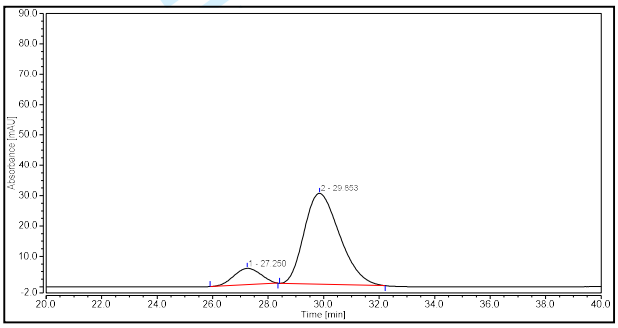
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (16.3 mg, 32% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 (t, J = 8.0 Hz, 1H), 7.34 – 7.29 (m, 3H), 7.26 – 7.22 (m, 4H), 7.18 – 7.17 (m, 1H), 7.08 (dd, J = 8.4, 1.2 Hz, 1H), 7.01 (dd, J = 7.7, 1.2 Hz, 1H), 6.93 (t, J = 7.5 Hz, 1H), 6.82 (dd, J = 8.2, 1.2 Hz, 1H), 4.84 – 4.81 (m, 1H), 4.65 (d, J = 9.1 Hz, 1H), 4.06 (s, 3H), 3.67 (d, J = 8.2 Hz, 1H), 3.09 – 3.07 (m, 2H), 3.01 (dd, J = 10.1, 5.3 Hz, 1H), 2.71 (d, J = 4.5 Hz, 1H), 1.95 (d, J = 10.9 Hz, 1H), 1.69 (d, J = 10.9 Hz, 1H), 1.56 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.8, 175.5, 168.0, 157.9, 155.4, 142.5, 138.7, 130.5, 128.3, 128.2, 128.1, 127.5, 126.5, 126.4, 122.1, 120.3, 118.8, 111.1, 110.1, 56.3, 55.3, 50.7, 48.4, 47.2, 46.0, 41.9, 41.6, 39.5, 23.1.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_5$, ($[M + Na]^+$): 533.2047, found: 533.2040.

$[\alpha]_D^{20}$ = 54 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 70:30, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 29.85 min, tr (minor) =27.25 min, 76% ee.

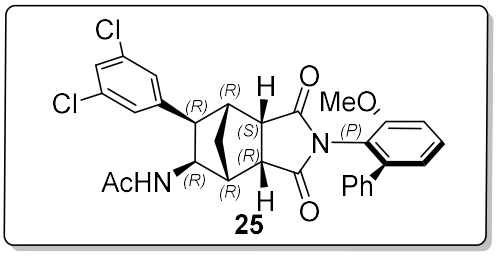




No.	Retention Time min	Area mAU*min	Relative Area %
1	27.223	12.942	50.06
2	30.140	12.911	49.94

No.	Retention Time min	Area mAU*min	Relative Area %
1	27.250	6.080	12.08
2	29.853	44.252	87.92

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-6-(3,5-dichlorophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 25



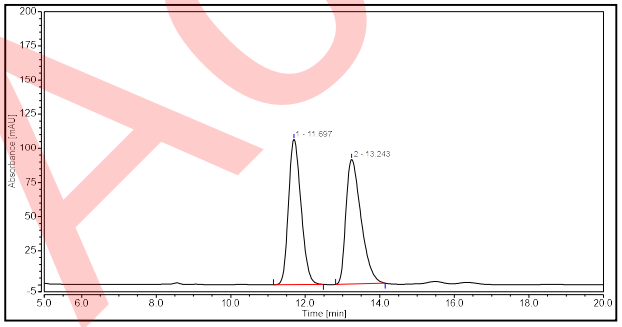
25

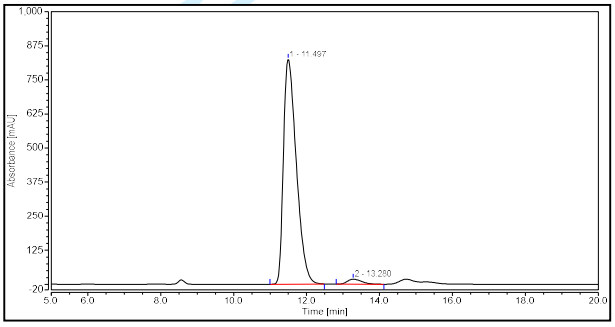
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (25.8 mg, 47% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.33 – 7.28 (m, 3H), 7.24 – 7.21 (m, 2H), 7.19 – 7.19 (m, 1H), 7.09 (dd, J = 8.5, 1.2 Hz, 1H), 7.01 (dd, J = 7.8, 1.2 Hz, 1H), 6.96 (d, J = 1.9 Hz, 2H), 5.05 – 5.00 (m, 1H), 4.79 (t, J = 8.8 Hz, 1H), 4.15 (s, 3H), 3.44 (d, J = 7.5 Hz, 1H), 3.12 – 3.07 (m, 1H), 3.03 – 2.98 (m, 1H), 2.71 (d, J = 5.4 Hz, 1H), 1.98 (d, J = 11.1 Hz, 1H), 1.75 (d, J = 11.1 Hz, 1H), 1.57 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.9, 175.7, 169.0, 155.1, 142.9, 142.4, 138.4, 134.8, 130.9, 132.4, 128.3, 127.8, 126.8, 122.4, 118.3, 111.1, 56.3, 52.3, 48.3, 47.9, 47.1, 45.1, 43.0, 39.8, 22.9.

HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{26}Cl_2N_2NaO_4$, ([M + Na]$^+$): 571.1162, found: 571.1169.

$[\alpha]_D^{20}$ = 82 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 11.50 min, tr (minor) =13.28 min, 95% ee.

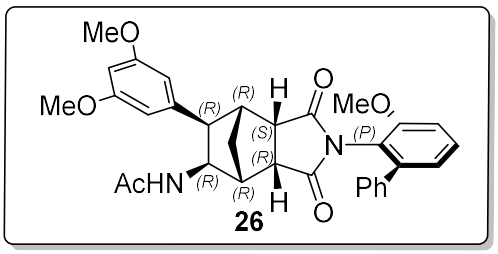




No.	Retention Time min	Area mAU*min	Relative Area %
1	11.697	41.458	49.17
2	13.243	42.852	50.83

No.	Retention Time min	Area mAU*min	Relative Area %
1	11.497	337.037	97.55
2	13.280	8.476	2.45

(*P*)- *N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-6-(3,5-dimethoxyphenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 26

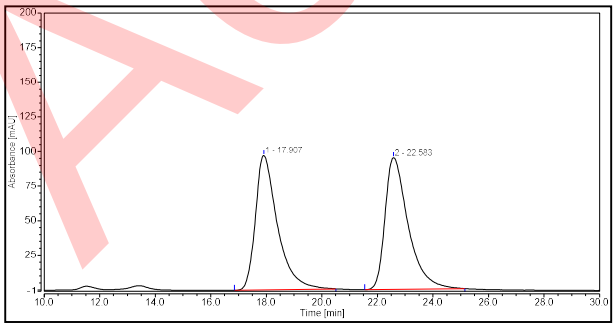


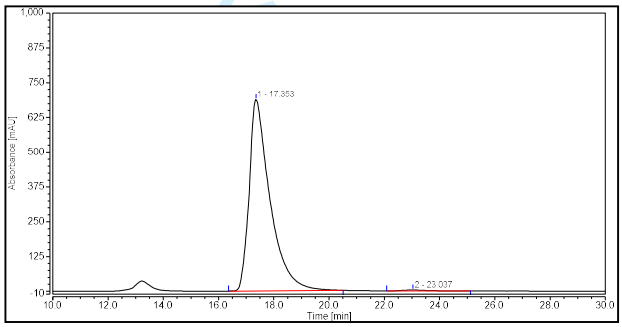
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (28.4 mg, 53% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 1H), 7.33 – 7.29 (m, 3H), 7.26 – 7.25(m, 2H), 7.09 (dd, J = 8.4, 1.2 Hz, 1H), 7.02 (dd, J = 7.7, 1.2 Hz, 1H), 6.29 (t, J = 2.2 Hz, 1H), 6.24 (d, J = 2.3 Hz, 2H), 4.88 – 4.87 (m, 1H), 4.81 – 4.78 (m, 1H), 4.15 (s, 3H), 3.74 (s, 6H), 3.46 (d, J = 8.3 Hz, 1H), 3.10 – 3.06(m, 2H), 2.99 (dd, J = 9.9, 5.3 Hz, 1H), 2.73 (d, J = 5.9 Hz, 1H), 2.00 (d, J = 11.1 Hz, 1H), 1.71 (d, J = 11.0 Hz, 1H), 1.55 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 169.0, 160.6, 155.1, 142.9, 141.1, 138.4, 130.6, 128.2, 128.1, 127.6, 122.3, 118.6, 110.9, 106.3, 98.2, 56.1, 55.3, 51.9, 48.4, 47.7, 47.0, 45.2, 42.7, 39.7, 23.1.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{32}N_2NaO_6$, ($[M + Na]^+$): 563.2153, found: 563.2158.

$[\alpha]_D^{20}$ = 80 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 17.35 min, tr (minor) =23.04 min, 99% ee.

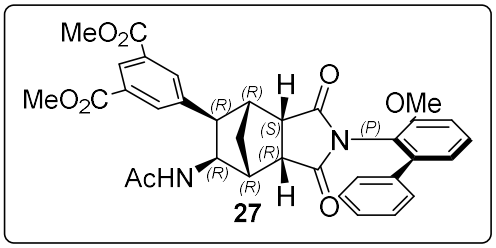




No.	Retention Time min	Area mAU*min	Relative Area %
1	17.907	89.632	49.34
2	22.583	92.018	50.66

No.	Retention Time min	Area mAU*min	Relative Area %
1	17.353	601.243	99.46
2	23.037	3.257	0.54

Dimethyl 5-((*3aS,4R,5R,6R,7R,7aR*)-6-acetamido-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)isophthalate 27

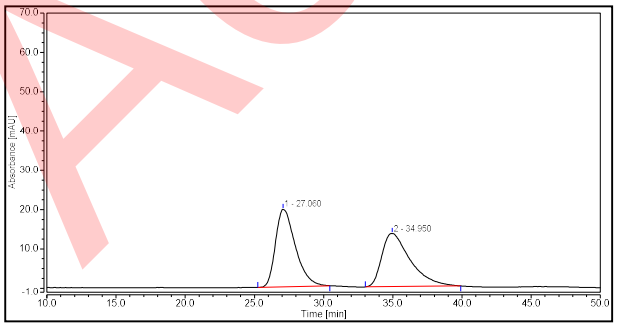


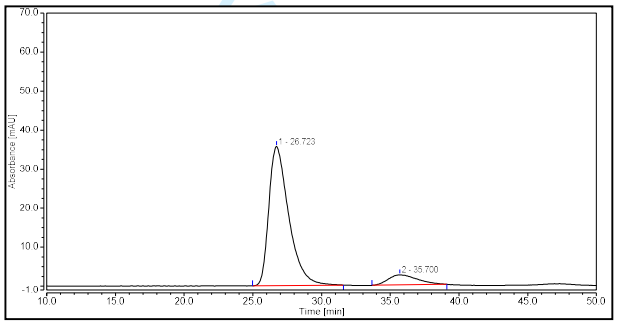
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (53.6 mg, 90% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.53 – 8.49 (m, 1H), 8.01 – 7.99 (m, 2H), 7.53 – 7.48 (m, 1H), 7.36 – 7.29 (m, 3H), 7.28 – 7.25 (m, 2H), 7.16 – 7.13 (m, 1H), 7.05 – 7.02 (m, 1H), 5.38 – 5.34 (m, 1H), 4.83 – 4.78 (m, 1H), 4.25 – 4.23 (m, 3H), 3.95 – 3.91 (m, 6H), 3.67 – 3.63 (m, 1H), 3.14 (dd, J = 10.7, 5.3 Hz, 1H), 3.04 (q, J = 9.3, 7.8 Hz, 2H), 2.78 – 2.75 (m, 1H), 2.24 – 2.22 (m, 1H), 1.81 (t, J = 11.1 Hz, 1H), 1.45– 1.43 (m, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.7, 168.6, 166.2, 166.1, 155.2, 155.2, 143.0, 140.3, 138.3, 133.9, 130.8, 130.3, 130.3, 128.9, 128.2, 128.2, 128.2, 128.1, 127.7, 122.2, 118.4, 118.3, 110.96, 110.94, 56.1, 52.7, 52.5, 48.6, 48.3, 46.9, 44.8, 43.8, 40.1, 22.5.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{32}N_2NaO_6$, ($[M + Na]^+$): 619.2051, found: 619.2051.

$[\alpha]_D^{20}$ = 18 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 35.70min, tr (minor) =26.72 min, 81% ee.

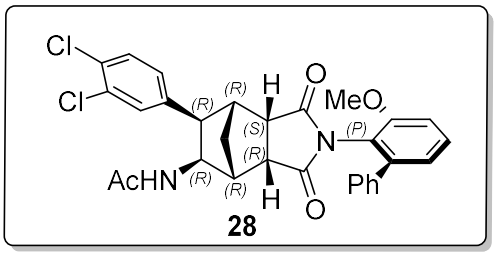




No.	Retention Time min	Area mAU*min	Relative Area %
1	27.060	32.965	50.53
2	34.950	32.272	49.47

No.	Retention Time min	Area mAU*min	Relative Area %
1	26.723	59.932	90.41
2	35.700	6.358	9.59

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-6-(3,4-dichlorophenyl)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxooctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 28



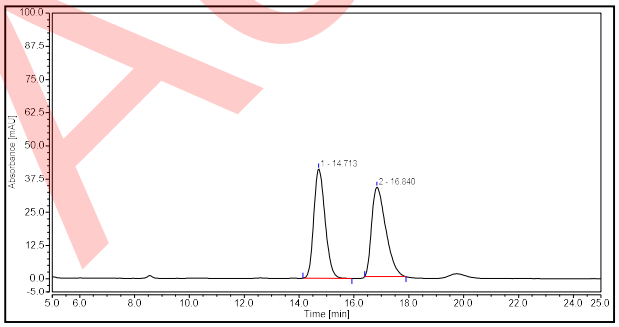
28

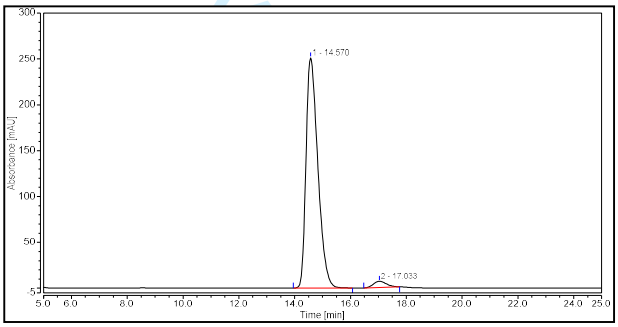
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (40.9 mg, 75% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (t, J = 8.0 Hz, 1H), 7.34 – 7.30 (m, 4H), 7.24 – 7.23 (m, 2H), 7.18 (d, J = 2.2 Hz, 1H), 7.10 (dd, J = 8.5, 1.2 Hz, 1H), 7.03 – 7.01 (m, 1H), 6.93 (dd, J = 8.4, 2.2 Hz, 1H), 5.17 (d, J = 9.2 Hz, 1H), 4.78 – 4.75 (m, 1H), 4.15 (s, 3H), 3.45 (d, J = 8.2 Hz, 1H), 3.10 – 3.07 (m, 1H), 3.01 – 2.96 (m, 2H), 2.69 (d, J = 5.6 Hz, 1H), 1.99 (d, J = 11.2 Hz, 1H), 1.72 (d, J = 11.8 Hz, 1H), 1.52 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.8, 175.6, 168.9, 155.1, 142.8, 139.3, 138.3, 132.1, 130.8, 130.5, 130.0, 129.5, 128.4, 128.2, 128.2, 127.7, 122.3, 118.4, 111.0, 56.2, 52.2, 48.3, 47.5, 47.0, 45.0, 43.1, 39.7, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{26}Cl_2N_2NaO_4$, ($[M + Na]^+$): 571.1162, found: 571.1167.

$[\alpha]_D^{20}$ = 90 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 14.57 min, tr (minor) =17.03 min, 94% ee.

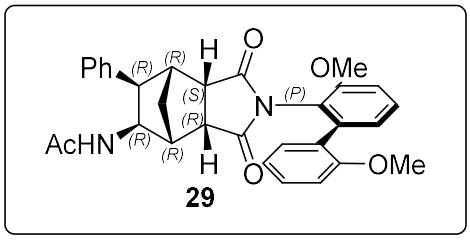




No.	Retention Time min	Area mAU*min	Relative Area %
1	14.713	19.663	49.41
2	16.840	20.133	50.59

No.	Retention Time min	Area mAU*min	Relative Area %
1	14.570	123.205	97.14
2	17.033	3.626	2.86

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(2',3-dimethoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 29



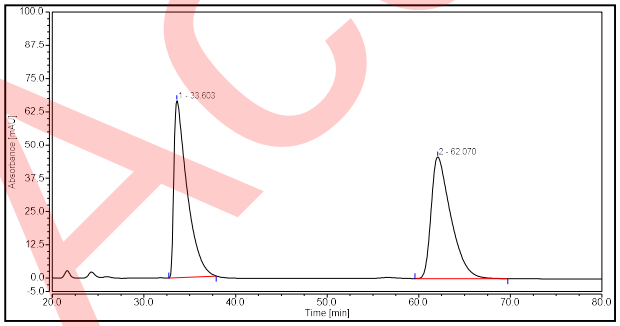
29

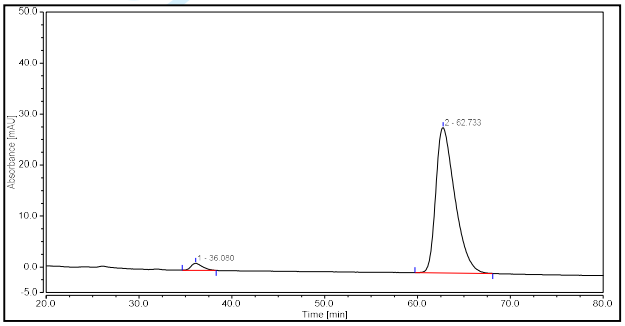
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (42.8 mg, 84% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.45 (t, J = 8.1 Hz, 1H), 7.29 – 7.24 (m, 3H), 7.17 (t, J = 7.4 Hz, 1H), 7.08 (dd, J = 13.0, 8.0 Hz, 5H), 6.94 – 6.85 (m, 2H), 4.86 – 4.74 (m, 2H), 4.13 (s, 3H), 3.71 (s, 3H), 3.50 (s, 1H), 3.08 – 3.03 (m, 2H), 2.99 – 2.92 (m, 1H), 2.73 (d, J = 5.6 Hz, 1H), 2.02 (d, J = 11.0 Hz, 1H), 1.71 (d, J = 11.0 Hz, 1H), 1.45 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.5, 179.9, 170.3, 157.5, 154.4, 142.2, 138.8, 130.1, 129.2, 128.4, 128.1, 127.4, 126.6, 124.1, 121.3, 120.4, 119.9, 111.3, 111.1, 56.2, 55.2, 52.1, 49.1, 47.6, 47.2, 44.7, 43.0, 40.1, 23.3.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_5$, ($[M + Na]^+$): 533.2047, found: 533.2037.

[α]$_D^{20}$ = 84 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 70:30, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 62.73 min, tr (minor) = 36.08 min, 94% ee.

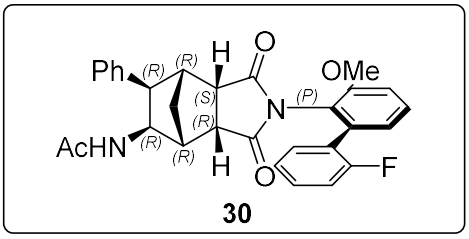




No.	Retention Time min	Area mAU*min	Relative Area %
1	33.603	111.815	49.56
2	62.070	113.804	50.44

No.	Retention Time min	Area mAU*min	Relative Area %
1	36.080	1.956	2.80
2	62.733	67.793	97.20

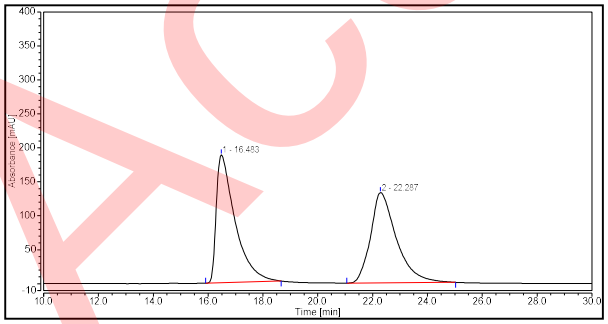
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(2'-fluoro-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl) acetamide 30

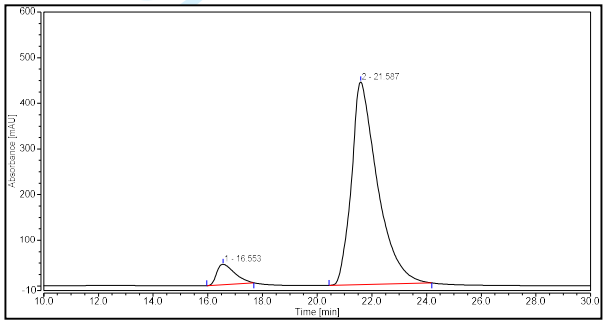


30

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (26.4 mg, 53% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (t, J = 8.1 Hz, 1H), 7.31 – 7.23 (m, 3H), 7.24 – 7.16 (m, 2H), 7.15 (d, J = 8.3 Hz, 1H),, 7.13 – 7.03 (m, 5H), 4.90 – 4.66 (m, 2H), 4.15 (s, 3H), 3.51 (d, J = 7.9 Hz, 1H), 3.19 – 3.08 (m, 2H), 3.04 – 2.99 (m, 1H), 2.75 (d, J = 5.5 Hz, 1H), 2.03 (d, J = 10.7 Hz, 1H), 1.75 (d, J = 11.1 Hz, 1H), 1.47 (s, 3H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.5, 175.1, 168.7, 159.5 (d, J = 248.4 Hz), 155.3, 138.6, 136.5, 131.1, 130.5, 129.7 (d, J = 8.0 Hz), 128.4, 128.0, 126.6, 125.7 (d, J = 15.7 Hz), 123.8 (d, J = 3.9 Hz), 122.9, 119.5, 115.7 (d, J = 21.8 Hz), 111.7, 56.2, 52.0, 48.5, 47.5, 47.1, 45.2, 42.9, 39.7, 22.9. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}N_2FNaO_4$, ($[M + Na]^+$): 521.1847, found: 521.1843. **$[\alpha]_D^{20}$** = 114 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 21.59 min, tr (minor) = 16.55 min, 87% ee.

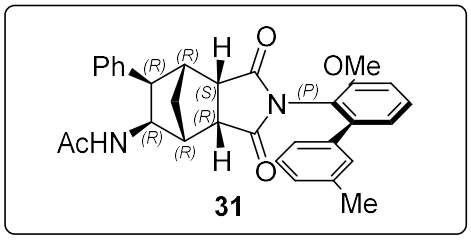




No.	Retention Time min	Area mAU*min	Relative Area %
1	16.483	149.273	50.66
2	22.287	145.406	49.34

No.	Retention Time min	Area mAU*min	Relative Area %
1	16.553	33.861	6.47
2	21.587	489.845	93.53

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-3'-methyl-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 31



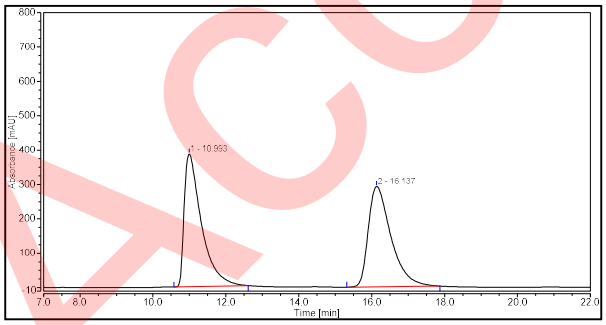
31

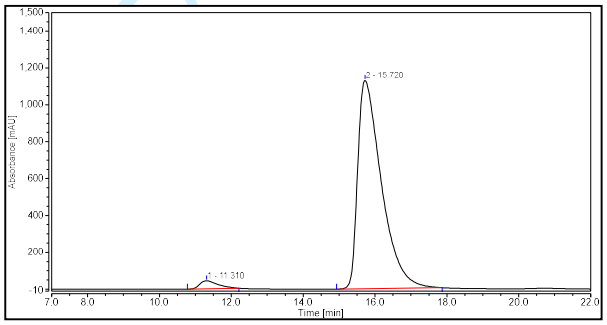
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (42.9 mg, 87% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.31 – 7.14 (m, 4H), 7.13 – 6.93 (m, 7H), 4.94 – 4.62 (m, 2H), 4.15 (s, 3H), 3.53 (d, J = 8.3 Hz, 1H), 3.17 – 2.90 (m, 3H), 2.72 (d, J = 5.7 Hz, 1H), 2.33 (s, 3H), 2.04 (d, J = 10.9 Hz, 1H), 1.73 (d, J = 11.1 Hz, 1H), 1.45 (s, 3H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.8, 155.2, 142.9, 138.7, 138.4, 137.8, 130.6, 129.1, 128.4, 128.3, 128.1, 127.9, 126.6, 125.1, 122.3, 118.6, 110.8, 56.2, 52.1, 48.5, 47.6, 47.1, 45.2, 43.0, 39.7, 22.8, 21.5.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_4$, ($[M + Na]^+$): 517.2098, found: 517.2099.

$[\alpha]_D^{20}$ = 110 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 °C, 227 nm); tr (major) = 15.72 min, tr (minor) = 11.31 min, 94% ee.

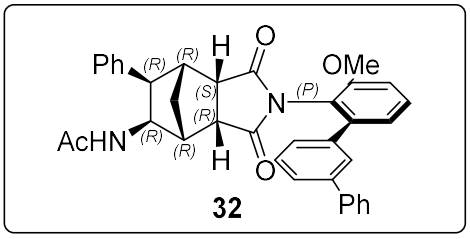




No.	Retention Time min	Area mAU*min	Relative Area %
1	10.993	211.923	50.16
2	16.137	210.602	49.84

No.	Retention Time min	Area mAU*min	Relative Area %
1	11.310	25.667	2.89
2	15.720	861.726	97.11

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-[1,1':3',1''-terphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 32



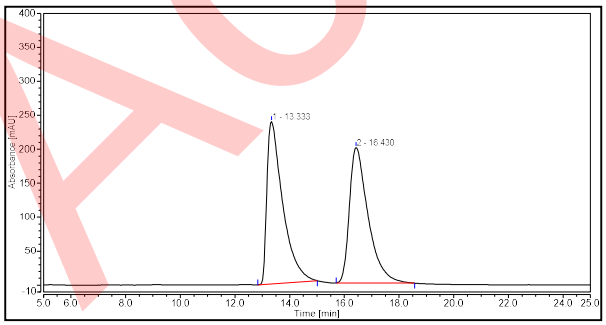
32

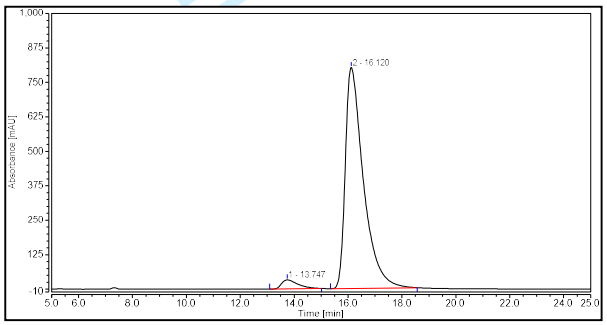
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (39.7 mg, 71% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 4H), 7.48 (t, J = 8.0 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 7.7 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.28 – 7.21 (m, 3H), 7.17 (t, J = 7.2 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 7.10 – 7.04 (m, 3H), 4.91 – 4.81 (m, 1H), 4.79 (t, J = 8.8 Hz, 1H), 4.16 (s, 3H), 3.54 (d, J = 8.2 Hz, 1H), 3.10 – 3.05 (m, 1H), 3.06 – 3.00 (m, 1H), 3.00 – 2.94 (m, 1H), 2.71 (d, J = 5.2 Hz, 1H), 2.01 (d, J = 11.3 Hz, 1H), 1.68 (d, J = 11.3 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.1, 175.8, 168.8, 155.3, 142.8, 140.8, 140.5, 138.9, 138.6, 130.7, 128.9, 128.5, 128.3, 128.1, 127.5, 127.1, 127.0, 126.6, 126.3, 122.2, 118.7, 111.1, 56.3, 52.1, 48.5, 47.6, 47.2, 45.2, 43.0, 39.7, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{36}H_{32}N_2NaO_4$, ($[M + Na]^+$): 579.2255, found: 579.2247.

$[\alpha]_D^{20}$ = 68 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 16.12 min, tr (minor) = 13.75 min, 93% ee.

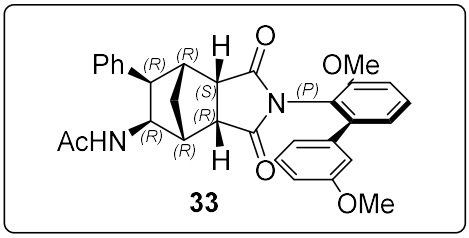




No.	Retention Time min	Area mAU*min	Relative Area %
1	13.333	160.776	50.39
2	16.430	158.318	49.61

No.	Retention Time min	Area mAU*min	Relative Area %
1	13.747	23.033	3.56
2	16.120	623.507	96.44

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3,3'-dimethoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 33



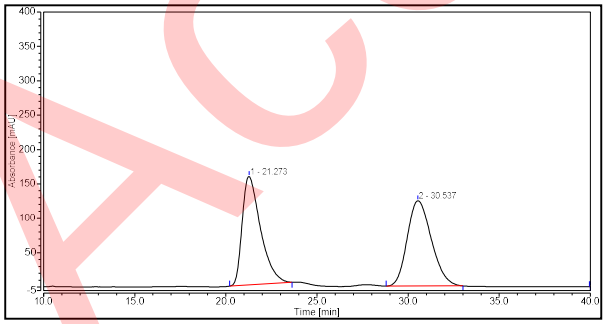
33

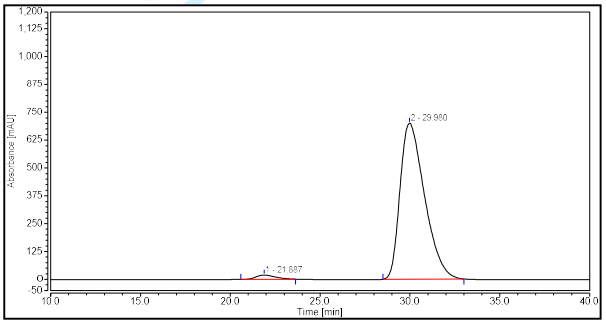
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (43.4 mg, 85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (t, J = 8.0 Hz, 1H), 7.29 – 7.13 (m, 4H), 7.12 – 7.06 (m, 3H), 7.03 – 6.99 (m, 1H), 6.86 – 6.76 (m, 3H), 4.93 – 4.84 (m, 1H), 4.78 (t, J = 8.8 Hz, 1H), 4.14 (s, 3H), 3.75 (s, 3H), 3.52 (d, J = 7.9 Hz, 1H), 3.13 – 3.06 (m, 2H), 3.05 – 2.98 (m, 1H), 2.72 (d, J = 5.3 Hz, 1H), 2.03 (d, J = 10.9 Hz, 1H), 1.72 (d, J = 10.8 Hz, 1H), 1.43 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.2, 175.9, 168.9, 159.3, 155.3, 142.8, 139.8, 138.7, 130.8, 129.2, 128.4, 128.2, 126.7, 122.2, 120.6, 118.6, 113.8, 113.5, 111.1, 56.3, 55.3, 52.1, 48.6, 47.8, 47.3, 45.2, 43.0, 39.8, 22.9.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_5$, ($[M + Na]^+$): 533.2047, found: 533.2039.

$[\alpha]_D^{20}$ = 74 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 75:25, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 29.98 min, tr (minor) = 21.89 min, 96% ee.

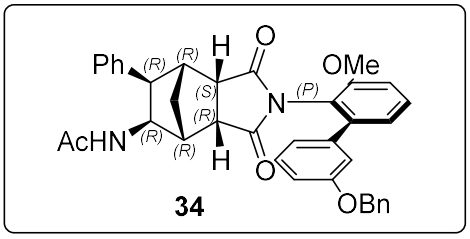




No.	Retention Time min	Area mAU*min	Relative Area %
1	21.273	184.111	49.15
2	30.537	190.445	50.85

No.	Retention Time min	Area mAU*min	Relative Area %
1	21.887	23.555	2.08
2	29.980	1107.317	97.92

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3'-(benzyloxy)-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 34



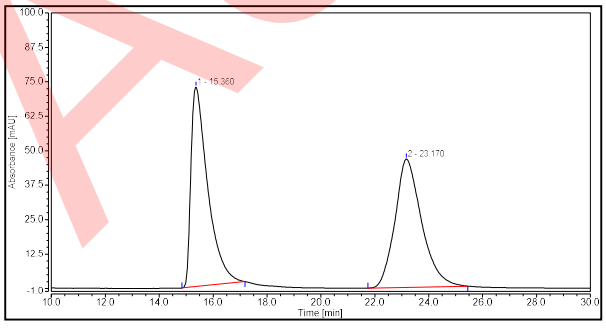
34

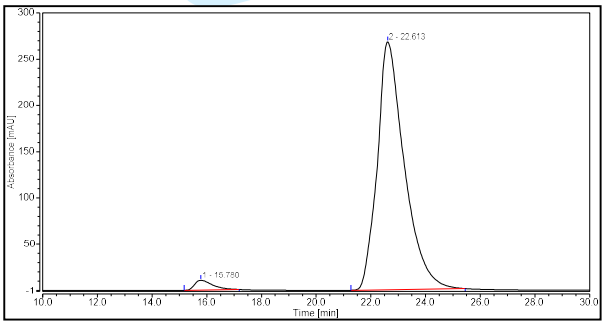
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (48.6mg, 83% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.45 (t, J = 8.1 Hz, 1H), 7.42 (d, J = 7.2 Hz, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.34 – 7.28 (m, 1H), 7.28 – 7.19 (m, 3H), 7.17 (t, J = 7.4 Hz, 1H), 7.12 – 7.05 (m, 3H), 7.00 (d, J = 7.5 Hz, 1H), 6.95 – 6.88 (m, 2H), 6.85 (d, J = 7.5 Hz, 1H), 5.02 (s, 2H), 4.93 – 4.86 (m, 1H), 4.77 (t, J = 8.8 Hz, 1H), 4.14 (s, 3H), 3.52 (d, J = 8.3 Hz, 1H), 3.07 (d, J = 5.1 Hz, 1H), 3.04 – 2.85 (m, 2H), 2.70 (d, J = 5.4 Hz, 1H), 2.11 – 1.98 (m, 1H), 1.69 (d, J = 10.8 Hz, 1H), 1.44 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.1, 175.8, 168.8, 158.5, 155.2, 142.7, 139.8, 138.7, 137.0, 130.7, 129.2, 128.6, 128.3, 128.1, 127.9, 127.5, 126.6, 122.2, 120.9, 118.6, 114.7, 114.4, 111.0, 69.8, 56.3, 52.2, 48.5, 47.6, 47.1, 45.2, 43.0, 39.7, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{37}H_{34}N_2NaO_5$, ($[M + Na]^+$): 609.2360, found: 609.2359.

$[\alpha]_D^{20}$ = 68 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 22.61 min, tr (minor) = 15.78 min, 95% ee.

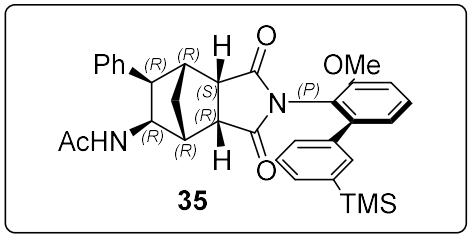




No.	Retention Time min	Area mAU*min	Relative Area %
1	15.360	52.291	49.55
2	23.170	53.237	50.45

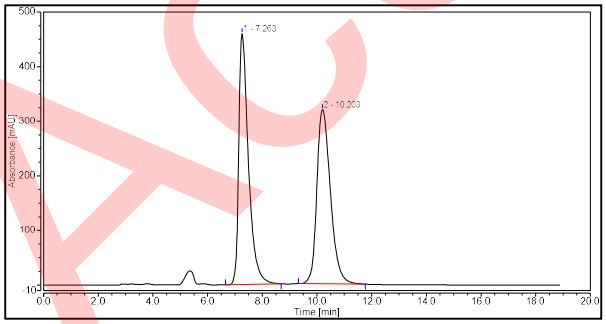
No.	Retention Time min	Area mAU*min	Relative Area %
1	15.780	8.058	2.55
2	22.613	307.726	97.45

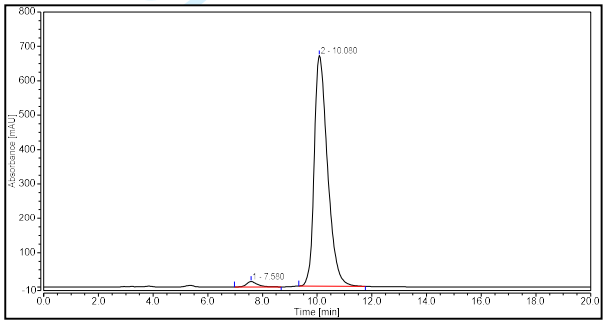
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-3'-(trimethylsilyl)-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 35



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (45.3mg, 82% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.39 – 7.38 (m, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.20 – 7.13 (m, 1H), 7.12 – 7.06 (m, 3H), 7.04 – 7.02 (m, 1H), 4.90 – 4.86 (m, 1H), 4.79 (t, J = 8.7 Hz, 1H), 4.15 (s, 3H), 3.53 (d, J = 8.2 Hz, 1H), 3.24 – 3.00 (m, 2H), 2.99 – 2.94 (m, 1H), 2.73 (d, J = 5.3 Hz, 1H), 2.04 (d, J = 11.0 Hz, 1H), 1.72 (d, J = 11.2 Hz, 1H), 1.45 (s, 3H), 0.25 (s, 9H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 177.0, 176.7, 169.8, 156.3, 144.2, 141.3, 139.7, 138.8, 134.0, 133.6, 131.7, 129.9, 129.4, 129.1, 128.7, 127.7, 123.4, 119.7, 112.0, 57.3, 53.1, 49.6, 48.7, 48.3, 46.3, 44.1, 40.8, 23.9, 0.0. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{33}H_{36}N_2SiNaO_4$, ($[M + Na]^+$): 575.2342, found: 575.2341. **$[\alpha]_D^{20}$** = 78 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 10.08 min, tr (minor) = 7.58 min, 96% ee.



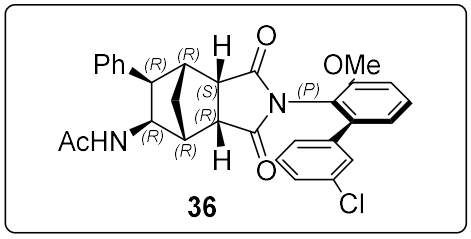


No.	Retention Time min	Area mAU*min	Relative Area %
1	7.263	188.412	50.64
2	10.203	183.681	49.36

No.	Retention Time min	Area mAU*min	Relative Area %
1	7.580	7.222	1.88
2	10.080	377.560	98.12

https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english

(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3'-chloro-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 36



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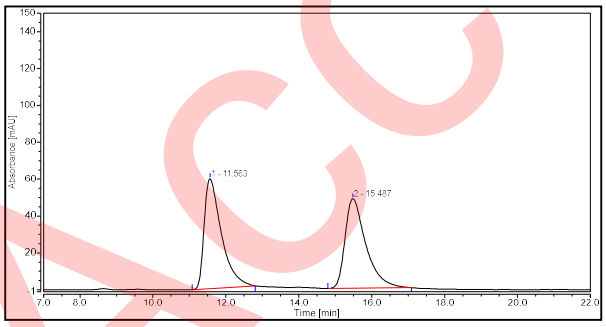
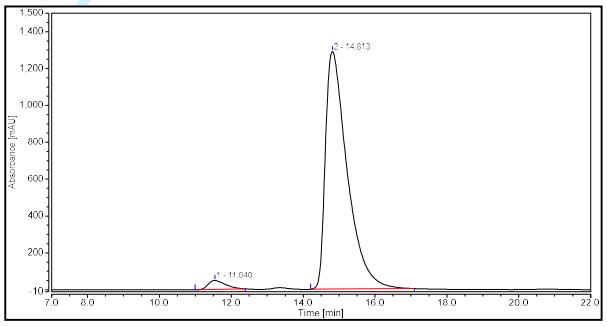
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (44.1 mg, 86% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (t, J = 8.1 Hz, 1H), 7.30 – 7.23 (m, 5H), 7.21 – 7.06 (m, 5H), 6.99 (d, J = 7.7 Hz, 1H), 4.92 – 4.85 (m, 1H), 4.79 (t, J = 8.9 Hz, 1H), 4.15 (s, 3H), 3.52 (d, J = 8.3 Hz, 1H), 3.24 – 2.96 (m, 3H), 2.74 (d, J = 5.5 Hz, 1H), 2.05 (d, J = 11.1 Hz, 1H), 1.75 (d, J = 11.1 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.7, 168.8, 155.3, 141.3, 140.2, 138.6, 134.0, 130.8, 129.4, 128.3, 128.1, 127.8, 126.6, 126.6, 122.0, 118.5, 111.5, 56.3, 52.1, 48.5, 47.7, 47.1, 45.2, 43.0, 39.8, 22.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}ClN_2NaO_4$, ($[M + Na]^+$): 537.1552, found: 537.1550. **$[\alpha]_D^{20}$** = 84 (c = 0.1, $CHCl_3$). **HPLC analysis**: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 °C, 227 nm); tr (major) = 14.81 min, tr (minor) = 11.54 min, 94% ee.

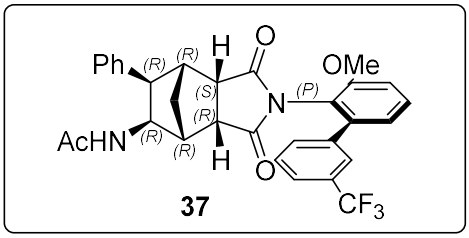




No.	Retention Time min	Area mAU*min	Relative Area %
1	11.563	32.696	50.36
2	15.487	32.227	49.64

No.	Retention Time min	Area mAU*min	Relative Area %
1	11.540	26.830	2.87
2	14.813	906.572	97.13

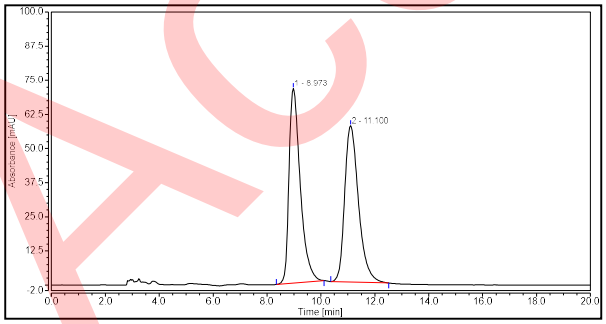
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 37

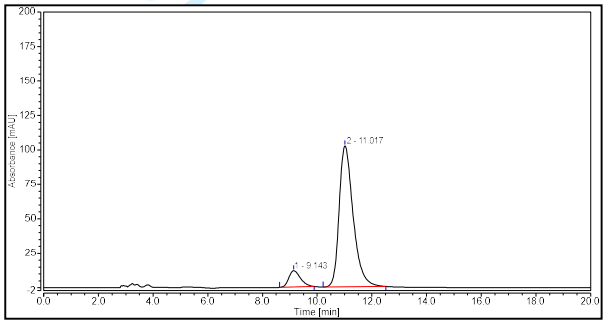


37

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (43.8mg, 80% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 – 7.55 (m, 1H), 7.54 – 7.44 (m, 4H), 7.28 (t, J = 7.8 Hz, 2H), 7.22 – 7.16 (m, 1H), 7.16 – 7.13 (m, 1H), 7.10 (d, J = 7.2 Hz, 2H), 7.05 – 7.02 (m, 1H), 4.92 – 4.58 (m, 2H), 4.17 (s, 3H), 3.53 (d, J = 8.1 Hz, 1H), 3.23 – 3.05 (m, 2H), 3.03 – 2.99 (m, 1H), 2.76 (d, J = 5.1 Hz, 1H), 2.05 (d, J = 11.1 Hz, 1H), 1.77 (d, J = 11.1 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.6, 168.8, 155.4, 141.1, 139.2, 138.5, 132.0, 130.9, 130.5 (q, J = 32.4 Hz), 128.8, 128.4, 128.0, 126.7, 124.9 (q, J = 4.0 Hz), 124.4 (q, J = 4.2 Hz), 124.0 (q, J = 272.9 Hz), 121.9, 118.6, 111.7, 56.3, 52.0, 48.5, 47.6, 47.1, 45.2, 42.9, 39.7, 22.9. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{31}H_{27}F_3N_2NaO_4$, ([M + Na]$^+$): 571.1815, found: 571.1807. **[α]$_D^{20}$** = 68 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 11.02 min, tr (minor) = 9.14 min, 82% ee.

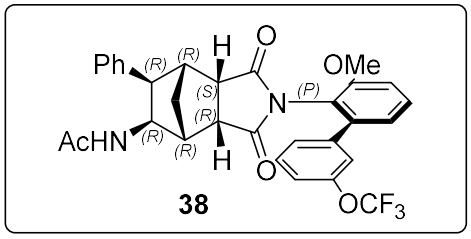




No.	Retention Time min	Area mAU*min	Relative Area %
1	8.973	34.457	50.23
2	11.100	34.146	49.77

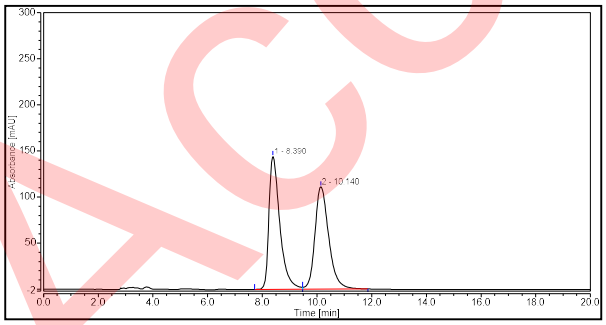
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.143	5.853	8.81
2	11.017	60.551	91.19

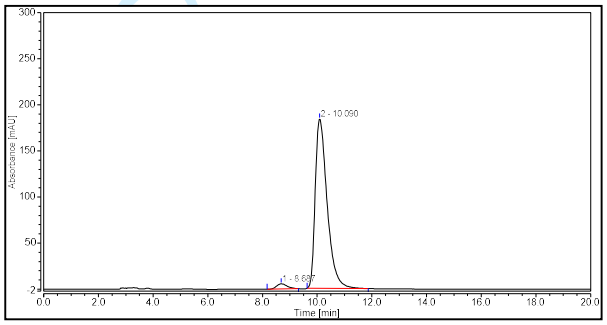
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-3'-(trifluoromethoxy)-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 38



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (49.1mg, 87% yield). **^{1}H NMR** ($CDCl_3$) δ 7.49 (t, J = 8.1 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.30 – 7.22 (m, 3H), 7.21 – 7.06 (m, 6H), 7.03 – 7.00 (m, 1H), 4.95 – 4.84 (m, 1H), 4.79 (t, J = 8.7 Hz, 1H), 4.16 (s, 3H), 3.52 (d, J = 8.3 Hz, 1H), 3.19 – 3.05 (m, 2H), 3.04 – 2.99 (m, 1H), 2.74 (d, J = 5.7 Hz, 1H), 2.05 (d, J = 11.1 Hz, 1H), 1.75 (d, J = 11.3 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.7, 168.8, 155.3, 148.7, 141.1, 140.4, 138.5, 130.9, 129.8, 128.3, 128.0, 127.2, 126.6, 122.0, 120.7, 120.5 (q, J = 257.1 Hz), 120.3, 118.5, 111.6, 56.3, 52.0, 48.5, 47.6, 47.1, 45.2, 43.0, 39.7, 22.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{31}H_{27}F_3N_2NaO_5$, ($[M + Na]^+$): 587.1764, found: 587.1766. **$[\alpha]_D^{20}$** = 74 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 10.09 min, tr (minor) = 8.69 min, 95% ee.

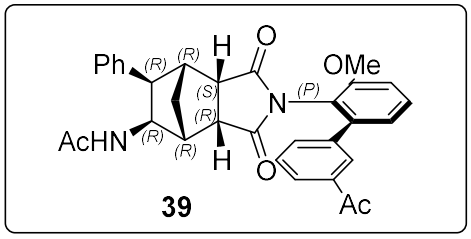




No.	Retention Time min	Area mAU*min	Relative Area %
1	8.390	66.635	50.60
2	10.140	65.044	49.40

No.	Retention Time min	Area mAU*min	Relative Area %
1	8.687	2.460	2.59
2	10.090	92.537	97.41

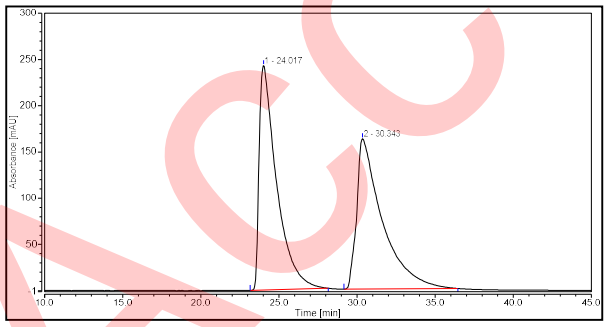
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3'-acetyl-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 39

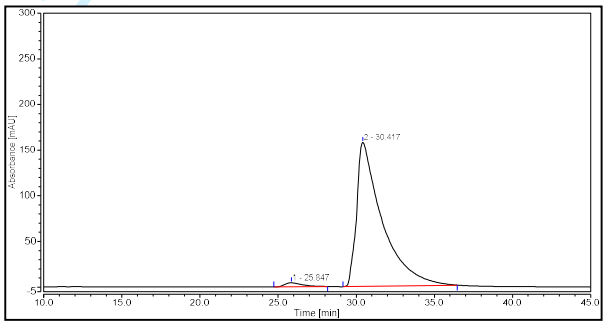


39

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (45.4mg, 87% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.98 – 7.75 (m, 2H), 7.55 – 7.36 (m, 3H), 7.33 – 6.97 (m, 7H), 4.95 – 4.74 (m, 2H), 4.17 (s, 3H), 3.53 (d, J = 8.3 Hz, 1H), 3.26 – 2.88 (m, 3H), 2.74 (d, J = 5.7 Hz, 1H), 2.58 (s, 3H), 2.06 (d, J = 11.2 Hz, 1H), 1.74 (d, J = 11.1 Hz, 1H), 1.46 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 197.9, 176.0, 175.8, 168.8, 155.3, 141.7, 138.8, 138.5, 137.1, 132.9, 130.9, 128.6, 128.5, 128.3, 128.1, 127.3, 126.6, 122.0, 118.6, 111.5, 56.3, 52.1, 48.5, 47.6, 47.2, 45.2, 43.0, 39.7, 26.7, 22.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{32}H_{30}N_2NaO_5$, ([M + Na]$^+$): 545.2047, found: 545.2042. **[α]$_D^{20}$** = 70 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 30.42 min, tr (minor) = 25.85 min, 96% ee.

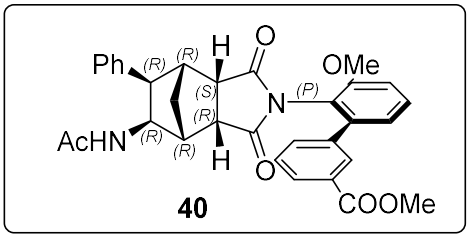




No.	Retention Time min	Area mAU*min	Relative Area %
1	24.017	313.501	50.45
2	30.343	307.861	49.55

No.	Retention Time min	Area mAU*min	Relative Area %
1	25.847	5.714	1.87
2	30.417	299.201	98.13

(*P*)-methyl2'-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-5-acetamido-1,3-dioxo-6-phenyloctahydro-2*H*-4,7-methanoisoindol-2-yl)-3'-methoxy-[1,1'-biphenyl]-3-carboxylate 40



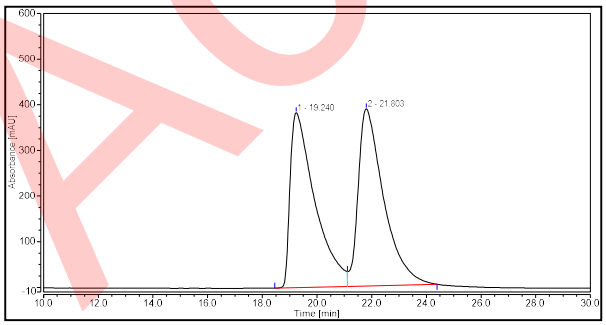
40

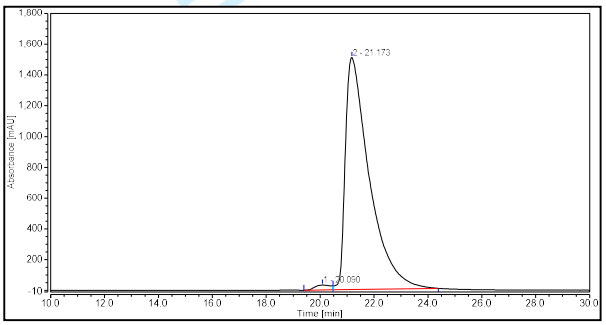
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (44.7mg, 83% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.02 – 7.87 (m, 2H), 7.52 – 7.44 (m, 2H), 7.40 (t, J = 7.7 Hz, 1H), 7.29 – 7.23 (m, 2H), 7.18 (t, J = 7.4 Hz, 1H), 7.14 – 7.12 (m, 1H), 7.09 (d, J = 7.5 Hz, 2H), 7.05 – 7.03 (m, 1H), 4.99 – 4.89 (m, 1H), 4.79 (t, J = 8.8 Hz, 1H), 4.16 (s, 3H), 3.90 (s, 3H), 3.52 (d, J = 8.3 Hz, 1H), 3.15 – 3.06 (m, 2H), 3.03 – 2.99 (m, 1H), 2.73 (d, J = 5.6 Hz, 1H), 2.05 (d, J = 11.1 Hz, 1H), 1.73 (d, J = 10.9 Hz, 1H), 1.46 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.7, 168.8, 166.8, 155.3, 141.6, 138.6, 138.6, 132.7, 130.8, 130.3, 129.4, 128.8, 128.3, 128.3, 128.1, 126.6, 122.0, 118.6, 111.5, 56.3, 52.2, 52.1, 48.5, 47.6, 47.1, 45.2, 43.0, 39.7, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{30}N_2NaO_6$, ($[M + Na]^+$): 561.1996, found: 561.1993.

$[\alpha]_D^{20}$ = 76 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 21.17 min, tr (minor) = 20.09 min, 97% ee.

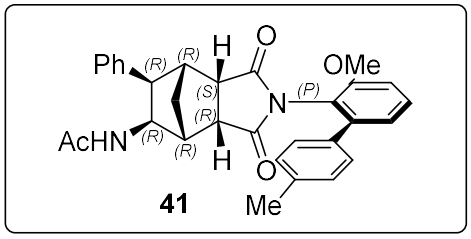




No.	Retention Time min	Area mAU*min	Relative Area %
1	19.240	400.416	48.92
2	21.803	418.103	51.08

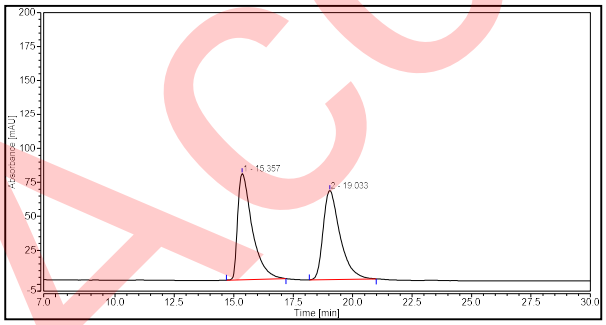
No.	Retention Time min	Area mAU*min	Relative Area %
1	20.090	21.271	1.35
2	21.173	1557.340	98.65

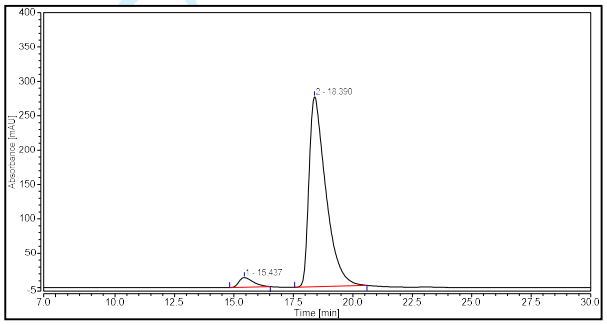
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3-methoxy-4'-methyl-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 41



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (28.4 mg, 57% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 (t, J = 8.0 Hz, 1H), 7.28 (t, J = 7.9 Hz, 2H), 7.22 – 7.16 (m, 1H), 7.17 – 7.03 (m, 7H), 7.02 –6.99 (m, 1H), 4.81 (t, J = 8.8 Hz, 1H), 4.77 – 4.65 (m, 1H), 4.15 (s, 3H), 3.55 (d, J = 8.3 Hz, 1H), 3.18 – 3.10 (m, 2H), 3.07 – 3.03 (m, 1H), 2.76 (d, J = 5.3 Hz, 1H), 2.34 (s, 3H), 2.04 (d, J = 11.0 Hz, 1H), 1.76 (d, J = 11.0 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.7, 155.2, 142.8, 138.7, 137.3, 135.5, 130.6, 128.9, 128.4, 128.1, 128.1, 126.6, 122.3, 118.6, 110.8, 56.2, 52.0, 48.5, 47.6, 47.1, 45.2, 42.9, 39.7, 22.9, 21.2. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_4$, ($[M + Na]^+$): 517.2098, found: 517.2093. **$[\alpha]_D^{20}$** = 76 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 18.39 min, tr (minor) = 15.44 min, 92% ee.

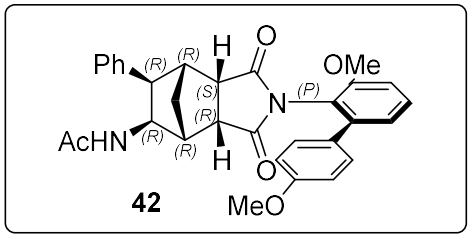




No.	Retention Time min	Area mAU*min	Relative Area %
1	15.357	55.352	50.67
2	19.033	53.898	49.33

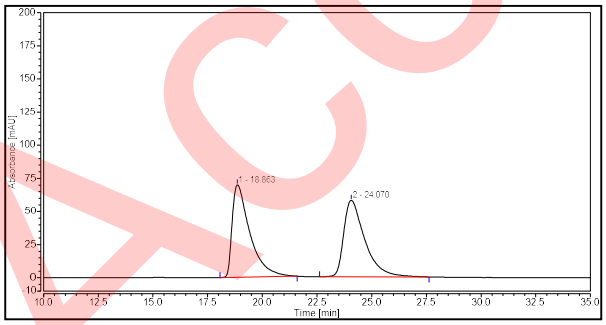
No.	Retention Time min	Area mAU*min	Relative Area %
1	15.437	9.727	4.11
2	18.390	226.988	95.89

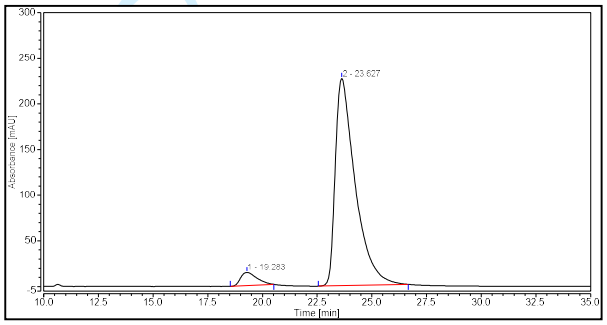
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(3,4'-dimethoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 42



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (22.4 mg, 44% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.45 (t, J = 8.0 Hz, 1H), 7.28 (t, J = 7.9 Hz, 2H), 7.22 – 7.15 (m, 3H), 7.13 – 7.04 (m, 3H), 7.01 – 6.98 (m, 1H), 6.88 – 6.82 (m, 2H), 4.81 (t, J = 8.8 Hz, 1H), 4.77 – 4.65 (m, 1H), 4.15 (s, 3H), 3.81 (s, 3H), 3.55 (d, J = 8.2 Hz, 1H), 3.15 – 3.11 (m, 2H), 3.08 – 3.04 (m, 1H), 2.76 (d, J = 5.3 Hz, 1H), 2.05 (d, J = 11.0 Hz, 1H), 1.76 (d, J = 10.9 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.7, 159.1, 155.2, 142.6, 138.6, 130.8, 130.6, 129.4, 128.4, 128.1, 126.6, 122.3, 118.7, 113.6, 110.7, 56.2, 55.2, 52.0, 48.5, 47.6, 47.2, 45.2, 42.9, 39.8, 22.9. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_5$, ($[M + Na]^+$): 533.2047, found: 533.2040. **$[\alpha]_D^{20}$** = 28 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 23.63 min, tr (minor) = 19.28 min, 90% ee.

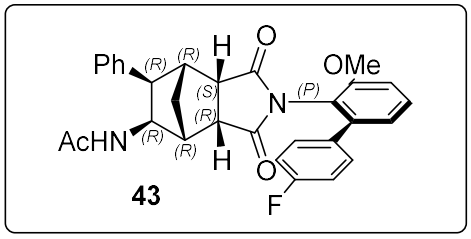




No.	Retention Time min	Area mAU*min	Relative Area %
1	18.863	65.633	50.54
2	24.070	64.221	49.46

No.	Retention Time min	Area mAU*min	Relative Area %
1	19.283	12.487	4.96
2	23.627	239.520	95.04

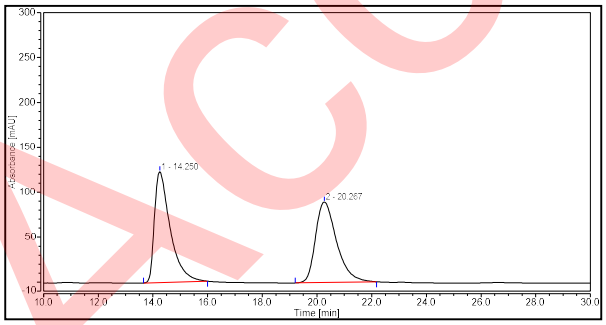
(*P*)-*N*-((3a*R*,4*R*,5*R*,6*R*,7*R*,7a*S*)-2-(4'-fluoro-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 43

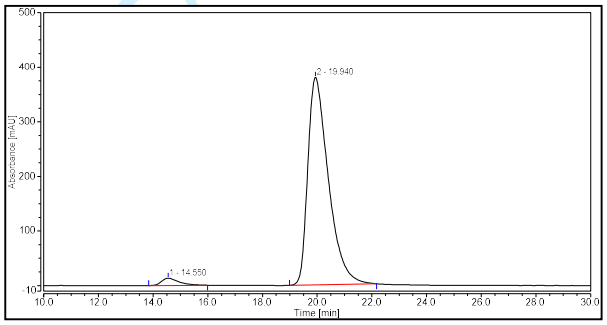


43

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (34.7 mg, 70% yield). **^{1}H NMR** ($CDCl_3$) δ 7.47 (t, J = 8.1 Hz, 1H), 7.30 – 7.24 (m, 2H), 7.25 – 7.16 (m, 3H), 7.13 – 7.06 (m, 3H), 7.04 – 6.95 (m, 3H), 4.93 – 4.69 (m, 2H), 4.15 (s, 3H), 3.53 (d, J = 8.1 Hz, 1H), 3.14 – 3.08 (m, 2H), 3.06 – 3.01 (m, 1H), 2.75 (d, J = 5.5 Hz, 1H), 2.05 (d, J = 11.1 Hz, 1H), 1.75 (d, J = 11.0 Hz, 1H), 1.47 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 168.8, 162.4 (d, J = 246.6 Hz), 155.2, 141.9, 138.5, 134.4 (d, J = 3.3 Hz), 130.7, 130.0 (d, J = 8.3 Hz), 128.4, 128.1, 126.7, 122.2, 118.7, 115.1 (d, J = 21.5 Hz), 111.2, 56.3, 52.0, 48.5, 47.6, 47.1, 45.2, 43.0, 39.7, 22.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}FN_2NaO_4$, ($[M + Na]^+$): 521.1847, found: 521.1844. **$[\alpha]_D^{20}$** = 78 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 °C, 227 nm); tr (major) = 19.94 min, tr (minor) = 14.55 min, 94% ee.

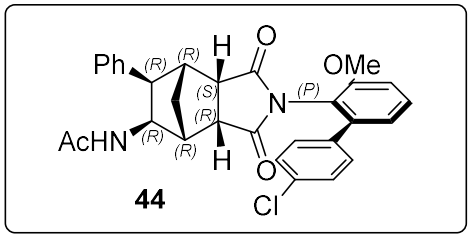




No.	Retention Time min	Area mAU*min	Relative Area %
1	14.250	82.371	50.70
2	20.267	80.081	49.30

No.	Retention Time min	Area mAU*min	Relative Area %
1	14.550	9.768	2.87
2	19.940	331.124	97.13

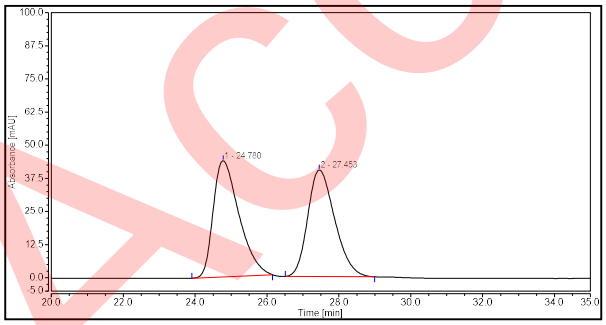
(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(4'-chloro-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyl-octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 44

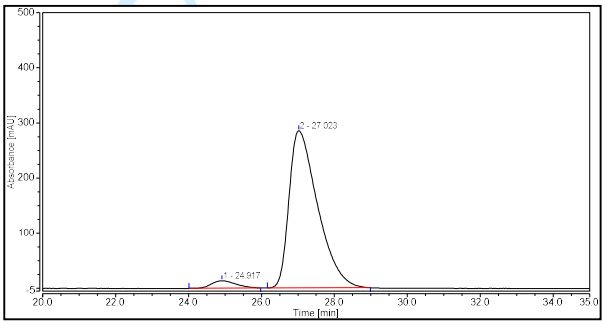


44

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (35.1 mg, 68% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.0 Hz, 1H), 7.29 – 7.23 (m, 4H), 7.22 – 7.15 (m, 3H), 7.13 – 7.04 (m, 3H), 6.97 – 6.94 (m, 1H), 4.80 – 4.75 (m, 2H), 4.14 (s, 3H), 3.60 – 3.46 (m, 1H), 3.16 – 3.07 (m, 2H), 3.06 – 3.01 (m, 1H), 2.74 (d, J = 5.3 Hz, 1H), 2.04 (d, J = 10.7 Hz, 1H), 1.75 (d, J = 11.0 Hz, 1H), 1.46 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.1, 175.9, 168.9, 155.3, 141.7, 138.6, 137.0, 133.9, 130.9, 129.7, 128.5, 128.5, 128.1, 126.7, 122.1, 118.6, 111.4, 56.3, 52.1, 48.5, 47.7, 47.2, 45.3, 43.2, 39.9, 23.0. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{27}ClN_2NaO_4$, ([M + Na]$^+$): 537.1552, found: 537.1548. **[α]$_D^{20}$** = 72 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 27.02 min, tr (minor) = 24.92 min, 92% ee.

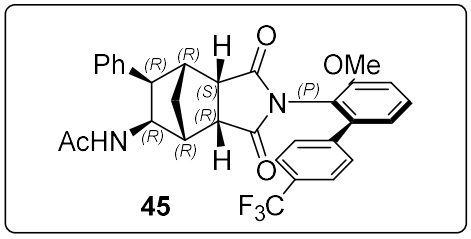




No.	Retention Time min	Area mAU*min	Relative Area %
1	24.780	36.515	51.06
2	27.453	34.993	48.94

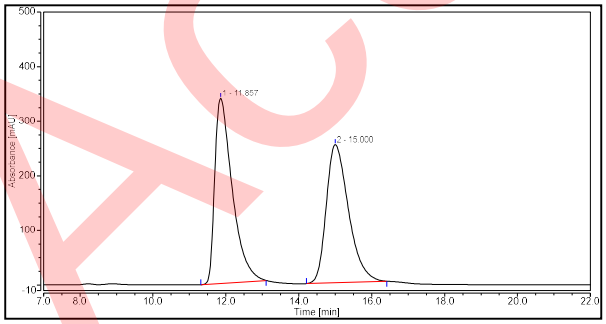
No.	Retention Time min	Area mAU*min	Relative Area %
1	24.917	10.483	3.89
2	27.023	259.361	96.11

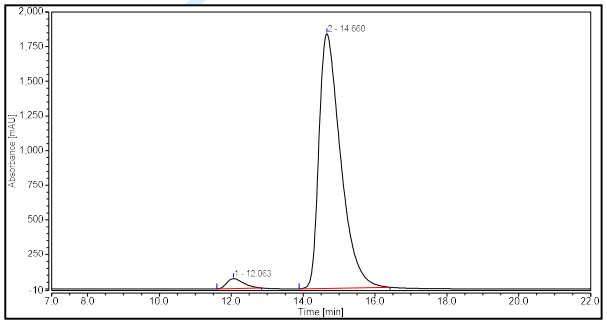
(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 45



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (48.2mg, 88% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 2H), 7.50 (t, J = 8.1 Hz, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.28 (t, J = 7.6 Hz, 2H), 7.23 – 7.17 (m, 1H), 7.17 – 7.14 (m, 1H), 7.10 (d, J = 7.5 Hz, 2H), 7.01 – 6.98 (m, 1H), 4.88 – 4.76 (m, 1H), 4.72 (d, J = 9.5 Hz, 1H), 4.18 (s, 3H), 3.54 (d, J = 8.2 Hz, 1H), 3.26 – 3.09 (m, 2H), 3.06 – 3.03 (m, 1H), 2.77 (d, J = 5.3 Hz, 1H), 2.05 (d, J = 11.0 Hz, 1H), 1.78 (d, J = 11.1 Hz, 1H), 1.49 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.6, 168.7, 155.3, 142.2, 141.5, 138.5, 130.9, 129.9 (q, J = 32.7 Hz), 128.7, 128.4, 128.0, 126.7, 125.1 (q, J = 3.4 Hz), 125.0 (q, J = 255.4 Hz), 121.9, 118.50, 111.7, 56.3, 52.0, 48.5, 47.6, 47.2, 45.3, 43.0, 39.8, 22.9. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{31}H_{27}F_3N_2NaO_4$, ($[M + Na]^+$): 571.1815, found: 571.1808. **$[\alpha]_D^{20}$** = 88 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 14.66 min, tr (minor) = 12.06 min, 94% ee.

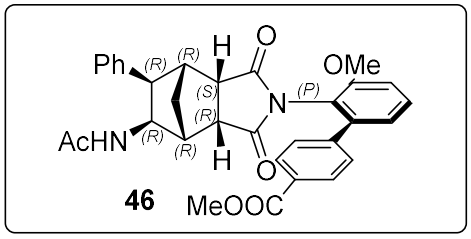




No.	Retention Time min	Area mAU*min	Relative Area %
1	11.857	189.265	51.42
2	15.000	178.792	48.58

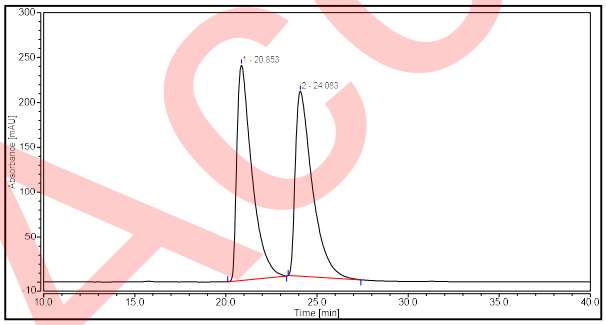
No.	Retention Time min	Area mAU*min	Relative Area %
1	12.063	38.621	2.93
2	14.660	1279.831	97.07

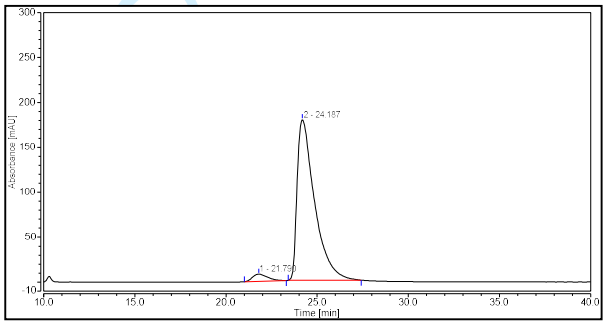
(*P*)-methyl2'-((*3aR,4R,5R,6R,7R,7aS*)-5-acetamido-1,3-dioxo-6-phenyloctahydro-2*H*-4,7-methanoisoindol-2-yl)-3'-methoxy-[1,1'-biphenyl]-4-carboxylate 46



Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (30.7mg, 57% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.99 (d, J = 7.9 Hz, 2H), 7.50 (t, J = 8.1 Hz, 1H), 7.37 – 7.23 (m, 4H), 7.23 – 6.96 (m, 5H), 4.86 – 4.76 (m, 2H), 4.16 (s, 3H), 3.92 (s, 3H), 3.52 (d, J = 8.0 Hz, 1H), 3.13 – 2.98 (m, 3H), 2.74 (d, J = 5.6 Hz, 1H), 2.05 (d, J = 11.0 Hz, 1H), 1.74 (d, J = 11.0 Hz, 1H), 1.47 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.7, 168.8, 166.9, 155.3, 143.2, 141.8, 138.5, 130.8, 129.4, 128.4, 128.4, 128.0, 126.6, 121.9, 118.5, 111.6, 56.3, 52.2, 52.0, 48.5, 47.6, 47.1, 45.2, 43.0, 39.7, 22.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{32}H_{30}N_2NaO_6$, ($[M + Na]^+$): 561.1996, found: 561.1996. **$[\alpha]_D^{20}$** = 70 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 24.19 min, tr (minor) = 21.80 min, 92% ee.

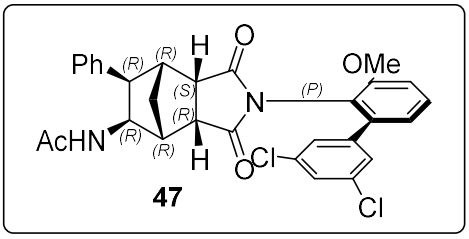




No.	Retention Time min	Area mAU*min	Relative Area %
1	20.853	230.695	50.79
2	24.083	223.558	49.21

No.	Retention Time min	Area mAU*min	Relative Area %
1	21.790	7.877	3.82
2	24.187	198.427	96.18

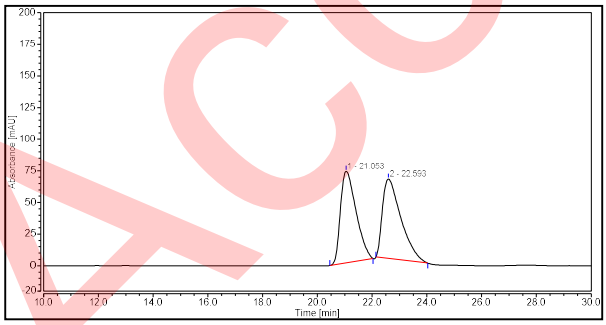
(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3',5'-dichloro-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 47

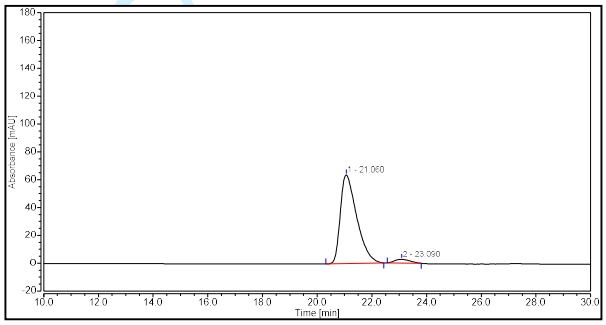


47

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (33.5 mg, 61% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49 (t, J = 8.1 Hz, 1H), 7.34 – 7.24 (m, 3H), 7.23 – 7.12 (m, 4H), 7.10 (d, J = 7.3 Hz, 2H), 6.99 – 6.97 (m, 1H), 4.84 – 4.78 (m, 2H), 4.16 (s, 3H), 3.53 (d, J = 6.2 Hz, 1H), 3.34 – 3.01 (m, 3H), 2.77 (d, J = 4.7 Hz, 1H), 2.07 (d, J = 11.0 Hz, 1H), 1.80 (d, J = 11.1 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.6, 168.8, 155.4, 141.2, 140.0, 138.5, 134.7, 131.0, 128.4, 128.0, 127.8, 126.8, 126.7, 121.8, 118.5, 112.0, 56.4, 52.0, 48.5, 47.7, 47.2, 45.2, 43.0, 39.8, 22.9. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{26}Cl_2N_2NaO_4$, ($[M + Na]^+$): 571.1162, found: 571.1171. **$[\alpha]_D^{20}$** = 74 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IE column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 21.060 min, tr (minor) = 23.09 min,92% ee.

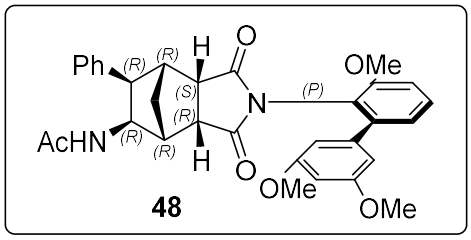




No.	Retention Time min	Area mAU*min	Relative Area %
1	21.053	47.768	49.16
2	22.593	49.409	50.84

No.	Retention Time min	Area mAU*min	Relative Area %
1	21.060	44.295	96.27
2	23.090	1.717	3.73

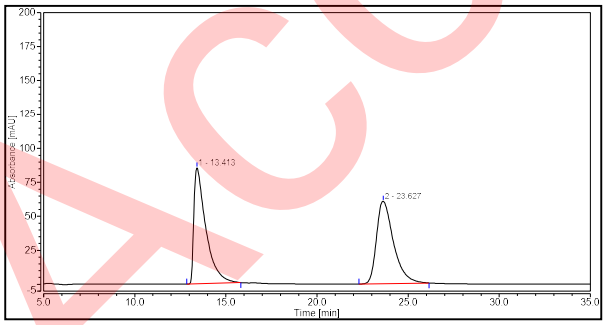
(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-1,3-dioxo-6-phenyl-2-(3,3',5'-trimethoxy-[1,1'-biphenyl]-2-yl)octahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 48

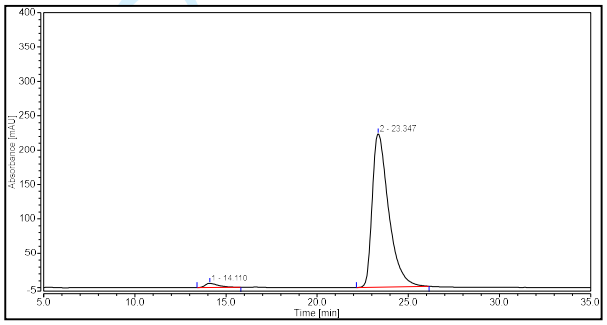


48

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (44.3 mg, 82% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.46 (t, J = 8.1 Hz, 1H), 7.28 – 7.24 (m, 2H), 7.18 (t, J = 7.4 Hz, 1H), 7.13 – 7.06 (m, 3H), 7.03 – 7.01 (m, 1H), 6.43 – 6.39 (m, 3H), 4.97 – 4.91 (m, 1H), 4.78 (t, J = 8.8 Hz, 1H), 4.14 (s, 3H), 3.74 (s, 6H), 3.54 (d, J = 8.3 Hz, 1H), 3.22 – 3.01 (m, 3H), 2.73 (d, J = 4.1 Hz, 1H), 2.05 (d, J = 11.0 Hz, 1H), 1.74 (d, J = 11.0 Hz, 1H), 1.45 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.1, 175.9, 168.8, 160.4, 155.2, 142.8, 140.3, 138.6, 130.7, 128.3, 128.1, 126.6, 122.1, 118.5, 111.1, 106.2, 100.3, 56.3, 55.4, 52.1, 48.6, 47.6, 47.2, 45.2, 43.0, 39.7, 22.8. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{32}H_{32}N_2NaO_6$, ($[M + Na]^+$): 563.2153, found: 563.2152. **$[\alpha]_D^{20}$** = 104 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 23.35 min, tr (minor) = 14.11 min, 96% ee.

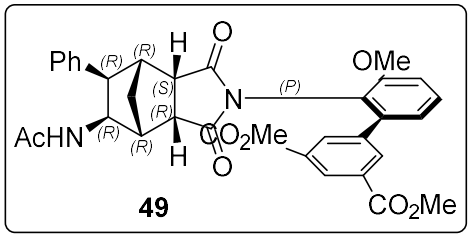




No.	Retention Time min	Area mAU*min	Relative Area %
1	13.413	65.707	49.99
2	23.627	65.734	50.01

No.	Retention Time min	Area mAU*min	Relative Area %
1	14.110	5.130	2.15
2	23.347	233.035	97.85

(*P*)-dimethyl 2'-((*3aR,4R,5R,6R,7R,7aS*)-5-acetamido-1,3-dioxo-6-phenyloctahydro-2*H*-4,7-methanoisoindol-2-yl)-3'-methoxy-[1,1'-biphenyl]-3,5-dicarboxylate 49



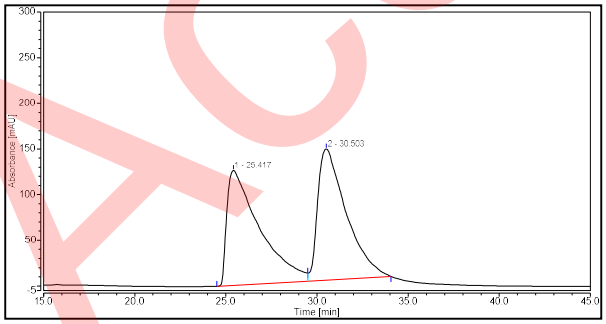
49

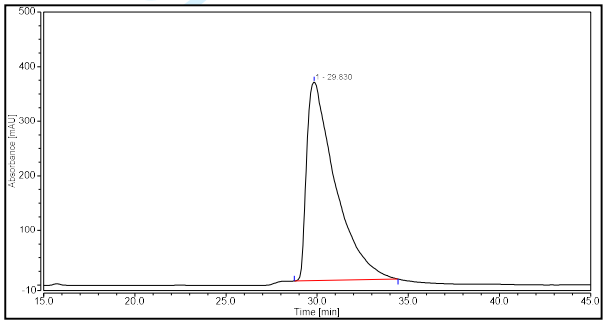
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (38.4 mg, 64% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.62 (t, J = 1.7 Hz, 1H), 8.15 (d, J = 1.7 Hz, 2H), 7.52 (t, J = 8.1 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.22 – 7.14 (m, 2H), 7.10 – 7.07 (m, 3H), 4.89 – 4.74 (m, 2H), 4.17 (s, 3H), 3.93 (s, 6H), 3.53 (d, J = 7.5 Hz, 1H), 3.18 – 3.08 (m, 2H), 3.05 – 3.01 (m, 1H), 2.76 (d, J = 5.2 Hz, 1H), 2.05 (d, J = 11.0 Hz, 1H), 1.77 (d, J = 11.0 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.8, 175.6, 168.8, 166.0, 155.4, 140.3, 139.1, 138.5, 133.5, 131.0, 130.8, 129.9, 128.3, 128.0, 126.6, 121.9, 118.7, 111.9, 56.4, 52.5, 52.1, 48.5, 47.6, 47.1, 45.2, 42.9, 39.7, 22.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{34}H_{32}N_2NaO_8$, ($[M + Na]^+$): 619.2051, found: 619.2060.

$[\alpha]_D^{20}$ = 58 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 88:12, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 29.83 min, >99% ee.

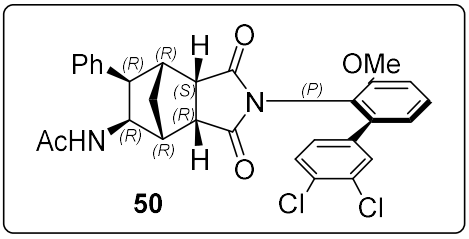




No.	Retention Time min	Area mAU*min	Relative Area %
1	25.417	260.700	49.98
2	30.503	260.937	50.02

No.	Retention Time min	Area mAU*min	Relative Area %
1	29.830	663.337	100.00
2	-	-	-

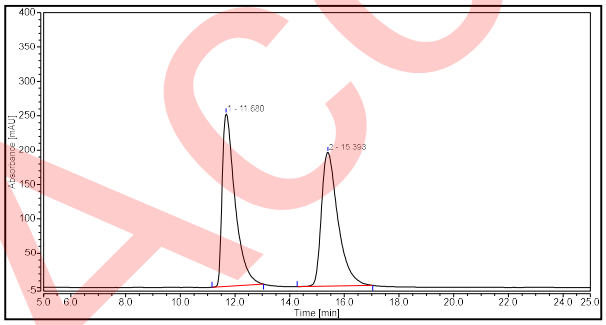
(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3',4'-dichloro-3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 50

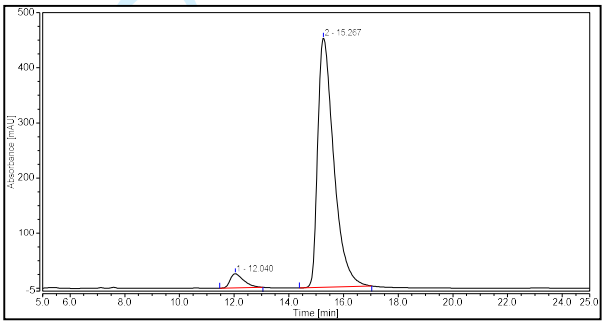


50

Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (34mg, 62% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (t, J = 8.1 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.31 – 7.25 (m, 2H), 7.20 (t, J = 7.3 Hz, 1H), 7.16 – 7.06 (m, 4H), 6.98 – 6.96 (m, 1H), 4.89 – 4.75 (m, 2H), 4.16 (s, 3H), 3.53 (d, J = 7.4 Hz, 1H), 3.29 – 3.01 (m, 3H), 2.77 (d, J = 5.0 Hz, 1H), 2.07 (d, J = 11.1 Hz, 1H), 1.79 (d, J = 11.1 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 175.9, 175.6, 168.8, 155.3, 140.4, 138.5, 138.4, 132.3, 132.0, 130.9, 130.2, 130.2, 128.4, 128.0, 127.7, 126.7, 121.9, 118.5, 111.8, 56.3, 52.0, 48.5, 47.6, 47.2, 45.3, 43.0, 39.8, 22.9. **HRMS** (ESI-TOF) (m/z): Calcd for $C_{30}H_{26}Cl_2N_2NaO_4$, ($[M + Na]^+$): 571.1162, found: 571.1166. **$[\alpha]_D^{20}$** = 78 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 15.27 min, tr (minor) = 12.04 min,91% ee.



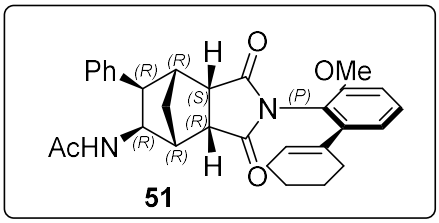


No.	Retention Time min	Area mAU*min	Relative Area %
1	11.680	137.426	50.19
2	15.393	136.358	49.81

No.	Retention Time min	Area mAU*min	Relative Area %
1	12.040	14.787	4.59
2	15.267	307.463	95.41

https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-2',3',4',5'-tetrahydro-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)acetamide 51



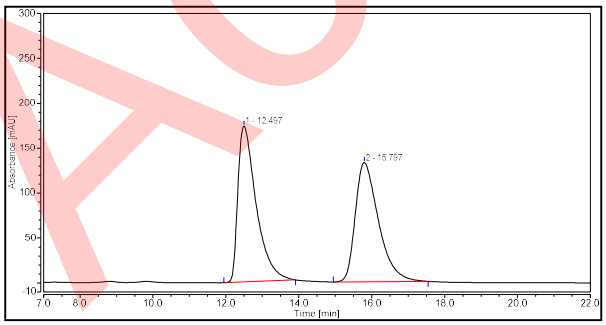
51

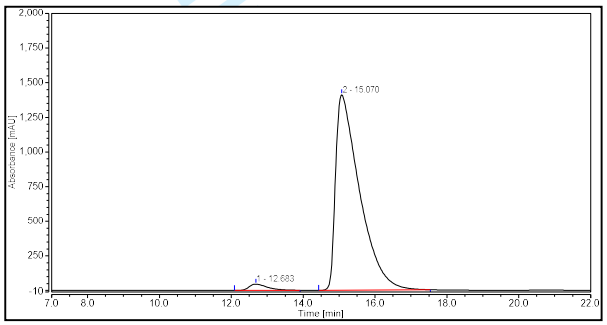
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (32.1 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 (t, J = 8.0 Hz, 1H), 7.28 (t, J = 7.7 Hz, 2H), 7.19 (t, J = 7.3 Hz, 1H), 7.11 (d, J = 7.5 Hz, 2H), 6.97 – 6.94 (m, 1H), 6.88 – 6.86 (m, 1H), 5.55 – 5.52 (m, 1H), 4.88 – 4.76 (m, 2H), 4.09 (s, 3H), 3.57 (d, J = 8.1 Hz, 1H), 3.30 – 3.27 (m, 2H), 3.20 (brs, 1H), 2.81 (brs, 1H), 2.19 – 2.15 (m, 2H), 2.10 (d, J = 11.0 Hz, 1H), 2.05 – 2.00 (m, 2H), 1.84 (d, J = 11.0 Hz, 1H), 1.70 – 1.62 (m, 2H), 1.61 – 1.53 (m, 2H), 1.47 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.3, 175.8, 168.8, 155.1, 145.1, 138.6, 135.3, 130.3, 128.4, 128.1, 126.6, 126.1, 120.6, 118.0, 109.9, 56.1, 52.1, 48.7, 47.6, 47.3, 45.3, 43.0, 39.8, 29.4, 25.5, 23.1, 22.8, 22.0.

HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{32}N_2NaO_4$, ($[M + Na]^+$): 507.2254, found: 507.2254.

$[\alpha]_D^{20}$ = 68 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 227 nm); tr (major) = 15.07 min, tr (minor) = 12.68 min, 95% ee.

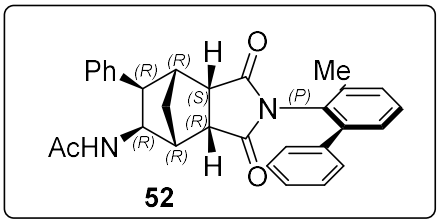




No.	Retention Time min	Area mAU*min	Relative Area %
1	12.497	101.061	50.80
2	15.797	97.871	49.20

No.	Retention Time min	Area mAU*min	Relative Area %
1	12.683	27.007	2.41
2	15.070	1091.811	97.59

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methyl-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1H-4,7-methanoisoindol-5-yl)acetamide 52

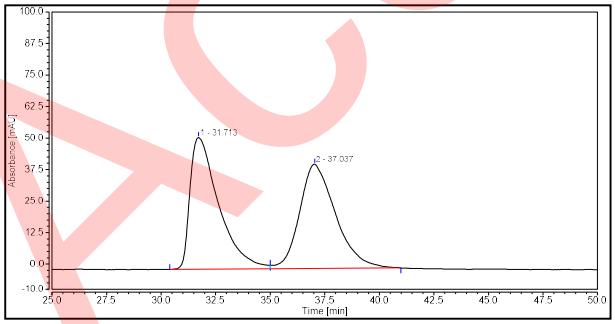


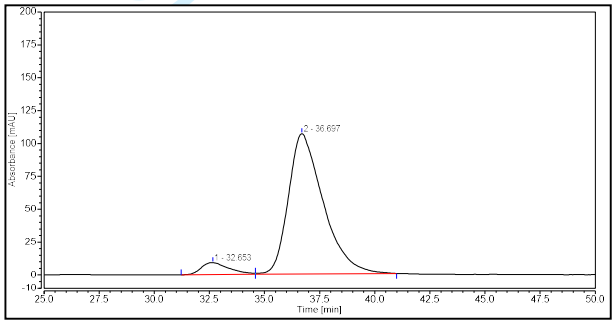
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (20.4 mg, 44% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 2H), 7.34 – 7.29 (m, 5H), 7.26 – 7.20 (m, 4H), 7.07 (d, J = 7.1 Hz, 2H), 4.71 – 4.69 (m, 1H), 4.62 (td, J = 8.7, 1.7 Hz, 1H), 3.42 (d, J = 8.4 Hz, 1H), 3.13 – 3.12 (m, 2H), 2.95 – 2.90 (m, 1H), 2.75 (d, J = 4.9 Hz, 1H), 2.54 (s, 3H), 2.03 (d, J = 11.0 Hz, 1H), 1.75 (d, J = 11.1 Hz, 1H), 1.50 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.2, 175.7, 168.8, 141.5, 139.2, 137.7, 136.4, 130.5, 129.7, 129.6, 128.6, 128.4, 128.3, 128.1, 128.0, 127.6, 127.0, 52.0, 48.7, 47.8, 47.3, 44.8, 42.5, 39.6, 22.8, 18.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{30}H_{28}N_2NaO_3$, ($[M + Na]^+$): 487.1992, found: 487.1996.

$[\alpha]_D^{20}$ = 58 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 92:8, v = 1.0 mL/min, 40 °C, 227 nm); tr (major) = 36.70 min, tr (minor) = 32,65 min, 87% ee.

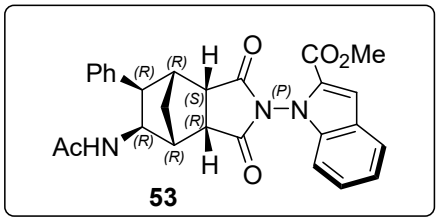




No.	Retention Time min	Area mAU*min	Relative Area %
1	31.713	79.734	50.14
2	37.037	79.288	49.86

No.	Retention Time min	Area mAU*min	Relative Area %
1	32.653	13.348	6.39
2	36.697	195.653	93.61

Methyl-*P*- 1-((*3aR,4R,5R,6R,7R,7aS*)-5-acetamido-1,3-dioxo-6-phenyloctahydro-2H-4,7-methanoisoindol-2-yl)-1H-indole-2-carboxylate 53



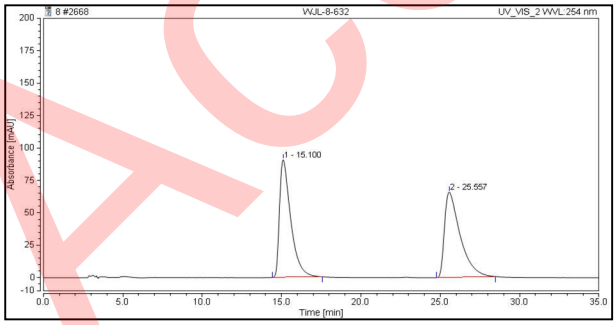
53

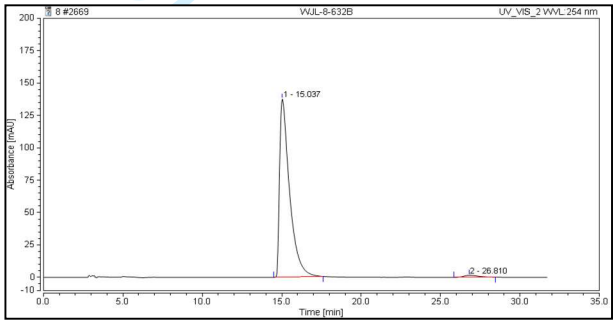
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (30.1mg, 64% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, J = 8.0 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.45 (s, 1H), 7.33 – 7.29 (m, 3H), 7.26 – 7.22 (m, 1H), 7.17 (d, J = 7.6 Hz, 2H), 5.02 (d, J = 8.9 Hz, 1H), 4.79 (t, J = 8.6 Hz, 1H), 3.84 (s, 3H), 3.55 (d, J = 8.5 Hz, 1H), 3.49 (brs, 2H) 3.31 (s, 1H), 2.92 (s, 1H), 2.18 (d, J = 11.2 Hz, 1H), 1.87 (d, J = 11.2 Hz, 1H), 1.54 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 173.6, 172.7, 169.2, 160.8, 138.1, 137.3, 128.6, 128.1, 127.7, 127.1, 125.1, 124.6, 123.3, 122.8, 112.2, 109.2, 52.5, 51.9, 48.4, 46.7, 45.6, 44.8, 42.9, 39.2, 22.7.

HRMS (ESI-TOF) (m/z): Calcd for $C_{27}H_{25}N_3NaO_5$, ($[M + Na]^+$): 494.1686, found: 494.1675.

$[\alpha]_D^{20}$ = 40 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 85:15, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 15.04 min, tr (minor) = 26.81 min, 96% ee.

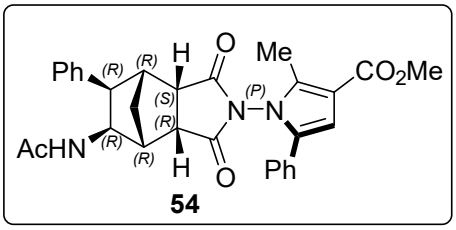




No.	Retention Time min	Area mAU*min	Relative Area %
1	15.100	74.261	49.74
2	25.557	75.046	50.26

No.	Retention Time min	Area mAU*min	Relative Area %
1	15.037	100.337	98.31
2	26.810	1.728	1.69

Methyl-*P*- 1-((*3aR,4R,5R,6R,7R,7aS*)-5-acetamido-1,3-dioxo-6-phenyloctahydro-2H-4,7-methanoisoindol-2-yl)-5-phenyl-1H-pyrrole-2-carboxylate 54



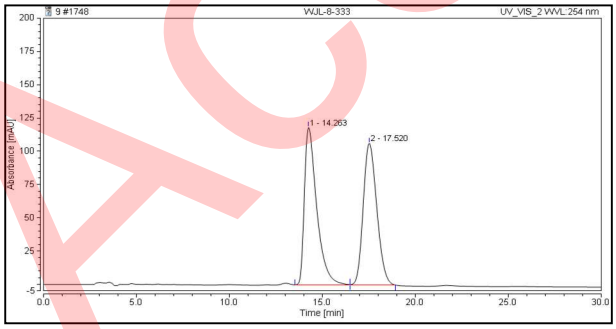
54

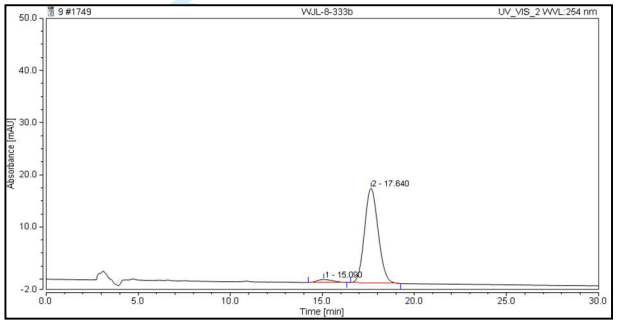
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (22.5 mg, 44% yield). **^{1}H NMR** ($CDCl_3$) δ 7.34 – 7.29 (M, 5H), 7.25 – 7.22 (m, 3H), 7.07 (d, J = 7.6 Hz, 2H), 6.72 (s, 1H), 4.75 – 4.73 (m, 1H), 4.59 – 4.56 (m, 1H), 3.85 (s, 3H), 3.36 (d, J = 8.8 Hz, 1H) 3.23 – 3.22 (m, 1H), 3.16 – 3.15 (m, 2H), 2.87 (d, J = 4.1 Hz, 1H), 2.71 (s, 3H), 2.10 (d, J = 11.2 Hz, 1H), 1.79 (d, J = 11.3 Hz, 1H), 1.53 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 172.7, 172.0, 169.0, 165.1, 136.9, 136.2, 133.3, 130.2, 128.8, 128.6, 128.4, 128.3, 127.9, 127.3, 112.4, 109.0, 52.0, 51.1, 47.8, 46.5, 45.0, 44.8, 42.5, 39.1, 29.7, 22.7.

HRMS (ESI-TOF) (m/z): Calcd for $C_{29}H_{27}N_3NaO_5$, ($[M + Na]^+$): 534.1999, found: 534.1992.

$[\alpha]_D^{20}$ = 28 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IG column (hexane: 2-propanol = 70:30, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 17.64 min, tr (minor) = 15.09 min, 92% ee.

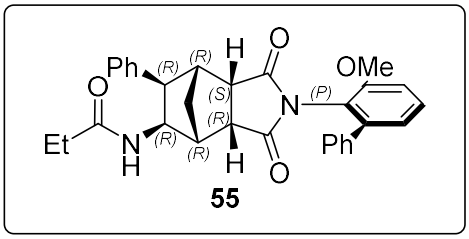




No.	Retention Time min	Area mAU*min	Relative Area %
1	14.263	91.155	50.28
2	17.520	90.129	49.72

No.	Retention Time min	Area mAU*min	Relative Area %
1	15.090	0.623	3.85
2	17.640	15.558	96.15

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)propionamide 55



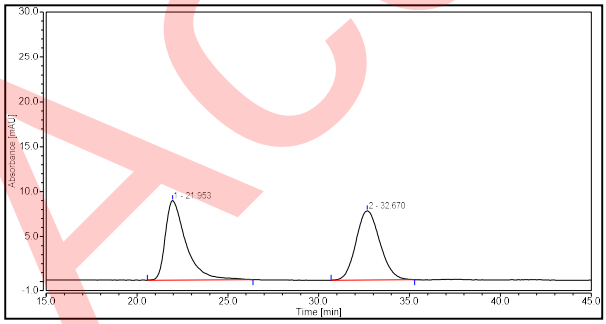
55

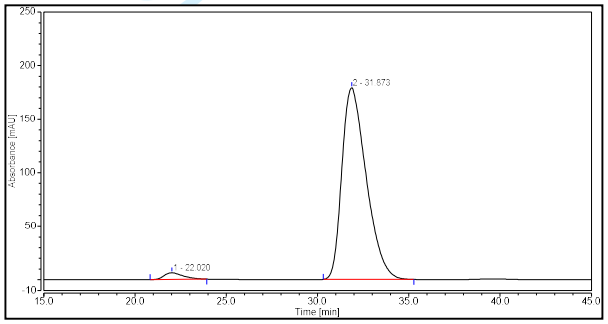
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (31.1 mg, 63% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.27 – 7.23 (m, 4H), 7.17 (t, J = 7.3 Hz, 1H), 7.13 – 7.05 (m, 3H), 7.03 – 7.00 (m, 1H), 4.92 – 4.68 (m, 2H), 4.17 (s, 3H), 3.53 (d, J = 7.6 Hz, 1H), 3.16 – 3.05 (m, 2H), 3.02 – 2.98 (m, 1H), 2.74 (d, J = 5.3 Hz, 1H), 2.05 (d, J = 11.3 Hz, 1H), 1.84 – 1.70 (m, 2H), 1.65 – 1.57 (m, 1H), 0.68 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 176.0, 175.8, 172.3, 155.2, 142.8, 138.7, 138.4, 130.6, 128.3, 128.2, 128.1, 128.1, 127.6, 126.6, 122.2, 118.6, 111.0, 56.3, 51.7, 48.5, 47.7, 47.1, 45.2, 43.1, 39.8, 29.5, 9.4.

HRMS (ESI-TOF) (m/z): Calcd for $C_{31}H_{30}N_2NaO_4$, ($[M + Na]^+$): 517.2098, found: 517.2096.

$[\alpha]_D^{20}$ = 68 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 31.87 min, tr (minor) = 22.02 min, 93% ee.

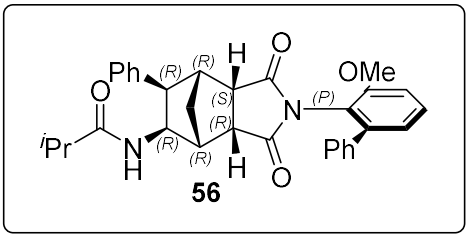




No.	Retention Time min	Area mAU*min	Relative Area %
1	21.953	11.668	49.76
2	32.670	11.779	50.24

No.	Retention Time min	Area mAU*min	Relative Area %
1	22.020	10.080	3.51
2	31.873	276.697	96.49

(*P*)-*N*-((*3aR,4R,5R,6R,7R,7aS*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-1,3-dioxo-6-phenyloctahydro-1*H*-4,7-methanoisoindol-5-yl)isobutyramide 56

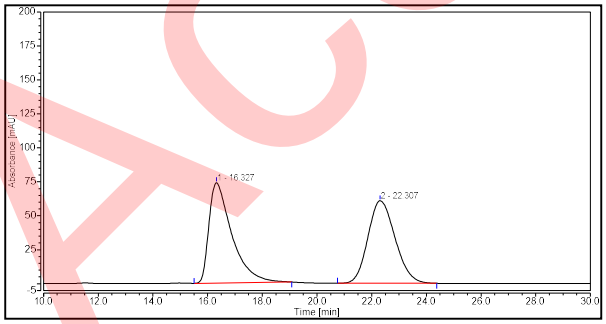


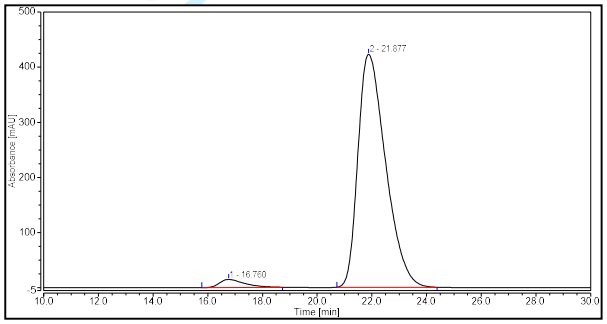
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (20.8mg, 41% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (t, J = 8.0 Hz, 1H), 7.31 – 7.27 (m, 3H), 7.26 – 7.19 (m, 4H), 7.15 (t, J = 7.3 Hz, 1H), 7.11 – 7.06 (m, 3H), 7.05 – 6.96 (m, 1H), 4.84 – 4.72 (m, 2H), 4.18 (s, 3H), 3.52 (d, J = 7.4 Hz, 1H), 3.15 – 3.06 (m, 2H), 3.03 – 2.96 (m, 1H), 2.74 (d, J = 5.3 Hz, 1H), 2.12 – 1.99 (m, 1H), 1.84 (p, J = 6.9 Hz, 1H), 1.76 (d, J = 11.0 Hz, 1H), 0.78 (d, J = 6.9 Hz, 3H), 0.58 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.1, 175.9, 175.3, 155.2, 142.9, 138.8, 138.5, 130.7, 128.5, 128.3, 128.3, 128.2, 127.7, 126.7, 122.3, 118.6, 111.0, 56.4, 51.6, 48.6, 47.8, 47.1, 45.4, 43.3, 40.1, 35.6, 19.3, 19.0.

HRMS (ESI-TOF) (m/z): Calcd for $C_{32}H_{32}N_2NaO_4$, ($[M + Na]^+$): 531.2254, found: 531.2254.

$[\alpha]_D^{20}$ = 70 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 ºC, 254 nm); tr (major) = 21.88 min, tr (minor) = 16.76 min, 94% ee.

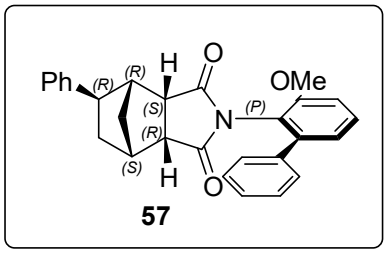




No.	Retention Time min	Area mAU*min	Relative Area %
1	16.327	71.640	50.57
2	22.307	70.035	49.43

No.	Retention Time min	Area mAU*min	Relative Area %
1	16.760	15.375	3.01
2	21.877	494.782	96.99

(*3aS,4R,5R,7S,7aR*)-2-(3-methoxy-[1,1'-biphenyl]-2-yl)-5-phenylhexahydro-1H-4,7-methanoisoindole-1,3(2H)-dione 57



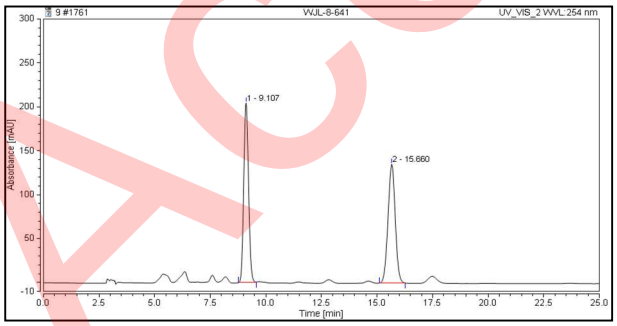
57

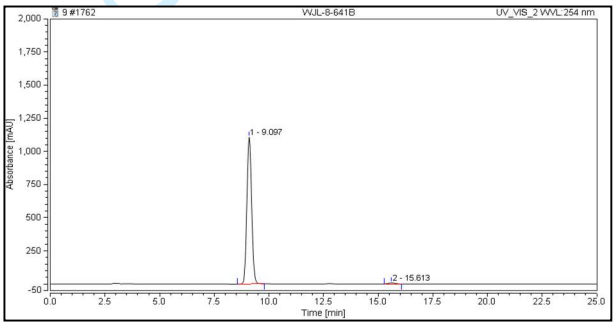
Prepared according to general procedure A on a 0.1 mmol scale, column chromatography (PE/EA = 2/1 to EA, v/v) afforded the title compound as a white foam (39.8 mg, 94% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 (t, J = 8.0 Hz, 1H), 7.35 – 7.28 (m, 7H), 7.23 – 7.19 (m, 3H), 7.04 (t, J = 7.1 Hz, 2H), 3.83 (s, 3H), 3.30 (dd, J = 9.1, 5.4 Hz, 1H), 3.04 (dd, J = 9.7, 5.3 Hz, 1H), 2.99 – 2.97 (m, 1H), 2.89 – 2.86 (m, 2H), 2.23 – 2.19 (m, 1H), 1.90 – 1.86 (m, 2H), 1.51 (d, J = 10.4 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 177.4, 177.3, 155.0, 145.4, 143.1, 138.4, 130.5, 128.5, 128.3, 128.1, 127.7, 127.1, 126.0, 122.5, 118.9, 110.9, 55.8, 49.2, 48.5, 45.9, 41.6, 39.9, 39.7, 32.8.

HRMS (ESI-TOF) (m/z): Calcd for $C_{28}H_{25}NNaO_3$, ($[M + Na]^+$): 446.1727, found: 446.1723.

$[\alpha]_D^{20}$ = -50 (c = 0.1, $CHCl_3$).

HPLC analysis: Daicel Chiralpak IA column (hexane: 2-propanol = 80:20, v = 1.0 mL/min, 40 °C, 254 nm); tr (major) = 9.10 min, tr (minor) = 15.61 min, 98% ee.

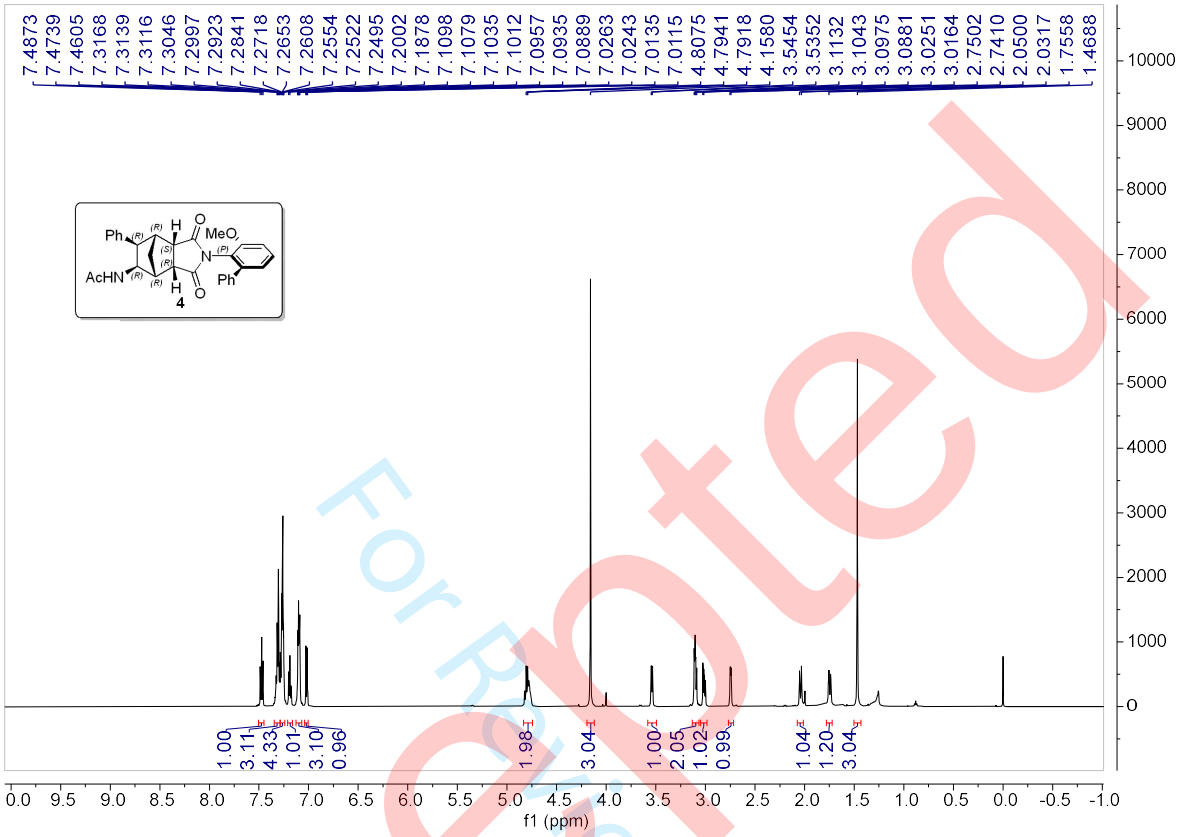




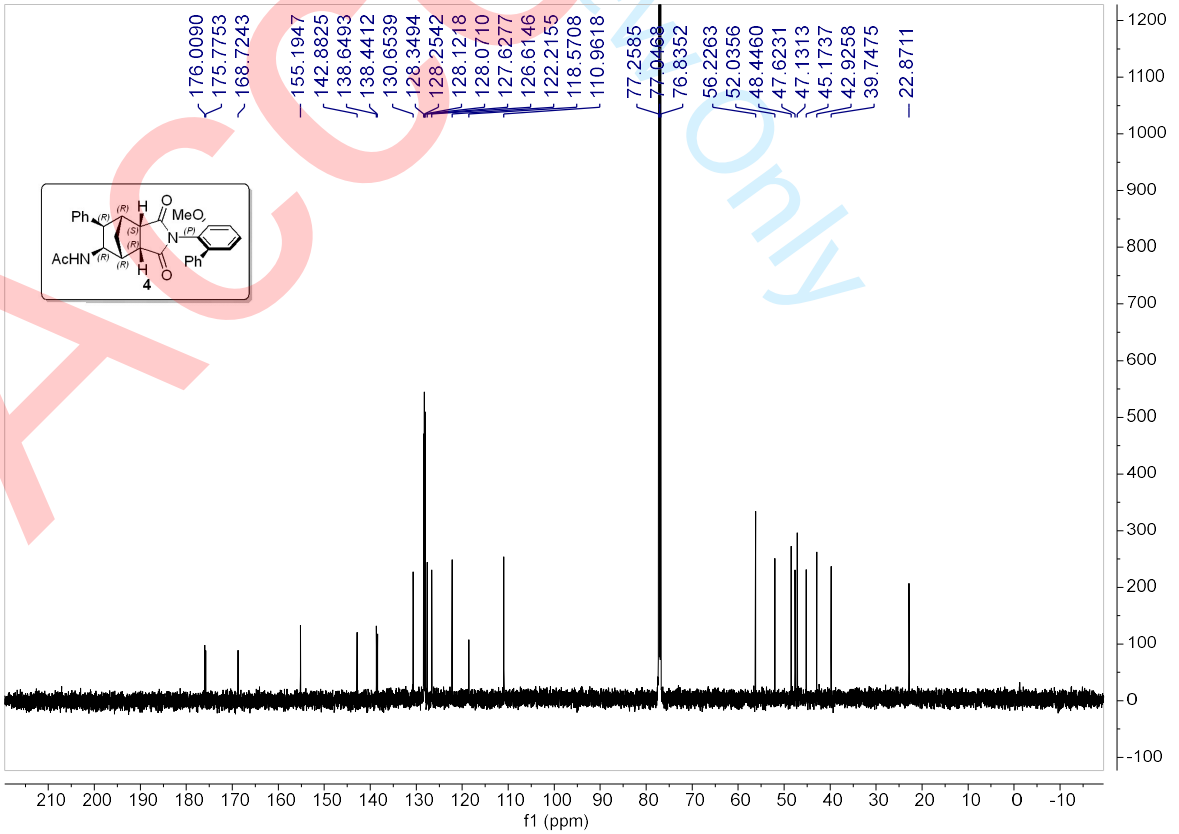
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.107	50.719	49.95
2	15.660	50.830	50.05

No.	Retention Time min	Area mAU*min	Relative Area %
1	9.097	279.453	99.01
2	15.613	2.799	0.99

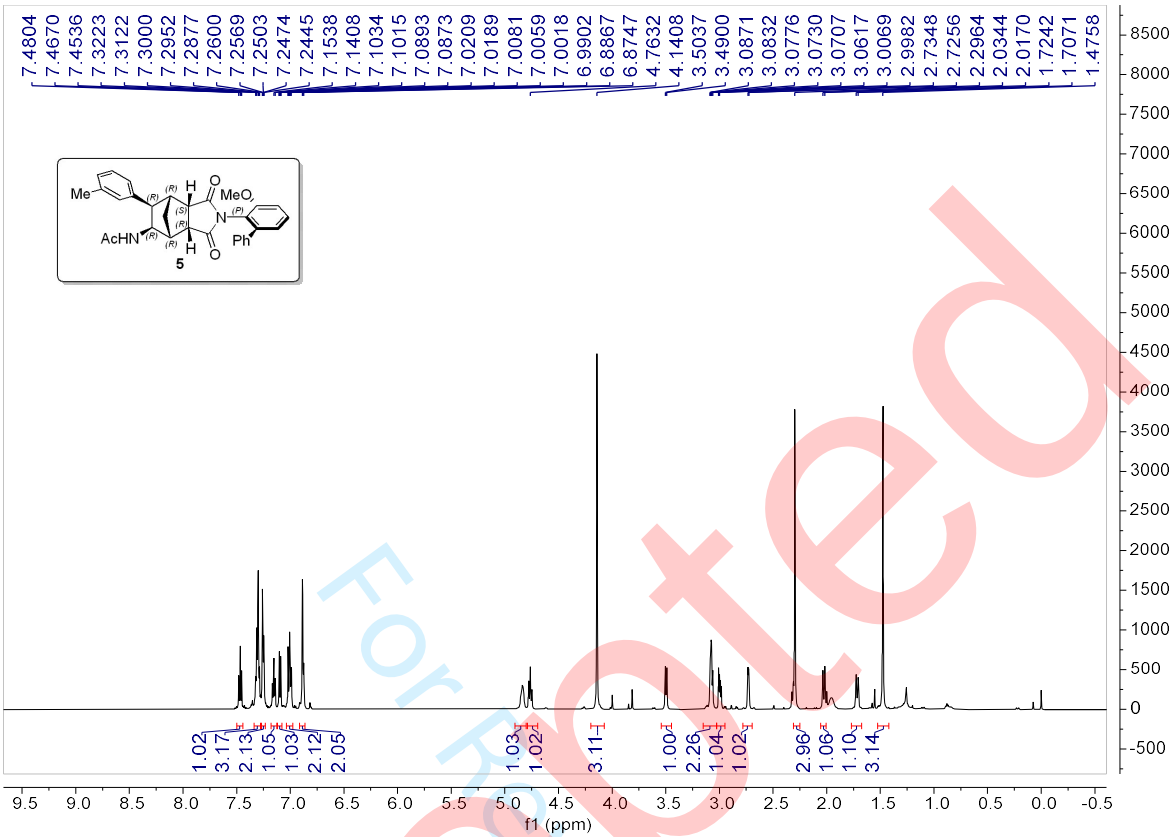
7. NMRspectrum



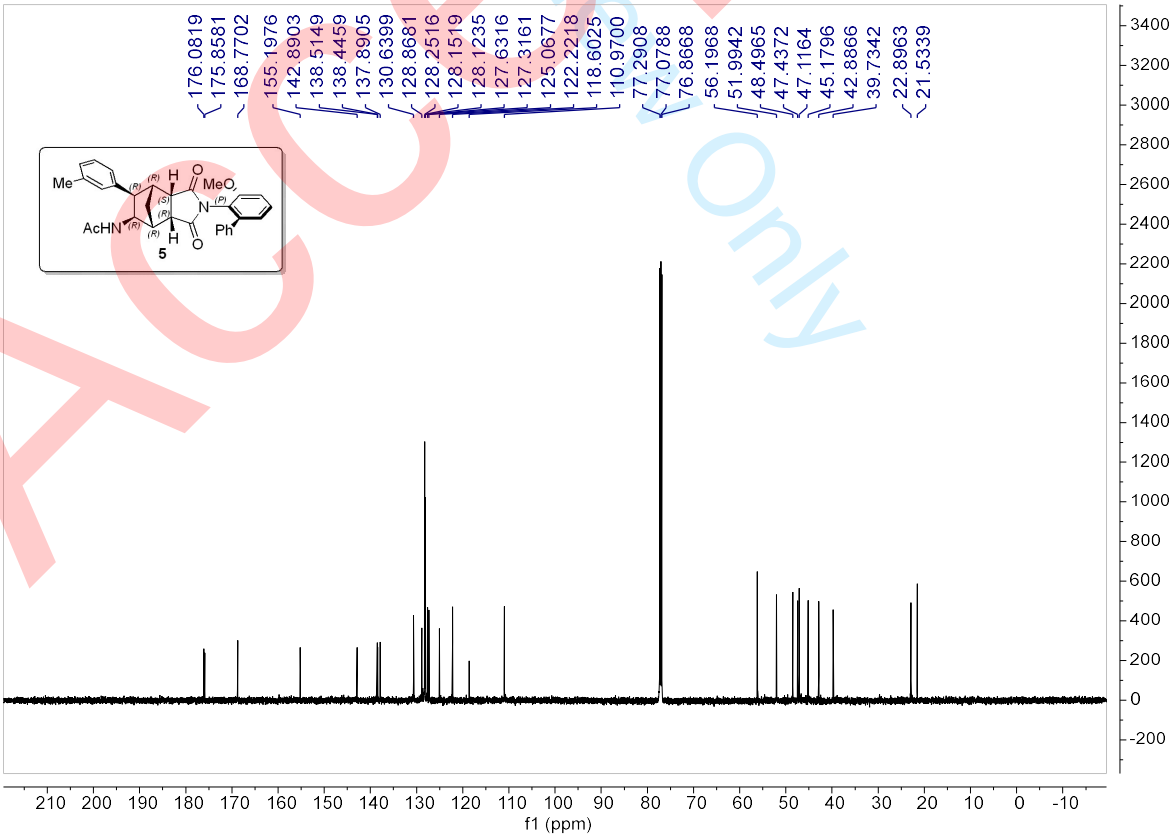
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 4



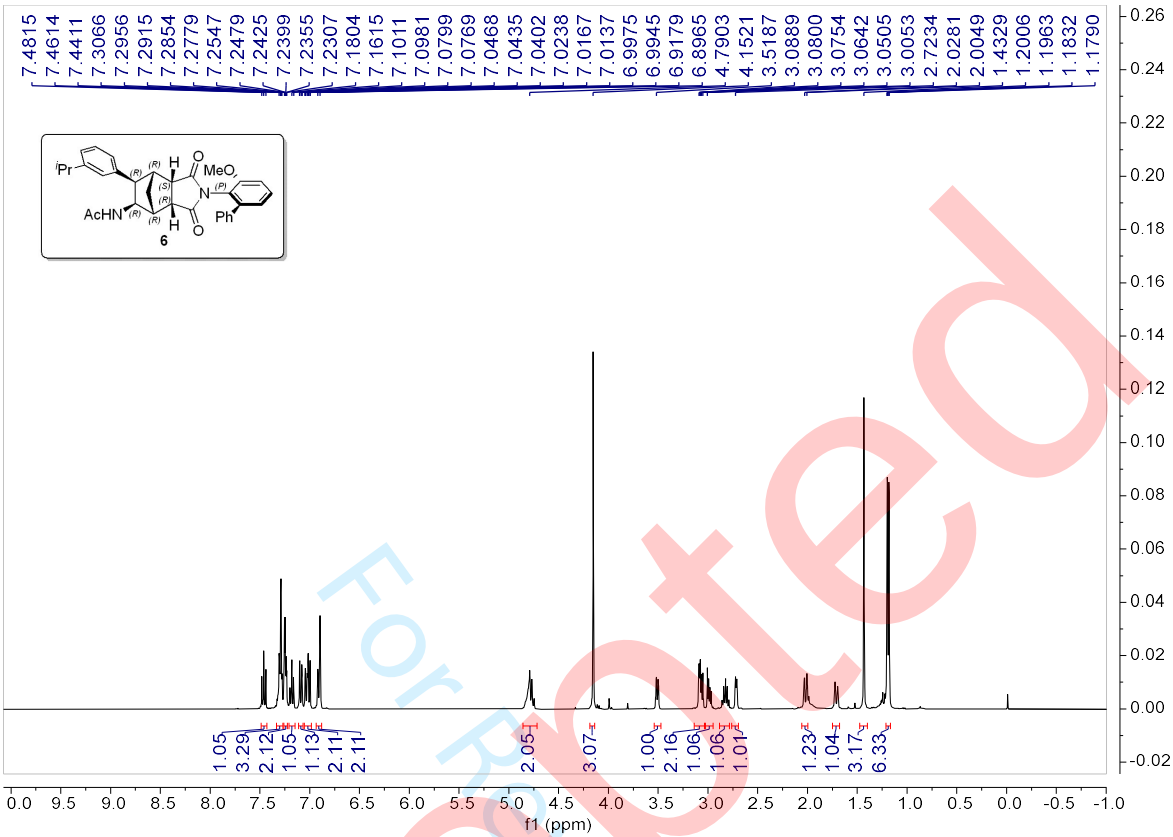
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 4



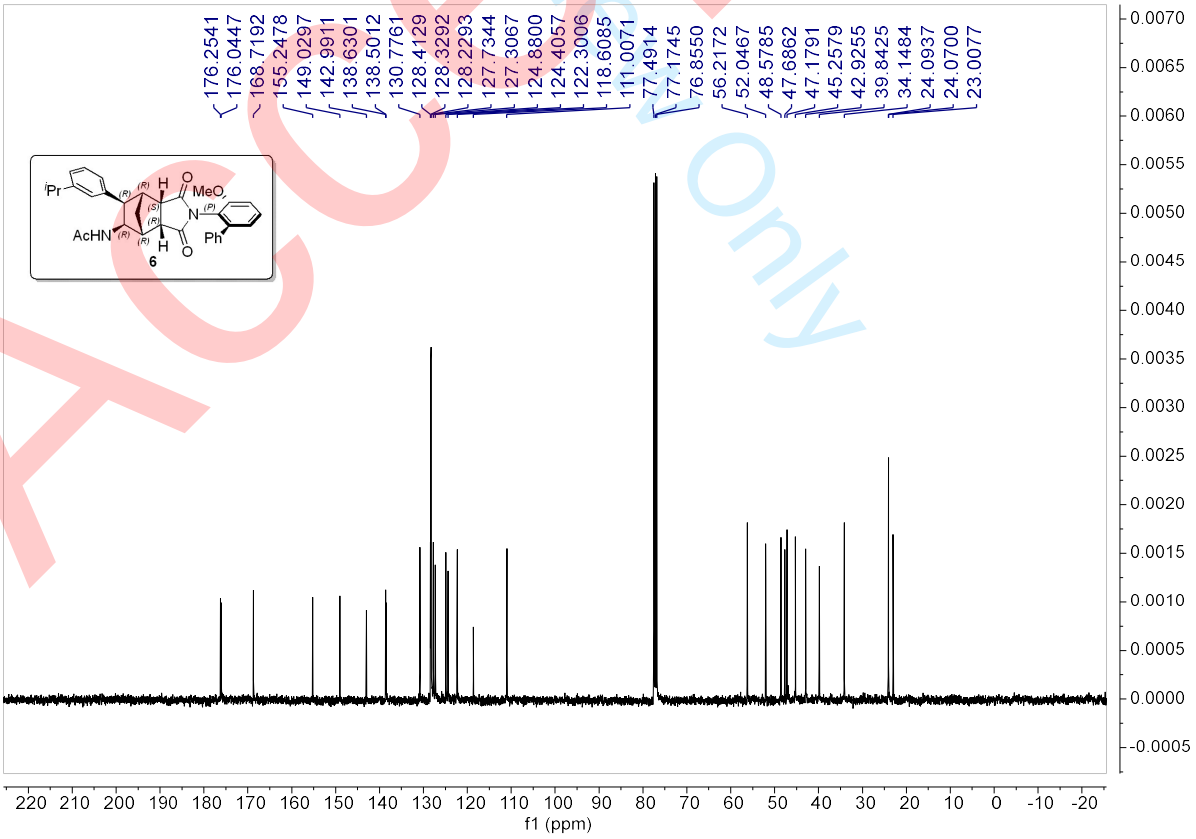
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 5



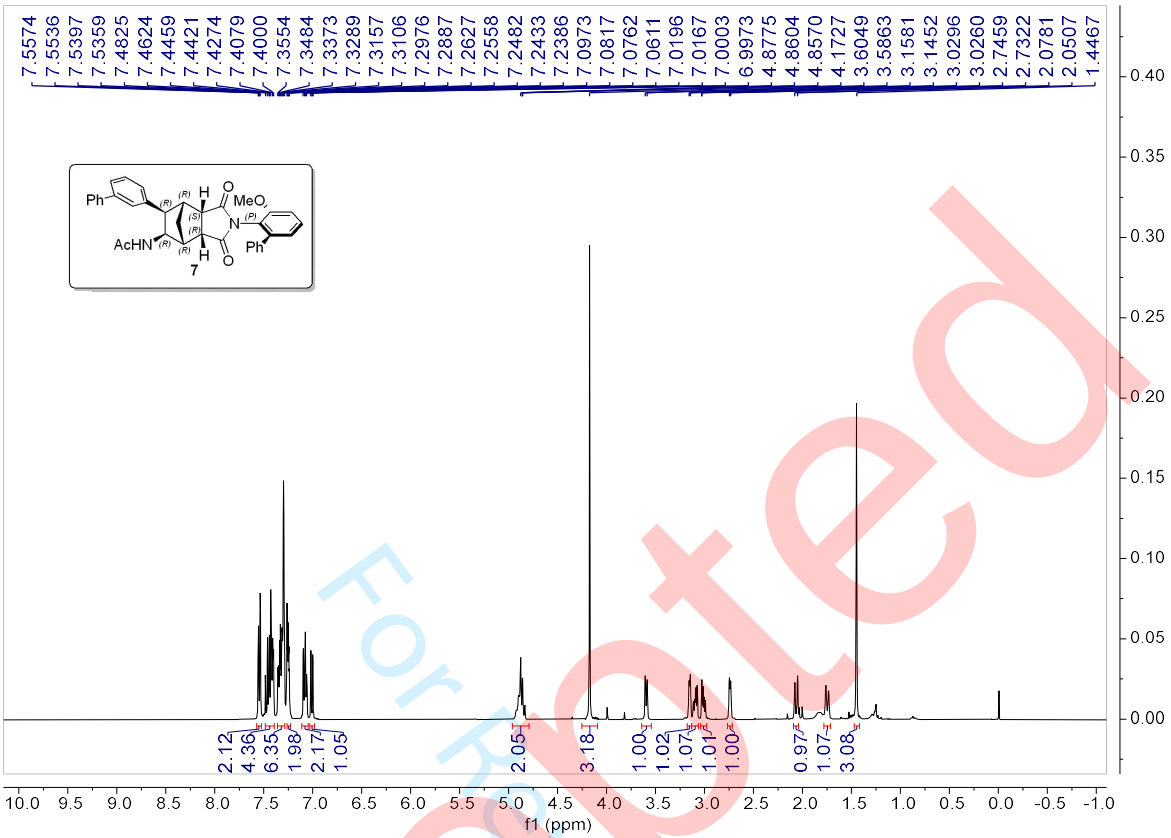
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 5



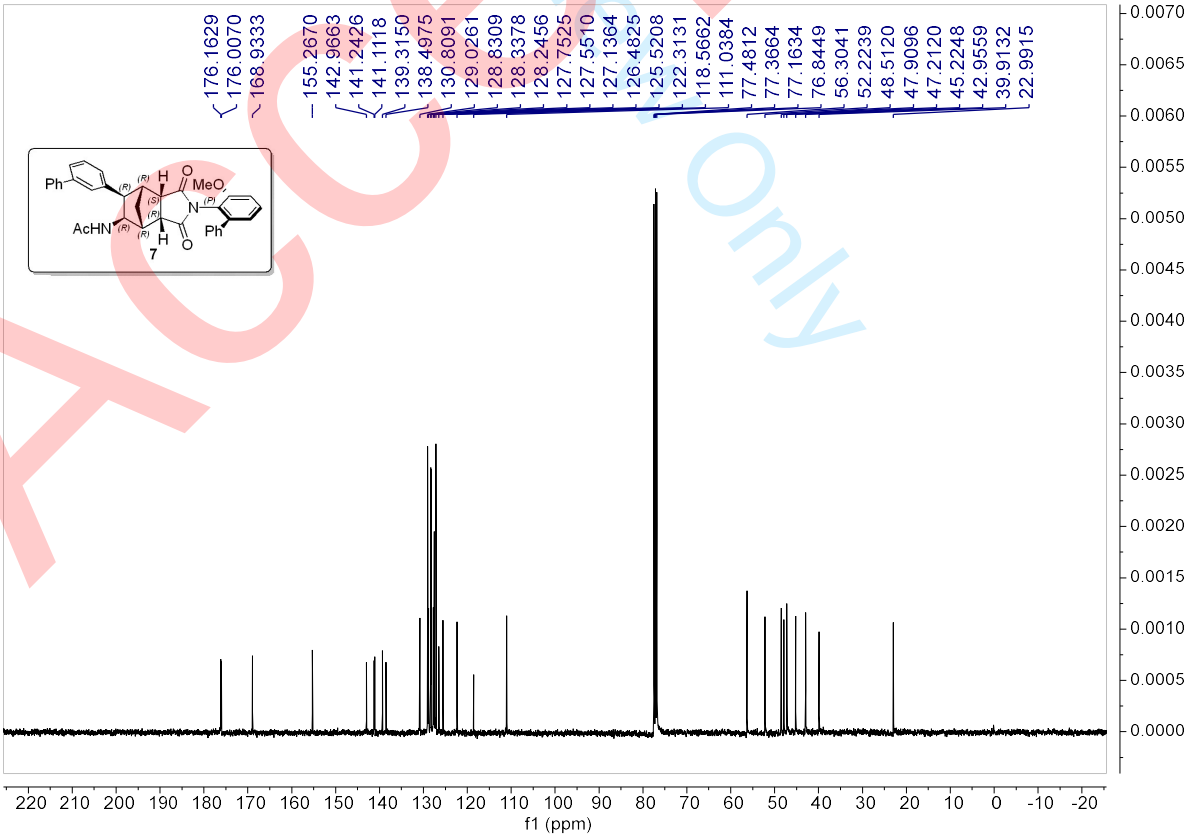
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 6



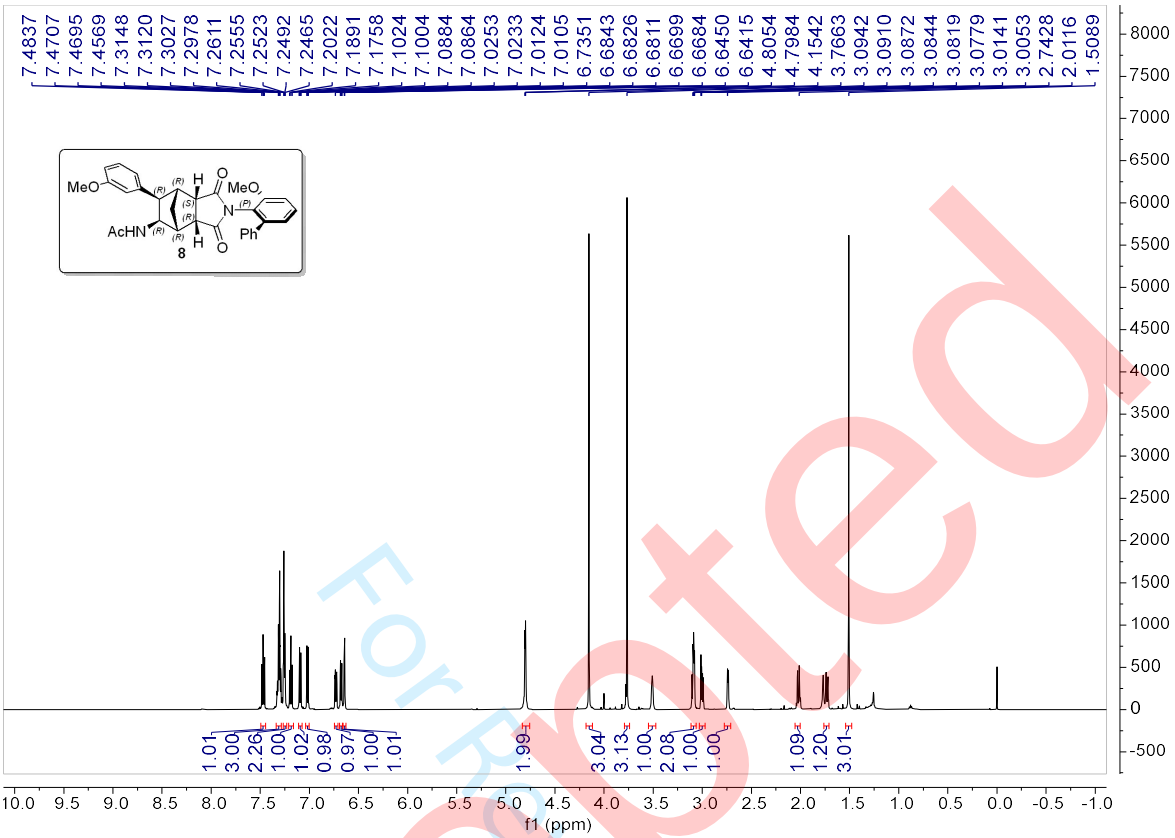
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 6



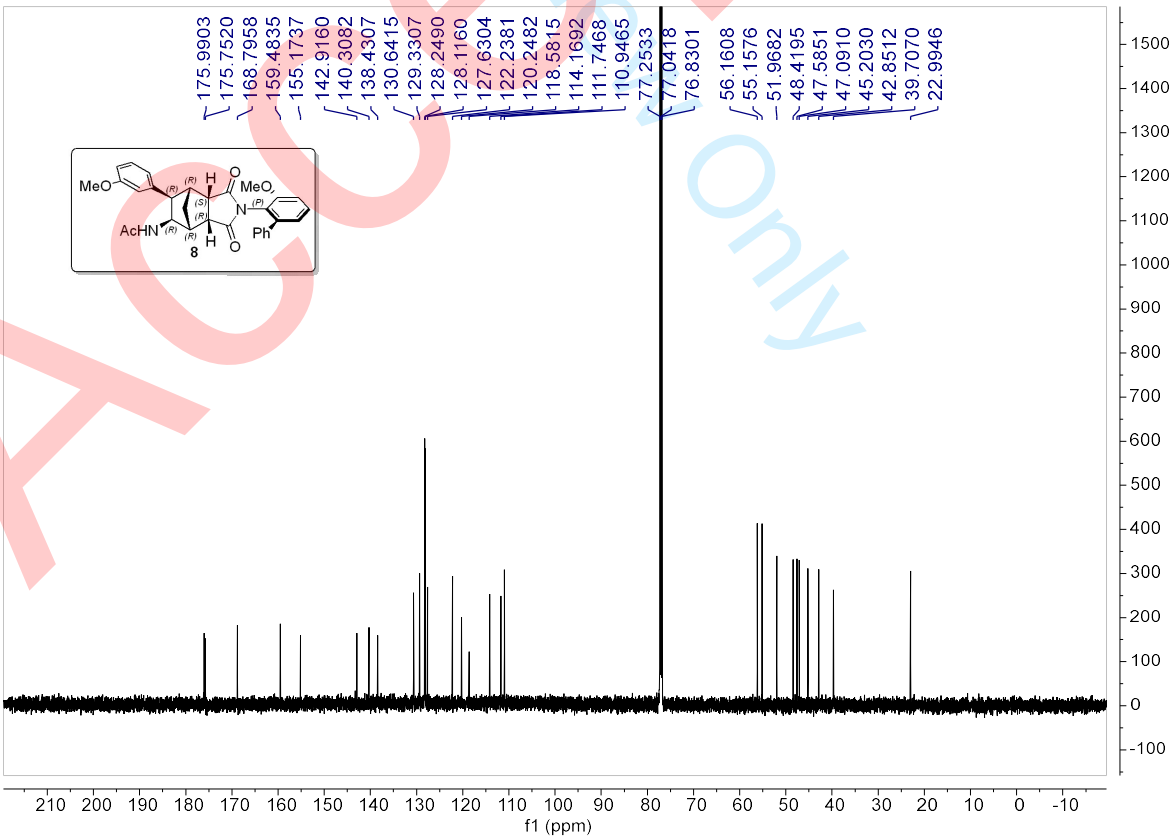
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 7



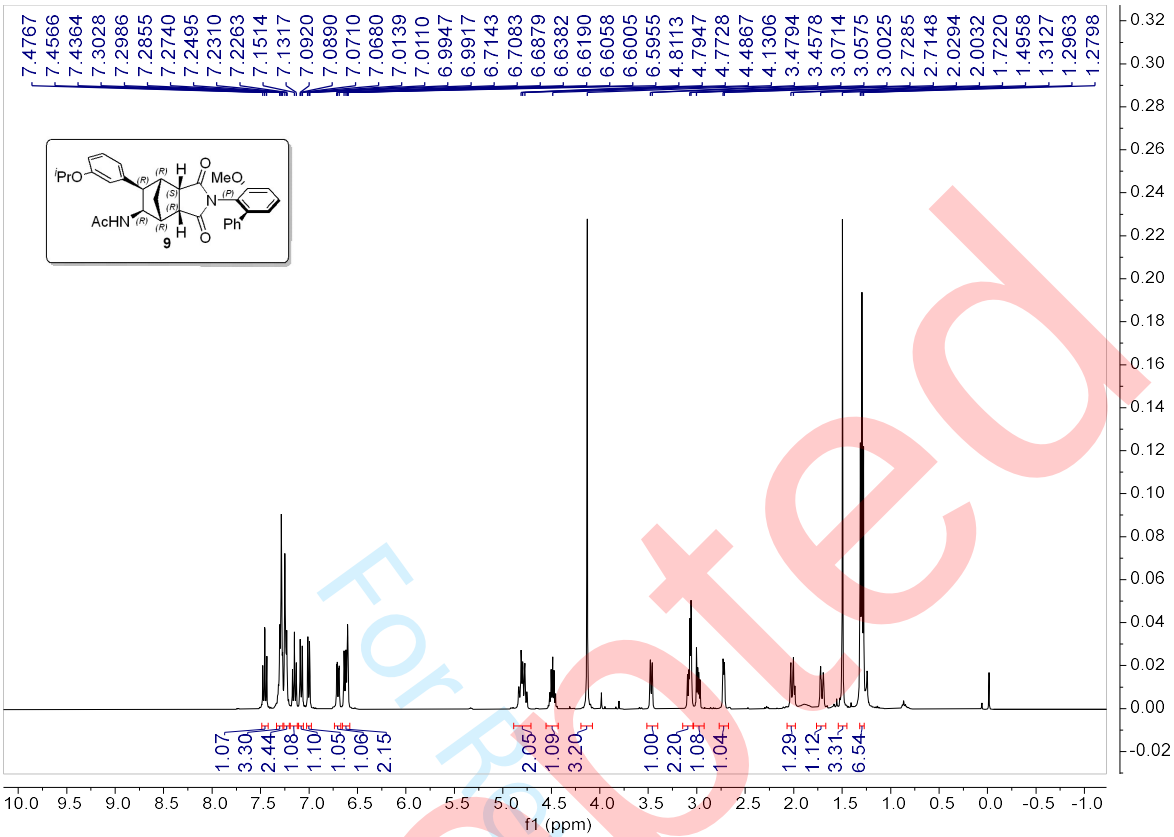
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 7



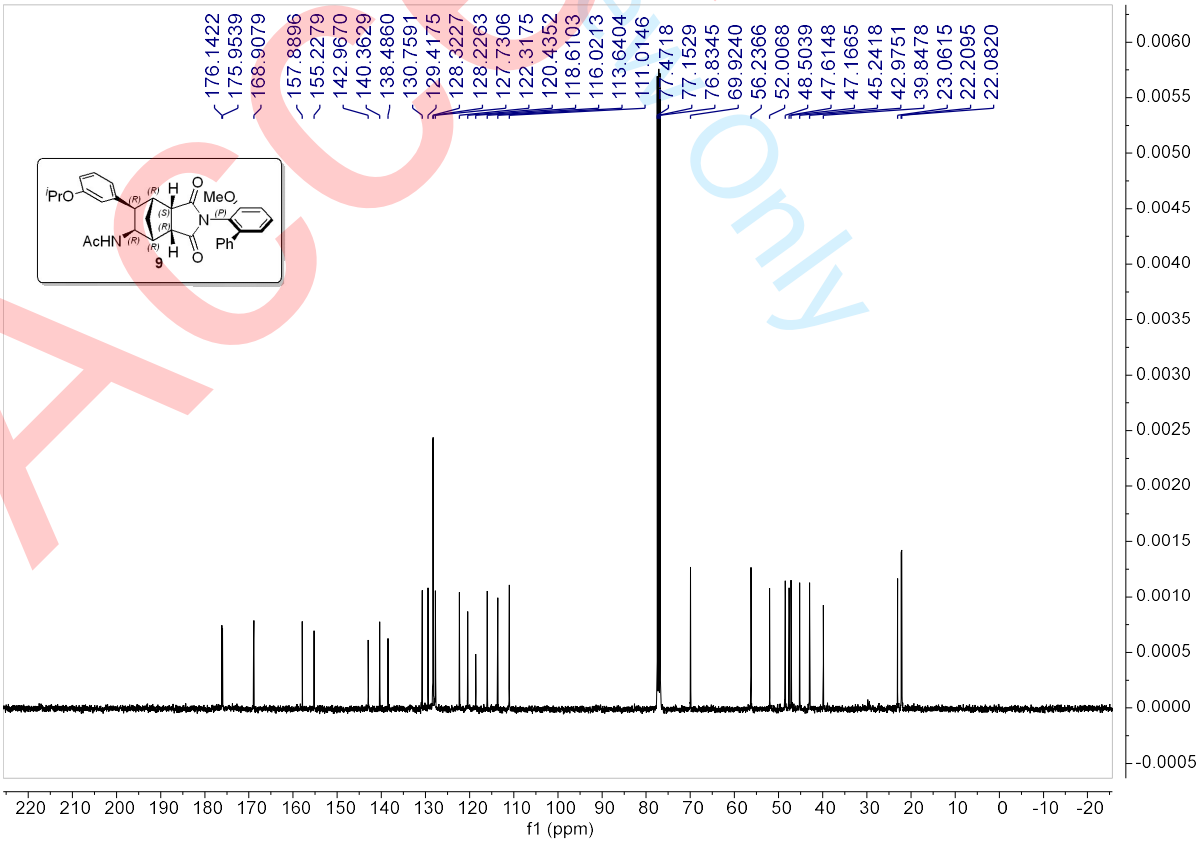
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 8



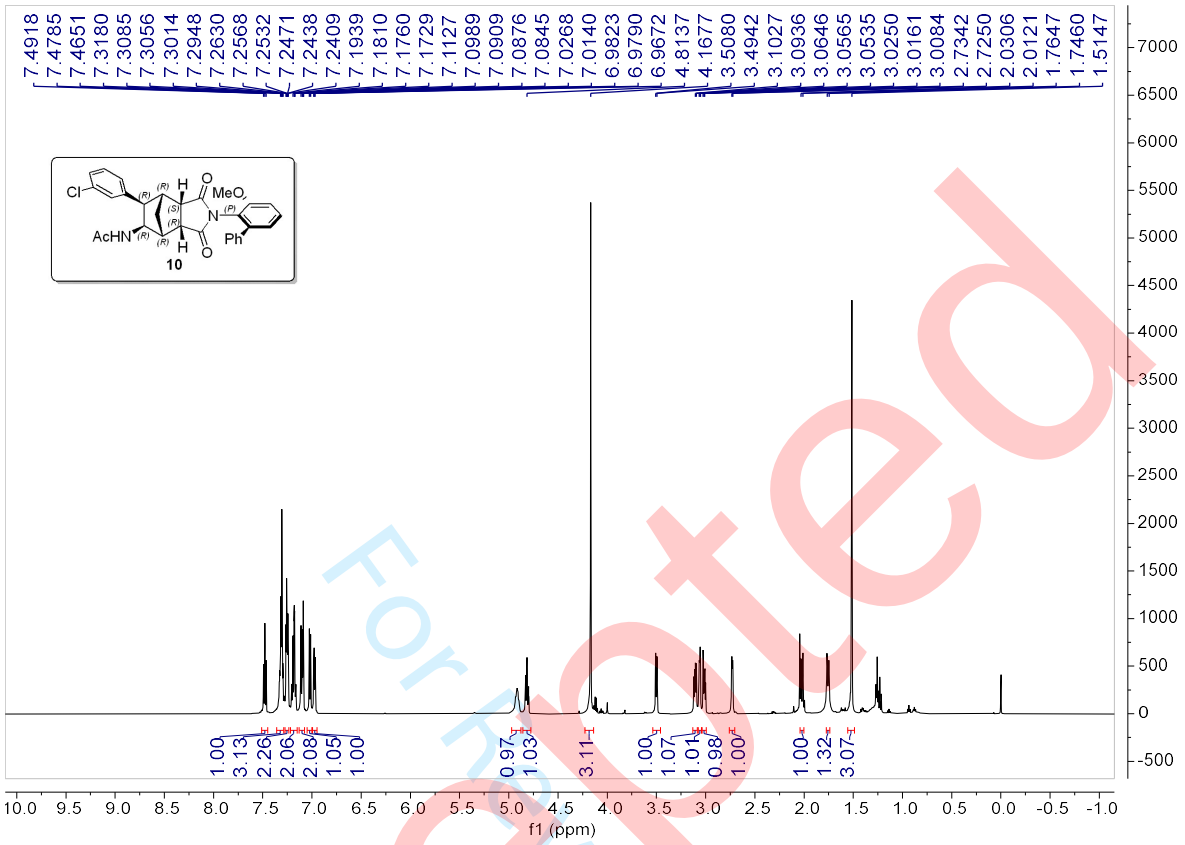
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 8



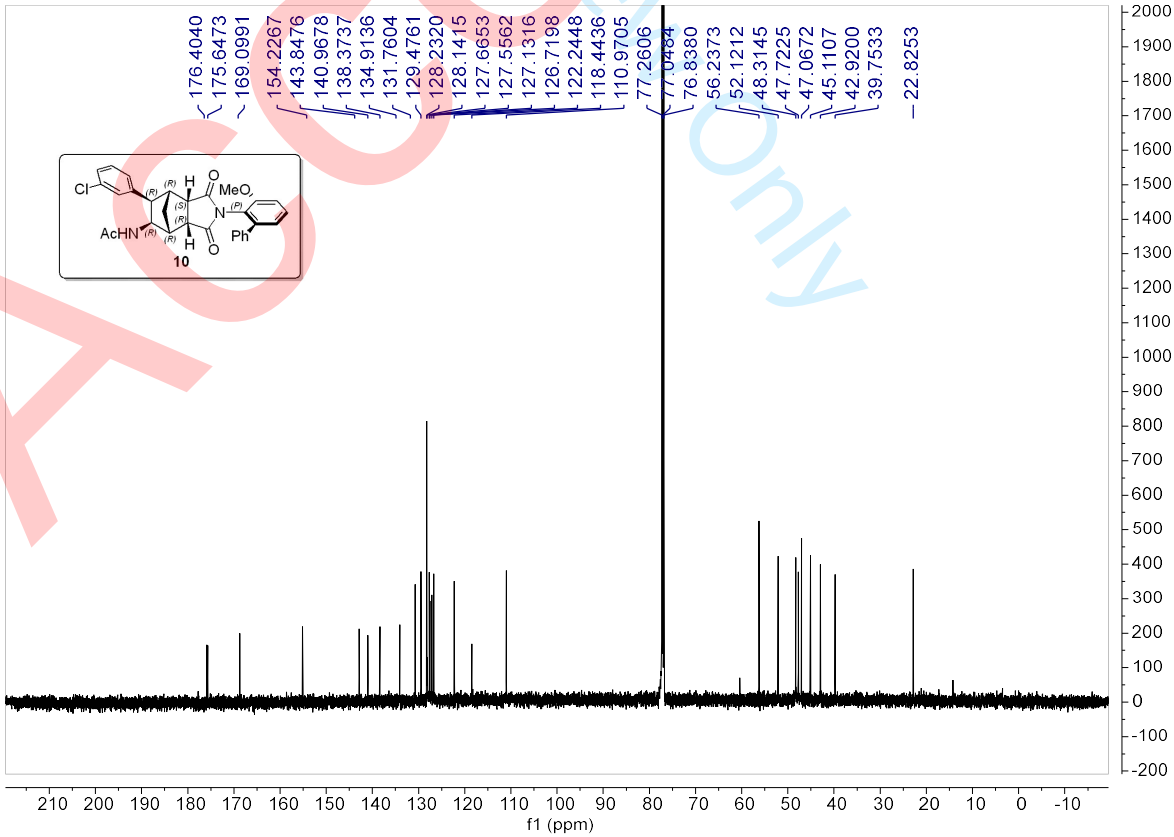
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 9



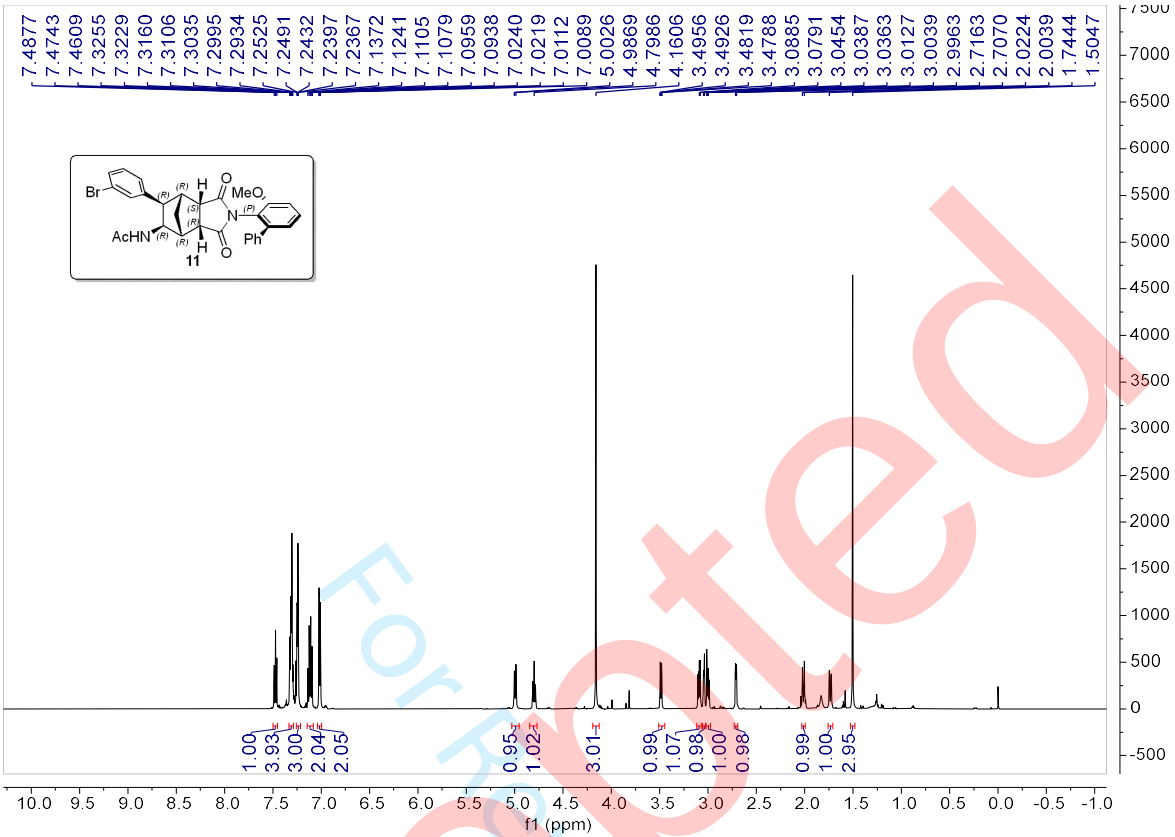
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 9



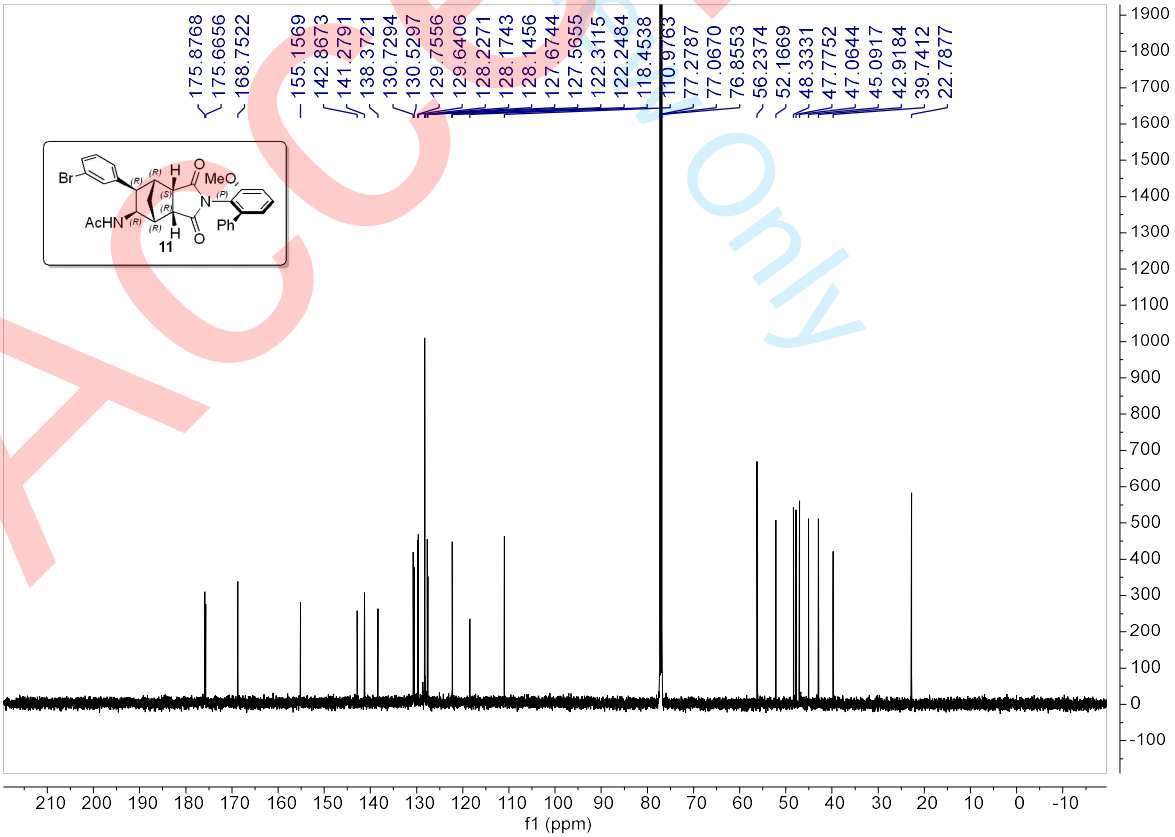
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 10



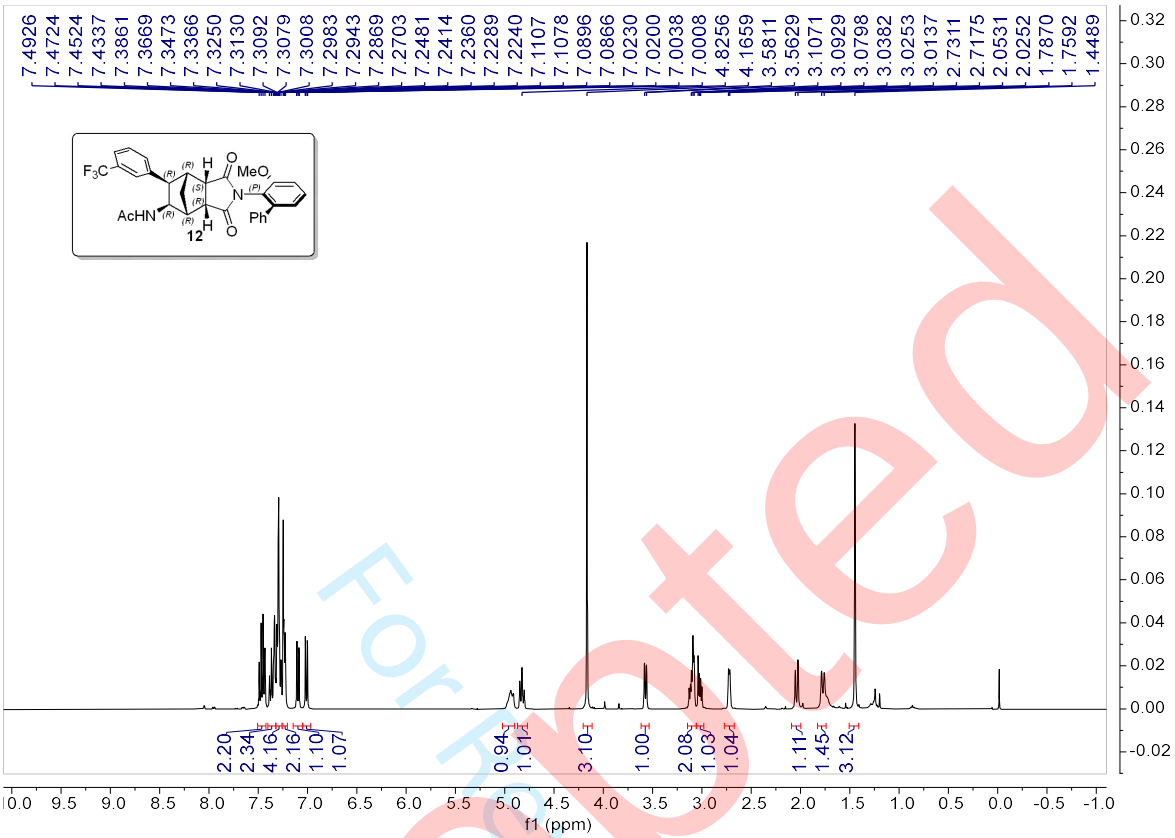
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 10



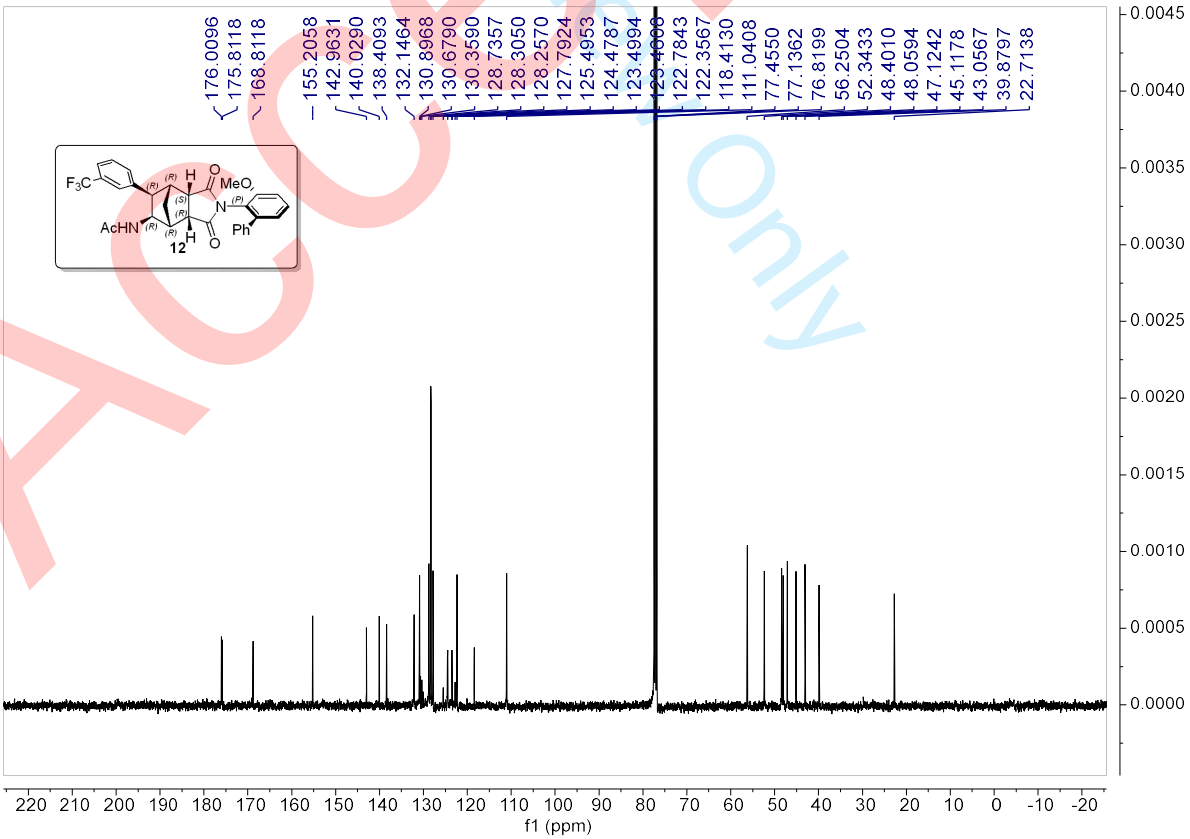
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 11



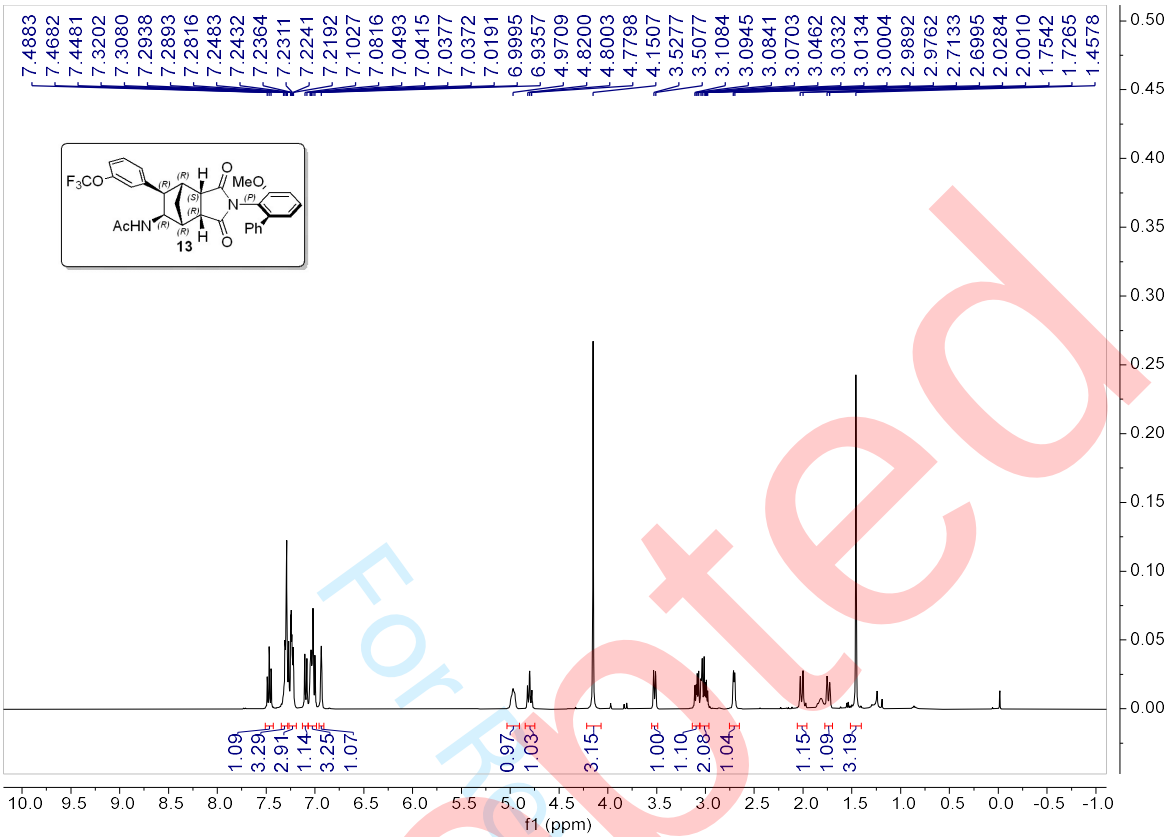
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 11



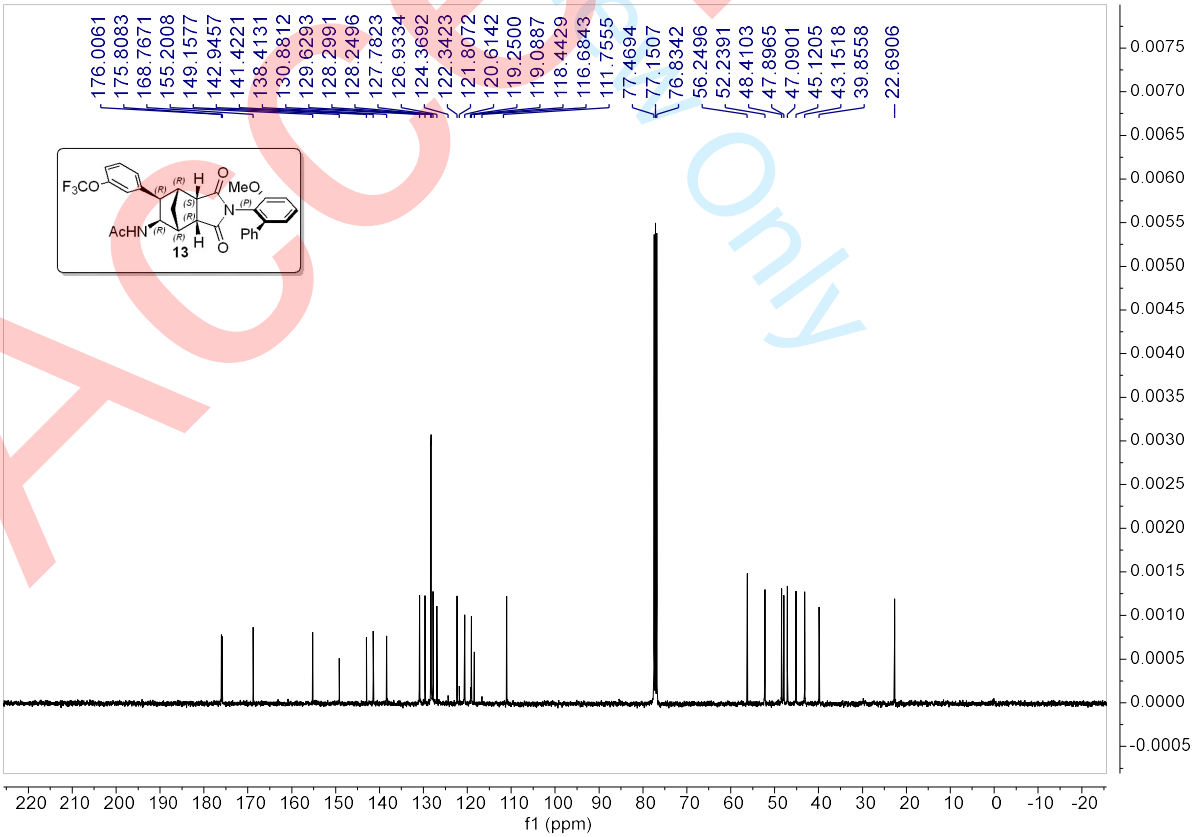
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 12



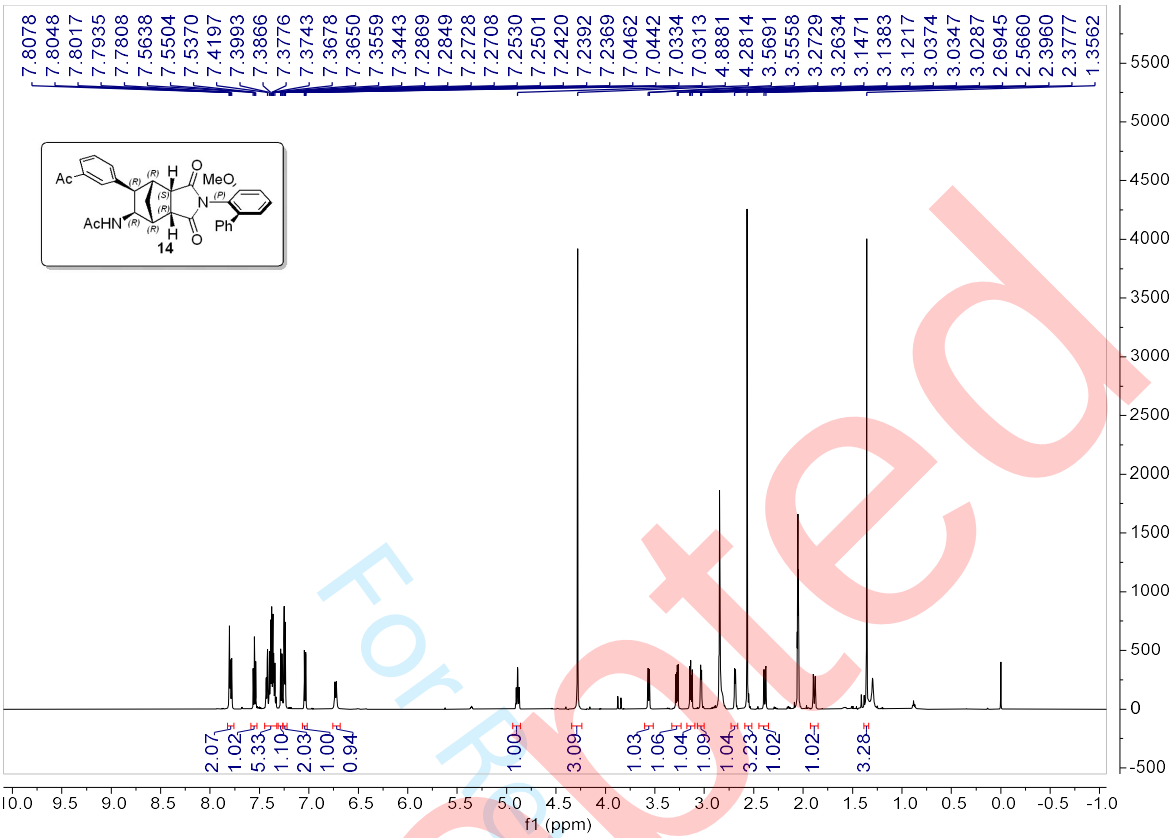
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 12



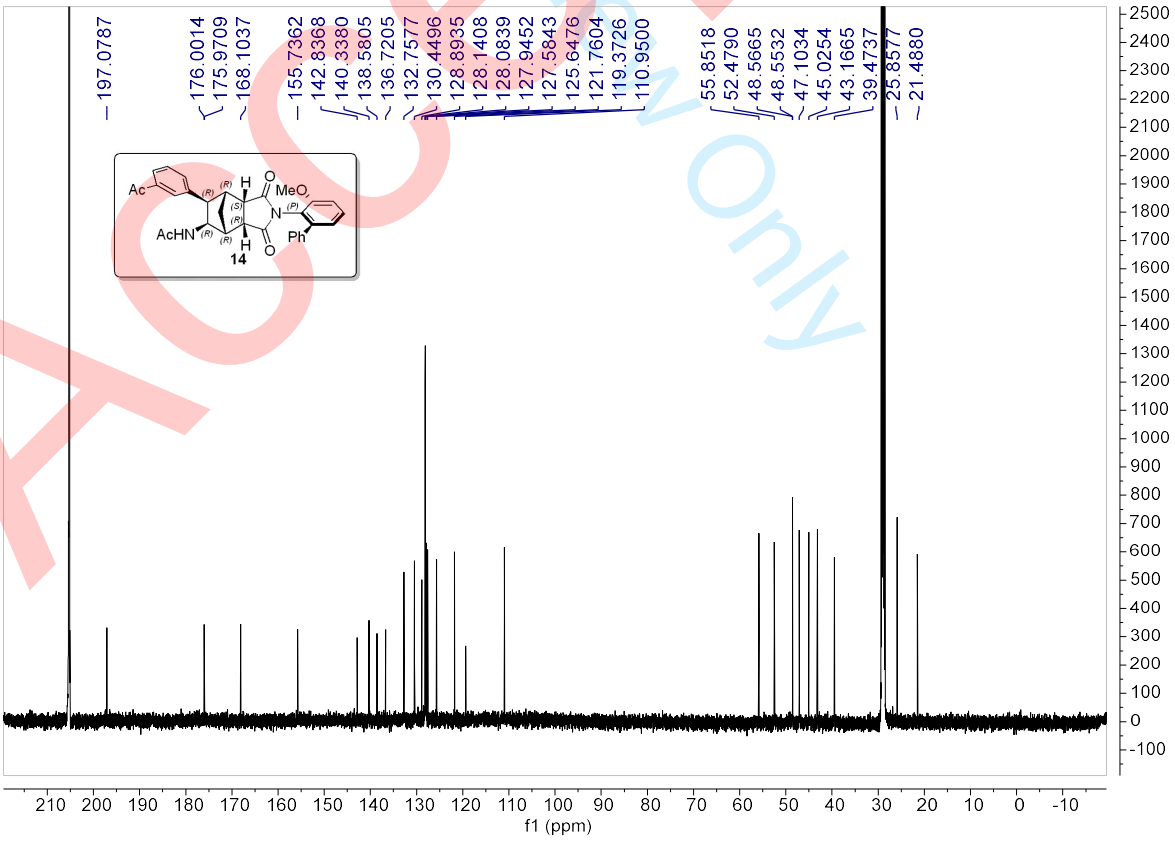
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 13



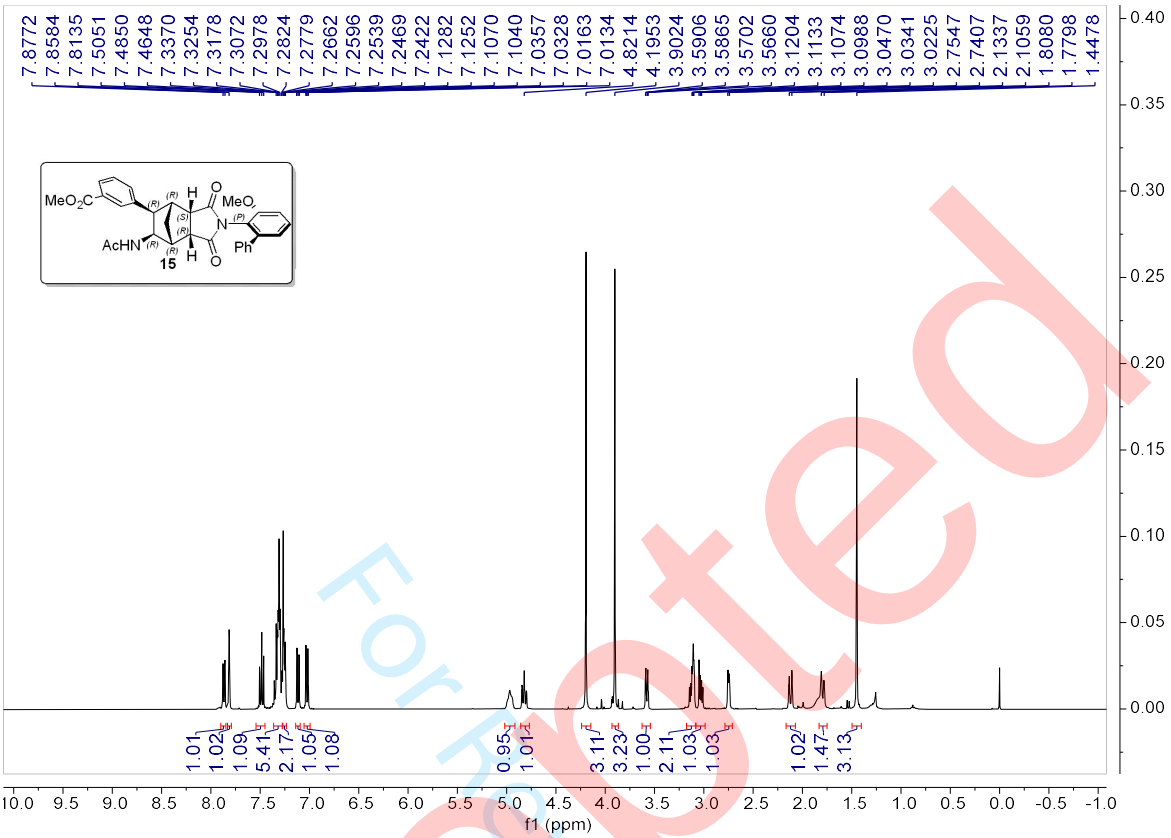
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 13



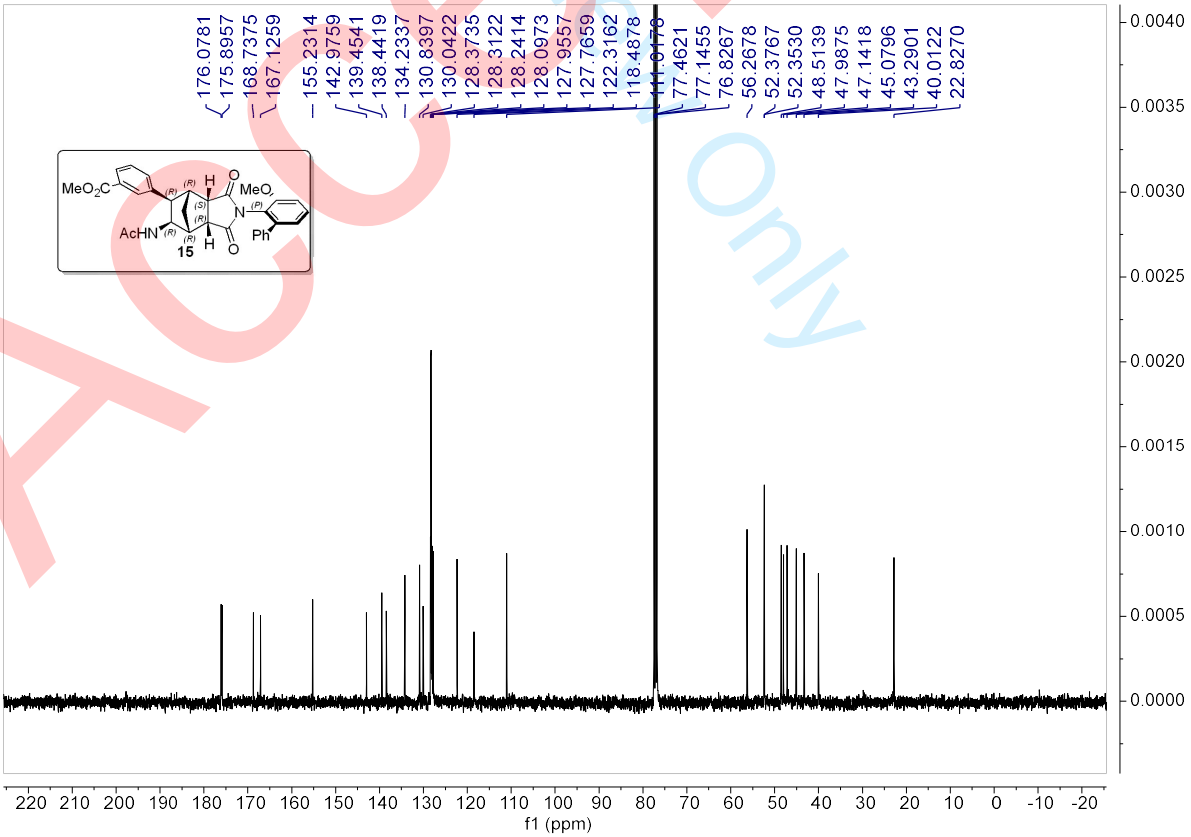
^{1}H NMR (600 MHz, acetone-d_6) spectrum of 14



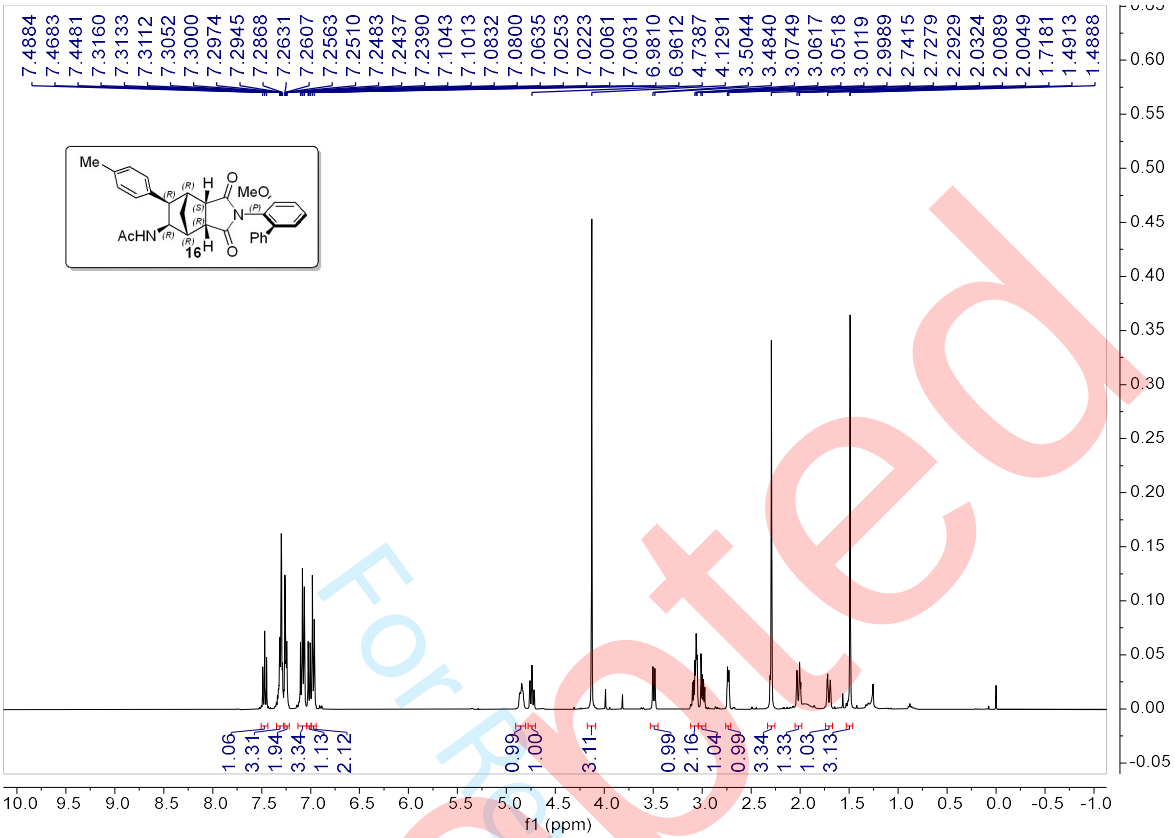
^{13}C NMR (100 MHz, acetone-d_6) spectrum of 14



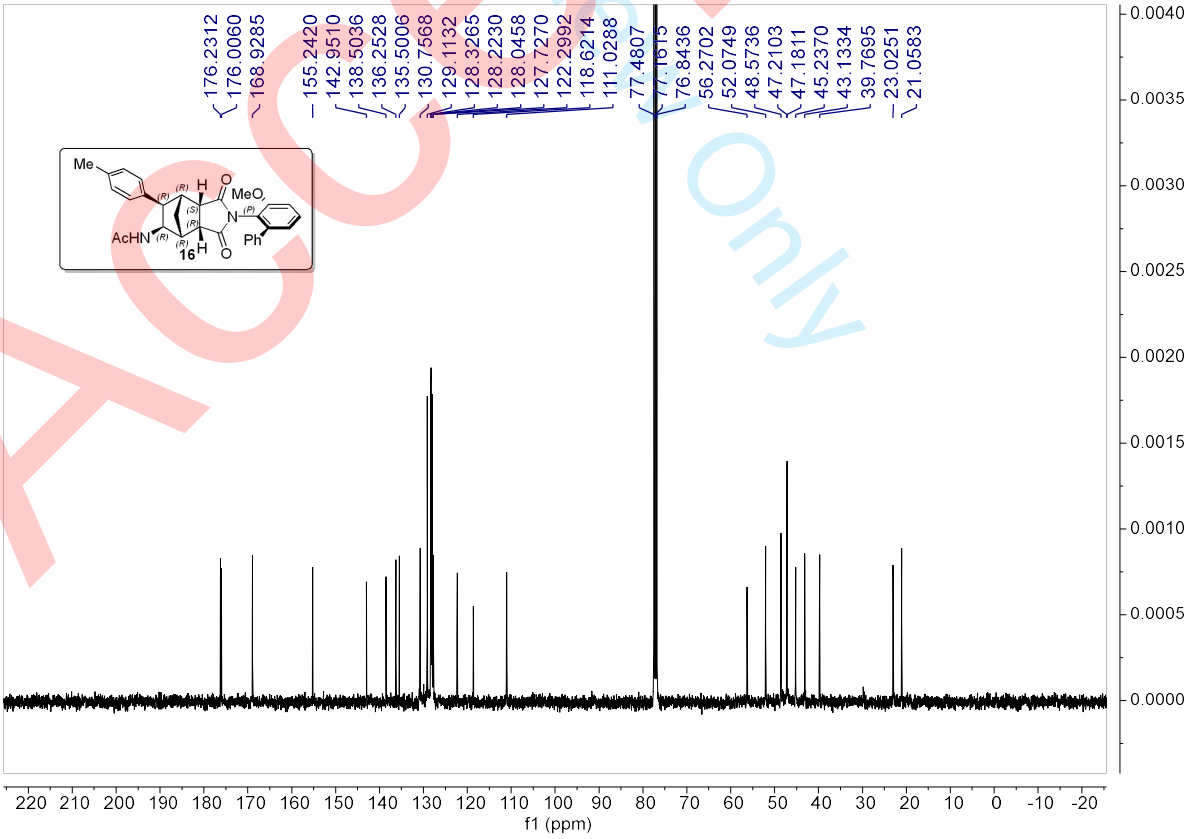
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 15



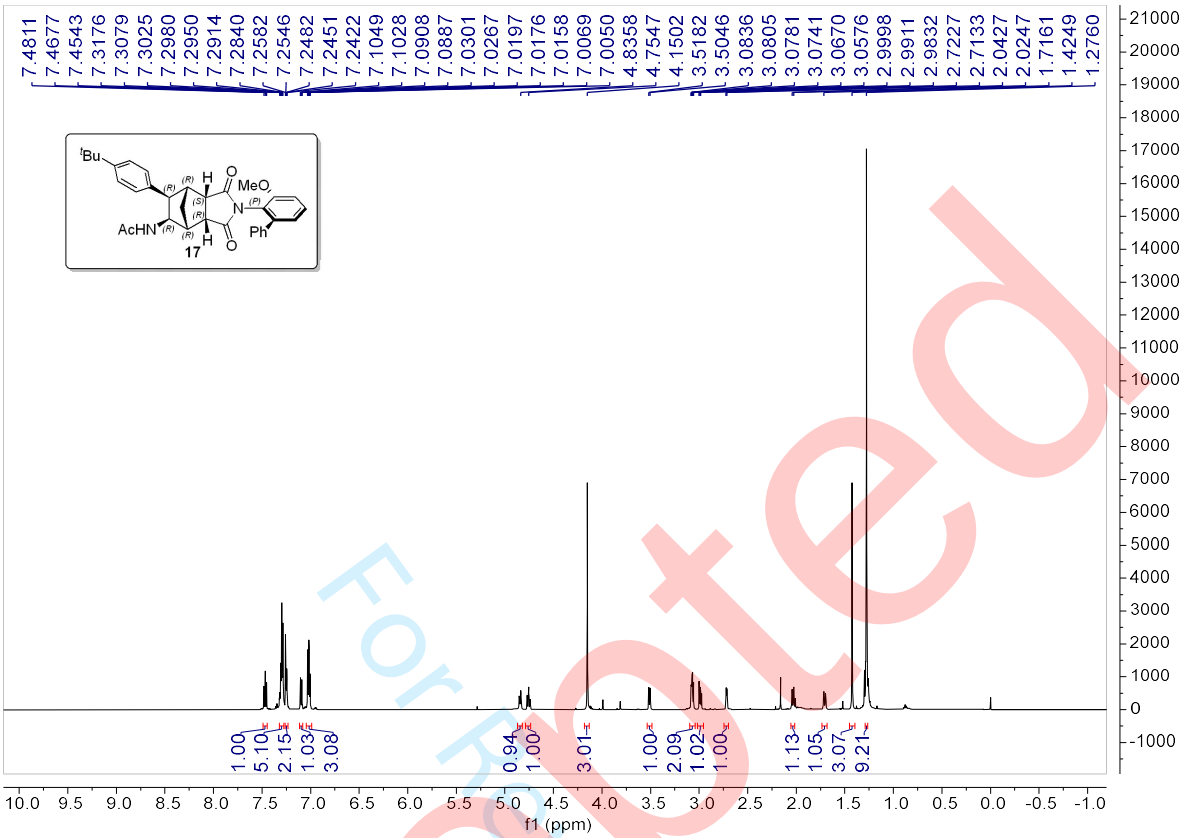
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 15



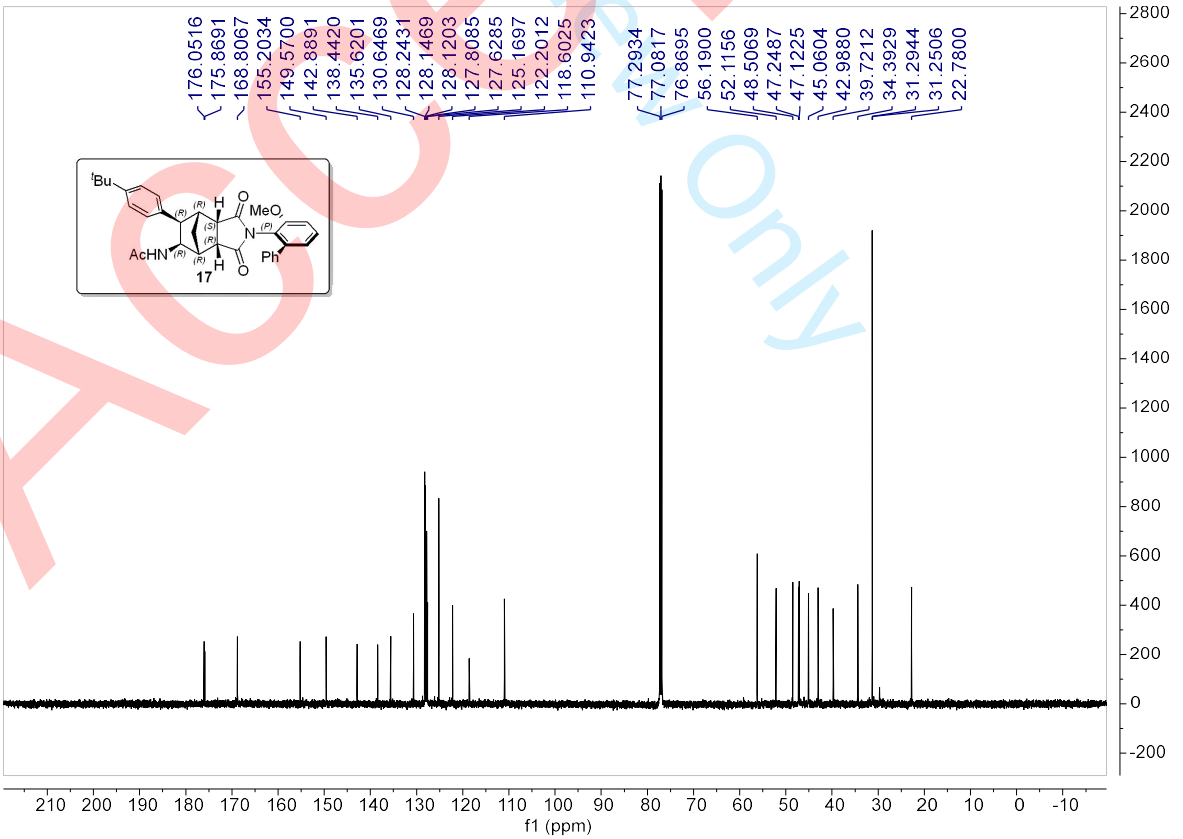
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 16



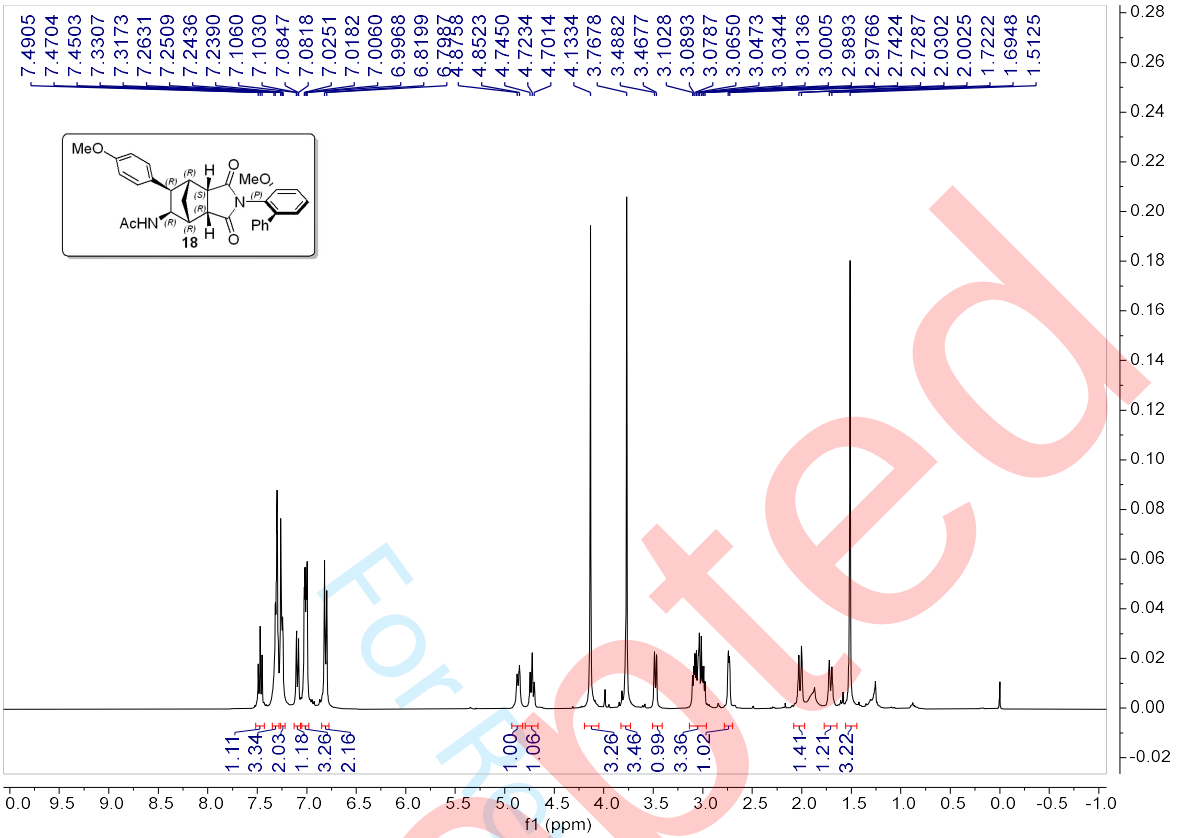
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 16



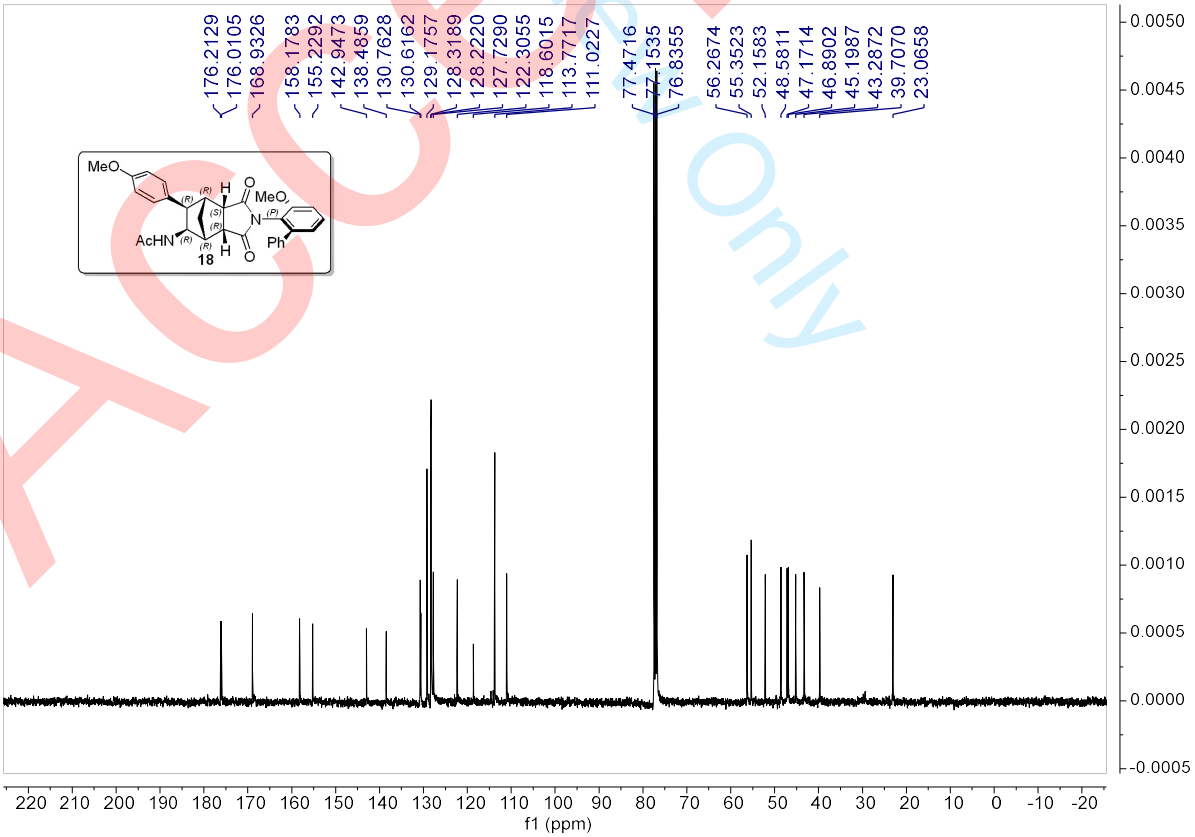
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 17



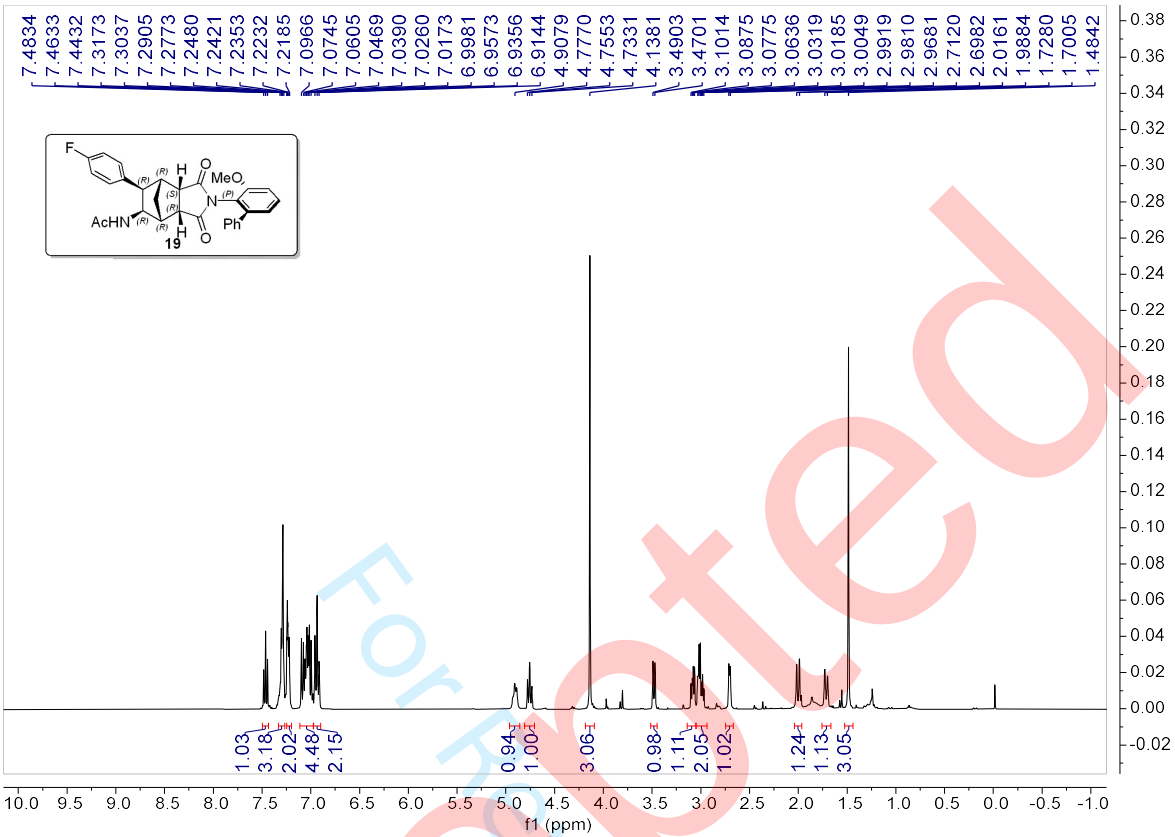
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 17



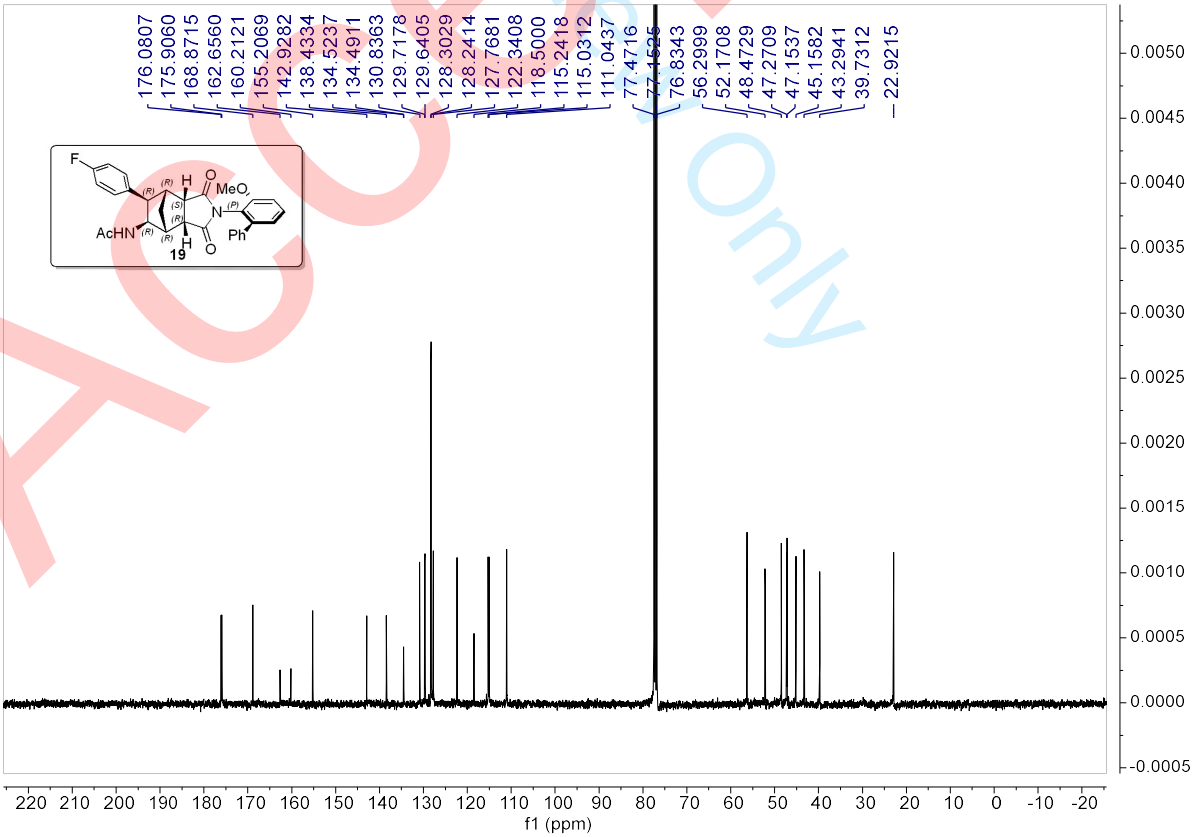
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 18



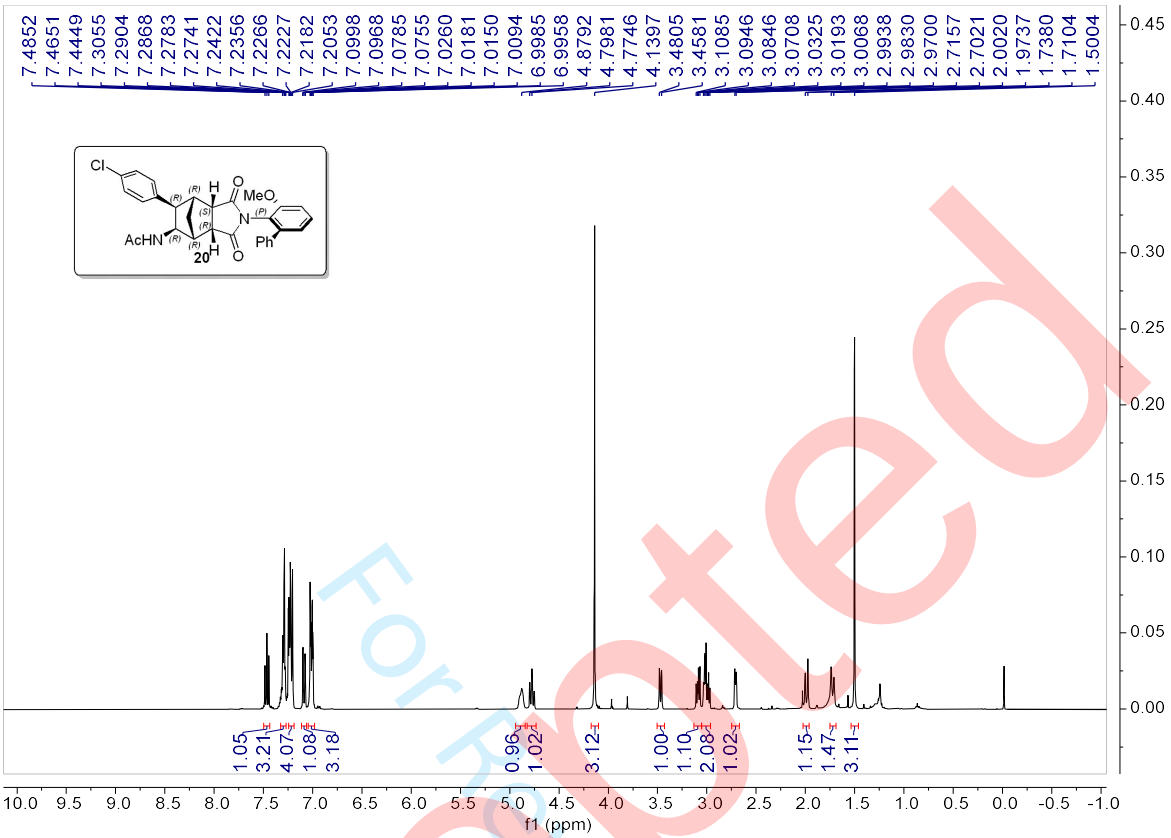
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 18



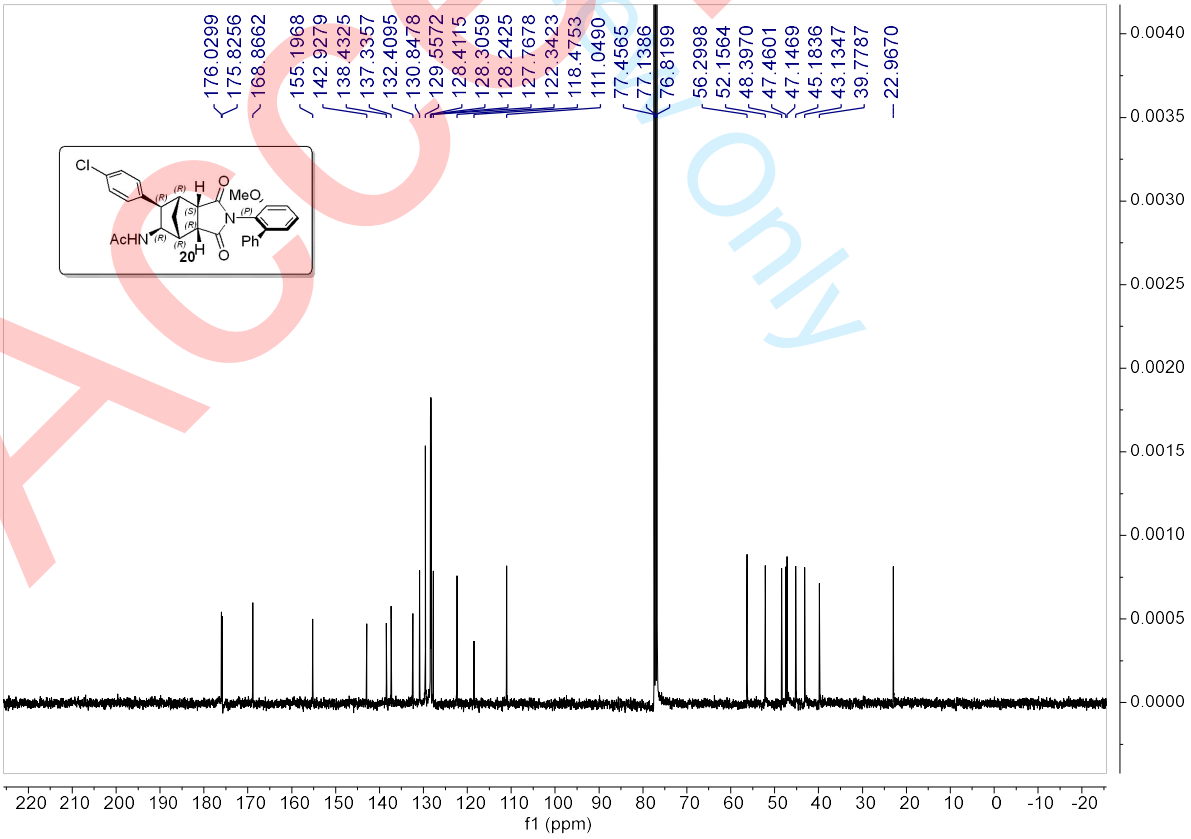
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 19



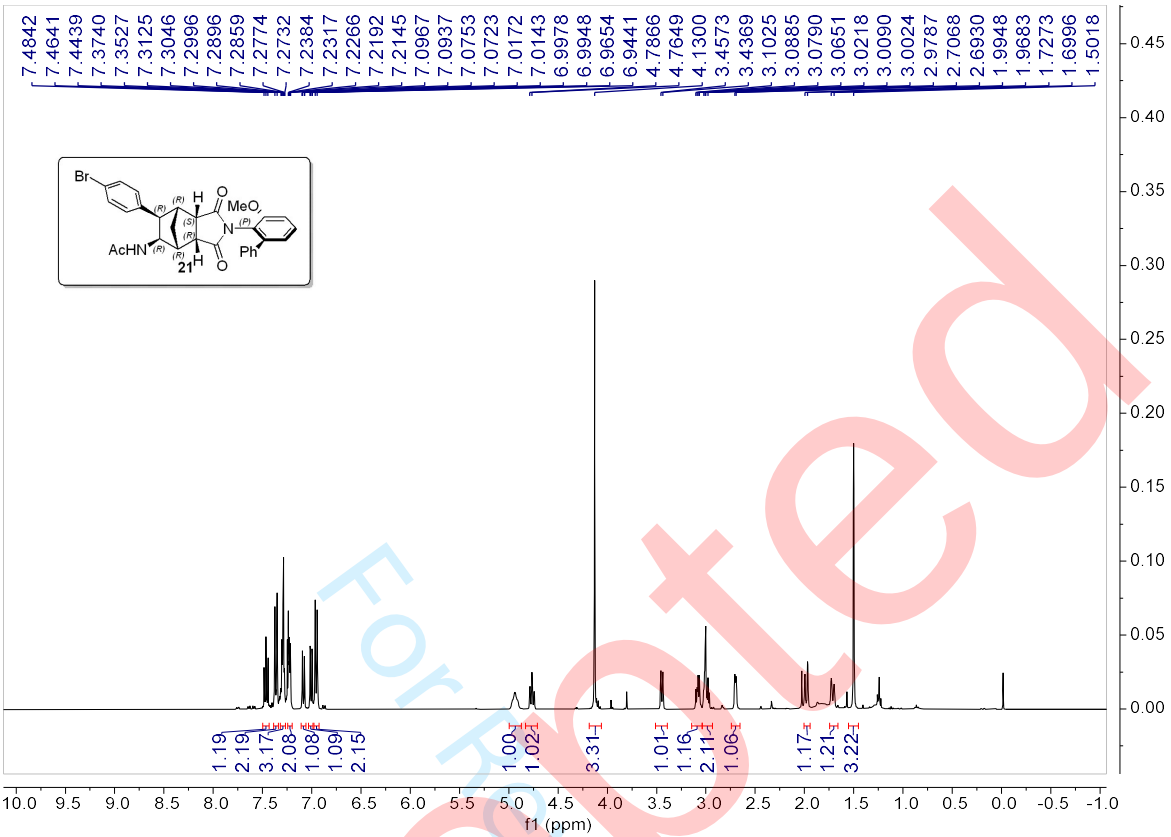
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 19



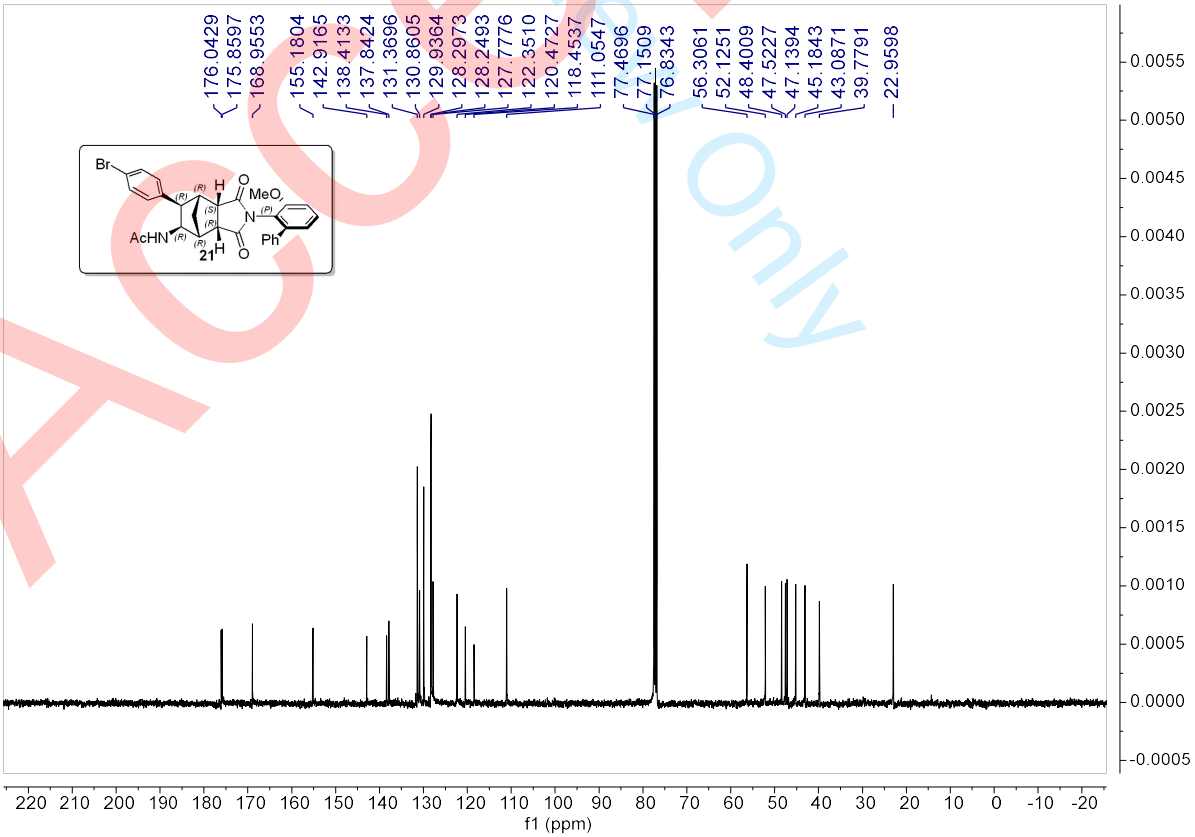
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 20



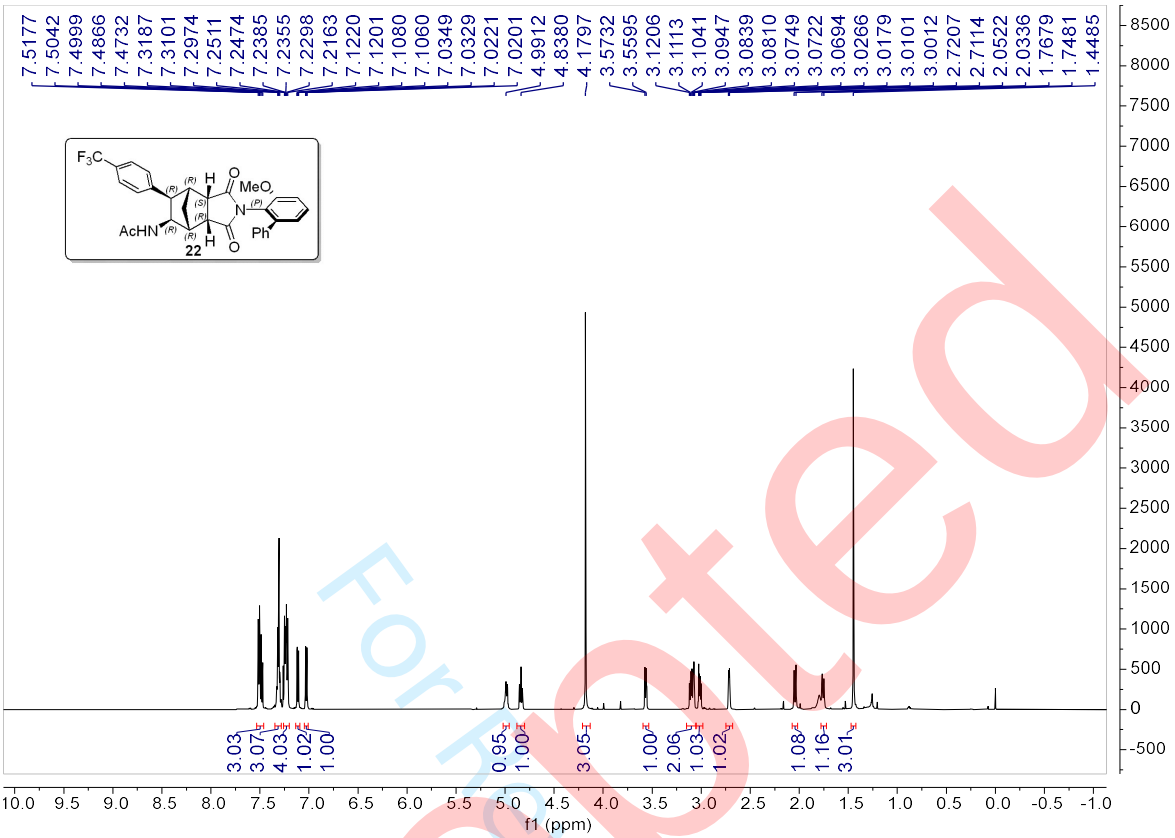
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 20



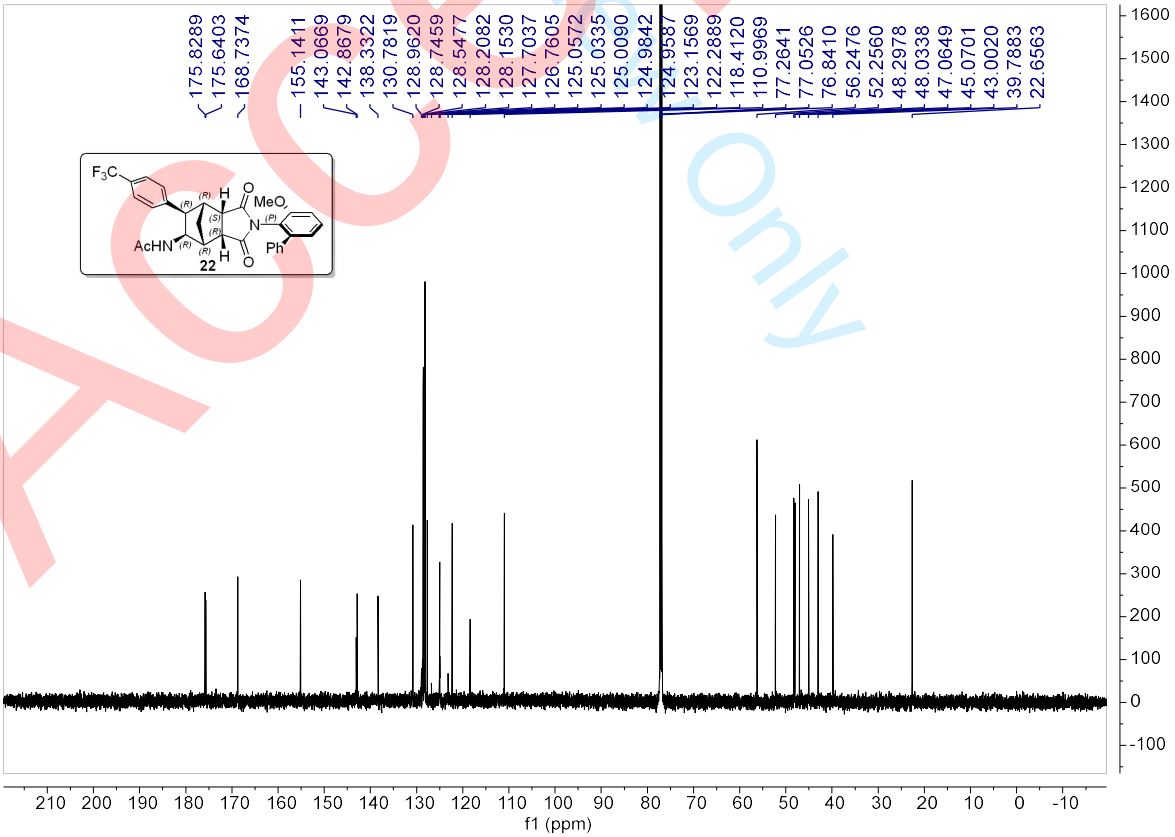
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 21



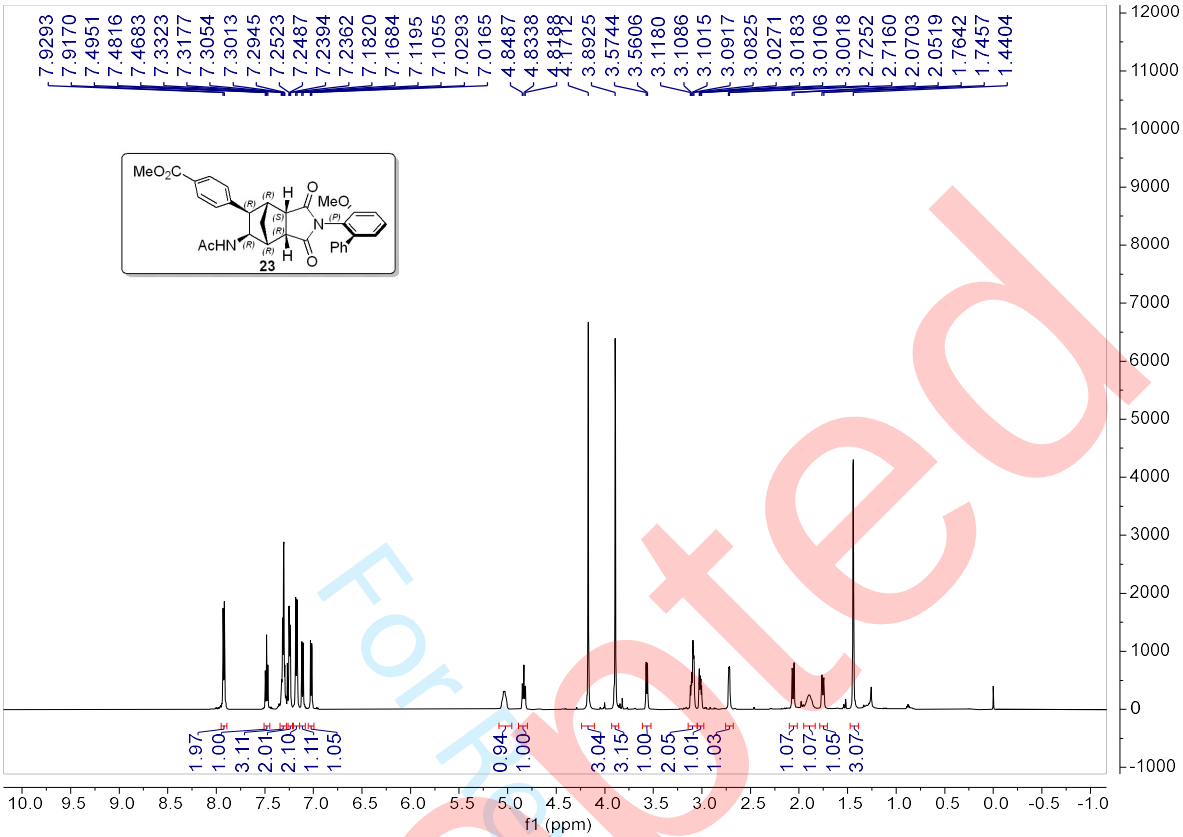
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 21



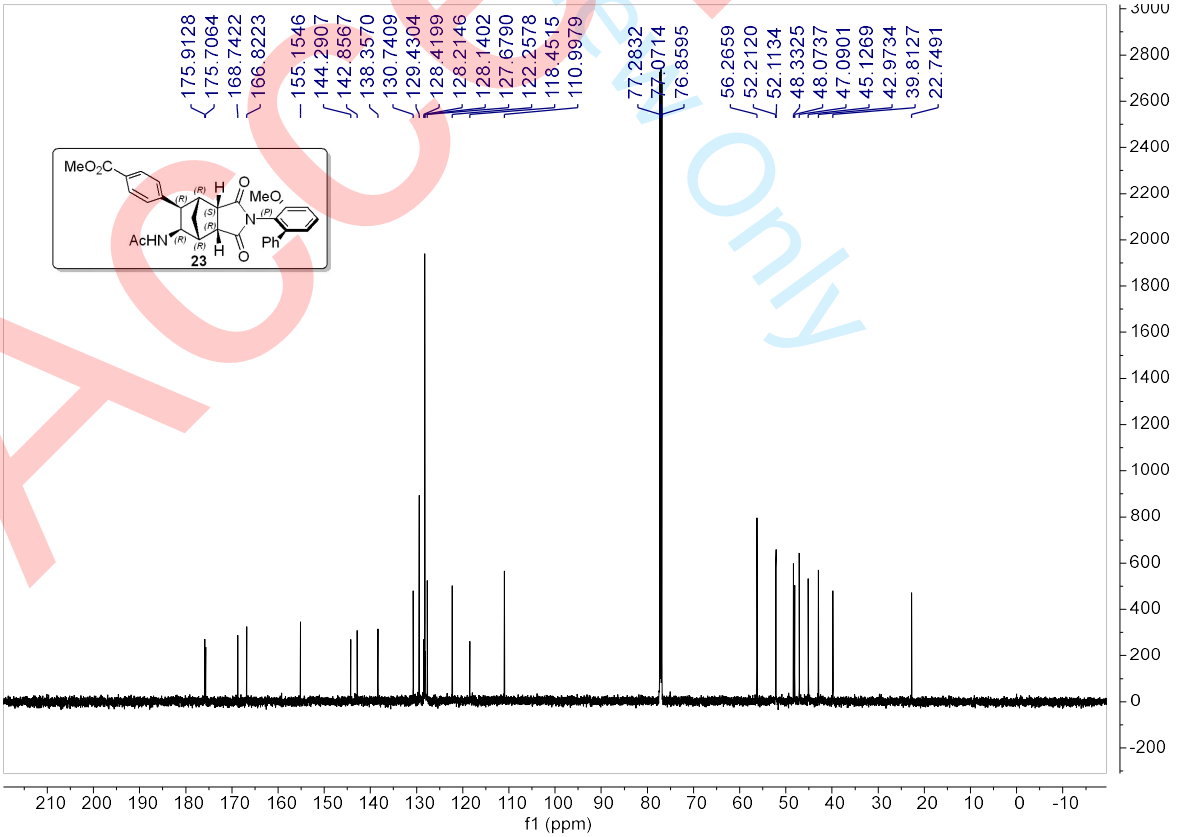
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 22



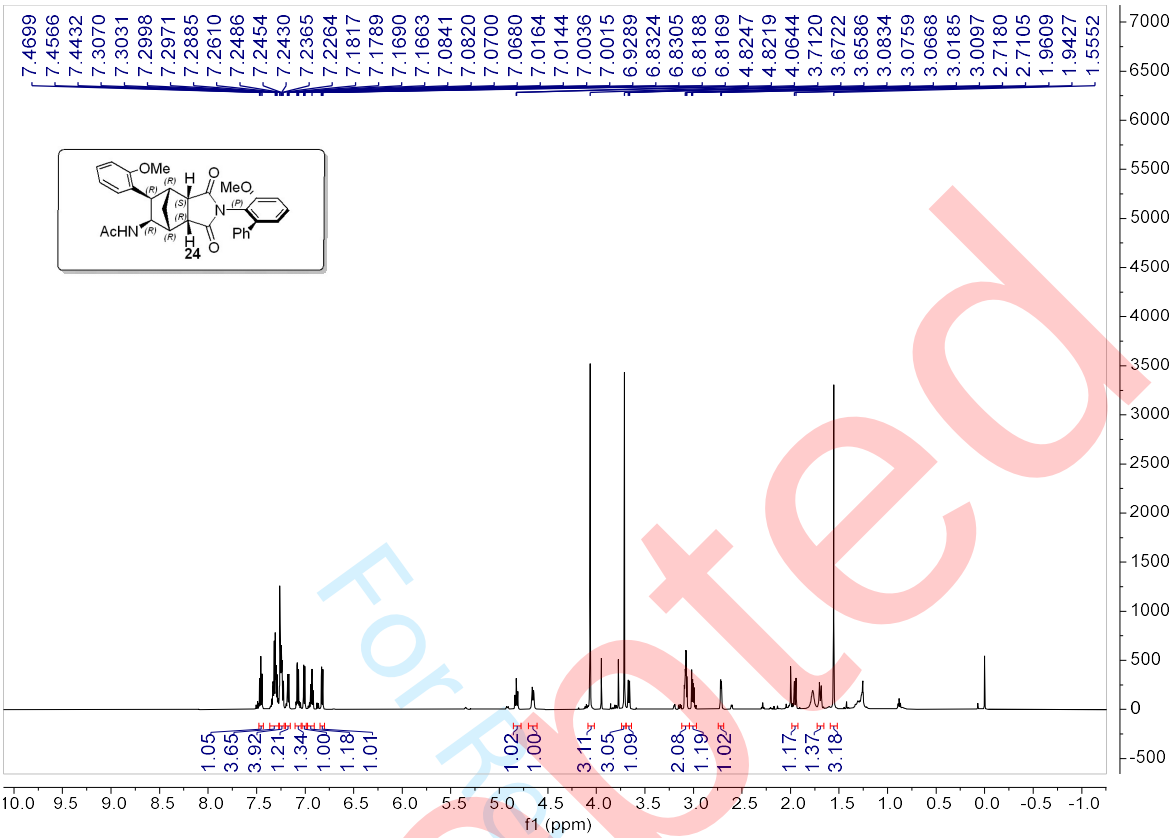
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 22



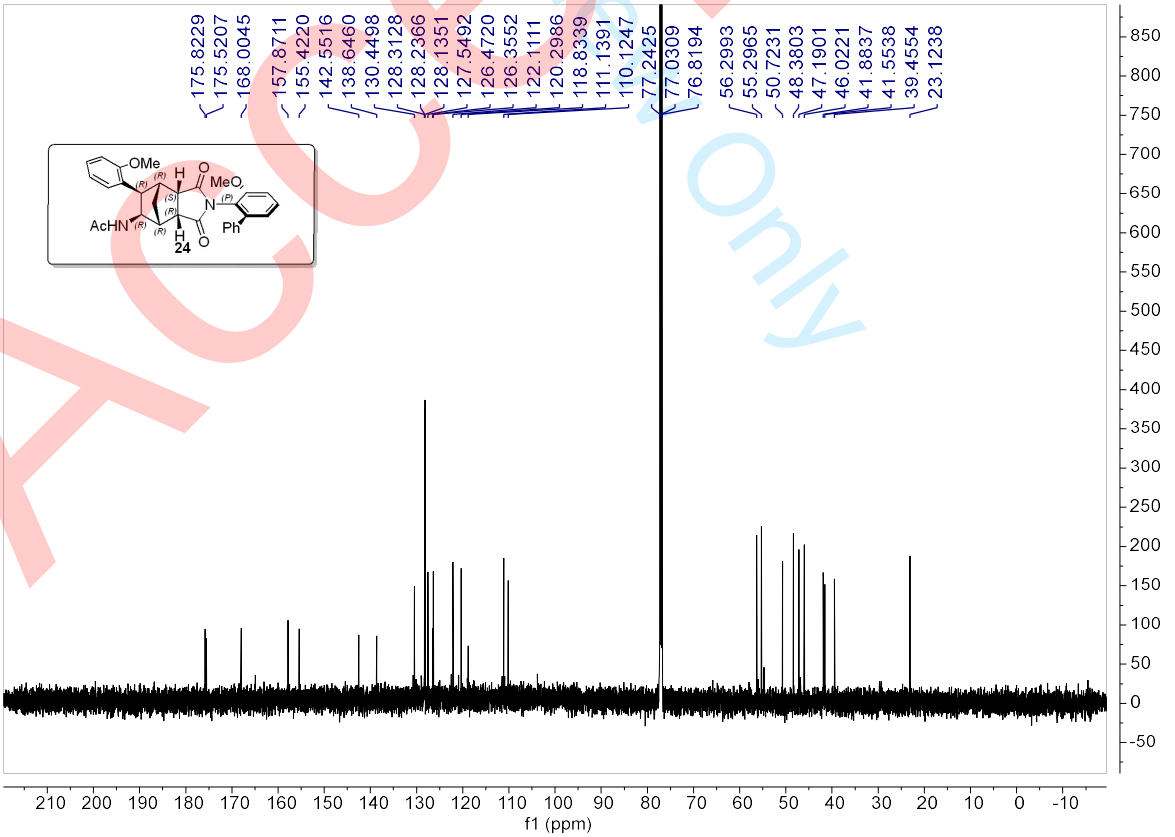
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 23



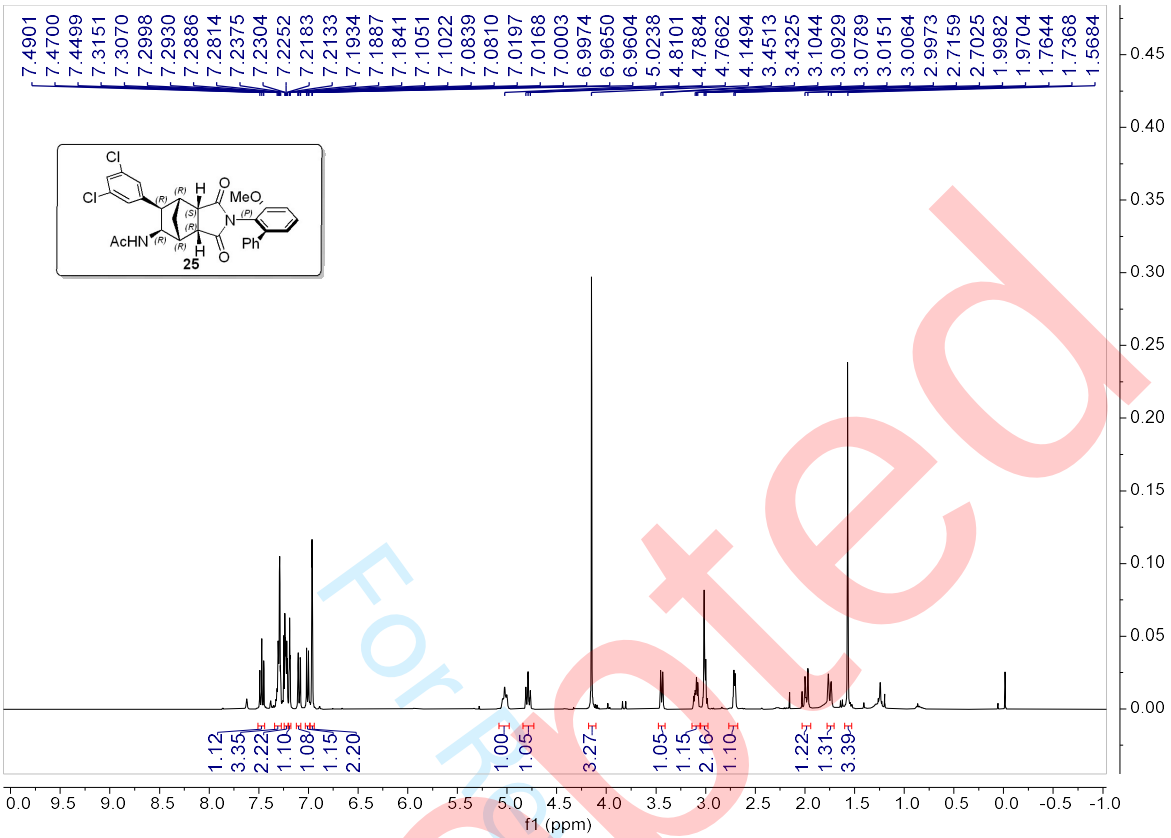
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 23



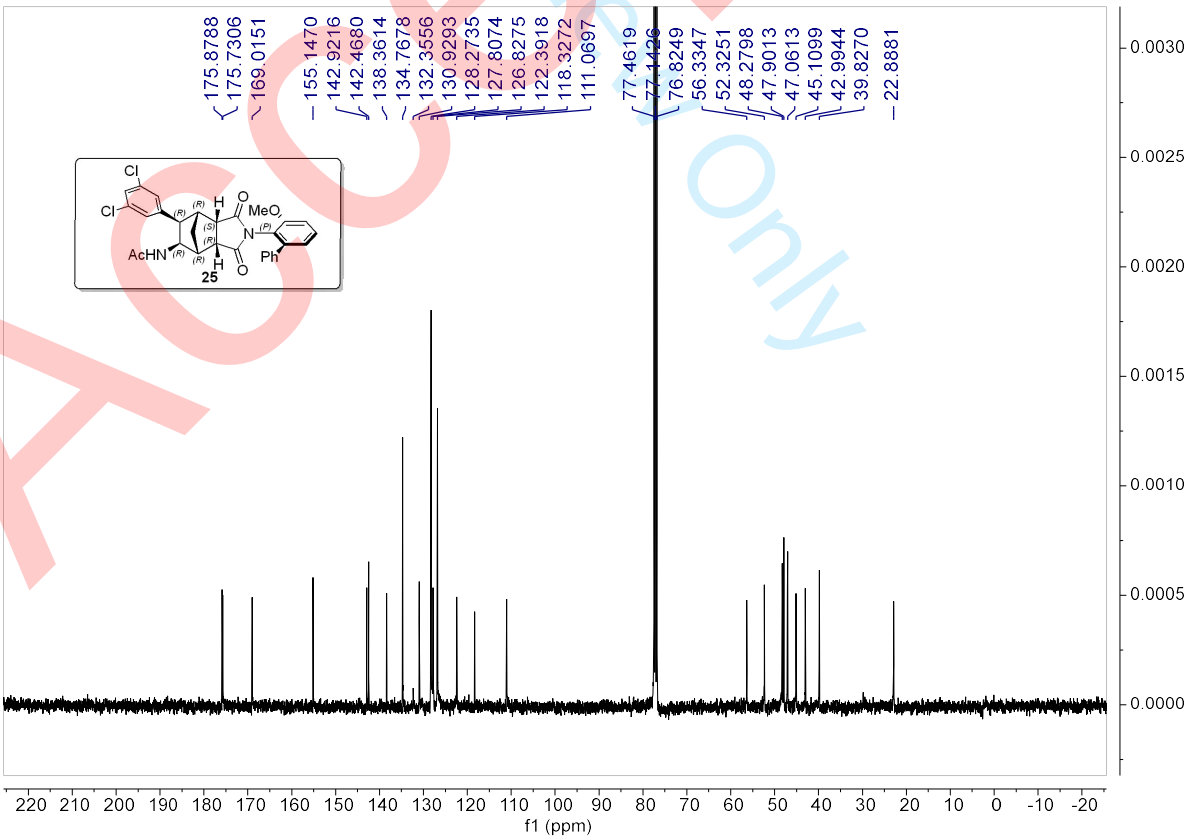
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 24



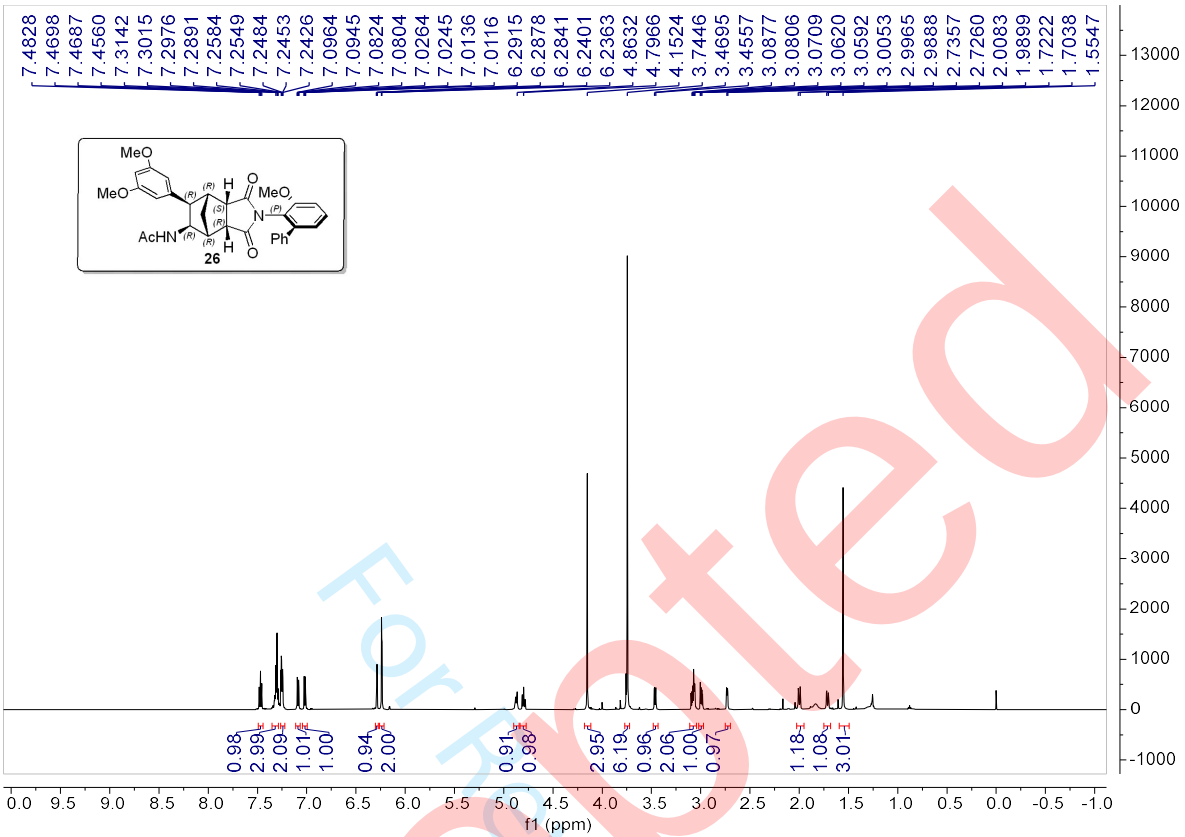
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 24



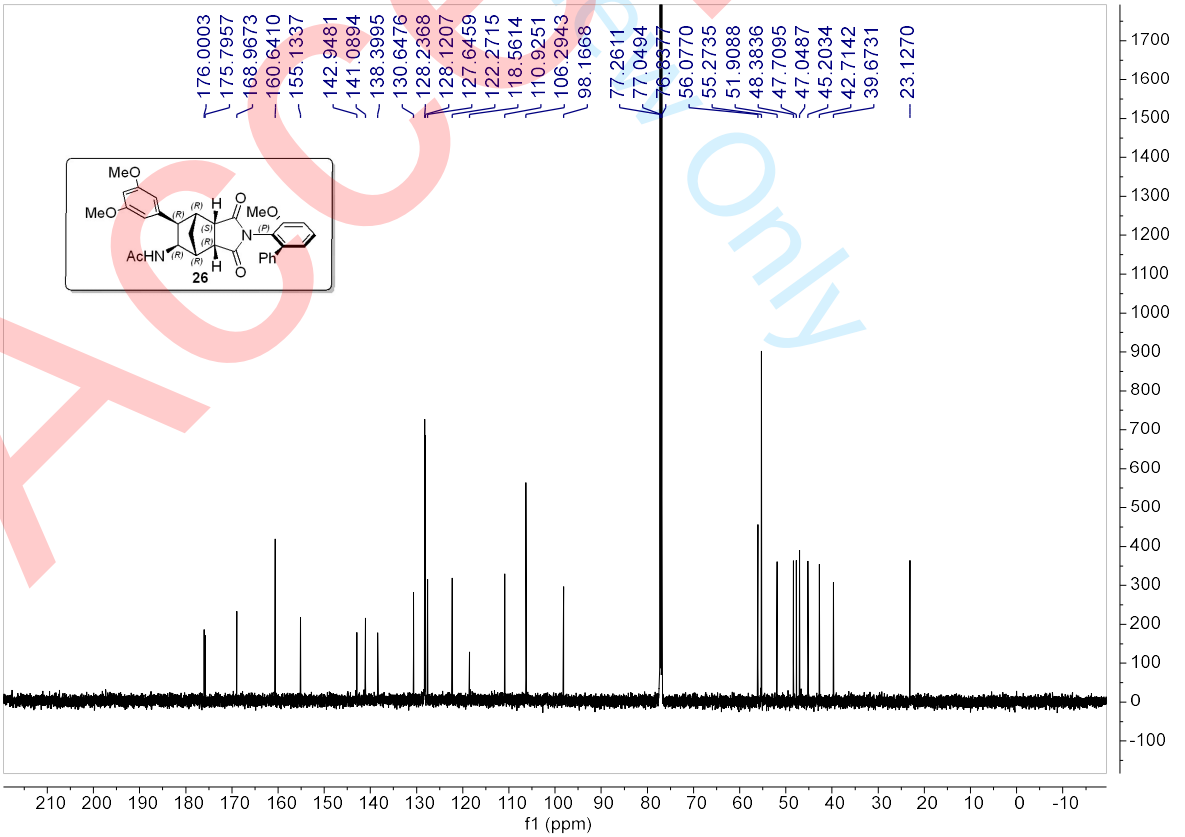
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 25



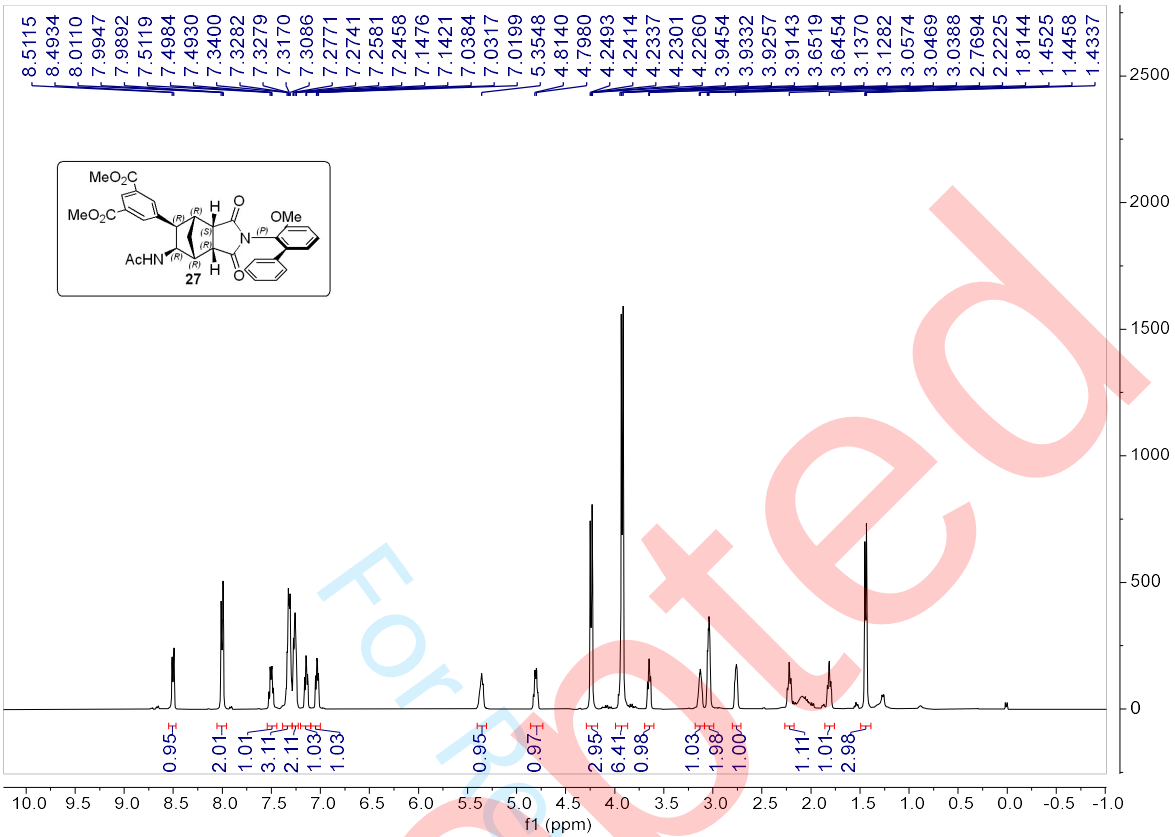
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 25



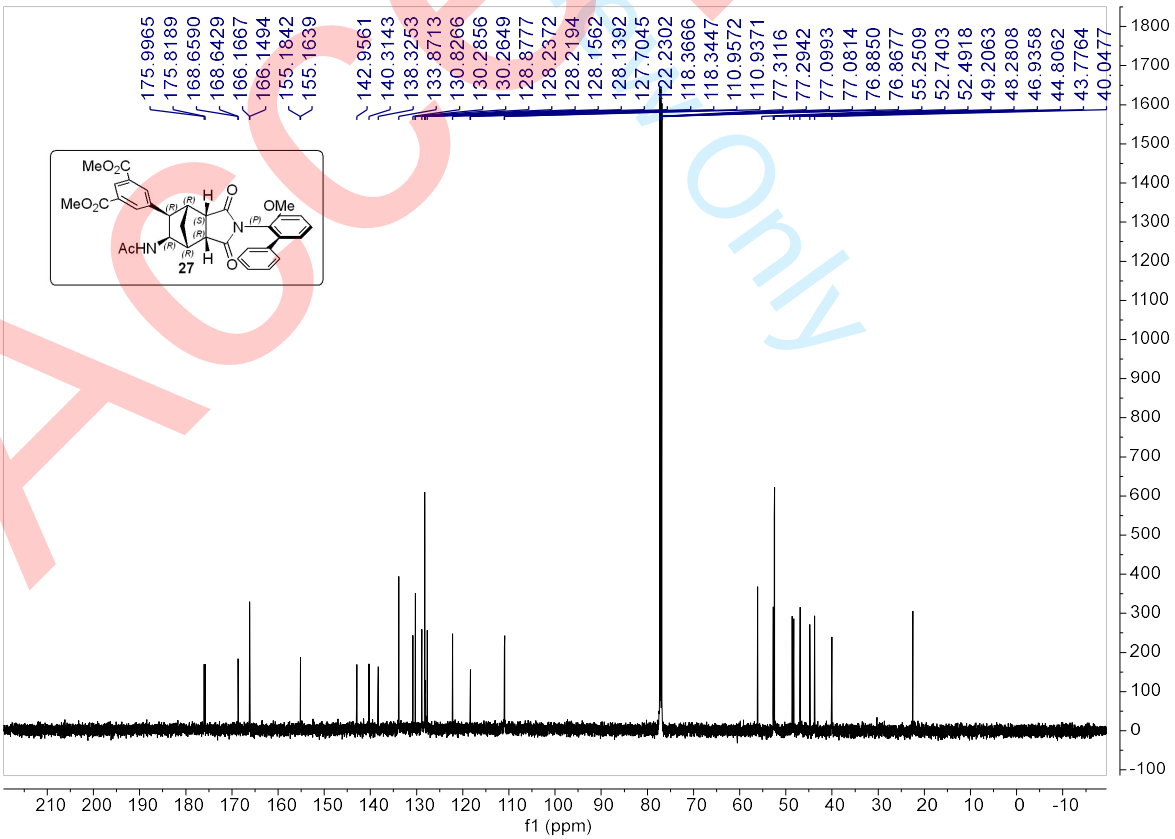
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 26



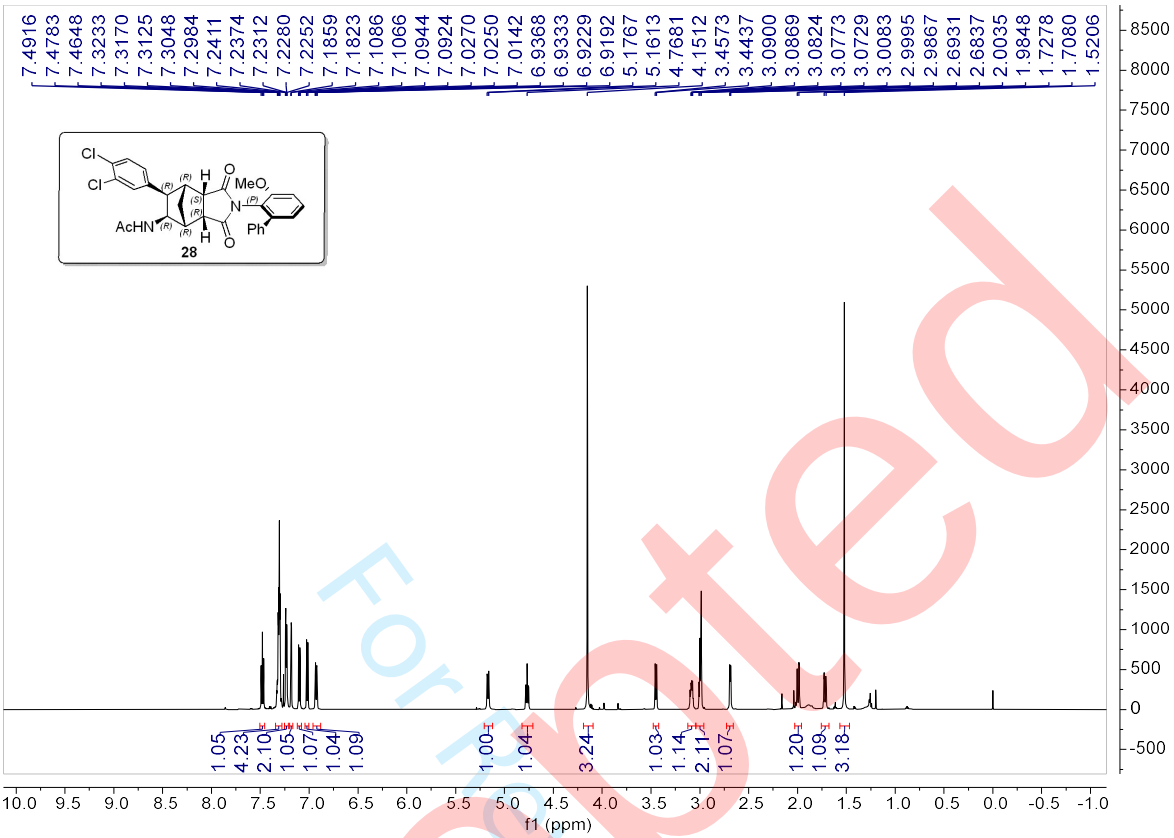
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 26



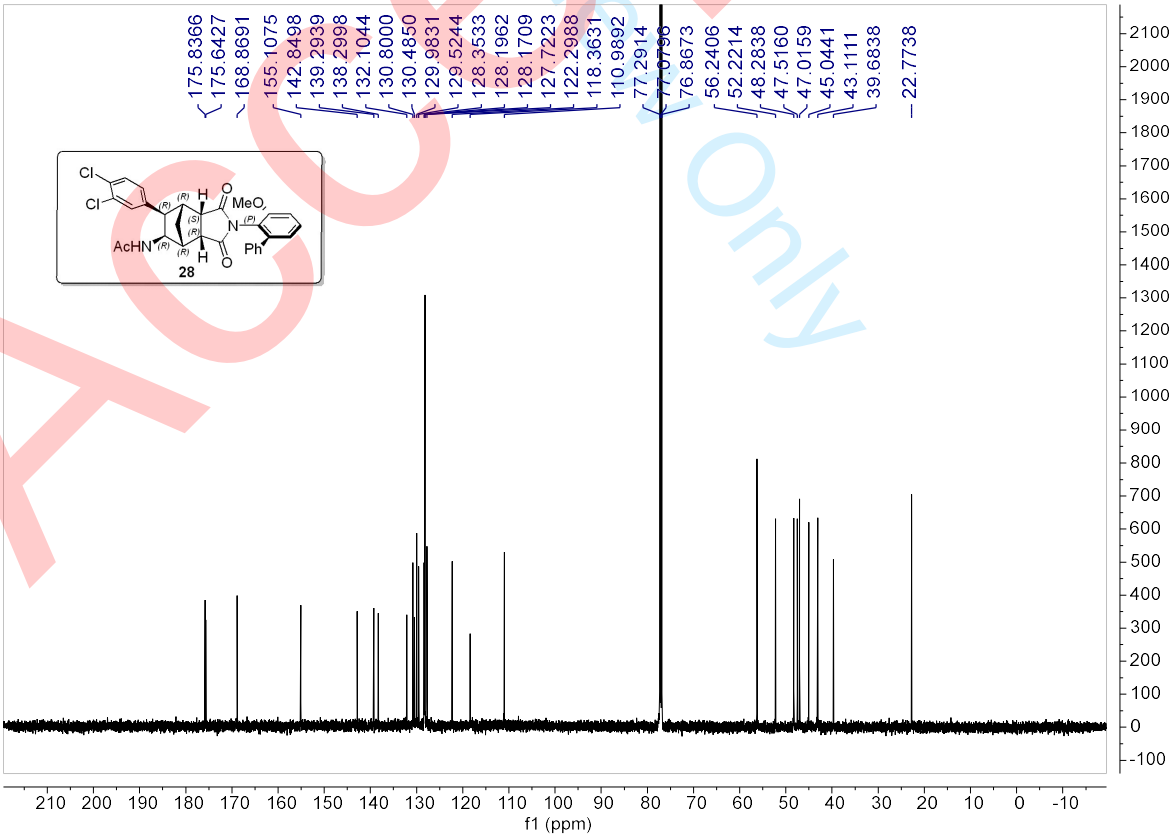
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 27



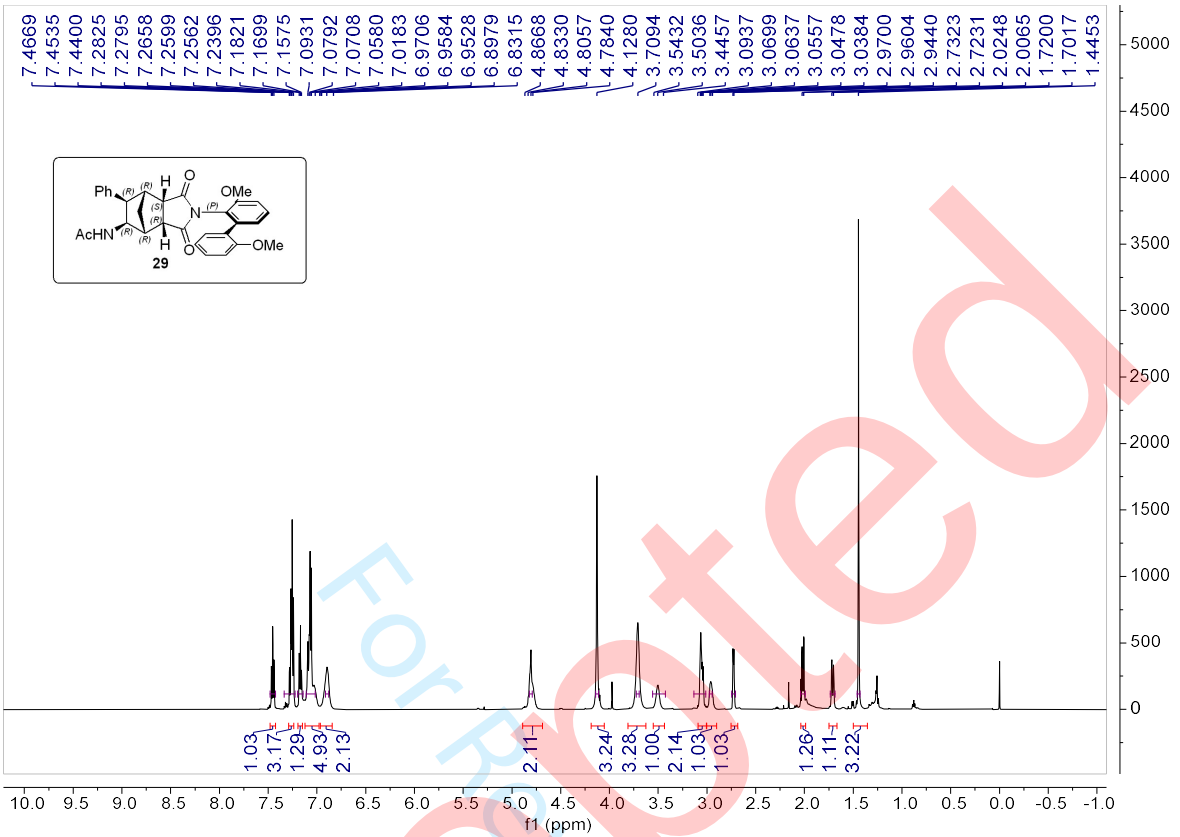
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 27



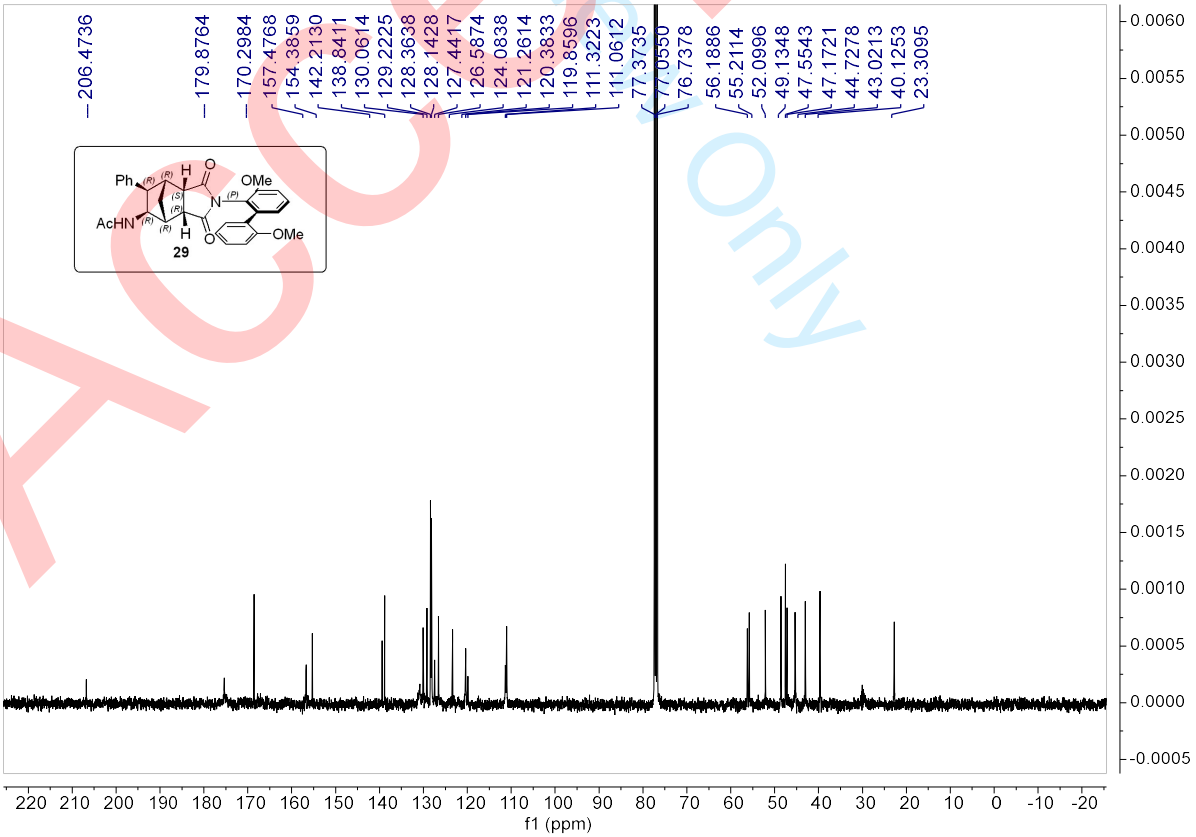
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 28



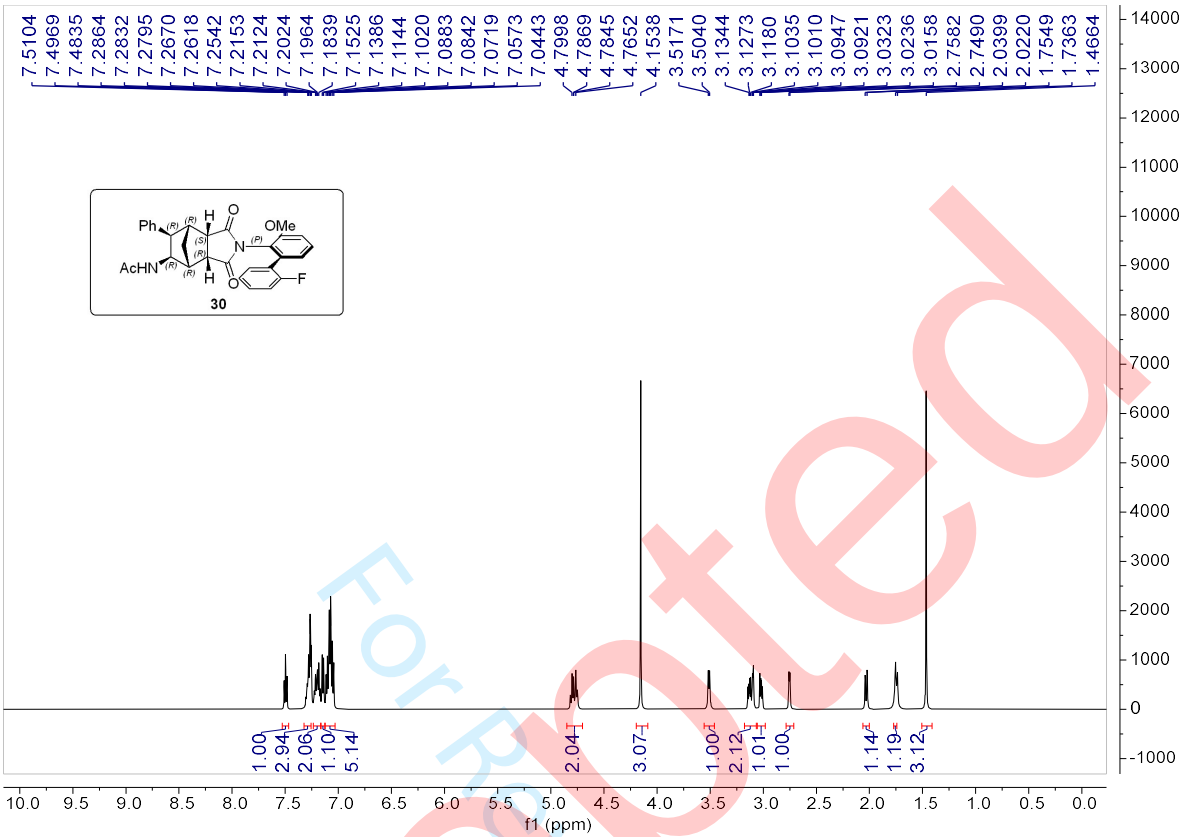
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 28



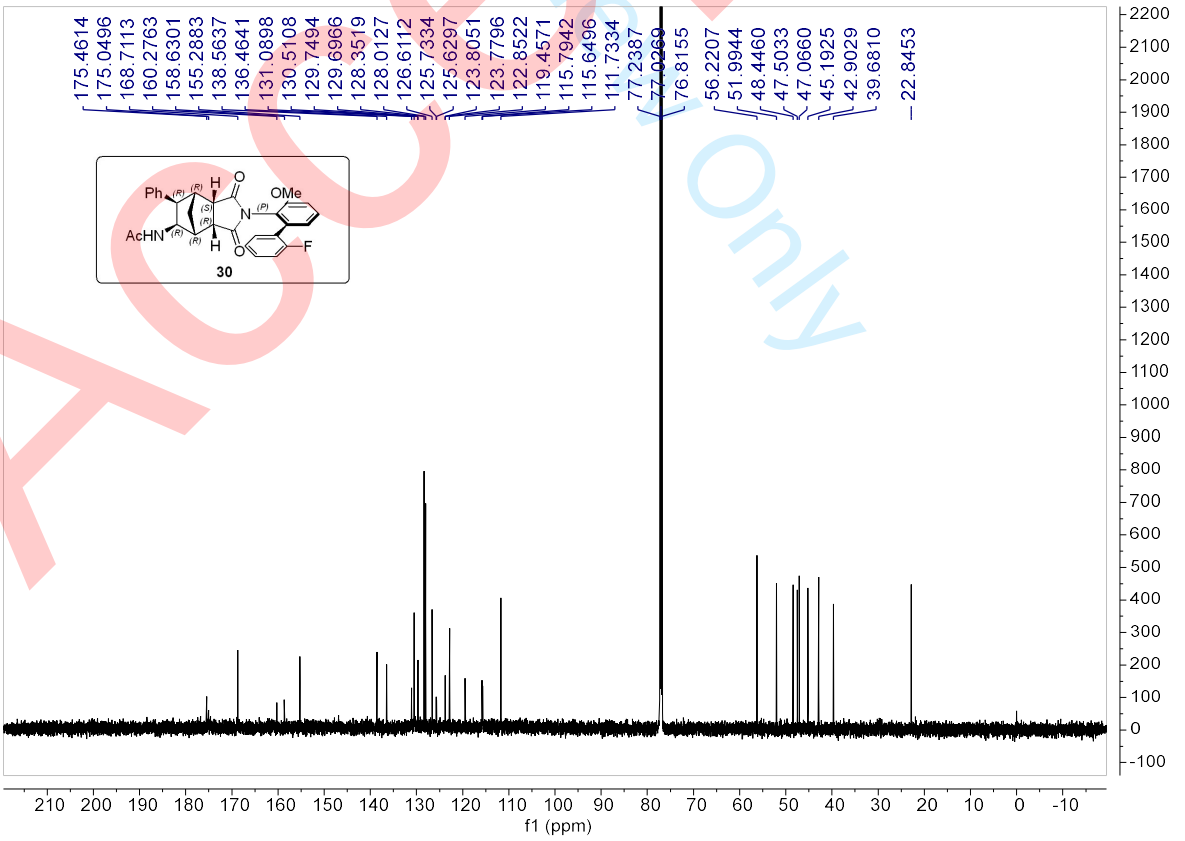
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 29



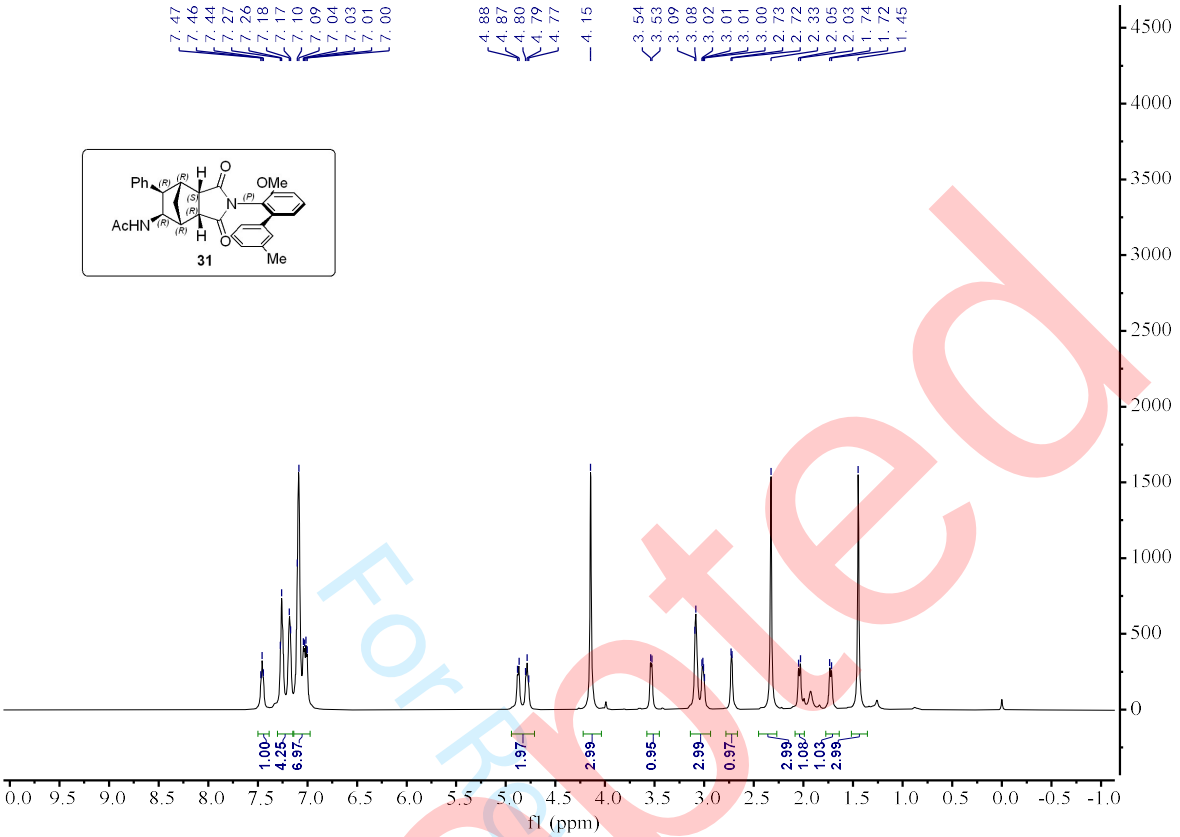
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 29



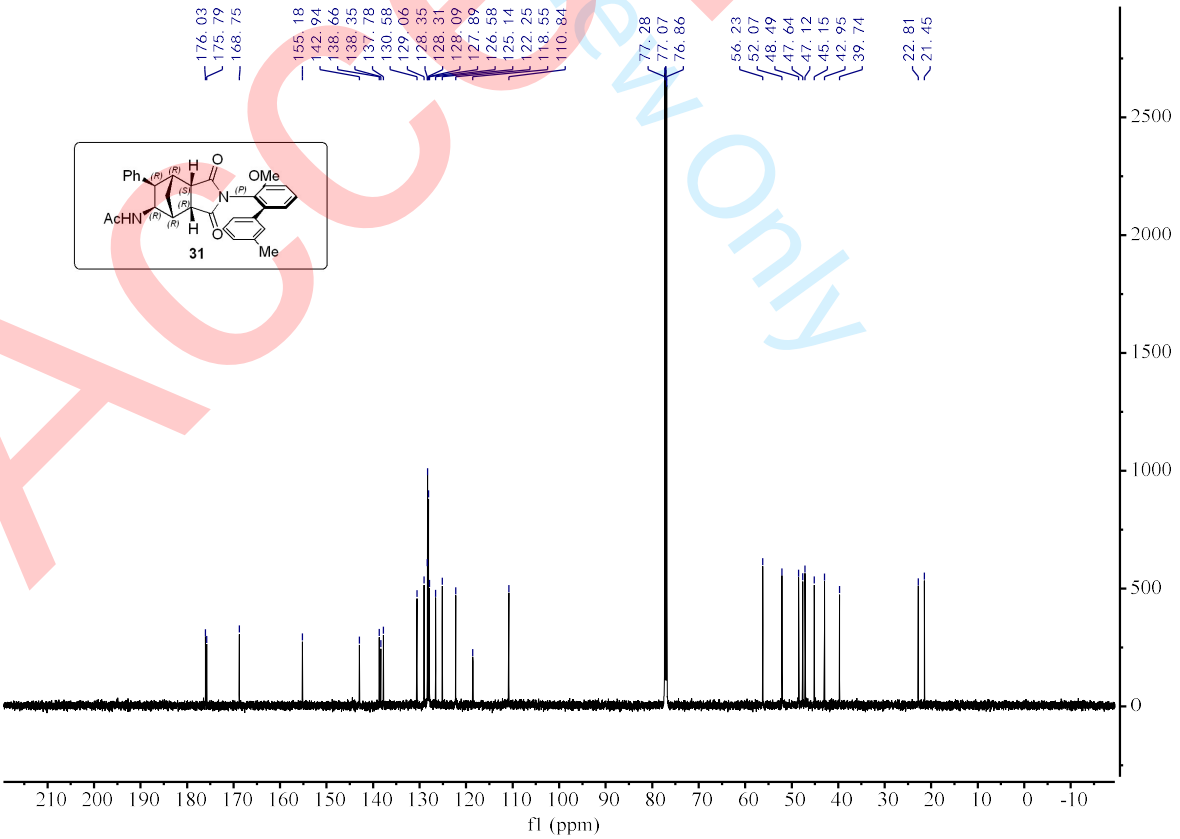
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 30



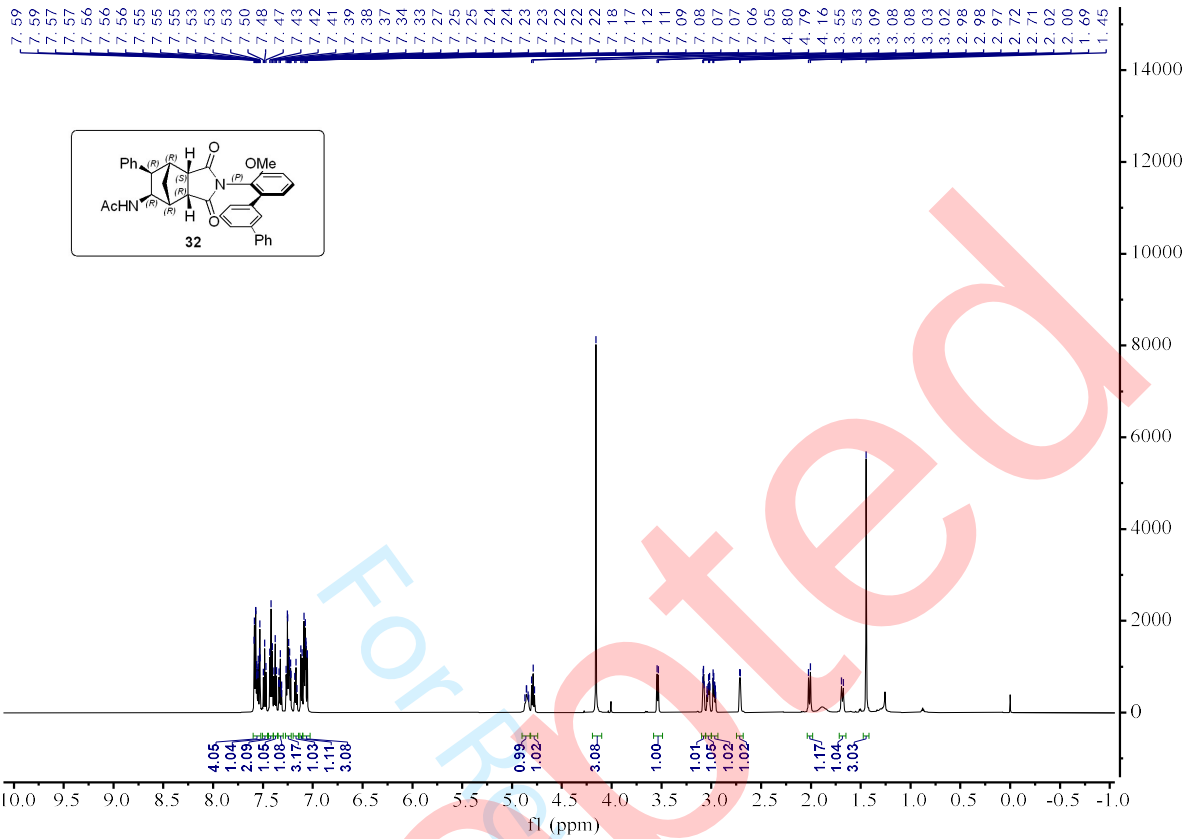
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 30



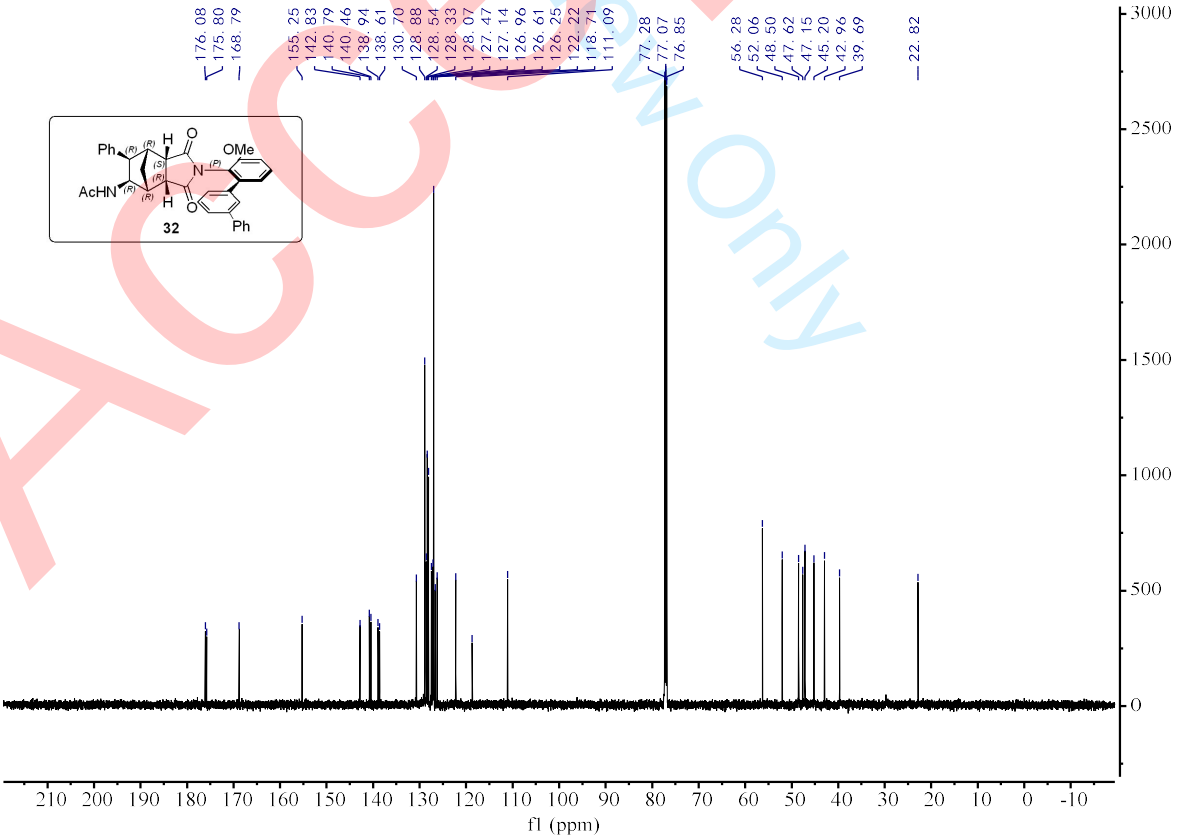
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 31



^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 31

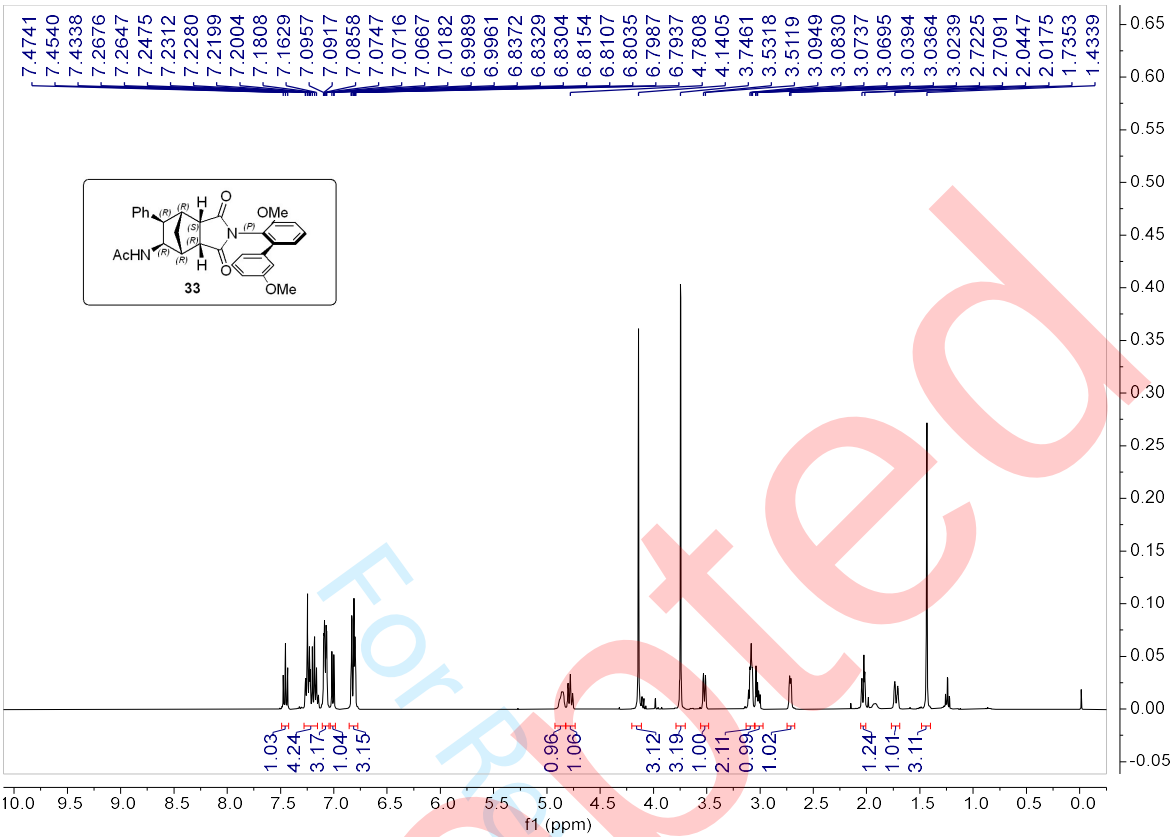


^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 32

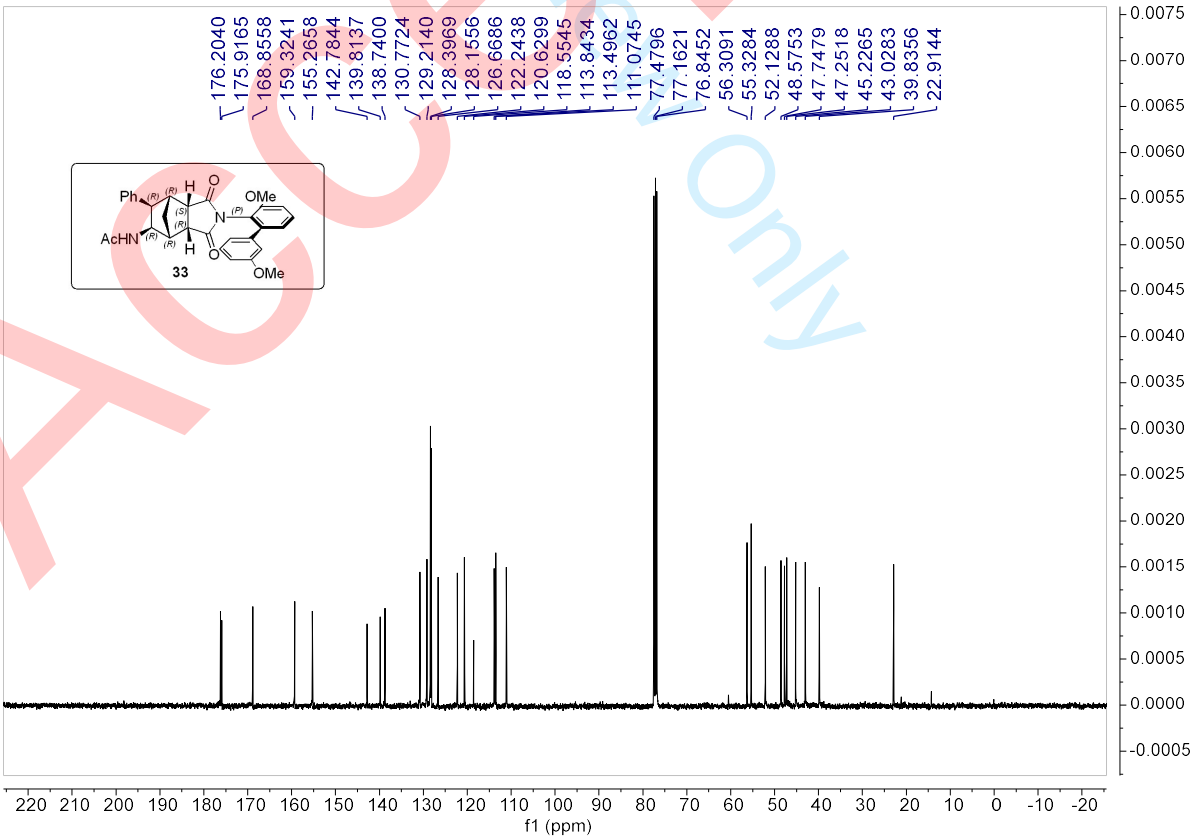


^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 32

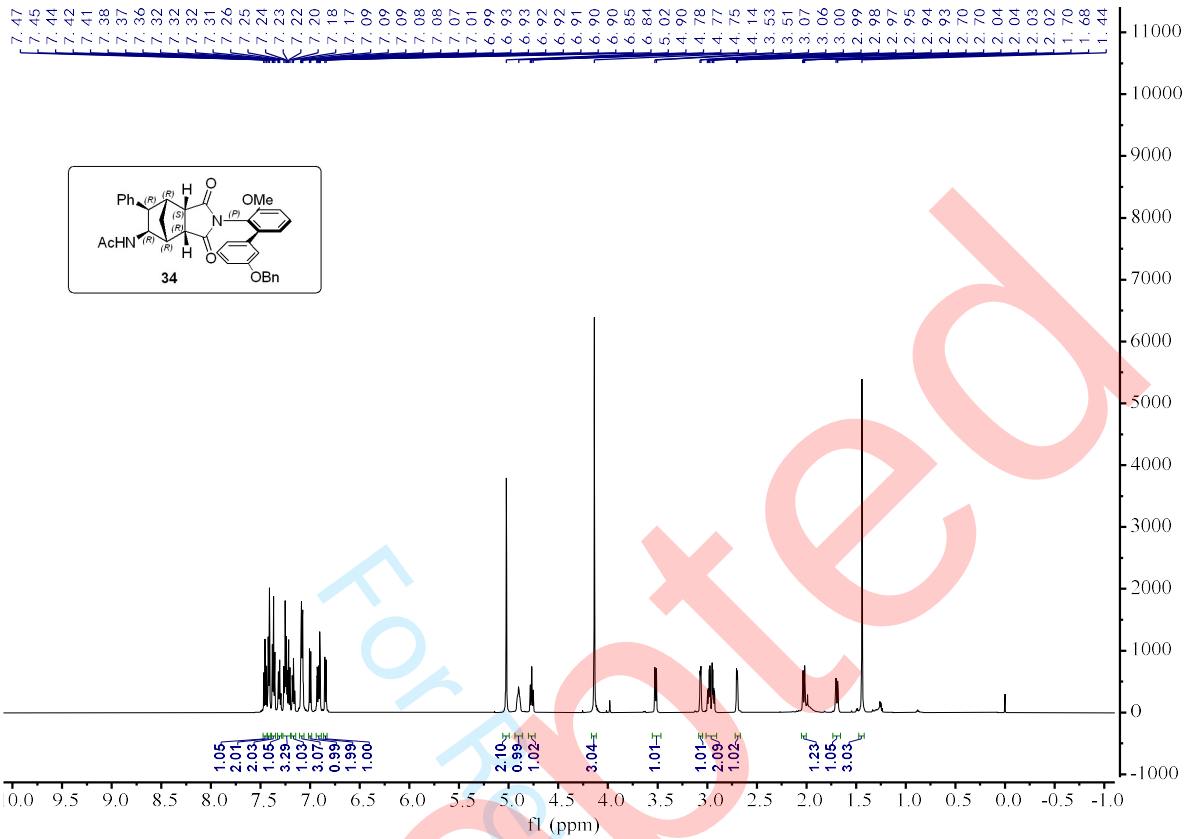
https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english



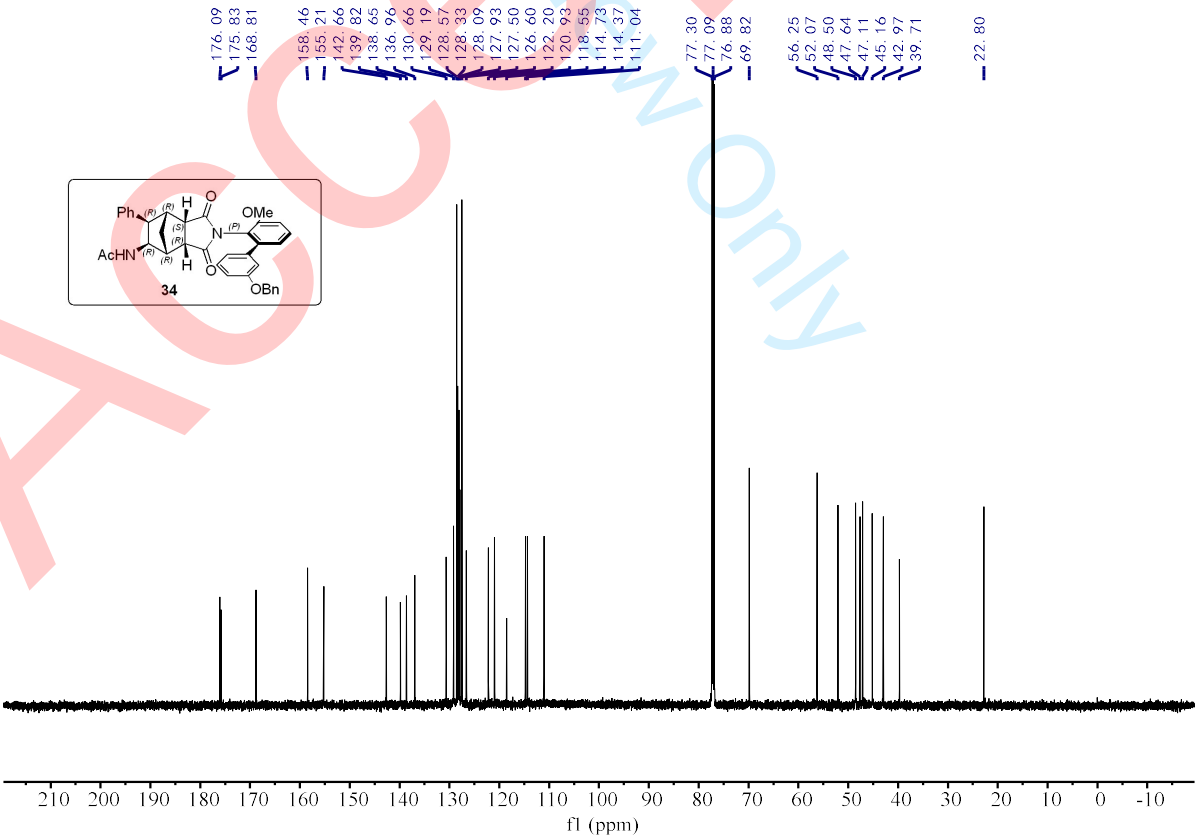
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 33



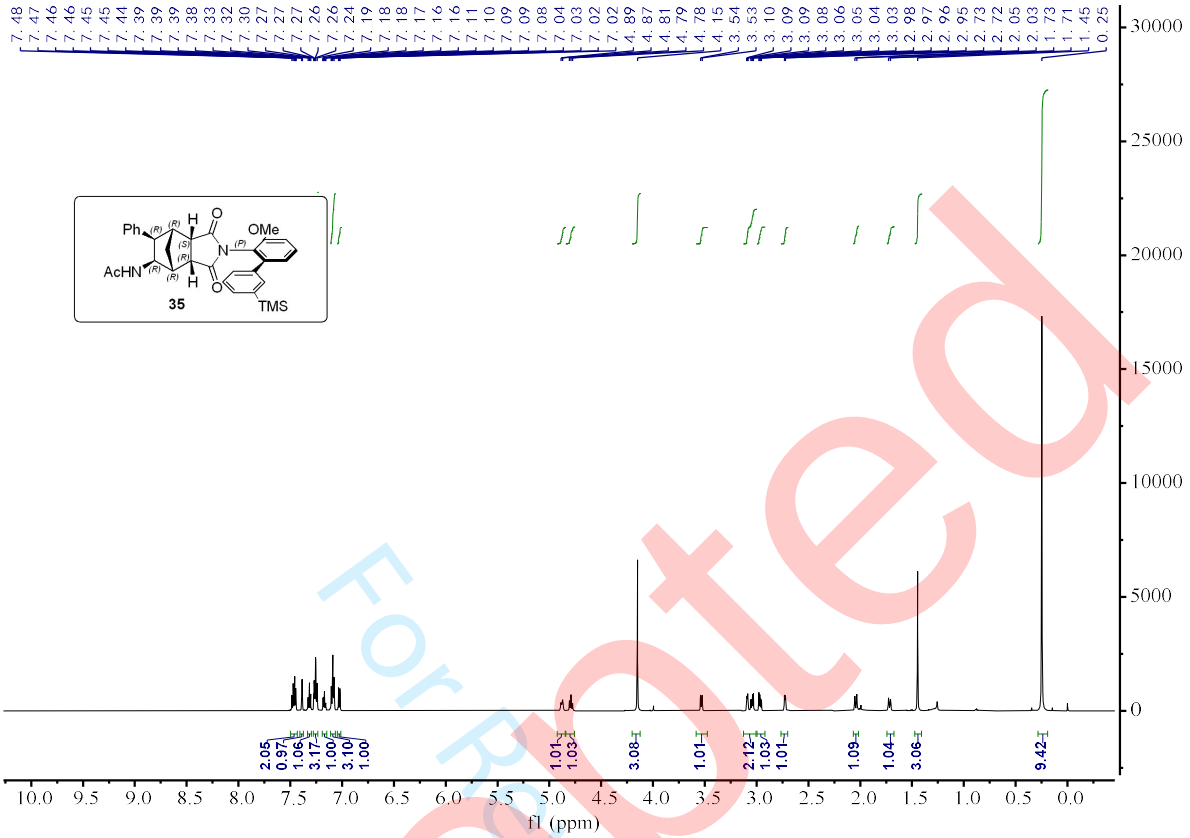
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 33



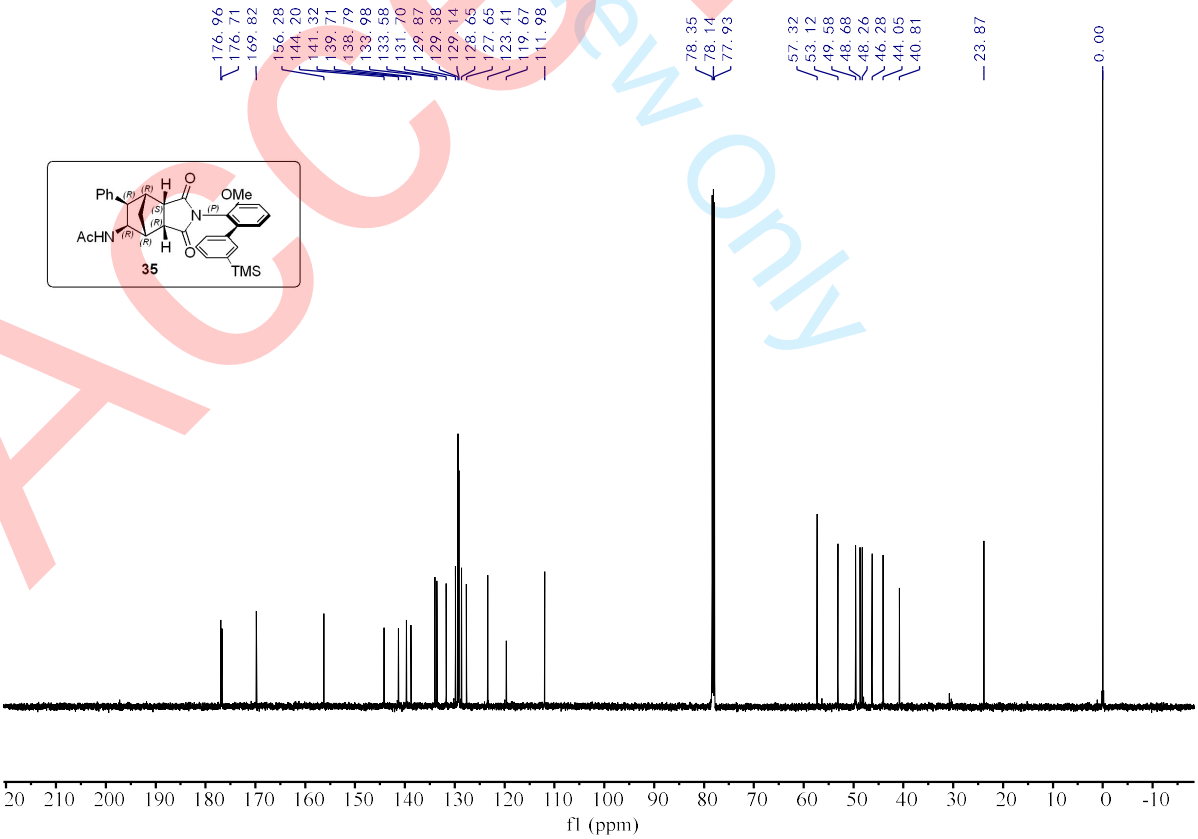
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 34



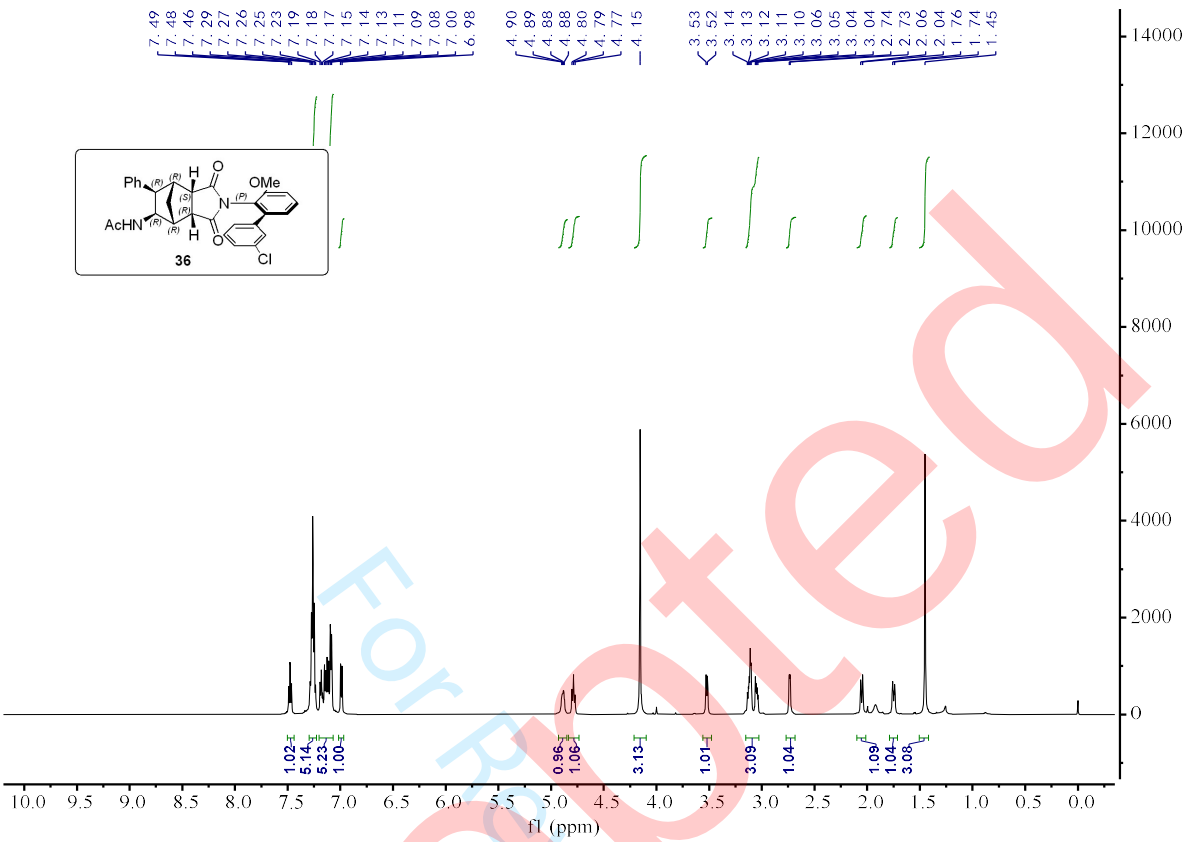
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 34



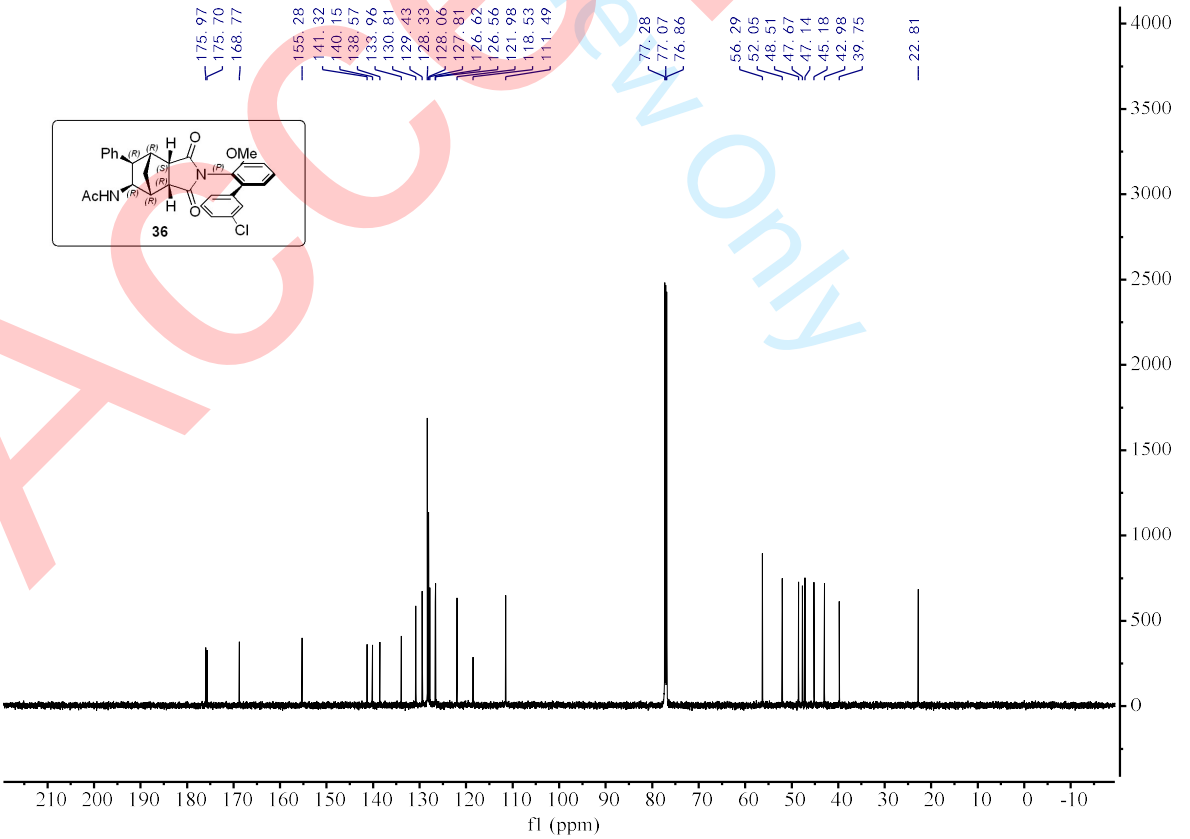
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 35



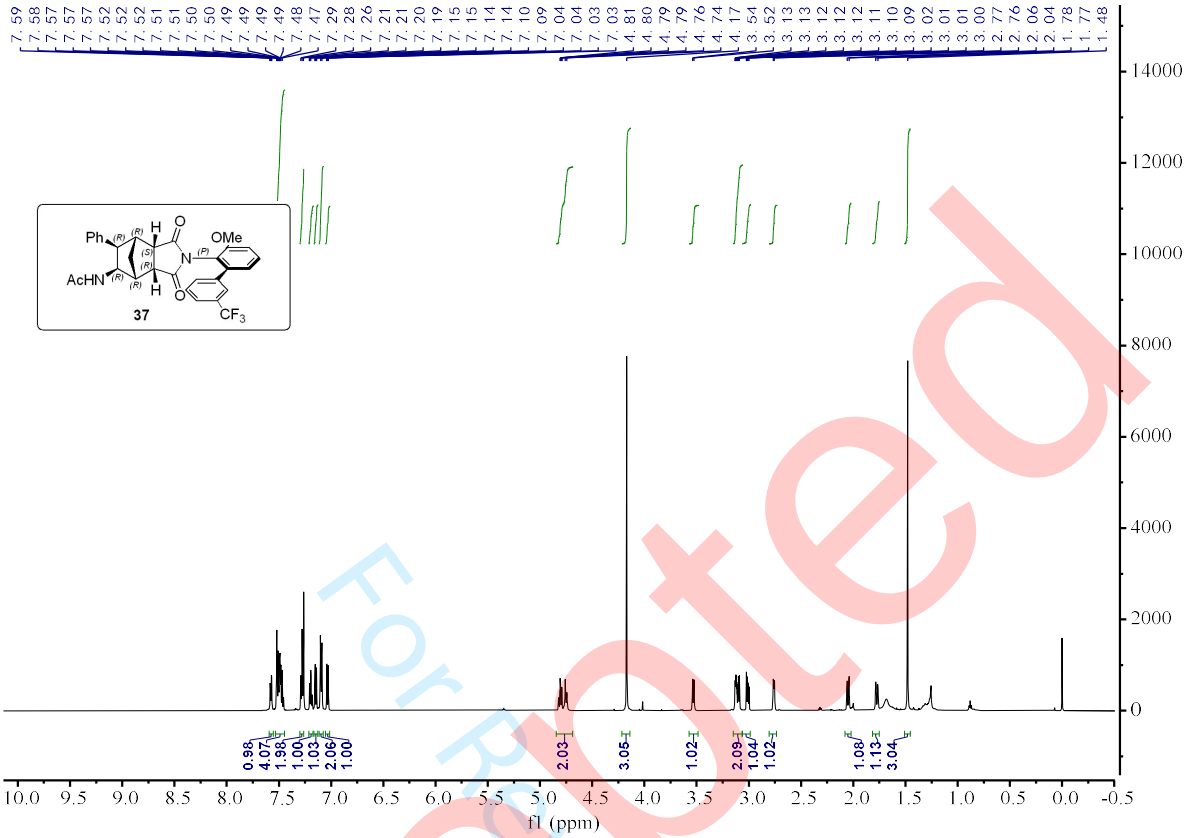
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 35



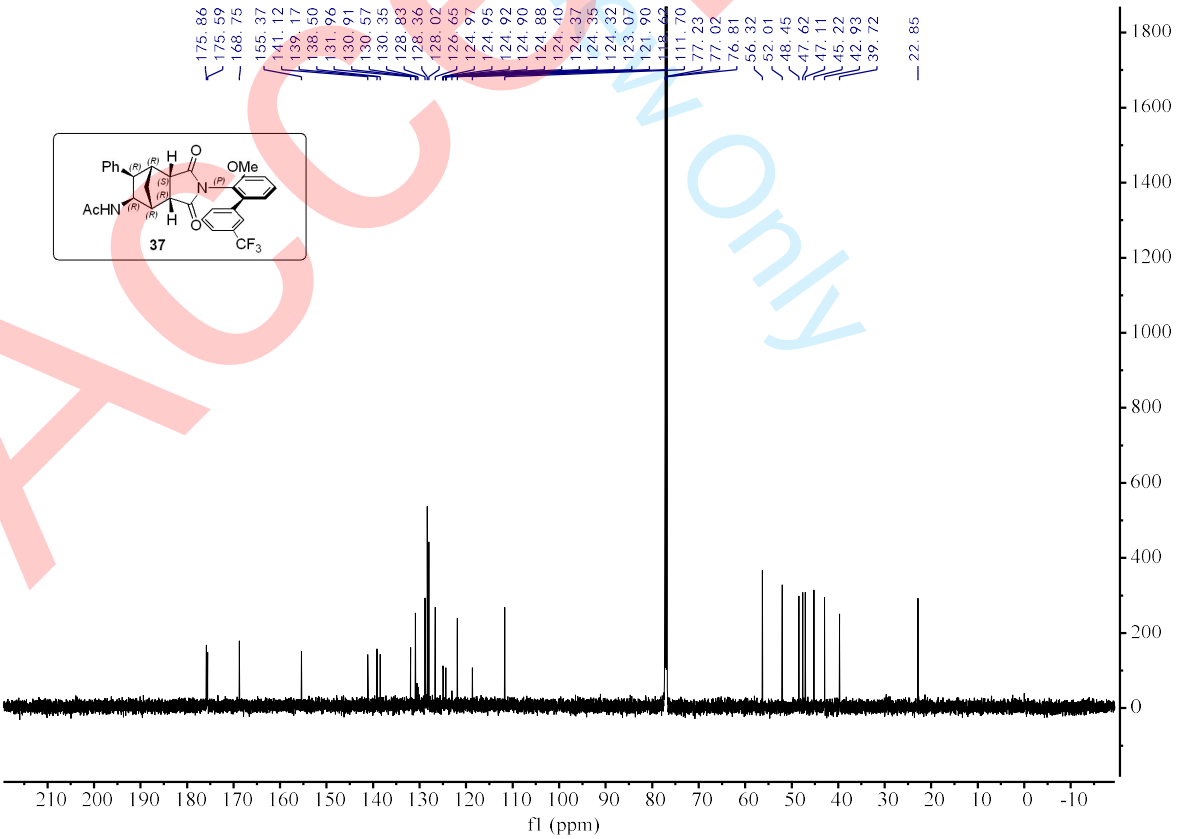
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 36



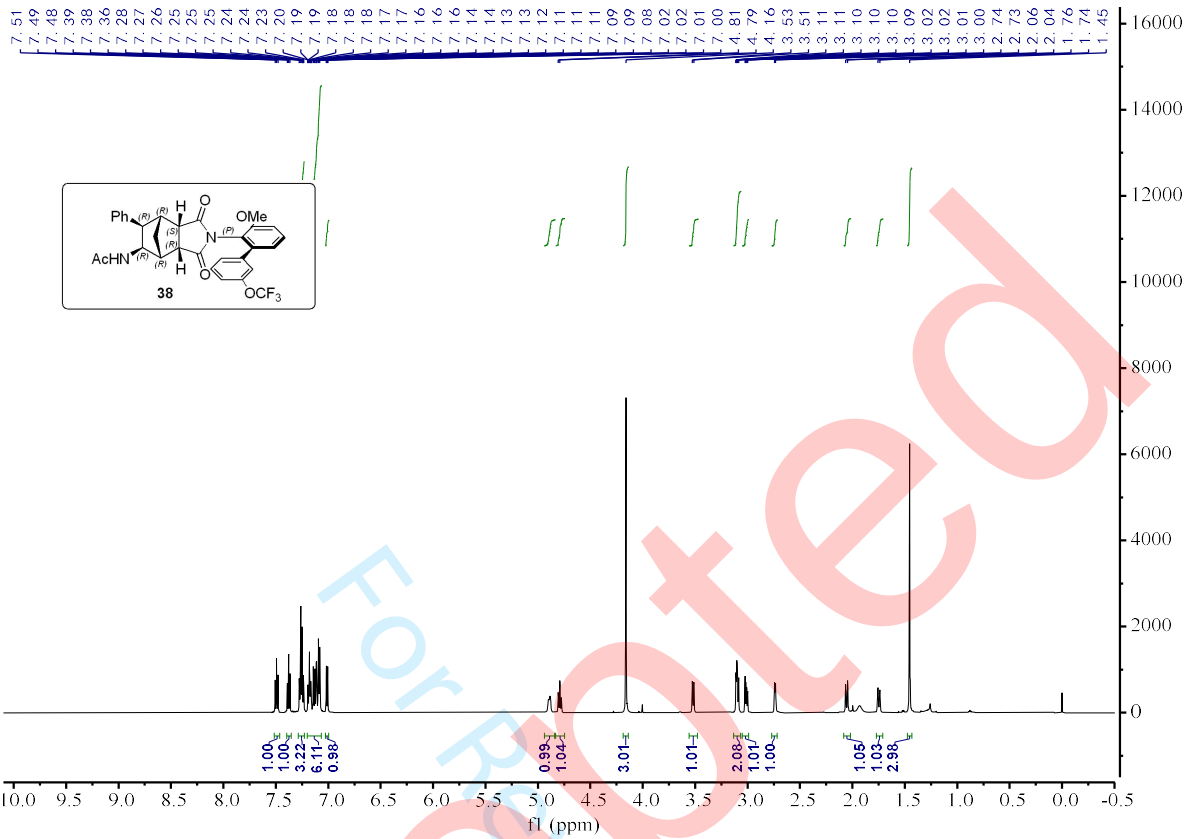
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 36



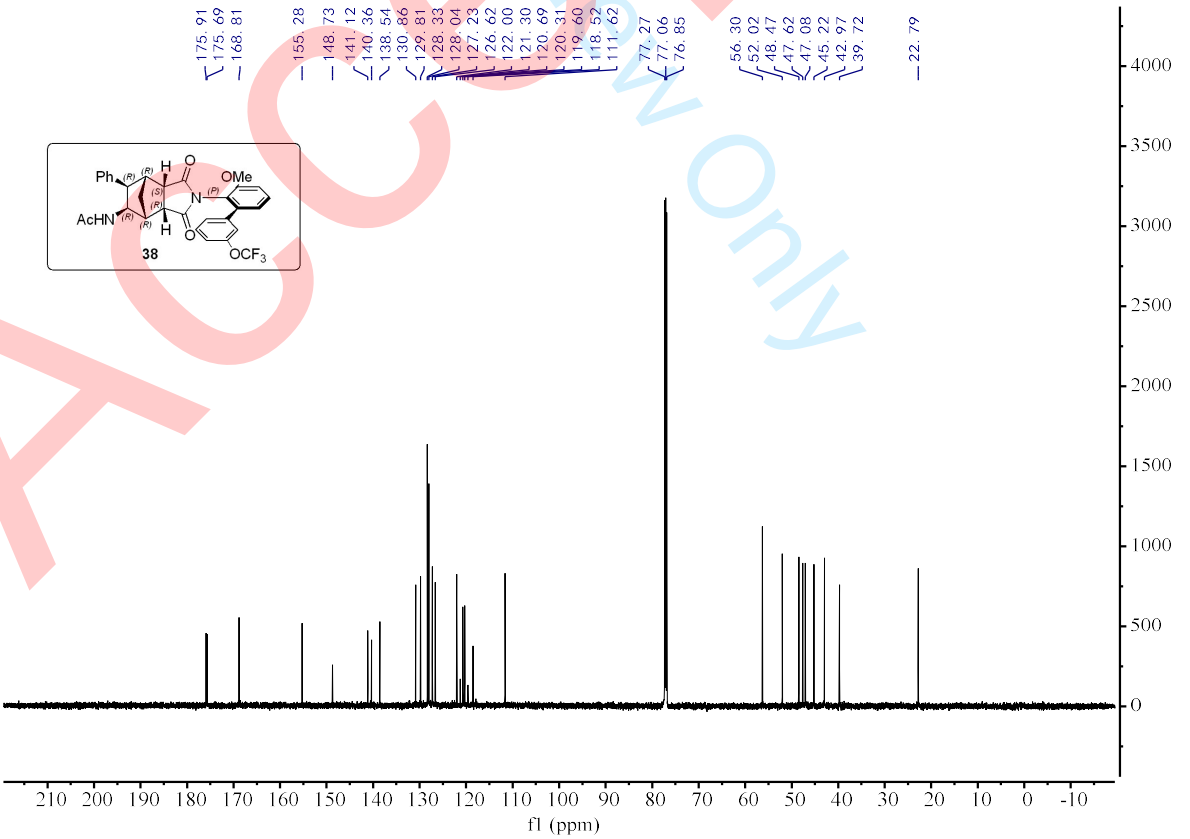
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 37



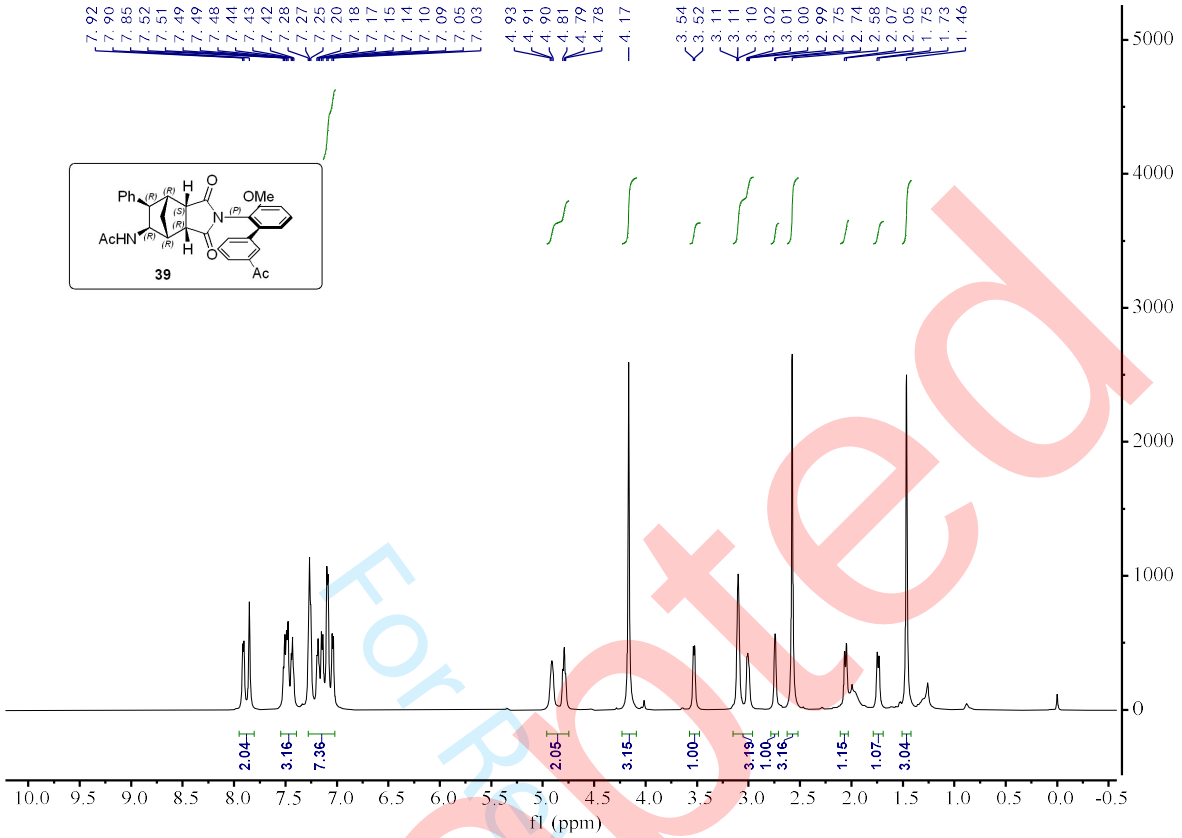
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 37



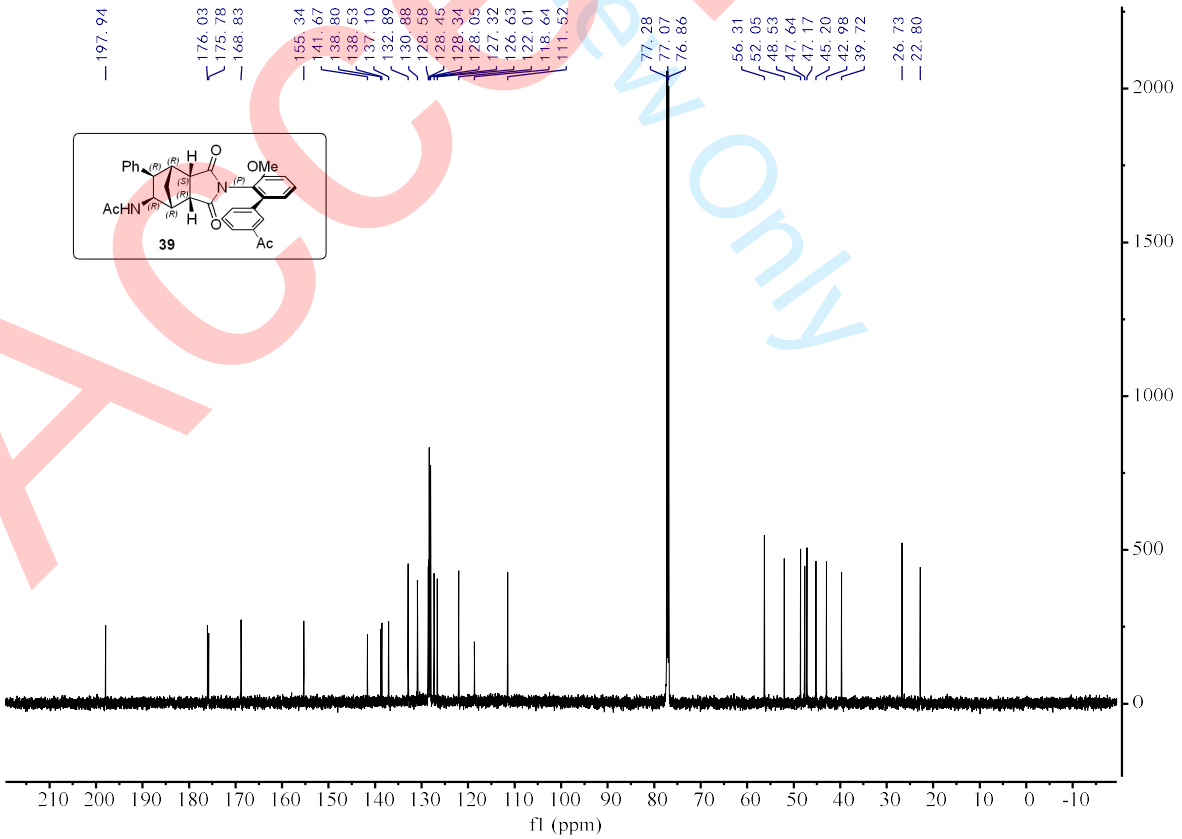
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 38



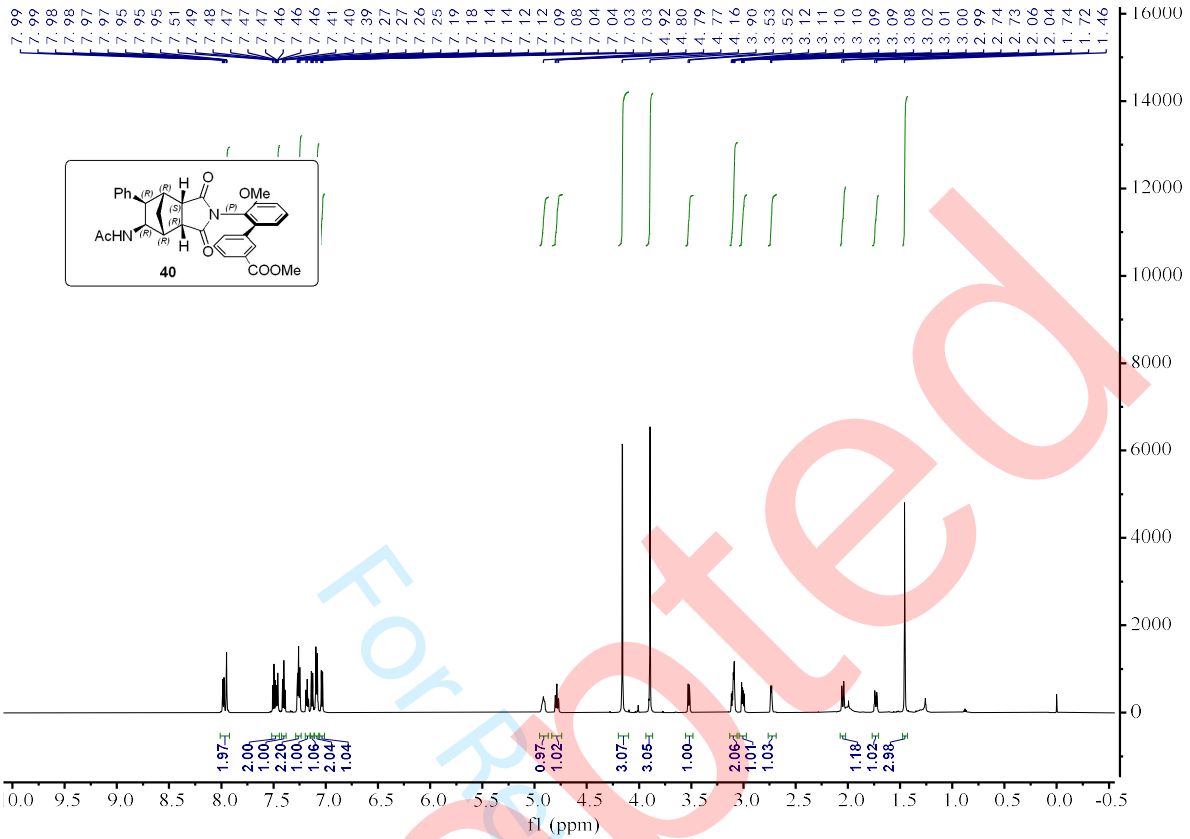
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 38



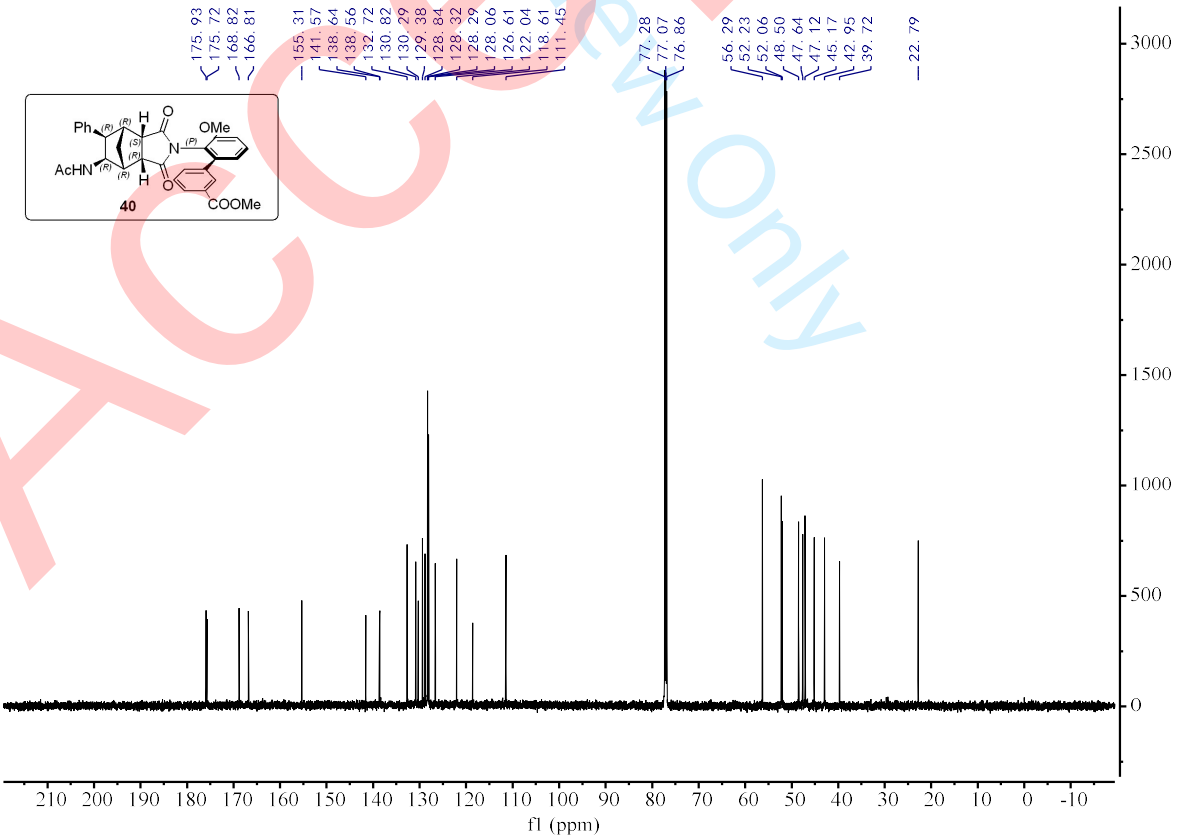
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 39



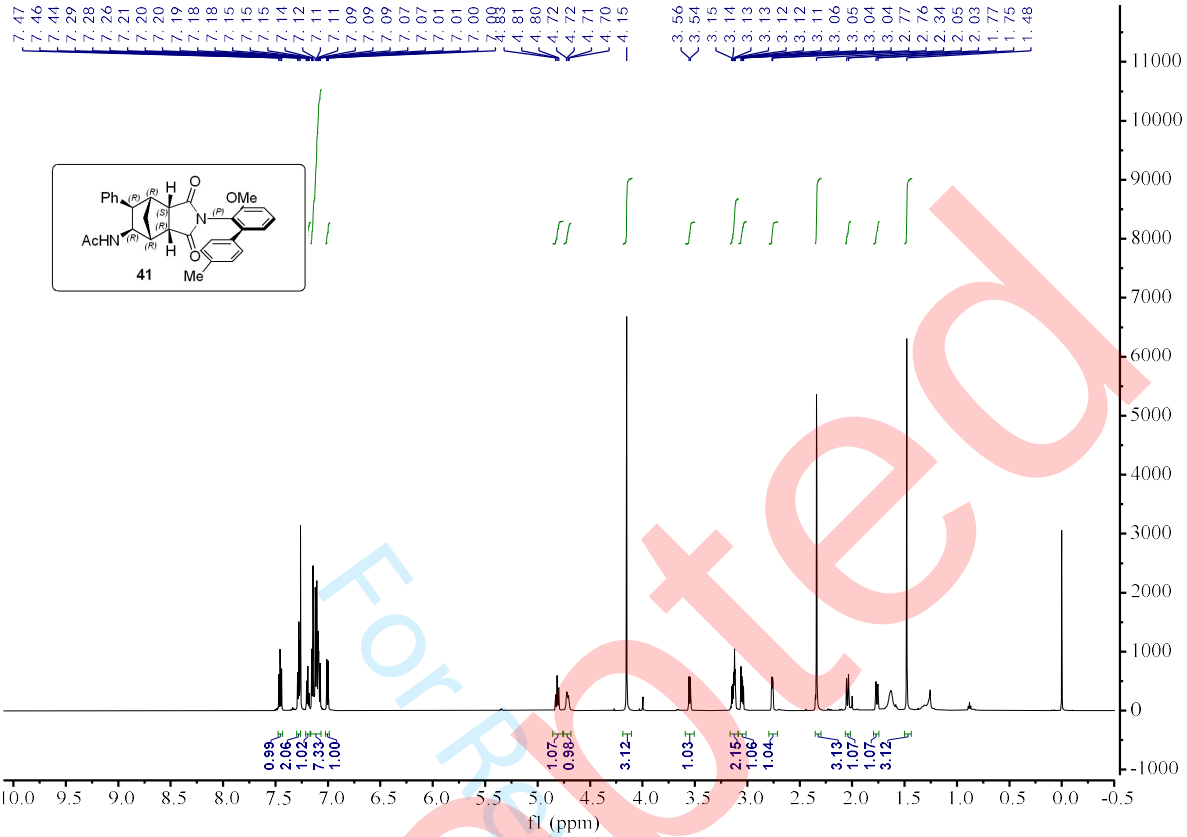
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 39



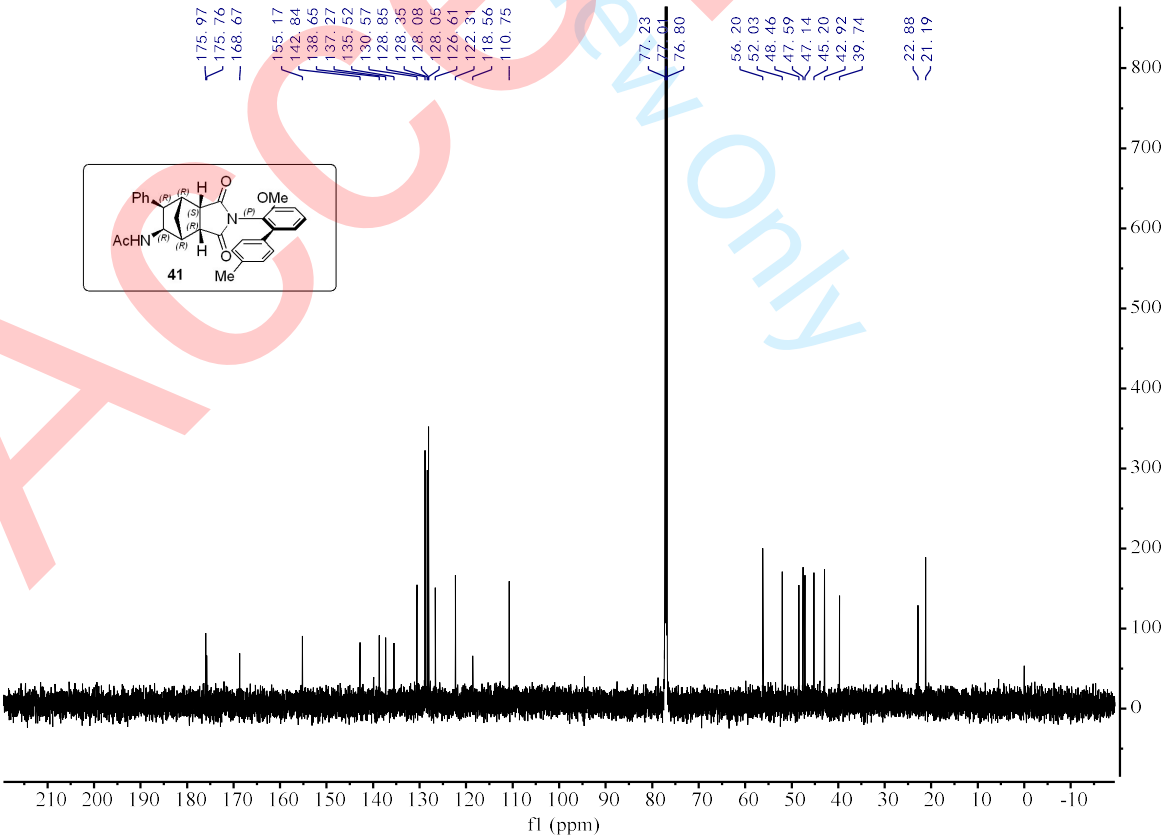
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 40



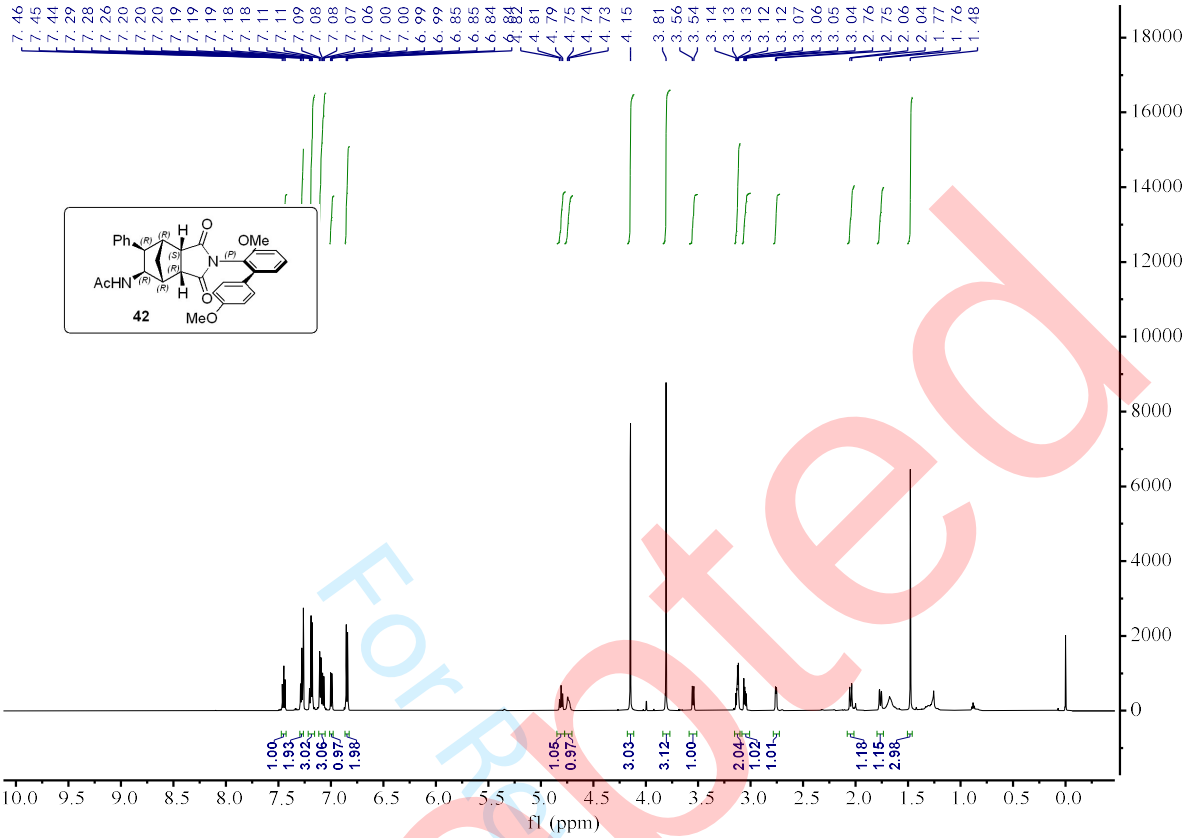
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 40



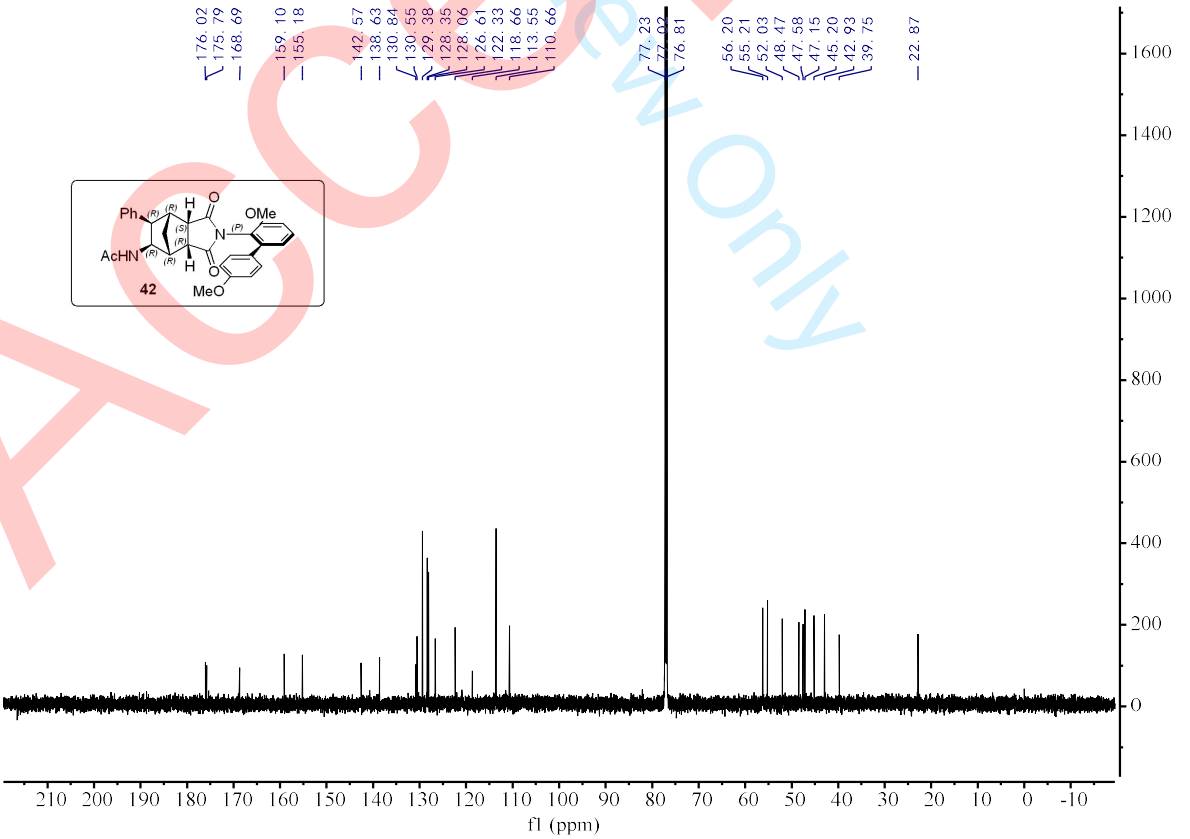
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 41



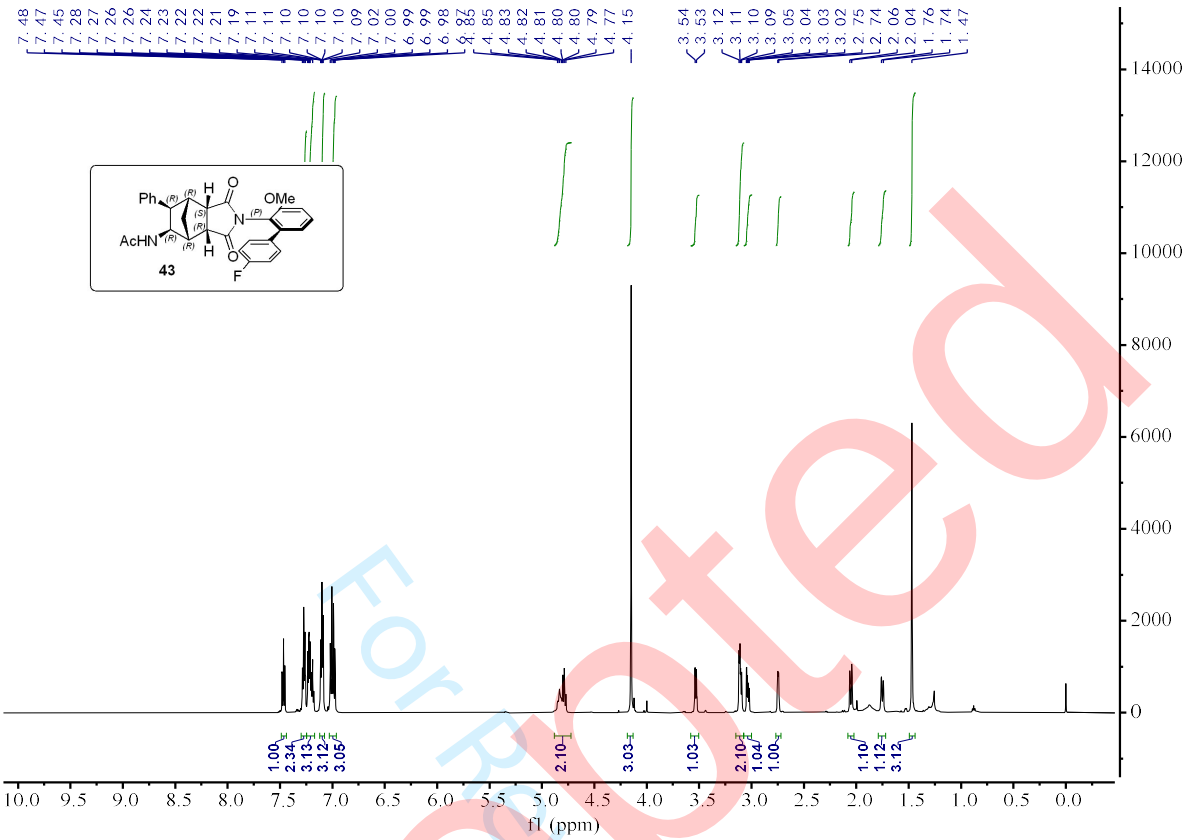
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 41



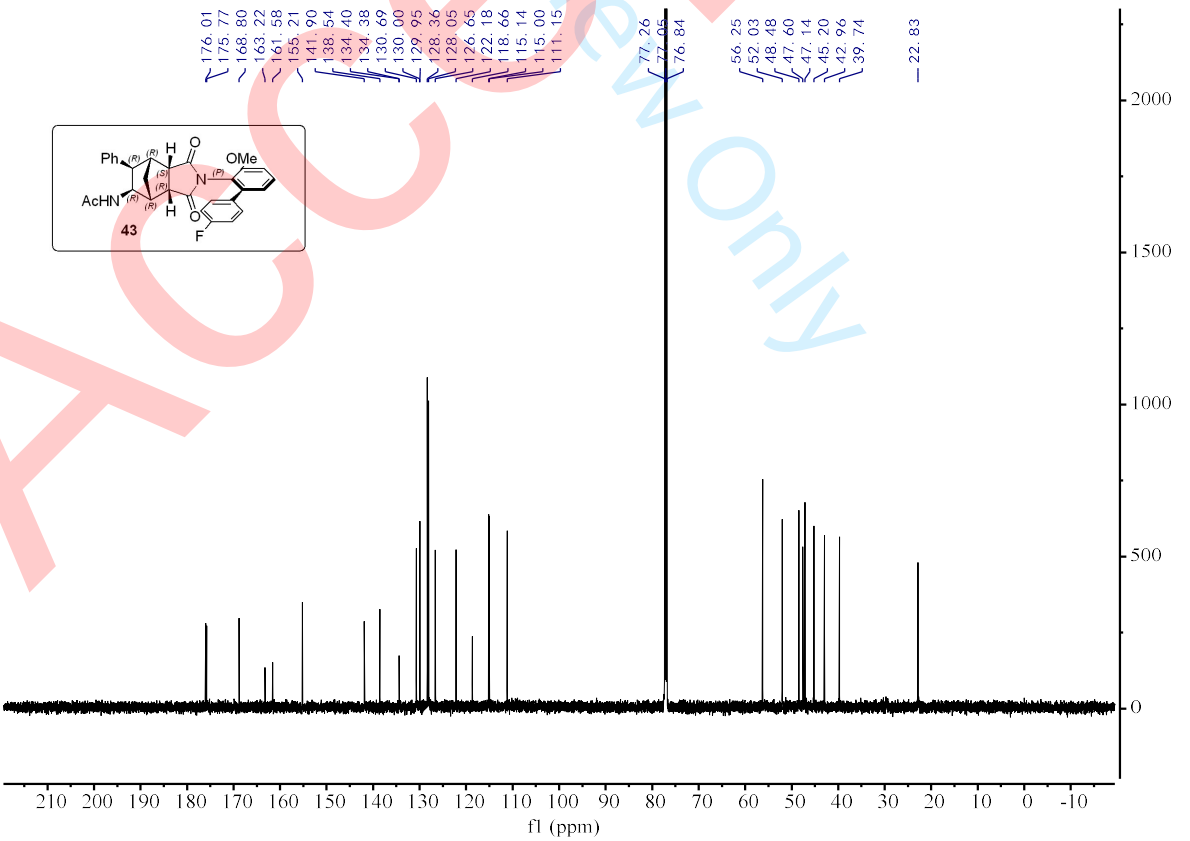
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 42



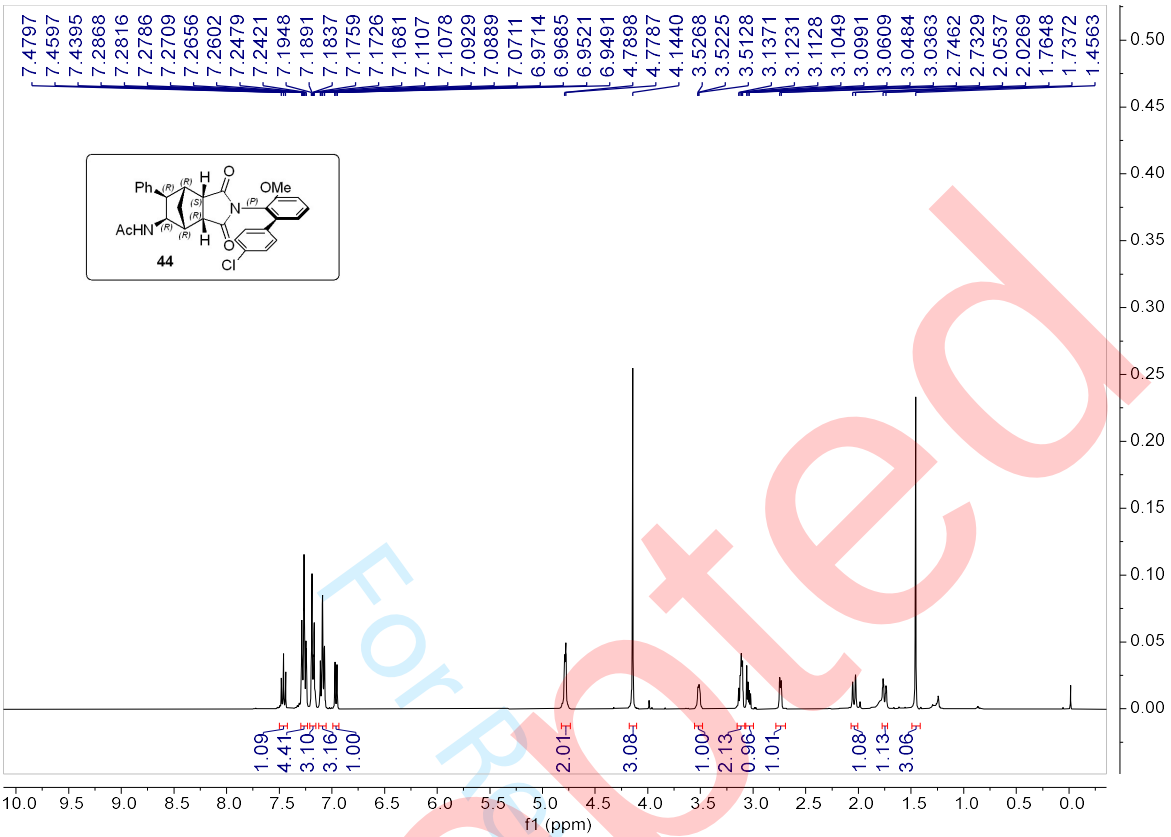
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 42



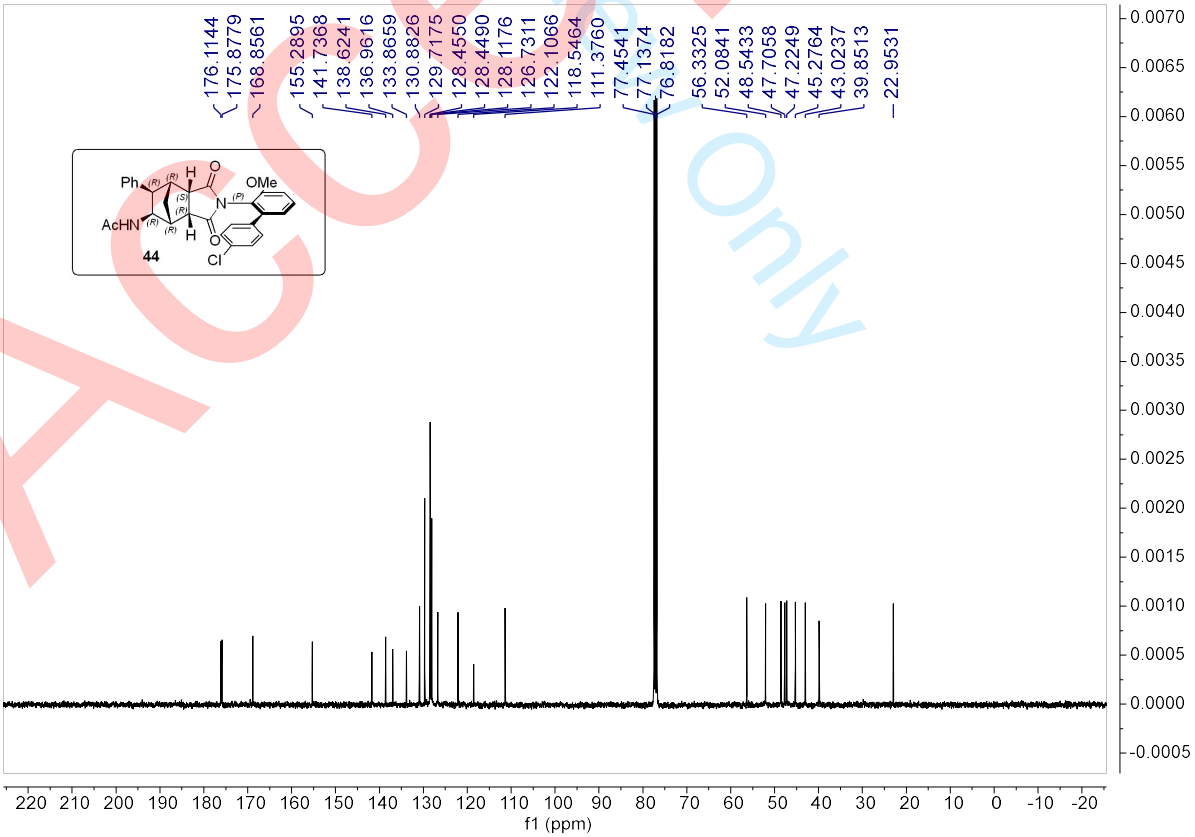
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 43



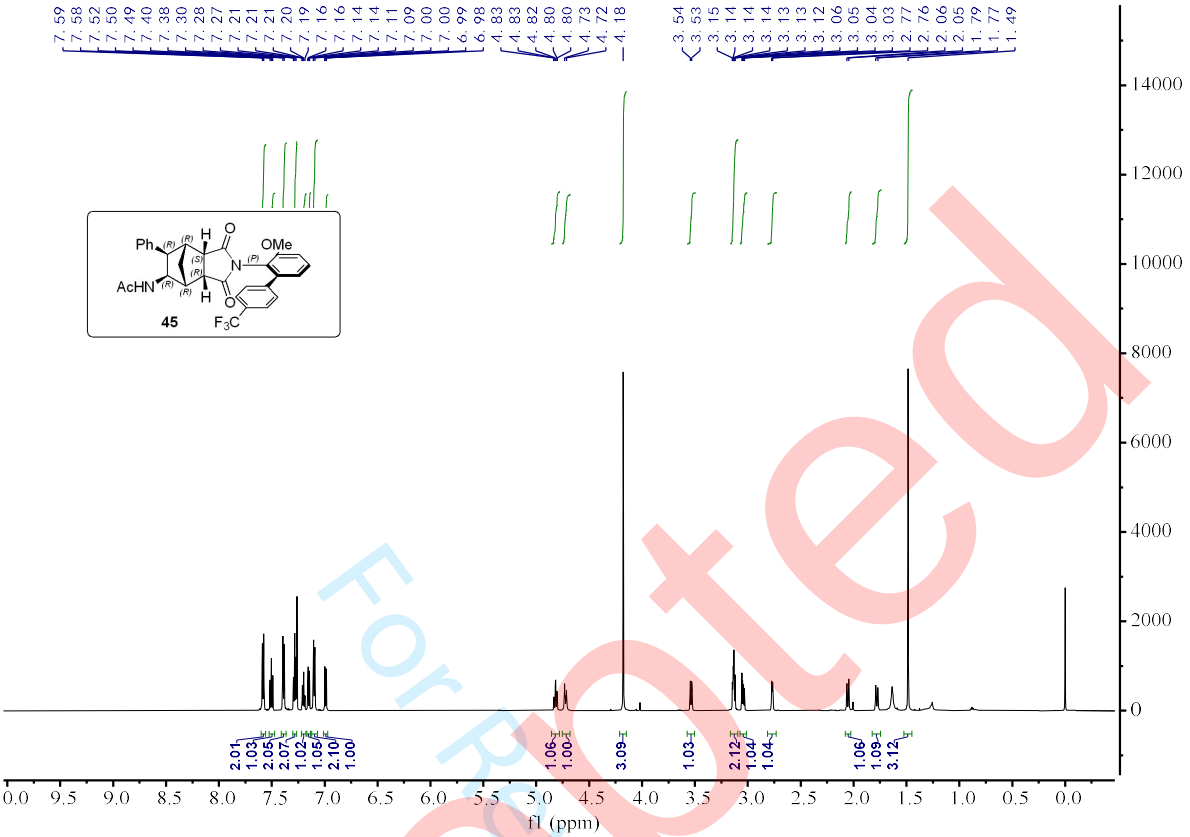
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 43



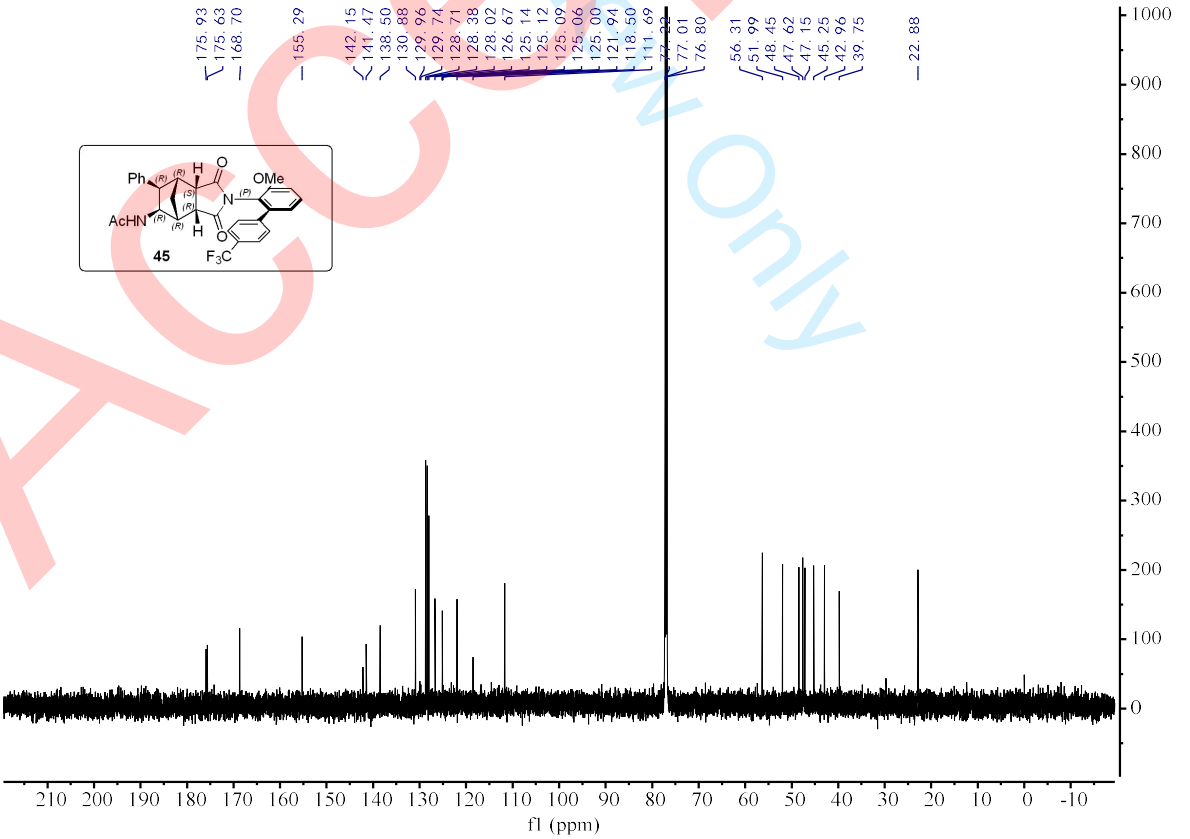
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 44



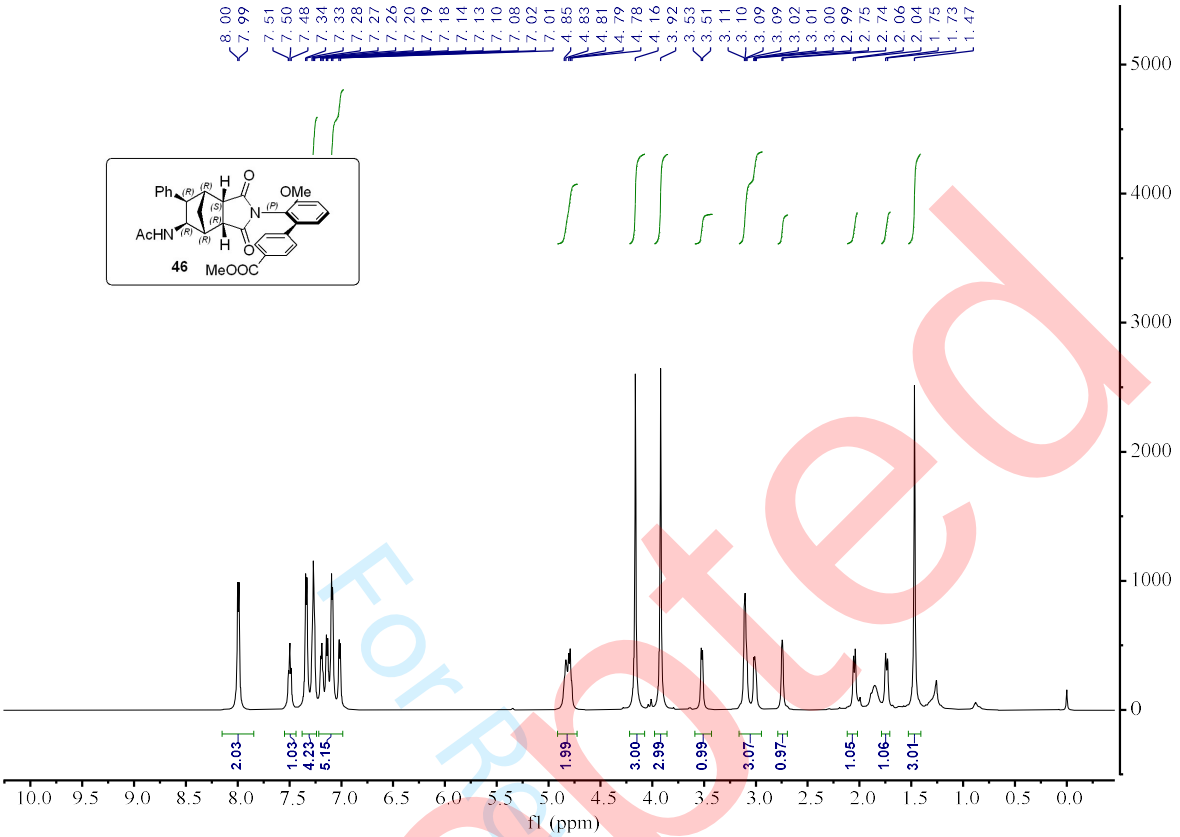
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of 44



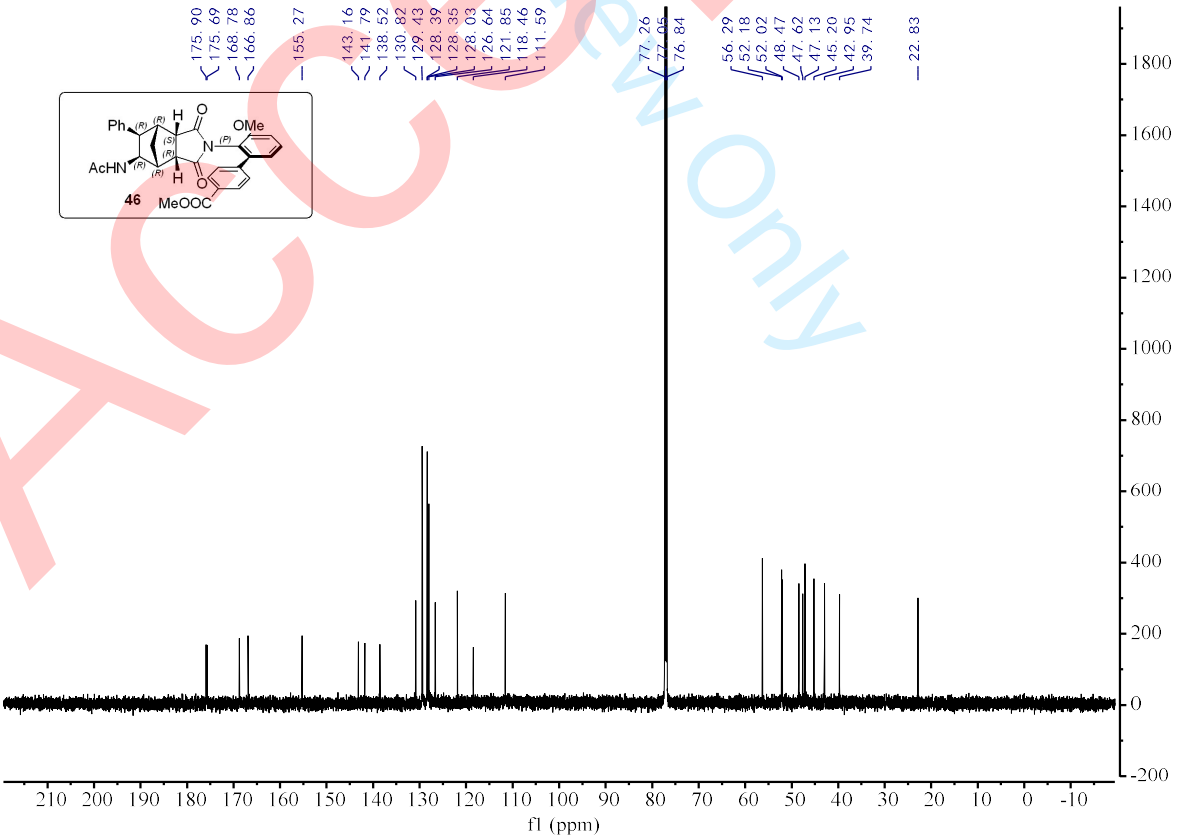
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 45



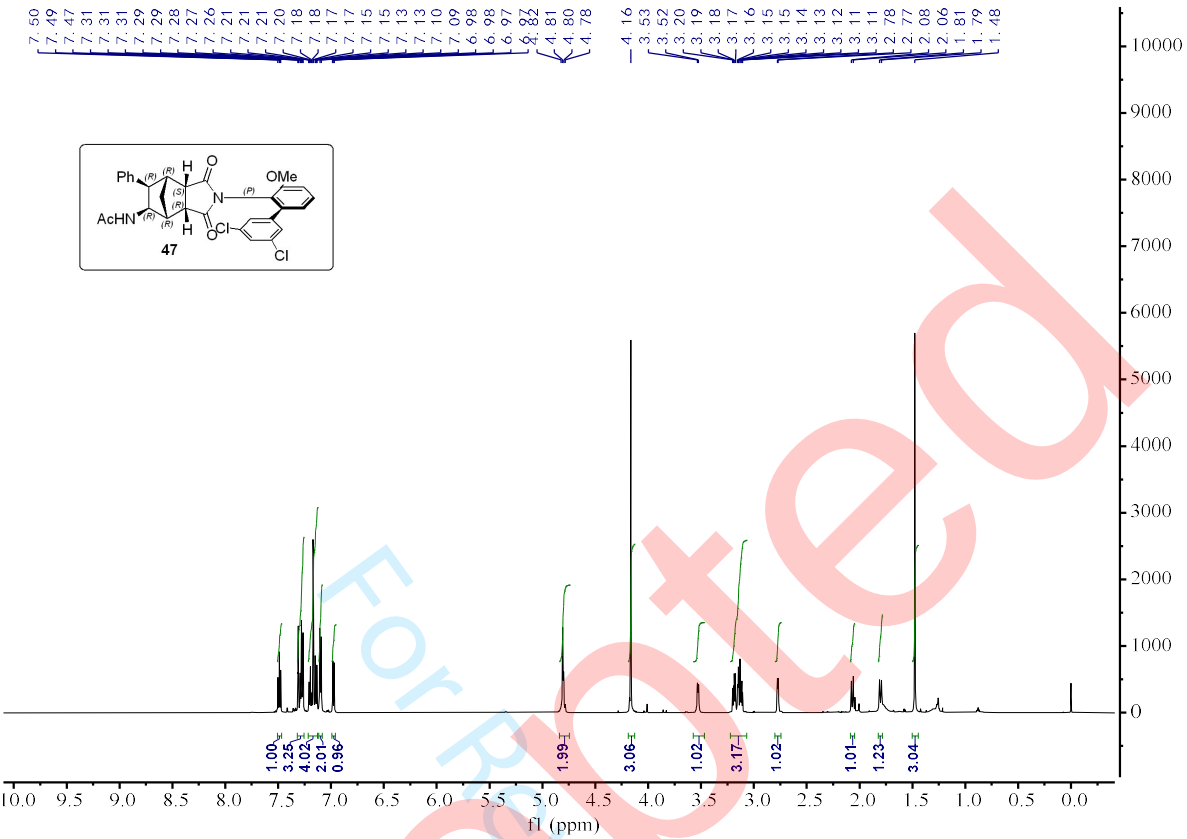
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 45



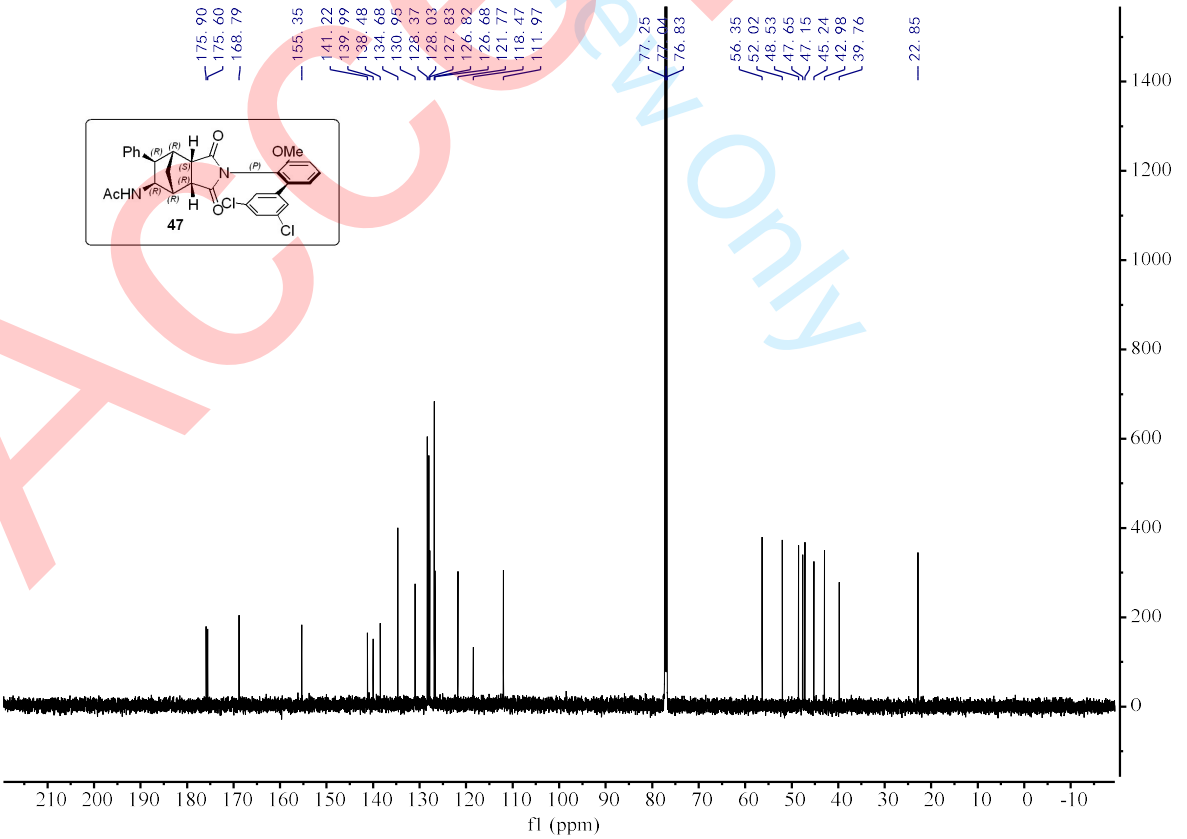
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 46



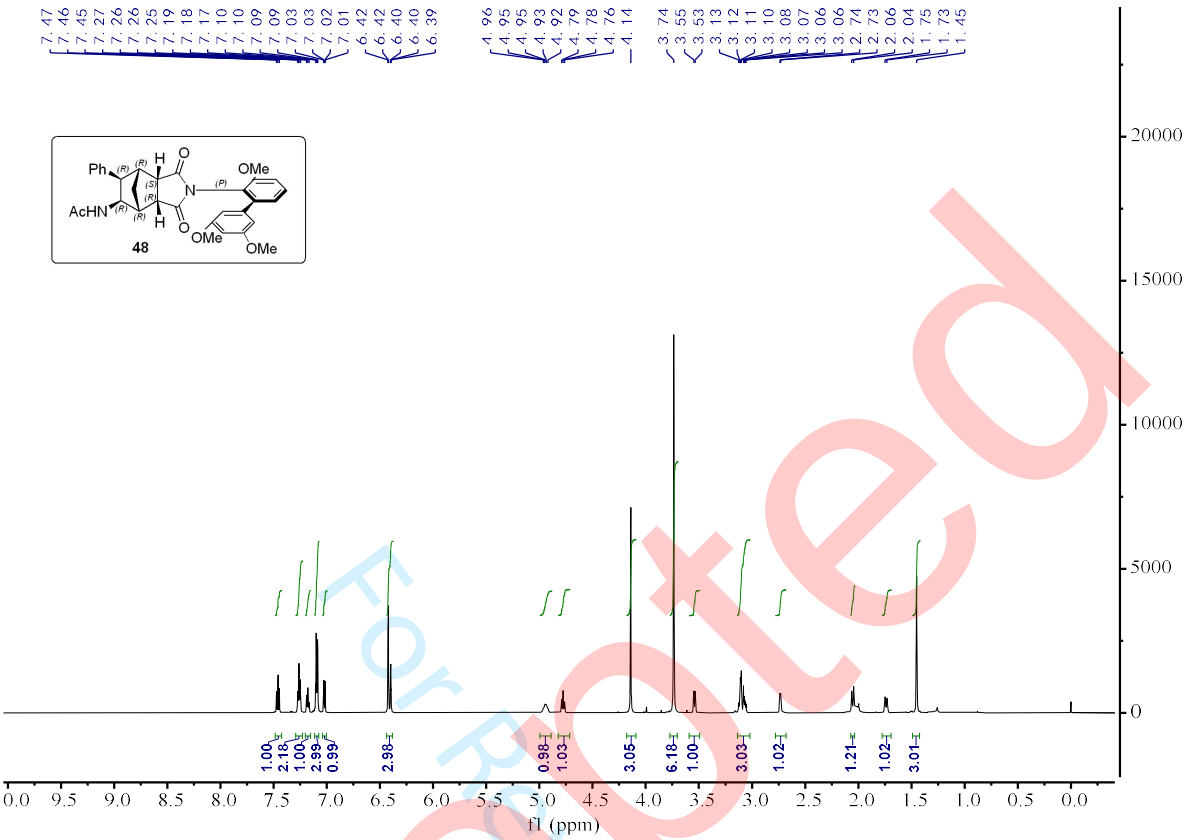
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 46



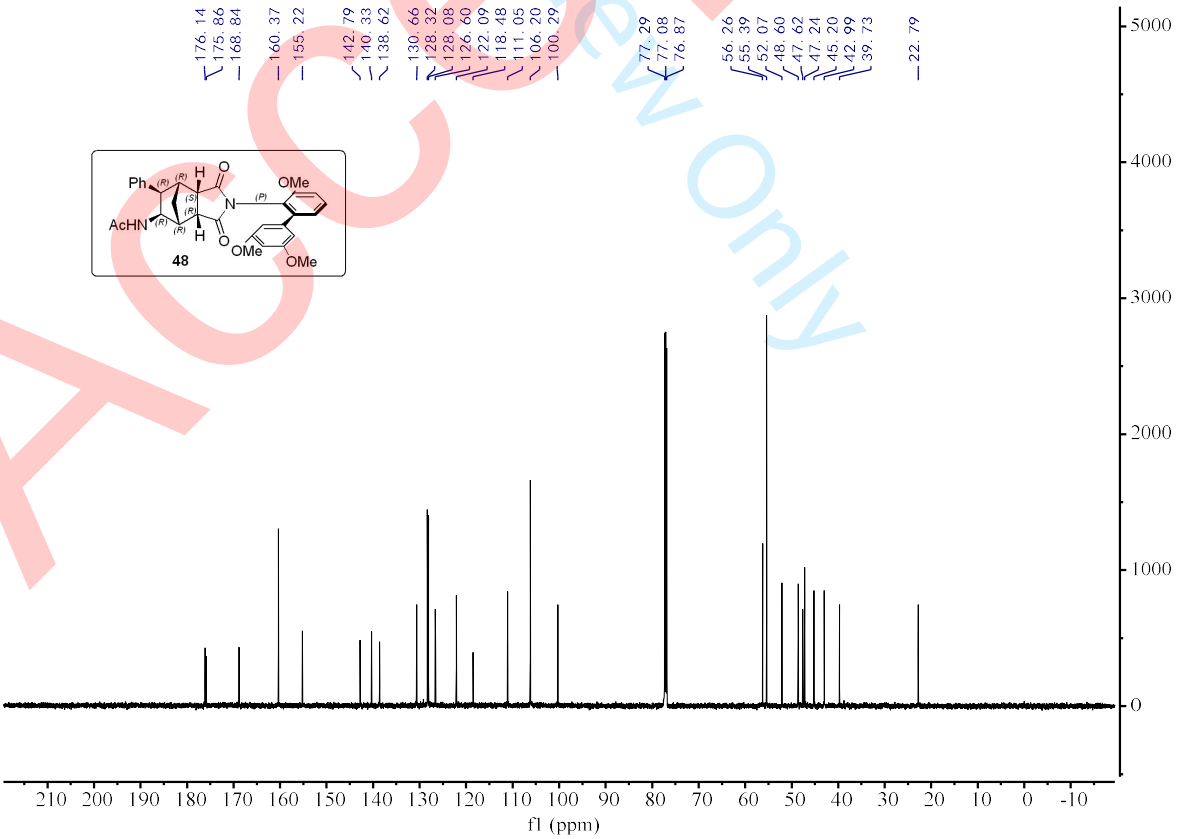
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 47



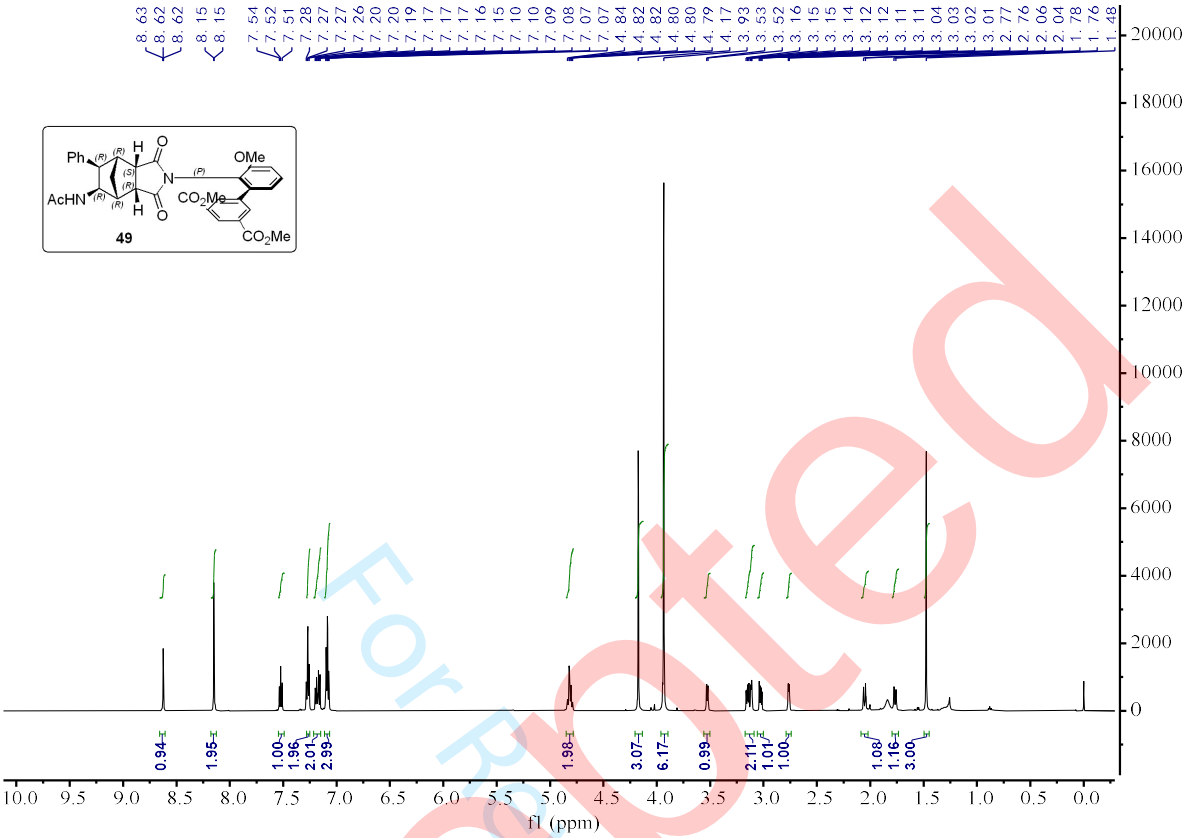
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 47



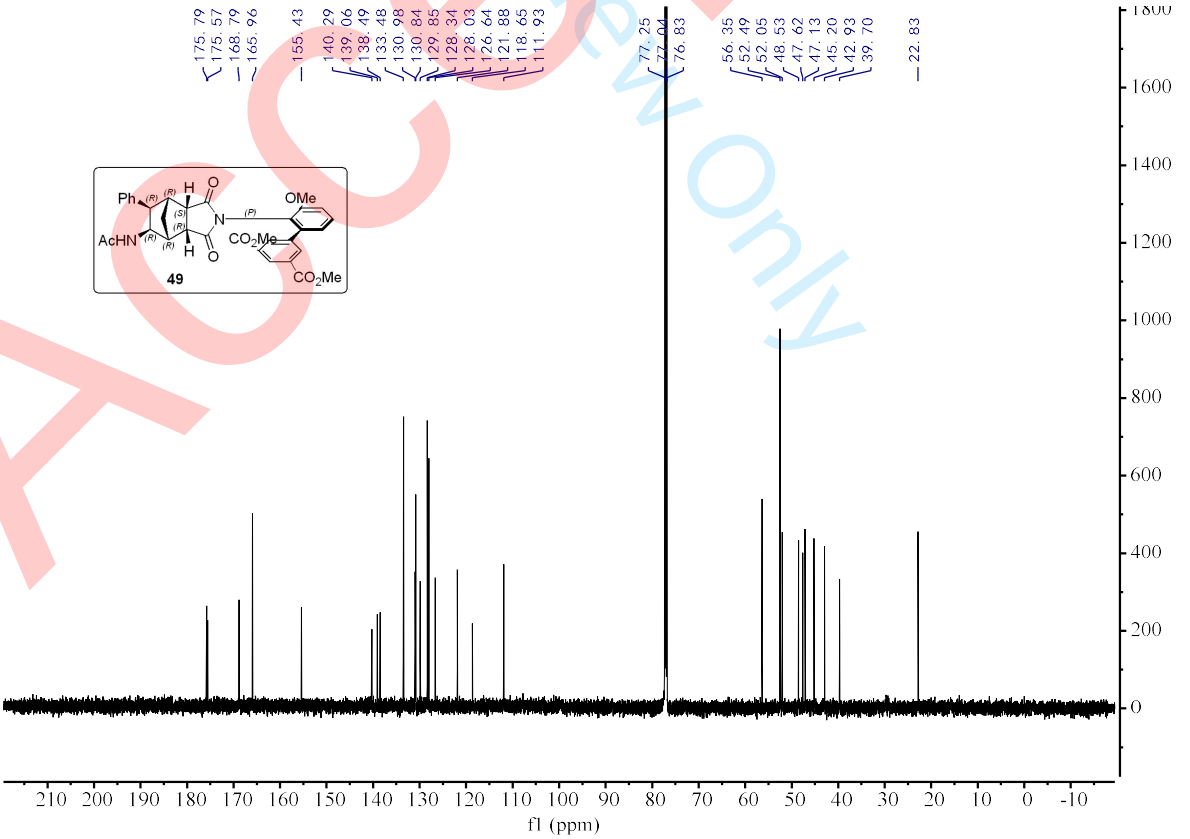
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 48



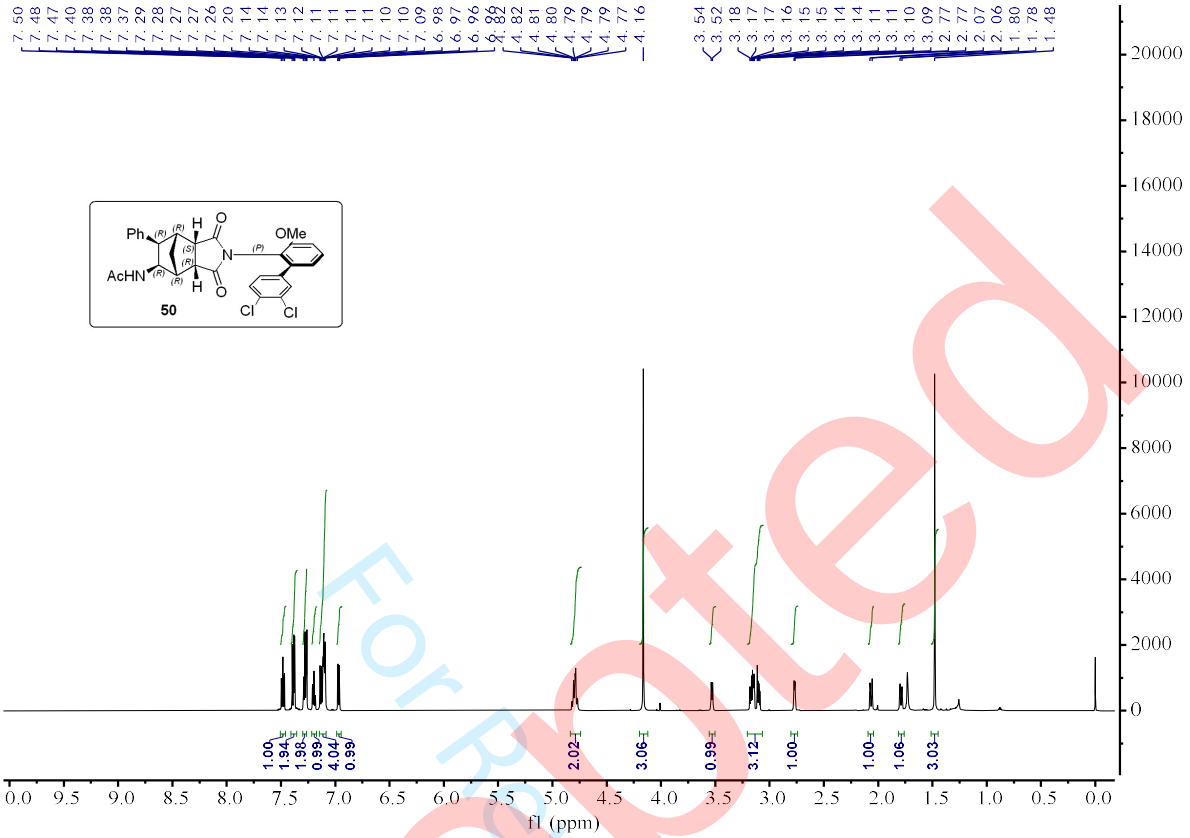
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 48



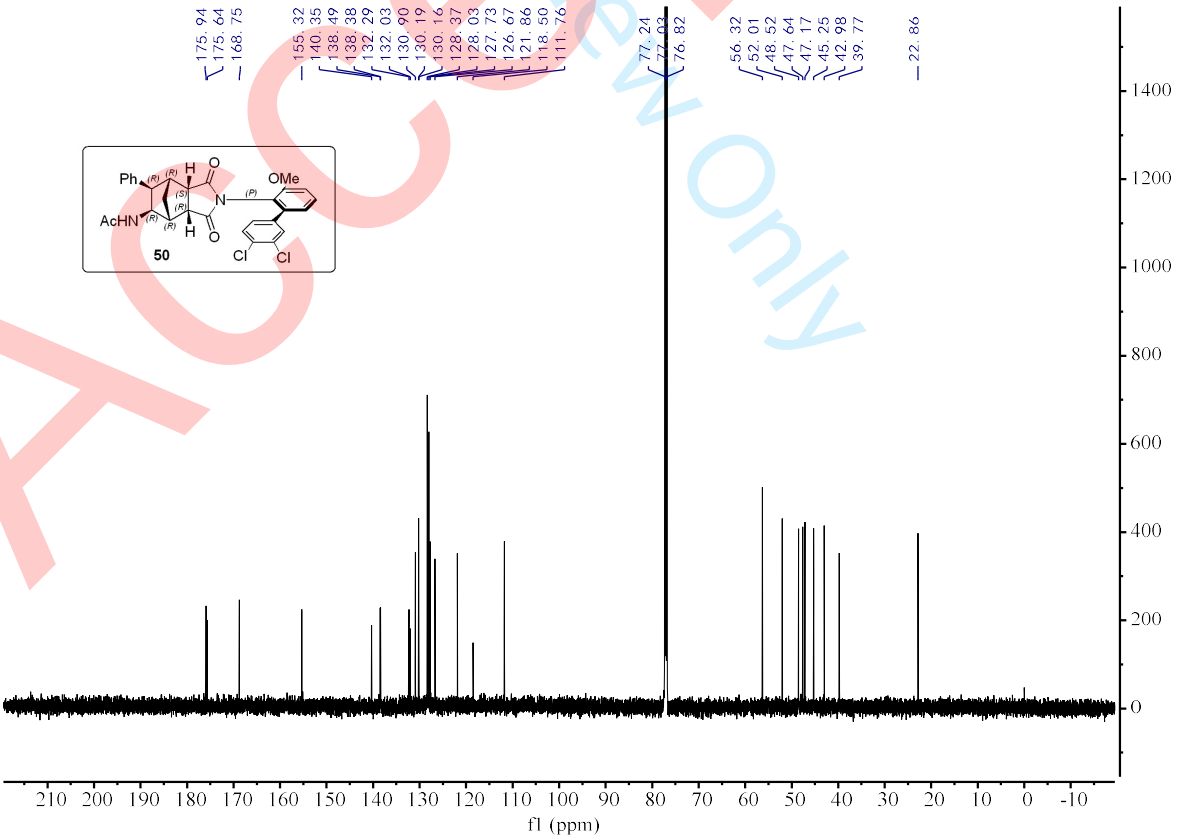
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 49



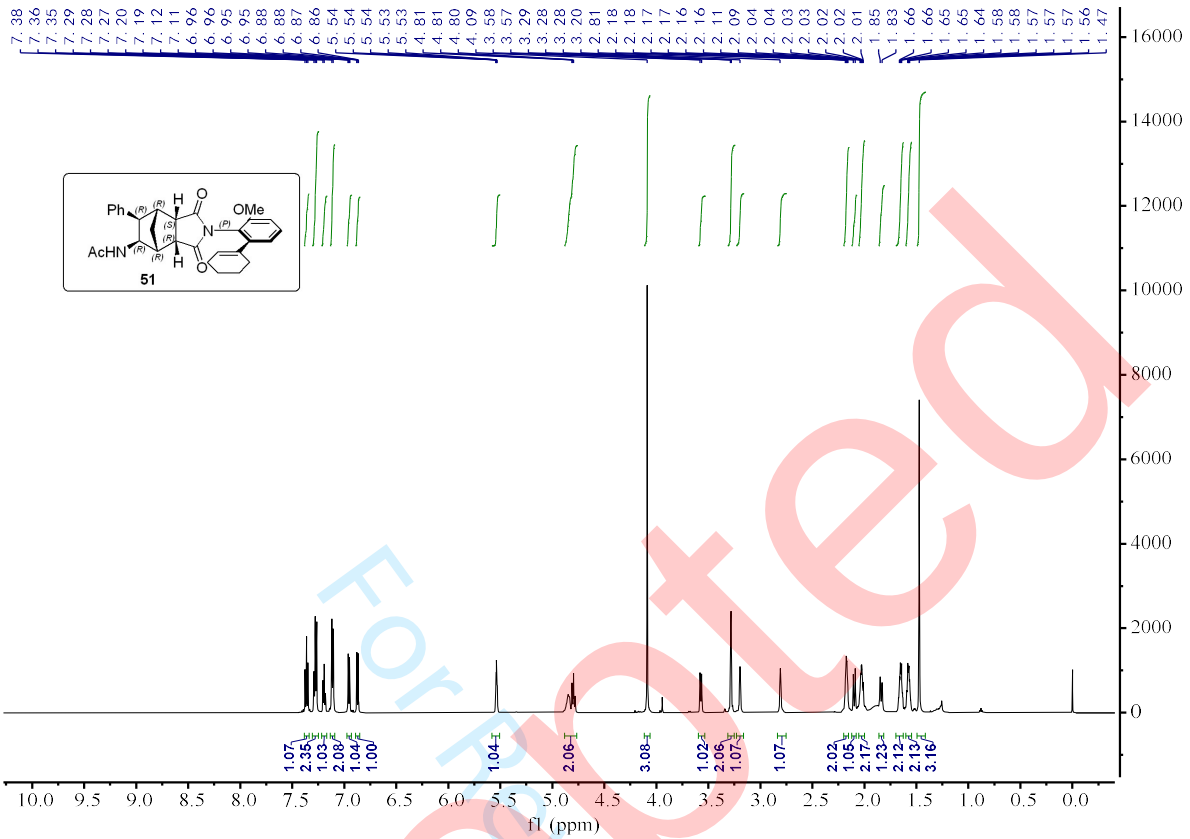
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 49



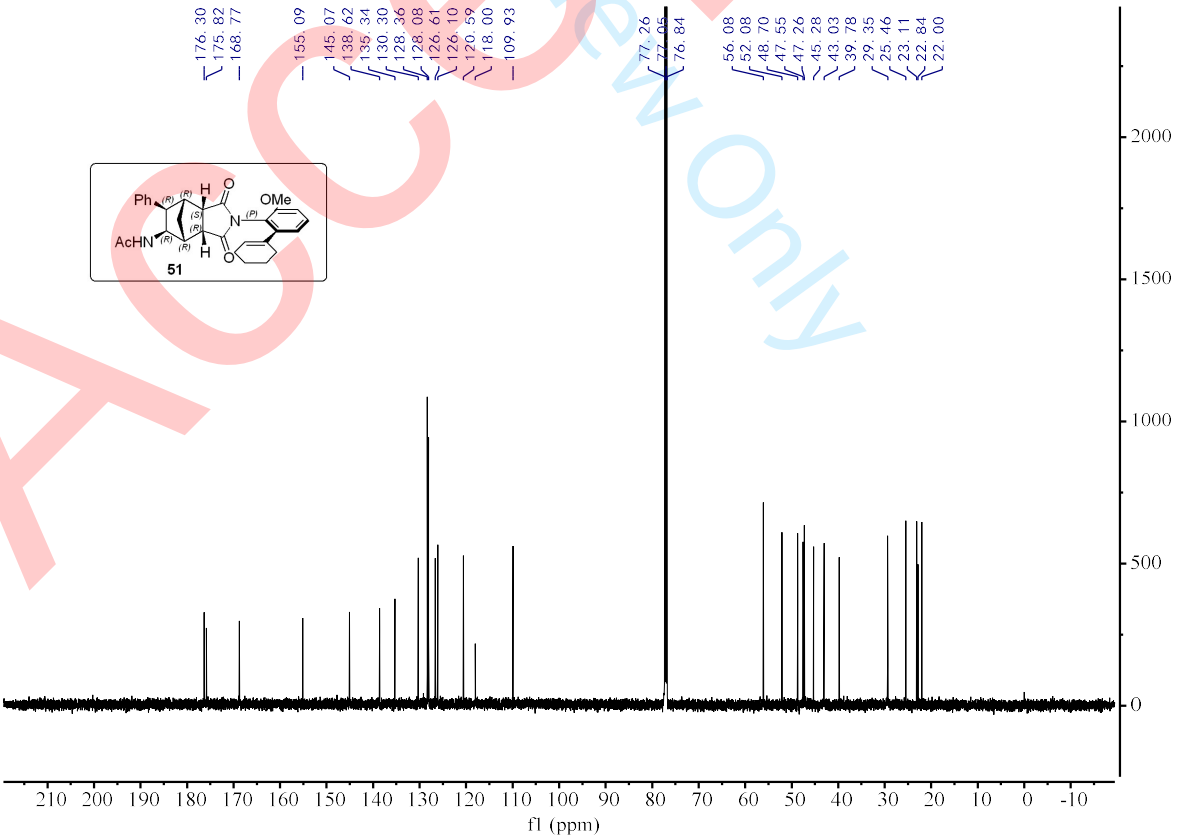
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 50



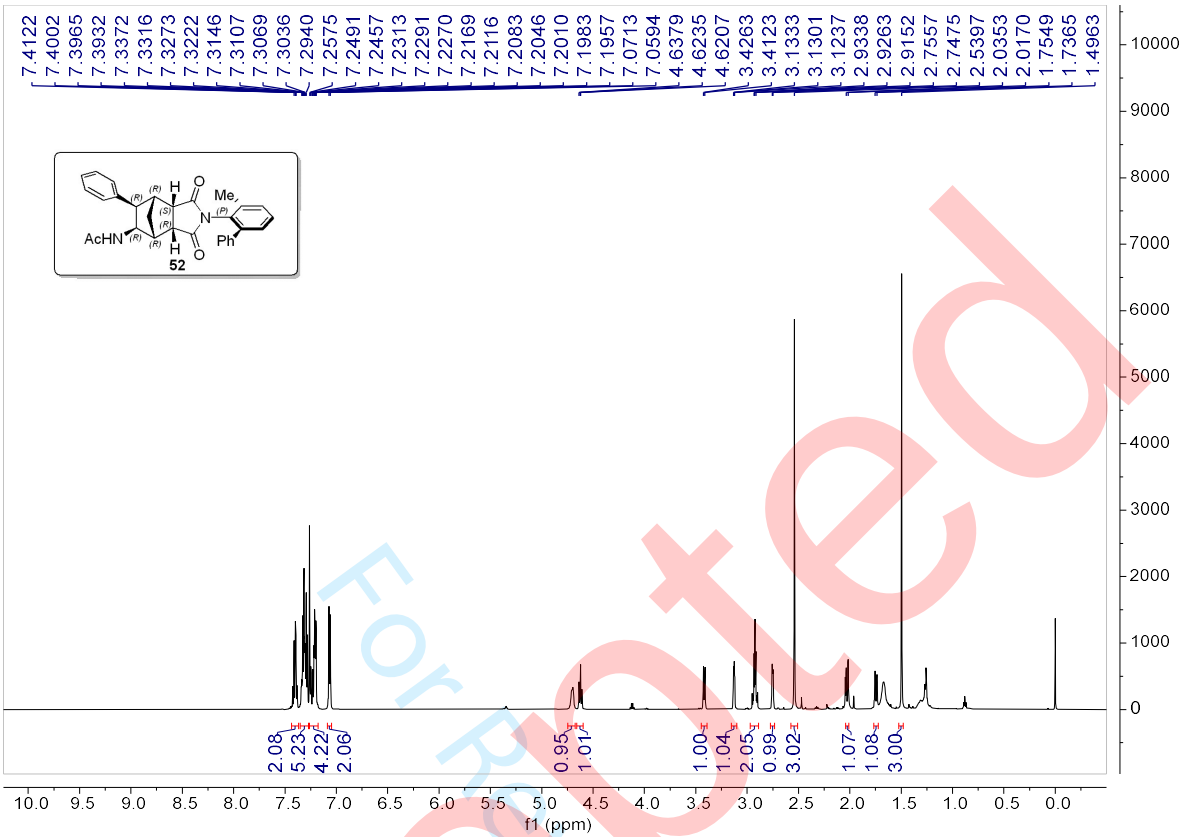
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 50



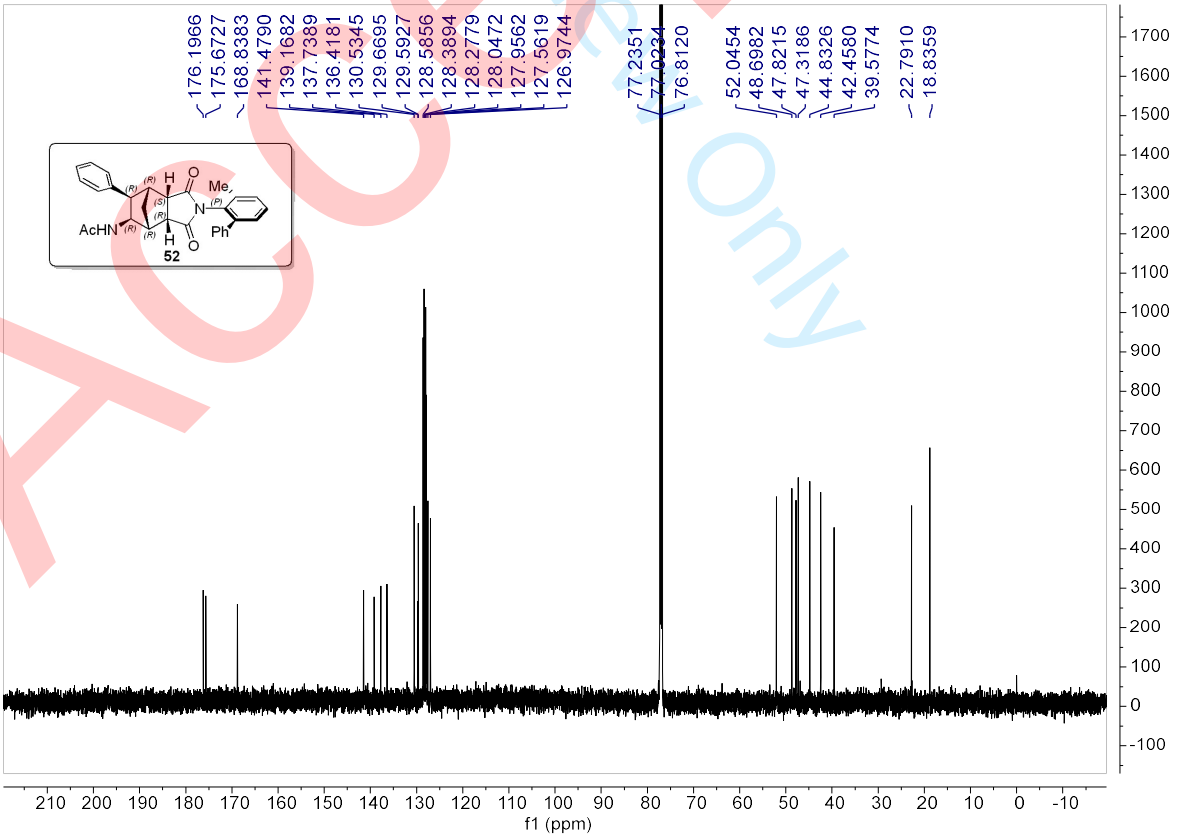
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 51



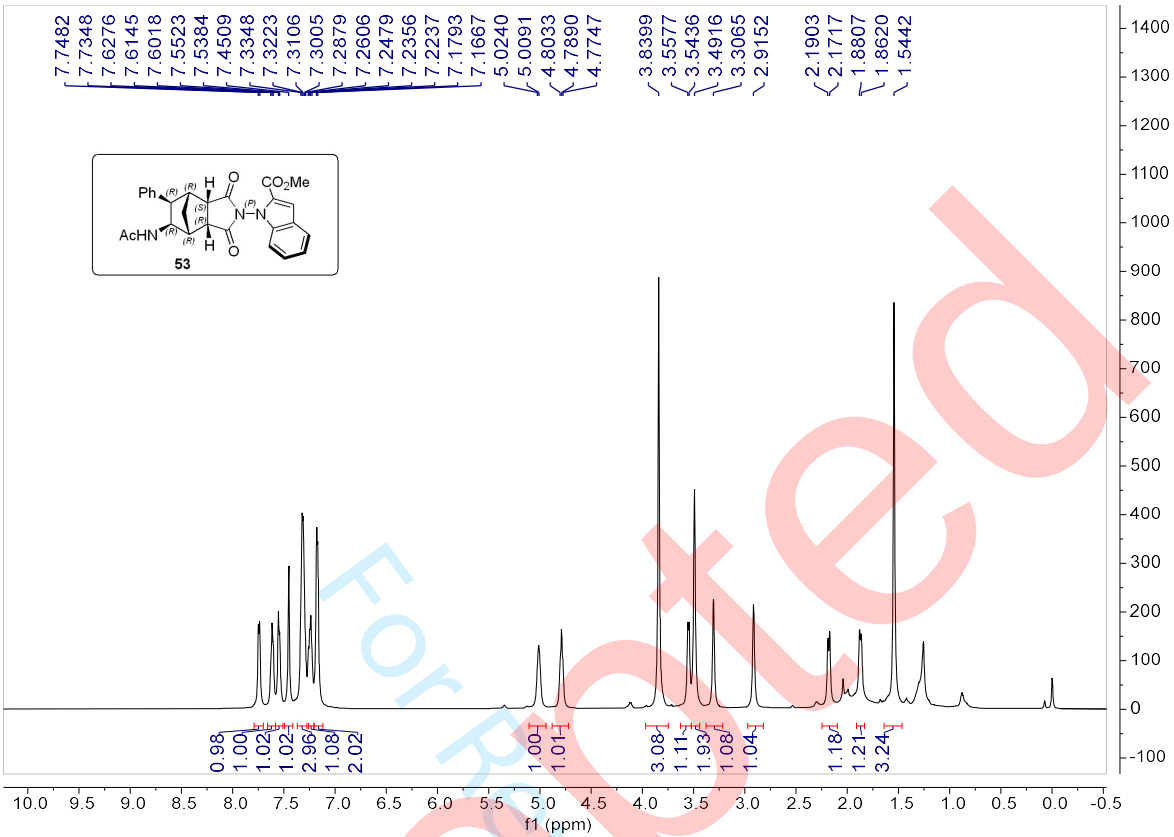
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 51



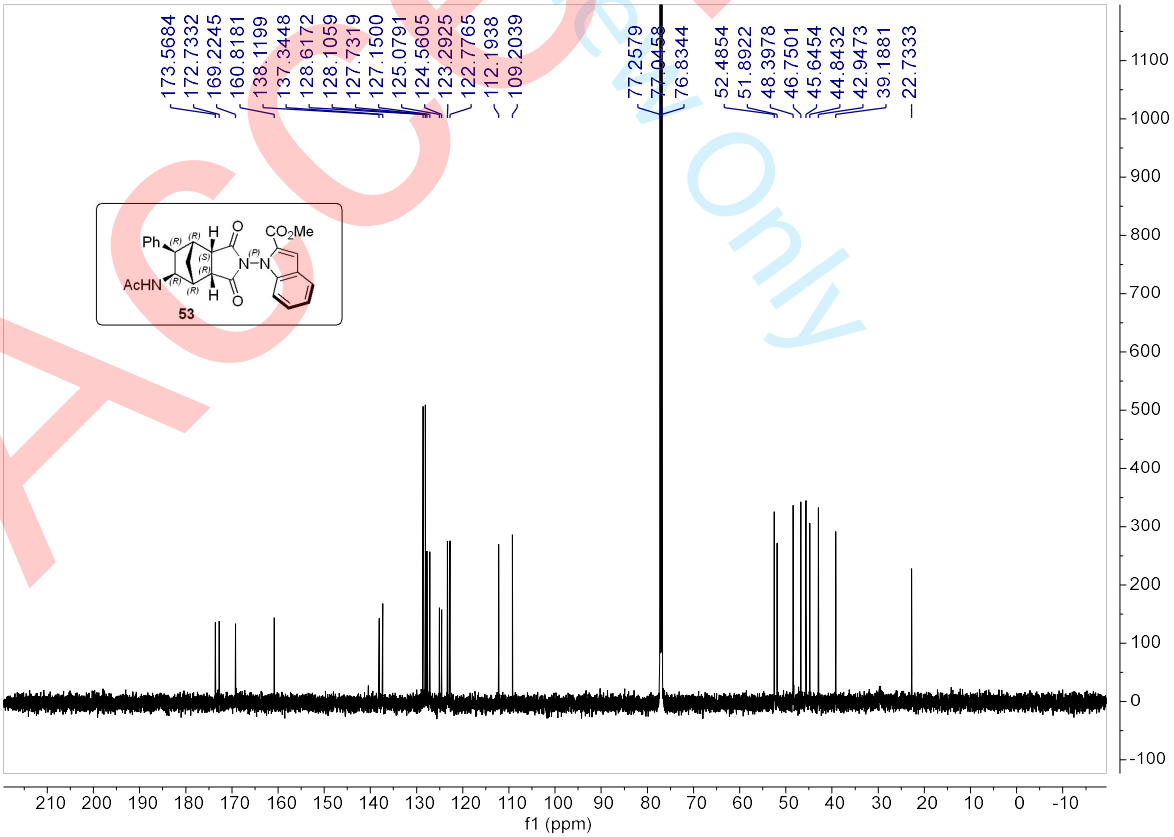
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 52



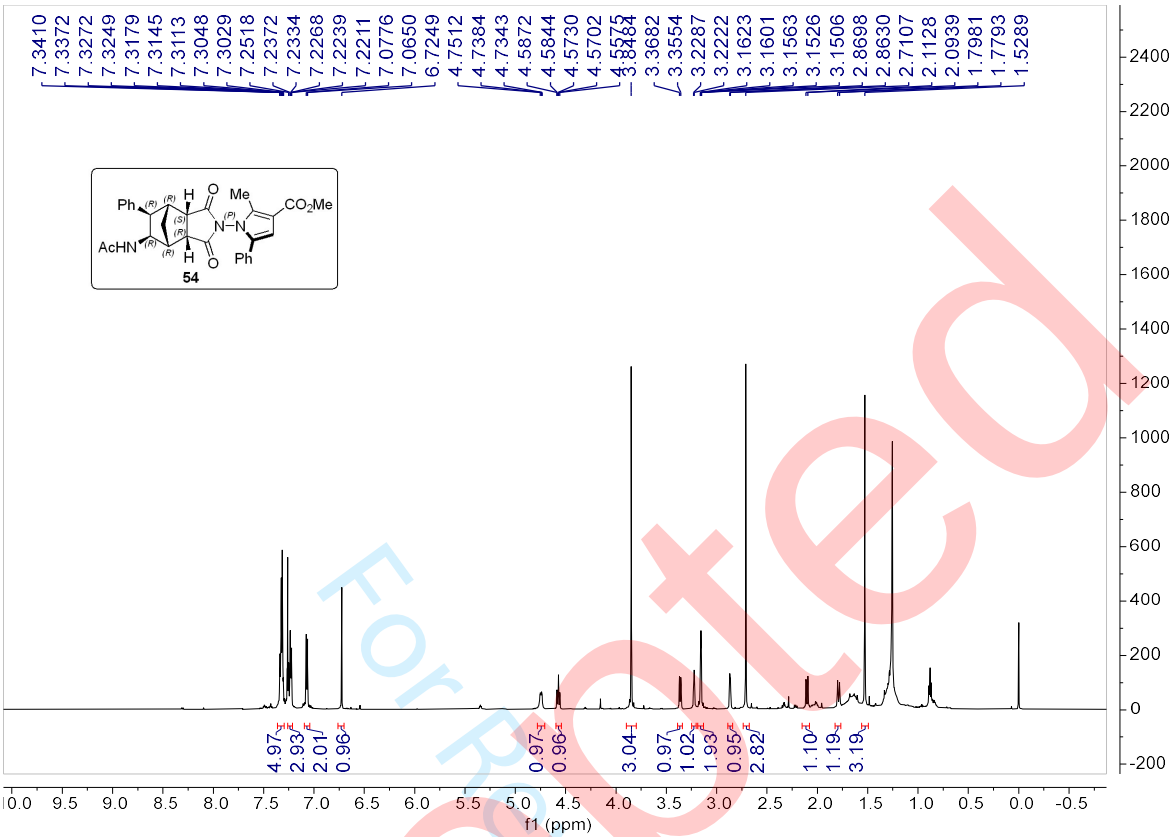
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 52



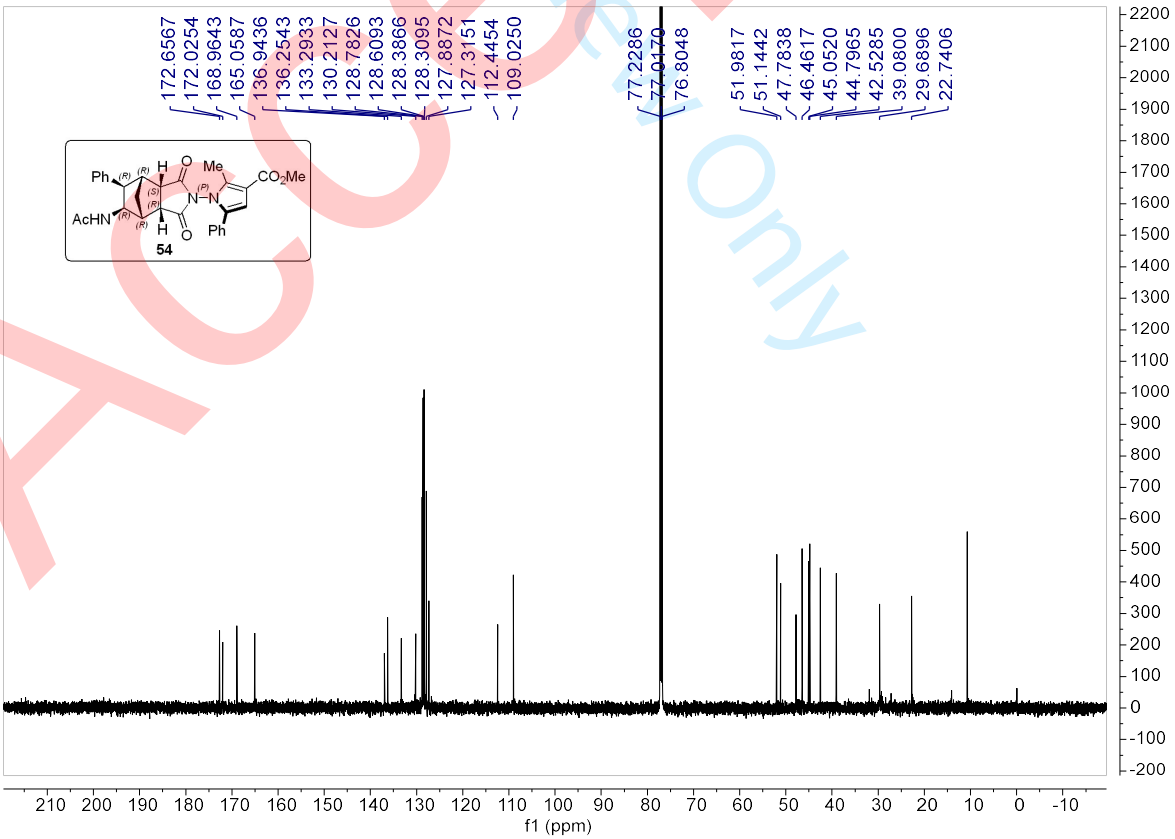
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 53



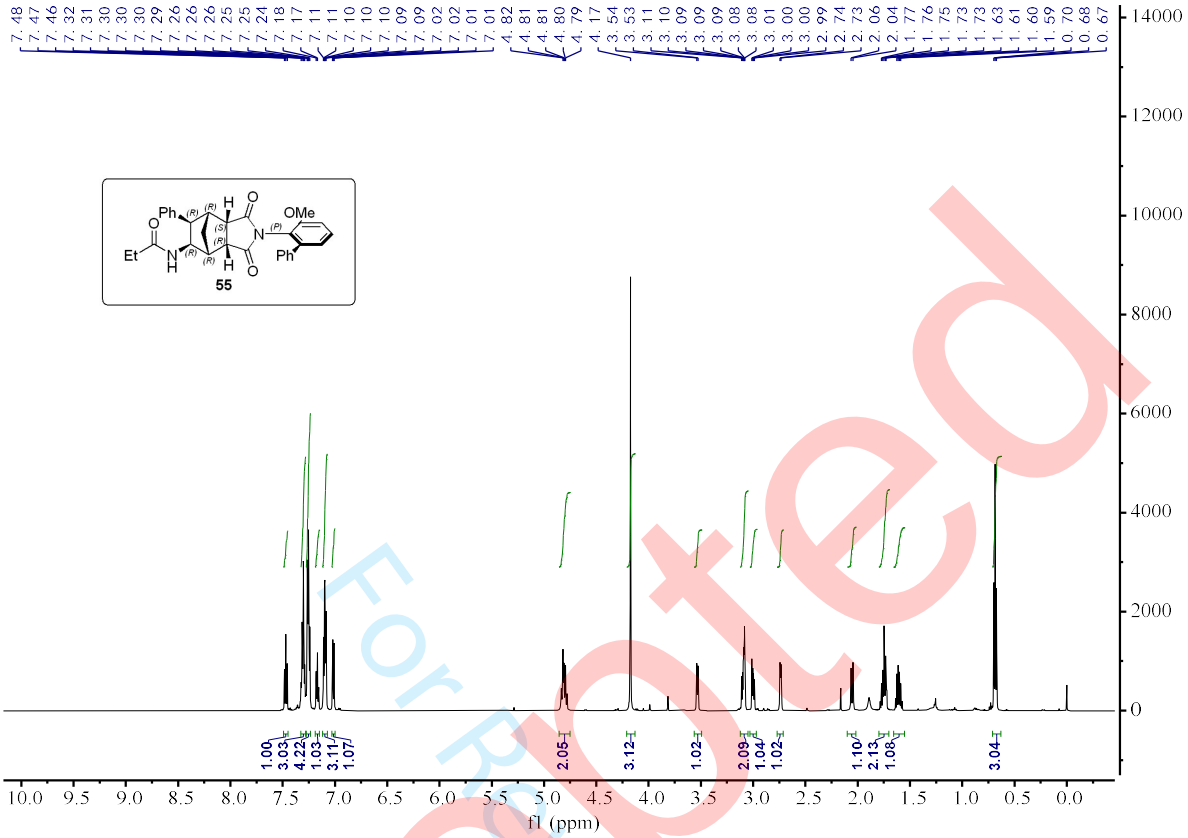
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 53



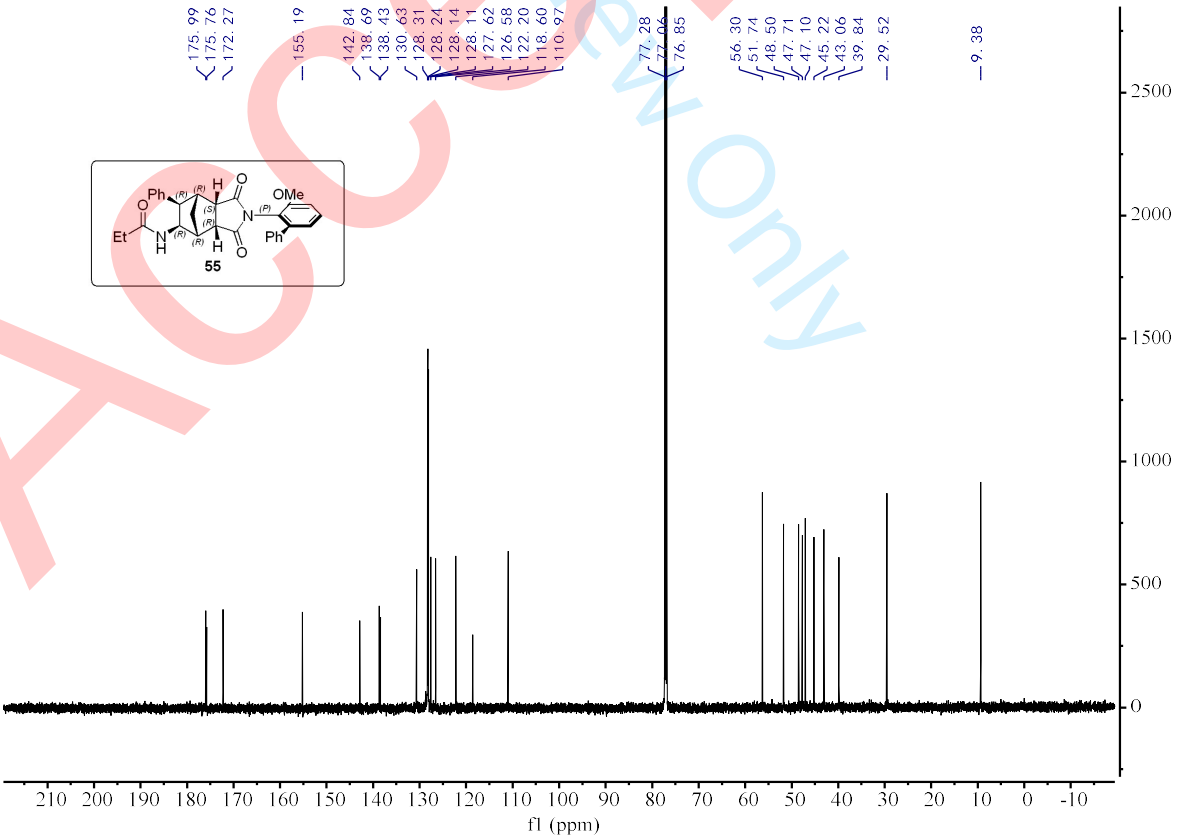
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 54



^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 54

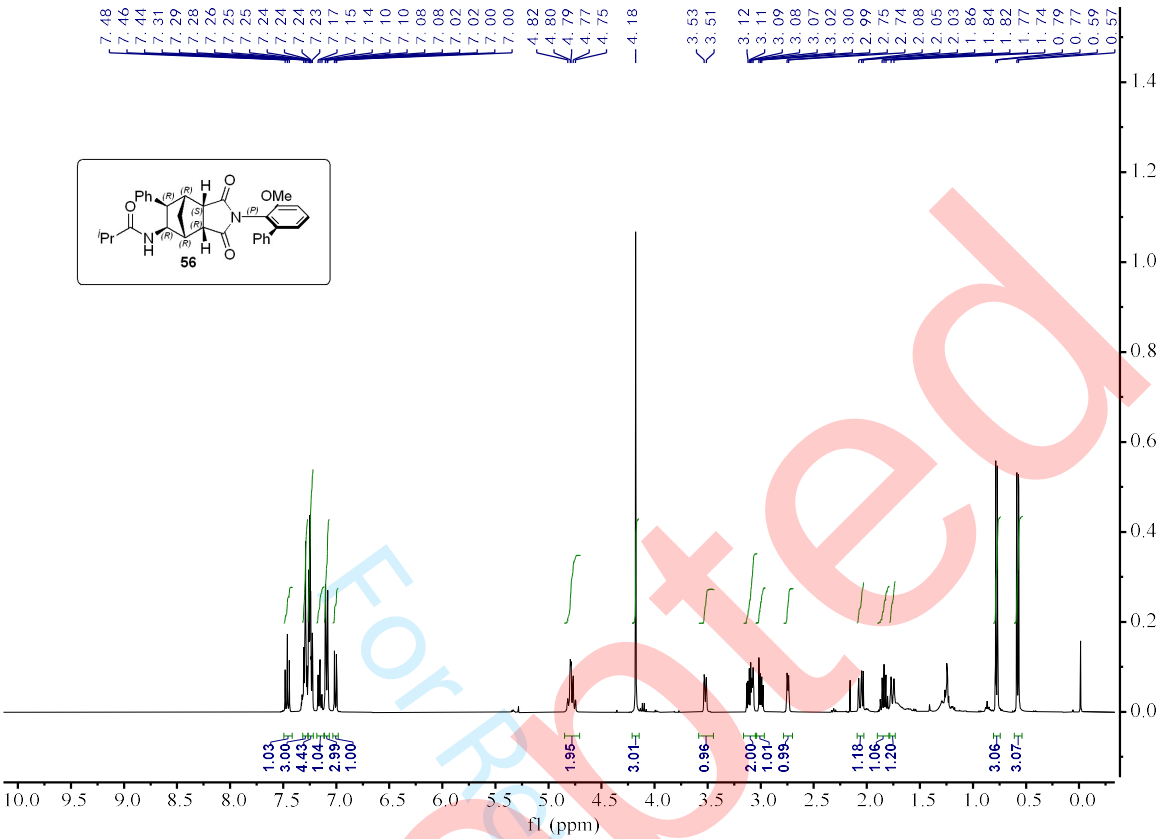


^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 55

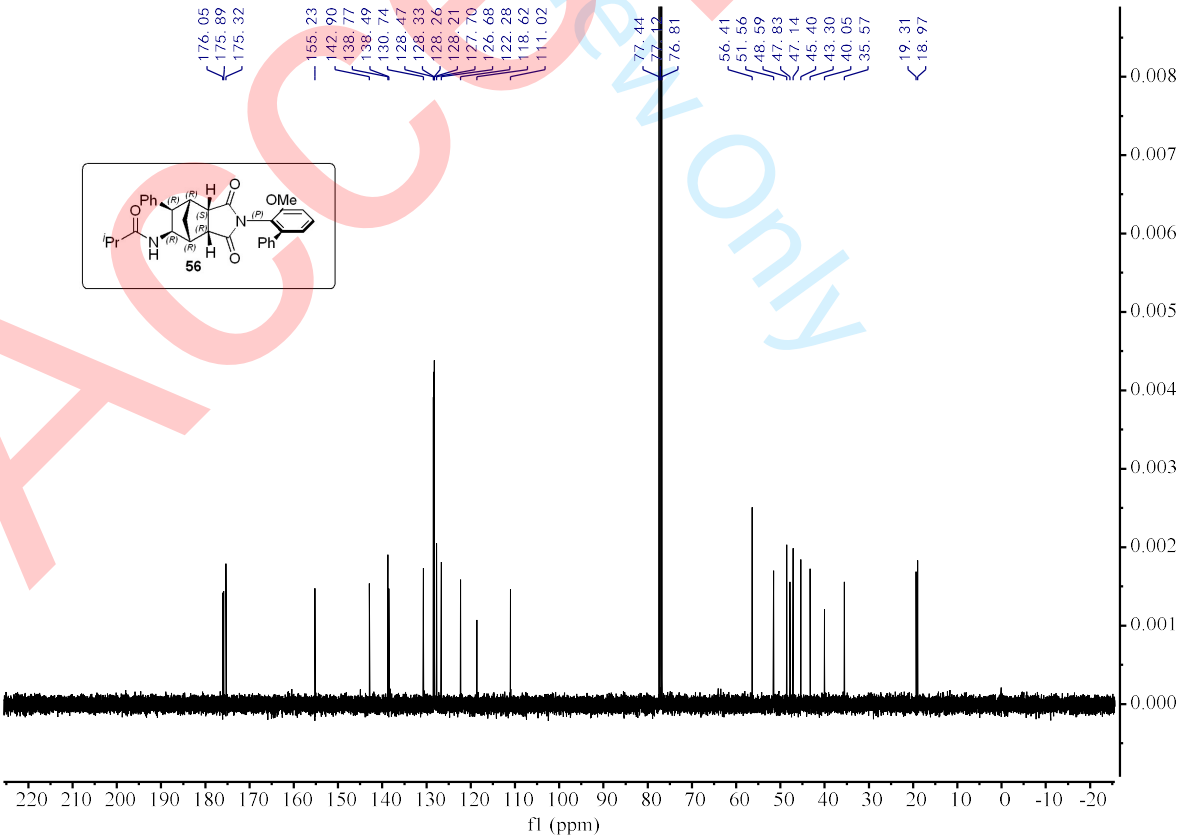


^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 55

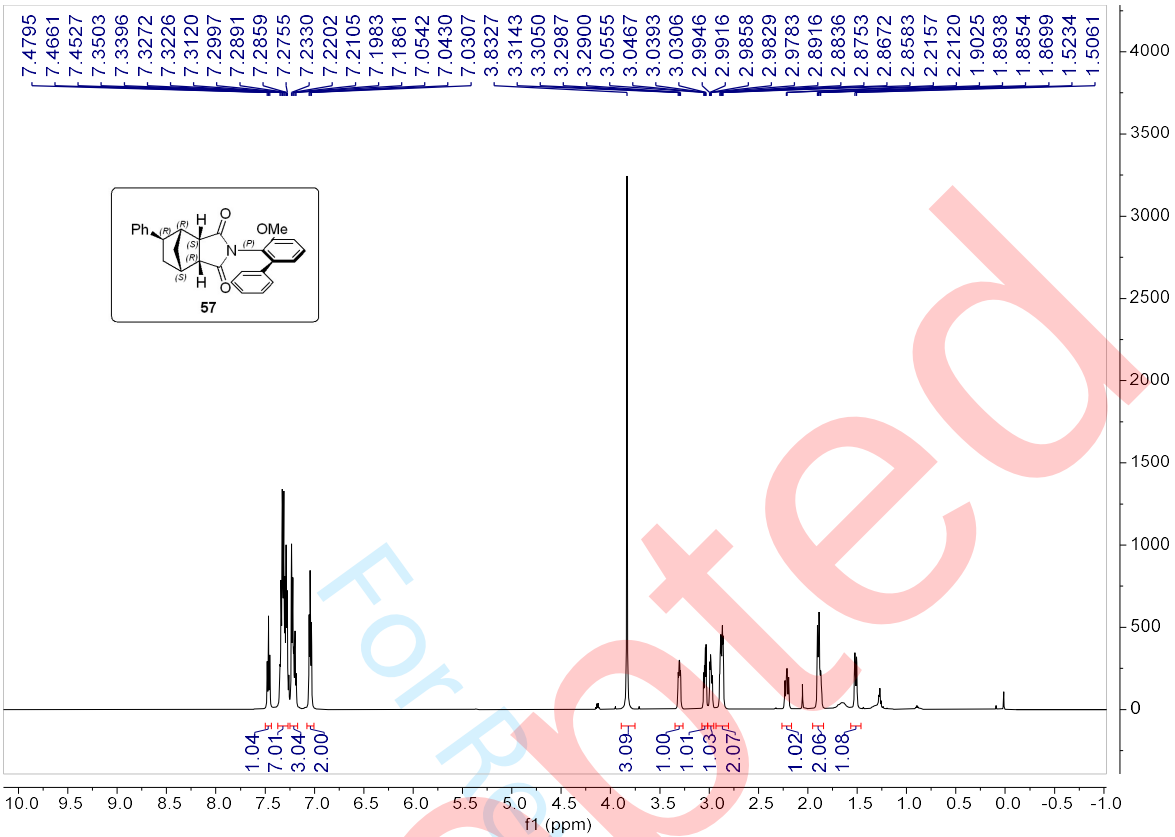
https://engine.scichina.com/doi/10.1007/s11426-023-1646-0
http://chem.scichina.com/english



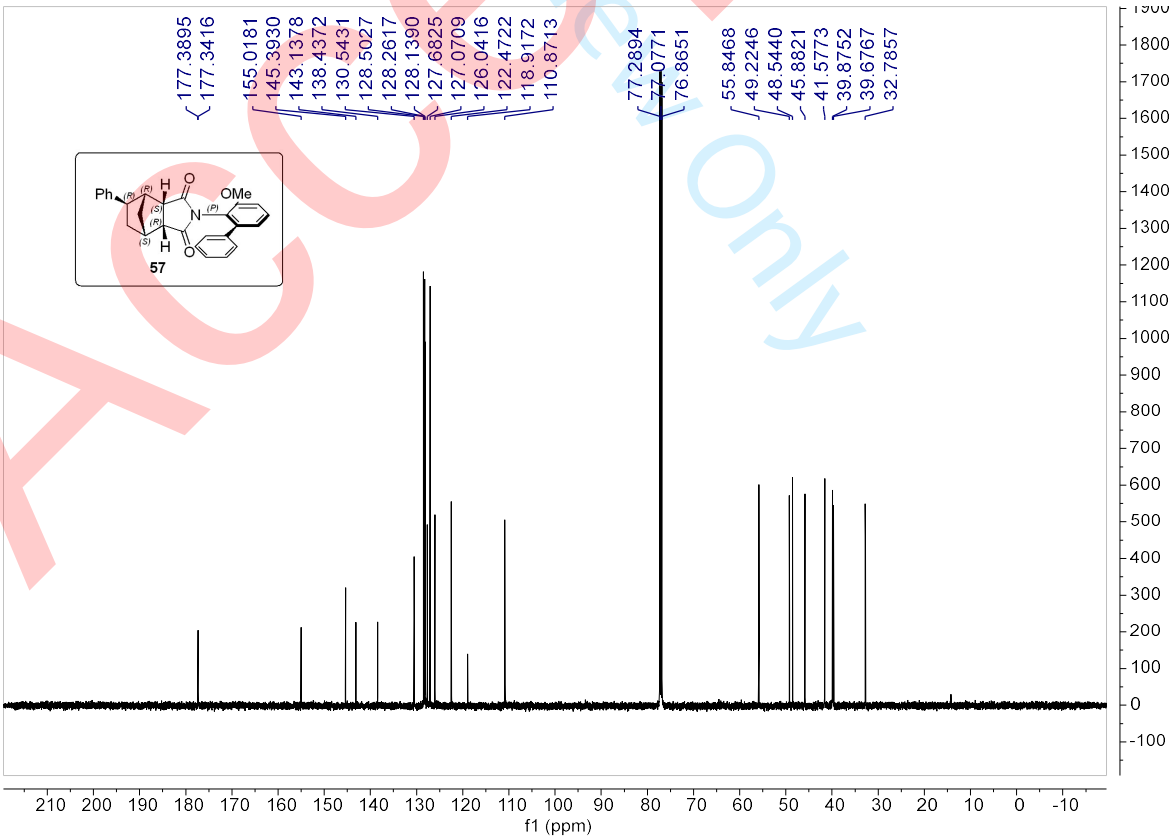
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 56



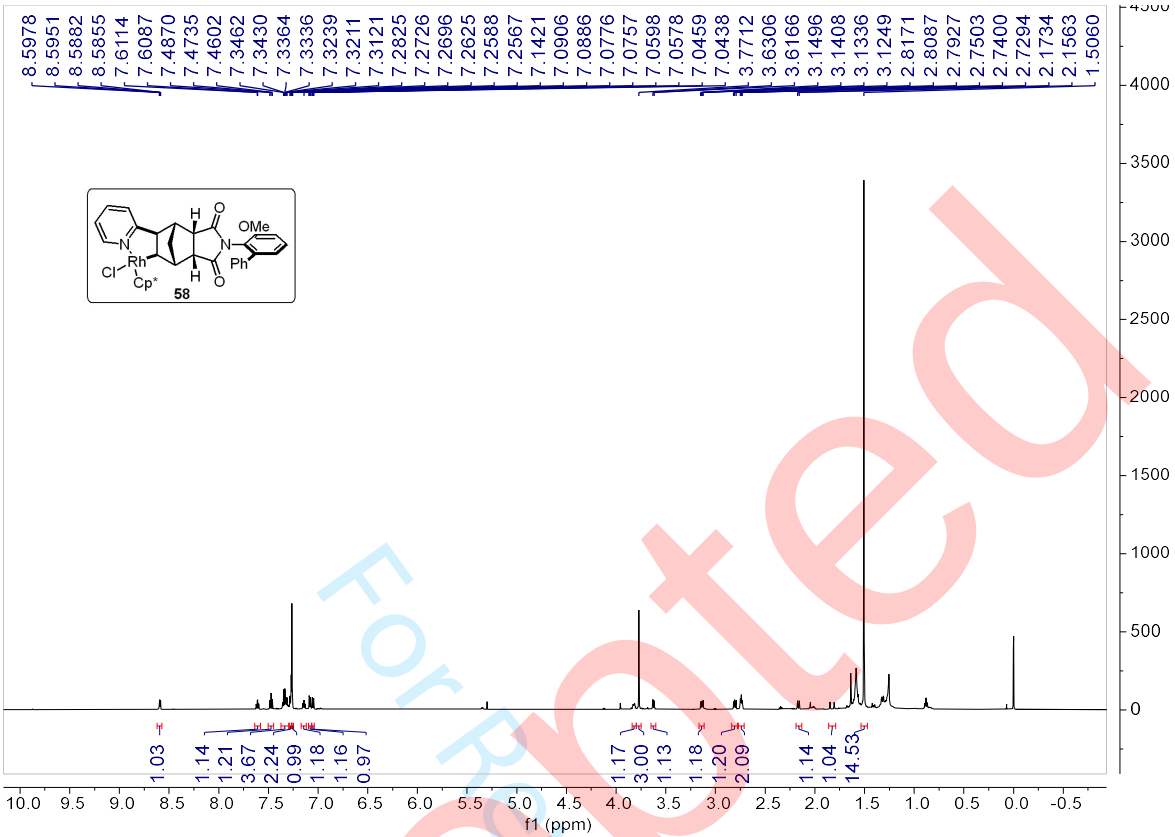
^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 56



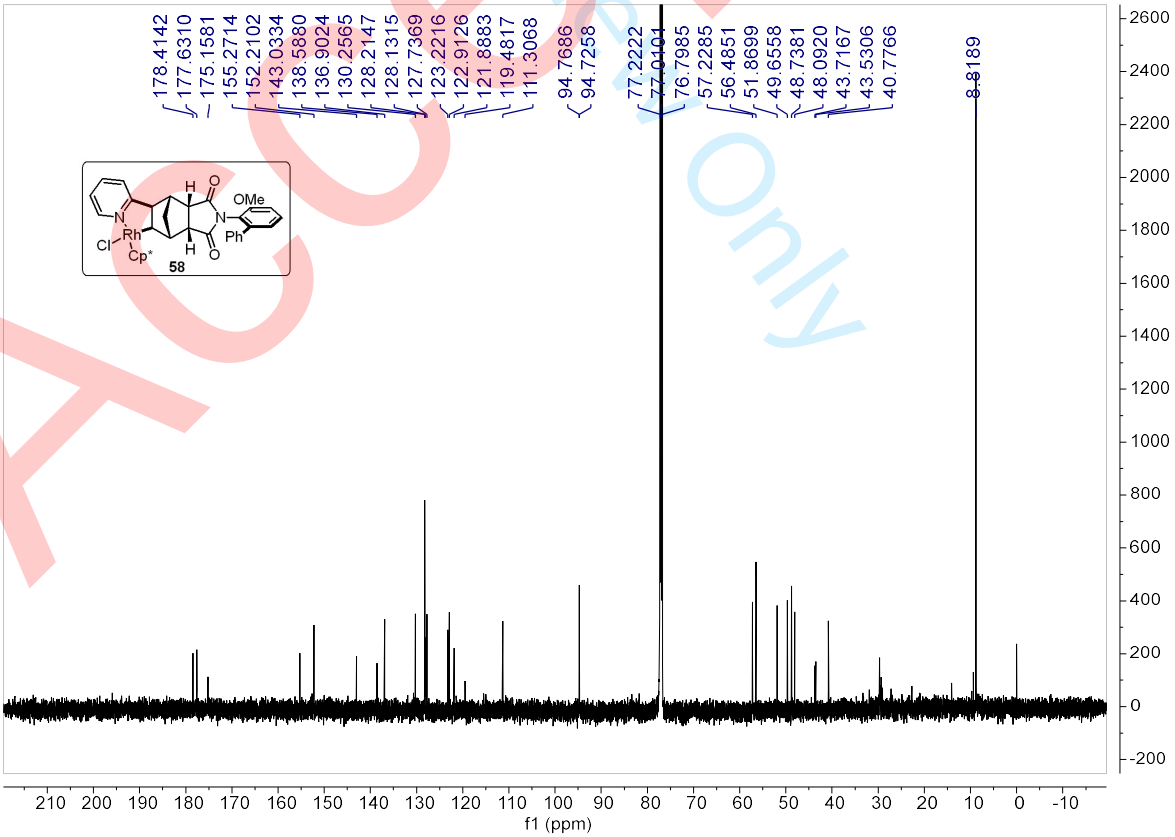
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 57



^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 57



^{1}H NMR (600 MHz, $CDCl_3$) spectrum of 58



^{13}C NMR (150 MHz, $CDCl_3$) spectrum of 58