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Dearomatization of electron poor six-membered N-heterocycles through [3 + 2] annulation with aminocyclopropanes†

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Many abundant and highly bioactive natural alkaloids contain an indolizidine skeleton. A simple, high yielding method to synthesize this scaffold from N-heterocycles was developed. A wide range of pyridines, quinolines and isoquinolines reacted with donor–acceptor (DA)-aminocyclopropanes *via* an ytterbium(III) catalyzed [3 + 2] annulation reaction to give tetrahydroindolizine derivatives. The products were obtained with high diastereoselectivities (dr > 20 : 1) as *anti*-isomers. Additionally, the formed aminals could be easily converted into secondary and tertiary amines through iminium formation followed by reduction or nucleophile addition. This transformation constitutes the first example of dearomatization of electron-poor six-membered heterocycles *via* [3 + 2] annulation with DA cyclopropanes.

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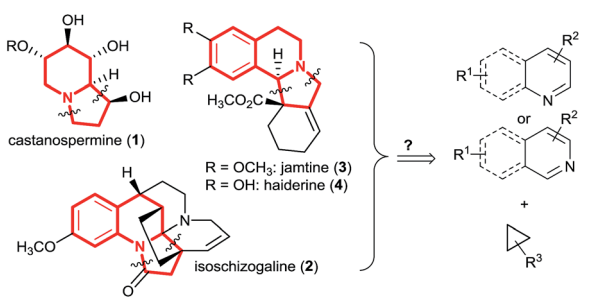
1. Introduction

The indolizidine skeleton is widely represented in bioactive alkaloids.[1] For example, castanospermine (**1**, Scheme 1) is a potent inhibitor of α-glucosidase I, an enzyme with a critical role in viral maturation, and was the lead structure for celgosivir which is currently under investigation for treatment of hepatitis C virus infection and dengue fever.[2] The indolizidine class of natural products also includes more complex polycyclic compounds incorporating further fused saturated or unsaturated rings.[3] For instance, isoschizogaline (**2**) contains a reduced quinoline core structure,[3a] whereas jamtine (**3**)[3b] or haiderine (**4**)[3c] can be seen as isoquinoline derived alkaloids. The construction of these polycyclic scaffolds by dearomatization of quinolines, isoquinolines or pyridines is highly attractive, due to the broad availability of the unsaturated heterocycles. Classic dearomatization strategies most often rely on the formation of a single bond, starting from activated pyridinium or (iso)quinolinium intermediates.[4] Dearomatization reactions through direct annulation *via* ring-extension of cyclopropanes would provide a more convergent synthesis (Scheme 1). Nevertheless, such processes are unknown.[5]

In this context, Lewis acid (LA) catalyzed [3 + 2] annulation reactions of donor–acceptor (DA) cyclopropanes with dipolarophiles have been intensively studied.[6] In particular, these reactions are highly successful with enol-ethers,[7] nitrosoarenes,[8] imines,[9] heteroatom substituted alkynes,[10] carbonyl compounds[11] and nitrones.[12] However, dearomative [3 + 2] annulation reactions were only intensively studied with indoles[13] and a single example was reported for benzothiazoles (Scheme 2).[14] Therefore, only [6,5,5] polycyclic ring systems can be currently accessed, although this approach would appear highly attractive for the synthesis of other polycyclic scaffolds as well. In fact, indole, with its high nucleophilicity and low aromatization energy (28 kcal mol^{-1} only for the pyrrole ring),[15] constitutes an ideal case for dearomatization reactions: the nucleophilic character leads to a fast reaction with Lewis acid activated DA cyclopropanes, and the lower aromatization energy makes isolation of the saturated products easier.



Scheme 1 Examples for indolizidine containing natural products and general retrosynthetic scheme.

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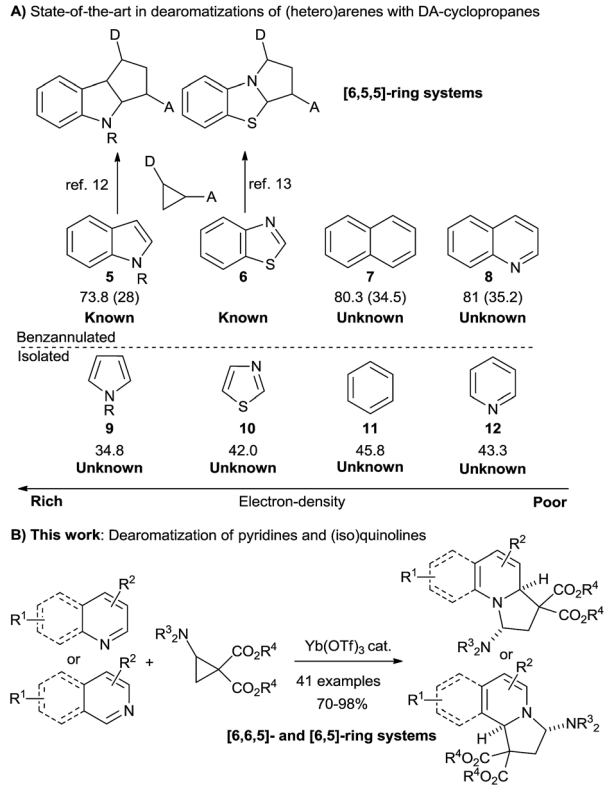
‡ Dr Chakrabarty has decided to stop his scientific career and cannot be contacted any more. He therefore did not see the final version of this manuscript. Based on his important contribution to the project, both J. P. and J. W. agree to include him as co-author and are convinced that he would agree to be included if he knew about this submission.



Scheme 2 Dearomatization *via* [3 + 2] annulations with DA-cyclopropanes.

Dearomatizing electron-poor quinolines with higher aromatization energy (35 kcal mol^{-1} for the pyridine ring) is much more challenging. In 2006, Pagenkopf and coworkers reported a method for the formation of indolizines *via* [3 + 2] annulation of pyridines or quinolines with DA cyclopropanes.[16a] In this work, dihydroindolizines were observed as intermediates, but they could be only isolated in very low yield and partially oxidized to indolizines. Therefore, the authors decided to completely aromatize the crude product with manganese(IV) oxide to obtain single, clean products. Later, Wang and coworkers used a similar approach with iodine as oxidant for indolizine synthesis.[16b]

Compared to bicyclic aromatic compounds, the dearomatization of monocyclic aromatics is even more challenging due to increased resonance stabilization. It is therefore not surprising that no dearomatizing [3 + 2] annulation was yet reported for these compounds.

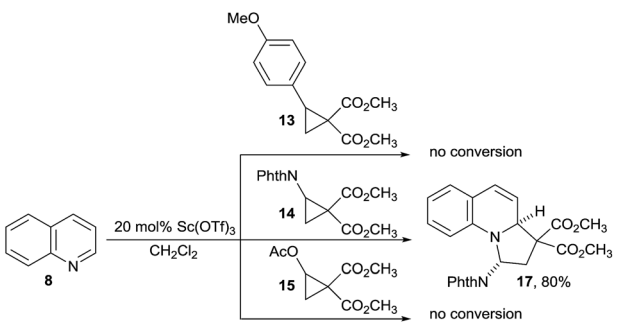
Herein we describe the dearomative [3 + 2] annulation of N-heterocycles with aminocyclopropanes to generate tetrahydroindolizines with high yield and stereoselectivity. Key for success were the exceptional properties of imido-substituted DA diester cyclopropanes, as other types of donor groups were not successful. A broad substrate scope including pyridines, quinolines, and isoquinolines is presented. The obtained aminals can be easily modified through iminium formation and subsequent reduction or nucleophile addition.

2. Results and discussion

2.1. Preliminary results and optimization

We started our investigations by examining the reactions of DA acceptor cyclopropanes with quinoline (**8**) using scandium triflate as a Lewis acid catalyst (Scheme 3). Under these conditions, no reactivity was observed using well-established aryl-substituted DA cyclopropane **13**.[6] We then wondered if DA cyclopropanes bearing a heteroatom donor group would be more reactive.[7c] Indeed, cyclopropane **14** bearing a phthalimide donor led to the formation of [3 + 2] annulation product **17** in 80% yield. Cyclopropane **14** is easily available in one step on multigram scale from *N*-vinylphthalimide and diazomalonates by Rh-catalyzed cyclopropanation.[17] In contrast, no conversion was observed with cyclopropane **15** bearing an oxygen donating group. This results further highlight the unique reactivity of imido-substituted DA cyclopropanes. Gratifyingly, compound **17** was stable enough to be isolated and fully characterized. The *cis*-relationship of the phthalimide and the hydrogen at ring junction was confirmed by X-ray analysis (Fig. 1).[18]

We then turned to the optimization of the [3 + 2] annulation. Product **17** was formed with >20 : 1 *anti* diastereoselectivity and 80% yield using $Sc(OTf)_3$ as catalyst (Table 1, entry 1). Nevertheless, this result could only be obtained with 1.5 equiv. of cyclopropane **14** and relatively low molarity (0.05 M) to prevent decomposition. Furthermore, the amount of $Sc(OTf)_3$ could not be reduced. Therefore, other Lewis acids were examined. No reaction was observed with $In(OTf)_3$ or $Cu(OTf)_2$ as catalysts (Table 1, entries 2 and 3) whereas the use of $Hf(OTf)_4$ resulted in full decomposition of the DA-cyclopropane **14** (Table 1, entry 4). Better results were obtained using $Yb(OTf)_3$ as catalyst. A first experiment gave 90% of the desired product **17** while the high diastereoselectivity was maintained (Table 1, entry 5). Furthermore, the mild conditions with $Yb(OTf)_3$ allowed us to conduct the reaction more concentrated (0.5 M), with only 1.05 equivalents **14** and at lower catalyst loading (5 mol%) without observing any decrease in yield (Table 1, entry 6).[19] The reaction proved to be easily scalable, as the yield did not change on 2 mmol scale. Eventual Brønsted acid catalysis of the reaction could be excluded by a control experiment with triflic acid (Table 1, entry 7). No reaction between **8** and *para*-methoxy phenyl or acetate substituted DA cyclopropanes (**13** and **15**) was again observed in presence of catalytic amounts of ytterbium(III) triflate (Table 1, entries 8 and 9).



Scheme 3 Preliminary results on the dearomatization of quinoline (**8**).

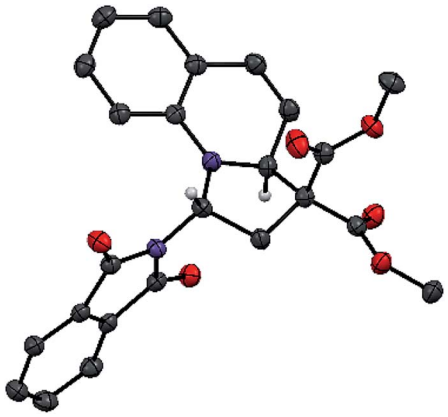


Fig. 1 Structure of compound **17** as determined by X-ray analysis. Some hydrogen atoms are omitted for clarity.

2.2. Scope of the [3 + 2] annulation

Next, the scope of the reaction was examined by submitting various quinolines to the optimized reaction conditions (Fig. 2). Substitution of the pyridine ring was examined first (Fig. 2A). Alkyl, alkynyl and halogen substituents were all well tolerated either in C3 or C4 position of the quinoline ring (products **20–25**). To our delight, *O*-acetylated cinchonidine with its highly basic amine worked well and furnished compound **22** in 76% yield and 1 : 1 dr. A broad range of versatile substituents such as aryl, halogens, trifluoromethyl, ester, nitrile and nitro were also tolerated on the arene ring (Fig. 2B, products **26–34**). Generally, no differences in term of reactivity were observed upon substitution of the benzene or the pyridine ring of the employed quinolines. Only 2- and 8-substituted quinolines did not react under the developed conditions (with the exception of the fluoro substituent, product **31**), probably due to increased steric hindrance. As a limitation, dearomatization of highly electron-rich 6-methoxy quinoline was not successful and compound **33** could not be obtained. Overall, the tolerance of functional groups attached to the quinoline is extremely broad, including in particular:

- Potentially sensitive π-systems, such as alkenes and alkynes (products **22**, **24** and **25**).

- Strongly electron-withdrawing groups, such as esters, cyano and nitro, which are useful precursors of amides or amines (products **29**, **30** and **34**).

- Halogens, which are easily further modified using cross-coupling chemistry (products **20** and **26**) or useful to diminish the electron-density of the heterocycle for pharmaceutical or agrochemical purposes (especially fluorine, products **27** and **31**)

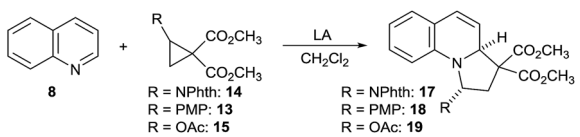
- Highly basic tertiary amines (product **22**).

The influence of different nitrogen substituents on the DA-cyclopropane was then investigated (Fig. 2C). Less electron donating phthalimide groups with chloro or nitro substituents gave the desired products **35** and **36** in good yields, but their stability was significantly lower compared to their unsubstituted relative **17**. Furthermore, maleimide, succinimide or a 2,3-naphthimide substituted DA cyclopropanes could also be used under the developed conditions (products **37–39**). Finally, different ester groups on the cyclopropane had low impact on the reaction outcome (Fig. 2D): replacing the methyl esters of **14** with benzyl or trifluoroethyl esters gave the desired products **40** and **41** in excellent yields. With a mixed diester, product **42** was isolated in 72% yield, and 3.5 : 1 dr at the additional stereogenic center.

At this point we wondered if the developed protocol for the dearomatization of quinoline could also be applied to other N-heterocycles. To our delight isoquinoline reacted equally well and furnished **43** with 83% yield and high diastereoselectivity (>20 : 1, Fig. 3A). Cyano and ester substituted isoquinolines reacted also well under the developed conditions (products **44** and **45**). The scope of the reaction could be extended to benzothiazole and benzoxazole (Fig. 3B, products **46** and **47**).

Further expansion of the scope to pyridines proved to be more difficult. Unsubstituted pyridines or pyridines with electron donating substituents did not react to form the desired products under the developed conditions. It is known, that nucleophilic ring opening of acceptor substituted cyclopropanes with pyridine furnishes betaine products.[20] Ring closure was expected to be more favored with electron deficient pyridines, as the positive charge of the betaine intermediate is then less stabilized. Indeed, the desired dearomative [3 + 2] annulation products of electron-deficient pyridines and **6a** were isolated with good yield and high diastereoselectivity (>20 : 1) when the catalyst loading was raised to 10 mol% and the concentration to 1 M (Fig. 3C). Nicotinonitrile as well as isonicotinonitrile gave the desired products **48** and **49** with high yield. 4-Methyl, bromo-, or alkyl-substituted nicotinonitrile could also be used (products **50–52**). Remarkably, the annulation reaction was completely regioselective for the less sterically hindered position. Such a high selectivity has been only rarely

Table 1 Optimization of the dearomative [3 + 2] annulation reaction of quinoline **8** and DA cyclopropanes **13–15**[a]



Entry	R	LA	Mol%	Yield[b]
1	NPhth	$Sc(OTf)_3$	20	80
2	NPhth	$In(OTf)_3$	20	No conversion
3	NPhth	$Cu(OTf)_2$	20	No conversion
4	NPhth	$Hf(OTf)_4$	20	Decomposition
5	NPhth	$Yb(OTf)_3$	20	90
6[c]	NPhth	$Yb(OTf)_3$	5	96 (95)[d]
7[e]	NPhth	TfOH	20	No conversion
8	PMP	$Yb(OTf)_3$	20	No conversion
9	OAc	$Yb(OTf)_3$	20	No conversion

[a] Reactions were carried out on 0.10 mmol scale with 1.5 equiv. of **13–15** in CH_2Cl_2 (0.05 M). [b] Isolated yields. [c] Reaction was carried out on 0.20 mmol scale with 1.05 equiv. of **14** in CH_2Cl_2 (0.50 M). [d] Reaction was carried out on 2.00 mmol scale with 1.05 equiv. of **14** in CH_2Cl_2 (0.50 M). [e] 0.2 M in CH_2Cl_2. Phth = phthalimide, Tf = trifluoromethylsulfonyl, PMP = *para* methoxyphenyl.

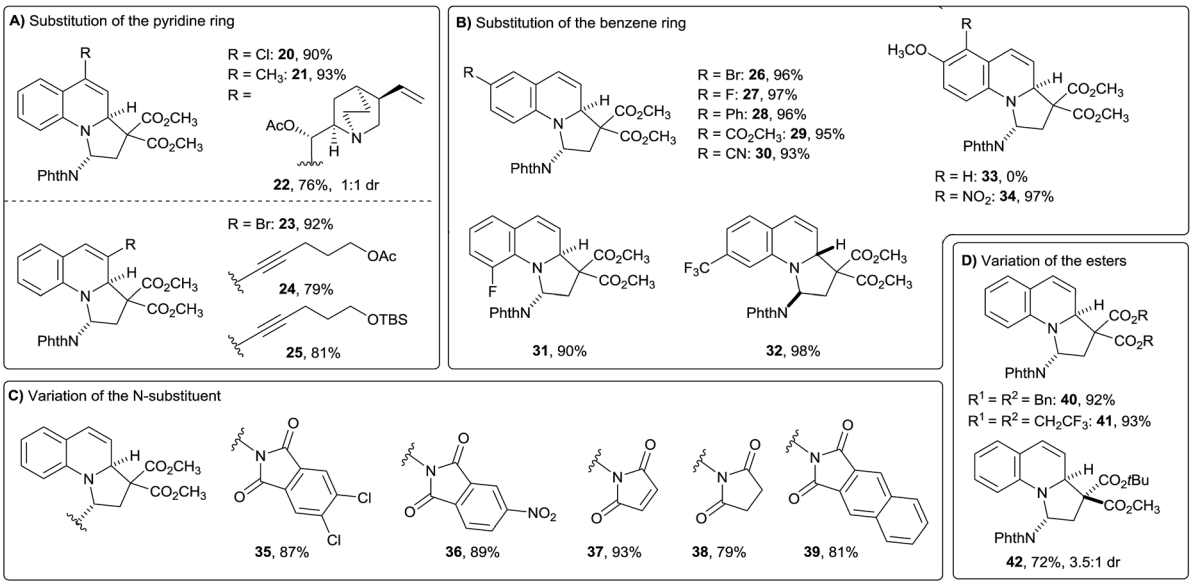


Fig. 2 Scope of the [3 + 2] annulation with quinolines. Reaction conditions: quinoline (0.20 mmol), DA-cyclopropane (0.21 mmol), $Yb(OTf)_3$ (5 mol%), CH_2Cl_2 (0.5 M). Unless noted otherwise products obtained with dr > 20 : 1. Phth = phthalimide, TBS = *tert*-butyldimethylsilyl.

reported for addition to pyridinium salts.[4h] Ethyl nicotinate derivative **53** could not be obtained, but 3,4- and 3,5-diester substituted pyridines gave the desired products **54** and **55** in good yields. Alternatively, installation of a more electron-withdrawing HFIP ester was also successful (product **56**). These active esters can be readily converted into different amides and esters.[21] Other electron-withdrawing groups on the nicotinate also led to good yields (products **57** and **58**). Finally, nitro-substituted pyridines also furnished the desired products **59–61** in 74–80% yield.

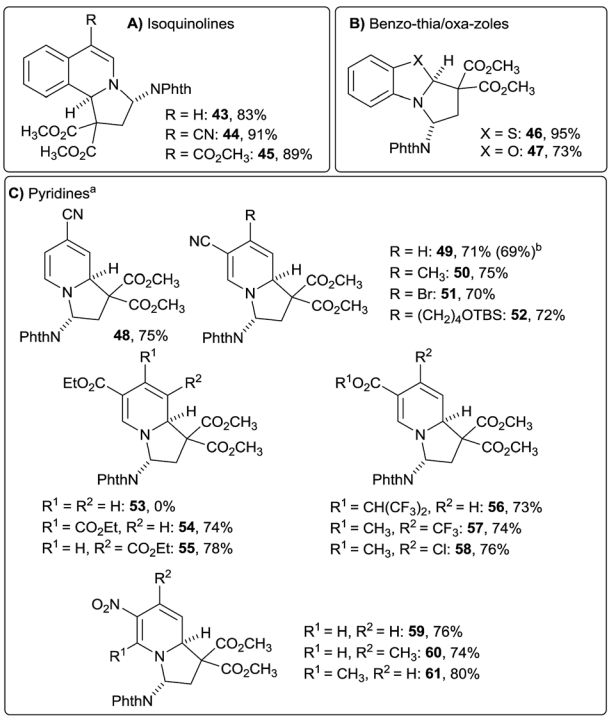
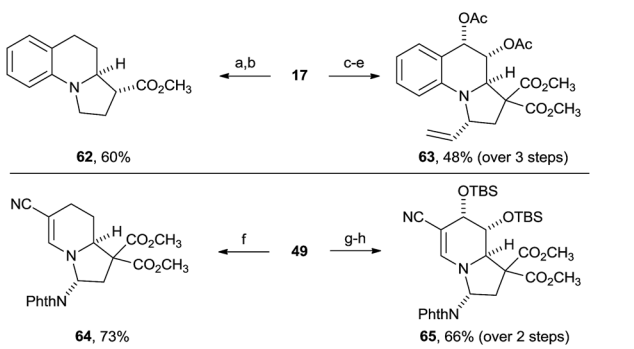


Fig. 3 Reaction conditions: N-heterocycle (0.20 mmol), **14** (0.21 mmol), $Yb(OTf)_3$ (5 mol%), CH_2Cl_2 (0.5 M). Unless noted otherwise products obtained with dr > 20 : 1. [a]Changes from normal reaction conditions: $Yb(OTf)_3$ (10 mol%), CH_2Cl_2 (1 M). [b]1 mmol scale. Phth = phthalimide, TBS = *tert*-butyldimethylsilyl.

2.3. Product functionalization

The obtained building blocks contain highly interesting functionalities for further modification, including in particular reactive alkenes and aminals. To further establish the synthetic

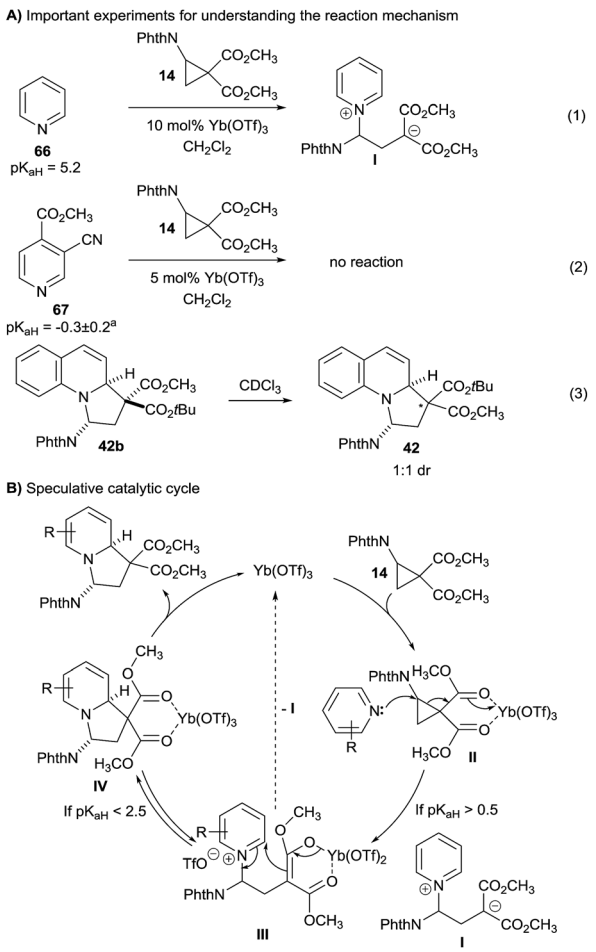


Scheme 4 Functionalization of products **17** and **49**. Reaction conditions: (a) H_2, $Pd(OH)_2$ (10% w/w), CH_3OH, 70%; (b) LiCl (5 equiv.), DMSO : H_2O 10 : 1, 140 °C, 85%; (c) OsO_4 (5 mol%), NMO·H_2O (1.2 equiv.), THF : acetone : H_2O (2 : 2 : 1); (d) Ac_2O (3 equiv.), DMAP (10 mol%), NEt_3 (4 equiv.), CH_2Cl_2, 71% dr > 20 : 1 (over 2 steps); (e) vinylMgBr (4 equiv.), $ZnCl_2$ (10 equiv.), THF, 50 °C, 68%, dr > 20 : 1; (f) H_2, $Pd(OH)_2$ (10% w/w), CH_3OH, 73%; (g) OsO_4 (5 mol%), NMO·H_2O (1.2 equiv.), acetone : H_2O (20 : 1), 0 °C; (h) TBSOTf, pyridine, CH_2Cl_2, 66%, dr > 20 : 1 (over 2 steps). Phth = phthalimide, TBS = *tert*-butyldimethylsilyl, NMO = *N*-methylmorpholine-*N*-oxide, THF = tetrahydrofuran, DMAP = *N*,*N*-dimethylpyridin-4-amine.

potential of the method, a few transformations of the dearomatization products were therefore examined (Scheme 4). Hydrogenation of the benzylic olefin and aminal of tetrahydrobenzoindolizine **17** and removal of one methyl ester group was achieved using Pearlman's catalyst, followed by Krapcho decarboxylation to give amine **62** in 60% overall yield. The phthalimido and the diester groups can therefore be considered as traceless activating and directing groups for the annulation reaction.

Selective dihydroxylation of the benzylic olefin from the convex side of the molecule was possible (dr > 20 : 1). After acetylation of the alcohols, the aminal was converted with high diastereoselectivity (dr > 20 : 1) into tertiary amine **63** through alkylation of the intermediary iminium with a vinyl zinc reagent, resulting in the stereoselective installation of four stereocenters around the tricyclic system.

Selective reduction of the more electron rich olefin of tetrahydroindolizine **49** furnished compound **64** in 73% yield. Moreover, selective dihydroxylation *via* osmium(VIII) catalysis and subsequent silylation of the diol gave compound **65** in high yield and high diastereoselectivity (dr > 20 : 1). Our methodology is therefore highly suited for accessing polysubstituted indolizidine rings frequently encountered in natural products (Scheme 1).



Scheme 5 Key experiments and speculative mechanism. [a]Predicted with ACD Labs.

2.4. Speculative reaction mechanism

Three experiments gave first insights into the reaction mechanism (Scheme 5A):

(1) When pyridine (**66**) was reacted with cyclopropane **14** using ytterbium triflate as catalyst, the desired product was not obtained. Full conversion of cyclopropane **14** was observed, but no pure product could be isolated from the reaction mixture. Nevertheless, a molecular ion corresponding to zwitterion **I** could be detected by mass spectroscopy.

(2) When highly electron-poor pyridine **67** was used, no reaction was observed (eqn (2)).

(3) Quinolizine **42** could be isolated with 3.5 : 1 dr at the diester center. However, after separation the minor isomer **42a** equilibrated to a 1 : 1 mixture just upon standing in deuterated chloroform (eqn (3)).

Based on these experiments and the well-established activation of DA diester cyclopropanes with Lewis acids,[11a] a first speculative mechanism can be proposed (Scheme 5B). Coordination of cyclopropane **14** by the Lewis acid led to activated intermediate **II**. Only sufficiently electron-rich pyridine (pK_{aH} > 0.5) are nucleophilic enough to react with this intermediate and give pyridinium **III**. At this point, reversible ring closure can occur to give coordinated product **IV**. The equilibrium lays on the product side for quinolines. For pyridines, this is the case only if the heterocycle is sufficiently electron poor (pK_{aH} < 2.5). If this is not the case, decoordination of the Lewis acid would free zwitterion **I**,[20] which could be the detected by mass spectroscopy. The high diastereoselectivity observed in the reaction is probably due to the higher stability of the products having the phthalimide group in the convex face of the polycyclic systems (thermodynamic control). From **IV**, the catalytic cycle is then closed by a simple ligand exchange on ytterbium.

3. Conclusion

In summary, a highly efficient method for the preparation of tetrahydroindolizine derivatives by dearomative [3 + 2] annulation reactions of pyridines, isoquinolines or quinolines and 2-aminocyclopropanes was developed. The fine modulation of the reactivity by the phthalimido group was essential for the success of this process. Excellent yields, high diastereoselectivities and a very broad substrate scope was achieved by employing ytterbium(III) triflate as catalyst. The reaction proved to be scalable and further functionalization of the obtained products was easily possible, setting the base for the synthesis of more complex bioactive compounds.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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18 X-ray data is available at the Cambridge Crystallographic Data Center (CCDC number: 1556244).† The relative configuration for other compounds was assumed to be the same on the basis of the similarity in their NMR-spectra.
19 Preliminary investigations showed that an enantioselective process should be possible, but highly challenging to develop, as so far no enantioselectivity higher than 18% was obtained. See Table S8 in the ESI.†
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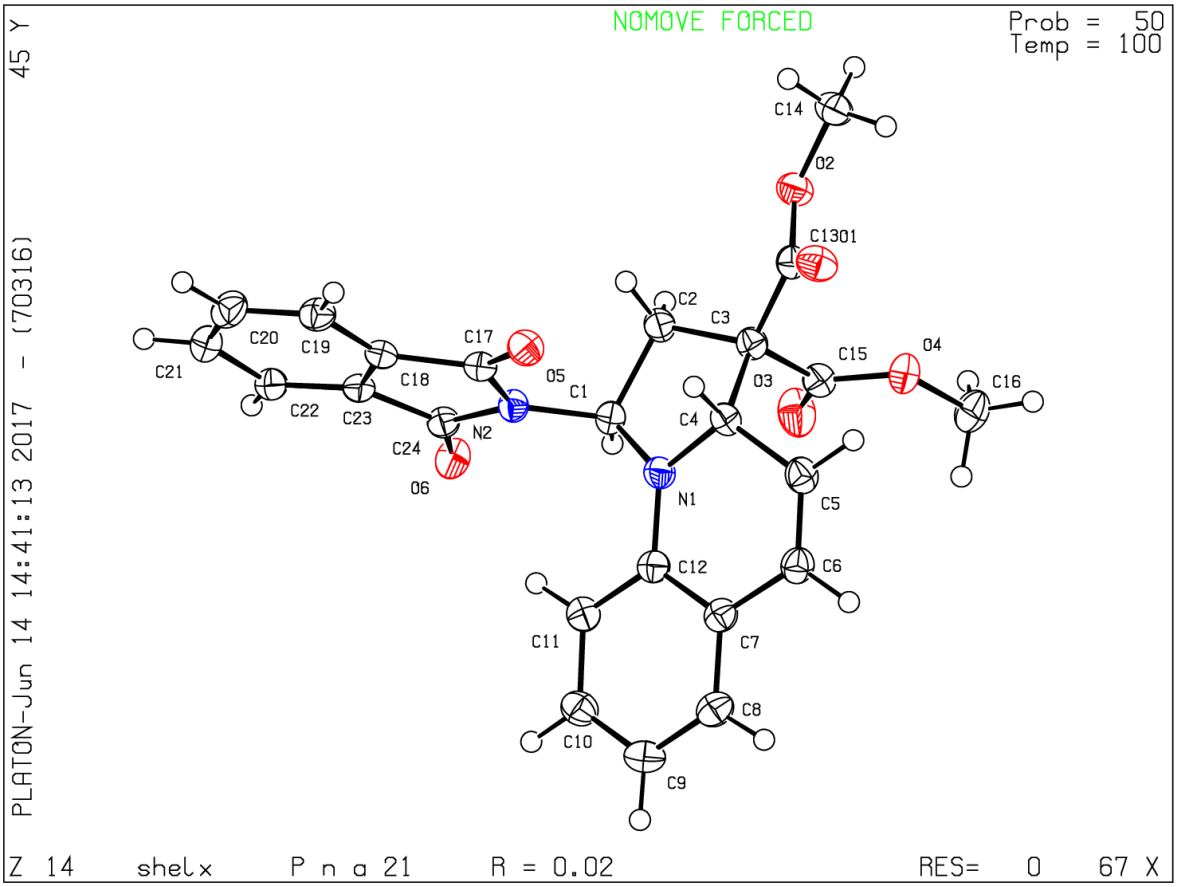
Content

1. X-ray diffraction analysis of compound 17



CCDC deposition number: 1556244

Table S1. Crystal data and structure refinement for compound **17**

Empirical formula	$C_{24}H_{20}N_2O_6$	
Formula weight	432.42	
Temperature	100.01(10) K	
Wavelength	1.54184 Å	
Crystal system	Orthorhombic	
Space group	*Pna*2$_1$	
Unit cell dimensions	a = 28.9068(4) Å	α= 90°.
	b = 7.90250(10) Å	β= 90°.
	c = 8.98890(10) Å	γ = 90°.
Volume	2053.39(4) Å^3	
Z	4	
Density (calculated)	1.399 Mg/m^3	
Absorption coefficient	0.846 mm^{-1}	
F(000)	904	
Crystal size	0.509 x 0.409 x 0.265 mm^3	
Theta range for data collection	5.797 to 75.495°.	
Index ranges	$-36 \le h \le 36$, $-9 \le k \le 9$, $-11 \le l \le 11$	
Reflections collected	35518	
Independent reflections	4206 [R_{int} = 0.0326]	
Completeness to θ = 67.684°	99.9 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.850 and 0.723	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4206 / 1 / 348	
Goodness-of-fit on F^2	1.059	
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0236, wR_2 = 0.0639	
R indices (all data)	R_1 = 0.0243, wR_2 = 0.0645	
Absolute structure parameter	0.01(5)	
Extinction coefficient	0.0012(2)	
Largest diff. peak and hole	0.186 and -0.133 e.Å^{-3}	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for compound **17**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	7071(1)	7430(2)	8003(1)	31(1)
O(2)	6456(1)	9031(2)	8589(1)	28(1)
O(3)	6155(1)	9739(2)	4455(2)	40(1)
O(4)	6861(1)	10163(1)	5425(2)	28(1)
O(5)	6107(1)	3180(2)	6928(1)	28(1)
O(6)	4927(1)	5102(2)	3972(1)	29(1)
N(1)	6306(1)	5697(2)	4369(2)	24(1)
N(2)	5585(1)	4517(2)	5362(2)	22(1)
C(1)	5855(1)	6043(2)	4984(2)	23(1)
C(2)	5951(1)	7102(2)	6398(2)	25(1)
C(3)	6453(1)	7729(2)	6229(2)	23(1)
C(4)	6677(1)	6213(2)	5381(2)	23(1)
C(5)	7124(1)	6551(2)	4597(2)	27(1)
C(6)	7193(1)	6080(2)	3193(2)	27(1)
C(7)	6828(1)	5288(2)	2309(2)	25(1)
C(8)	6908(1)	4733(2)	862(2)	29(1)
C(9)	6554(1)	4069(2)	-1(2)	31(1)
C(10)	6111(1)	3976(2)	596(2)	29(1)
C(11)	6021(1)	4511(2)	2044(2)	25(1)
C(12)	6379(1)	5161(2)	2917(2)	22(1)
C(13)	6702(1)	8019(2)	7697(2)	24(1)
C(14)	6674(1)	9411(2)	10007(2)	32(1)
C(15)	6464(1)	9325(2)	5267(2)	25(1)
C(16)	6908(1)	11653(2)	4490(2)	33(1)
C(17)	5726(1)	3275(2)	6378(2)	23(1)
C(18)	5320(1)	2151(2)	6596(2)	22(1)
C(19)	5265(1)	788(2)	7539(2)	27(1)
C(20)	4835(1)	7(2)	7551(2)	31(1)
C(21)	4476(1)	569(2)	6646(2)	29(1)
C(22)	4533(1)	1950(2)	5694(2)	25(1)
C(23)	4962(1)	2725(2)	5701(2)	21(1)
C(24)	5128(1)	4247(2)	4884(2)	23(1)

Table S3. Bond lengths [Å] and angles [°] for compound **17**. (Symmetry transform. used to gen. equiv. atoms)

O(1)-C(13)	1.195(2)	C(11)-H(11)	0.99(2)
O(2)-C(13)	1.339(2)	C(14)-H(14A)	0.9800
O(2)-C(14)	1.454(2)	C(14)-H(14B)	0.9800
O(3)-C(15)	1.199(2)	C(14)-H(14C)	0.9800
O(4)-C(15)	1.332(2)	C(16)-H(16A)	0.9800
O(4)-C(16)	1.453(2)	C(16)-H(16B)	0.9800
O(5)-C(17)	1.209(2)	C(16)-H(16C)	0.9800
O(6)-C(24)	1.211(2)	C(17)-C(18)	1.485(2)
N(1)-C(12)	1.389(2)	C(18)-C(19)	1.380(2)
N(1)-C(1)	1.442(2)	C(18)-C(23)	1.387(2)
N(1)-C(4)	1.464(2)	C(19)-C(20)	1.388(3)
N(2)-C(17)	1.401(2)	C(19)-H(19)	0.93(3)
N(2)-C(24)	1.405(2)	C(20)-C(21)	1.392(3)
N(2)-C(1)	1.476(2)	C(20)-H(20)	0.96(2)
C(1)-C(2)	1.547(2)	C(21)-C(22)	1.397(2)
C(1)-H(1)	0.94(2)	C(21)-H(21)	0.97(3)
C(2)-C(3)	1.542(2)	C(22)-C(23)	1.383(2)
C(2)-H(2A)	0.99(2)	C(22)-H(22)	1.03(2)
C(2)-H(2B)	0.98(2)	C(23)-C(24)	1.488(2)
C(3)-C(13)	1.520(2)	C(13)-O(2)-C(14)	114.64(13)
C(3)-C(15)	1.529(2)	C(15)-O(4)-C(16)	114.95(14)
C(3)-C(4)	1.561(2)	C(12)-N(1)-C(1)	123.82(14)
C(4)-C(5)	1.496(2)	C(12)-N(1)-C(4)	123.84(13)
C(4)-H(4)	1.02(2)	C(1)-N(1)-C(4)	111.78(13)
C(5)-C(6)	1.331(3)	C(17)-N(2)-C(24)	111.51(13)
C(5)-H(5)	1.00(2)	C(17)-N(2)-C(1)	124.65(13)
C(6)-C(7)	1.462(2)	C(24)-N(2)-C(1)	123.39(13)
C(6)-H(6)	1.00(2)	N(1)-C(1)-N(2)	114.27(13)
C(7)-C(8)	1.392(2)	N(1)-C(1)-C(2)	104.79(13)
C(7)-C(12)	1.411(2)	N(2)-C(1)-C(2)	110.32(13)
C(8)-C(9)	1.387(3)	N(1)-C(1)-H(1)	111.0(13)
C(8)-H(8)	0.98(2)	N(2)-C(1)-H(1)	106.2(12)
C(9)-C(10)	1.391(3)	C(2)-C(1)-H(1)	110.3(12)
C(9)-H(9)	0.94(3)	C(3)-C(2)-C(1)	105.19(13)
C(10)-C(11)	1.393(3)	C(3)-C(2)-H(2A)	113.3(13)
C(10)-H(10)	0.97(2)	C(1)-C(2)-H(2A)	109.5(14)
C(11)-C(12)	1.396(2)	C(3)-C(2)-H(2B)	108.8(13)

C(1)-C(2)-H(2B)	110.4(13)	O(1)-C(13)-O(2)	124.76(16)
H(2A)-C(2)-H(2B)	109.5(19)	O(1)-C(13)-C(3)	124.32(15)
C(13)-C(3)-C(15)	110.88(13)	O(2)-C(13)-C(3)	110.92(13)
C(13)-C(3)-C(2)	114.18(14)	O(2)-C(14)-H(14A)	109.5
C(15)-C(3)-C(2)	109.91(13)	O(2)-C(14)-H(14B)	109.5
C(13)-C(3)-C(4)	110.10(13)	H(14A)-C(14)-H(14B)	109.5
C(15)-C(3)-C(4)	110.35(13)	O(2)-C(14)-H(14C)	109.5
C(2)-C(3)-C(4)	101.01(12)	H(14A)-C(14)-H(14C)	109.5
N(1)-C(4)-C(5)	112.95(14)	H(14B)-C(14)-H(14C)	109.5
N(1)-C(4)-C(3)	102.39(12)	O(3)-C(15)-O(4)	124.76(17)
C(5)-C(4)-C(3)	116.76(13)	O(3)-C(15)-C(3)	123.63(15)
N(1)-C(4)-H(4)	109.5(11)	O(4)-C(15)-C(3)	111.60(14)
C(5)-C(4)-H(4)	109.1(11)	O(4)-C(16)-H(16A)	109.5
C(3)-C(4)-H(4)	105.7(12)	O(4)-C(16)-H(16B)	109.5
C(6)-C(5)-C(4)	121.74(16)	H(16A)-C(16)-H(16B)	109.5
C(6)-C(5)-H(5)	123.3(12)	O(4)-C(16)-H(16C)	109.5
C(4)-C(5)-H(5)	114.9(12)	H(16A)-C(16)-H(16C)	109.5
C(5)-C(6)-C(7)	121.79(16)	H(16B)-C(16)-H(16C)	109.5
C(5)-C(6)-H(6)	120.4(12)	O(5)-C(17)-N(2)	125.13(15)
C(7)-C(6)-H(6)	117.7(12)	O(5)-C(17)-C(18)	128.90(15)
C(8)-C(7)-C(12)	119.47(15)	N(2)-C(17)-C(18)	105.97(13)
C(8)-C(7)-C(6)	121.55(15)	C(19)-C(18)-C(23)	121.71(15)
C(12)-C(7)-C(6)	118.91(15)	C(19)-C(18)-C(17)	129.77(15)
C(9)-C(8)-C(7)	121.31(17)	C(23)-C(18)-C(17)	108.46(14)
C(9)-C(8)-H(8)	122.5(14)	C(18)-C(19)-C(20)	117.10(16)
C(7)-C(8)-H(8)	116.1(14)	C(18)-C(19)-H(19)	120.5(14)
C(8)-C(9)-C(10)	118.92(17)	C(20)-C(19)-H(19)	122.3(14)
C(8)-C(9)-H(9)	120.6(15)	C(19)-C(20)-C(21)	121.47(17)
C(10)-C(9)-H(9)	120.4(15)	C(19)-C(20)-H(20)	120.1(14)
C(9)-C(10)-C(11)	121.00(17)	C(21)-C(20)-H(20)	118.4(14)
C(9)-C(10)-H(10)	118.8(14)	C(20)-C(21)-C(22)	121.19(16)
C(11)-C(10)-H(10)	120.2(14)	C(20)-C(21)-H(21)	118.9(15)
C(10)-C(11)-C(12)	119.99(16)	C(22)-C(21)-H(21)	119.9(15)
C(10)-C(11)-H(11)	118.2(13)	C(23)-C(22)-C(21)	116.76(15)
C(12)-C(11)-H(11)	121.8(13)	C(23)-C(22)-H(22)	125.1(13)
N(1)-C(12)-C(11)	121.80(15)	C(21)-C(22)-H(22)	118.1(13)
N(1)-C(12)-C(7)	118.89(14)	C(22)-C(23)-C(18)	121.76(15)
C(11)-C(12)-C(7)	119.31(15)	C(22)-C(23)-C(24)	130.10(15)

C(18)-C(23)-C(24)	108.10(13)	O(6)-C(24)-C(23)	129.02(15)
O(6)-C(24)-N(2)	125.05(15)	N(2)-C(24)-C(23)	105.92(13)

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for compound **17**.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	29(1)	36(1)	29(1)	-2(1)	-5(1)	5(1)
O(2)	28(1)	31(1)	27(1)	-5(1)	0(1)	1(1)
O(3)	38(1)	38(1)	43(1)	12(1)	-17(1)	-7(1)
O(4)	24(1)	24(1)	35(1)	5(1)	0(1)	-2(1)
O(5)	24(1)	33(1)	27(1)	1(1)	-6(1)	1(1)
O(6)	23(1)	33(1)	32(1)	10(1)	-4(1)	0(1)
N(1)	20(1)	29(1)	24(1)	-4(1)	0(1)	-3(1)
N(2)	21(1)	23(1)	24(1)	1(1)	-1(1)	-2(1)
C(1)	22(1)	22(1)	25(1)	1(1)	1(1)	-2(1)
C(2)	23(1)	24(1)	29(1)	-4(1)	2(1)	-2(1)
C(3)	22(1)	23(1)	24(1)	-1(1)	-1(1)	-1(1)
C(4)	23(1)	22(1)	25(1)	-2(1)	-2(1)	-1(1)
C(5)	21(1)	27(1)	32(1)	-3(1)	0(1)	0(1)
C(6)	22(1)	27(1)	31(1)	0(1)	2(1)	0(1)
C(7)	26(1)	22(1)	25(1)	3(1)	1(1)	2(1)
C(8)	28(1)	30(1)	28(1)	2(1)	3(1)	3(1)
C(9)	35(1)	34(1)	23(1)	-2(1)	-2(1)	5(1)
C(10)	31(1)	30(1)	26(1)	-1(1)	-5(1)	1(1)
C(11)	26(1)	25(1)	26(1)	1(1)	-2(1)	1(1)
C(12)	26(1)	19(1)	23(1)	3(1)	-1(1)	2(1)
C(13)	26(1)	21(1)	25(1)	0(1)	0(1)	-3(1)
C(14)	33(1)	37(1)	27(1)	-8(1)	0(1)	-4(1)
C(15)	25(1)	24(1)	26(1)	-1(1)	-1(1)	0(1)
C(16)	33(1)	27(1)	39(1)	8(1)	5(1)	0(1)
C(17)	25(1)	24(1)	20(1)	-1(1)	0(1)	1(1)
C(18)	24(1)	22(1)	20(1)	-3(1)	1(1)	1(1)
C(19)	31(1)	26(1)	24(1)	2(1)	-1(1)	2(1)
C(20)	36(1)	28(1)	29(1)	7(1)	4(1)	-1(1)
C(21)	29(1)	29(1)	30(1)	2(1)	2(1)	-6(1)
C(22)	24(1)	27(1)	23(1)	-1(1)	0(1)	-2(1)
C(23)	23(1)	23(1)	19(1)	-2(1)	2(1)	1(1)
C(24)	23(1)	23(1)	22(1)	-1(1)	1(1)	1(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for compound **17**.

	x	y	z	U(eq)
H(1)	5672(7)	6660(30)	4310(20)	23(5)
H(2A)	5722(8)	8030(30)	6470(30)	35(6)
H(2B)	5930(7)	6390(30)	7280(30)	33(6)
H(4)	6727(7)	5290(20)	6160(20)	21(5)
H(5)	7368(7)	7090(30)	5220(30)	30(5)
H(6)	7496(7)	6310(20)	2690(20)	25(5)
H(8)	7224(8)	4870(30)	490(30)	34(6)
H(9)	6615(8)	3650(30)	-960(30)	41(6)
H(10)	5861(8)	3540(30)	-20(30)	36(6)
H(11)	5700(7)	4440(30)	2410(20)	27(5)
H(14A)	7006	9584	9856	49
H(14B)	6626	8464	10694	49
H(14C)	6537	10440	10426	49
H(16A)	6898	11316	3441	49
H(16B)	7203	12211	4701	49
H(16C)	6653	12438	4697	49
H(19)	5510(8)	410(30)	8130(30)	34(6)
H(20)	4780(8)	-950(30)	8190(30)	33(6)
H(21)	4180(9)	-10(30)	6690(30)	42(6)
H(22)	4252(7)	2360(30)	5090(30)	30(5)

Table S6. Torsion angles [°] for compound **17**.

C(12)-N(1)-C(1)-N(2)	76.2(2)
C(4)-N(1)-C(1)-N(2)	-112.13(15)
C(12)-N(1)-C(1)-C(2)	-162.91(15)
C(4)-N(1)-C(1)-C(2)	8.74(17)
C(17)-N(2)-C(1)-N(1)	59.5(2)
C(24)-N(2)-C(1)-N(1)	-128.82(16)
C(17)-N(2)-C(1)-C(2)	-58.23(19)
C(24)-N(2)-C(1)-C(2)	113.43(16)
N(1)-C(1)-C(2)-C(3)	16.44(17)
N(2)-C(1)-C(2)-C(3)	139.89(14)
C(1)-C(2)-C(3)-C(13)	-151.30(13)
C(1)-C(2)-C(3)-C(15)	83.38(16)
C(1)-C(2)-C(3)-C(4)	-33.19(16)
C(12)-N(1)-C(4)-C(5)	15.4(2)
C(1)-N(1)-C(4)-C(5)	-156.26(14)
C(12)-N(1)-C(4)-C(3)	141.81(15)
C(1)-N(1)-C(4)-C(3)	-29.84(17)
C(13)-C(3)-C(4)-N(1)	158.69(13)
C(15)-C(3)-C(4)-N(1)	-78.59(15)
C(2)-C(3)-C(4)-N(1)	37.66(16)
C(13)-C(3)-C(4)-C(5)	-77.40(18)
C(15)-C(3)-C(4)-C(5)	45.33(19)
C(2)-C(3)-C(4)-C(5)	161.57(15)
N(1)-C(4)-C(5)-C(6)	-13.2(2)
C(3)-C(4)-C(5)-C(6)	-131.54(17)
C(4)-C(5)-C(6)-C(7)	3.4(3)
C(5)-C(6)-C(7)-C(8)	-177.23(16)
C(5)-C(6)-C(7)-C(12)	5.9(2)
C(12)-C(7)-C(8)-C(9)	0.6(2)
C(6)-C(7)-C(8)-C(9)	-176.30(17)
C(7)-C(8)-C(9)-C(10)	0.6(3)
C(8)-C(9)-C(10)-C(11)	-1.1(3)
C(9)-C(10)-C(11)-C(12)	0.4(3)
C(1)-N(1)-C(12)-C(11)	-16.3(2)
C(4)-N(1)-C(12)-C(11)	173.04(15)
C(1)-N(1)-C(12)-C(7)	163.36(14)
C(4)-N(1)-C(12)-C(7)	-7.3(2)

C(10)-C(11)-C(12)-N(1)	-179.55(15)
C(10)-C(11)-C(12)-C(7)	0.8(2)
C(8)-C(7)-C(12)-N(1)	179.08(15)
C(6)-C(7)-C(12)-N(1)	-4.0(2)
C(8)-C(7)-C(12)-C(11)	-1.3(2)
C(6)-C(7)-C(12)-C(11)	175.71(15)
C(14)-O(2)-C(13)-O(1)	1.0(2)
C(14)-O(2)-C(13)-C(3)	-178.56(13)
C(15)-C(3)-C(13)-O(1)	-107.51(18)
C(2)-C(3)-C(13)-O(1)	127.69(18)
C(4)-C(3)-C(13)-O(1)	14.9(2)
C(15)-C(3)-C(13)-O(2)	72.02(16)
C(2)-C(3)-C(13)-O(2)	-52.78(18)
C(4)-C(3)-C(13)-O(2)	-165.57(13)
C(16)-O(4)-C(15)-O(3)	-1.6(3)
C(16)-O(4)-C(15)-C(3)	177.12(14)
C(13)-C(3)-C(15)-O(3)	-145.69(18)
C(2)-C(3)-C(15)-O(3)	-18.5(2)
C(4)-C(3)-C(15)-O(3)	92.0(2)
C(13)-C(3)-C(15)-O(4)	35.57(19)
C(2)-C(3)-C(15)-O(4)	162.76(14)
C(4)-C(3)-C(15)-O(4)	-86.69(17)
C(24)-N(2)-C(17)-O(5)	177.73(15)
C(1)-N(2)-C(17)-O(5)	-9.8(3)
C(24)-N(2)-C(17)-C(18)	-1.79(17)
C(1)-N(2)-C(17)-C(18)	170.73(14)
O(5)-C(17)-C(18)-C(19)	4.4(3)
N(2)-C(17)-C(18)-C(19)	-176.13(16)
O(5)-C(17)-C(18)-C(23)	-178.23(16)
N(2)-C(17)-C(18)-C(23)	1.26(17)
C(23)-C(18)-C(19)-C(20)	0.3(3)
C(17)-C(18)-C(19)-C(20)	177.37(17)
C(18)-C(19)-C(20)-C(21)	0.2(3)
C(19)-C(20)-C(21)-C(22)	-0.3(3)
C(20)-C(21)-C(22)-C(23)	-0.1(3)
C(21)-C(22)-C(23)-C(18)	0.7(2)
C(21)-C(22)-C(23)-C(24)	-176.95(16)
C(19)-C(18)-C(23)-C(22)	-0.8(2)

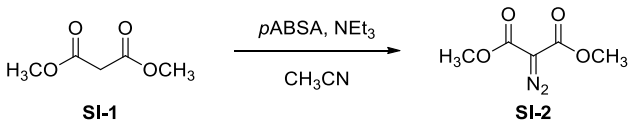
C(17)-C(18)-C(23)-C(22)	-178.39(15)
C(19)-C(18)-C(23)-C(24)	177.33(15)
C(17)-C(18)-C(23)-C(24)	-0.32(17)
C(17)-N(2)-C(24)-O(6)	-177.52(16)
C(1)-N(2)-C(24)-O(6)	9.9(3)
C(17)-N(2)-C(24)-C(23)	1.60(17)
C(1)-N(2)-C(24)-C(23)	-171.03(14)
C(22)-C(23)-C(24)-O(6)	-3.8(3)
C(18)-C(23)-C(24)-O(6)	178.32(17)
C(22)-C(23)-C(24)-N(2)	177.12(16)
C(18)-C(23)-C(24)-N(2)	-0.74(17)

2. General methods

All reactions were carried out in oven- or flame dried glassware under nitrogen atmosphere, unless stated otherwise. For quantitative flash chromatography, distilled technical grade solvents were used. THF, Et_2O, CH_3CN and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 7 ppm, Karl-Fischer titration). NEt_3 was dried by distillation over CaH_2 under nitrogen atmosphere. All chemicals were purchased and used as received unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC aluminium plates and visualized with UV-light, permanganate, CAM or *p*-anisaldehyde stains. ^{1}H-NMR spectra were recorded at room temperature on a Brucker DPX-400 400 MHz spectrometer in chloroform-d or D6-DMSO; all signals are reported in ppm with the internal chloroform signal at 7.26 ppm or the internal D6-DMSO signal at 2.50 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, integration, coupling constant(s) in Hz, interpretation). ^{13}C-NMR spectra were recorded with 1H-decoupling on a Bruker DPX-400 101 MHz spectrometer in chloroform-d or D6-DMSO; all signals are reported in ppm with the internal chloroform signal at 77.00 ppm or the internal DMSO signal at 39.51 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO4100-S and a ZnSe prism and are reported as cm^{-1} (w = weak, m = medium, s = strong). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. Melting points were measured on a Buechi B-540 melting point apparatus and were not corrected.

3. Synthesis of diazo compounds

Dimethyl 2-diazomalonate (**SI-2**).



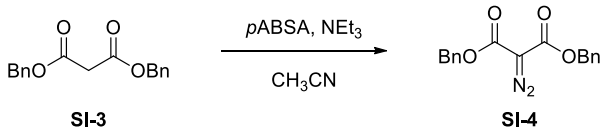
SI-1 **SI-2**

Following a modified procedure,[1] triethylamine (9.23 mL, 66.6 mmol, 2.4 equiv.) and dimethyl malonate **SI-1** (3.19 mL, 27.8 mmol, 1 equiv.) were added to a solution of *p*ABSA (10.0 g, 41.6 mmol, 1.5 equiv.) in CH_3CN (111 mL, 0.25 M) at room temperature and the resulting mixture was stirred for 18 hours at room temperature. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (50 mL), the remaining solids were filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 5:1) and 4.28 g (27.1 mmol, 98%) of the title compound **SI-2** were isolated as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 6H, C*H*$_3$).

^{1}H-NMR data match the literature report.[1]

Dibenzyl 2-diazomalonate (**SI-4**).



SI-3 **SI-4**

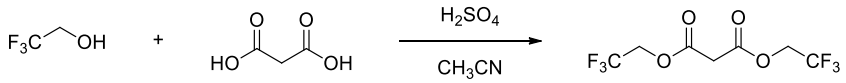
Following a modified procedure,[2] triethylamine (1.33 mL, 9.60 mmol, 2.4 equiv.) and dibenzyl malonate **SI-3** (1.00 mL, 4.00 mmol, 1 equiv.) were added to a solution of *p*ABSA (1.44 g, 6.00 mmol, 1.5 equiv.) in CH_3CN (16.0 mL, 0.25 M) at room temperature and the resulting mixture was stirred for 18 hours at room temperature. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (20 mL), the remaining solids were filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1) and 1.19 g (3.83 mmol, 96%) of the title compound **SI-4** were isolated as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.28 (m, 10H, Ar*H*), 5.28 (s, 4H, C*H*$_2$).

^{1}H-NMR data match the literature report.[1]

[1] F. de Nanteuil, J. Waser, *Angew. Chem. Int. Ed.,* **2011**, *50*, 12075–12079.

Bis(2,2,2-trifluoroethyl) malonate (**SI-7**).



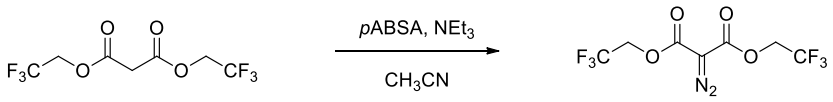
SI-5 **SI-6** **SI-7**

Following a modified procedure,[2] H_2SO_4 (1.00 mL, 18.8 mmol, 0.25 equiv.) was added to a solution of trifluoroethanol **SI-5** (29.9 mL, 415 mmol, 5.4 equiv.) and malonic acid **SI-6** (8.00 g, 77.0 mmol, 1 equiv.) in toluene (40.0 mL, 1.9 M) and the resulting mixture was heated to reflux for 8 hours. After cooling to room temperature, toluene (80.0 mL) was added and the mixture was washed with aq. NaOH (200 mL, 1 M), water (200 mL) and brine (200 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated which afforded 6.80 g (25.4 mmol, 33%) of the title compound **SI-7** as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.55 (q, *J* = 8.2 Hz, 4H, OC*H*$_2$), 3.61 (s, 2H, C*H*$_2$).

^{1}H-NMR data match the literature report.[2]

Bis(2,2,2-trifluoroethyl) 2-diazomalonate (**SI-8**).



SI-7 **SI-8**

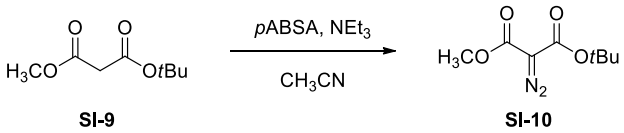
Following a modified procedure,[2] triethylamine (6.00 mL, 43.3 mmol, 2.4 equiv.) and bis(trifluorethyl)malonate **SI-7** (4.84 g, 18.0 mmol, 1 equiv.) were added to a solution of *p*ABSA (6.50 g, 27.1 mmol, 1.5 equiv.) in CH_3CN (72.0 mL, 0.25 M) at room temperature and the resulting mixture was stirred for 18 hours at room temperature. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (50 mL), the solids were filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 5:1) and 5.26 g (17.9 mmol, 99%) of the title compound **SI-8** were isolated as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.63 (q, *J* = 8.2 Hz, 4H, OC*H*$_2$).

^{1}H-NMR data match the literature report.[2]

[2] F. de Nanteuil, J. Loup, and J. Waser *Org. Lett.* **2013**, *15*, 3738-3741.

1-*tert*-Butyl 3-methyl 2-diazomalonate (**SI-10**).



SI-9 **SI-10**

Following a modified procedure,[3] triethylamine (1.97 mL, 14.2 mmol, 2.4 equiv.) and *tert*-butyl methyl malonate **SI-9** (1.00 mL, 5.91 mmol, 1 equiv.) were added to a solution of *p*ABSA (2.13 g, 8.87 mmol, 1.5 equiv.) in CH_3CN (23 mL, 0.25 M) at room temperature and the resulting mixture was stirred for 18 hours at room temperature. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (25 mL), the remaining solids were filtered and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 20:1 to 10:1) and 1.05 g (5.24 mmol, 89%) of the title compound **SI-10** were isolated as a yellow oil.

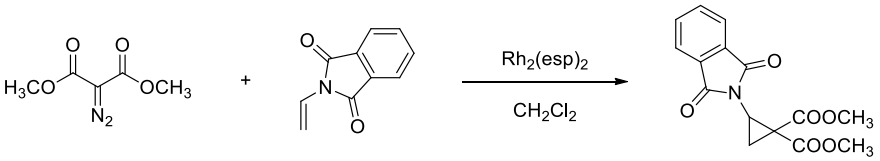
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3H, C*H*$_3$), 1.50 (s, 9H, C(C*H*$_3$)$_3$).

HRMS (ESI) calcd. for $C_8H_{13}N_2O_4^+$ $[M+H]^+$ 201.0870; found 201.0690.

^{1}H-NMR data match the literature report.[3]

4. Synthesis of aminocyclopropanes

Bimethyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**14**).



SI-2 **SI-11** **14**

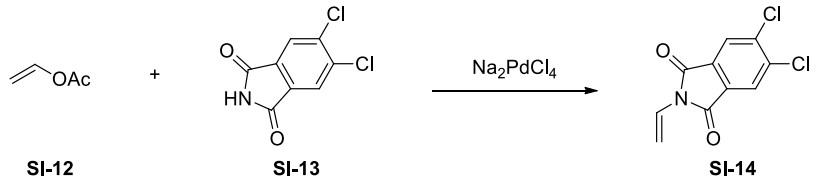
Following a modified procedure,[1] a solution of dimethyldiazomalonate **SI-2** (2.21 g, 14.0 mmol, 1.1 equiv.) in CH_2Cl_2 (10.0 mL) was added over 5 minutes at 0 °C to a solution of $Rh_2(esp)_2$ (19.0 mg, 25.0 µmol, 0.2 mol%) and *N*-vinyl-phtalimide **SI-11** (2.20 g, 12.7 mmol, 1 equiv.) in CH_2Cl_2 (40 mL). The reaction mixture was stirred for 16 hours while warming to room temperature. Thereafter the solvent was evaporated and the residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to pentane:EtOAc 4:1) affording 3.23 g (10.7 mmol, 84%) of the title compound **14** as a colorless oil.

[3] F. de Simone, T. Saget, F. Benfatti, S. Almeida, J. Waser *Chem. Eur. J.* **2011**, *17,* 14527-14538.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 3.83 (s, 3H, OC*H*$_3$), 3.70 (dd, *J* = 8.5, 6.6 Hz, 1H, C*H*-Phth), 3.62 (s, 3H, OC*H*$_3$), 2.71 (t, *J* = 6.6 Hz, 1H, CH_2), 2.04 (dd, *J* = 8.5, 6.6 Hz, 1H, CH_2).

^{1}H-NMR data match the literature report.[1]

5,6-Dichloro-2-vinylisoindoline-1,3-dione (**SI-14**).



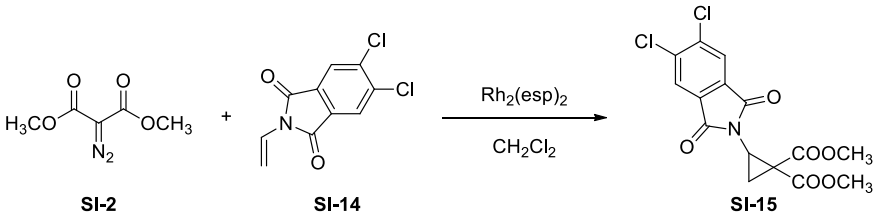
SI-12 **SI-13** **SI-14**

Following a modified procedure,[7] Na_2PdCl_4 (27.0 mg, 92 µmol, 2 mol%) was added to a stirred solution of 4,5-dichlorophthalimide (**SI-13**) (1.00 g, 4.63 mmol, 1.00 equiv.) in vinyl acetate (**SI-12**) (11.5 mL, 124 mmol, 26.8 equiv.), and the mixture was heated under reflux for 48 h. After solvent evaporation, the crude was purified by Biotage (SNAP Cartridge KP-Sil 25 g, 8:2 Hexane/EtOAc) to obtain 1.25 g (4.63 mmol, 46%) of the title compound **SI-14** as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.96 (s, 2H, Ar*H*), 6.84 (dd, *J* = 16.4, 9.8 Hz, 1H, N-*CH*), 6.09 (dd, *J* = 16.4, 0.3 Hz, 1H, *=CH*), 5.10 (dd, *J* = 9.8, 0.3 Hz, 1H, *=CH*).

^{1}H-NMR data match the literature report.[7]

Dimethyl 2-(5,6-dichloro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**SI-15**).



SI-2 **SI-14** **SI-15**

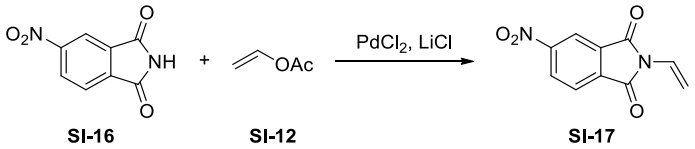
Following a modified procedure,[8] a solution of dimethyl diazomalonate (**SI-2**) (0.51 mL, 4.40 mmol, 1.5 equiv.) in CH_2Cl_2 (8.0 mL) was added dropwise over 5 minutes to a solution of 5,6-dichloro-2-vinylisoindoline- 1,3-dione (**SI-14**) (72.0 mg, 3.00 mmol, 1 equiv.) and $Rh_2(esp)_2$ (4.50 mg, 5.90 µmol, 0.2 mol%) in CH_2Cl_2 (4.0 mL) at 0 °C. After stirring the resulting mixture overnight at room temperature, the solution was concentrated under reduced pressure. Purification by Biotage (SNAP cartridge KP-Sil

25 g, hexane:EtOAc 95:5 to 6:4) afforded 810 mg (2.20 mmol, 74%) of the title compound **SI-15** as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (s, 2H, Ar*H*), 3.82 (s, 3H, OC*H*$_3$), 3.66 (dd, *J* = 8.5, 6.5 Hz, 1H, C*H*-Phth), 3.63 (s, 3H, OC*H*$_3$), 2.64 (dd, *J* = 6.5. 6.5 Hz, 1H, C*H*$_2$), 2.07-2.01 (m, 1H, C*H*$_2$).

^{1}H-NMR data match the literature report.[8]

5-Nitro-2-vinylisoindoline-1,3-dione (**SI-17**).

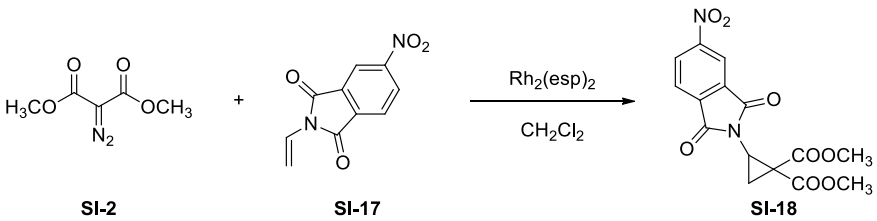


Following a modified procedure,[4] $PdCl_2$ (92 mg, 0.52 mmol, 10 mol%) and LiCl (221 mg, 5.20 mmol, 1 equiv.) were added to a solution of 5-nitrosoindoline-1,3-dione (**SI-16**) (1.00 g, 5.20 mmol, 1 equiv.) in vinyl acetate (**SI-12**) (12.9 mL, 139 mmol, 27 equiv.) and the mixture was heated to reflux for 20 hours. After cooling to room temperature the solvent was evaporated and the residue was purified by column chromatography (hexane:EtOAc 4:1 to 1:1) affording 1.14 g (5.23 mmol, quant.) of the title compound **SI-17** as a bright yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.68 (dd, *J* = 2.0, 0.5 Hz, 1H, Ar*H*), 8.63 (dd, *J* = 8.1, 2.0 Hz, 1H, Ar*H*), 8.08 (m, 1H, Ar*H*), 6.88 (dd, *J* = 16.4, 9.8 Hz, 1H, *CH*-N), 6.14 (dd, *J* = 16.4, 0.5 Hz, 1H, =*CH*$_2$), 5.16 (dd, *J* = 9.8, 0.5 Hz, 1H, =*CH*$_2$) ppm.

^{1}H-NMR data match the literature report.[4]

Dimethyl 2-(5-nitro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**SI-18**).



Following a modified procedure,[4] a solution of dimethyldiazomalonate (**SI-2**) (0.12 g 0.77 mmol, 1.2 equiv.) in CH_2Cl_2 (1.0 mL) was added over 5 minutes to a solution of 5-nitro-2-vinylisoindoline-1,3-

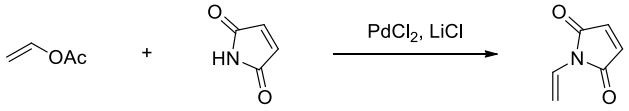
[4] F. de Nanteuil, E. Serrano, D. Perrotta, and J. Waser *J. Am. Chem. Soc.* **2014** *136*, 6239-6242.

dione (**SI-17**) (0.13 g, 0.64 mmol, 1 equiv.) and $Rh_2(esp)_2$ (1 mg, 1.2 µmol, 0.2 mol%) in CH_2Cl_2 (1.6 mL) at 0 °C and the resulting mixture was stirred for 16 hours while warming to room temperature. Thereafter the solvent was evaporated and the residue was purified by column chromatography (silica, hexane:EtOAc 6:4) affording 0.18 g (0.53 mmol, 83%) of the title compound **SI-18** as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.61 (m, 2H, Ar*H*), 8.03 (d, *J* = 8.1 Hz, 1H, Ar*H*), 3.83 (s, 3H, OCH_3), 3.70 (m, 1H, C*H*-N), 3.62 (s, 3H, OCH_3), 2.63 (m, 1H, CH_2), 2.07 (m, 1H, CH_2).

^{1}H-NMR data match the literature report.[4]

1-Vinyl-1H-pyrrole-2,5-dione (**SI-20**).



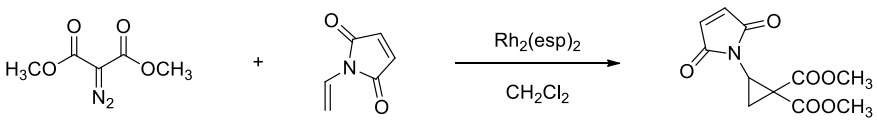
SI-12 **SI-19** **SI-20**

Following a modified procedure,[7] maleimide (**SI-19**) (1.30 g, 13.4 mmol, 1 equiv.), palladium(II) chloride (240 mg, 1.34 mmol, 0.1 equiv.), lithium chloride (57.0 mg, 1.34 mmol, 0.1 equiv.) and vinyl acetate (**SI-12**) (33.2 mL, 359 mmol, 27 equiv.) were added in a microwave tube sealed with a microwave cap. After stirring at 80 °C for 23 h, the resulting mixture was cooled down to room temperature. Purification by Biotage (SNAP cartridge KP-Sil 50 g, hexane:EtOAc 93:7 to 40:60) afforded 1.74 g (14.1 mmol, quant.) of the title compound **SI-20** as a bright yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.74 (s, 2H, *CH*-*C*=*O*), 6.67 (dd, *J* = 16.4, 9.8 Hz, 1H, C*H*-N), 5.87 (d, *J* = 16.4 Hz, 1H, =CH_2), 4.94 (d, *J* = 9.8 Hz, 1H, =CH_2).

^{1}H-NMR data match the literature report.[7]

Dimethyl 2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)cyclopropane-1,1-dicarboxylate (**SI-21**).



SI-2 **SI-20** **SI-21**

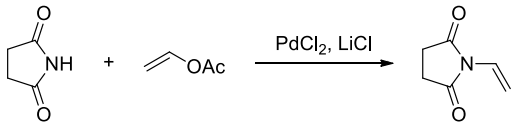
Following a modified procedure,[8] a solution of dimethyl diazomalonate (**SI-2**) (96 mg, 0.61 mmol, 1.5 equiv.) in CH_2Cl_2 (1.0 mL) was added dropwise over 5 minutes to a solution of 1-vinyl-1*H*-pyrrole-2,5-dione (**SI-20**) (50 mg, 0.41 mmol, 1 equiv.) and $Rh_2(esp)_2$ (0.7 mg, 0.9 µmol, 0.2 mol%) in CH_2Cl_2

(2.0 mL) at 0 °C. The resulting mixture was stirred for 5 hours at room temperature and thereafter concentrated under reduced pressure. Purification by Biotage (SNAP cartridge KP-Sil 10 g, hexane/EtOAc 95:5 to 70:30) afforded 66.9 mg (0.264 mmol, 65%) of the title compound **SI-21** as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.67 (s, 2H, C*H*-C=O), 3.79 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 3.56-3.51 (m, 1H, C*H*-N), 2.56 (dd, *J* = 6.4, 6.5 Hz, 1H, CH_2), 1.96-1.91 (m, 1H, CH_2) ppm.

^{1}H-NMR data match the literature report.[8]

1-Vinylpyrrolidine-2,5-dione (**SI-23**).



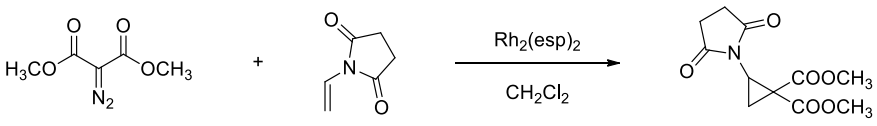
SI-22 **SI-12** **SI-23**

Following a modified procedure,[5] succinimide (**SI-22**) (1.00 g, 10.1 mmol, 1.00 equiv.), vinyl acetate (**SI-12**) (25.0 mL, 270 mmol, 26.8 eq) and Na_2PdCl_4 (59.0 mg, 0.202 mmol, 2.00 mol%) were heated under reflux for 72 hours. After solvent evaporation, the crude was purified by Biotage (SNAP Cartridge KP-Sil 50 g, 7:3 Hexane/EtOAc) to obtain the title compound **SI-23** (1.22 g, 9.78 mmol, 97%) as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.68 (dd, *J* = 16.4, 9.9 Hz, 1H, N-C*H*), 6.08 (d, *J* = 16.4 Hz, 1H, =C*H*), 5.06 (d, *J* = 9.9 Hz, 1H, =C*H*), 2.72 (s, 4H, CH_2) ppm.

^{1}H-NMR data match the literature report.[5]

Dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (**SI-24**).



SI-2 **SI-23** **SI-24**

Following a modified procedure,[4] a solution of dimethyldiazomalonate (**SI-2**) (300 mg, 4.80 mmol, 1.2 equiv.) in CH_2Cl_2 (4 mL) was added over 5 minutes to a solution of *N*-vinyl-succinimide (**SI-23**) (500 mg, 4.00 mmol, 1.00 equiv.), and $Rh_2(esp)_2$ (3.0 mg, 4.0 µmol, 0.10 mol%) in CH_2Cl_2 (15 mL) at 0 °C

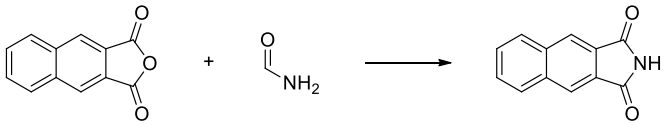
[5] E. Bayer, K. Geckeler, *Angew. Chem. Int. Ed.* **1979**, *18*, 533.

and the mixture was warmed to room temperature over 16 hours. Thereafter the solvent was evaporated and the residue was purified by Biotage (SNAP Cartridge KP-Sil 50 g, 1:1 hexane/EtOAc) affording the title compound **SI-24** as a yellow solid (801 mg, 3.14 mmol, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.78 (s, 3H, OC*H*$_3$), 3.68 (s, 3H, OC*H*$_3$), 3.45 (dd, *J* = 8.5, 6.5 Hz, 1H, N-C*H*), 2.73-2.58 (m, 4H, O=C-C*H*$_2$), 2.45 (dd, *J* = 6.5, 6.5 Hz, 1H, C*H*$_2$), 1.93 (dd, *J* = 8.5, 6.5 Hz, 1H, C*H*$_2$) ppm.

^{1}H-NMR data match the literature report.[4]

1H-Benzo[*f*]isoindole-1,3(2*H*)-dione (**SI-27**).



SI-25 **SI-26** **SI-27**

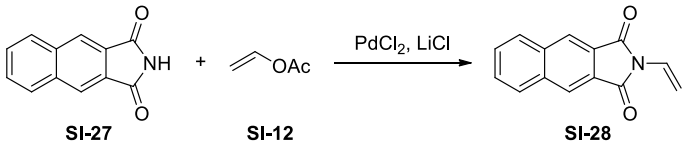
Following a modified procedure,[6] naphtho[2,3-*c*]furan-1,3-dione (**SI-25**) (500 mg, 2.52 mmol, 1 equiv.) and formamide **SI-26** (10.0 mL, 252 mmol, 100 equiv.) were added in a 20 mL microwave vial and sealed with a microwave cap. The mixture was stirred until the product was completely dissolved. The mixture was heated twice at 200 °C for 30 sec with 10 sec pre-stirring, using Biotage Initiator 2.0 microwave reactor. The mixture was cooled to 0 °C and cold water (10 mL) was added into the tube. The solid was filtrated over a filter paper, washed with water (15 mL) and hexane (20 mL) and dried under reduced pressure to afford 432 mg (2.19 mmol, 87%) of the title compound **SI-27** as a beige solid which was used without further purification.

^{1}H NMR (400 MHz, [D6]-DMSO) δ = 11.5 (s, 1H, *NH*), 8.45 (s, 2H, Ar*H*), 8.26 (dd, *J* = 6.6, 3.3 Hz, 2H, Ar*H*), 7.76 (dd, *J* = 6.6, 3.3 Hz, 2H, Ar*H*).

^{1}H-NMR data match the literature report.[6]

[6] K. Kacprzak, *Synth. Commun.* **2003**, *33*, 1499-1507.

2-Vinyl-1H-benzo[*f*]isoindole-1,3(2*H*)-dione (**SI-28**).



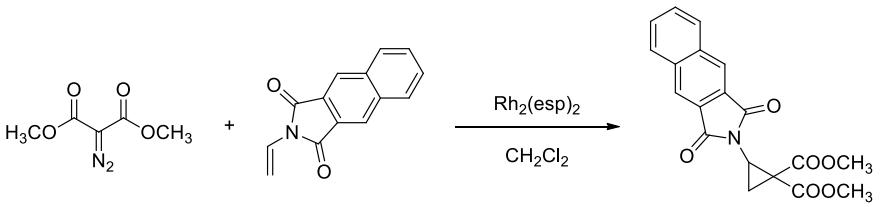
SI-27 **SI-12** **SI-28**

Following a modified procedure,[7] 1*H*-benzo[*f*]isoindole-1,3(2*H*)-dione (**SI-27**) (1.70 g, 8.62 mmol, 1 equiv.), palladium(II) chloride (0.15 g, 0.86 mmol, 0.1 equiv.), lithium chloride (40 mg, 0.86 mmol, 0.1 equiv.) and vinyl acetate (**SI-12**) (21.4 mL, 231 mmol, 27 equiv.) were added in a microwave tube sealed with a microwave cap. After stirring for 31 h at 80 °C, the resulting mixture was cooled down to room temperature. Purification by silica gel chromatography (hexane:EtOAc 17:1 to 10:1) afforded 1.26 g (5.66 mmol, 66%) the title compound **SI-28** as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.37 (s, 2H, Ar*H*), 8.07 (dd, *J* = 6.3, 3.4 Hz, 2H, Ar*H*), 7.72 (dd, *J* = 6.3, 3.4 Hz, 2H, Ar*H*), 6.97 (dd, *J* = 16.4, 9.8 Hz, 1H, Phth-*CH*), 6.20 (d, *J* = 16.4 Hz, 1H, =*CH*), 5.12 (d, *J* = 9.8 Hz, 1H, =*CH*).

^{1}H-NMR data match the literature report.[7]

Dimethyl 2-(1,3-dioxo-1H-benzo[f]isoindol-2(3*H*)-yl)cyclopropane-1,1-dicarboxylate (**SI-29**).



SI-2 **SI-28** **SI-29**

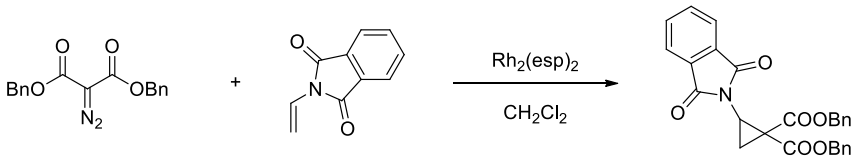
Following a modified procedure,[8] a solution of dimethyl 2-diazomalonate (**SI-2**) (20 mg, 1.30 mmol, 1.5 equiv.) in dichloromethane (2.00 mL) was added dropwise over 5 minutes to a solution of 2-vinyl-1*H*-benzo[*f*]isoindole- 1,3(2*H*)-dione (**SI-28**) (0.19 g, 0.85 mmol, 1 equiv.) and $Rh_2(esp)_2$ (1 mg, 1.70 µmol, 0.2 mol%) in CH_2Cl_2 (3.00 mL) at 0 °C. After stirring the resulting mixture for 26 hours at room temperature the solution was concentrated under reduced pressure. Purification by silica gel chromatography (hexane:EtOAc 8:2 to 6:4) afforded 0.28 g (0.80 mmol, 94%) the title compound **SI-29** as a colorless solid.

[7] N. Baret, J.-P. Dulcere, J. Rodriguez, J.-M. Pons, R. Faure, *Eur. J. Org. Chem.* **2000**, 1507-1516.
[8] F. Gonzalez-Bobes, M. D. B. Fenster, S. Kiau, L. Kolla, S. Kolotuchin, M. Soumeillant, *Adv. Synth. Catal.* **2008**, *350*, 813.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.34 (s, 2H, Ar*H*), 8.06 (dd, *J* = 6.2, 3.3 Hz, 2H, Ar*H*), 7.70 (dd, *J* = 6.2, 3.3 Hz, 2H, Ar*H*), 3.84 (s, 3H, OC*H*$_3$), 3.77 (dd, *J* = 8.5, 6.5 Hz, 1H C*H*-N), 3.60 (s, 3H, OC*H*$_3$), 2.78 (dd, *J* = 6.5, 6.5 Hz, 1H, C*H*$_2$), 2.08 (dd, *J* = 8.5, 6.5, 1H, C*H*$_2$).

^{1}H-NMR data match the literature report.[8]

Dibenzyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**SI-30**).



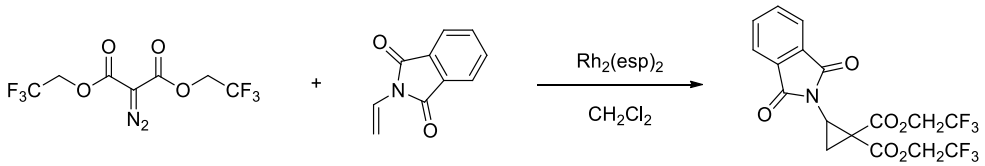
SI-4 **SI-11** **SI-30**

Following a modified procedure,[2] a solution of dibenzyl diazomalonate **SI-4** (1.19 g, 3.83 mmol, 1.1 equiv.) in CH_2Cl_2 (5 mL) was added over 5 minutes at 0 °C to a solution of $Rh_2(esp)_2$ (6 mg, 7 µmol, 0.2 mol%) and *N*-vinyl-phtalimide (**SI-11**) (604 mg, 3.49 mmol, 1 equiv.) in CH_2Cl_2 (9 mL). The reaction mixture was stirred for 16 hours while warming to room temperature. Thereafter the solvent was evaporated and the residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to pentane:EtOAc 4:1) affording 625 mg (1.37 mmol, 39%) of the title compound **SI-30** as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 5.5, 3.2 Hz, 2H, *Phth*), 7.73 – 7.66 (m, 2H, *Phth*), 7.35 – 7.30 (m, 5H, Ar*H*), 7.23 – 7.12 (m, 5H, Ar*H*), 5.29 – 5.17 (m, 2H, C*H*$_2$Ph), 5.04 – 4.95 (m, 2H, C*H*$_2$Ph), 3.78 – 3.70 (m, 1H, C*H*-Phth), 2.79 (dd, *J* = 6.5, 6.5 Hz, 1H, C*H*$_2$), 2.05 (dd, *J* = 8.5, 6.5 Hz, 1H, C*H*$_2$).

^{1}H-NMR data match the literature report.[2]

Bis(2,2,2-trifluoroethyl) 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**SI-31**).



SI-8 **SI-11** **SI-31**

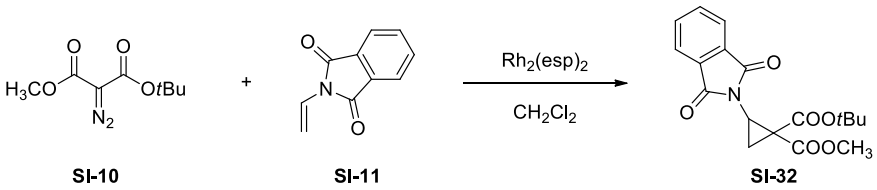
Following a modified procedure,[2] a solution of bis(trifluoroethyl)diazomalonate **SI-8** (5.26 g, 17.9 mmol, 1.1 equiv.) in CH_2Cl_2 (13 mL) was added over 5 minutes at 0 °C to a solution of $Rh_2(esp)_2$ (25 mg, 33 µmol, 0.2 mol%) and *N*-vinyl-phtalimide (**SI-11**) (2.82 g, 16.3 mmol, 1 equiv.) in CH_2Cl_2 (30 mL). The reaction mixture was stirred for 16 hours while warming to room temperature. Thereafter

the solvent was evaporated and the residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to pentane:EtOAc 7:3) affording 5.18 g (11.8 mmol, 73%) of the title compound **SI-31** as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 4.62 (q, *J* = 8.2 Hz, 2H, C*H*$_2$CF$_3$), 4.53 – 4.26 (m, 2H, C*H*$_2$CF$_3$), 3.84 (dd, *J* = 8.5, 6.9 Hz, 1H, C*H*-Phth), 2.91 (dd, *J* = 6.9, 6.9 Hz, 1H, C*H*$_2$), 2.20 (dd, *J* = 8.5, 6.9 Hz, 1H, C*H*$_2$).

^{1}H-NMR data match the literature report.[2]

1-*tert*-Butyl 1-methyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**SI-32**).



SI-10 **SI-11** **SI-32**

A solution of *tert*-butyl methyl diazomalonate (**SI-10**) (1.05 g, 5.24 mmol, 1.1 equiv.) in CH_2Cl_2 (5 mL) was added over 5 minutes at 0 °C to a solution of $Rh_2(esp)_2$ (7.2 mg, 9.5 µmol, 0.2 mol%) and *N*-vinyl-phtalimide (**SI-11**) (826 mg, 4.77 mmol, 1 equiv.) in CH_2Cl_2 (12 mL). The reaction mixture was stirred for 16 hours while warming to room temperature. Thereafter the solvent was evaporated and the residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to pentane:EtOAc 4:1) affording 1.26 g (3.65 mmol, 77%) of the title compound (**SI-32**) as a colorless oil.[9]

R_f: 0.5 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.67 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.61 – 6.52 (m, 1H, C*H*-Phth), 3.56 (s, 3H, OC*H*$_3$), 2.57 (dd, *J* = 6.4, 6.4 Hz, 1H, CH_2), 1.89 (dd, *J* = 8.5, 6.4 Hz, 1H, CH_2), 1.45 (s, 9H, C(C*H*$_3$)$_3$);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.9, 167.4, 166.9, 134.3, 131.4, 123.4, 82.5, 52.7, 34.3, 34.2, 27.9, 19.0 ppm;

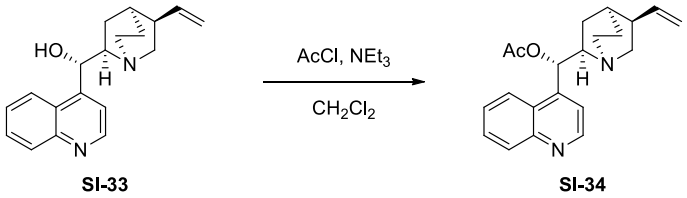
IR (film): $\tilde{\nu}$ = 2349 (w), 2139 (w), 1777 (m), 1764 (m), 1724 (s), 1438 (w), 1393 (w), 1331 (m), 1304 (m), 1275 (w), 1223 (w), 1201 (w), 1174 (w), 1132 (m), 1092 (w), 1058 (w), 982 (w), 957 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{18}H_{19}NNaO_6^+$ $[M+Na]^+$ 368.1105; found 368.1109.

[9] The compound was isolated as a single diastereoisomer of which the relative configuration was not assigned.

5. Substrate synthesis

(*S*)-Quinolin-4-yl((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl acetate (**SI-34**).



SI-33 **SI-34**

Following a modified procedure,[10] NEt_3 (0.71 mL, 5.1 mmol, 1.5 equiv.) followed by acetyl chloride (0.32 mL, 4.4 mmol, 1.3 equiv.) were added to a suspension of cinchonine (**SI-33**) (1.00 g, 3.40 mmol, 1 equiv.) in CH_2Cl_2 (17 mL, 0.2 M) at room temperature and the resulting mixture was stirred for 16 hours. Thereafter water (20 mL) was added, the mixture was stirred for 30 minutes, then sat. aq. K_2CO_3 (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The comb. org. extracts were washed with brine (20 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, EtOAc:MeOH 30:1) and 1.10 g (3.27 mmol, 96%) of the title compound **SI-34** were isolated as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (d, *J* = 4.5 Hz, 1H, Ar*H*), 8.21 (d, *J* = 8.6 Hz, 1H, Ar*H*), 8.16 – 8.09 (m, 1H, Ar*H*), 7.72 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H, Ar*H*), 7.60 (ddd, *J* = 8.4, 6.8, 1.3 Hz, 1H, Ar*H*), 7.38 (d, *J* = 4.5 Hz, 1H, Ar*H*), 6.58 (d, *J* = 6.9 Hz, 1H, C*H*), 6.02 (ddd, *J* = 17.4, 10.5, 7.3 Hz, 1H, C*H*=CH_2), 5.18 – 5.02 (m, 2H, CH=CH_2), 3.30 (q, *J* = 8.5 Hz, 1H, C*H*), 2.92 (d, *J* = 9.2 Hz, 2H, CH_2), 2.73 (ddd, *J* = 22.3, 14.6, 7.0 Hz, 2H, CH_2), 2.27 (q, *J* = 8.4 Hz, 1H, C*H*), 2.13 (s, 3H, C(O)CH_3), 1.85 (dd, *J* = 18.2, 7.6 Hz, 2H, C*H and* CH_2), 1.59 – 1.51 (m, 3H, CH_2 *and* CH_2) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.8, 149.9, 148.6, 145.4, 140.2, 130.4, 129.2, 126.8, 126.0, 123.4, 118.5, 114.9, 73.7, 59.5, 49.8, 49.0, 39.7, 27.8, 26.3, 23.6, 21.1;

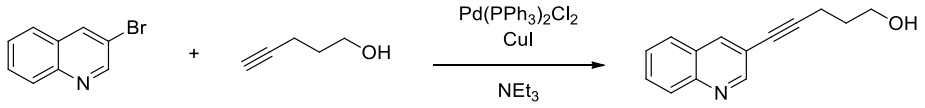
IR (film): $\tilde{\nu}$ = 2940 (w), 2874 (w), 2364 (w), 2320 (w), 1747 (m), 1594 (w), 1510 (w), 1457 (w), 1374 (w), 1276 (m), 1264 (s), 1231 (s), 1026 (m), 911 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{25}N_2O_2^+$ $[M+H]^+$ 337.1911; found 337.1911.

The analytical data match the literature report.[10]

[10] J. Qi, A. B. Beeler, Q. Zhang, J. A. Porco *J. Am. Chem. Soc.* **2010**, *132*, 13642-13644.

5-(Quinolin-3-yl)pent-4-yn-1-ol (**SI-37**).



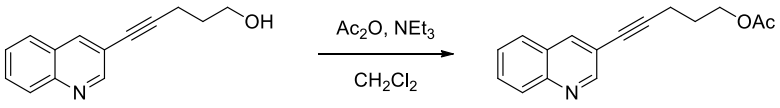
SI-35 **SI-36** **SI-37**

Following a modified procedure,[11] $Pd(PPh_3)_2Cl_2$ (0.14 g, 0.20 mmol, 5 mol%) and pent-4-yn-1-ol (**SI-36**) (1.86 mL, 20.0 mmol, 5 equiv.) were added to a solution of 3-bromo-quinoline (**SI-35**) (0.54 mL, 4.00 mmol, 1 equiv.) and CuI (76 mg, 0.40 mmol, 10 mol%) in triethylamine (8.00 mL, 0.5 M) at room temperature and the resulting mixture was then refluxed for 18 hours. Thereafter the reaction mixture was cooled to room temperature and filtered through a plug of Celite®. The filtrate was washed with brine (15 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 5:2) and 760 mg (3.60 mmol, 90%) of the title compound **SI-37** were isolated as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87 (s, 1H, Ar*H*), 8.19 (d, *J* = 1.6 Hz, 1H, Ar*H*), 8.12 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.77 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.71 (ddd, *J* = 8.3, 6.9, 1.6 Hz, 1H, Ar*H*), 7.56 (t, *J* = 6.9 Hz, 1H, Ar*H*), 3.86 (t, *J* = 6.1 Hz, 2H, C*H*$_2$-OH), 2.63 (t, *J* = 7.0 Hz, 2H, C≡C-C*H*$_2$), 1.92 (p, *J* = 6.6 Hz, 2H, CH_2-C*H*$_2$-CH_2);
^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.2, 146.3, 138.3, 129.9, 129.0, 127.4, 127.3, 127.2, 117.9, 93.2, 78.2, 61.5, 31.3, 16.1 ppm;
IR (film): $\tilde{\nu}$ = 3333 (w), 2946 (w), 2361 (w), 2231 (w), 1570 (w), 1490 (m), 1433 (w), 1350 (w), 1266 (m), 1126 (w), 1059 (s), 947 (w), 909 (s) cm^{-1};
HRMS (ESI) calcd. for $C_{14}H_{14}NO^+$ $[M+H]^+$ 212.1070; found 212.1075.

The analytical data match the literature report.[11]

5-(Quinolin-3-yl)pent-4-yn-1-yl acetate (**SI-38**).



SI-37 **SI-38**

Ac_2O was added to a solution of alcohol **SI-37** (200 mg, 0.947 mmol, 1 equiv.) and triethylamine (0.21 mL, 1.5 mmol, 1.6 equiv.) in CH_2Cl_2 (1.90 mL, 0.5 M) and the resulting mixture was stirred for 16 hours at room temperature. The reaction was quenched by the addition of sat. aq. $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The comb. org. extracts were washed with brine (20 mL) and

[11] A. Jean, J. Blanchet, J. Rouden, J. Maddalunob, M. de Paolis *Chem. Commun.* **2013**, *49*, 1651-1653.

dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 177 mg (0.70 mmol, 77%) of the title compound **SI-38** were isolated as a colorless oil.

R_f: 0.5 (silica, pentane:EtOAc 4:1);

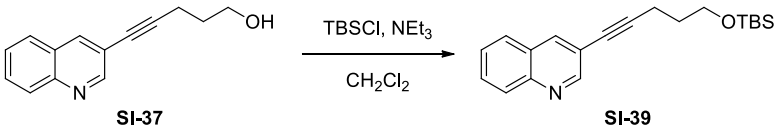
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 2.1 Hz, 1H, Ar*H*), 8.10 (d, *J* = 2.1 Hz, 1H, Ar*H*), 8.02 (dd, *J* = 8.3, 1.3 Hz, 1H, Ar*H*), 7.68 (dd, *J* = 8.3, 1.3 Hz, 1H, Ar*H*), 7.62 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H, Ar*H*), 7.47 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H, Ar*H*), 4.20 (t, *J* = 6.3 Hz, 2H, C*H*$_2$-OAc), 2.53 (t, *J* = 7.0 Hz, 2H, C≡C-C*H*$_2$), 2.02 (s, 3H, C(O)C*H*$_3$), 1.97 – 1.88 (m, 2H, CH_2-C*H*$_2$-CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.0, 152.2, 146.4, 138.2, 129.82, 129.1, 127.4, 127.3, 127.2, 117.8, 92.3, 78.5, 63.1, 27.65, 20.9, 16.3 ppm;

IR (film): $\tilde{\nu}$ = 2964 (w), 2901 (w), 2364 (w), 2327 (w), 2233 (w), 1736 (s), 1568 (w), 1490 (w), 1366 (m), 1238 (s), 1125 (w), 1043 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{16}H_{16}NO_2^+$ $[M+H]^+$ 254.1176; found 254.1185.

3-(5-((*tert*-Butyldimethylsilyl)oxy)pent-1-yn-1-yl)quinoline (**SI-39**).



SI-37 **SI-39**

TBSCl (214 mg, 1.42 mmol, 1.5 equiv.) was added to a solution of alcohol **SI-37** (200 mg, 0.947 mmol, 1 equiv.) and triethylamine (0.21 mL, 1.5 mmol, 1.6 equiv.) in CH_2Cl_2 (1.60 mL, 0.5 M) and the resulting mixture was stirred for 16 hours at room temperature. The reaction was quenched by the addition of sat. aq. NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The comb. org. extracts were washed with brine (20 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1) and 275 mg (0.85 mmol, 89%) of the title compound **SI-39** were isolated as a colorless oil.

R_f: 0.5 (silica, pentane:EtOAc 10:1);

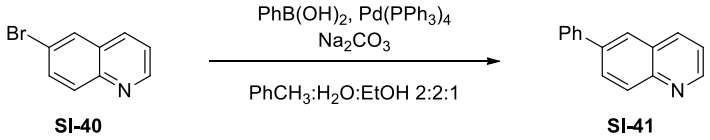
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87 (t, *J* = 1.6 Hz, 1H, Ar*H*), 8.16 (t, *J* = 2.6 Hz, 1H, Ar*H*), 8.11 – 8.04 (m, 1H, Ar*H*), 7.80 – 7.73 (m, 1H, Ar*H*), 7.69 (m, 1H, Ar*H*), 7.59 – 7.49 (m, 1H, Ar*H*), 3.85 – 3.71 (m, 2H, C*H*$_2$-OTBS), 2.57 (td, *J* = 7.0, 1.7 Hz, 2H, C≡C-C*H*$_2$), 1.92 – 1.78 (m, 2H, CH_2-C*H*$_2$-CH_2), 0.92 (s, 9H, Si-*tBu*), 0.09 (s, 6H, Si-*(CH$_3$)$_2$*);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.5, 146.5, 138.2, 129.9, 129.3, 127.6, 127.5, 127.3, 118.3, 93.8, 78.1, 61.6, 31.7, 26.1, 18.5, 16.1, -5.2 ppm.

IR (film): $\tilde{\nu}$ = 2953 (m), 2929 (m), 2856 (m), 2365 (w), 2233 (w), 1490 (w), 1472 (w), 1463 (w), 1276 (m), 1258 (s), 1103 (s), 1071 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{20}H_{28}NOSi^+$ $[M+H]^+$ 326.1935; found 326.1945.

6-Phenylquinoline (**SI-41**).



SI-40 **SI-41**

Following a modified procedure,[12] a mixture of 6-bromo-quinoline (**SI-40**) (0.70 mL, 5.00 mmol, 1 equiv.), sodium carbonate (2.12 g, 20.0 mmol, 4 equiv.), phenylboronic acid (732 mg, 6.00 mmol, 1.2 equiv.), water (4 mL), toluene (4 mL) and ethanol (2 mL) was degassed by nitrogen bubbling, then $Pd(PPh_3)_4$ (0.29 g, 0.25 mmol, 5 mol%) was added and the mixture was heated to 75 °C for 12 hours. Thereafter the mixture was filtered through a plug of celite®, the filtrate was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined org. extracts were washed with brine (20 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1 to 1:1) and 740 mg (3.61 mmol, 72%) of the title compound **SI-41** were isolated as a red-brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.93 (dd, *J* = 4.3, 1.7 Hz, 1H, Ar*H*), 8.23 (dt, *J* = 7.4, 2.6 Hz, 2H, Ar*H*), 8.04 – 7.95 (m, 2H, Ar*H*), 7.77 – 7.67 (m, 2H, Ar*H*), 7.51 (dd, *J* = 8.4, 6.9 Hz, 2H, Ar*H*), 7.47 – 7.38 (m, 2H, Ar*H*) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.0, 147.2, 140.2, 139.5, 136.6, 129.6, 129.4, 129.0, 128.5, 127.8, 127.4, 125.4, 121.4 ppm.

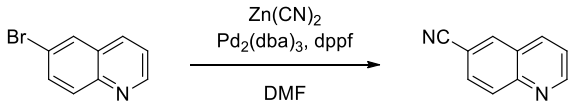
IR (film): $\tilde{\nu}$ = 3015 (w), 2326 (w), 1903 (w), 1775 (w), 1685 (w), 1591 (m), 1489 (s), 1444 (m), 1328 (m), 1276 (s), 1261 (s), 1188 (w), 1123 (m), 1040 (w), 891 (m), 845 (s) cm^{-1}.

HRMS (ESI) calcd. for $C_{15}H_{12}N^+$ $[M+H]^+$ 206.0964; found 206.0967.

The analytical data match the literature report.[12]

[12] L. Mengozzi, A. Gualandi, P.-G. Cozzi *Eur. J. Org. Chem*. **2016**, *19*, 3200-3207.

Quinoline-6-carbonitrile (**SI-42**).



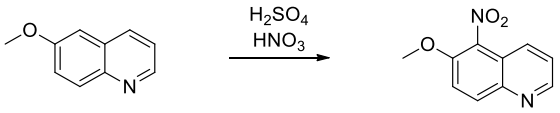
SI-40 **SI-42**

Following a modified procedure,[13] 6-bromoquinoline (**SI-40**) (0.70 mL, 5.00 mmol, 1 equiv.), $Zn(CN)_2$ (881 mg, 7.50 mmol, 1.5 equiv.) and dppf (0.28 mg, 0.50 mmol, 10 mol%) were dissolved in DMF (10 mL, 0.5 M), the mixture was degassed by N_2 bubbling for 10 minutes, then Pd_2dba_3 (0.23 g, 0.25 mmol, 5 mol%) was added and the mixture was heated to 130 °C for 14 hours. After cooling to room temperature the reaction was quenched with water (20 mL) and the mixture was extracted with EtOAc (3 x 20 mL). The comb. org. extracts were washed with brine (20 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by column chromatography (silica, pentane:EtOAc 5:1) and 581 mg (3.77 mmol, 75%) of the title compound **SI-42** were isolated as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.07 (dd, *J* = 4.3, 1.7 Hz, 1H, Ar*H*), 8.30 – 8.16 (m, 3H, Ar*H*), 7.88 (dd, *J* = 8.7, 1.7 Hz, 1H, Ar*H*), 7.56 (dd, *J* = 8.4, 4.3 Hz, 1H, Ar*H*);
^{13}C NMR (101 MHz, $CDCl_3$): δ = 153.1, 149.0, 136.5, 134.1, 131.0, 130.2, 127.6, 122.7, 118.5, 110.5 ppm.
IR (film): $\tilde{\nu}$ = 2987 (s), 2901 (m), 2328 (w), 1764 (w), 1699 (w), 1543 (w), 1509 (w), 1413 (m), 1339 (m), 1233 (s), 1059 (s) cm^{-1};
HRMS (ESI) calcd. for $C_{10}H_7N_2^+$ $[M+H]^+$ 155.0604; found 155.0603.

The analytical data match the literature report.[13]

6-Methoxy-5-nitroquinoline (**SI-44**).



SI-43 **SI-44**

Following a modified procedure,[14] 6-methoxy-quinoline (**SI-43**) (1.00 mL, 7.22 mmol) was added dropwise to a mixture of H_2SO_4 (4.00 mL) and HNO_3 (4.00 mL) at 0 °C and the resulting mixture was stirred for 1 hour. The reaction was basified with sat. aq. Na_2CO_3 and extracted with CH_2Cl_2 (3 x 50 mL). The comb. org. extracts were washed with brine (50 mL) and dried over $MgSO_4$. The drying agent was

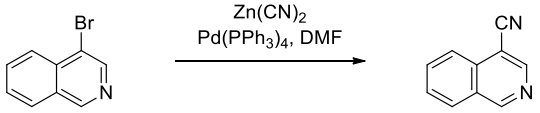
[13] F. Zhao, J. Zhang, L. Zhang, Y. Hao, C. Shi, G. Xia, J. Yu, , Y. Liu *Bioorg.Med. Chem.* **2016**, *24,* 4281-4290.
[14] H.-Y. Lee, J.-Y. Chang, C.-Y. Nien, C.-C. Kuo, K.-H. Shih, C.-H. Wu, C.-Y. Chang, W.-Y. Lai, J.-P. Liou *J. Med. Chem.* **2011**, *54*, 8517-8525.

filtered off and the solvent was evaporated. The crude product was purified by column chromatography (SiO_2, pentane:EtOAc 1:1) and 1.14 g (5.58 mmol, 77%) of the title compound **SI-44** were isolated as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (dd, *J* = 4.1, 1.5 Hz, 1H, Ar*H*), 8.28 (d, *J* = 9.5 Hz, 1H, Ar*H*), 8.08 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.59 (d, *J* = 9.5Hz, 1H, Ar*H*), 7.53 (dd, *J* = 8.7, 4.1 Hz, 1H, Ar*H*), 4.08 (s, 3H, OCH_3).
^{13}C NMR (101 MHz, $CDCl_3$): δ = 149.5, 149.2, 142.3, 134.6, 134.1, 129.2, 123.6, 121.4, 116.3, 57.2 ppm;
IR (film): $\tilde{\nu}$ = 2978 (s), 2909 (m), 2350 (w), 1648 (w), 1516 (w), 1389 (w), 1245 (w), 1068 (s), 878 (w) cm^{-1};
HRMS (ESI) calcd. for $C_{10}H_9N_2O_3^+$ $[M+H]^+$ 205.0608; found 205.0612.

The analytical data match the literature report.[14]

Isoquinoline-4-carbonitrile (**SI-46**).



SI-45 **SI-46**

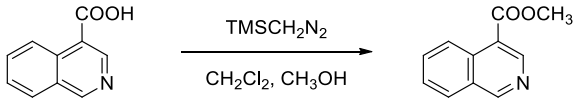
Following a modified procedure,[15] $Pd(PPh_3)_4$ (0.29 g, 0.25 mmol, 8 mol%) was added in one portion to a solution of 4-bromoisoquinoline (**SI-45**) (624 mg, 3.00 mmol, 1 equiv.) and $Zn(CN)_2$ (352 mmol, 3.00 mmol, 1 equiv.) in DMF (5 mL, 0.6 M) and the resulting mixture was heated to 80 °C for 16 hours. The reaction was quenched with sat. aq. Na_2CO_3 (10 mL) and the mixture was extracted 3 times with CH_2Cl_2 (10 mL). The combined org. extracts were washed with brine (15 mL) and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 4:1) and 412 mg (2.67 mmol, 89%) of the title compound **SI-46** were isolated as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.30 (s, 1H, Ar*H*), 8.76 (s, 1H, Ar*H*), 8.07 – 7.92 (m, 2H, Ar*H*), 7.81 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H, Ar*H*), 7.68 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H, Ar*H*);
^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.9, 147.9, 134.0, 132.7, 128.9, 128.2, 127.1, 123.6, 115.6, 105.5;
IR (film): $\tilde{\nu}$ = 3058 (w), 2230 (m), 1623 (m), 1578 (w), 1502 (m), 1390 (m), 1380 (m), 1268 (s), 1221 (w), 1149 (w), 909 (m) cm^{-1};
HRMS (ESI) calcd. for $C_{10}H_7N_2^+$ $[M+H]^+$ 155.0604; found 155.0602.

The analytical data match the literature report.[15]

[15] J. C. Barrow, B. D. Dorsey, H. G. Selnick, P. L. Ngo WO2001070229 A1.

Methyl isoquinoline-4-carboxylate (**SI-48**).



SI-47 **SI-48**

TMS diazomethane (1.08 mL, 2.17 mmol, 2 M in Et_2O) was added dropwise to a suspension of isoquinoline-4-carboxylic acid **SI-47** (250 mg, 1.44 mmol) in CH_2Cl_2 (10 mL) and CH_3OH (4 mL) at 0 °C. The resulting mixture was stirred for 16 hours while warming to room temperature, then the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 3:1) affording 232 mg (1.24 mmol, 86%) of the title compound **SI-48** as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.38 (s, 1H), 9.19 (s, 1H), 8.96 (dq, *J* = 8.8, 0.9 Hz, 1H), 8.05 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.91 – 7.81 (m, 1H), 7.69 (m, 1H), 4.04 (s, 3H);

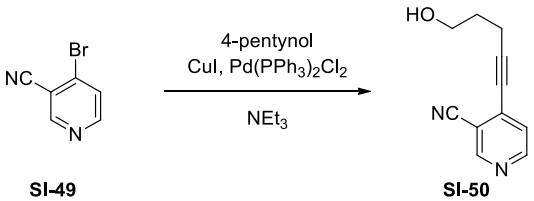
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.8, 156.9, 146.7, 133.9, 132.3, 128.4, 128.3, 127.7, 125.0, 120.5, 52.3;

IR (film): $\tilde{\nu}$ = 3014 (w), 2958 (w), 1722 (s), 1624 (w), 1572 (w), 1505 (m), 1436 (m), 1378 (w), 1294 (s), 1238 (w), 1208 (s), 1143 (m), 1045 (m), 1023 (w), 918 (w), 866 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{11}H_{10}NO_2^+$ $[M+H]^+$ 188.0706; found 188.0713.

The analytical data match the literature report.[16]

4-(5-Hydroxypent-1-yn-1-yl)nicotinonitrile (**SI-50**).



SI-49 **SI-50**

4-Pentynol (712 µL, 7.65 mmol, 4 equiv.) was added to a degassed (pump and freeze, 3 cycles) solution of 4-bromonicotinonitrile (**SI-49**) (350 mg, 1.91 mmol, 1 equiv.) $Pd(PPh_3)_2Cl_2$ (67 mg, 10 µmol, 5 mol%) and CuI (36 mg, 0.19 mmol, 10 mol%) in NEt_3 (3.8 mL, 0.5 M) and the resulting mixture was heated to 40 °C for 1.5 hours. After cooling to room temperature, sat. aq. NH_4Cl (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined org. extracts were washed with brine and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 1:1 to 1:2) and 332 mg (1.78 mmol, 93%) of the title compound **SI-50** were isolated as an orange oil.

[16] J. R. Martinelli, D. A. Watson, D. M. Freckmann, T. E. Barder, S. L. Buchwald *J. Org. Chem.* **2008**, *73*, 7102-7107.

R_f: 0.2 (silica, pentane:EtOAc 1:1);

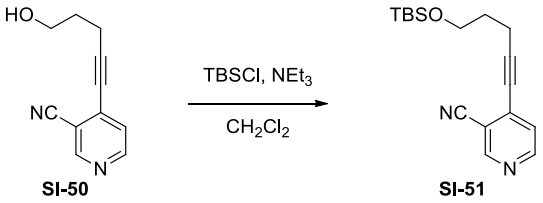
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (s, 1H, Ar*H*), 8.69 (d, *J* = 5.2 Hz, 1H, Ar*H*), 7.36 (d, *J* = 5.2 Hz, 1H, Ar*H*), 3.85 (t, *J* = 6.1 Hz, 2H, C*H*$_2$OH), 2.67 (t, *J* = 6.9 Hz, 2H, C≡C-C*H*$_2$), 1.91 (p, *J* = 6.5 Hz, 3H, C*H*$_2$ and O*H* underneath);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.5, 152.3, 135.6, 125.5, 115.8, 112.2, 103.4, 75.9, 61.0, 30.6, 16.2 ppm.

IR (film): $\tilde{\nu}$ = 3396 (w), 2932 (w), 2877 (w), 2235 (m), 1584 (s), 1537 (w), 1486 (w), 1409 (w), 1186 (w), 1058 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{11}H_{11}N_2O^+$ $[M+H]^+$ 187.0866; found 187.0865.

4-(5-((*tert*-Butyldimethylsilyl)oxy)pent-1-yn-1-yl)nicotinonitrile (**SI-51**).



TBSCl (389 mg, 2.58 mmol, 1.5 equiv.) was added to a solution of **SI-50** (320 mg, 1.78 mmol, 1 equiv.) and NEt_3 (480 µL, 3.44 mmol, 2 equiv.) in CH_2Cl_2 (3.4 mL) at room temperature and the mixture was stirred for 16 hours. The reaction was quenched with sat. aq. NH_4Cl (15 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined org. extracts were washed with brine and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 5:1) and 404 mg (1.35 mmol, 78%) of the title compound **SI-51** were isolated as an orange oil.

R_f: 0.7 (silica, pentane:EtOAc 2:1);

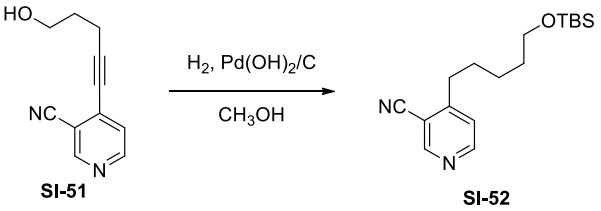
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (d, *J* = 0.9 Hz, 1H, Ar*H*), 8.68 (d, *J* = 5.3 Hz, 1H, Ar*H*), 7.35 (dd, *J* = 5.3, 0.9 Hz, 1H, Ar*H*), 3.77 (t, *J* = 5.9 Hz, 2H, C*H*$_2$OTBS), 2.63 (t, *J* = 7.1 Hz, 2H, C≡C-C*H*$_2$), 1.86 (tt, *J* = 7.1, 5.9 Hz, 2H, C*H*$_2$), 0.90 (s, 9H, C(C*H*$_3$)$_3$), 0.07 (s, 6H, Si(C*H*$_3$)$_2$);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.6, 152.2, 135.7, 125.6, 115.7, 112.1, 104.0, 75.6, 61.2, 31.1, 25.9, 18.3, 16.2, -5.4 ppm;

IR (film): $\tilde{\nu}$ = 2956 (m), 2931 (w), 2855 (w), 2236 (w), 1583 (m), 1537 (w), 1485 (w), 1408 (w), 1107 (s), 838 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{17}H_{25}N_2OSi^+$ $[M+H]^+$ 301.1731; found 301.1730.

4-(5-((*tert*-Butyldimethylsilyl)oxy)pentyl)nicotinonitrile (**SI-52**).



$Pd(OH)_2/C$ (34 mg, 20% Pd, 10%$_{w/w}$) was added to a solution of **SI-51** (340 mg, 1.13 mmol) in CH_3OH (2.3 mL, 0.5 M) and the resulting mixture was purged with hydrogen and thereafter stirred for 18 hours under H_2-atmosphere (1 atm). Then the mixture was filtered through a plug of Celite® and concentrated. The residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 5:1) affording 243 mg (0.80 mmol, 71%) of the title compound **SI-52** as a colorless oil.

R_f: 0.7 (silica, pentane:EtOAc 2:1);

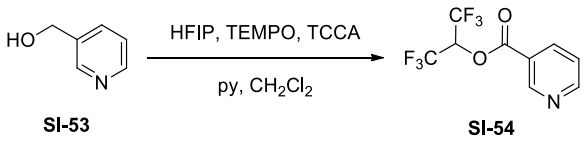
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 0.8 Hz, 1H, Ar*H*), 8.65 (d, *J* = 5.2 Hz, 1H, Ar*H*), 7.26 (dd, *J* = 5.2, 0.8 Hz, 1H, Ar*H*), 3.60 (t, *J* = 6.3 Hz, 2H, CH_2OTBS), 2.90 – 2.77 (m, 2H, Ar-CH_2), 1.76 – 1.65 (m, 2H CH_2), 1.60 – 1.50 (m, 2H CH_2), 1.47 – 1.36 (m, 2H CH_2), 0.86 (s, 9H, C(CH_3)$_3$), 0.02 (s, 6H Si(CH_3)$_2$) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 155.3, 152.9, 152.5, 123.9, 115.9, 110.4, 62.7, 34.0, 32.3, 29.6, 25.9, 25.4, 18.3, -5.3 ppm.

IR (film): $\tilde{\nu}$ = 2931 (w), 2857 (w), 2229 (w), 1590 (w), 1556 (w), 1472 (w), 1463 (w), 1407 (w), 1255 (m), 834 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{17}H_{25}N_2OSi^+$ $[M+H]^+$ 301.1731; found 301.1730.

1,1,1,3,3,3-Hexafluoropropan-2-yl nicotinate (**SI-54**).



Following a modified procedure,[17] TEMPO (161 mg, 1.03 mmol, 5 mol%) followed by trichloroisocyanuric acid (5.75 g, 24.7 mmol, 1.2 equiv.) were added to a solution of pyridine-3-ylmethanol (**SI-53**) (2.00 mL, 20.6 mmol, 1 equiv.) in CH_2Cl_2 (41.2 mL, 0.5 M) at 0 °C and the resulting mixture was stirred for 2 hours. Thereafter pyridine (6.70 mL, 82.0 mmol, 4 equiv.) followed by 1,1,1,3,3,3-hexafluoropropan-2-ol (4.40 mL, 41.2 mmol, 2 equiv.) were added and stirring was continued for 16 hours at room temperature. The reaction mixture was filtered through a plug of

[17] J.-M. Vatéle *Synlett* **2015**, *26*, 2280-2284.

Celite® and concentrated. The residue was purified by column chromatography (silica, pentane:EtOAc 5:1) affording 4.53 g (16.6 mmol, 81%) of the title compound **SI-54** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.28 (dd, *J* = 2.2, 0.8 Hz, 1H, Ar*H*), 8.86 (dd, *J* = 4.9, 1.7 Hz, 1H, Ar*H*), 8.42 (ddd, *J* = 8.0, 2.2, 1.7 Hz, 1H, Ar*H*), 7.54 (ddd, *J* = 8.0, 4.9, 0.8 Hz, 1H, Ar*H*), 6.02 (p, *J* = 6.0 Hz, 1H, C*H*$(CF_3)_2$);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.9, 154.5, 151.0, 138.3, 124.0, 123.4, 120.7 (q, *J* = 282.6 Hz), 67.1 (p, *J* = 67.2 Hz);

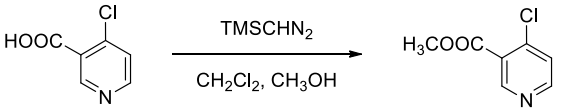
^{19}F NMR (376 MHz, $CDCl_3$): δ = -75.60 (d, *J* = 5.8 Hz);

IR (film): $\tilde{\nu}$ = 1764 (m), 1595 (w), 1426 (w), 1386 (w), 1361 (w), 1297 (m), 1266 (m), 1197 (s), 1101 (s), 1017 (w), 912 (m) cm^{-1};

HRMS (ESI) calcd for $C_9H_6F_6NO_2^+$ $[M+H]^+$ 274.0297; found 274.0300.

The analytical data match the literature report.[18]

Methyl 4-chloronicotinate (**SI-56**).



SI-55 **SI-56**

Following a modified procedure,[19] trimethylsilyldiazomethane (4.76 mL, 9.52 mmol, 1.5 equiv.) was added dropwise to a suspension of chloronicotinic acid (**SI-55**) (1.00 g, 6.35 mmol, 1 equiv.) in a mixture of CH_2Cl_2 (5.5 mL) and methanol (2.2 mL) at 0 °C. The resulting mixture was warmed to room temperature and stirred for 1 hour, then concentrated and the residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 5:1) affording 1.02 g (5.92 mmol, 93%) of the title compound **SI-56** as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.03 (t, *J* = 0.6 Hz, 1H), 8.58 (dd, *J* = 5.4, 0.6 Hz, 1H), 7.49 – 7.28 (m, 1H), 3.97 (s, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.2, 152.6, 152.2, 144.2, 125.9, 125.8, 52.7 ppm;

IR (film): $\tilde{\nu}$ = 3003 (w), 2953 (w), 1725 (s), 1627 (w), 1573 (m), 1436 (m), 1292 (s), 1275 (s), 1130 (m), 1082 (s), 1046 (w), 955 (w), 832 (m) cm^{-1};

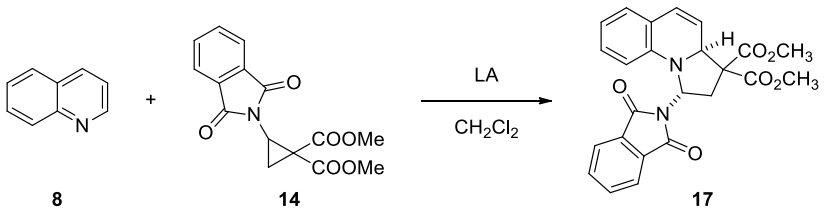
HRMS (ESI) calcd. for $C_7H_7ClNO_2^+$ $[M+H]^+$ 172.0160; found 172.0161.

The analytical data match the literature report.[19]

[18] C. B. Kelly, M. A. Mercadante, R. J. Wiles, N. E. Leadbeater *Org. Lett.* **2013**, *15*, 2222-2225.
[19] D. Norton, D. Andreotti, S. E. Ward, R. Profeta, S. Spada, H. S. Price WO 2012098400 A1.

6. Optimization of the reaction

Table S7 Optimization of the annulation of quinoline (**8**) and cyclopropane **14**.



8 **14** **17**

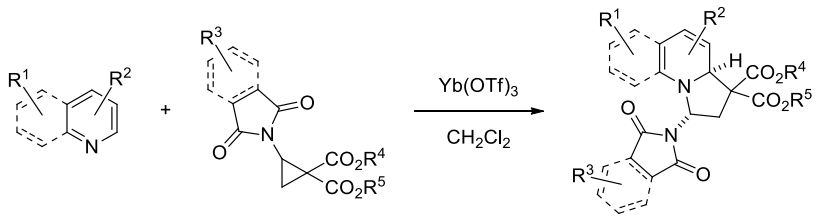
Entry	14	Lewis Acid (mol%)	Conc.	Result[a]	Comment[b]
1	1.0 equiv.	$Sc(OTf)_3$ (20 mol%)	0.1 M	30% of **17**	full conversion of cyclopropane
2	1.0 equiv.	$Sc(OTf)_3$ (20 mol%)	0.05 M	62% of **17**	full conversion of cyclopropane
3	1.5 equiv.	$Sc(OTf)_3$ (20 mol%)	0.1 M	69% of **17**	full conversion of cyclopropane
4	1.5 equiv.	$Sc(OTf)_3$ (20 mol%)	0.05 M	80% of **17**	full conversion of cyclopropane
5	1.5 equiv.	$Sn(OTf)_2$ (20 mol%)	0.05 M	no conversion	
6	1.5 equiv.	$In(OTf)_3$ (20 mol%)	0.05 M	no conversion	
7	1.5 equiv.	$Cu(OTf)_2$ (20 mol%)	0.05 M	no conversion	
8	1.5 equiv.	$Hf(OTf)_4$ (20 mol%)	0.05 M	decomposition	
9	1.5 equiv.	$FeCl_3$ (20 mol%)	0.05 M	no conversion	
10	1.5 equiv.	$FeCl_2$ (20 mol%)	0.05 M	no conversion	
11	1.5 equiv.	$InCl_3$ (20 mol%)	0.05 M	no conversion	
12	1.5 equiv.	$MgCl_2$ (20 mol%)	0.05 M	no conversion	
13	1.5 equiv.	$Yb(OTf)_3$ (20 mol%)	0.05 M	90% of **17**	remaining cyclopropane
14	1.1 equiv.	$Yb(OTf)_3$ (20 mol%)	0.05 M	88% of **17**	
15	1.05 equiv.	$Yb(OTf)_3$ (10 mol%)	0.05 M	89% of **17**	reaction time: 2 days
16	1.05 equiv.	$Yb(OTf)_3$ (5 mol%)	0.05 M	96% of **17**	reaction time: 4 days
17	1.05 equiv.	$Yb(OTf)_3$ (5 mol%)	0.5 M	96% of **17**	reaction time: 16 hours
18	1.05 equiv.	HOTf (20 mol%)	0.2 M	no conversion	

[a] Yields determined by isolation; [b] remaining cyclopropane was detected by TLC.

Experimental procedure for optimization

A vial was charged with cyclopropane **14**, the Lewis acid and quinoline **8** (0.10 mmol, 1.00 equiv.) in the glovebox, then capped, removed from the glovebox and CH_2Cl_2 was added. The mixture was stirred, if not stated otherwise in the table, for 16 hours, then concentrated and the residue was purified by column chromatography.

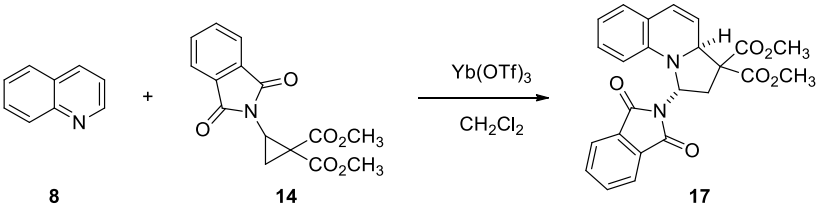
7. General procedure



A vial was charged with cyclopropane (0.21 mmol, 1.05 equiv.), $Yb(OTf)_3$ (0.01 mmol, 5 mol% or 0.02 mmol, 10 mol%) and the *N*-heterocyclic compound (0.20 mmol, 1.00 equiv.) in the glovebox, then capped, removed from the glovebox and CH_2Cl_2 was added. The mixture was stirred for the indicated time, then concentrated and the residue was purified by column chromatography to afford the title compound.

8. Scope of the reaction with quinolines

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**17**).



8 **14** **17**

Following the general procedure quinoline (**8**) (260 mg, 2.00 mmol, 1.00 equiv.), cyclopropane **14** (640 mg, 2.10 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (62 mg, 0.10 mmol, 5 mol%) were stirred in CH_2Cl_2 (4.0 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 820 mg (1.90 mmol, 95%) of the title compound **17** were isolated as a yellow oil which was crystallized from EtOAc by overlaying it with pentane.

Performing the reaction with quinoline **8** (26 mg, 0.20 mmol), **14** (64 mg, 0.21 mmol) and $Yb(OTf)_3$ (6 mg, 0.01 mmol) afforded 83 mg (0.19 mmol, 96%) of the title compound **17**.

mp: 127-129 °C;

R_f: 0.3 (silica, pentane:EtOAc 4:1);

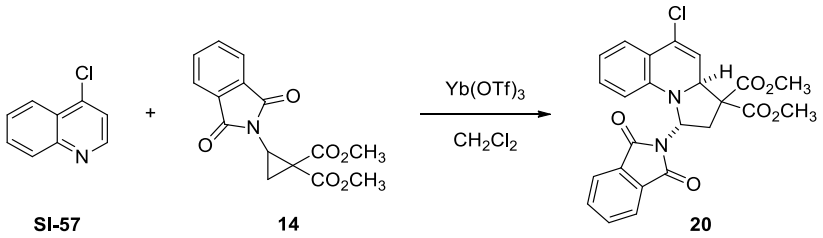
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.95 (td, *J* = 7.9, 1.6 Hz, 1H, Ar*H*), 6.78 (dd, *J* = 7.4, 1.6 Hz, 1H, Ar*H*), 6.55 (td, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 6.42 (d, *J* = 7.9 Hz, 1H, Ar*H*), 6.30 (dd, *J* = 10.2, 2.0 Hz, 1H, C=C*H*), 6.21 (dd, *J* = 8.6, 5.9 Hz, 1H, N-C*H*-Phth), 5.94 (t, *J* = 2.5 Hz, 1H, C*H*-N), 5.85 (dd, *J* = 10.2, 2.9 Hz, 1H, CH=C*H*), 3.82 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 2.98 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.53 (dd, *J* = 13.7, 5.9 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.0, 169.1, 167.7, 141.6, 134.3, 131.7, 129.5, 127.2, 126.2, 123.4, 120.4, 119.4, 118.0, 109.7, 67.3, 65.3, 64.4, 52.7, 52.6, 35.3 ppm;

IR (film): $\tilde{\nu}$ = 3050 (w), 2996 (w), 2953 (w), 1721 (s), 1604 (w), 1497 (w), 1458 (w), 1442 (w), 1390 (w), 1357 (m), 1321 (m), 1273 (s), 1222 (w), 1141 (w), 1078 (w), 969 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{20}N_2NaO_6^+$ $[M+Na]^+$ 455.1214; found 455.1223.

***anti*-Dimethyl 5-chloro-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**20**).



SI-57 **14** **20**

Following the general procedure 4-chloroquinoline (**SI-57**) (33 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 84 mg (0.18 mmol, 90%) of the title compound **20** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 4:1);

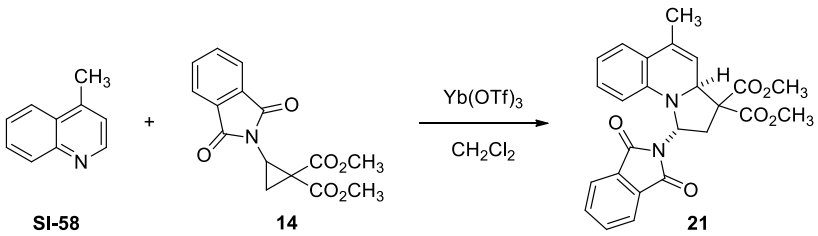
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.32 (dd, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 7.03 (td, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 6.63 (td, *J* = 7.5, 1.0 Hz, 1H, Ar*H*), 6.44 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.20 (dd, *J* = 8.6, 5.9 Hz, 1H, C*H*-Phth), 6.06 (d, *J* = 3.3 Hz, 1H, C*H*=CCl), 5.97 (d, *J* = 3.3 Hz, 1H, C*H*-N), 3.83 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 3.00 (dd, *J* = 13.8, 8.6 Hz, 1H, CH_2), 2.51 (dd, *J* = 13.8, 5.9 Hz, 1H, CH_2) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.6, 168.7, 167.6, 142.1, 134.4, 131.5, 130.8, 129.6, 125.2, 123.5, 118.2, 118.1, 117.1, 109.9, 67.1, 65.1, 65.0, 52.9, 52.8, 35.0 ppm;

IR (film): $\tilde{\nu}$ = 2955 (w), 2925 (w), 2852 (w), 1772 (w), 1732 (s), 1710 (s), 1647 (w), 1598 (w), 1491 (m), 1458 (w), 1436 (w), 1396 (w), 1354 (w), 1276 (m), 1266 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{20}ClN_2O_6^+$ $[M+H]^+$ 467.1004; found 467.0997.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-5-methyl-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**21**).



SI-58 **14** **21**

Following the general procedure lepidine (**SI-58**) (29 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 83 mg (0.19 mmol, 93%) of the title compound **21** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 4:1);

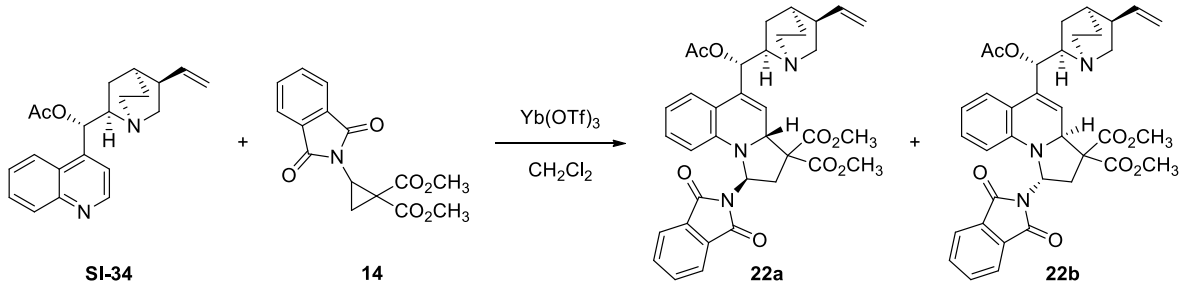
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.98 (td, *J* = 7.3, 1.3 Hz, 2H, Ar*H*), 6.60 (td, *J* = 7.3, 1.3 Hz, 1H, Ar*H*), 6.44 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.22 (dd, *J* = 8.6, 5.9 Hz, 1H, C*H*-Phth), 5.87 (dd, *J* = 3.1, 1.6 Hz, 1H, C*H*-N), 5.73 (dd, *J* = 3.1, 1.6 Hz, 1H, C*H*=CCH$_3$), 3.82 (s, 3H, OC*H$_3$*), 3.59 (s, 3H, OC*H$_3$*), 2.98 (dd, *J* = 13.7, 8.6 Hz, 1H, C*H$_2$*), 2.51 (dd, *J* = 13.7, 5.9 Hz, 1H, C*H$_2$*), 1.98 (t, *J* = 1.6 Hz, 3H, C*H$_3$*);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.0, 169.3, 167.7, 141.8, 134.3, 131.7, 130.7, 129.3, 123.8, 123.4, 120.6, 117.8, 117.8, 109.7, 67.6, 65.2, 64.1, 52.7, 52.5, 35.3, 19.0;

IR (film): $\tilde{\nu}$ 2987 (s), 2972 (s), 2902 (m), 2362 (w), 1717 (w), 1406 (w), 1395 (w), 1384 (w), 1276 (w), 1258 (w), 1231 (w), 1076 (s), 1066 (s), 1057 (s) cm^{-1};

HRMS (ESI) calcd for $C_{25}H_{23}N_2O_6^+$ $[M+H]^+$ 447.1551; found 447.1548.

(1*R*,3a*R*)-Dimethyl 5-((*S*)-acetoxy((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**22a**) and **(1*S*,3a*S*)-dimethyl 5-((*S*)-acetoxy((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**22b**)



SI-34 **14** **22a** **22b**

Following the general procedure **SI-34** (67 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, EtOAc:CH_3OH 30:1 to 20:1) and 97 mg (0.15 mmol, 76%) of the title compounds **22a** and **22b** were isolated as a yellow oil and 1:1 mixture of diastereoisomers.[20]

R_f: 0.1 (silica, EtOAc: CH_3OH 30:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 5.7 Hz, 4H), 7.78 – 7.69 (m, 4H), 7.18 (m, 2H, Ar*H*), 7.00 (m, 2H, Ar*H*), 6.63 (m, 2H, Ar*H*), 6.44 (m, 2H, Ar*H*), 6.17 (m, 2H, C*H*-Phth), 6.06 – 5.87 (m, 6H, =C*H*-N, C*H*-O and C*H*=CH_2), 5.84 (d, *J* = 8.1 Hz, 2H, C=C*H*), 5.29 – 4.96 (m, 4H, =CH_2), 3.82 (m, 6H, OCH_3), 3.62 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3), 3.23 – 2.86 (m, 12H, 3 x CH_2), 2.63 – 2.27 (m, 4H, CH_2), 2.14 (s, 6H, C(O)CH_3), 1.97 – 1.43 (m, 10H, CH_2, 3 x CH);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.0, 169.6, 169.2, 169.1, 168.7, 167.8, 167.7, 142.0, 141.6, 139.1, 138.7, 134.4, 132.7, 132.2, 131.6, 130.0, 129.7, 123.5, 123.1, 118.5, 118.1, 117.4, 116.8, 115.9, 115.6, 110.4, 67.9, 66.5, 65.3, 64.7, 64.0, 63.7, 57.4, 57.3, 53.1, 52.9, 52.8, 52.7, 50.0, 49.8, 49.2, 49.0, 38.8, 38.5, 35.7, 34.9, 27.8, 27.7, 25.4, 25.1, 21.2, 21.2;[21]

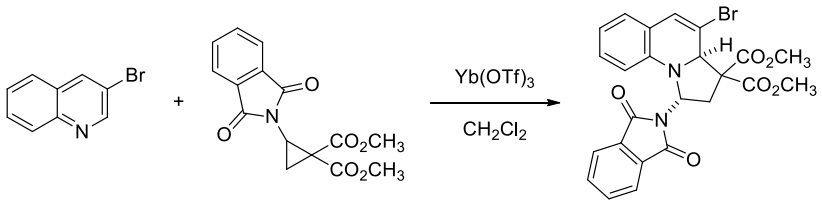
IR (film): $\tilde{\nu}$ 2987 (w), 2958 (w), 2902 (w), 1732 (s), 1714 (s), 1599 (w), 1498 (w), 1458 (w), 1437 (w), 1396 (w), 1363 (w), 1328 (w), 1268 (m), 1231 (s), 1211 (m), 1126 (w), 1105 (w), 1078 (m), 1031 (m), 967 (w), 919 (w), 879 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{36}H_{38}N_3O_8^+$ $[M+H]^+$ 640.2653; found 640.2647.

[20] The diastereomeric ratio was determined by integration of the methyl esters in the ^{1}H-NMR. Both the diastereoisomers were not individually assigned due to overlapping signals in ^{1}H-NMR.

[21] Some olefinic carbons are overlapping.

***anti*-Dimethyl 4-bromo-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**23**).



SI-35 **14** **23**

Following the general procedure 6-bromoquinoline (**SI-35**) (41 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 94 mg (0.18 mmol, 92%) of the title compound **23** were isolated as an orange oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);

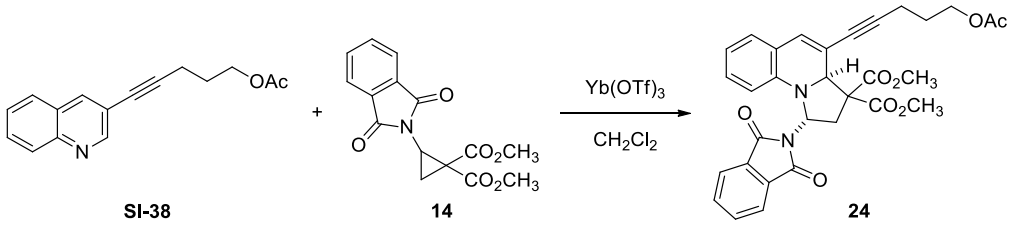
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.05 – 6.90 (m, 1H, Ar*H*), 6.76 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 6.74 – 6.65 (m, 1H, C*H*=CBr), 6.58 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 6.42 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.28 (d, *J* = 1.4 Hz, 1H, C*H*-N), 6.15 (dd, *J* = 8.4, 7.0 Hz, 1H, C*H*-Phth), 3.84 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 3.11 (dd, *J* = 13.0, 8.4 Hz, 1H, CH_2), 2.72 (dd, *J* = 13.0, 7.0 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 168.4, 167.5, 140.2, 134.4, 131.6, 130.0, 129.5, 126.8, 123.6, 118.9, 118.6, 115.4, 109.7, 70.5, 66.8, 65.5, 52.9, 52.7, 37.1 ppm;

IR (film): $\tilde{\nu}$ = 2955 (w), 2901 (w), 1772 (w), 1731 (m), 1714 (s), 1598 (w), 1495 (m), 1398 (w), 1365 (w), 1352 (w), 1264 (s), 1229 (w), 1134 (m), 1079 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{18}BrN_2O_6$ [M+] 509.0343; found 509.0359.

***anti*-Dimethyl 4-(5-acetoxypent-1-yn-1-yl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**24**).



SI-38 **14** **24**

Following the general procedure **SI-38** (51 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M)

for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 88 mg (0.16 mmol, 79%) of the title compound **24** were isolated as a yellow oil.

R_f: 0.2 (silica, pentane:EtOAc 4:1);

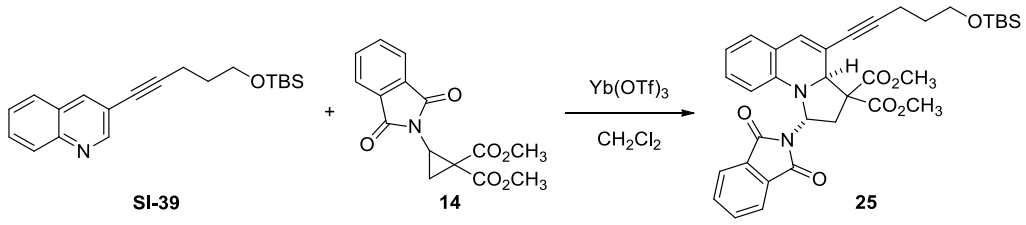
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.93 (td, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 6.75 (dd, *J* = 7.4, 1.5 Hz, 1H, Ar*H*), 6.54 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.50 (d, *J* = 1.5 Hz, 1H, C*H*=C), 6.38 (d, *J* = 8.0 Hz, 1H, Ar*H*), 6.17 – 6.08 (m, 2H, C*H*-N and C*H*-Phth), 4.19 (t, *J* = 6.3 Hz, 2H, CH_2-O), 3.80 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.04 (dd, *J* = 13.1, 8.4 Hz, 1H, CH_2), 2.63 (dd, *J* = 13.1, 6.5 Hz, 1H, CH_2), 2.45 (t, *J* = 7.0 Hz, 2H, C≡C-CH_2), 2.06 (s, 3H, COCH_3), 1.88 (p, *J* = 6.7 Hz, 2H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.9, 169.3, 168.7, 167.5, 140.9, 134.3, 131.6, 131.4, 130.0, 127.2, 123.5, 123.4, 119.2, 118.3, 114.5, 109.5, 91.9, 79.1, 67.0, 66.6, 65.1, 63.1, 52.6, 52.5, 37.3, 27.6, 20.9, 16.4 ppm;

IR (film): $\tilde{\nu}$ 2954 (w), 2851 (w), 1773 (w), 1731 (s), 1711 (s), 1597 (w), 1495 (w), 1459 (w), 1436 (w), 1397 (w), 1365 (w), 1353 (w), 1259 (s), 1242 (s), 1134 (w), 1075 (w), 1044 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{23}H_{24}NO_6$ [M+] 410.1598; found 410.1605.

***anti*-Dimethyl 4-(5-((*tert*-butyldimethylsilyl)oxy)pent-1-yn-1-yl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**25**).



Following the general procedure **SI-39** (65 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 6:1) and 88 mg (0.16 mmol, 81%) of the title compound **25** were isolated as a yellow oil.

R_f: 0.5 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.93 (td, *J* = 7.6, 1.5 Hz, 1H, Ar*H*), 6.76 (dd, *J* = 7.6, 1.5 Hz, 1H, Ar*H*), 6.60 – 6.51 (m, 1H, Ar*H*), 6.49 (d, *J* = 1.5 Hz, 1H, C*H*=C), 6.38 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.17 – 6.08 (m, 2H, C*H*-N and C*H*-Phth), 3.81 (s, 3H, OCH_3), 3.72 (t, *J* = 6.0 Hz, 2H, CH_2O), 3.65 (s, 3H, OCH_3), 3.05 (dd, *J* = 13.1, 8.4 Hz, 1H, CH_2), 2.67 (dd, *J*

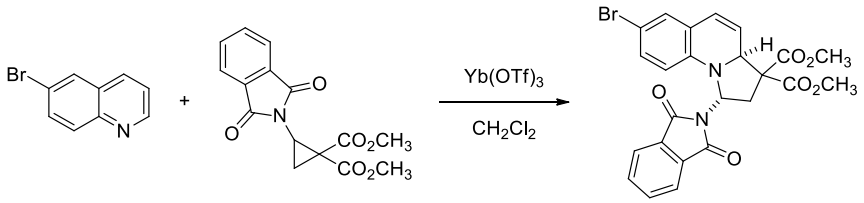
= 13.1, 6.6 Hz, 1H, CH_2), 2.43 (t, *J* = 7.2 Hz, 2H, C≡CCH_2), 1.81 – 1.72 (m, 2H, CH_2), 0.90 (s, 9H, SiC$(CH_3)_3$), 0.07 (s, 6H, Si$(CH_3)_2$);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 168.7, 167.5, 140.9, 134.3, 131.7, 130.9, 129.9, 127.2, 123.5, 119.4, 118.3, 114.9, 109.5, 93.3, 78.5, 67.2, 66.6, 65.2, 61.7, 52.6, 52.5, 37.4, 31.8, 25.9, 18.3, 16.1, -5.4;

IR (film): $\tilde{\nu}$ 2953 (w), 2946 (w), 2856 (w), 1773 (w), 1731 (s), 1714 (s), 1598 (w), 1495 (w), 1460 (w), 1354 (w), 1289 (w), 1259 (m), 1134 (w), 1099 (m), 1076 (m), 836 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{27}H_{36}NO_5Si$ [M+] 482.2357; found 482.2363.

***anti*-Dimethyl 7-bromo-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**26**).



SI-40 **14** **26**

Following the general procedure 6-bromoquinoline (**SI-40**) (42 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 98 mg (0.19 mmol, 96%) of the title compound **26** were isolated as an orange oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);

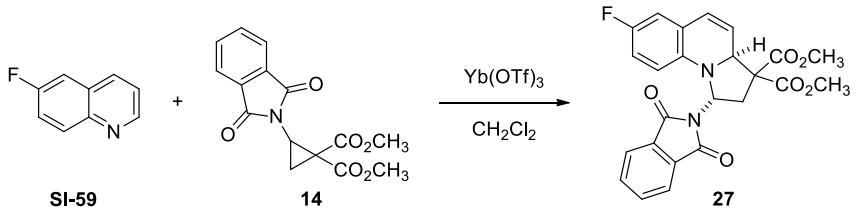
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.00 (dd, *J* = 8.6, 2.4 Hz, 1H, Ar*H*), 6.86 (d, *J* = 2.4 Hz, 1H, Ar*H*), 6.30 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.24 – 6.19 (m, 1H, CH=C*H*), 6.14 (dd, *J* = 8.7, 5.9 Hz, 1H, C*H*-Phth), 5.93 – 5.86 (m, 2H, CH=C*H* and C*H*-N), 3.81 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 2.96 (dd, *J* = 13.7, 8.7 Hz, 1H, CH_2), 2.52 (dd, *J* = 13.7, 5.9 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.8, 168.9, 167.6, 140.7, 134.4, 131.8, 131.5, 129.4, 125.1, 123.5, 121.8, 121.3, 111.4, 109.9, 67.1, 65.1, 64.3, 52.7, 52.7, 35.1;

IR (film): $\tilde{\nu}$ = 3466 (w), 3058 (w), 2956 (w), 2851 (w), 1772 (w), 1733 (s), 1709 (s), 1490 (m), 1436 (w), 1396 (w), 1352 (w), 1327 (w), 1266 (s), 1214 (m), 1179 (w), 1156 (w), 1130 (m), 1112 (m), 1087 (m), 970 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{18}BrN_2O_6$ [M+] 509.0343; found 509.0343.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-7-fluoro-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**27**).



Following the general procedure 6-fluoroquinoline (**SI-59**) (29 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 87 mg (0.19 mmol, 97%) of the title compound **27** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.64 (td, *J* = 8.6, 3.0 Hz, 1H, Ar*H*), 6.51 (dd, *J* = 8.6, 3.0 Hz, 1H, Ar*H*), 6.34 (dd, *J* = 8.9, 4.3 Hz, 1H, Ar*H*), 6.23 (dd, *J* = 10.0, 2.1 Hz, 1H, CH=C*H*), 6.16 (dd, *J* = 8.6, 5.9 Hz, 1H, C*H*-Phth), 5.97 – 5.86 (m, 2H, C*H*-N and C*H*=CH), 3.81 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 2.96 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.52 (dd, *J* = 13.7, 5.9 Hz, 1H, CH_2);

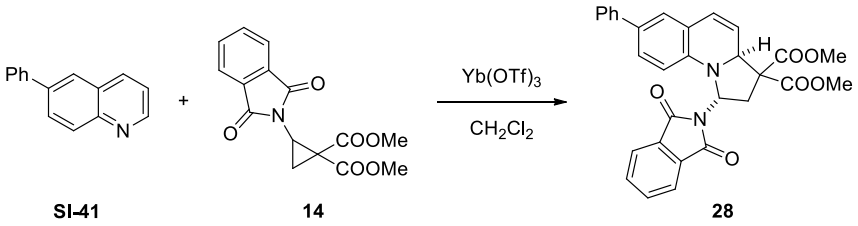
^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.0, 169.0, 167.7, 155.9 (d, *J* = 235.5 Hz), 138.1 (d, *J* = 1.9 Hz), 134.4, 131.6, 125.4 (d, *J* = 2.0 Hz), 123.5, 122.3, 120.4 (d, *J* = 7.5 Hz), 115.1 (d, *J* = 22.2 Hz), 113.7 (d, *J* = 23.9 Hz), 110.3 (d, *J* = 7.4 Hz), 67.8, 65.4, 64.4, 52.7, 52.7, 35.1;

^{19}F NMR (376 MHz, $CDCl_3$) δ = -127.77 (td, *J* = 8.6, 4.3 Hz) ppm.

IR (film): $\tilde{\nu}$ = 2958 (w), 2849 (w), 1773 (w), 1732 (s), 1709 (s), 1498 (s), 1436 (w), 1396 (w), 1352 (w), 1276 (s), 1246 (s), 1219 (m), 1160 (m), 1111 (m), 1078 (m), 952 (w), 873 (m) cm^{-1};

HRMS (ESI) calcd for $C_{24}H_{20}FN_2O_6^+$ $[M+H]^+$ 451.1300; found 451.1205.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-7-phenyl-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**28**).



SI-41 **14** **28**

Following the general procedure 6-phenylquinoline (**SI-41**) (41 mg, 0.20 mmol, 1.00 equiv.), cycloproane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 98 mg (0.19 mmol, 96%) of the title compound **28** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 4:1);

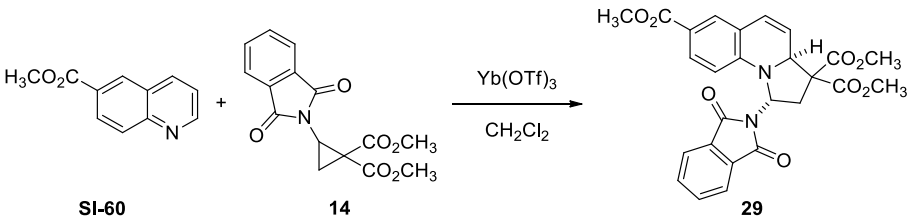
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.50 – 7.42 (m, 2H, Ar*H*), 7.35 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 7.06 (d, *J* = 2.2 Hz, 1H, Ar*H*), 6.52 (d, *J* = 8.4 Hz, 1H, Ar*H*), 6.39 (dd, *J* = 10.2, 2.9 Hz, 1H, C*H*=CH), 6.27 (dd, *J* = 8.6, 5.9 Hz, 1H, C*H*-Phth), 5.97 (dd, *J* = 2.9, 1.9 Hz, 1H, C*H*-N), 5.92 (dd, *J* = 10.2, 2.9 Hz, 1H, CH=C*H*), 3.84 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 3.02 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.57 (dd, *J* = 13.7, 5.9 Hz, 1H,CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.0, 169.1, 167.8, 141.1, 140.7, 134.4, 131.7, 131.0, 128.6, 128.1, 126.3, 126.2, 126.1, 125.9, 123.5, 120.9, 119.8, 110.1, 67.2, 65.3, 64.5, 52.8, 52.8, 35.4 ppm;

IR (film): $\tilde{\nu}$ 1774 (w), 1732 (s), 1711 (s), 1651 (w), 1609 (w), 1488 (m), 1436 (w), 1395 (w), 1352 (m), 1327 (m), 1265 (s), 1219 (w), 1180 (w), 1131 (w), 1113 (w), 1077 (m), 1019 (w), 970 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{30}H_{25}N_2O_6^+$ $[M+H]^+$ 509.1707; found 509.1711.

***anti*-Trimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3,7(3a*H*)-tricarboxylate** (**29**).



SI-60 **14** **29**

Following the general procedure methyl quinoline-6-carboxylate (**SI-60**) (37 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography

(silica, pentane:EtOAc 10:1 to 4:1) and 93 mg (0.19 mmol, 95%) of the title compound **29** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 4:1);

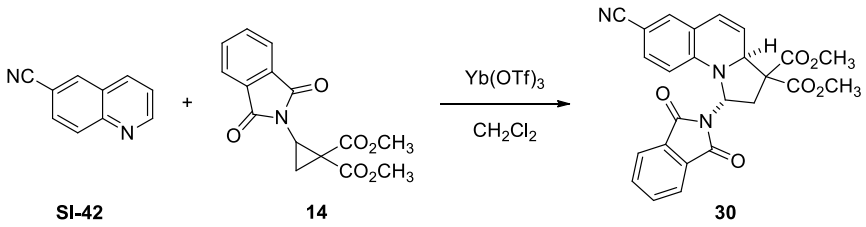
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.64 (dd, *J* = 8.6, 2.0 Hz, 1H, Ar*H*), 7.44 (d, *J* = 2.0 Hz, 1H, Ar*H*), 6.43 (d, *J* = 8.6 Hz, 1H, Ar*H*), 6.33 (dd, *J* = 10.2, 2.0 Hz, 1H, CH=C*H*), 6.22 (dd, *J* = 8.7, 6.0 Hz, 1H, C*H*-Phth), 5.97 – 5.93 (m, 1H, C*H*-N), 5.89 (dd, *J* = 10.2, 2.9 Hz, 1H, C*H*=CH), 3.81 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 2.98 (dd, *J* = 13.7, 8.7 Hz, 1H, CH_2), 2.53 (dd, *J* = 13.7, 6.0 Hz, 1H, CH_2) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 168.7, 167.5, 166.8, 145.4, 134.5, 131.8, 131.5, 128.5, 125.8, 123.6, 120.8, 119.5, 119.0, 109.2, 66.5, 64.9, 64.3, 52.8, 52.7, 51.5, 35.1;

IR (film): $\tilde{\nu}$ 2988 (w), 2956 (w), 2902 (w), 1773 (w), 1733 (m), 1708 (s), 1603 (w), 1506 (w), 1432 (w), 1393 (w), 1353 (w), 1276 (s), 1201 (m), 1151 (w), 1111 (m), 1078 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{26}H_{23}N_2O_8^+$ $[M+H]^+$ 491.1449; found 491.1446.

***anti*-Dimethyl 7-cyano-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**30**).



SI-42 **14** **30**

Following the general procedure methyl quinoline-6-carboxylate (**SI-42**) (31 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 85 mg (0.19 mmol, 93%) of the title compound **30** were isolated as a yellow oil.

R_f: 0.2 (silica, pentane:EtOAc 4:1);

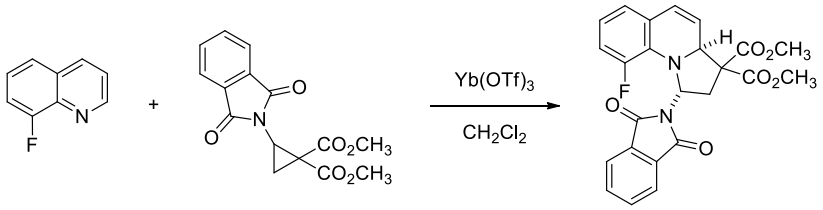
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.19 (dd, *J* = 8.5, 2.0 Hz, 1H, Ar*H*), 6.99 (d, *J* = 2.0 Hz, 1H, Ar*H*), 6.44 (d, *J* = 8.5 Hz, 1H, CH=C*H*), 6.30 – 6.23 (m, 1H, Ar*H*), 6.17 (dd, *J* = 8.8, 6.0 Hz, 1H, C*H*-Phth), 5.97 – 5.89 (m, 2H, C*H*-N and C*H*=CH), 3.80 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 2.97 (dd, *J* = 13.8, 8.8 Hz, 1H, CH_2), 2.54 (dd, *J* = 13.8, 6.0 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.5, 168.5, 167.4, 144.8, 134.5, 134.0, 131.3, 130.2, 124.8, 123.6, 122.0, 119.9, 119.6, 109.9, 100.2, 66.1, 64.7, 64.2, 52.8, 52.8, 34.8;

IR (film): $\tilde{\nu}$ 2956 (w), 2925 (w), 2853 (w), 2215 (m), 1773 (m), 1749 (m), 1731 (s), 1713 (s), 1602 (m), 1505 (s), 1462 (w), 1393 (w), 1354 (w), 1277 (s), 1240 (m), 1215 (m), 1176 (m), 1146 (m), 1107 (w), 1089 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{26}H_{23}N_2O_8^+$ $[M+H]^+$ 491.1449; found 491.1446.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-9-fluoro-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**31**).



SI-61 **14** **31**

Following the general procedure 8-fluoroquinoline (**SI-61**) (29 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 81 mg (0.18 mmol, 90%) of the title compound **31** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H, *Phth*), 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H, *Phth*), 6.70 (ddd, *J* = 13.8, 8.1, 1.6 Hz, 1H, Ar*H*), 6.59 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 6.51 (td, *J* = 7.5, 4.4 Hz, 1H, Ar*H*), 6.39 – 6.24 (m, 2H, C*H*-Phth and C*H*=CH), 5.96 (dd, *J* = 10.1, 3.1 Hz, 1H, CH=C*H*), 5.91 (dd, *J* = 3.1, 1.6 Hz, 1H, C*H*-N), 3.79 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 2.98 (dd, *J* = 13.8, 8.6 Hz, 1H, CH_2), 2.27 (dd, *J* = 13.8, 6.2 Hz, 1H, CH_2);

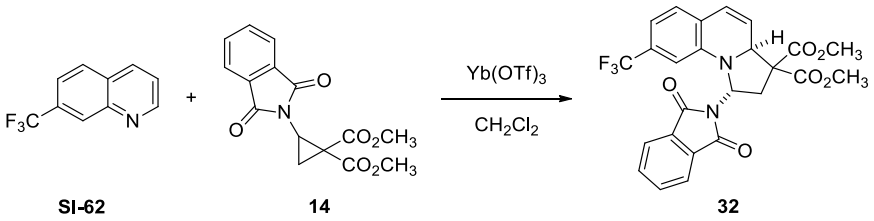
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.9, 168.9, 167.5, 150.1 (d, *J* = 238.3 Hz), 134.0, 131.9, 130.4 (d, *J* = 8.7 Hz), 125.5 (d, *J* = 4.0 Hz), 123.21, 123.15, 123.1 (d, *J* = 2.2 Hz), 122.5, 119.0 (d, *J* = 8.1 Hz), 117.1 (d, *J* = 22.9 Hz), 70.5 (s, *J* = 5.1 Hz), 65.7, 64.8, 52.7, 52.7, 36.2;

^{19}F NMR (376 MHz, $CDCl_3$) δ = -131.20 (dt, *J* = 13.8, 3.2 Hz);

IR (film): $\tilde{\nu}$ = 3003 (w), 2955 (w), 2845 (w), 1773 (w), 1732 (s), 1710 (s), 1611 (w), 1475 (m), 1397 (w), 1353 (m), 1267 (s), 1246 (m), 1219 (m), 1114 (m), 1077 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{19}FN_2NaO_6^+$ $[M+Na]^+$ 473.1119; found 473.1124.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-8-(trifluoromethyl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**32**).



SI-62 **14** **32**

Following the general procedure 7-(trifluormethyl)quinoline (**SI-62**) (39 mg, 0.20 mmol, 1.00 equiv.), cyclopropane **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 98 mg (0.20 mmol, 98%) of the title compound **32** were isolated as a yellow oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.85 (d, *J* = 7.6 Hz, 1H, Ar*H*), 6.79 (dd, *J* = 7.6, 1.5 Hz, 1H, Ar*H*), 6.72 (s, 1H, Ar*H*), 6.33 (dd, *J* = 10.0, 1.5 Hz, 1H, CH=C*H*), 6.22 (dd, *J* = 8.7, 5.8 Hz, 1H, C*H*-Phth), 6.01 – 5.92 (m, 2H, C*H*-N and C*H*=CH), 3.83 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 2.99 (dd, *J* = 13.8, 8.7 Hz, 1H, CH_2), 2.58 (dd, *J* = 13.8, 5.8 Hz, 1H, CH_2) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.9, 168.9, 167.7, 141.8, 134.5, 131.5, 131.2 (q, *J* = 31.9 Hz), 127.2, 125.3, 123.6, 122.9, 122.3, 114.9 (q, *J* = 3.6 Hz), 106.4 (q, *J* = 3.5 Hz), 66.9, 65.2, 64.3, 52.8, 52.8, 34.9;[22]

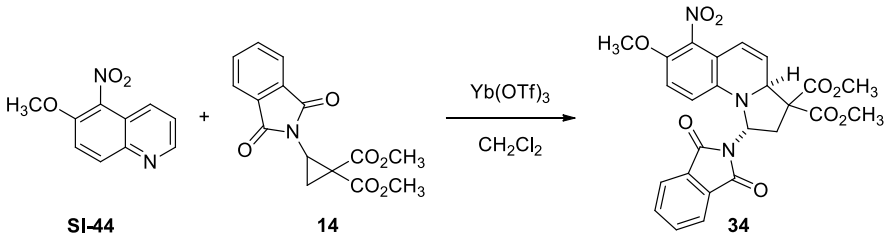
^{19}F NMR (376 MHz, $CDCl_3$) δ = -63.1 (s) ppm.

IR (film): $\tilde{\nu}$ = 2959 (w), 2924 (w), 2365 (w), 1772 (w), 1732 (s), 1709 (s), 1509 (w), 1453 (m), 1436 (w), 1396 (w), 1355 (w), 1327 (w), 1270 (m), 1224 (w), 1143 (w), 1111 (m), 1078 (s), 1046 (w), 1002 (w) cm^{-1};

HRMS (ESI) calcd for $C_{25}H_{18}F_3N_2O_6^+$ $[M+H]^+$ 499.1111; found 499.1109.

[22] The CF_3 carbon was not observed.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-7-methoxy-6-nitro-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**34**).



SI-44 **14** **34**

Following the general procedure 6-methoxy-5-nitroquinoline (**SI-44**) (41 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1) and 98 mg (0.19 mmol, 97%) of the title compound **34** were isolated as a yellow oil.

R_f: 0.1 (silica, pentane:EtOAc 4:1);

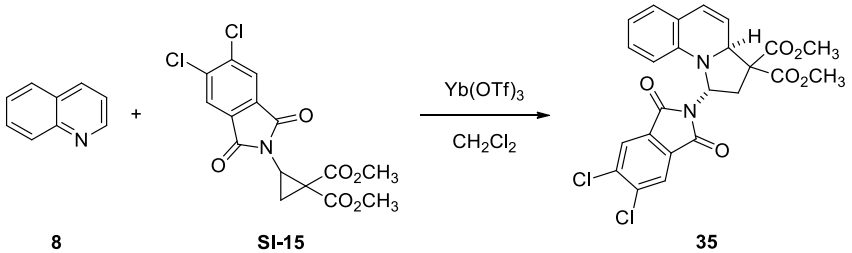
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.75 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.66 (d, *J* = 9.0 Hz, 1H, C*H*=CH), 6.47 (d, *J* = 9.0 Hz, 1H, CH=C*H*), 6.22 – 6.11 (m, 2H, C*H*-Phth and Ar*H*), 6.08 (dd, *J* = 10.5, 3.0 Hz, 1H, Ar*H*), 5.88 (dd, *J* = 2.9, 2.0 Hz, 1H, C*H*-N), 3.81 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.97 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.53 (dd, *J* = 13.7, 5.9 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 168.7, 167.7, 142.7, 139.2, 135.9, 134.5, 131.5, 125.7, 123.6, 118.7, 113.5, 112.3, 111.5, 67.6, 65.1, 63.9, 56.8, 52.9, 35.0;

IR (film): $\tilde{\nu}$ 2957 (w), 2923 (w), 2849 (w), 1771 (w), 1733 (s), 1713 (s), 1532 (m), 1494 (m), 1437 (w), 1395 (w), 1355 (m), 1329 (w), 1277 (s), 1243 (w), 1222 (w), 1133 (w), 1114 (w), 1077 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{25}H_{22}N_3O_9^+$ $[M+H]^+$ 508.1351; found 508.1367.

***anti*-Dimethyl 1-(5,6-dichloro-1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**35**).



8 **SI-15** **35**

Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-15** (78 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M)

for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 87 mg (0.17 mmol, 87%) of the title compound **35** were isolated as a red oil.

R_f: 0.2 (silica, pentane:EtOAc 4:1);

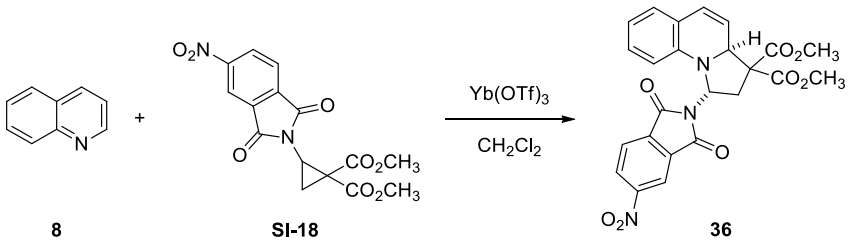
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 2H, *Phth*), 6.94 (t, *J* = 7.7 Hz, 1H, Ar*H*), 6.78 (d, *J* = 7.1 Hz, 1H, Ar*H*), 6.57 (t, *J* = 7.1 Hz, 1H, Ar*H*), 6.32 (dd, *J* = 12.6, 9.0 Hz, 2H, C*H*=CH and Ar*H*), 6.18 (dd, *J* = 8.4, 5.8 Hz, 1H, C*H*-Phth), 5.93 – 5.78 (m, 2H, C*H*-N and C*H*=CH), 3.83 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.00 (dd, *J* = 13.7, 8.4 Hz, 1H, CH_2), 2.48 (dd, *J* = 13.7, 5.8 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.8, 168.9, 165.7, 141.3, 139.2, 130.7, 129.5, 127.2, 126.2, 125.5, 120.3, 119.4, 118.3, 109.5, 67.8, 65.2, 64.3, 52.8, 52.7, 35.3 ppm;

IR (film): $\tilde{\nu}$ 2955 (w), 1773 (w), 1732 (s), 1708 (s), 1596 (w), 1492 (w), 1437 (w), 1386 (w), 1345 (s), 1264 (s), 1221 (m), 1134 (w), 1110 (m), 1083 (w), 955 (w), 908 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{19}Cl_2N_2O_6^+$ $[M+H]^+$ 501.0615; found 501.0615.

***anti*-Dimethyl 1-(5-nitro-1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**36**).



Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-18** (73 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 2:1) and 85 mg (0.18 mmol, 89%) of the title compound **36** were isolated as a red oil.

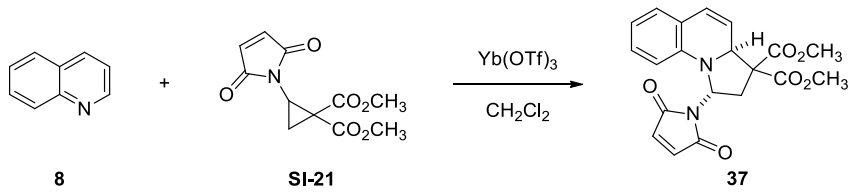
R_f: 0.1 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, *J* = 20.3 Hz, 2H, *Phth*), 8.04 (d, *J* = 6.2 Hz, 1H, *Phth*), 6.92 (t, *J* = 7.6 Hz, 1H, Ar*H*), 6.76 (d, *J* = 7.0 Hz, 1H, Ar*H*), 6.55 (t, *J* = 7.0 Hz, 1H, Ar*H*), 6.30 (dd, *J* = 13.6, 8.8 Hz, 2H, Ar*H* and C*H*=CH), 6.26 – 6.16 (m, 1H, C*H*-Phth), 5.92 – 5.79 (m, 2H, C*H*-N and CH=C*H*), 3.84 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.03 (dd, *J* = 13.0, 8.1 Hz, 1H, CH_2), 2.50 (dd, *J* = 13.0, 5.8 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 168.8, 165.6, 165.3, 151.7, 141.2, 135.9, 133.0, 129.5, 129.4, 127.2, 126.1, 124.7, 120.2, 119.4, 118.8, 118.4, 109.5, 68.1, 65.1, 64.3, 52.8, 52.7, 35.3 ppm;

IR (film): $\tilde{\nu}$ 3007 (w), 2989 (w), 2957 (w), 1780 (w), 1730 (s), 1719 (s), 1599 (w), 1542 (m), 1494 (w), 1436 (w), 1397 (w), 1340 (m), 1276 (s), 1263 (s), 1221 (w), 1137 (w), 1109 (w), 1079 (w) cm^{-1};
HRMS (ESI) calcd. for $C_{24}H_{20}N_3O_8^+$ $[M+H]^+$ 478.1245; found 478.1242.

***anti*-Dimethyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**37**).

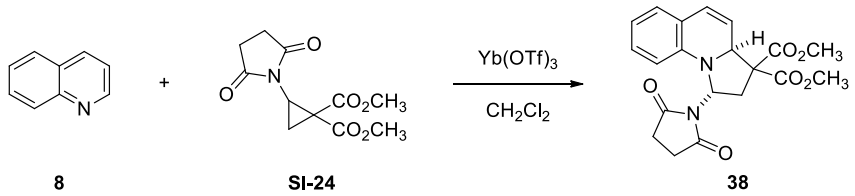


8 **SI-21** **37**

Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-21** (53 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 71 mg (0.19 mmol, 93%) of the title compound **37** were isolated as a colorless oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (td, *J* = 7.8, 1.6 Hz, 1H, Ar*H*), 6.78 (dd, *J* = 7.4, 1.6 Hz, 1H, Ar*H*), 6.69 (s, 2H, *Mal*), 6.57 (td, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 6.39 – 6.22 (m, 2H, C*H*=CH and Ar*H*), 6.01 (dd, *J* = 8.6, 5.9 Hz, 1H, C*H*-Mal), 5.82 (dd, *J* = 10.1, 2.9 Hz, 1H, CH=C*H*), 5.78 (dd, *J* = 2.9, 1.9 Hz, 1H, C*H*-N), 3.80 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3), 2.92 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.38 (dd, *J* = 13.7, 5.9 Hz, 1H, CH_2);
^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.1, 169.8, 169.0, 141.5, 134.3, 129.5, 127.2, 126.3, 120.3, 119.4, 118.2, 109.5, 67.0, 65.2, 64.2, 52.7, 52.6, 35.3;
IR (film): $\tilde{\nu}$ 2959 (w), 2901 (w), 1731 (s), 1704 (s), 1651 (w), 1599 (w), 1495 (w), 1460 (w), 1436 (w), 1406 (w), 1355 (m), 1265 (s), 1221 (w), 1159 (m), 1101 (w), 1081 (m), 1054 (w), 911 (w) cm^{-1};
HRMS (ESI) calcd for $C_{20}H_{17}N_2O_6$ [M+] 381.1081; found 381.1079.

***anti*-Dimethyl 1-(2,5-dioxopyrrolidin-1-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**38**).



8 **SI-24** **38**

Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-24** (26 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 61 mg (0.16 mmol, 79%) of the title compound **38** were isolated as a colorless oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);

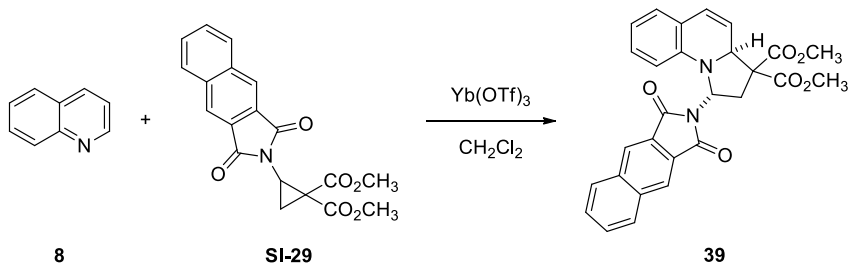
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (td, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 6.78 (dd, *J* = 7.4, 1.5 Hz, 1H, Ar*H*), 6.57 (td, *J* = 7.4, 0.9 Hz, 1H, Ar*H*), 6.34 – 6.24 (m, 2H, Ar*H* and C*H*=CH), 6.04 (dd, *J* = 8.6, 5.9 Hz, 1H, C*H*-Succ), 5.84 – 5.76 (m, 2H, CH=C*H* and C*H*-N), 3.79 (s, 3H, OCH_3), 3.58 (s, 3H, OCH_3), 2.84 (dd, *J* = 13.6, 8.6 Hz, 1H, CH_2), 2.69 (s, 4H*, Succ*), 2.40 (dd, *J* = 13.6, 5.9 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.7, 169.9, 169.0, 141.6, 129.5, 127.2, 126.1, 120.4, 119.4, 118.1, 109.7, 68.2, 65.4, 64.6, 52.7, 52.6, 34.2, 28.1;

IR (film): $\tilde{\nu}$ 2954 (w), 2127 (w), 1732 (s), 1702 (s), 1599 (w), 1496 (w), 1459 (w), 1436 (w), 1398 (w), 1353 (m), 1310 (w), 1266 (s), 1222 (m), 1176 (s), 1150 (w), 1100 (w), 1085 (m), 1053 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{20}H_{20}N_2NaO_6^+$ $[M+Na]^+$ 407.1214; found 407.1208.

***anti*-Dimethyl 1-(1,3-dioxo-1H-benzo[f]isoindol-2(3H)-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**39**).



8 **SI-29** **39**

Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-29** (74 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 78 mg (0.16 mmol, 81%) of the title compound **39** were isolated as a yellow oil.

R_f: 0.5 (silica, pentane:EtOAc 4:1);

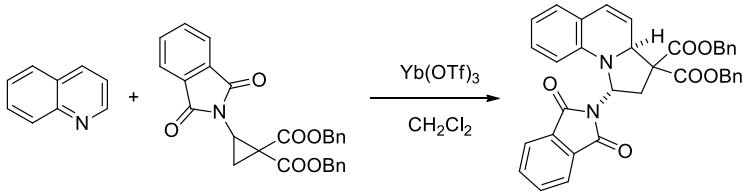
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (s, 2H, *Naphth*), 8.05 (dd, *J* = 6.3, 3.3 Hz, 2H, *Naphth*), 7.69 (dd, *J* = 6.3, 3.3 Hz, 2H, *Naphth*), 6.96 (td, *J* = 8.0, 1.6 Hz, 1H, Ar*H*), 6.79 (dd, *J* = 7.3, 1.6 Hz, 1H, Ar*H*), 6.60 – 6.51 (m, 1H, Ar*H*), 6.48 (d, *J* = 8.0 Hz, 1H, Ar*H*), 6.37 – 6.22 (m, 2H, C*H*-Phth and CH=C*H*), 6.01 (dd, *J* = 2.5 Hz, 1H, C*H*-N), 5.88 (dd, *J* = 10.2, 2.5 Hz, 1H, C*H*=CH), 3.84 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 3.02 (dd, *J* = 13.7, 8.7 Hz, 1H, CH_2), 2.60 (dd, *J* = 13.7, 5.9 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.0, 169.2, 167.4, 141.7, 135.5, 130.3, 129.6, 129.3, 127.3, 127.2, 126.3, 125.0, 120.5, 119.5, 118.1, 109.9, 67.6, 65.4, 64.5, 52.7, 52.7, 35.2;

IR (film): $\tilde{\nu}$ 2955 (w), 1765 (m), 1731 (s), 1704 (s), 1650 (w), 1600 (w), 1496 (w), 1459 (w), 1339 (s), 1310 (w), 1265 (s), 1220 (m), 1149 (m), 1136 (m), 1112 (m), 1083 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{28}H_{22}N_2NaO_6^+$ $[M+Na]^+$ 505.1370; found 505.1370.

***anti*-Dibenzyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**40**).



Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-30** (96 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 107 mg (0.18 mmol, 92%) of the title compound **40** were isolated as a yellow oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);

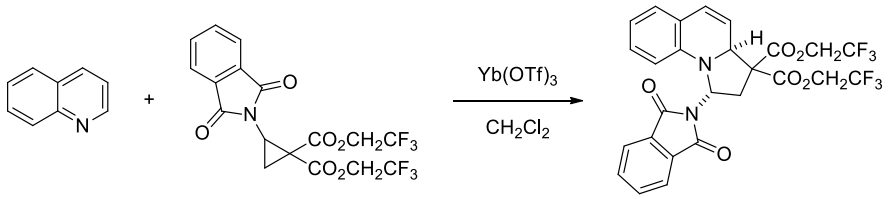
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 5.4, 3.0 Hz, 2H, *Phth*), 7.70 (dd, *J* = 5.4, 3.0 Hz, 2H, *Phth*), 7.35 – 7.16 (m, 8H, Ar*H*), 7.10 – 7.01 (m, 2H, Ar*H*), 6.94 (td, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 6.72 (dd, *J* = 7.3, 1.5 Hz, 1H, Ar*H*), 6.55 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.38 (d, *J* = 10.0 Hz, 1H, C*H*=CH), 6.19 – 6.10 (m, 2H, C*H*-Phth and Ar*H*), 5.99 (t, *J* = 2.4 Hz, 1H, C*H*-N), 5.79 (dd, *J* = 10.0, 2.4 Hz, 1H, CH=C*H*), 5.22 (m, 2H, CH_2Ph), 5.02 (m, 2H, CH_2Ph), 3.00 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.54 (dd, *J* = 13.7, 5.8 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.4, 168.4, 167.7, 141.5, 135.1, 134.7, 134.3, 131.6, 129.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 127.3, 126.3, 123.4, 120.2, 119.4, 118.0, 109.7, 67.6, 67.3, 67.2, 65.4, 64.5, 35.3 ppm;

IR (film): $\tilde{\nu}$ 3033 (w), 2960 (w), 1772 (w), 1730 (s), 1712 (s), 1599 (w), 1497 (w), 1459 (w), 1351 (m), 1265 (s), 1203 (m), 1134 (m), 1072 (m), 909 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{36}H_{29}N_2O_6^+$ $[M+H]^+$ 585.2020; found 585.2018.

***anti-bis*(2,2,2-Trifluoroethyl) 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**41**).



Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-31** (92 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 106 mg (0.186 mmol, 93%) of the title compound **41** were isolated as a yellow oil.

R_f: 0.4 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.99 (td, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 6.80 (dd, *J* = 7.4, 1.5 Hz, 1H, Ar*H*), 6.59 (td, *J* = 7.4, 0.9 Hz, 1H, Ar*H*), 6.49 (d, *J* = 7.9 Hz, 1H, Ar*H*), 6.35 (dd, *J* = 10.2, 2.0 Hz, 1H, C*H*=CH), 6.27 (dd, *J* = 8.7, 5.7 Hz, 1H, C*H*-Phth), 6.06 (dd, *J* = 2.9, 2.0 Hz, 1H, C*H*-N), 5.82 (dd, *J* = 10.2, 2.9 Hz, 1H, CH=C*H*), 4.70 – 4.55 (m, 2H, C$H_2$$CF_3$), 4.52 – 4.36 (m, 2H, C$H_2$$CF_3$), 3.07 (dd, *J* = 13.9, 8.7 Hz, 1H, CH_2), 2.63 (dd, *J* = 13.9, 5.7 Hz, 1H, CH_2);

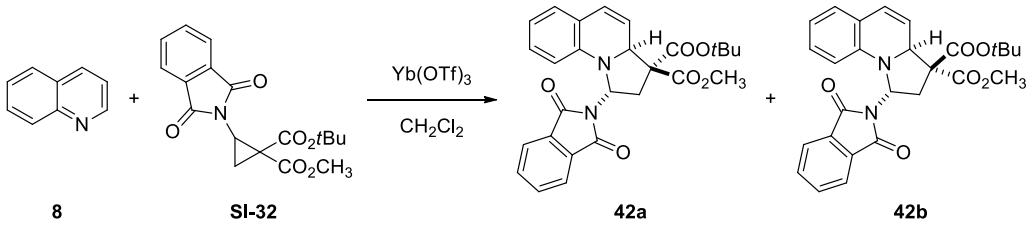
^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.7, 167.5, 166.4, 141.1, 134.4, 131.6, 129.8, 127.5, 127.3, 123.6, 122.5 (q, *J* = 276.4 Hz), 122.3 (q, *J* = 277.2 Hz), 119.1, 118.9, 118.5, 109.9, 66.7, 65.0, 64.8, (d, *J* = 24.9 Hz), 61.3 (q, *J* = 37.8 Hz), 61.2 (*J* = 37.0 Hz), 35.2;

^{19}F NMR (376 MHz, $CDCl_3$) δ = -73.68 (t, *J* = 8.4 Hz), -73.74 (t, *J* = 8.4 Hz);

IR (film): $\tilde{\nu}$ 2976 (w), 2901 (w), 1753 (m), 1712 (s), 1600 (w), 1497 (w), 1461 (w), 1405 (w), 1352 (w), 1310 (w), 1276 (m), 1236 (w), 1166 (s), 1132 (m), 1110 (m), 1087 (m), 977 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{26}H_{18}F_6N_2NaO_6^+$ $[M+Na]^+$ 591.0961; found 591.0962.

***rac*-(1*R*,3*S*,3a*R*)-3-*tert*-Butyl 3-methyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**42a**) and ***rac*-(1*R*,3*R*,3a*R*)-3-*tert*-Butyl 3-methyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**42b**)



8 **SI-32** **42a** **42b**

Following the general procedure quinoline (**8**) (26 mg, 0.20 mmol, 1.00 equiv.), **SI-32** (73 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) affording **42a** (53 mg, 0.11 mmol, 56%) and **42b** (15 mg, 0.05 mmol, 16%) as yellow oils.[23]

42a

R_f: 0.51 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.95 (td, *J* =8.0, 1.6 Hz, 1H, Ar*H*), 6.78 (dd, *J* = 7.3, 1.6 Hz, 1H, Ar*H*), 6.55 (td, *J* = 7.3, 1.0 Hz, 1H, Ar*H*), 6.41 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.33 – 6.26 (m, 1H, C*H*=CH), 6.11 (dd, *J* = 8.6, 6.1 Hz, 1H, C*H*-Phth), 5.98 – 5.82 (m, 2H, C*H*-N and CH=C*H*), 3.81 (s, 3H, OCH_3), 2.88 (dd, *J* = 13.7, 8.6 Hz, 1H, CH_2), 2.51 (dd, *J* = 13.7, 6.1 Hz, 1H, CH_2), 1.25 (s, 9H, C(CH_3)$_3$);

^{13}C NMR (101 MHz, $CDCl_3$): 169.4, 168.6, 167.7, 142.2, 134.3, 131.7, 129.5, 127.1, 126.4, 123.4, 120.5, 119.6, 118.0, 109.7, 83.0, 68.1, 66.1, 64.2, 52.5, 35.2, 27.6;

IR (film): $\tilde{\nu}$ 2981 (w), 1772 (w), 1710 (s), 1600 (w), 1496 (w), 1459 (w), 1394 (w), 1367 (w), 1263 (s), 1227 (w), 1151 (m), 1134 (m), 1078 (m), 1050 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{27}H_{27}N_2O_6^+$ $[M+H]^+$ 475.1864; found 475.1872.

[23] The minor diasteroisomer **30b** slowly converts into the major diastereoisomer **30a** in $CDCl_3$.

42b

R_f: 0.49 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 5.6, 3.3 Hz, 2H, *Phth*), 7.73 (dd, *J* = 5.6, 3.3 Hz, 2H, *Phth*), 6.95 (t, *J* = 7.9 Hz, 1H, Ar*H*), 6.77 (d, *J* = 7.2 Hz, 1H, Ar*H*), 6.54 (t, *J* = 7.2 Hz, 1H, Ar*H*), 6.40 (d, *J* = 7.9 Hz, 1H, Ar*H*), 6.28 (d, *J* = 10.1 Hz, 1H, C*H*=CH), 6.19 (dd, *J* = 8.2, 6.5 Hz, 1H, C*H*-Phth), 5.95 – 5.79 (m, 2H, C*H*-N and CH=C*H*), 3.64 (s, 3H, OCH_3), 2.94 (dd, *J* = 13.7, 8.2 Hz, 1H, CH_2), 2.50 (dd, *J* = 13.7, 6.5 Hz, 1H, CH_2), 1.51 (s, 9H, C(CH_3)$_3$);

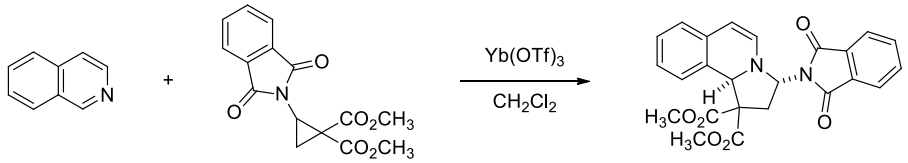
^{13}C NMR (101 MHz, $CDCl_3$): 170.5, 167.7, 167.7, 141.8, 134.3, 131.8, 129.5, 127.1, 126.1, 123.5, 120.9, 119.5, 117.9, 109.7, 82.4, 67.3, 66.1, 64.3, 52.4, 35.5, 27.9 ppm;

IR (film): $\tilde{\nu}$ 2981 (w), 1777 (w), 1726 (s), 1714 (s), 1600 (w), 1497 (w), 1459 (w), 1395 (w), 1354 (w), 1276 (m), 1262 (m), 1219 (w), 1149 (w), 1135 (m), 1112 (w), 1050 (w), 844 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{27}H_{27}N_2O_6^+$ $[M+H]^+$ 475.1864; found 475.1868.

9. Scope of the reaction with isoquinolines

***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydropyrrolo[2,1-a]isoquinoline-1,1(10b*H*)-dicarboxylate** (**43**).



SI-63 **14** **43**

Following the general procedure isoquinoline (**SI-63**) (26 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 72 mg (0.17 mmol, 83%) of the title compound **43** were isolated as a yellow oil.

R_f: 0.2 (silica, pentane:EtOAc 4:1);

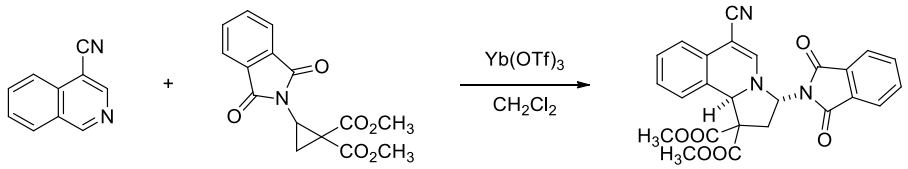
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.55 – 7.50 (m, 1H, Ar*H*), 7.09 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.01 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 6.80 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 6.16 (d, *J* = 7.6 Hz, 1H, CH=C*H*-N), 6.10 (s, 1H, C*H*-N), 6.07 (dd, *J* = 9.0, 5.3 Hz, 1H, C*H*-Phth), 5.12 (d, *J* = 7.6 Hz, 1H, N-CH=C*H*), 3.86 (s, 3H, OCH_3), 3.35 (s, 3H, OCH_3), 3.02 (dd, *J* = 13.7, 9.0 Hz, 1H, CH_2), 2.85 (dd, *J* = 13.7, 5.3 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 170.0, 168.1, 134.4, 134.3, 131.9, 131.8, 128.1, 127.8, 127.0, 125.3, 123.9, 123.6, 98.4, 69.6, 67.7, 64.9, 52.8, 52.5, 34.2;

IR (film): $\tilde{\nu}$ 2960 (w), 2358 (w), 1774 (w), 1731 (s), 1714 (s), 1635 (w), 1462 (w), 1436 (w), 1371 (w), 1356 (w), 1329 (w), 1271 (w), 1214 (w), 1141 (w), 1093 (w), 1062 (w), 914 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{21}N_2O_6^+$ $[M+H]^+$ 433.1394; found 433.1404.

***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydropyrrolo[2,1-a]isoquinoline-1,1(10b*H*)-dicarboxylate** (**44**).



SI-46 **14** **44**

Following the general procedure isoquinoline-4-carbonitrile (**SI-46**) (31 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2

(0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 3:1) and 83 mg (0.18 mmol, 91%) of the title compound **44** were isolated as a yellow oil.

R_f: 0.1 (silica, pentane:EtOAc 3:1);

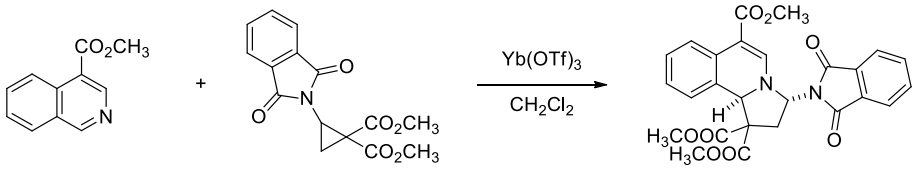
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.56 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.25 – 7.15 (m, 2H, Ar*H*), 7.15 – 7.07 (m, 1H, Ar*H*), 6.98 (s, 1H, C=C*H*-N), 6.16 (s, 1H, C*H*-N), 6.11 (dd, *J* = 8.9, 5.2 Hz, 1H, C*H*-Phth), 3.89 (s, 3H, OCH_3), 3.37 (s, 3H, OCH_3), 3.03 (dd, *J* = 14.1, 8.9 Hz, 1H, CH_2), 2.93 (dd, *J* = 14.1, 5.2 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 169.5, 167.6, 143.7, 134.7, 131.3, 128.8, 127.6, 126.9, 126.8, 124.7, 123.8, 122.4, 118.2, 82.3, 67.4, 67.0, 63.9, 53.1, 52.7, 34.0;

IR (film): $\tilde{\nu}$ 2956 (w), 2251 (w), 2207 (m), 1835 (w), 1776 (w), 1730 (s), 1730 (s), 1713 (s), 1623 (s), 1571 (w), 1497 (w), 1457 (m), 1436 (w), 1366 (m), 1353 (m), 1327 (m), 1272 (m), 1206 (m), 1117 (m), 1092 (m), 1064 (m), 910 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{25}H_{20}N_3O_6^+$ $[M+H]^+$ 458.1347; found 458.1346.

***anti*-Trimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydropyrrolo[2,1-a]isoquinoline-1,1,6(10b*H*)-tricarboxylate** (**45**).



SI-48 **14** **45**

Following the general procedure methyl isoquinoline-4-carboxylate (**SI-48**) (37 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 87 mg (0.18 mmol, 89%) of the title compound **45** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (dd, *J* = 8.1, 1.4 Hz, 1H, Ar*H*), 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.54 (d, *J* = 7.7 Hz, 1H, Ar*H*), 7.50 (s, 1H, C*H*=C($COOCH_3$)), 7.17 (td, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.05 (td, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 6.19 – 6.11 (m, 2H, Ar-C*H*-N and C*H*-Phth), 3.87 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.32 (s, 3H, OCH_3), 3.03 (dd, *J* = 13.9, 9.0 Hz, 1H, CH_2), 2.87 (dd, *J* = 13.9, 5.3 Hz, 1H, CH_2);

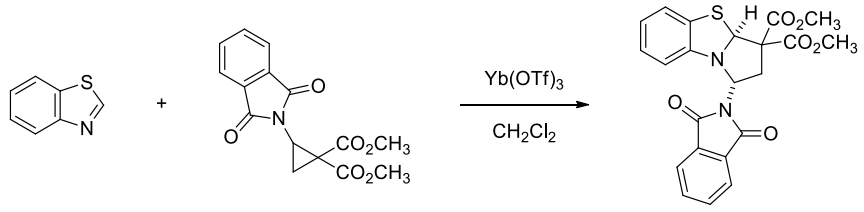
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.9, 169.5, 167.6, 166.2, 144.4, 134.6, 131.4, 128.7, 128.2, 127.2, 125.5, 125.4, 123.8, 123.7, 98.5, 68.0, 67.0, 64.3, 52.9, 52.6, 50.7, 34.3;

IR (film): $\tilde{\nu}$ 3499 (w), 2938 (w), 2830 (w), 1738 (s), 1636 (s), 1417 (m), 1298 (m), 1246 (m), 1176 (m), 1157 (m), 940 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{26}H_{23}N_2O_8^+$ $[M+H]^+$ 491.1449; found 491.1449.

10. Scope of the reaction with benzo- thia/oxa-zole

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydrobenzo[d]pyrrolo[2,1-b]thiazole-3,3(3a*H*)-dicarboxylate** (**46**).



SI-64 **14** **46**

Following the general procedure benzothiazole (**SI-64**) (27 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 83 mg (0.19 mmol, 95%) of the title compound **46** were isolated as a colorless oil.

R_f: 0.6 (silica, pentane:EtOAc 4:1);

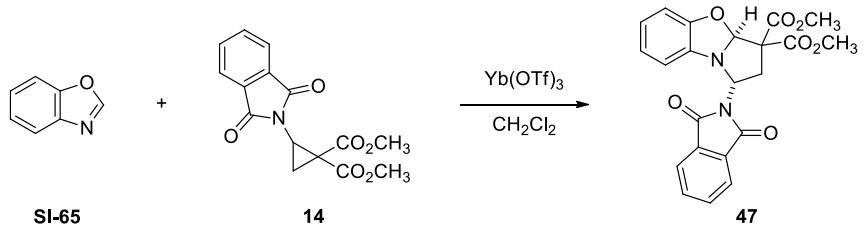
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.4, 3.1 Hz, 2H, *Phth*), 7.75 (dd, *J* = 5.4, 3.1 Hz, 2H, *Phth*), 6.94 (ddd, *J* = 9.0, 7.9, 1.2 Hz, 2H, Ar*H*), 6.71 (td, *J* = 7.5, 1.2 Hz, 1H, Ar*H*), 6.65 (d, *J* = 7.8 Hz, 1H, C*H*-Phth), 6.30 (s, 1H, S-C*H*-N), 6.20 (t, *J* = 7.9 Hz, 1H, Ar*H*), 3.85 (s, 3H, OCH_3), 3.45 (s, 3H, OCH_3), 2.95 (d, *J* = 7.8 Hz, 2H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.4, 168.8, 167.6, 147.1, 134.4, 131.6 (3C overlapping, two of them symmetric), 125.6, 123.5, 121.2, 120.9, 109.2, 74.1, 69.9, 66.7, 53.0, 52.5, 35.0;

IR (film): $\tilde{\nu}$ 2956 (w), 2364 (w), 2257 (w), 1773 (w), 1748 (m), 1724 (m), 1716 (s), 1583 (w), 1472 (m), 1393 (w), 1364 (m), 1350 (m), 1333 (m), 1297 (m), 1273 (m), 1220 (w), 1131 (m), 1070 (w), 1036 (w), 971 (w), 907 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{22}H_{18}N_2NaO_6S^+$ $[M+Na]^+$ 461.0778; found 461.0773.

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydrobenzo[d]pyrrolo[2,1-b]oxazole-3,3(3a*H*)-dicarboxylate** (**47**).



SI-65 **14** **47**

Following the general procedure benzoxazole (**SI-65**) (24 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (6 mg, 0.01 mmol, 5 mol%) were stirred in CH_2Cl_2 (0.4 mL, 0.5 M) for 16 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1) and 62 mg (0.15 mmol, 73%) of the title compound **47** were isolated as a colorless oil.

R_f: 0.5 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 5.3, 3.0 Hz, 2H, *Phth*), 7.77 (dd, *J* = 5.3, 3.0 Hz, 2H, *Phth*), 6.79 (pd, *J* = 7.5, 1.4 Hz, 2H, Ar*H*), 6.75 – 6.67 (m, 3H, O-C*H*-N and Ar*H*), 6.09 (dd, *J* = 8.4, 6.8 Hz, 1H, C*H*-Phth), 3.92 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 3.12 – 2.95 (m, 2H, CH_2);

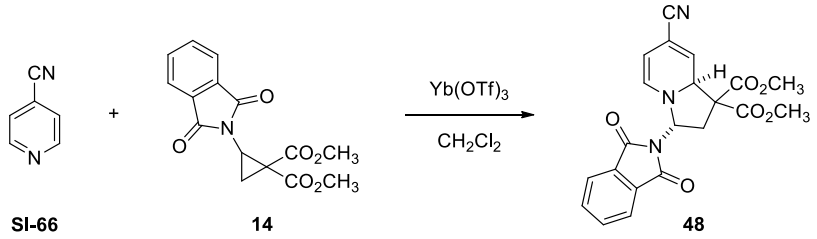
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 168.3, 167.5, 149.8, 138.4, 134.4, 131.7, 123.6, 122.2, 121.9, 110.5, 108.0, 101.7, 70.5, 65.8, 53.3, 53.1, 34.3 ppm;

IR (film): $\tilde{\nu}$ 2957 (w), 1737 (s), 1720 (s), 1487 (m), 1437 (w), 1363 (m), 1279 (m), 1252 (s), 1127 (m), 1054 (w), 898 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{22}H_{19}N_2O_7^+$ $[M+H]^+$ 423.1187; found 423.1179.

11. Scope of the reaction with pyridines

***anti*-Dimethyl 7-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**48**).



SI-66 **14** **48**

Following the general procedure isonicotinonitrile (**SI-66**) (21 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 10:1 to 3:1) and 61 mg (0.15 mmol, 75%) of the title compound **48** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 3:1);

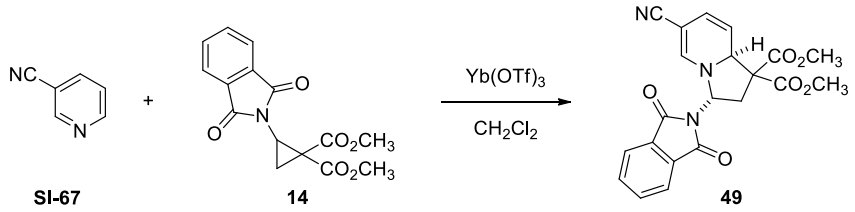
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.76 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.08 (dt, *J* = 7.5, 0.7 Hz, 1H, CH=C*H*N), 6.04 – 5.92 (m, 2H, N-C*H*-Phth and C=C*H*-CHN), 5.64 (d, *J* = 3.4 Hz, 1H, C*H*-N), 4.52 (dd, *J* = 7.4, 1.6 Hz, 1H, C*H*=CHN), 3.82 (s, 6H, 2 OCH_3), 2.80 (dd, *J* = 13.8, 8.5 Hz, 1H, CH_2), 2.64 (dd, *J* = 13.9, 6.1 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.8, 168.4, 167.8, 134.6, 134.6, 131.5, 125.8, 123.7, 117.5, 111.6, 91.7, 68.0, 66.7, 63.3, 53.2, 53.0, 32.1 ppm;

IR (film): $\tilde{\nu}$ 2958 (w), 2226 (w), 1775 (w), 1732 (s), 1712 (s), 1633 (w), 1572 (w), 1436 (w), 1354 (w), 1328 (w), 1271 (m), 1218 (w), 1130 (w), 1088 (w), 972 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{16}N_3O_6$ [M+] 406.1034; found 406.1036.

***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**49**).



Following the general procedure nicotinonitrile (**SI-67**) (104 mg, 1.00 mmol, 1.00 equiv.), **14** (318 mg, 1.05 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (62 mg, 0.10 mmol, 10 mol%) were stirred in CH_2Cl_2 (1.0 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 280 mg (0.69 mmol, 69%) of the title compound **49** were isolated as a yellow oil.

Performing the reaction with **SI-67** (21 mg, 0.20 mmol), **14** (64 mg, 0.21 mmol) and $Yb(OTf)_3$ (12 mg, 20 µmol) afforded 58 mg (0.14 mmol, 71%) of the title compound **49**.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

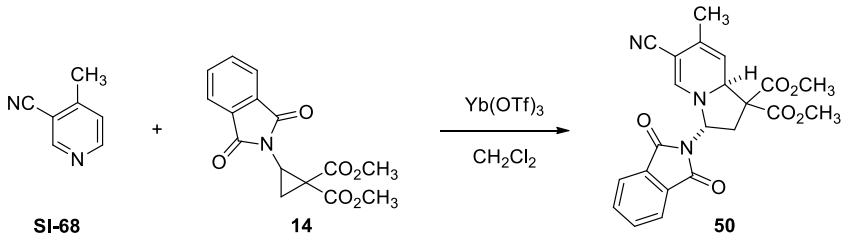
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.76 (t, *J* = 1.2 Hz, 1H, C=C*H*-N), 6.07 (dd, *J* = 8.6, 6.3 Hz, 1H, C*H*-NPhth), 5.81 (dt, *J* = 10.3, 1.7 Hz, 1H, C*H*=CH-CHN), 5.57 (t, *J* = 2.2 Hz, 1H, N-C*H*-CH=CH), 5.37 (ddd, *J* = 10.2, 2.4, 1.0 Hz, 1H, CH=C*H*-CHN), 3.82 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 2.82 (dd, *J* = 14.0, 8.6 Hz, 1H, CH_2), 2.72 (dd, *J* = 13.9, 6.3 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 168.4, 167.5, 143.8, 134.8, 131.3, 123.9, 121.4, 119.7, 113.9, 79.4, 67.2, 66.0, 62.7, 53.1, 53.0, 32.1 ppm;

IR (film): $\tilde{\nu}$ 3007 (w), 2956 (w), 2257 (w), 2203 (m), 1776 (w), 1713 (s), 1644 (m), 1577 (m), 1435 (w), 1394 (w), 1353 (m), 1332 (m), 1273 (s), 1226 (m), 1128 (m), 1100 (m), 981 (w), 910 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{18}N_3O_6^+$ $[M+H]^+$ 408.1190; found 408.1186.

***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-7-methyl-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**50**).



SI-68 **14** **50**

Following the general procedure 3-cyano-4-methylpyridine (**SI-68**) (24 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 3:1 to 2:1) and 63 mg (0.15 mmol, 75%) of the title compound **50** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

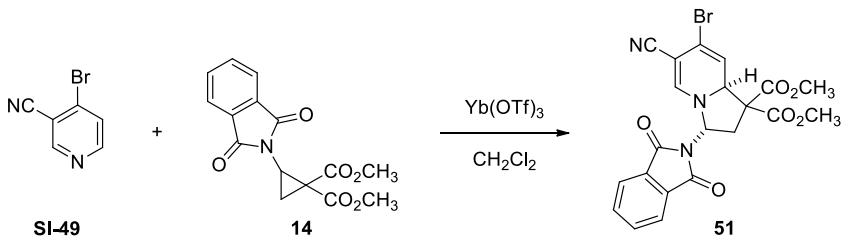
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.78 (s, 1H, C*H*=C(CN)), 6.06 (dd, *J* = 8.6, 6.2 Hz, 1H, N-C*H*-Phth), 5.51 (t, *J* = 2.0 Hz, 1H, N-C*H*-CH=C(CH_3)), 5.18 – 5.11 (m, 1H, C*H*=C(CH_3)), 3.81 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.81 (dd, *J* = 14.0, 8.6 Hz, 1H, CH_2), 2.71 (dd, *J* = 14.0, 6.2 Hz, 1H, CH_2), 1.80 (t, *J* = 1.6 Hz, 3H, CH_3);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.8, 168.6, 167.5, 144.0, 134.7, 131.4, 128.4, 123.8, 119.1, 109.4, 82.4, 67.1, 66.0, 63.5, 53.0, 52.9, 32.2, 19.4;

IR (film): $\tilde{\nu}$ 3056 (w), 2956 (w), 2202 (w), 1777 (w), 1718 (s), 1660 (w), 1585 (w), 1436 (w), 1351 (w), 1329 (w), 1266 (s), 1130 (w), 1092 (m), 909 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{22}H_{19}N_3NaO_6^+$ $[M+Na]^+$ 444.1166; found 444.1165.

***anti*-Dimethyl 7-bromo-6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**51**).



SI-49 **14** **51**

Following the general procedure 4-bromopyridine-3-carbonitrile (**SI-49**) (37 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica,

pentane:EtOAc 4:1 to 2:1) and 68 mg (0.14 mmol, 70%) of the title compound **51** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

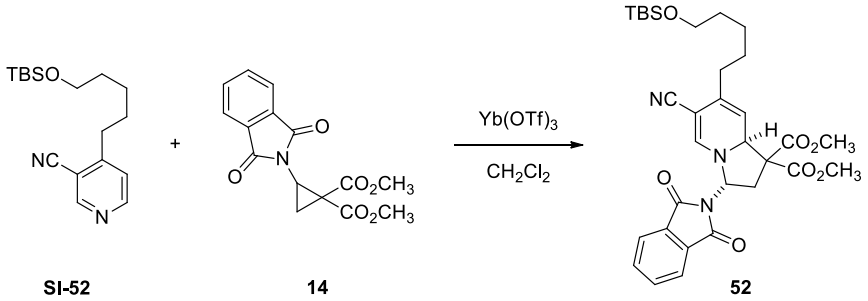
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.79 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.81 (s, 1H, N-C*H*=C(CN)), 6.08 (dd, *J* = 8.6, 6.3 Hz, 1H, N-C*H*-Phth), 5.70 (d, *J* = 2.5 Hz, 1H, C(Br)=C*H*), 5.58 (d, *J* = 2.5 Hz, 1H, N-C*H*-CH=C(Br)), 3.83 (s, 6H, OCH_3), 2.84 (dd, *J* = 14.0, 8.6 Hz, 1H, CH_2), 2.73 (dd, *J* = 13.9, 6.3 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 168.0, 167.3, 144.8, 134.9, 131.2, 124.0, 117.9, 114.3, 113.1, 83.5, 66.8, 65.7, 65.1, 53.4, 53.2, 32.1 ppm;

IR (film): $\tilde{\nu}$ 2956 (w), 2208 (w), 1730 (s), 1712 (s), 1626 (m), 1577 (m), 1434 (w), 1351 (m), 1273 (s), 1133 (m), 1103 (m), 1001 (m), 912 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{15}BrN_3O_6^+$ $[M+H]^+$ 484.0139; found 484.0130.

***anti*-Dimethyl 7-(5-((*tert*-butyldimethylsilyl)oxy)pentyl)-6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**52**).



SI-52 **14** **52**

Following the general procedure **SI-52** (61 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 3:1 to 2:1) and 88 mg (0.15 mmol, 72%) of the title compound **52** were isolated as a yellow oil containing minor impurities which could not be removed.

R_f: 0.5 (silica, pentane:EtOAc 2:1);

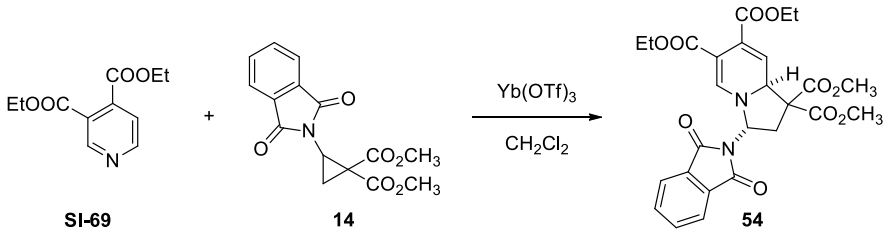
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.79 (s, 1H, N-C*H*=C(CN)), 6.07 (dd, *J* = 8.6, 6.3 Hz, 1H, C*H*Pthth), 5.55 (dt, *J* = 2.4, 1.3 Hz, 1H, C*H*-CH-N), 5.12 (dd, *J* = 2.4, 1.3 Hz, 1H, N-C*H*-CH), 3.83 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.59 (t, *J* = 6.6 Hz, 2H, CH_2-OTBS), 2.82 (dd, *J* = 14.1, 8.6 Hz, 1H, CH_2-CHPhth), 2.73 (dd, *J* = 14.1, 6.3 Hz, 1H, CH_2-CHPhth), 2.09 (t, *J* = 7.6 Hz, 2H, C-CH_2), 1.56 – 1.40 (m, 4H, 2x CH_2), 1.34 (m, 2H, CH_2), 0.87 (s, 9H, C(CH_3)$_3$), 0.03 (s, 6H, Si(CH_3)$_2$);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.8, 168.6, 167.5, 144.4, 134.8, 132.8, 131.4, 123.9, 119.1, 109.0, 82.1, 67.2, 66.1, 63.5, 63.1, 53.0 (2 C), 33.3, 32.6, 32.3, 28.2, 26.0, 25.3, 18.3, -5.3;

IR (film): $\tilde{\nu}$ 2953 (w), 2931 (w), 2857 (w), 2202 (w), 1777 (w), 1716 (s), 1602 (w), 1470 (w), 1436 (w), 1394 (w), 1351 (w), 1327 (w), 1273 (w), 1217 (w), 1099 (m), 912 (m), 836 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{32}H_{42}N_3O_7Si^+$ $[M+H]^+$ 608.2787; found 608.2767.

***anti*-6,7-Diethyl 1,1-dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6,7(8a*H*)-tetracarboxylate** (**54**).



Following the general procedure dietyl pyridine-3,4-dicarboxylate (**SI-69**) (45 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 78 mg (0.15 mmol, 74%) of the title compound **54** were isolated as a yellow oil.

R_f: 0.2 (silica, pentane:EtOAc 2:1);

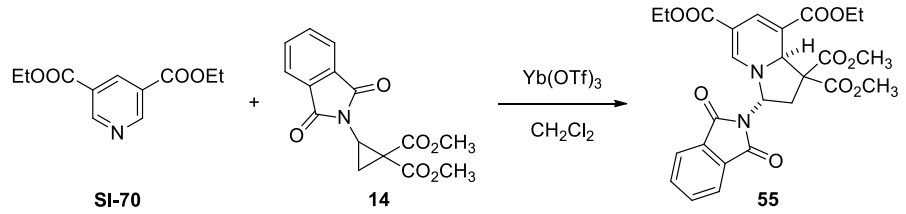
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.19 (s, 1H, N-C*H*=C(COOEt)), 6.12 (dd, *J* = 8.6, 6.3 Hz, 1H, C*H*-Phth), 5.67 – 5.54 (m, 2H, N-C*H*-CH and N-CH-C*H*=C(COOEt)), 4.20 (qd, *J* = 7.1, 4.0 Hz, 2H, OCH_2), 4.06 (qd, *J* = 7.1, 2.5 Hz, 2H, OCH_2), 3.81 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.86 (dd, *J* = 13.9, 8.6 Hz, 1H, CH_2), 2.65 (dd, *J* = 13.9, 6.3 Hz, 1H, CH_2), 1.26 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.17 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.5, 168.3, 168.0, 167.4, 164.6, 142.9, 134.7, 131.4, 130.6, 123.8, 114.6, 97.9, 67.1, 65.6, 63.0, 61.0, 59.7, 53.1, 53.0, 32.6, 14.3, 14.0 ppm;

IR (film): $\tilde{\nu}$ 2999 (w), 2968 (w), 2238 (w), 1786 (w), 1742 (s), 1702 (s), 1653 (w), 1557 (m), 1459 (m), 1342 (m), 1283 (s), 1166 (s), 1082 (s), 1043 (m), 982 (w), 934 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{26}H_{27}N_2O_{10}^+$ $[M+H]^+$ 527.1660; found 527.1669.

***anti*-6,8-Diethyl 1,1-dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6,8(8a*H*)-tetracarboxylate** (**55**).



Following the general procedure dietyl pyridine-3,5-dicarboxylate (**SI-70**) (45 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 82 mg (0.16 mmol, 78%) of the title compound **55** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

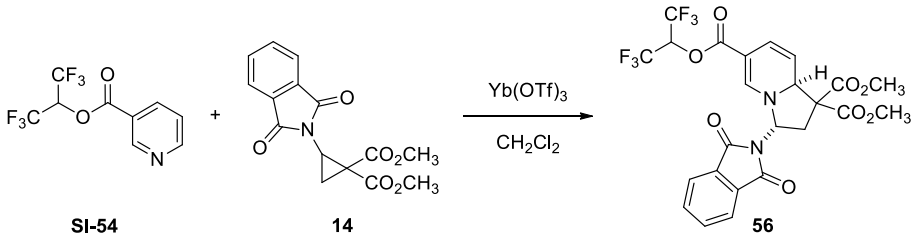
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.77 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.42 (t, *J* = 1.4 Hz, 1H, N-C*H*=C(COOEt)), 7.30 (d, *J* = 1.4 Hz, 1H, (COOEt)C-C*H*=C(COOEt)), 6.09 (d, *J* = 1.4 Hz, 1H, N-C*H*-C(COOEt)), 5.98 (dd, *J* = 8.1 Hz, 1H, C*H*-Phth), 4.28 – 4.00 (m, 4H, 2xOCH_2), 3.83 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.97 (m, 2H, CH_2), 1.27 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.20 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 167.9, 167.0, 165.2, 165.0, 145.6, 134.7, 131.7, 131.4, 123.8, 114.4, 99.0, 66.4, 65.7, 65.4, 60.2, 59.8, 52.9, 35.0, 14.4, 14.2

IR (film): $\tilde{\nu}$ 2983 (w), 2956 (w), 2261 (w), 1779 (w), 1718 (s), 1687 (s), 1634 (m), 1557 (m), 1435 (w), 1368 (w), 1330 (m), 1270 (m), 1225 (s), 1131 (s), 1089 (m), 1023 (w), 910 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{26}H_{27}N_2O_{10}^+$ $[M+H]^+$ 527.1660; found 527.1642.

***anti*-6-(1,1,1,3,3,3-Hexafluoropropan-2-yl) 1,1-dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6(8a*H*)-tricarboxylate** (**56**).



Following the general procedure 1,1,1,3,3,3-hexafluoropropan-2-yl nicotinate (**SI-54**) (55 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column

chromatography (silica, pentane:EtOAc 5:1 to 4:1) and 84 mg (0.15 mmol, 73%) of the title compound **56** were isolated as a yellow oil.

R_f: 0.5 (silica, pentane:EtOAc 2:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.38 (s, 1H, (COOR)C=C*H*-N), 6.32 (dt, *J* = 10.5, 1.8 Hz, 1H, CH=C*H*-C(COOR)), 6.17 (dd, *J* = 8.7, 6.2 Hz, 1H, N-C*H*-Phth), 5.81 (quint, *J* = 6.3 Hz, 1H, C*H*(CCF_3)$_2$), 5.65 (t, *J* = 2.2 Hz, 1H, N-C*H*), 5.39 (dd, *J* = 10.5, 2.2 Hz, 1H, N-CH-C*H*=CH), 3.84 (s, 3H, OC*H*$_3$), 3.78 (s, 3H, OC*H*$_3$), 2.88 (dd, *J* = 14.0, 8.7 Hz, 1H, CH_2), 2.72 (dd, *J* = 14.0, 6.2 Hz, 1H, CH_2);

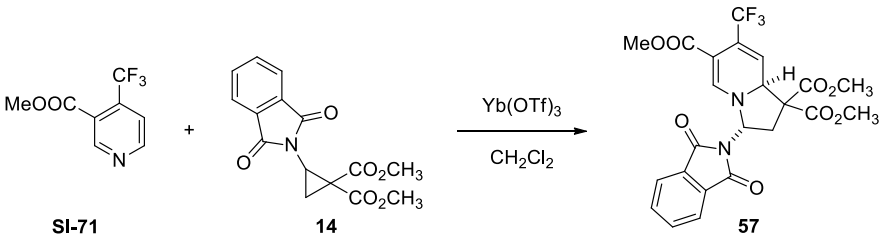
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.6, 168.4, 167.4, 161.9, 145.3, 134.8, 131.4, 123.9, 121.5, 120.7 (q, *J* = 282.9 Hz), 112.3, 95.8, 67.1, 65.6, 65.5 (quint, *J* = 34.5 Hz), 63.4, 53.1, 53.0, 32.6;

^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.3 – –73.4 (m);

IR (film): $\tilde{\nu}$ 2958 (w), 2259 (w), 1715 (s), 1638 (w), 1574 (m), 1436 (w), 1352 (m), 1274 (m), 1195 (m), 1099 (s), 982 (w), 907 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{24}H_{18}F_6N_2NaO_8^+$ $[M+Na]^+$ 599.0860; found 599.0850.

***anti*-Trimethyl 3-(1,3-dioxoisoindolin-2-yl)-7-(trifluoromethyl)-2,3-dihydroindolizine-1,1,6(8a*H*)-tricarboxylate** (**57**).



SI-71 **14** **57**

Following the general procedure methyl 4-(trifluormethyl)nicotinate (**SI-71**) (41 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and Yb(OTf)$_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 75 mg (0.15 mmol, 74%) of the title compound **57** were isolated as a yellow oil.

R_f: 0.4 (silica, pentane:EtOAc 2:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.79 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.36 (s, 1H, N-C*H*=C(COOMe)), 6.14 (dd, *J* = 8.6, 6.3 Hz, 1H, N-C*H*-Phth), 5.97 (s, 1H, C*H*=C(CF_3)), 5.67 (dd, *J* = 2.7 Hz, 1H, N-C*H*-CH=C(CF_3)), 3.84 (s, 3H, OC*H*$_3$), 3.77 (s, 3H, OC*H*$_3$), 3.62 (s, 3H, OC*H*$_3$), 2.89 (dd, *J* = 13.9, 8.6 Hz, 1H, C*H*$_2$), 2.68 (dd, *J* = 13.9, 6.3 Hz, 1H, C*H*$_2$);

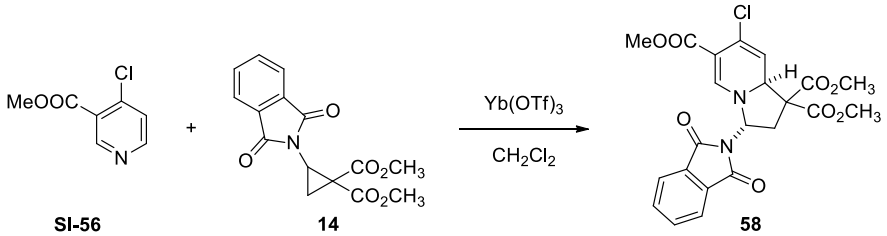
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.2, 168.1, 167.4, 163.9, 145.1, 134.8, 131.4, 126.0 (q, *J* = 32.2 Hz), 123.9, 116.6 (q, *J* = 7.8 Hz), 95.2, 67.1, 65.7, 62.6, 53.2, 53.1, 51.0, 32.6; [24]

^{19}F NMR (376 MHz, $CDCl_3$): δ = –63.3 (s);

IR (film): $\tilde{\nu}$ 2956 (w), 2372 (w), 2350 (m), 1713 (s), 1642 (w), 1572 (m), 1436 (m), 1354 (m), 1326 (m), 1289 (m), 1222 (w), 1142 (s), 1089 (m), 1013 (m), 916 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{23}H_{20}F_3N_2O_8^+$ $[M+H]^+$ 509.1166; found 509.1136.

***anti*-Trimethyl 7-chloro-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6(8a*H*)-tricarboxylate** (**58**).



SI-56 **14** **58**

Following the general procedure methyl 4-chloronicotinate (**SI-56**) (34 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 μmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 72 mg (0.15 mmol, 76%) of the title compound **58** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.79 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.33 (s, 1H, N-C*H*=C($COOCH_3$)), 6.13 (dd, *J* = 8.7, 6.3 Hz, 1H, C*H*-Phth), 5.63 (d, *J* = 2.7 Hz, 1H, C*H*=CCl), 5.46 (d, *J* = 2.7 Hz, 1H, N-C*H*-CH), 3.83 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3), 2.86 (dd, *J* = 13.9, 8.7 Hz, 1H, CH_2), 2.68 (dd, *J* = 13.9, 6.3 Hz, 1H, CH_2);

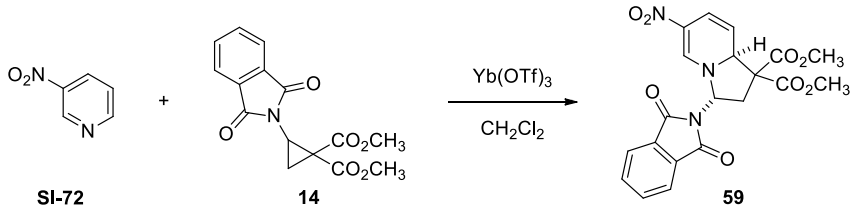
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.6, 168.3, 167.4, 164.1, 144.8, 134.8, 131.4, 127.6, 123.9, 111.3, 97.3, 67.1, 65.8, 64.8, 53.3, 53.1, 50.9, 32.7;

IR (film): $\tilde{\nu}$ 2955 (w), 1777 (w), 1732 (s), 1715 (s), 1626 (w), 1566 (w), 1435 (w), 1354 (m), 1327 (m), 1263 (m), 1149 (m), 1016 (w), 917 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{22}H_{20}ClN_2O_8^+$ $[M+H]^+$ 475.0903; found 475.0900.

[24] The CF_3 carbon was not observed.

***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-6-nitro-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**59**).



Following the general procedure 3-nitropyridine (**SI-72**) (25 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 4:1 to 2:1) and 65 mg (0.15 mmol, 76%) of the title compound **59** were isolated as a red oil.

R_f: 0.2 (silica, pentane:EtOAc 2:1);

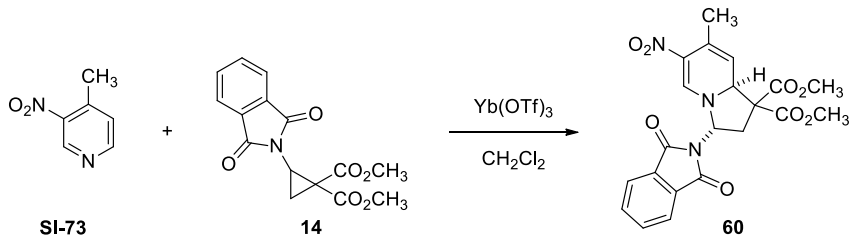
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.87 (d, *J* = 1.7 Hz, 1H, C=C*H*N), 7.81 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 6.72 (dt, *J* = 10.8, 2.1 Hz, 1H, NCH=CH=C*H*), 6.22 (dd, *J* = 8.6, 6.7 Hz, 1H, C*H*-NPhth), 5.67 (t, *J* = 2.1 Hz, 1H, NC*H*-CH=CH), 5.43 (dd, *J* = 10.8, 2.1 Hz, 1H, NCH-C*H*=CH), 3.85 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 2.91 (dd, *J* = 13.9, 8.6 Hz, 1H, CH_2), 2.79 (dd, *J* = 13.9, 6.7 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.2, 168.0, 167.2, 141.6, 135.0, 131.2, 124.4, 124.0, 119.3, 112.5, 66.8, 65.0, 63.9, 53.3, 53.2, 32.7 ppm;

IR (film): $\tilde{\nu}$ 2958 (w), 1780 (w), 1715 (s), 1635 (m), 1577 (m), 1549 (w), 1490 (w), 1435 (w), 1361 (w), 1267 (m), 1223 (m), 1181 (s), 1131 (w), 1085 (s), 982 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{20}H_{18}N_3O_8^+$ $[M+H]^+$ 428.1088; found 428.1092.

***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-7-methyl-6-nitro-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**60**).



Following the general procedure 4-methyl-3-nitropyridine (**SI-73**) (28 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 3:1 to 2:1) and 65 mg (0.15 mmol, 74%) of the title compound **60** were isolated as a red oil.

R_f: 0.2 (silica, pentane:EtOAc 2:1);

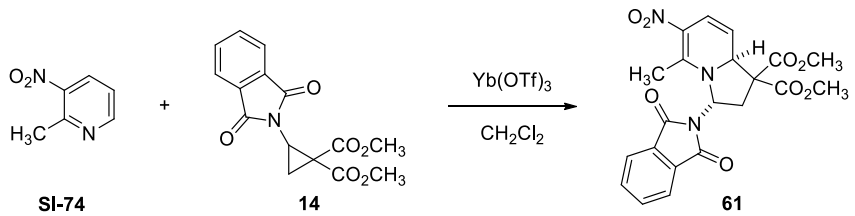
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1H, C=C*H*-N), 7.89 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.80 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.21 (dd, *J* = 8.5, 6.8 Hz, 1H, N-C*H*-Phth), 5.58 (t, *J* = 2.0 Hz, 1H, N-C*H*-CH), 5.12 (t, *J* = 1.7 Hz, 1H, (CH_3)C=C*H*), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.88 (dd, *J* = 13.9, 8.5 Hz, 1H, CH_2), 2.75 (dd, *J* = 13.9, 6.8 Hz, 1H, CH_2), 2.15 (t, *J* = 1.7 Hz, 3H, CH_3);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.3, 168.2, 167.1, 143.2, 134.9, 131.3, 129.2, 125.9, 124.0, 110.5, 66.8, 65.1, 64.1, 53.2, 53.1, 32.8, 21.5;

IR (film): $\tilde{\nu}$ 2957 (w), 1778 (w), 1715 (s), 1671 (m), 1640 (m), 1571 (m), 1497 (w), 1434 (w), 1359 (w), 1265 (s), 1234 (m), 1169 (s), 1079 (s), 1041 (m), 942 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{20}N_3O_8^+$ $[M+H]^+$ 442.1245; found 442.1241.

***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-5-methyl-6-nitro-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate** (**61**).



Following the general procedure 2-methyl-3-nitropyridine (**SI-74**) (28 mg, 0.20 mmol, 1.00 equiv.), **14** (64 mg, 0.21 mmol, 1.05 equiv.) and $Yb(OTf)_3$ (12 mg, 20 µmol, 10 mol%) were stirred in CH_2Cl_2 (0.2 mL, 1 M) for 3 hours. The crude product was purified by column chromatography (silica, pentane:EtOAc 3:1 to 2:1) and 71 mg (0.15 mmol, 80%) of the title compound **61** were isolated as a yellow oil.

R_f: 0.3 (silica, pentane:EtOAc 2:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.79 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.84 (dd, *J* = 10.7, 2.3 Hz, 1H, C*H*-C(NO_2)), 6.42 (dd, *J* = 8.5, 6.8 Hz, 1H, C*H*-Phth), 5.77 (t, *J* = 2.3 Hz, 1H, N-C*H*-CH), 5.40 (dd, *J* = 10.7, 2.3 Hz, 1H, n-CH-C*H*=CH), 3.80 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 2.95 (dd, *J* = 13.7, 8.5 Hz, 1H, CH_2), 2.50 (dd, *J* = 13.7, 6.8 Hz, 1H, CH_2), 2.40 (s, 3H, CH_3);

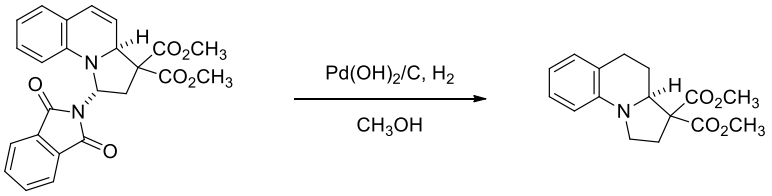
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.1, 167.8, 166.6, 154.7, 135.0, 130.9, 125.1, 124.0, 121.3, 110.7, 65.1, 64.9, 63.8, 53.2, 53.1, 34.9, 18.0;

IR (film): $\tilde{\nu}$ 2977 (w), 2277 (w), 1788 (w), 1748 (s), 1557 (m), 1487 (w), 1282 (s), 1254 (s), 1216 (s), 1175 (s), 1105 (m), 1024 (m), 930 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{20}N_3O_8^+$ $[M+H]^+$ 442.1245; found 442.1251.

12. Product modification

Dimethyl 1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**SI-75**).



17 **SI-75**

$Pd(OH)_2$/C (3 mg, 20% Pd, 10%$_{w/w}$) was added to a solution of **17** (30 mg, 70 µmol) in CH_3OH (0.4 mL, 0.17 M), the mixture was purged with H_2 and stirred for 18 hours. Thereafter the mixture was filtered through a plug of celite® and concentrated. The residue product was purified by column chromatograohy (SiO_2, pentane:EtOAc 50:1) and 14 mg (50 µmol, 70%) of the title compound **SI-75** were isolated as a yellow oil.

R_f: 0.8 (silica, pentane:EtOAc 4:1);

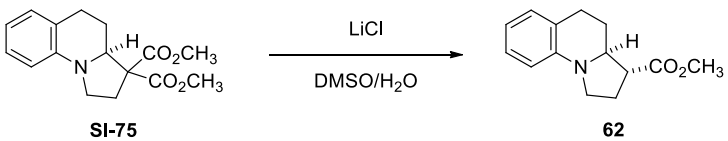
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 – 7.04 (m, 1H, Ar*H*), 6.98 (d, *J* = 7.4 Hz, 1H, Ar*H*), 6.59 (td, *J* = 7.3, 1.1 Hz, 1H, Ar*H*), 6.39 (dd, *J* = 8.1, 1.1 Hz, 1H, Ar*H*), 4.03 (dd, *J* = 11.5, 2.9 Hz, 1H, C*H*), 3.79 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.62 (q, *J* = 8.4 Hz, 1H, CH_2), 3.32 (td, *J* = 9.3, 2.4 Hz, 1H, CH_2), 2.99 – 2.87 (m, 1H, CH_2), 2.80 (ddd, *J* = 16.2, 4.7, 2.4 Hz, 1H, CH_2), 2.73 (ddd, *J* = 13.1, 7.8, 2.4 Hz, 1H, CH_2), 2.34 (ddt, *J* = 12.3, 5.1, 2.7 Hz, 1H, CH_2), 2.22 (ddd, *J* = 13.1, 9.6, 8.8 Hz, 1H, CH_2), 1.37 (tdd, *J* = 12.7, 11.6, 4.7 Hz, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 169.8, 144.1, 128.3, 127.2, 121.0, 115.7, 110.2, 62.1, 61.9, 52.6, 52.4, 45.7, 31.8, 27.8, 23.9;

IR (film): $\tilde{\nu}$ = 2954 (w), 2925 (w), 2854 (w), 1732 (s), 1605 (m), 1576 (w), 1506 (m), 1480 (w), 1460 (m), 1436 (m), 1365 (w), 1314 (m), 1270 (s), 1221 (m), 1199 (m), 1172 (m), 1090 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{16}H_{19}NNaO_4^+$ $[M+Na]^+$ 312.1206; found 312.1205.

(3*S*,3a*R*)-methyl 1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinoline-3-carboxylate (**62**).



SI-75 **62**

LiCl (37 mg, 0.86 mmol) was added to a solution of **SI-75** (50 mg, 0.17 mmol) in DMSO:H_2O 10:1 (0.88 mL, 0.2 M) at room temperature and the resulting mixture was then heated for 5 hours to 140 °C.

The mixture was cooled to room temperature, quenched with sat. aq. NH_4Cl (5 mL) and extracted with DCM (3x15 mL). The combined org. extracts were washed with brine (10 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatograohy (SiO_2, pentane:EtOAc 50:1) and 34 mg (0.15 mmol, 85%) of the title compound **62** were isolated as a yellow oil.

R_f: 0.5 (silica, pentane:EtOAc 20:1);

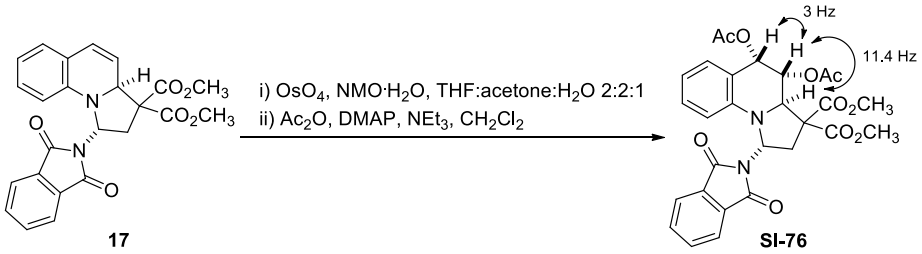
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 – 7.04 (m, 1H, Ar*H*), 7.00 (d, *J* = 7.3 Hz, 1H, Ar*H*), 6.60 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.41 (d, *J* = 8.1 Hz, 1H, Ar*H*), 3.75 (s, 3H, OCH_3), 3.65 – 3.53 (m, 1H, N-C*H*), 3.43 (td, *J* = 9.1, 2.3 Hz, 1H, N-CH_2), 3.31 (td, *J* = 9.3, 7.5 Hz, 1H, N-CH_2), 2.86 (m, 1H, Ar-CH_2), 2.78 (m, 1H, Ar-CH_2), 2.67 (m, 1H, C*H*-COOMe), 2.41 – 2.19 (m, 3H, CH_2), 1.56 – 1.41 (m, 1H, CH_2) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.4, 144.1, 128.5, 127.2, 121.3, 115.8, 110.2, 60.5, 51.9, 50.0, 46.4, 27.8, 27.6, 26.4 ppm;

IR (film): $\tilde{\nu}$ = 2952 (w), 2849 (w), 1737 (s), 1605 (m), 1506 (m), 1460 (w), 1352 (m), 1312 (w), 1279 (w), 1204 (w), 1054 (w), 1021 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{14}H_{18}NO_2^+$ $[M+H]^+$ 232.1332; found 232.1339.

***rac*-(1*R*,3a*S*,4*S*,5*R*)-Dimethyl 4,5-diacetoxy-1-(1,3-dioxoisoindolin-2-yl)-1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**SI-76**).



OsO_4 (0.38 mL, 60 µmol, 4% in water, 5 mol%) was added to a solution of **17** (510 mg, 1.18 mmol, 1 equiv.) and NMO·H_2O (261 mg, 1.93 mmol, 1.2 equiv.) in THF:acetone:water (2:2:1, 5.0 mL, 0.23 M) at room temperature and the resulting mixture was stirred for 18 hours. The reaction was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined org. extracts were washed with brine and dried over $MgSO_4$. The drying agent was filtered off and the solution was concentrated. The crude product was dissolved in CH_2Cl_2 (2.0 mL, 0.58 M), DMAP (14 mg, 0.12 mmol, 0.1 equiv.), NEt_3 (0.66 mL, 4.7 mmol, 4 equiv.) and Ac_2O (0.33 mL, 3.5 mmol, 3 equiv.) were added and the resulting mixture was stirred for 16 hours. The reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined org. extracts were washed with brine (15 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by

column chromatography (silica, pentane:EtOAc 2:1) and 0.46 g (0.84 mmol, 71%) of the title compound **SI-76** were isolated as a colorless oil.

R_f: 0.3 (silica, pentane:EtOAc 1:1);

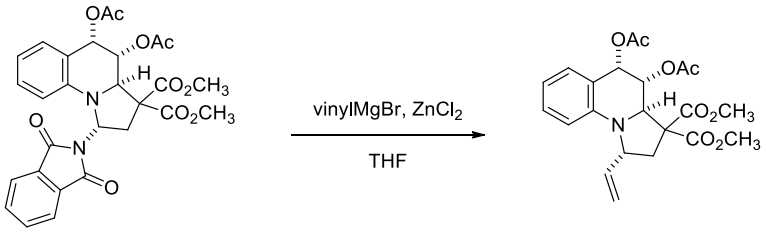
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.71 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.22 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.14 (ddd, *J* = 8.7, 7.5, 1.6 Hz, 1H, Ar*H*), 6.67 (td, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 6.55 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.32 (dd, *J* = 8.4, 6.0 Hz, 1H, C*H*-Phth), 6.14 (d, *J* = 3.0 Hz, 1H, Ar-C*H*-OAc), 5.41 (d, *J* = 11.4 Hz, 1H, C*H*-N), 5.05 (dd, *J* = 11.4, 3.0 Hz, 1H, C*H*-OAc), 3.82 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.29 (dd, *J* = 13.5, 8.3 Hz, 1H, CH_2), 2.79 (dd, *J* = 13.5, 6.0 Hz, 1H, CH_2), 2.14 (s, 3H, O*Ac*), 2.06 (s, 3H, O*Ac*);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 169.8, 169.2, 168.8, 167.6, 140.3, 134.3, 131.8, 131.5, 131.1, 123.6, 117.9, 117.5, 110.8, 69.3, 68.8, 62.9, 61.3, 60.0, 53.3, 52.8, 38.2, 21.3, 20.7;

IR (film): $\tilde{\nu}$ = 3016 (w), 2951 (w), 1742 (s), 1716 (s), 1610 (w), 1500 (w), 1374 (m), 1266 (s), 1243 (m), 1222 (m), 1188 (w), 1139 (w), 1053 (s), 1025 (m), 968 (w), 913 (w) cm^{-1};

HRMS (ESI) calcd. for $C_{28}H_{26}N_2NaO_{10}^+$ $[M+Na]^+$ 573.1480; found 573.1490.

***rac*-(1*S*,3a*S*,4*S*,5*R*)-Dimethyl 4,5-diacetoxy-1-vinyl-1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**63**).



SI-76 **63**

Vinylmagnesium bromide (0.47 mL, 0.33 mmol, 0.7 M in THF, 4 equiv.) was added dropwise to a solution of dry $ZnCl_2$ (0.11 g, 0.82 mmol, 10 equiv.) in THF (1 mL) and the resulting mixture was stirred for 10 minutes at room temperature. Thereafter a solution of **SI-76** (45 mg, 82 µmol, 1 equiv.) in THF (3.5 mL) was added dropwise and the resulting mixture was heated to 50 °C for 18 hours. Thereafter, the reaction was cooled to room temperature and quenched with sat. aq. NH_4Cl (10 mL). The mixture was extracted with CH_2Cl_2 (3 x 20 mL), the combined org. extracts were washed with brine (20 mL) and dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 3:1) and 24 mg (0.056 mmol, 68%) of the title compound **63** were isolated as a colorless oil.

R_f: 0.6 (silica, pentane:EtOAc 1:1);

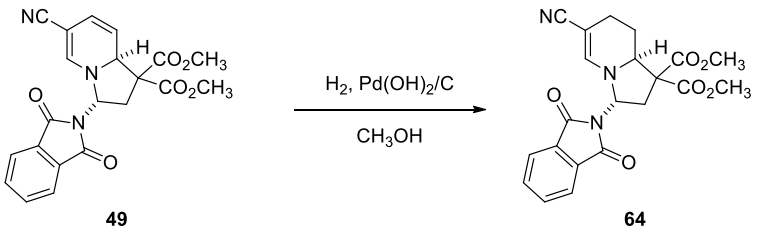
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 – 7.11 (m, 2H, Ar*H*), 6.65 (td, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 6.56 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.15 (d, *J* = 3.0 Hz, 1H, Ar-C*H*-OAc), 5.77 (ddd, *J* = 17.1, 10.2, 7.0 Hz, 1H, C*H*=CH_2), 5.31 (dt, *J* = 17.2, 1.1 Hz, 1H, CH=CH_2), 5.24 (dt, *J* = 10.2, 1.1 Hz, 1H, CH=CH_2), 5.13 (dd, *J* = 11.3, 3.0 Hz, 1H, CH-C*H*-OAc), 4.76 (d, *J* = 11.3 Hz, 1H, N-C*H*-CHOAc), 4.47 (q, *J* = 7.6 Hz, 1H, N-C*H*-CH=CH_2), 3.78 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.07 (dd, *J* = 13.1, 7.7 Hz, 1H, CH_2), 2.15 (dd, *J* = 13.1, 8.0 Hz, 1H, CH_2), 2.10 (s, 3H, O*Ac*), 2.01 (s, 3H, O*Ac*).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.4, 169.8, 169.6, 169.0, 142.7, 138.5, 131.3, 130.5, 116.9, 116.8, 116.5, 111.9, 69.4, 69.1, 60.4, 60.2, 60.1, 53.1, 52.8, 41.1, 21.3, 20.7;

IR (film): $\tilde{\nu}$ = 2675 (w), 2350 (w), 1739 (s), 1610 (w), 1498 (w), 1372 (w), 1261 (m), 1242 (m), 1224 (m), 1179 (w), 1060 (s), 1026 (m), 954 (w), 912 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{22}H_{26}NO_8^+$ $[M+H]^+$ 432.1653; found 432.1652.

***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3,8,8a-tetrahydroindolizine-1,1(7*H*)-dicarboxylate** (**64**).



49 **64**

$Pd(OH)_2$/C (12 mg, 10%$_{w/w}$, 20% Pd) was added to a solution of **49** (0.12 mg, 0.30 mmol) in methanol (3 mL), the mixture was purged with hydrogen and then stirred for 8 hours under hydrogen atmosphere. The mixture was filtered through a plug of Celite®, concentrated and the residue was purified by column chromatography (silica, pentane:EtOAc 2:1) affording 88 mg (0.22 mmol, 73%) of the title compound **64**.

R_f: 0.2 (silica, pentane:EtOAc 2:1);

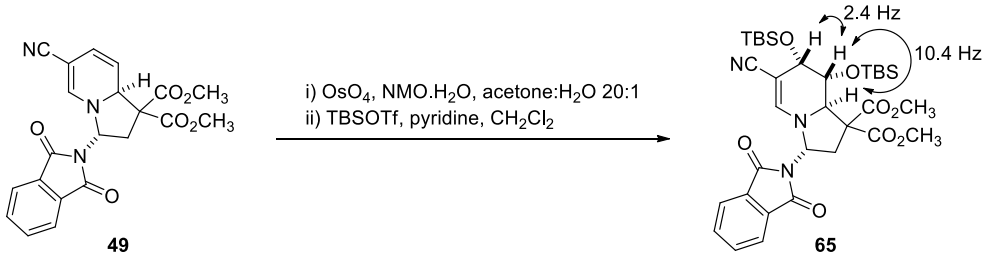
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H, *Phth*), 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.74 (d, *J* = 1.6 Hz, 1H, N-C*H*=C(CN)), 6.02 (dd, *J* = 8.2, 6.6 Hz, 1H, C*H*-Phth), 4.35 (dd, *J* = 11.4, 3.3 Hz, 1H, N-C*H*-CH_2), 3.81 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.89 (qd, *J* = 14.0, 7.4 Hz, 2H, CH_2), 2.42 – 2.29 (m, 2H, CH_2), 2.27 – 2.18 (m, 1H, CH_2), 1.24 – 1.13 (m, 1H, CH_2);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.5, 168.9, 167.5, 141.2, 134.7, 131.3, 123.7, 121.6, 77.6, 65.0, 62.2, 59.8, 53.0, 52.9, 34.7, 23.4, 22.5;

IR (film): $\tilde{\nu}$ = 2955 (w), 2854 (w), 2193 (m), 1776 (w), 1733 (s), 1714 (s), 1623 (s), 1438 (w), 1397 (w), 1353 (m), 1324 (m), 1272 (m), 1219 (w), 1151 (m), 1106 (m), 972 (w), 913 (m) cm^{-1};

HRMS (ESI) calcd. for $C_{21}H_{20}N_3O_6^+$ [M+H]$^+$ 410.1347; found 410.1348.

***rac*-(3*R*,7*R*,8*S*,8a*S*)-Dimethyl 7,8-bis((*tert*-butyldimethylsilyl)oxy)-6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3,8,8a-tetrahydroindolizine-1,1(7*H*)-dicarboxylate** (**65**).



OsO_4 (0.21 mL, 0.026 mmol, 4% in water, 5 mol%) was added to a solution of **49** (214 mg, 0.525 mmol, 1 equiv.) and NMO·H_2O (85 mg, 0.63 mmol, 1.2 equiv.) in acetone:water 20:1 (5.25 mL, 0.1 M) at 0 °C. The resulting mixture was stirred for 16 hours, while warming to room temperature, then the solvent was evaporated and the residue was dried in high vacuo. The residue was suspended in CH_2Cl_2 (2.5 mL) and pyridine (0.21 mL, 2.6 mmol, 5 equiv.) followed by TBSOTf (0.48 mL, 2.1 mmol, 4 equiv.) were added. The resulting mixture was stirred for 18 hours at room temperature and thereafter quenched with sat. aq. NH_4Cl (10 mL). The mixture was extracted with Et_2O (3 x 15 mL), the combined org. extracts were washed with brine (10 mL) and then dried over $MgSO_4$. The drying agent was filtered off and the solvent was evaporated. The residue was purified by column chromatography (silica, pentane:EtOAc 4:1) affording 231 mg (0.345 mmol, 66%) of the title compound **65** as a colorless oil.

R_f: 0.2 (silica, pentane:EtOAc 4:1);

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H, *Phth*), 6.75 (s, 1H, N-C*H*=C(CN)), 6.03 (t, *J* = 7.8 Hz, 1H, C*H*-Phth), 5.09 (d, *J* = 10.4 Hz, 1H, N-C*H*-CH(OTBS)), 4.27 (d, *J* = 2.4 Hz, 1H, C(CN)-C*H*(OTBS)), 3.82 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.72 (dd, *J* = 10.4, 2.4 Hz, 1H, (CN)C-CH-C*H*-CHN), 3.06 (dd, *J* = 13.2, 7.8 Hz, 1H, CH_2), 2.96 (dd, *J* = 13.2, 7.8 Hz, 1H, CH_2), 0.92 (s, 9H, C(CH_3)$_3$), 0.89 (s, 9H, C(CH_3)$_3$), 0.15 (s, 3H, SiCH_3), 0.13 (s, 3H, SiCH_3), 0.04 (s, 3H, SiCH_3), -0.06 (s, 3H, SiCH_3) ppm;

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.0, 168.2, 167.0, 143.6, 134.8, 131.3, 123.8, 121.1, 80.2, 70.7, 67.8, 64.9, 61.2, 61.0, 53.0, 52.9, 36.5, 25.9, 25.5, 18.1, 17.9, -3.2, -3.5, -4.8, -5.5 ppm;

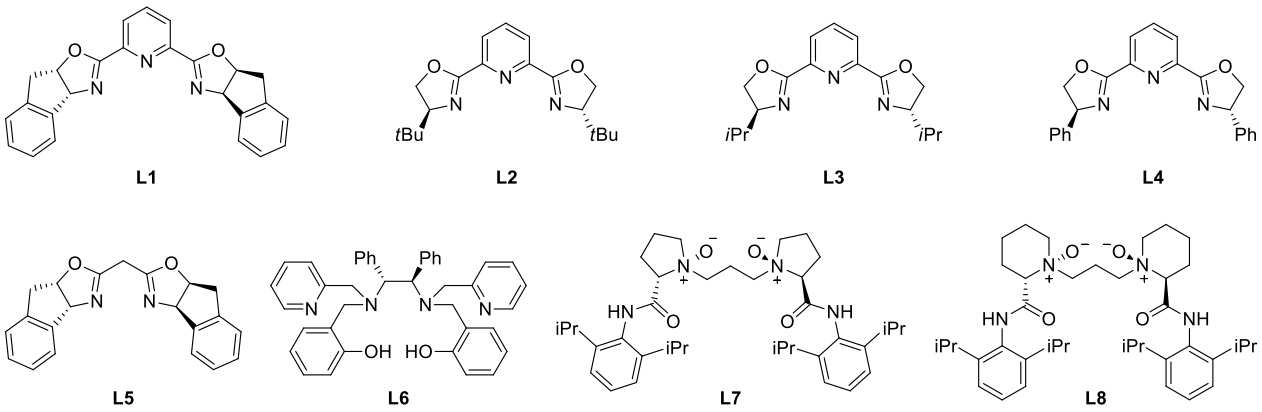
IR (film): $\tilde{\nu}$ = 2954 (w), 2930 (w), 2894 (w), 2857 (w), 2195 (w), 1720 (s), 1618 (s), 1472 (w), 1360 (w), 1255 (m), 1133 (m), 1109 (m), 958 (m), 913 (m), 840 (s) cm^{-1};

HRMS (ESI) calcd. for $C_{33}H_{47}N_3NaO_8Si_2^+$ [M+Na]$^+$ 692.2794; found 692.2797.

13. Attempts towards the Enantioselective Dearomatization

Table S8 Screening of chiral ligands for the annulation reaction.

8 1 equiv. | **14** 1.05 equiv. | 5 mol% | 6 mol% | **17**



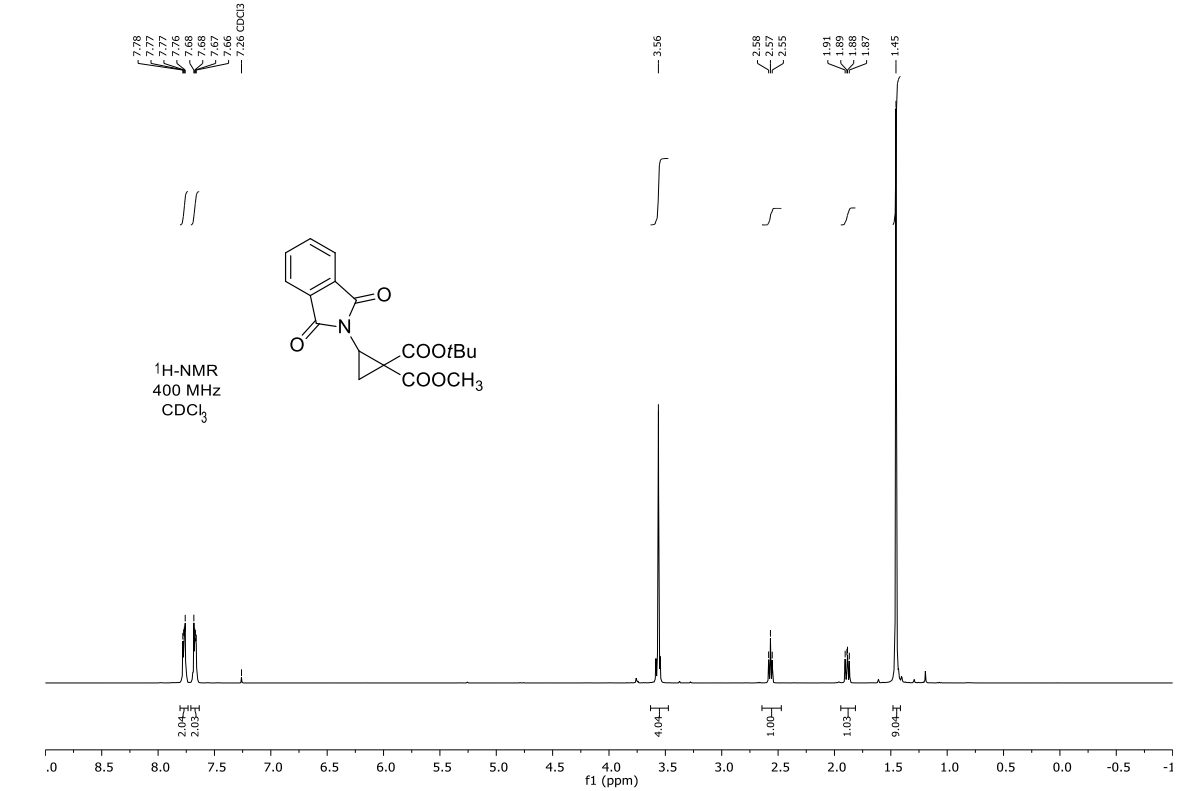
Entry	Lewis Acid	Ligand	Solvent	Yield	ee
1	$Yb(OTf)_3$	**L1**	CH_2Cl_2	88%	0%
2	$Sc(OTf)_3$	**L1**	CH_2Cl_2	90%	12%
3	$Sc(OTf)_3$	**L1**	PhCl	56%	9%
4	MgI_2	**L1**	CH_2Cl_2	81%	6%
5	$La(OTf)_3$	**L1**	CH_2Cl_2	91%	10%
6	$La(OTf)_3$	**L1**	THF	84%	10%
7	$Zn(OTf)_2$	**L1**	CH_2Cl_2	no conversion	-
8	$Zn(NTf_2)_2$	**L1**	CH_2Cl_2	9%	18%
9	$Sc(OTf)_3$	**L2**	CH_2Cl_2	55%	1%
10	$Sc(OTf)_3$	**L3**	CH_2Cl_2	35%	1%
11	$Sc(OTf)_3$	**L4**	CH_2Cl_2	44%	2%
12	$Cu(OTf)_2$	**L5**	CH_2Cl_2	no conversion	-
13	$Ni(OTf)_2$	**L5**	CH_2Cl_2	93%	6%
14	$Zn(OTf)_2$	**L5**	CH_2Cl_2	83%	10%
15	$Yb(OTf)_3$	**L6**	CH_2Cl_2	93%	0%
16	$Yb(OTf)_3$	**L7**	CH_2Cl_2	87%	0%
17	$Sc(OTf)_3$	**L7**	CH_2Cl_2	85%	0%
18	$Yb(OTf)_3$	**L8**	CH_2Cl_2	83%	0%
19	$Sc(OTf)_3$	**L8**	CH_2Cl_2	88%	0%

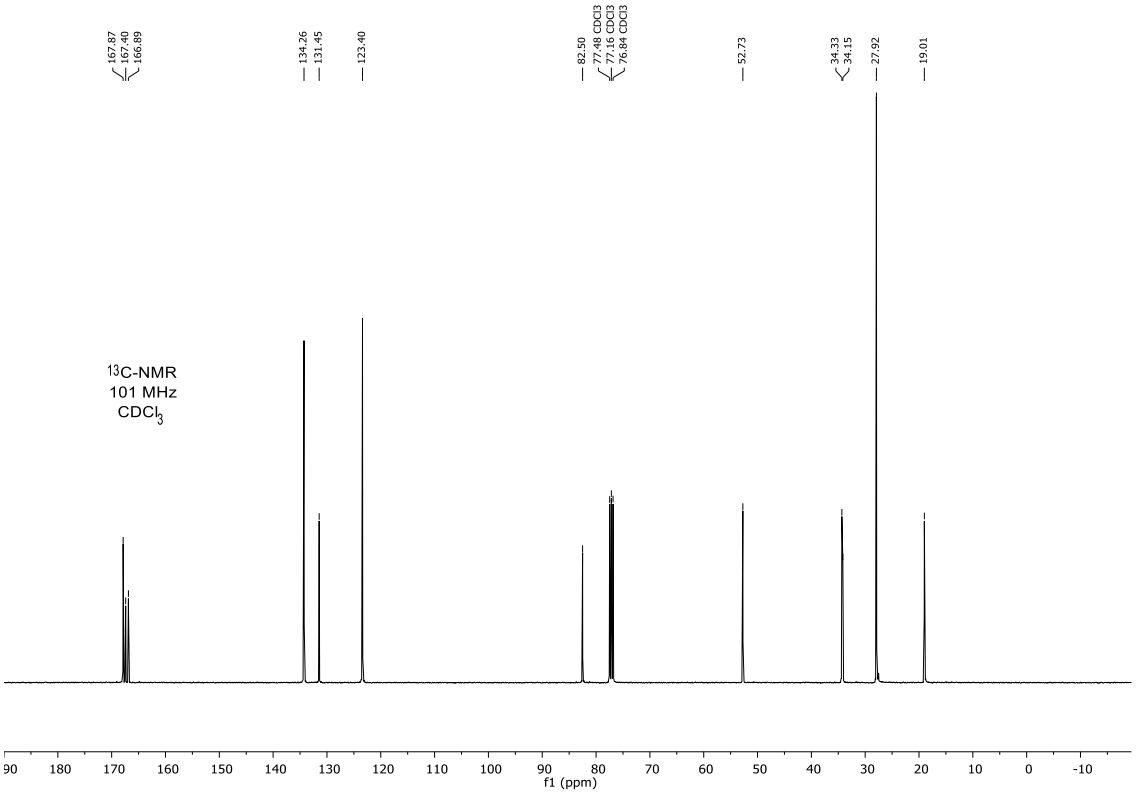
General procedure for the attempted enantioselective dearomatization

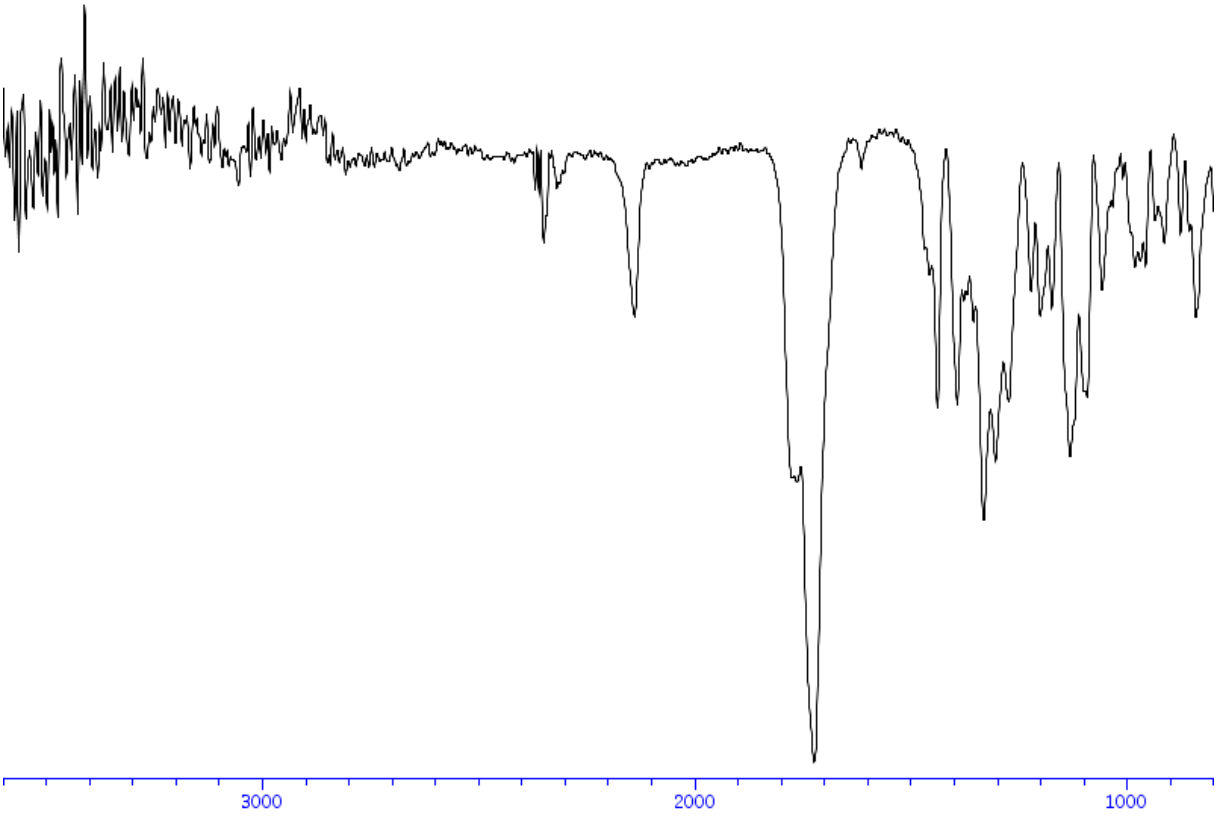
A vial was charged with the ligand (0.06 mmol, 6 mol%) and the Lewis acid (0.05 mmol, 5 mol%) in the glovebox, then CH_2Cl_2 (0.1 mL) was added and the resulting mixture was stirred for 3 hours at room temperature. Thereafter a solution of the cyclopropane **14** in CH_2Cl_2 (0.1 mL) was added, followed by quinoline **8** (0.10 mmol, 1.00 equiv.) and stirring of the mixture was continued for 16 hours at room temperature. The solvent was then evaporated and the residue was purified by column chromatography (silica, pentane:EtOAc 10:1 to 4:1). The enantiomeric excess was determined by chiral HPLC. Chiralcel IA, hexane:*i*PrOH 60:40, 1 mL/min, 31 min, t_{R1} = 10.2 min, t_{R2} 14.4 min, λ = 254 nm.

14. Spectra of new compounds

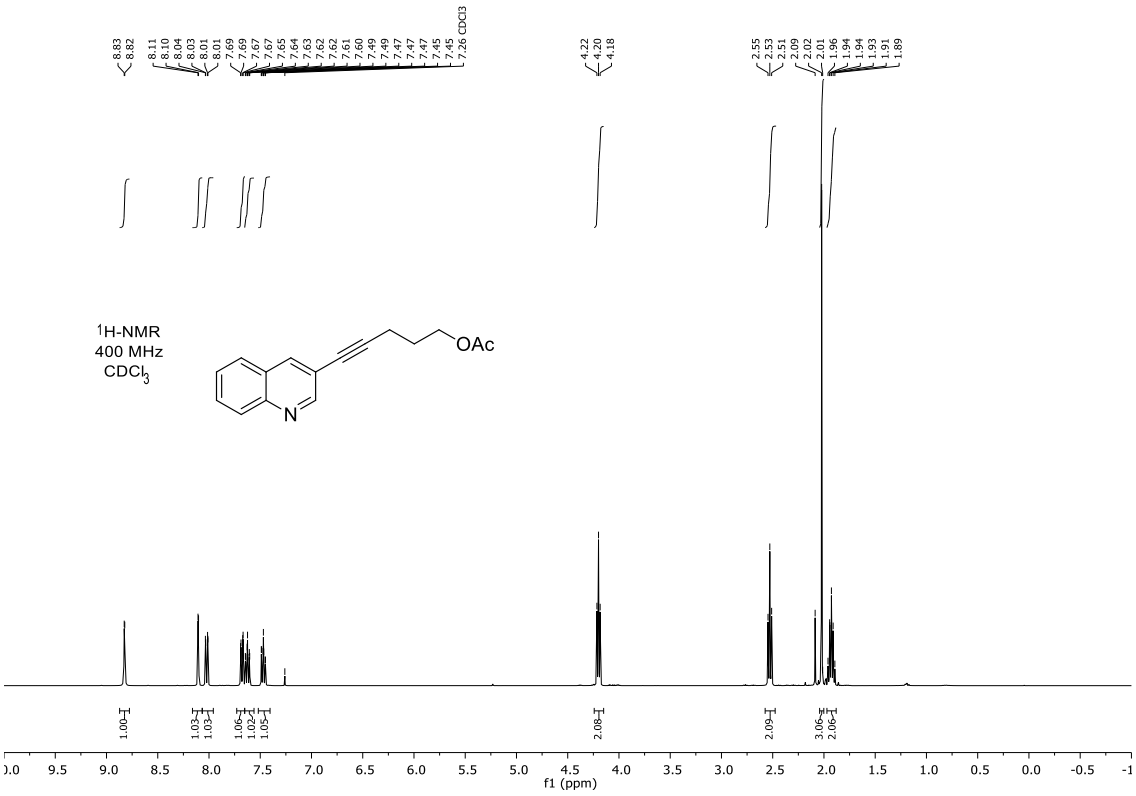
1-*tert*-Butyl 1-methyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (SI-32).

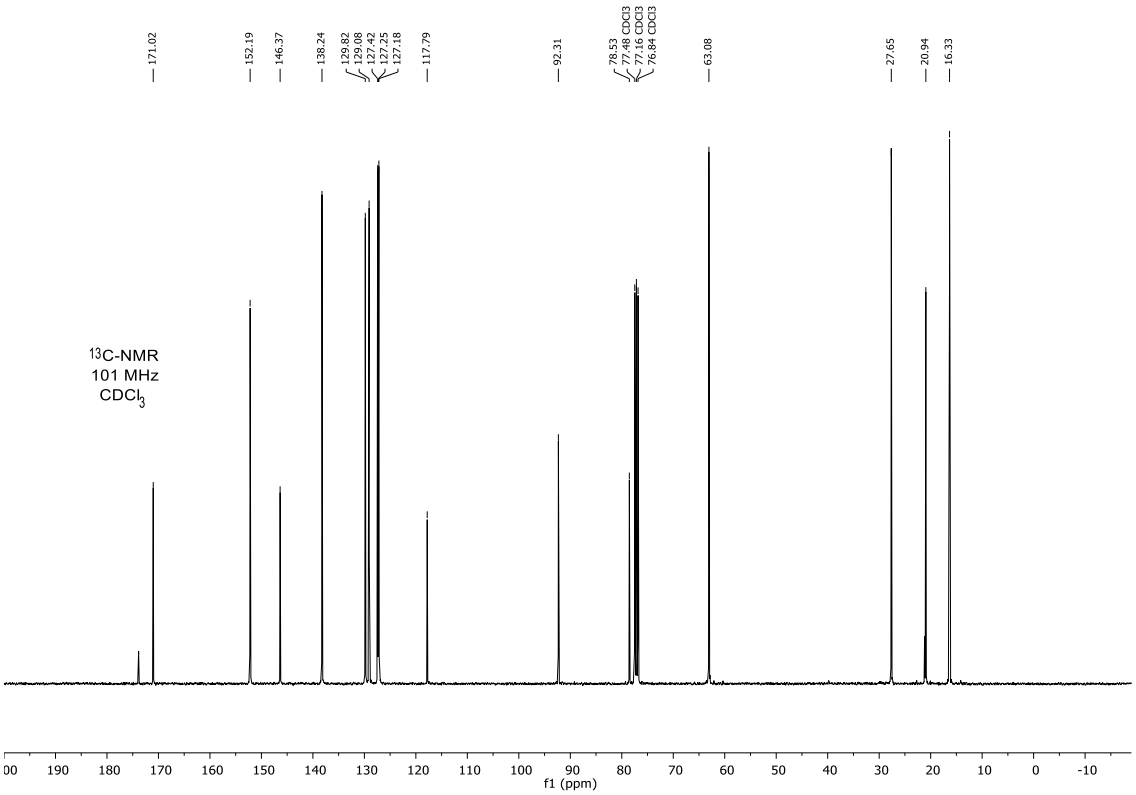


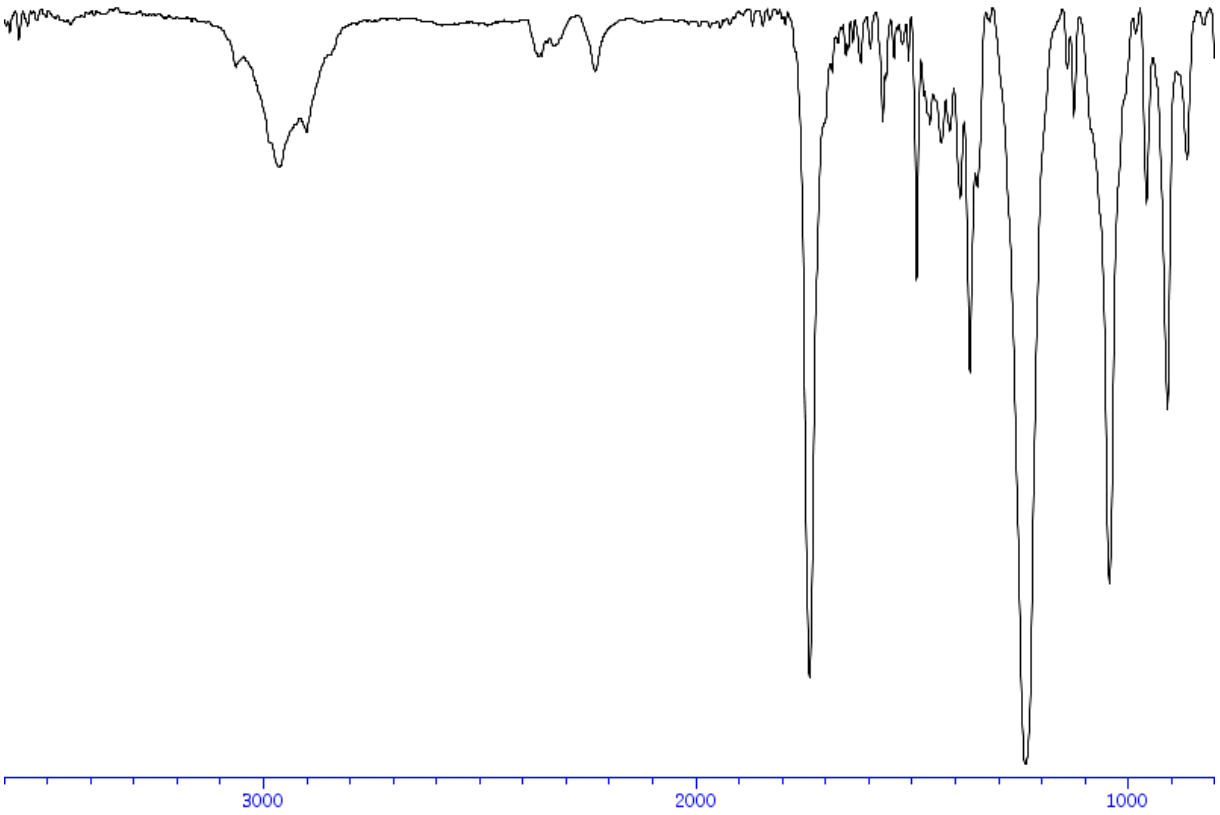




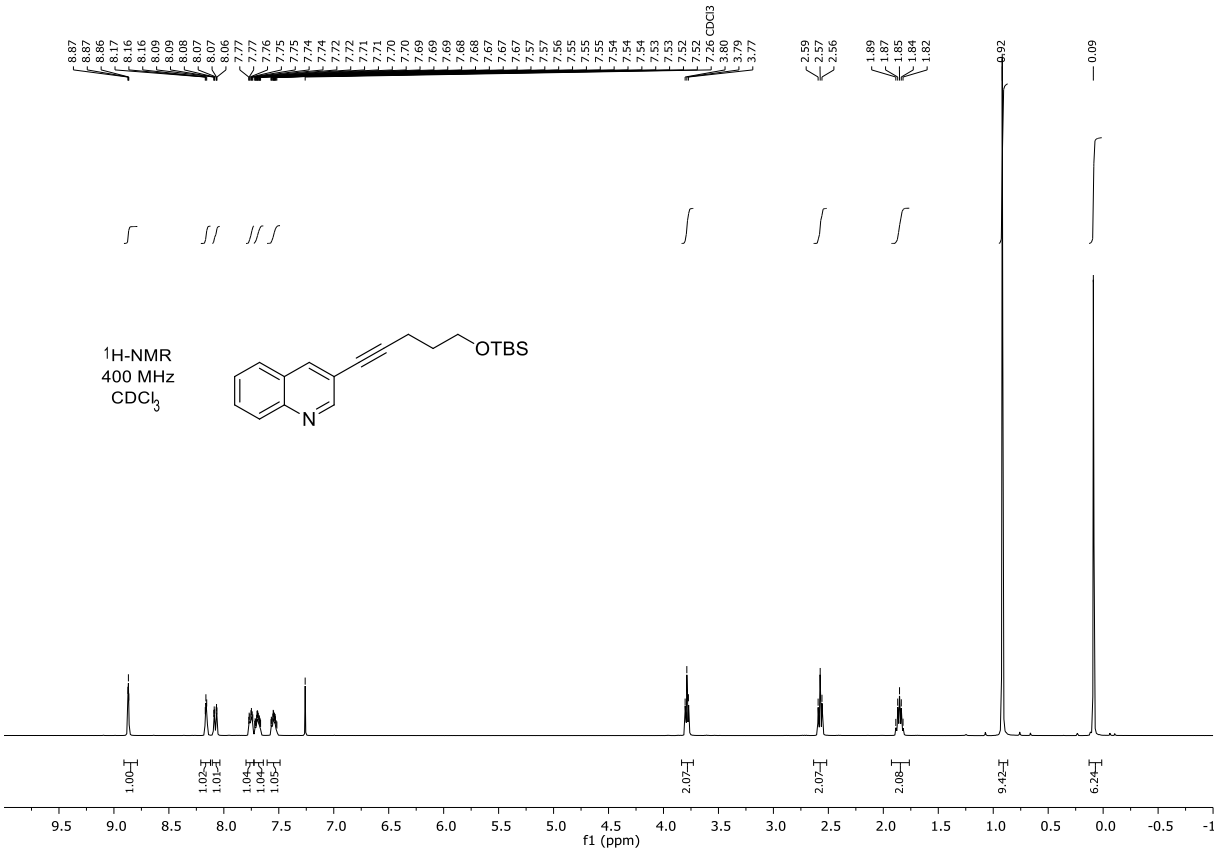
5-(Quinolin-3-yl)pent-4-yn-1-yl acetate (**SI-38**).

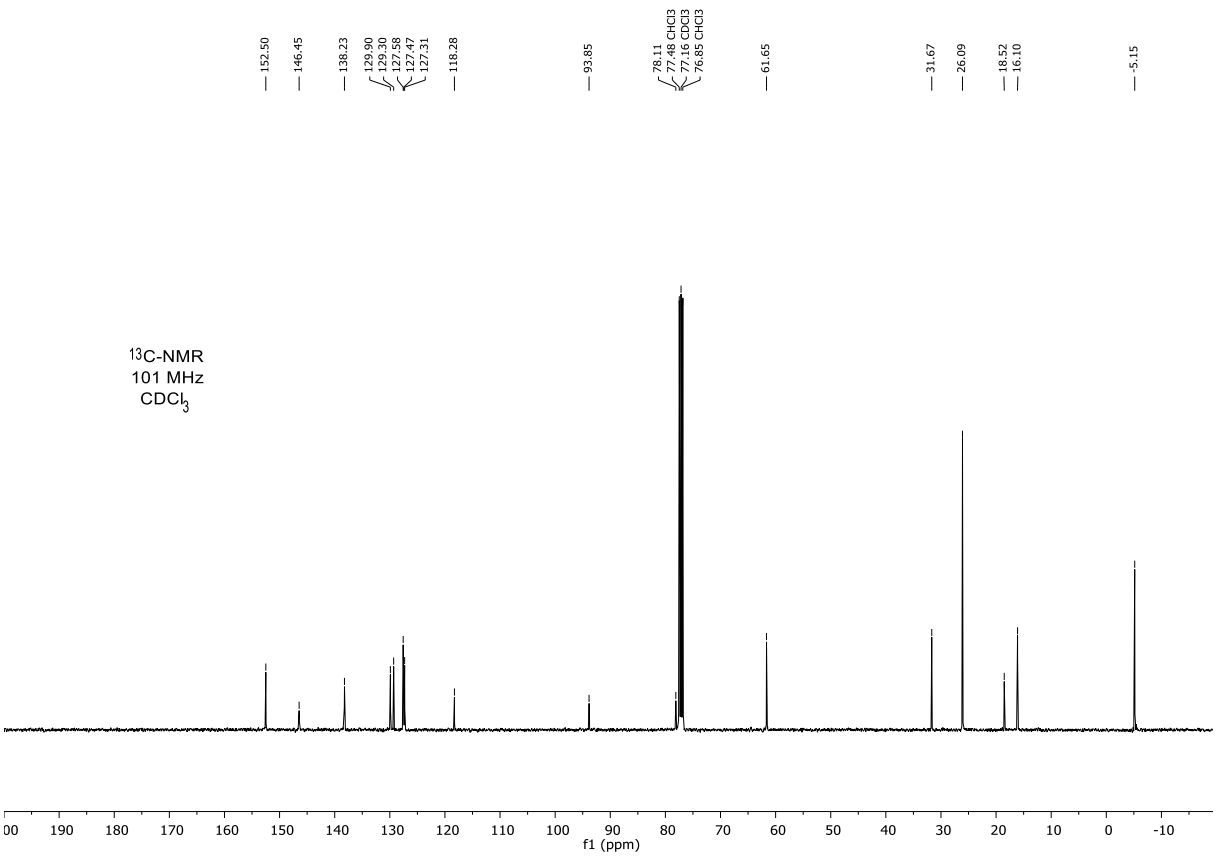


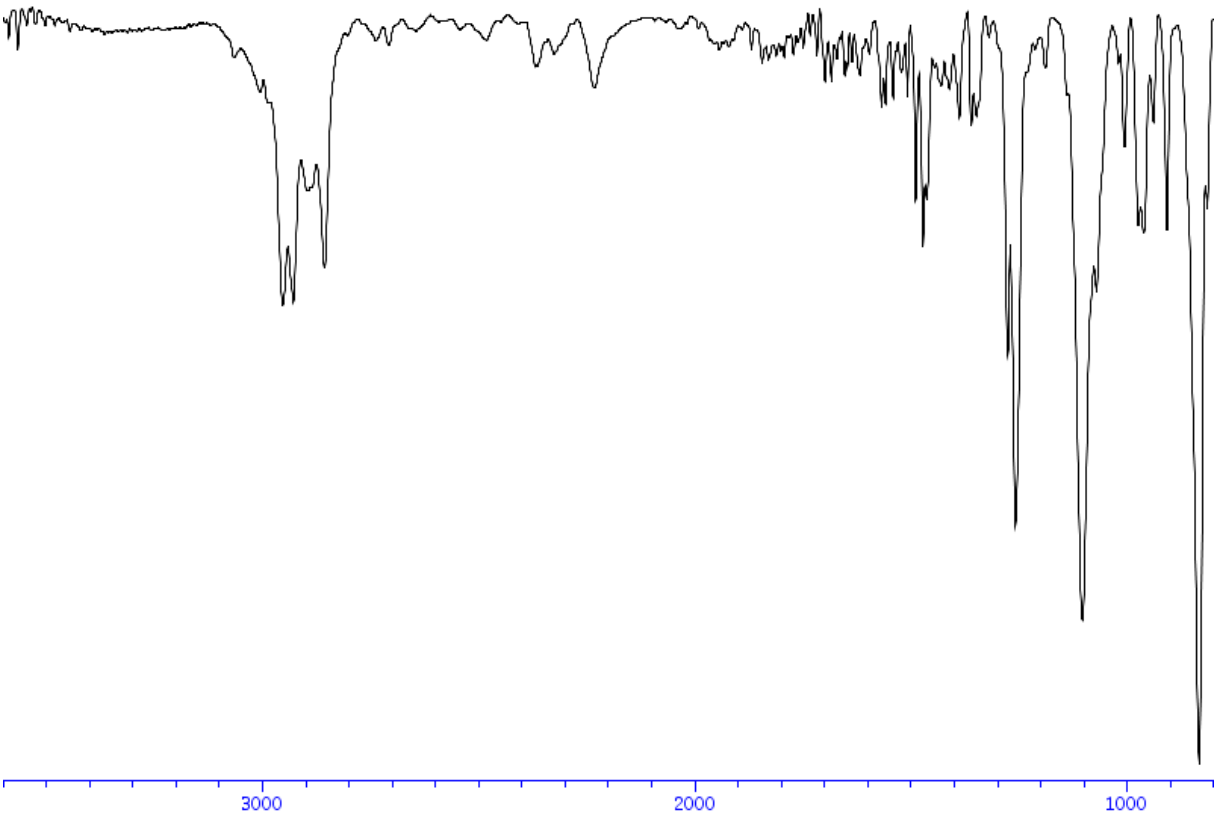

171.02
152.19
146.37
138.24
129.82
129.08
127.42
127.25
127.18
117.79
92.31
78.53
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
63.08
27.65
20.94
16.33
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

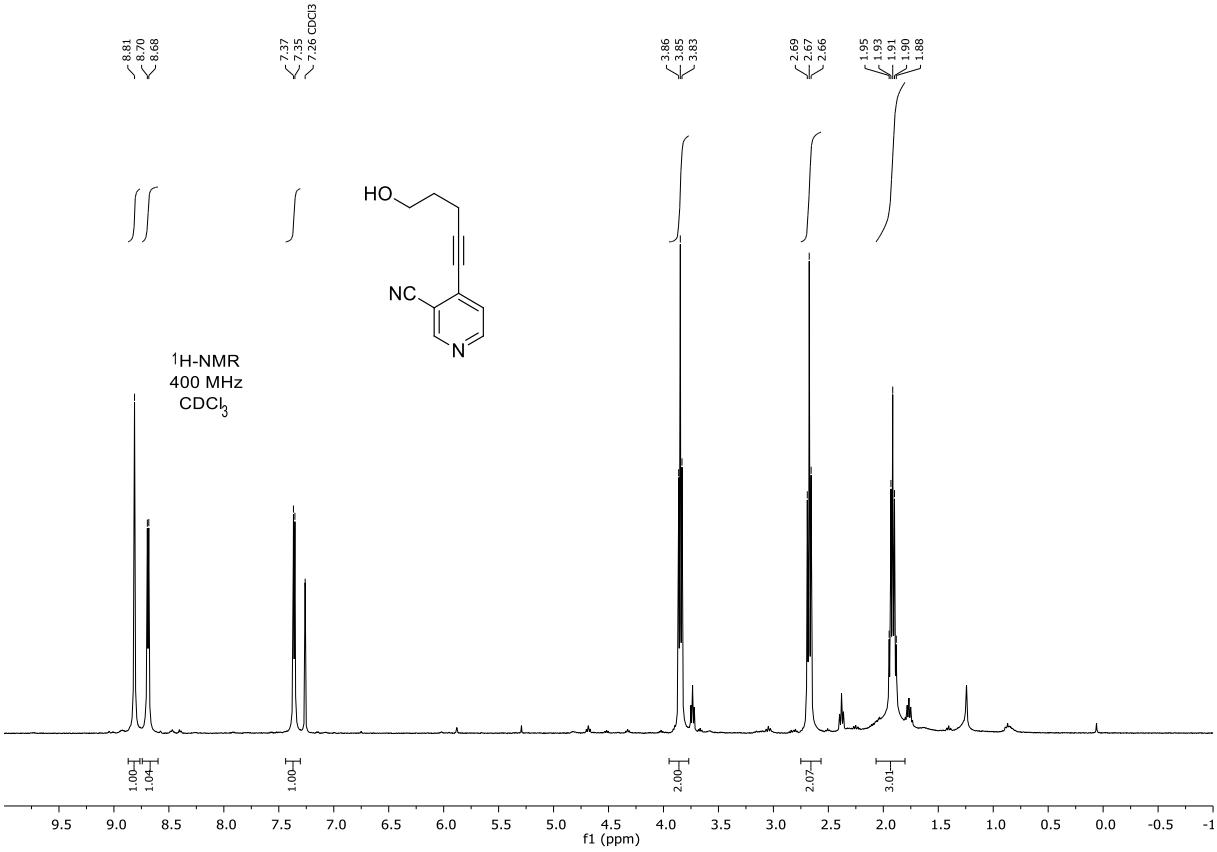
3-(5-((*tert*-Butyldimethylsilyl)oxy)pent-1-yn-1-yl)quinoline (SI-39).

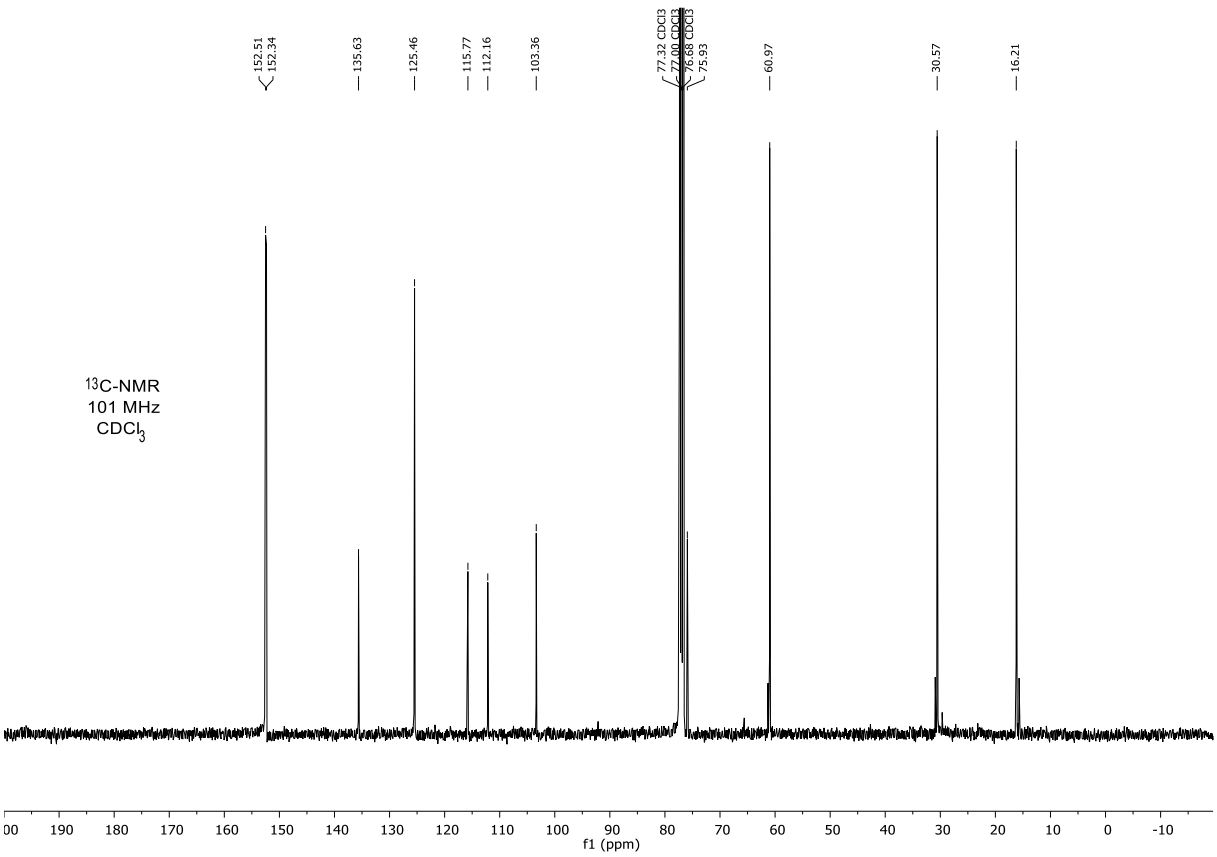


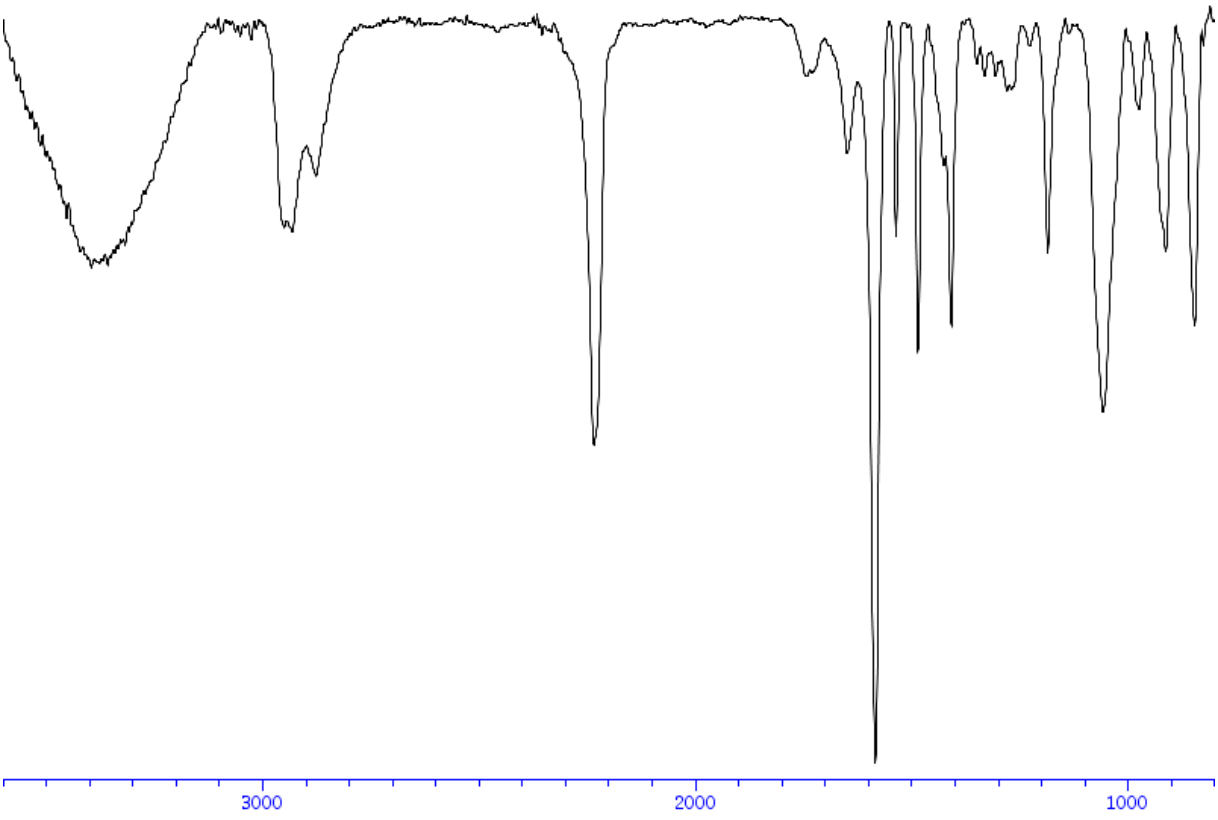




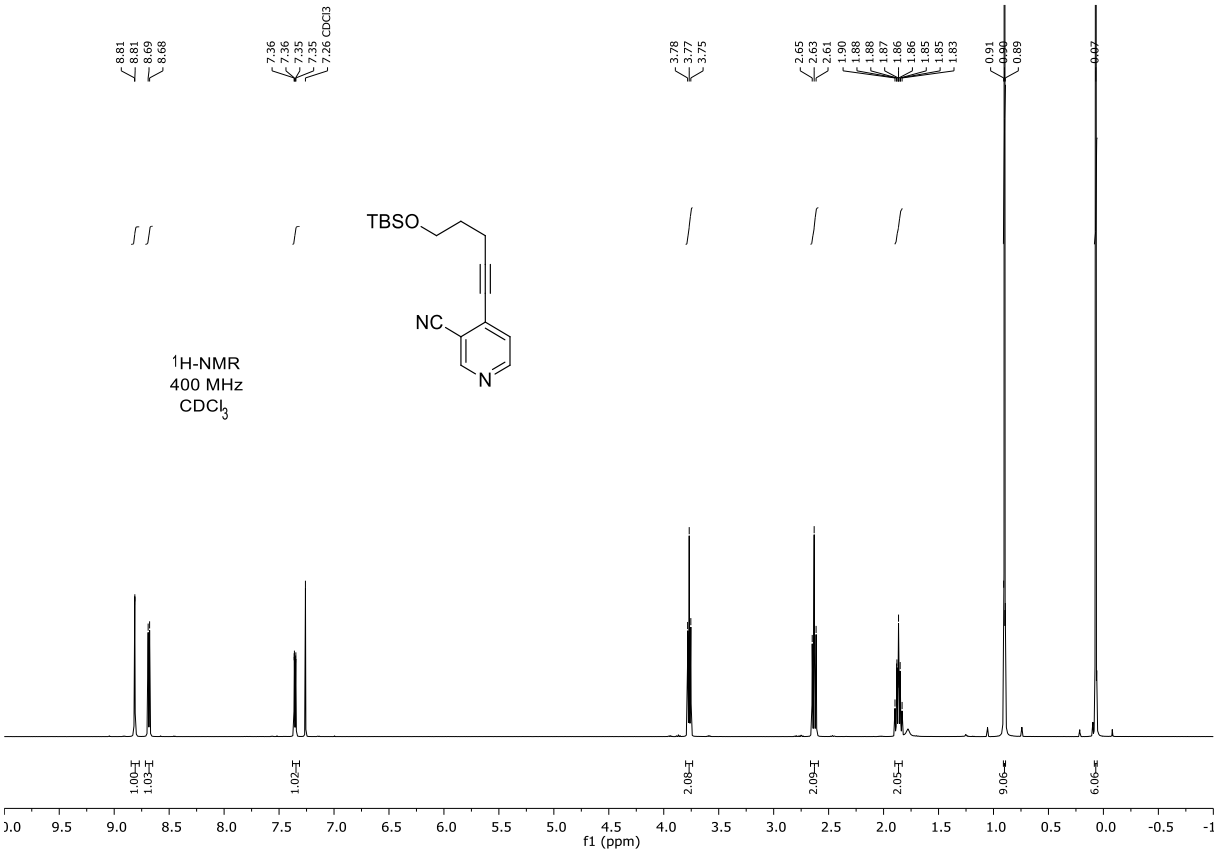
4-(5-Hydroxypent-1-yn-1-yl)nicotinonitrile (SI-50).

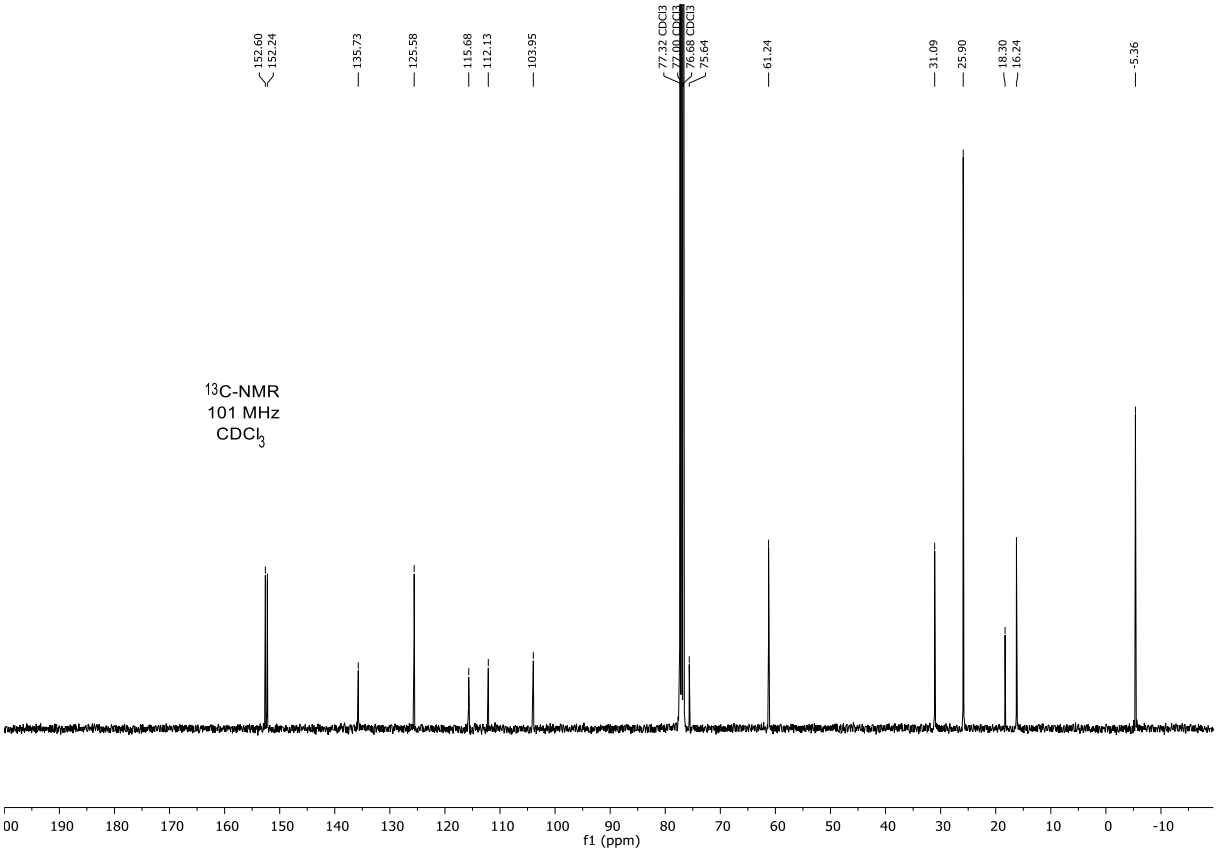


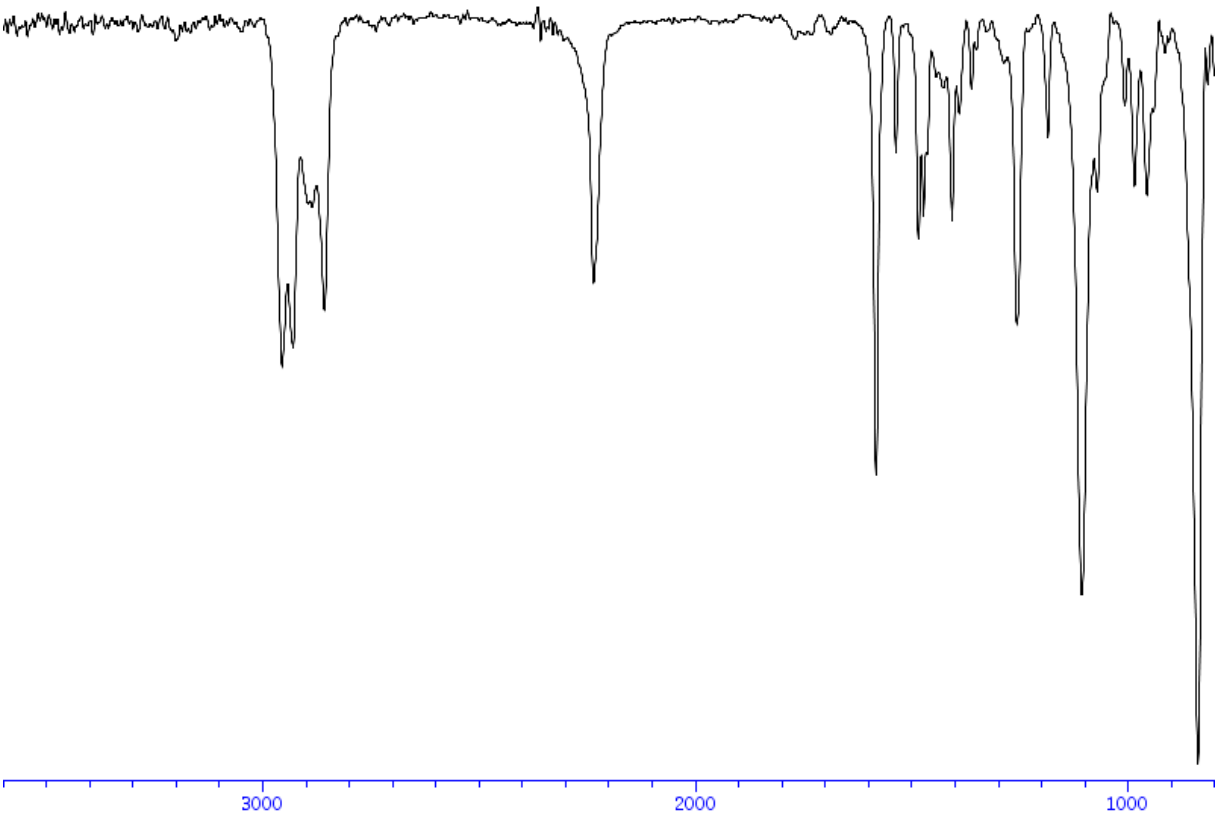

152.51
152.34
135.63
125.46
115.77
112.16
103.36
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
75.93
60.97
30.57
16.21
13C-NMR
101 MHz
CDCl3
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


3000
2000
1000

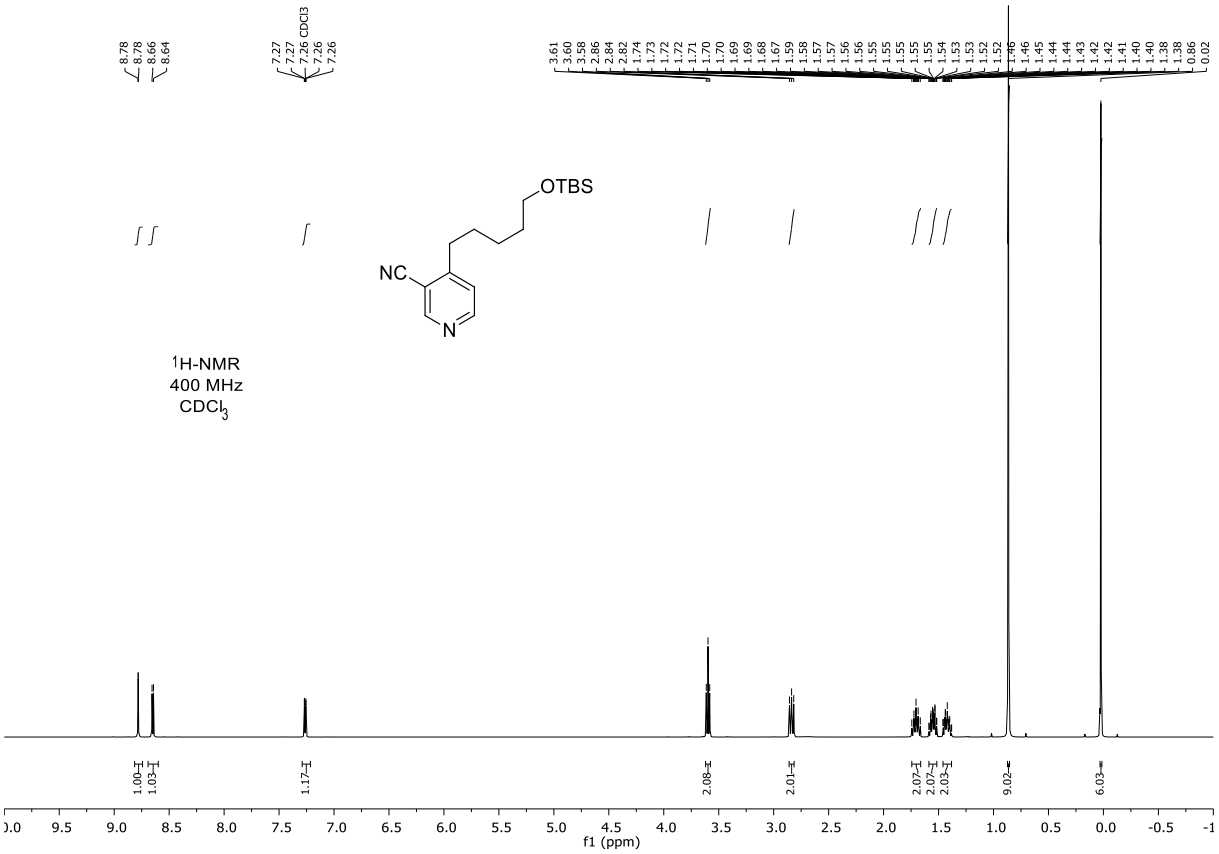
4-(5-((*tert*-Butyldimethylsilyl)oxy)pent-1-yn-1-yl)nicotinonitrile (**SI-51**).

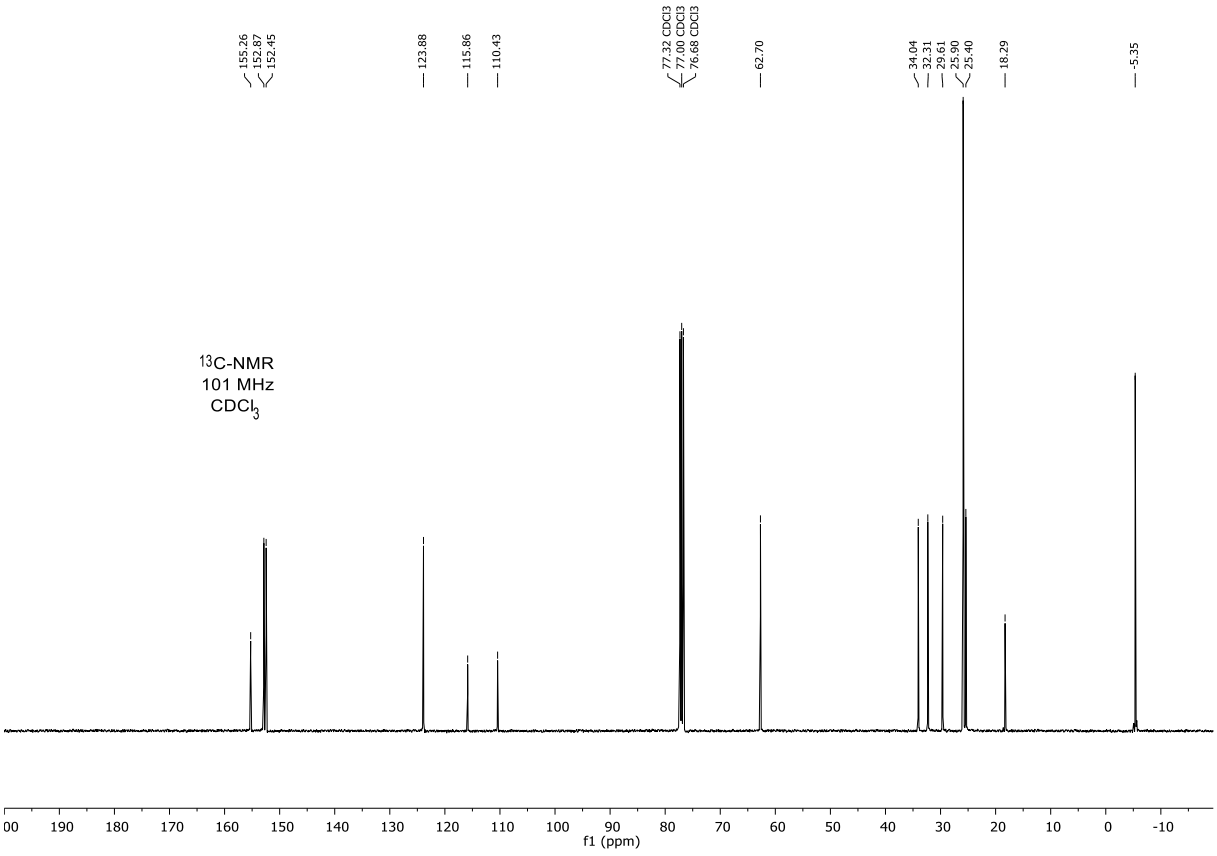


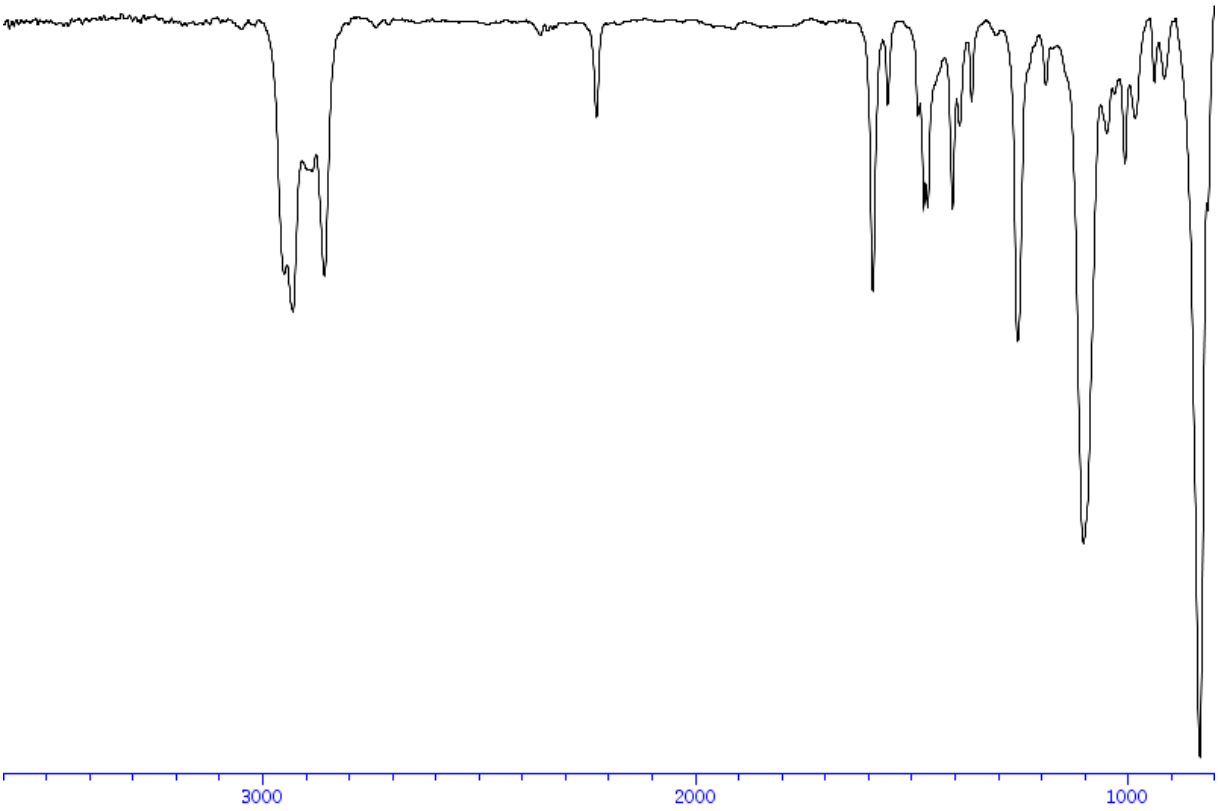




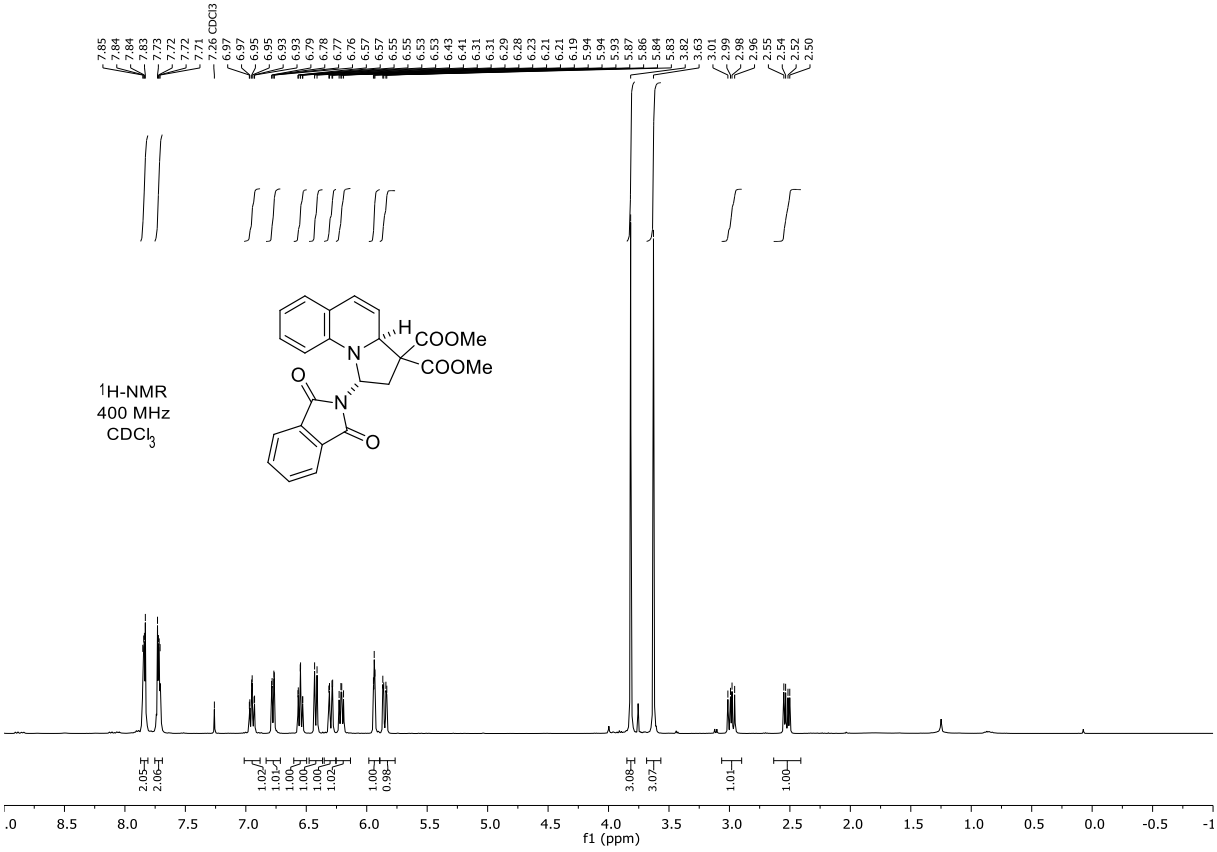
4-(5-((*tert*-Butyldimethylsilyl)oxy)pentyl)nicotinonitrile (SI-52).

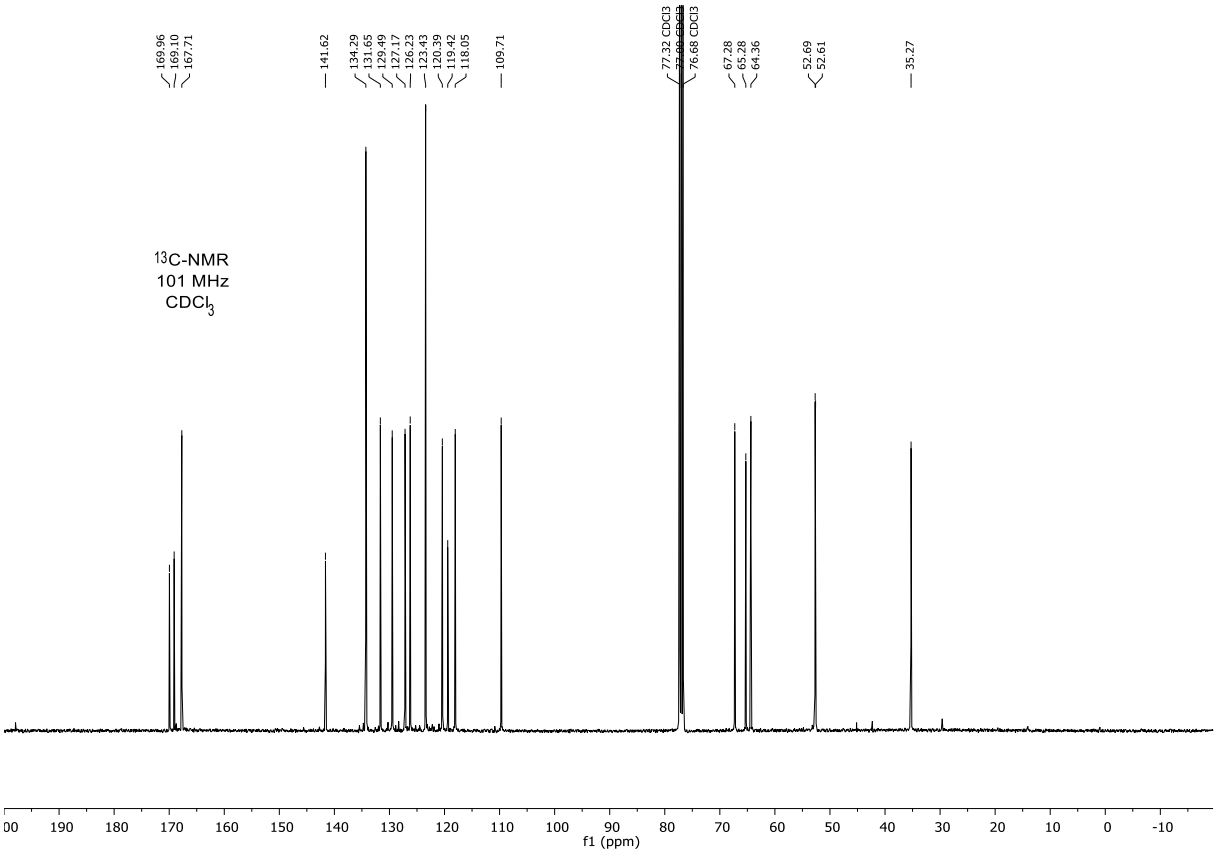


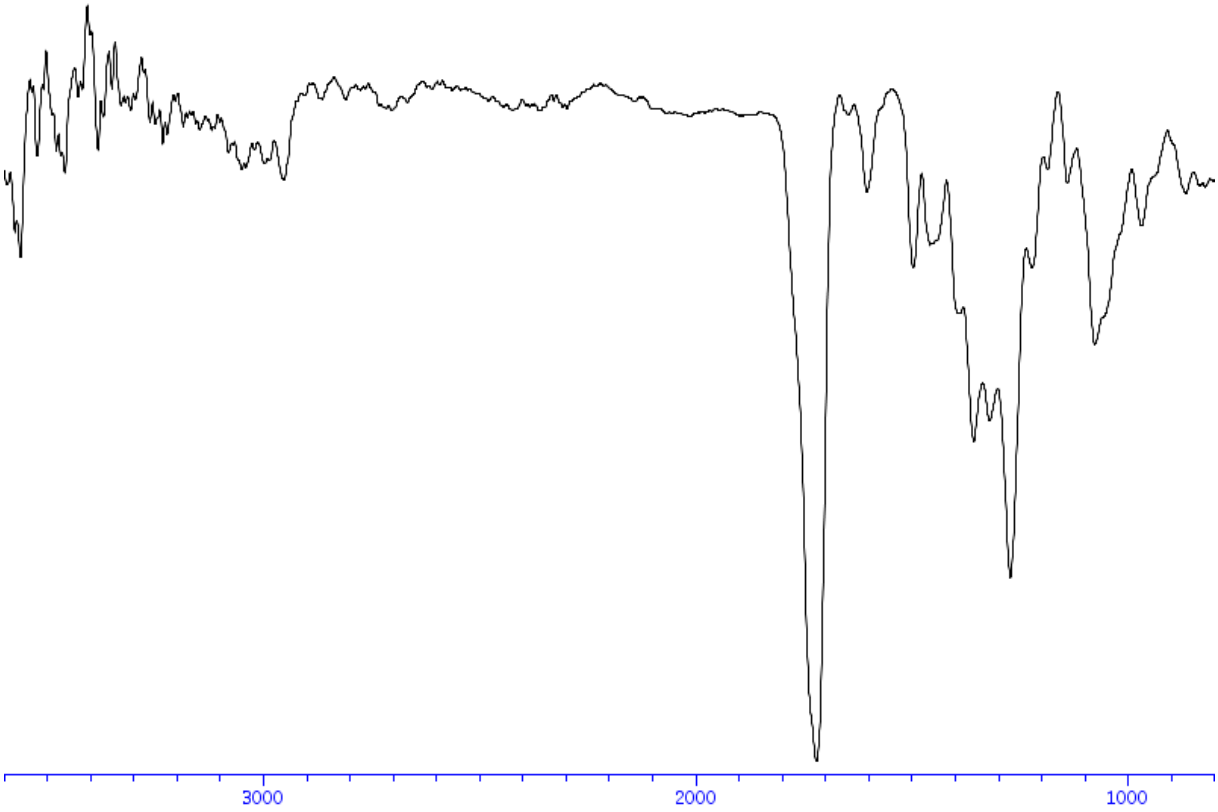

155.26
152.87
152.45
123.88
115.86
110.43
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
62.70
34.04
32.31
29.61
25.90
25.40
18.29
-5.35
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

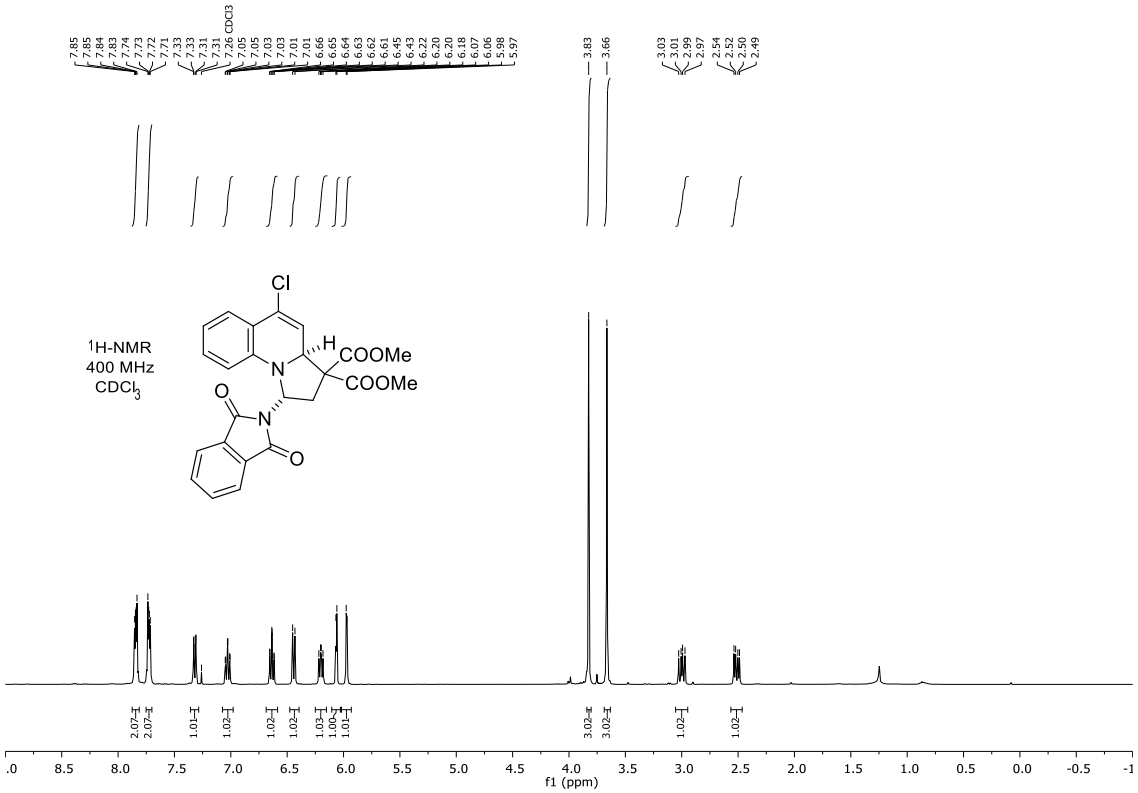
***anti*-Dimethyl 1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (17).**

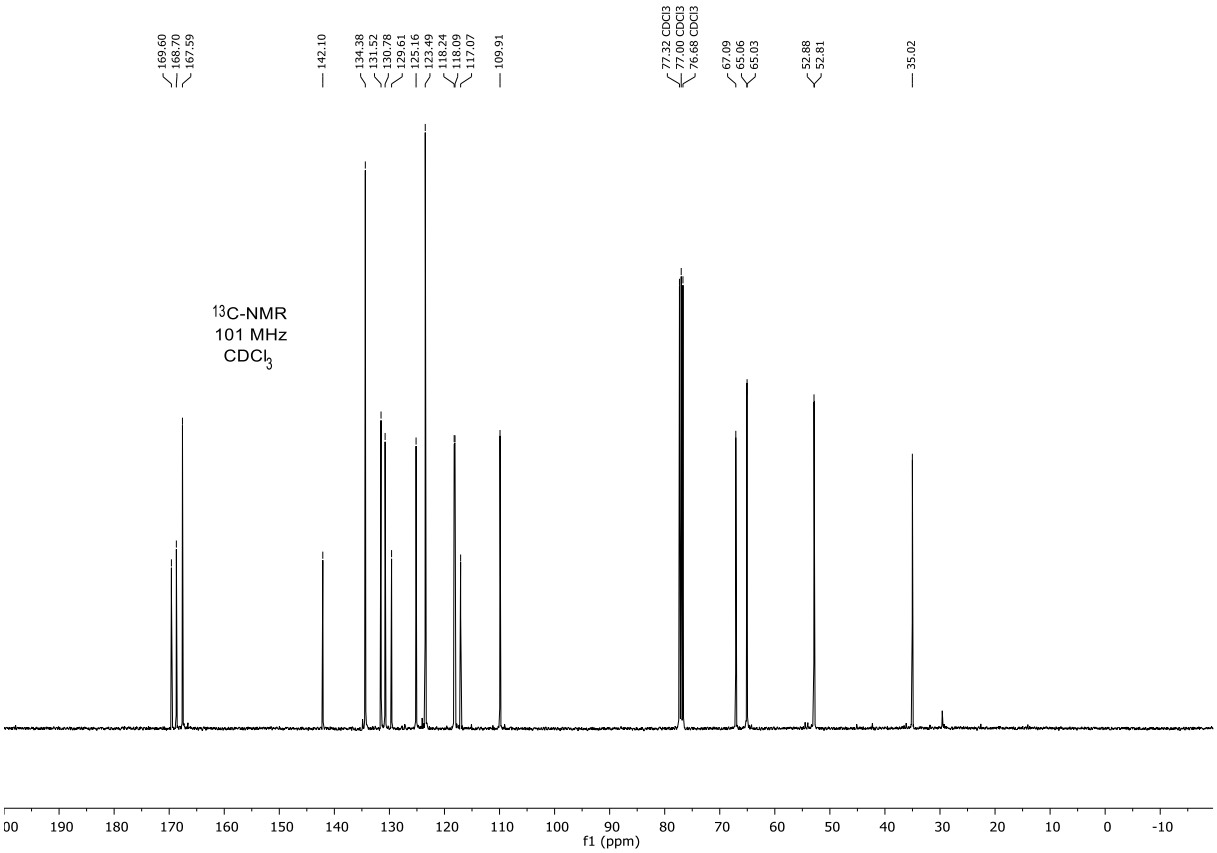


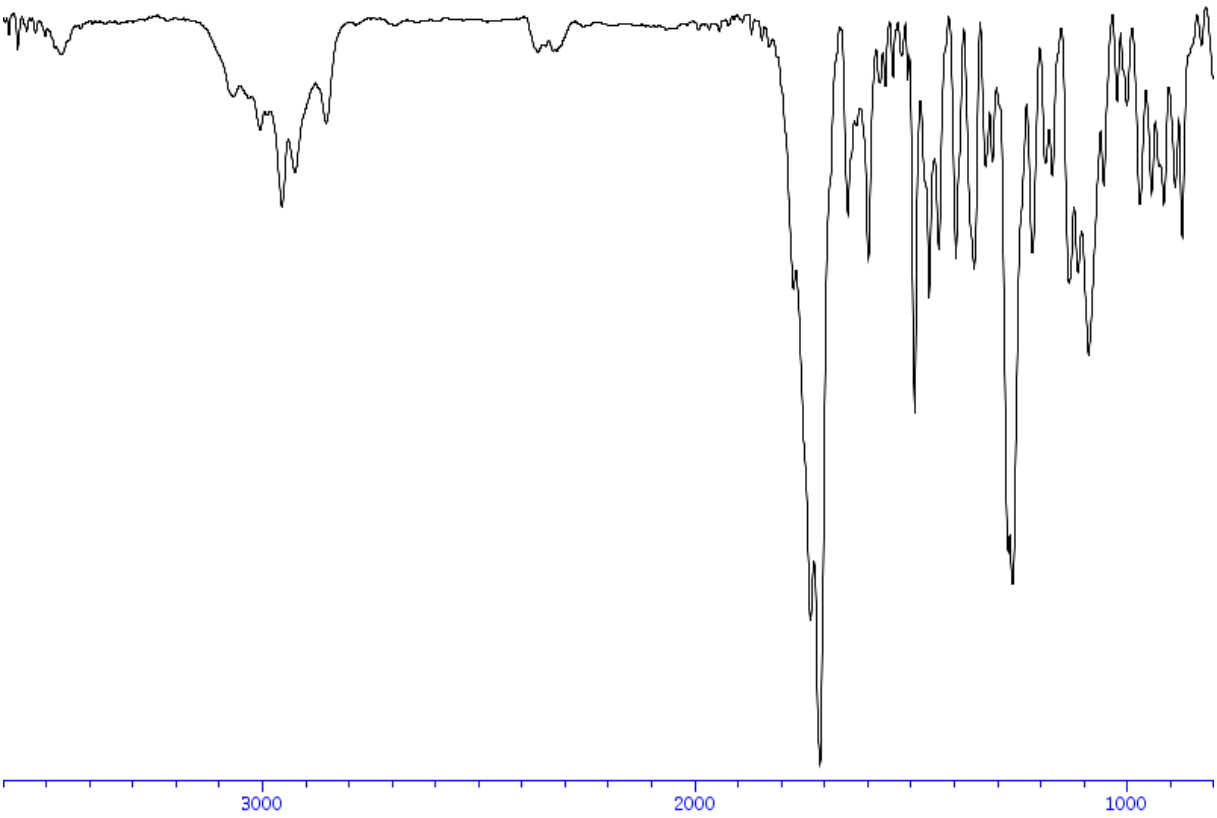




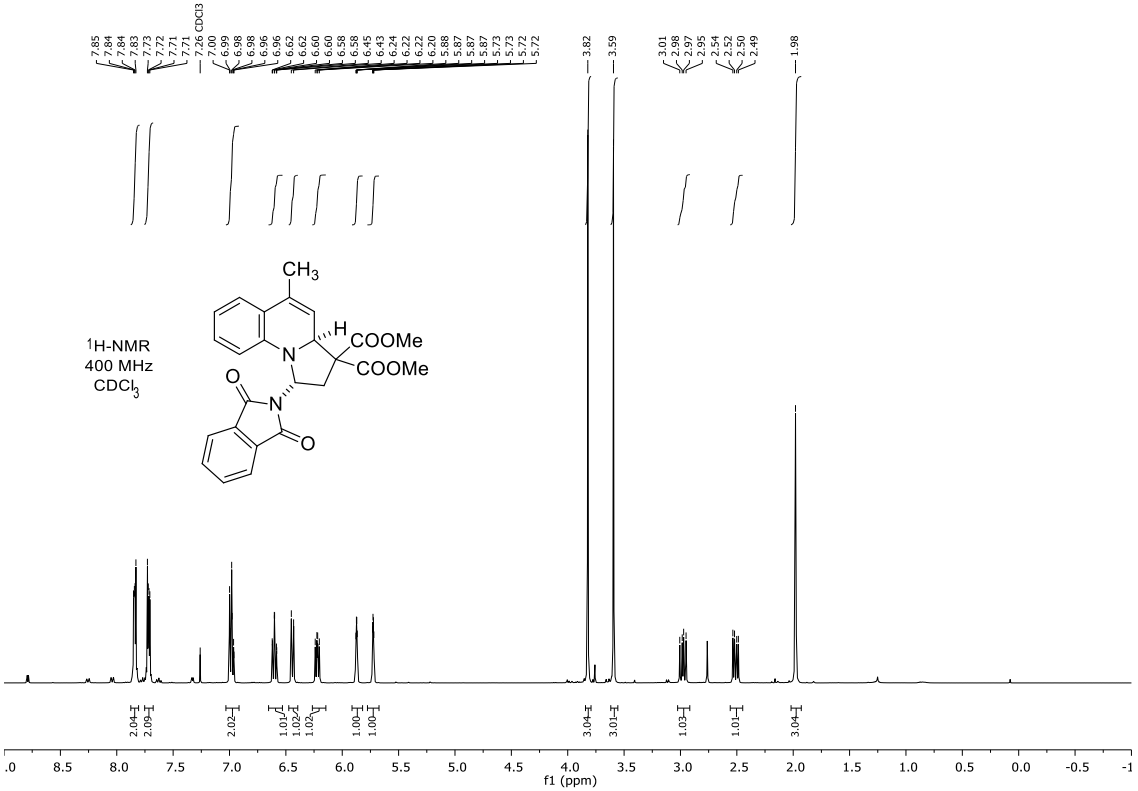
***anti*-Dimethyl 5-chloro-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (20).**

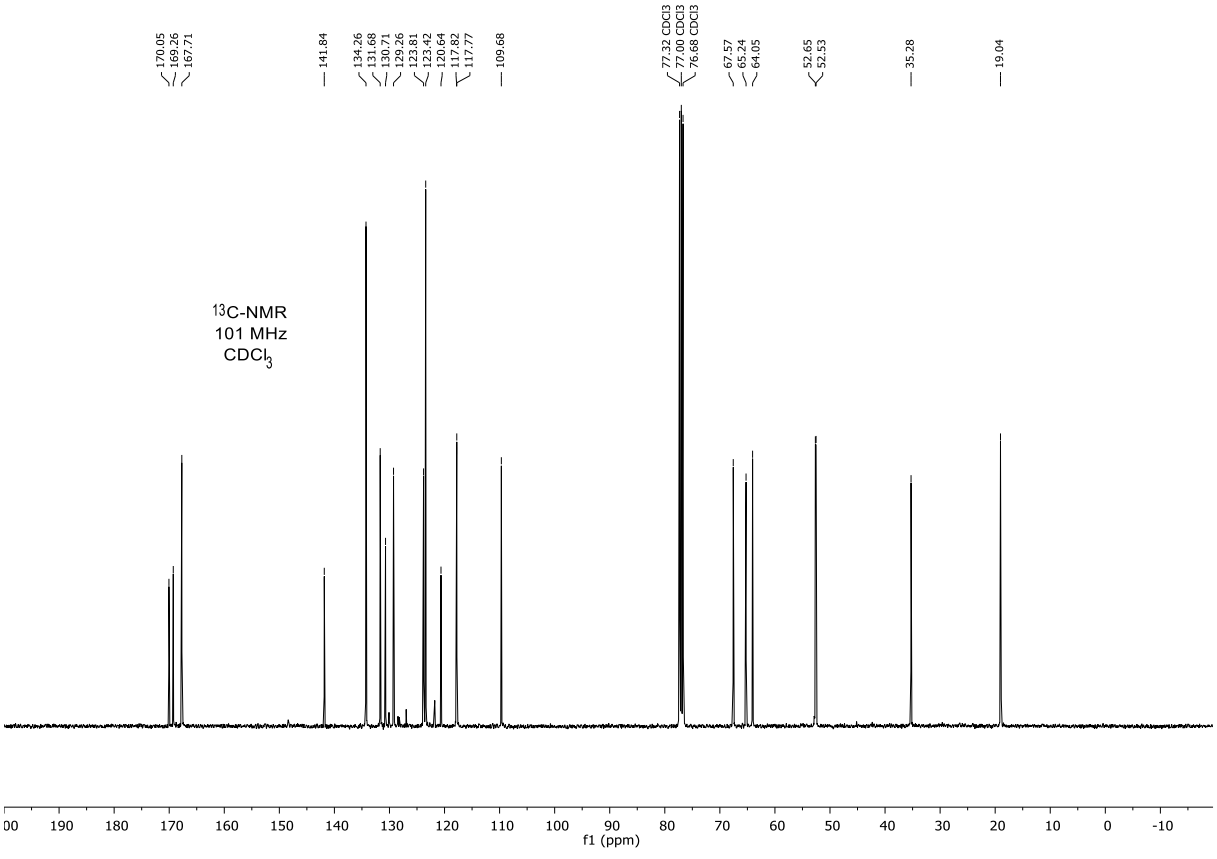


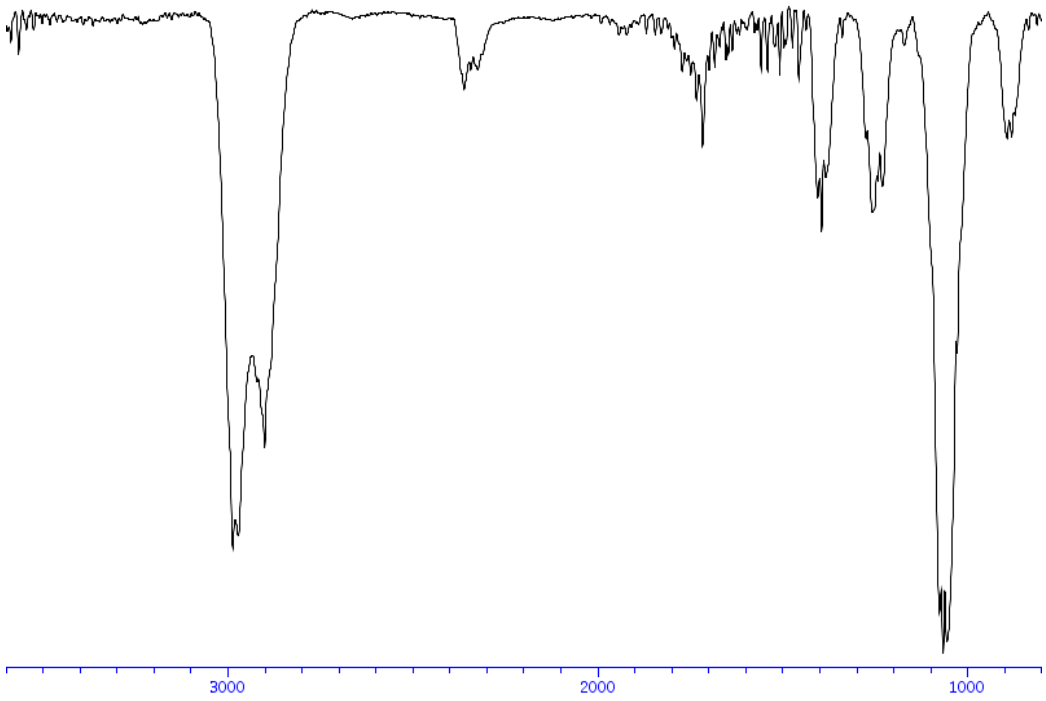

169.60
168.70
167.59
142.10
134.38
131.52
130.78
129.61
125.16
123.49
118.24
118.09
117.07
109.91
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
67.09
65.06
65.03
52.88
52.81
35.02
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

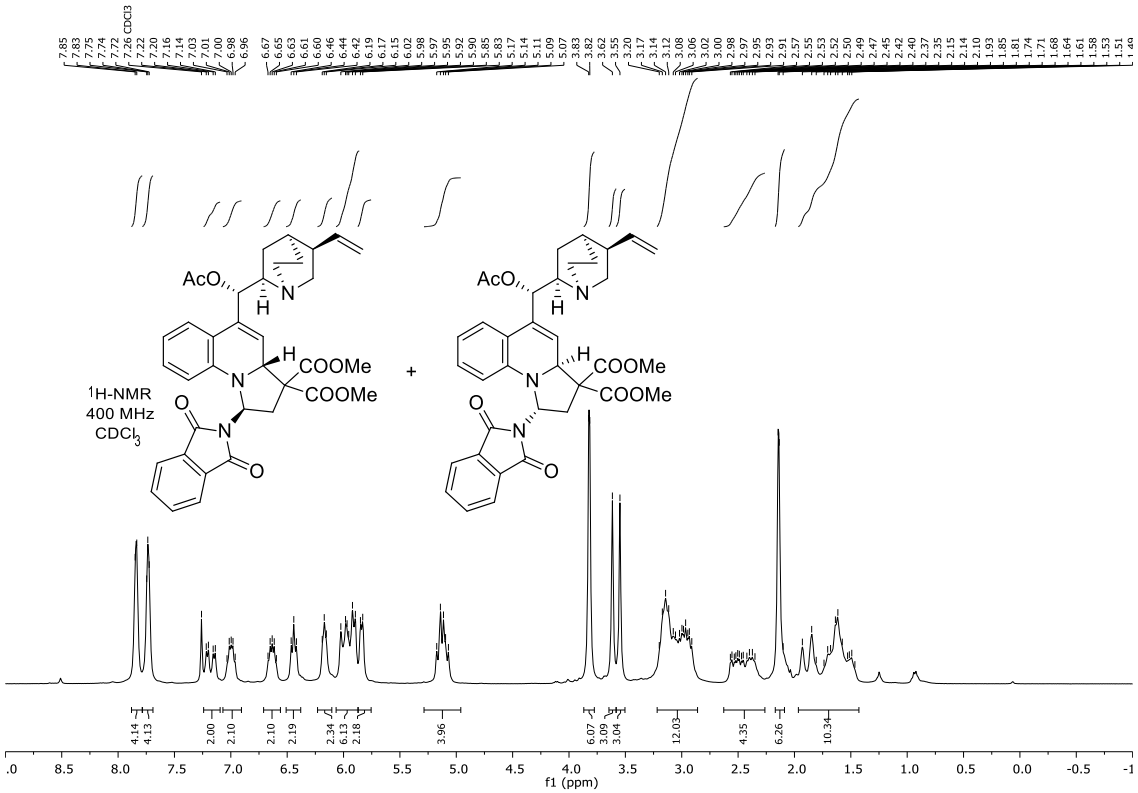
***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-5-methyl-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**21**).

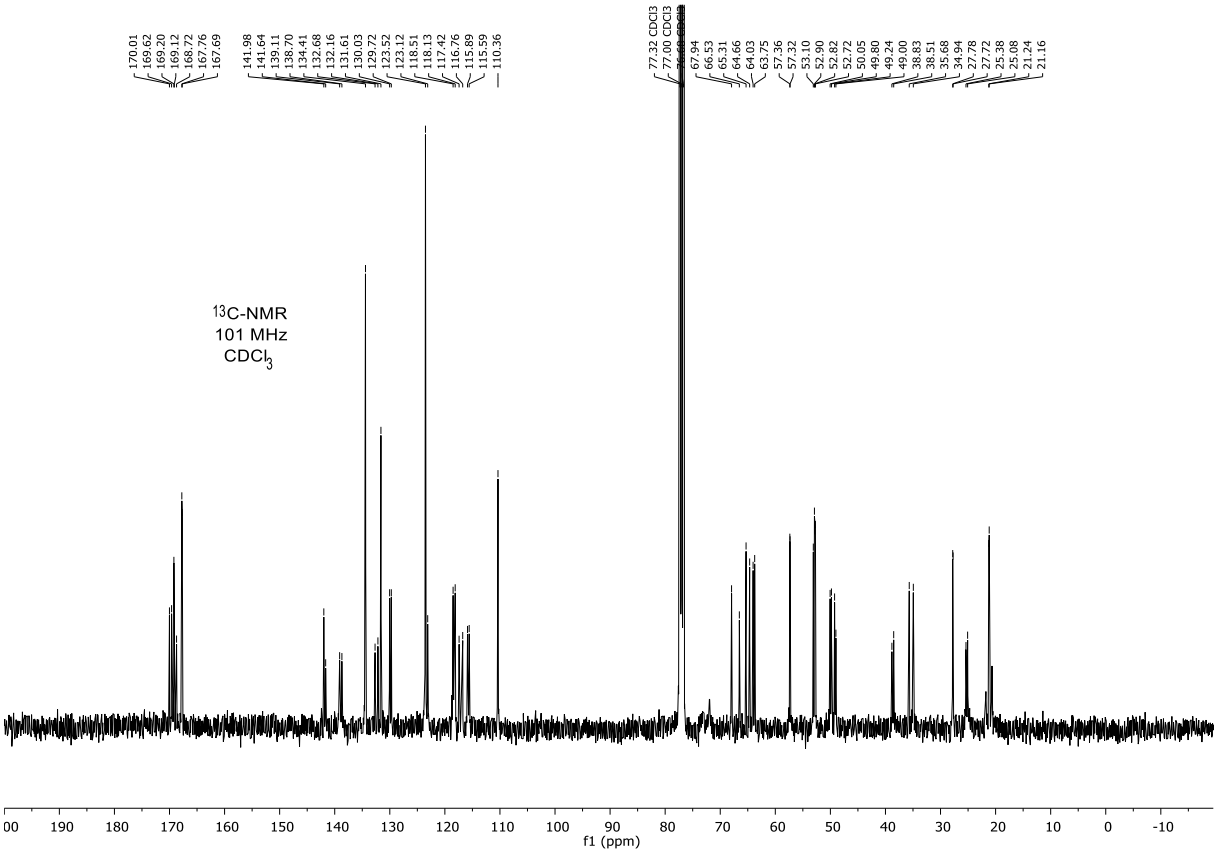


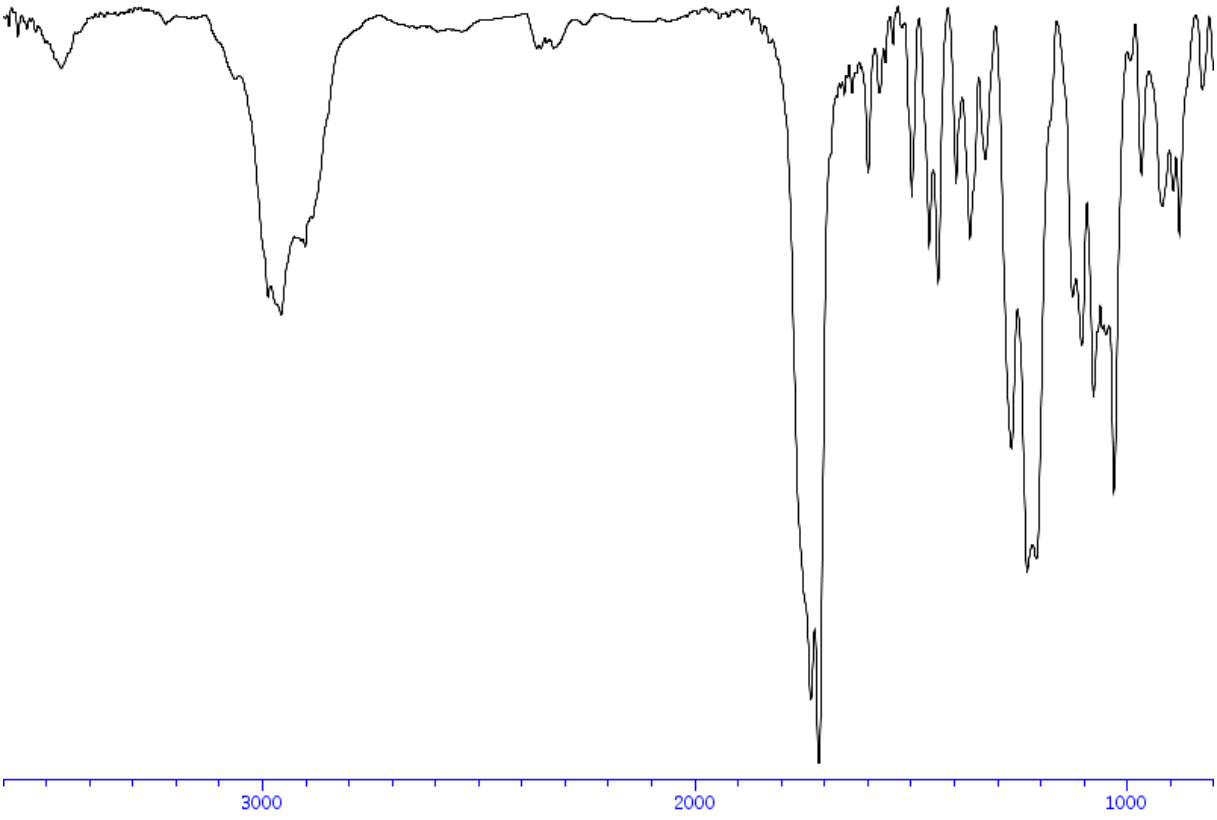




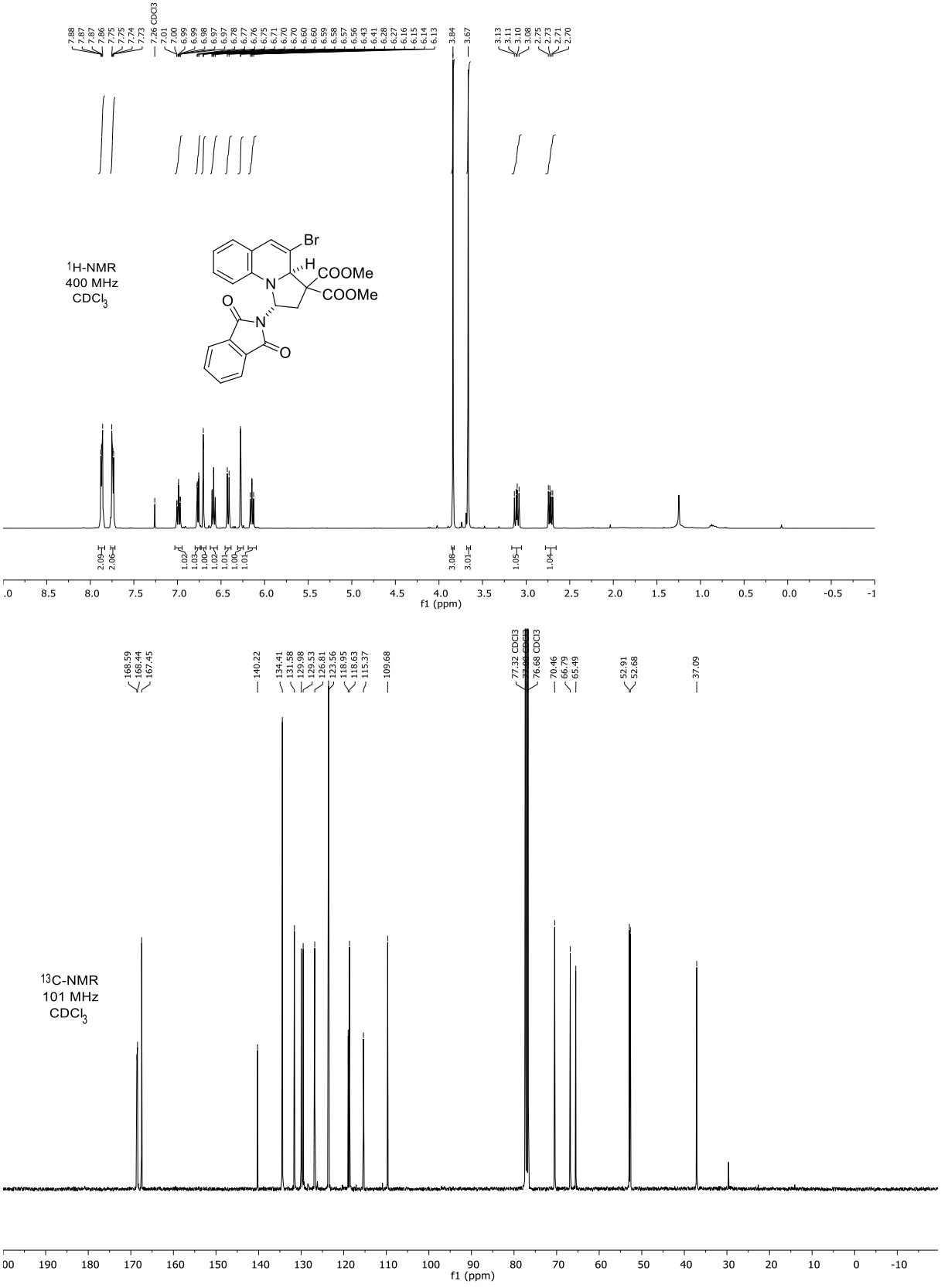
(1*R*,3a*R*)-Dimethyl 5-((*S*)-acetoxy((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**22a**) and **(1*S*,3a*S*)-dimethyl 5-((*S*)-acetoxy((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**22b**).

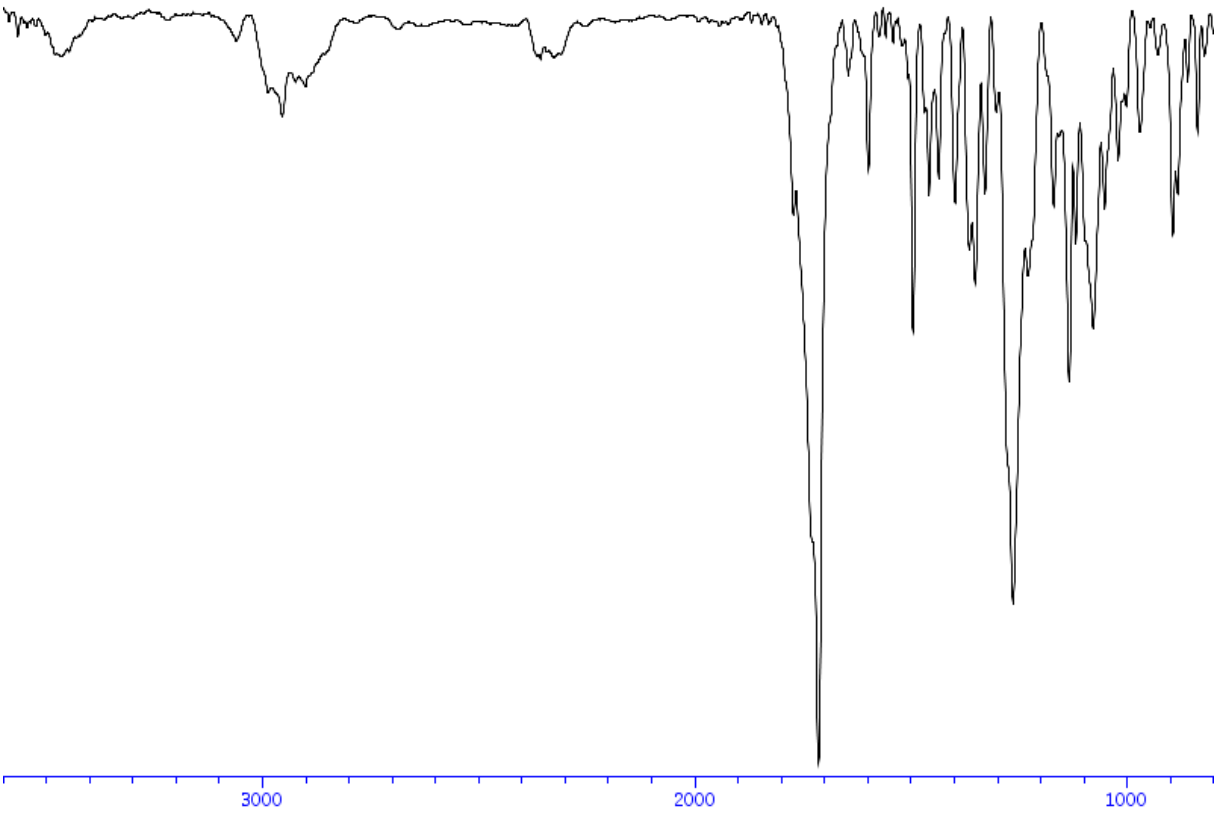



170.01
169.62
169.20
169.12
168.72
167.76
167.69
141.98
141.64
139.11
138.70
134.41
132.68
132.16
131.61
130.03
129.72
123.52
123.12
118.51
118.13
117.42
116.76
115.89
115.59
110.36
77.32 CDCl3
77.00 CDCl3
67.94
66.53
65.31
64.66
64.03
63.75
57.36
57.32
53.10
52.90
52.82
52.72
50.05
49.80
49.24
49.00
38.83
38.51
35.68
34.94
27.78
27.72
25.38
25.08
21.24
21.16
13C-NMR
101 MHz
CDCl3
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

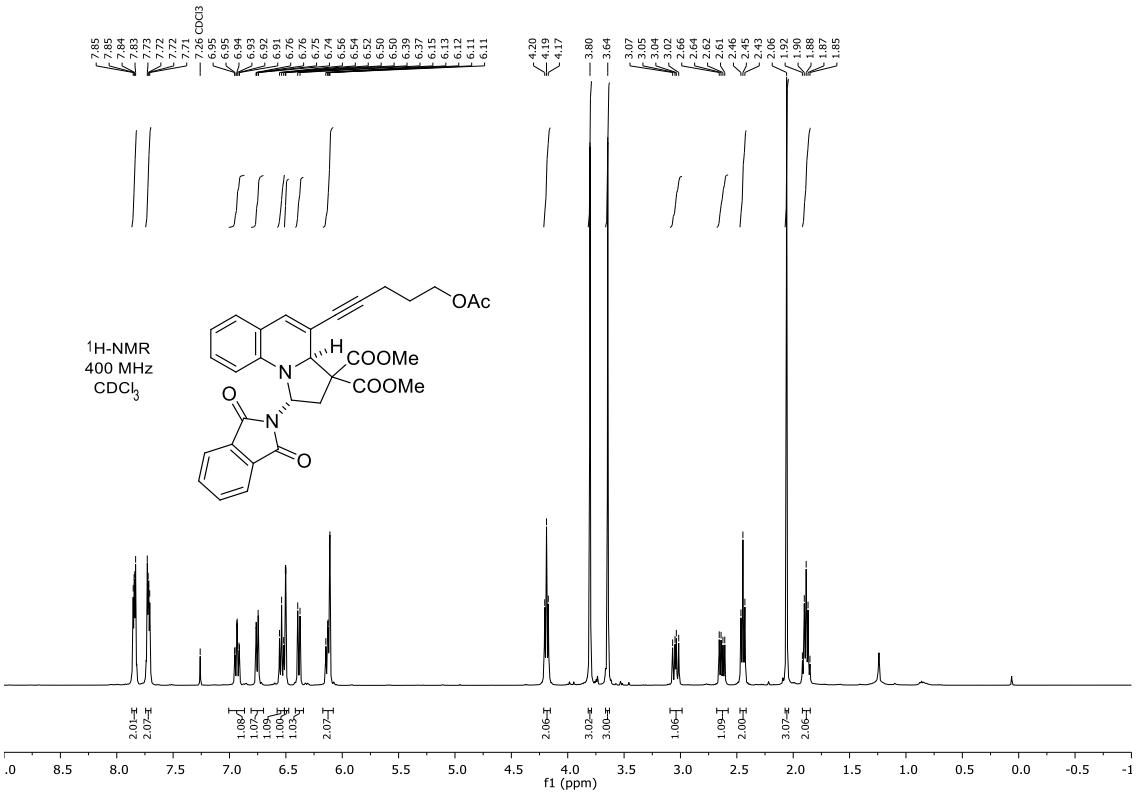

3000
2000
1000

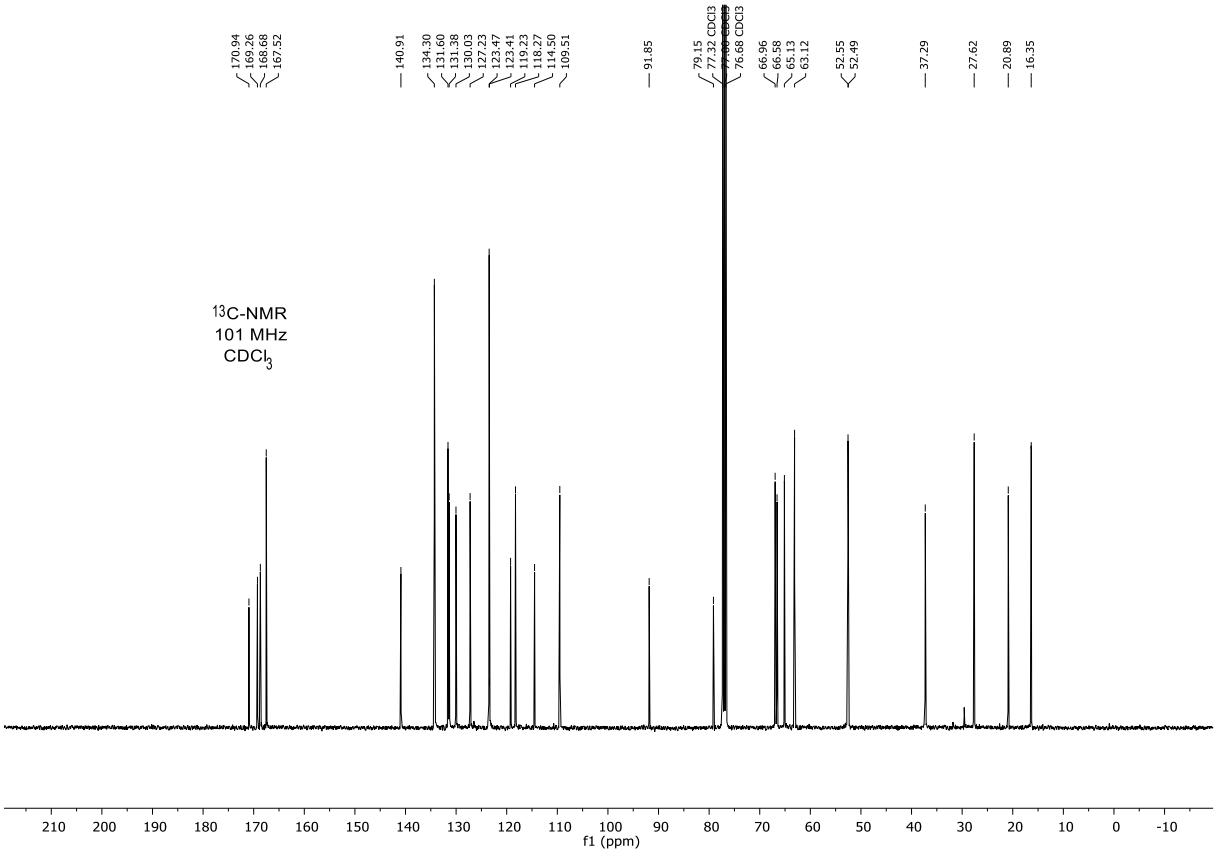
***anti*-Dimethyl 4-bromo-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**23**).

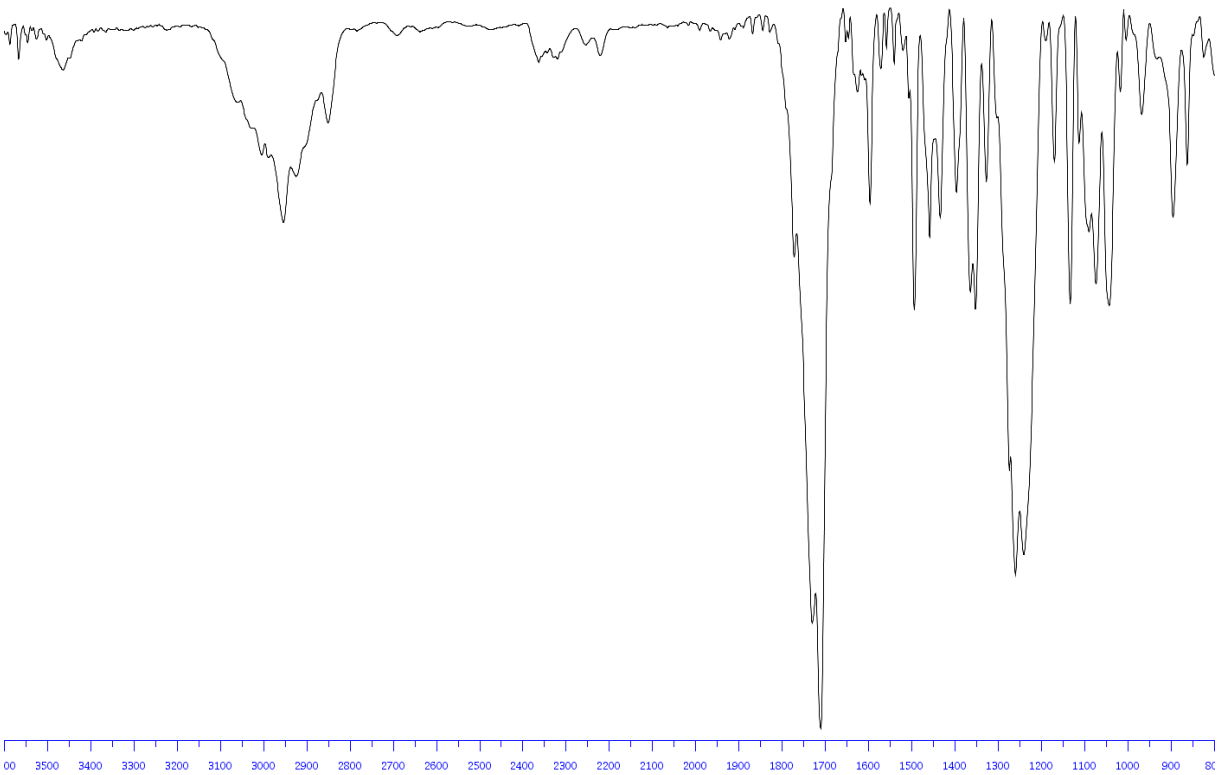




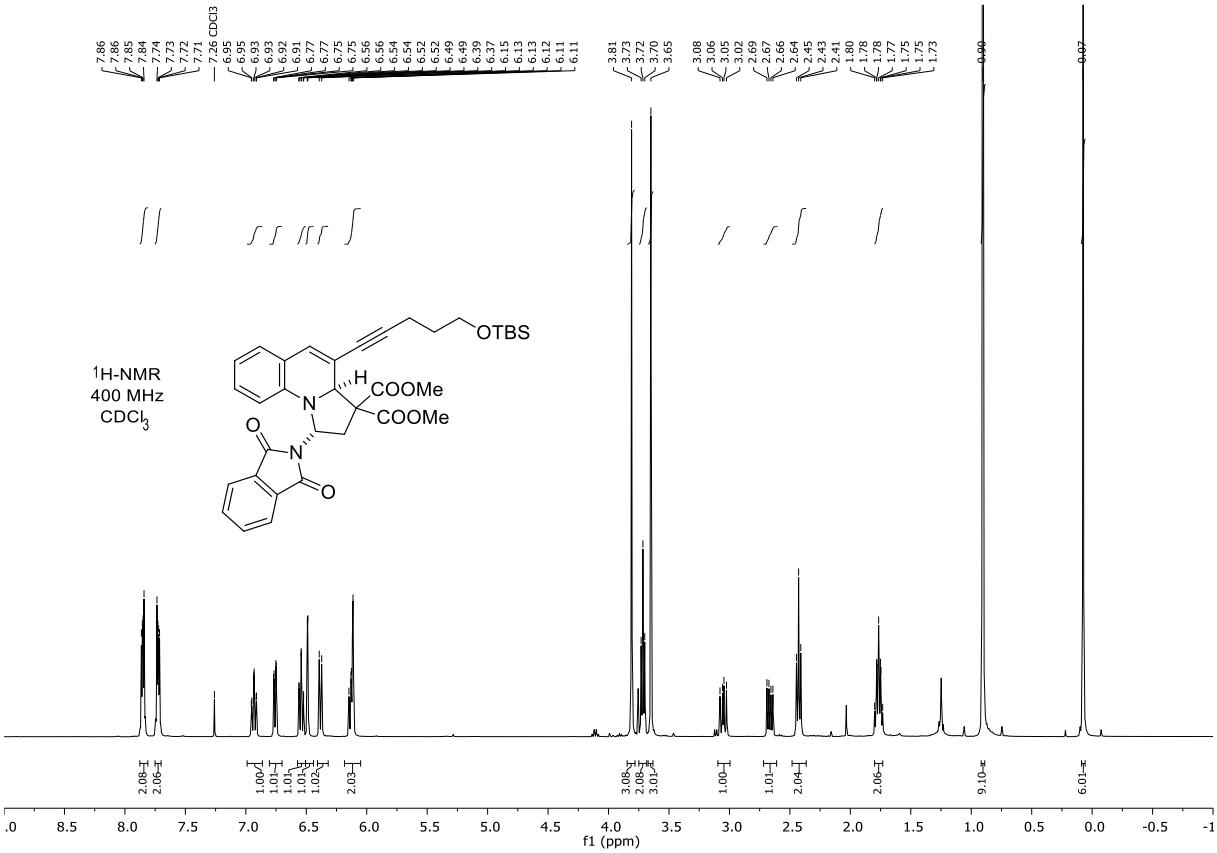
***anti*-Dimethyl 4-(5-acetoxypent-1-yn-1-yl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**24**).

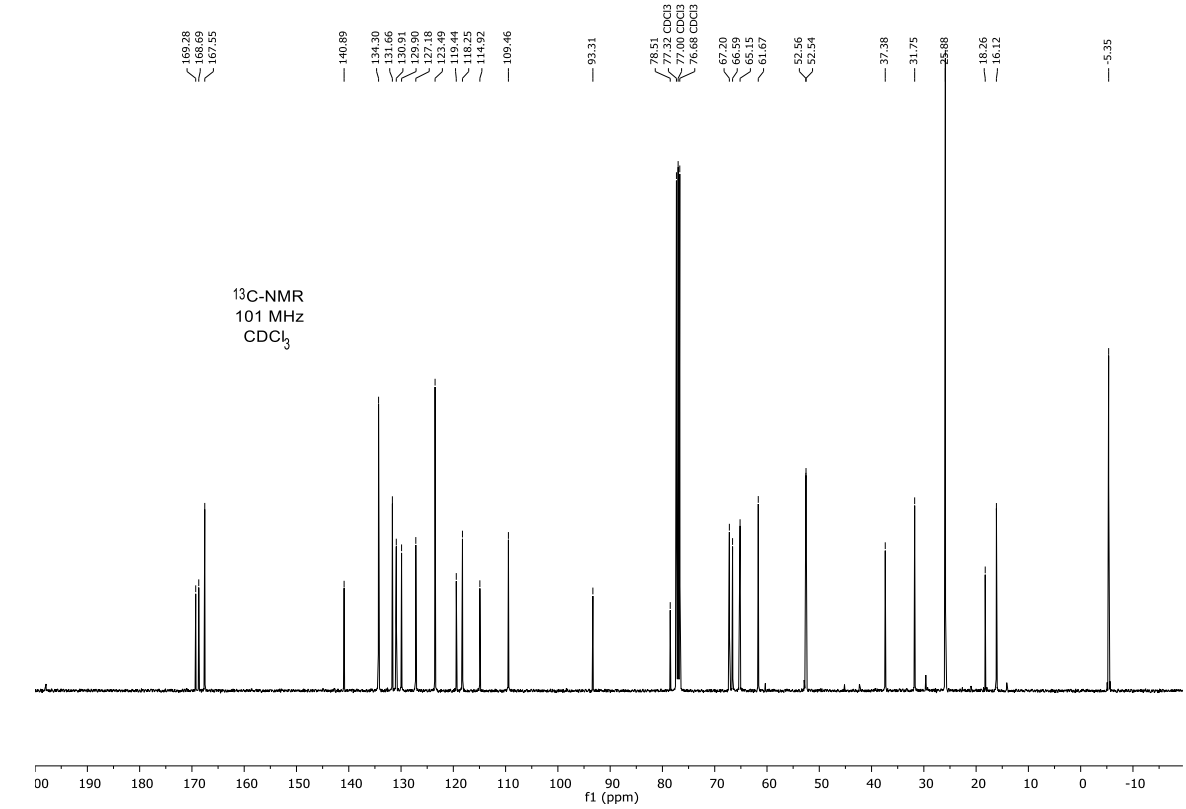


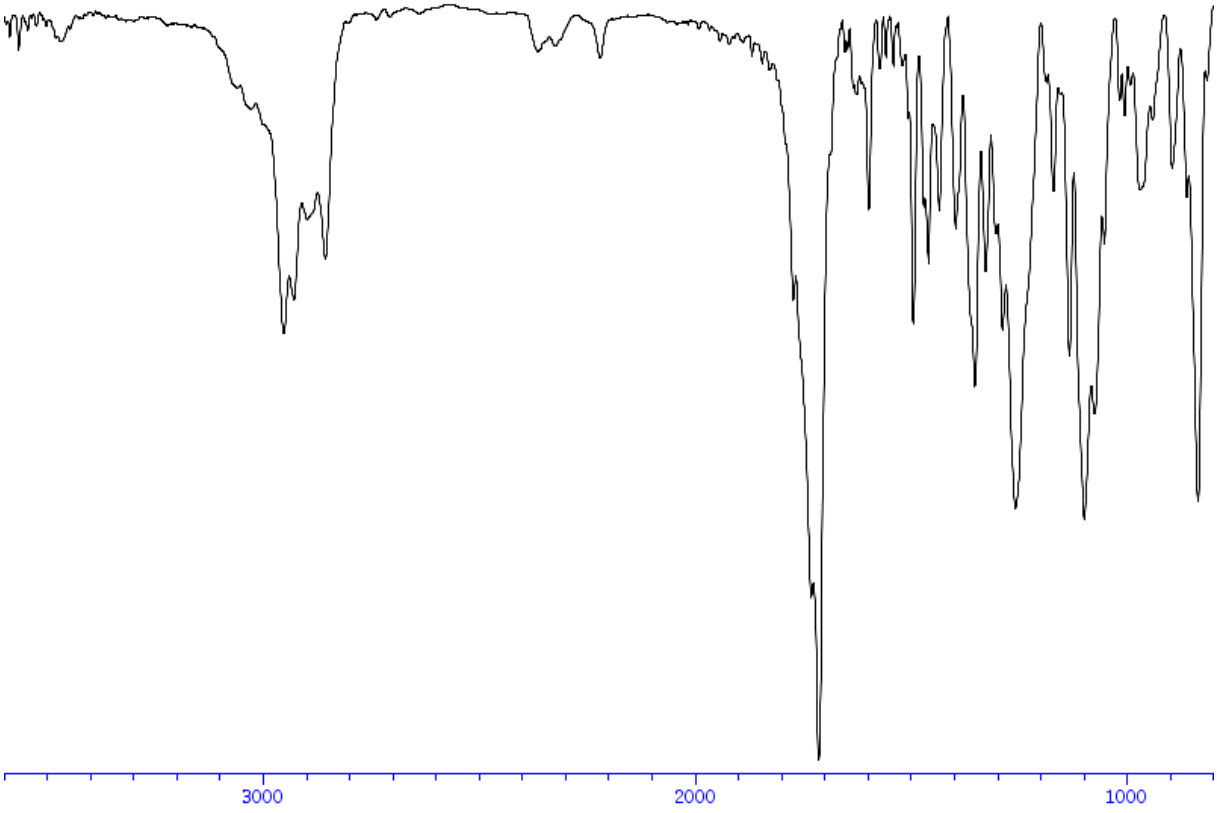

170.94
169.26
168.68
167.52
140.91
134.30
131.60
131.38
130.03
127.23
123.47
123.41
119.23
118.27
114.50
109.51
91.85
79.15
77.32 CDCl3
76.68 CDCl3
66.96
66.58
65.13
63.12
52.55
52.49
37.29
27.62
20.89
16.35
13C-NMR
101 MHz
CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



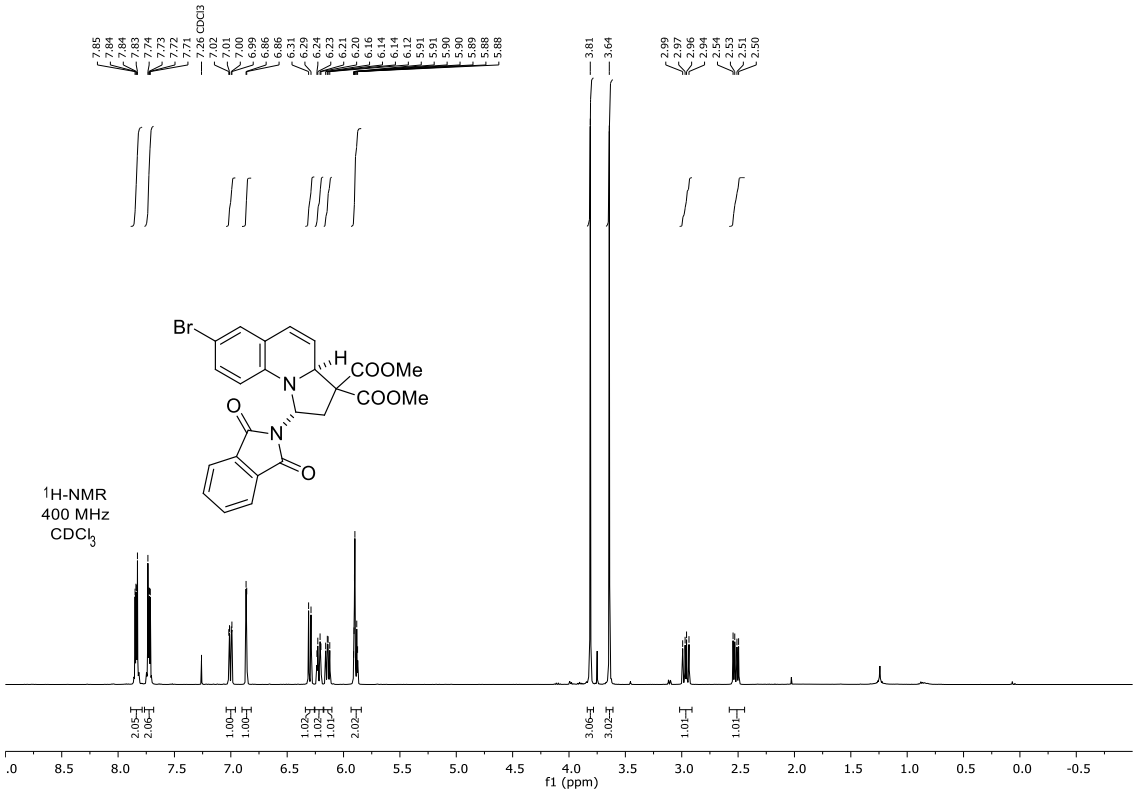
***anti*-Dimethyl 4-(5-((*tert*-butyldimethylsilyl)oxy)pent-1-yn-1-yl)-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**25**).

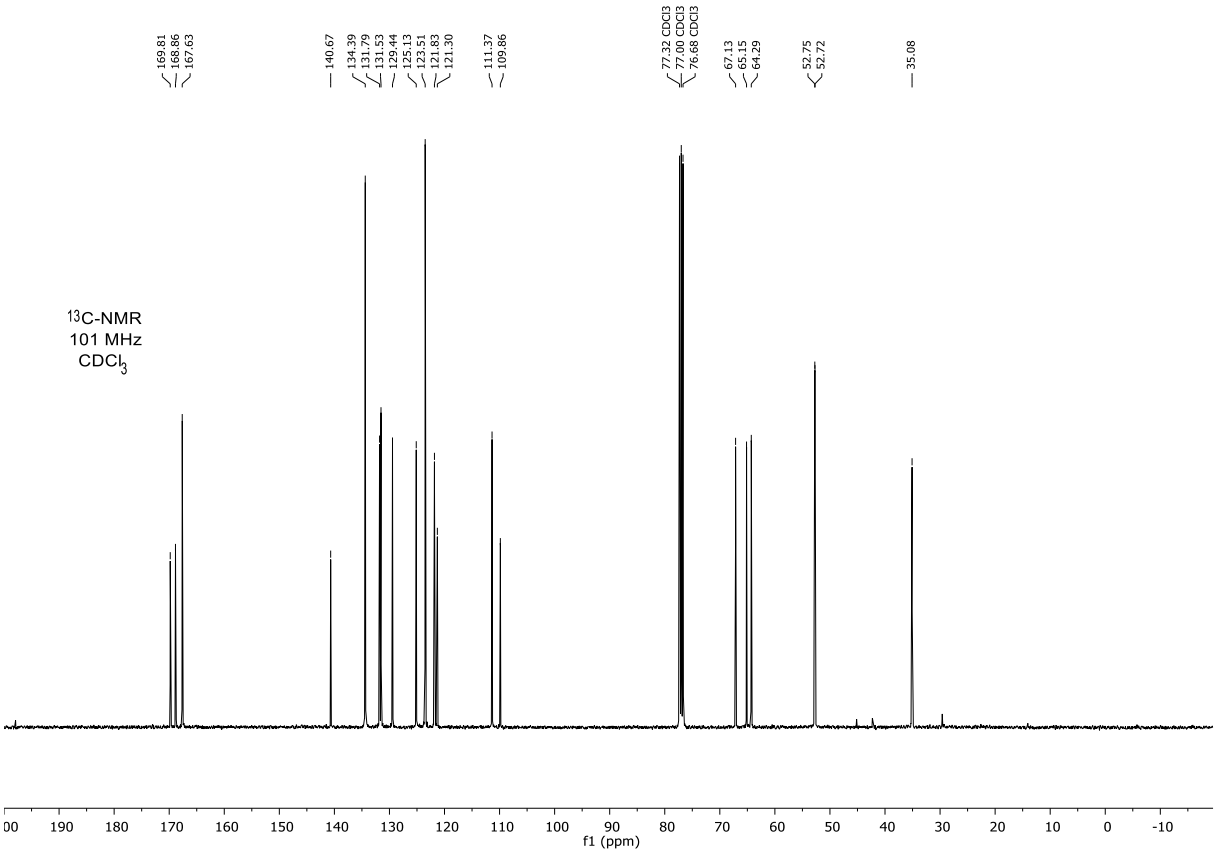


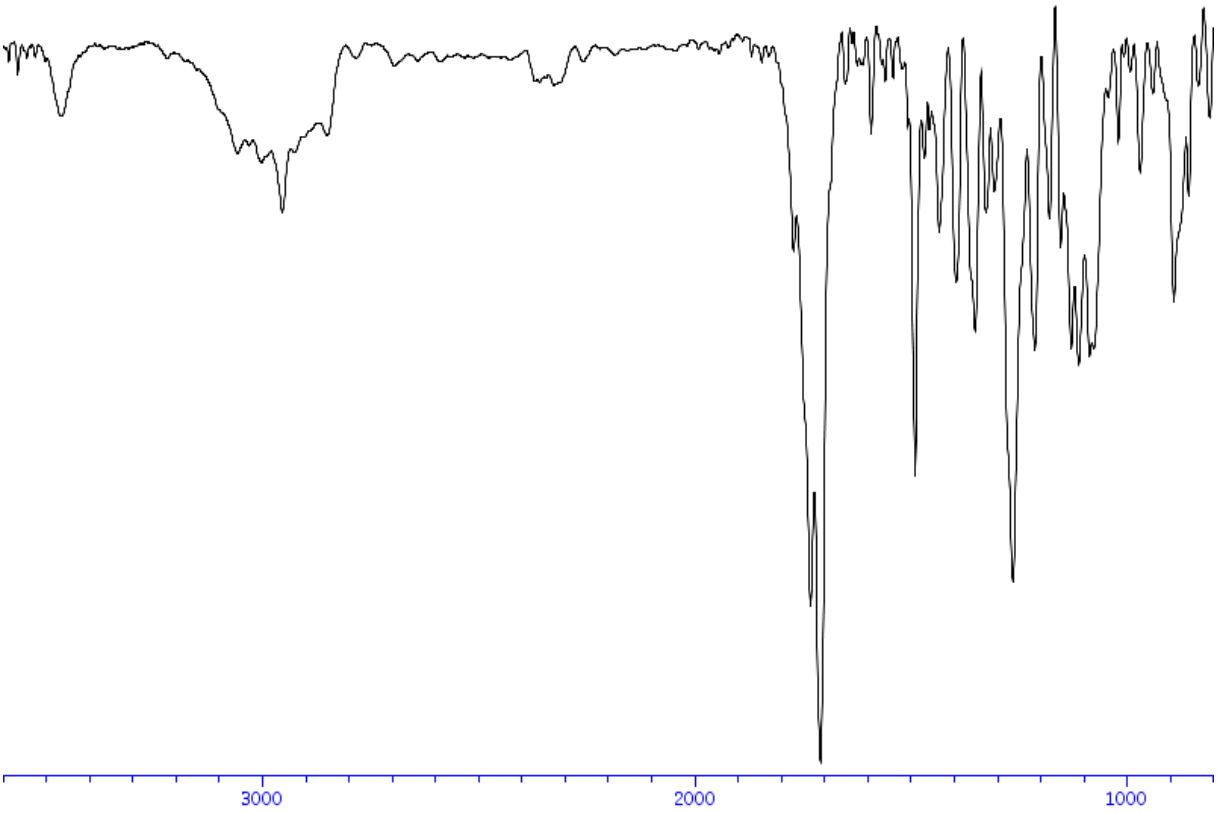




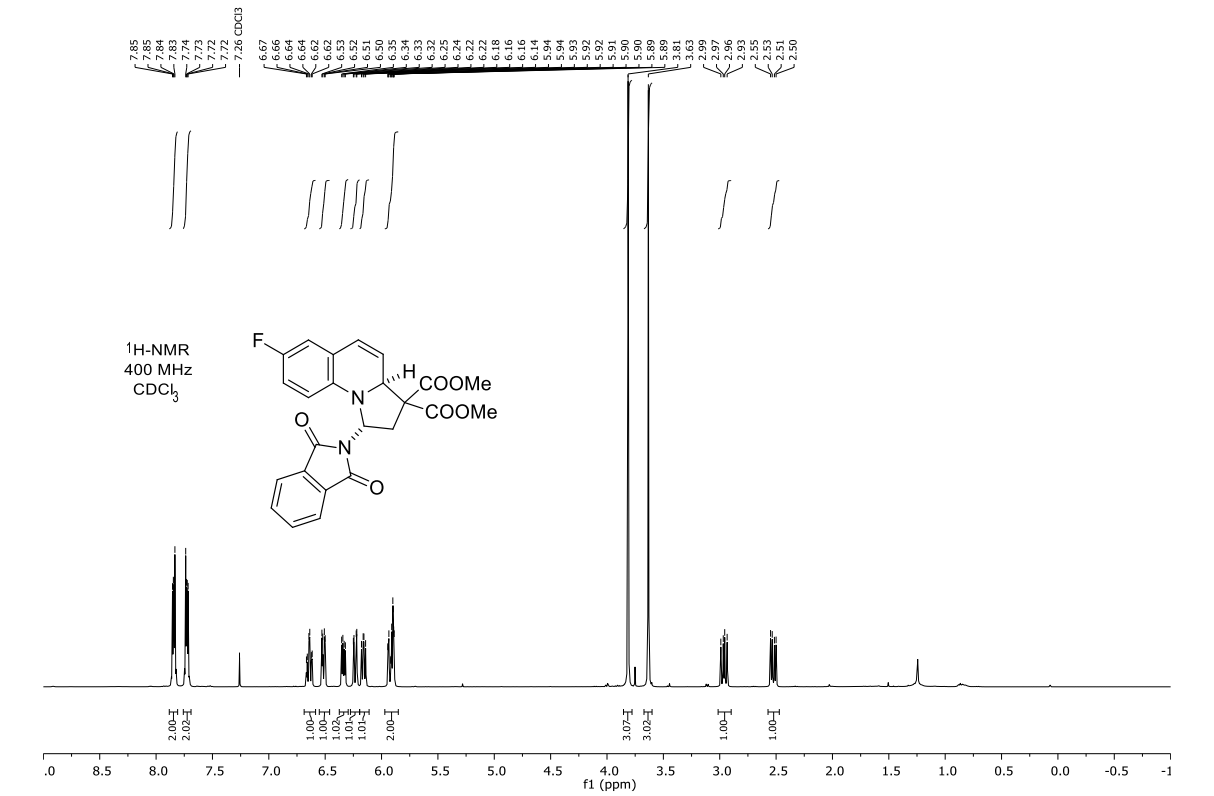
***anti*-Dimethyl 7-bromo-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (26).**

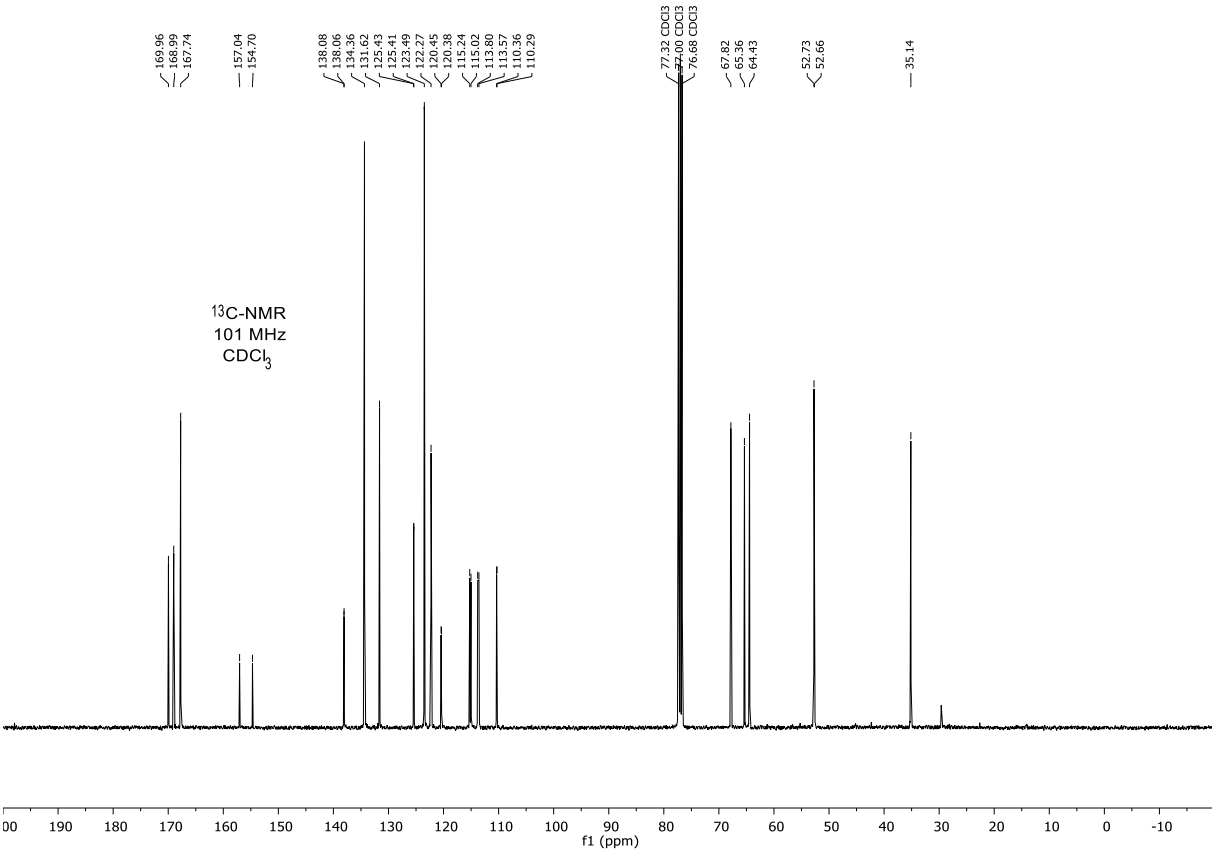


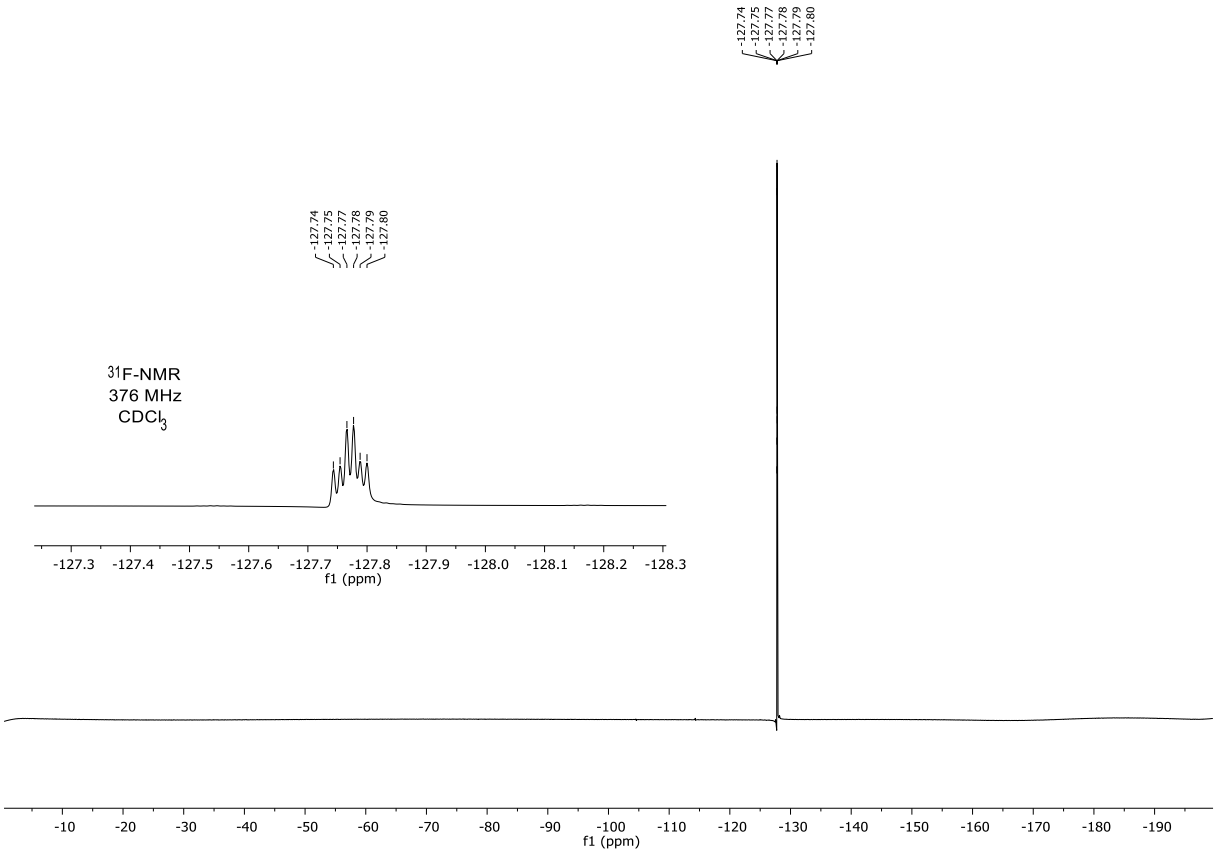

169.81
168.86
167.63
140.67
134.39
131.79
131.53
129.44
125.13
123.51
121.83
121.30
111.37
109.86
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
67.13
65.15
64.29
52.75
52.72
35.08
13C-NMR
101 MHz
CDCl3
f1 (ppm)

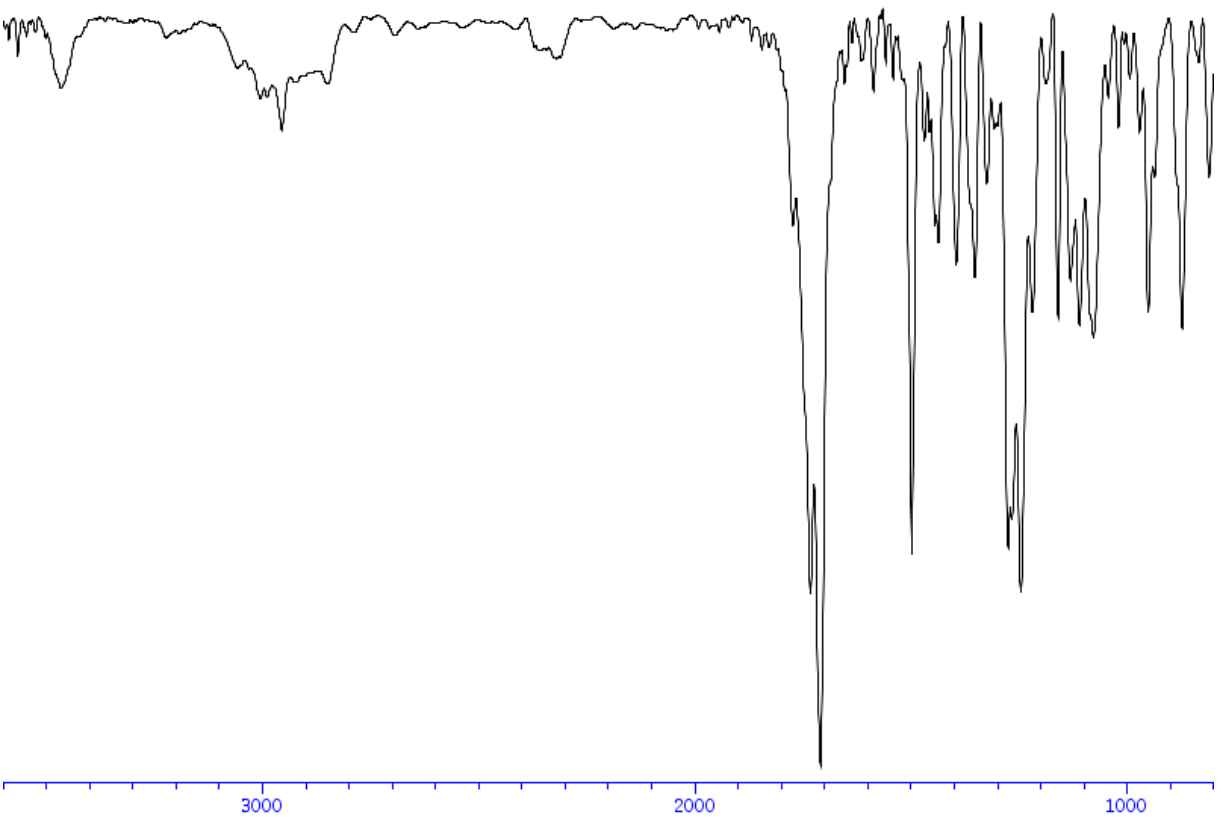

3000
2000
1000

***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-7-fluoro-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (27).**

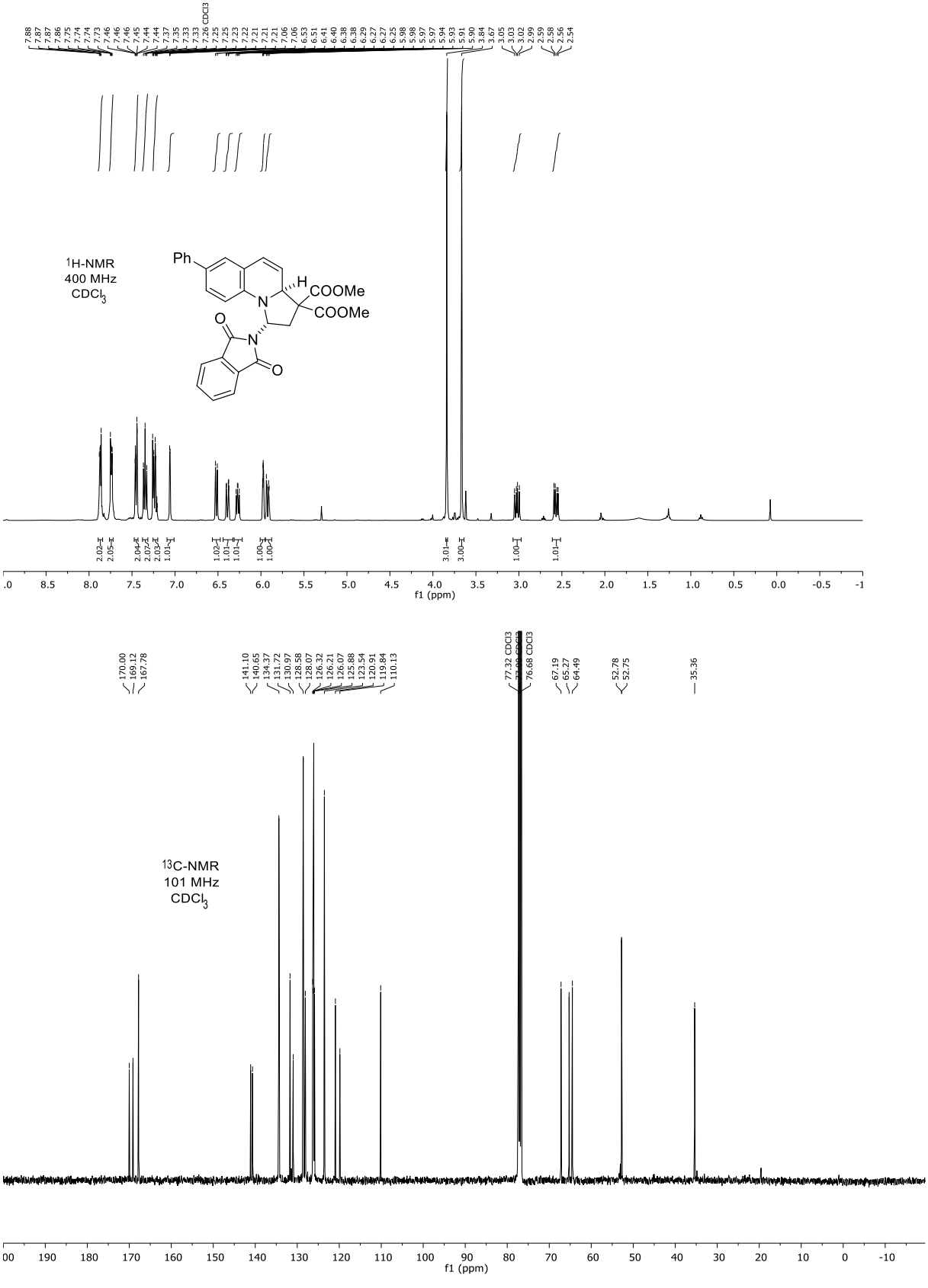


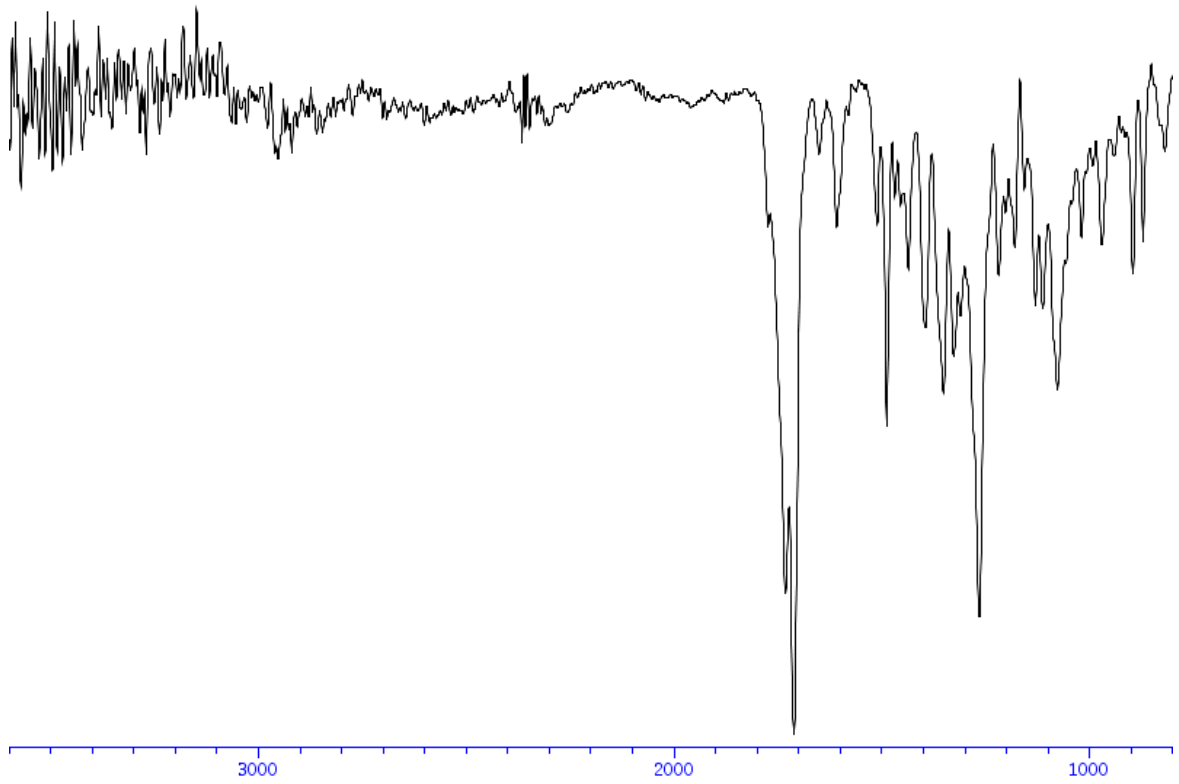



-127.74
-127.75
-127.77
-127.78
-127.79
-127.80
31F-NMR
376 MHz
CDCl3
-127.3 -127.4 -127.5 -127.6 -127.7 -127.8 -127.9 -128.0 -128.1 -128.2 -128.3
f1 (ppm)
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

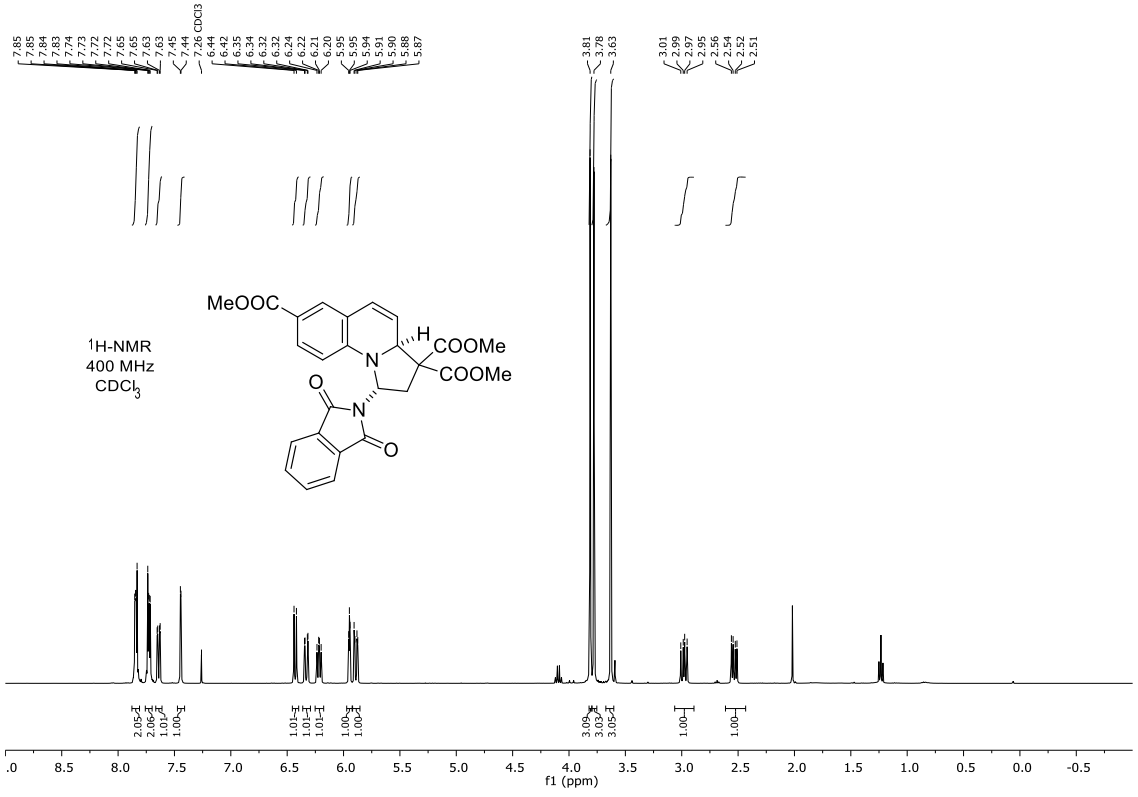

3000
2000
1000

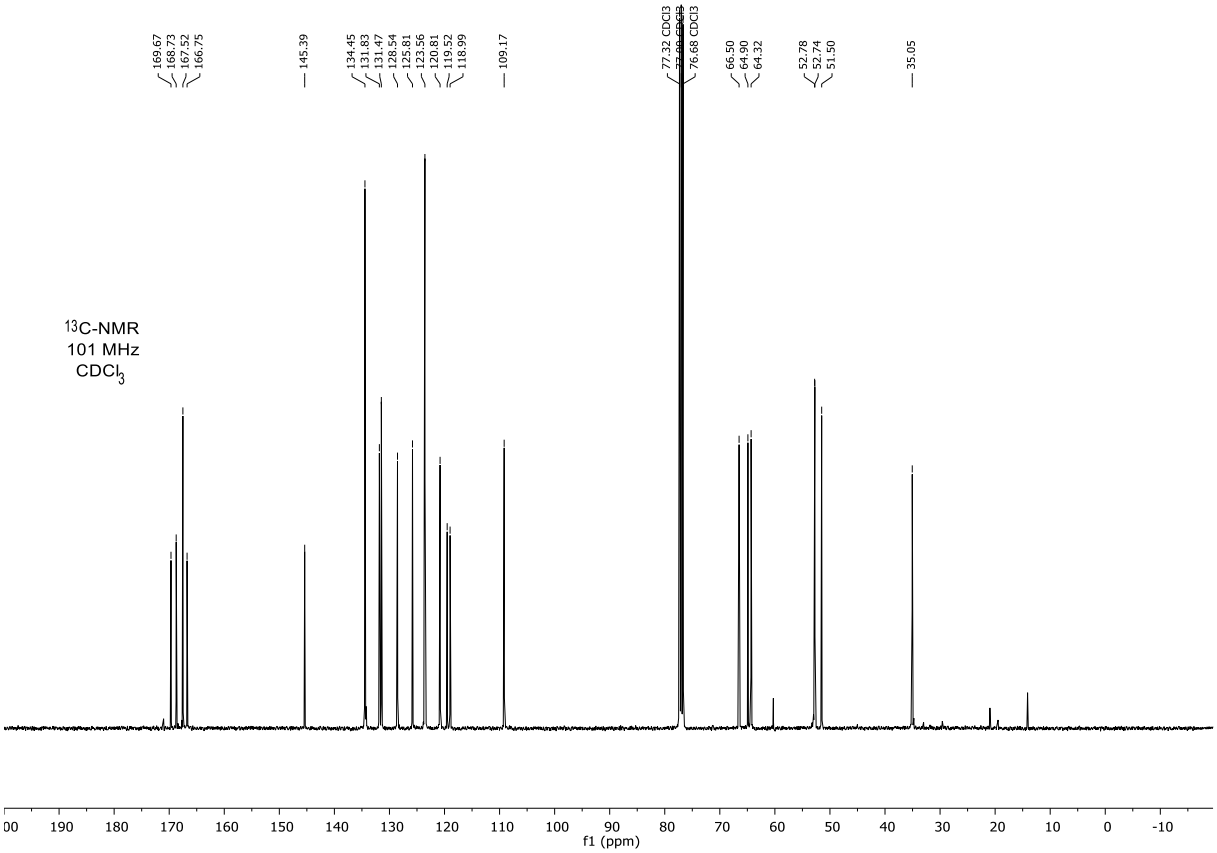
***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-7-phenyl-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**28**).

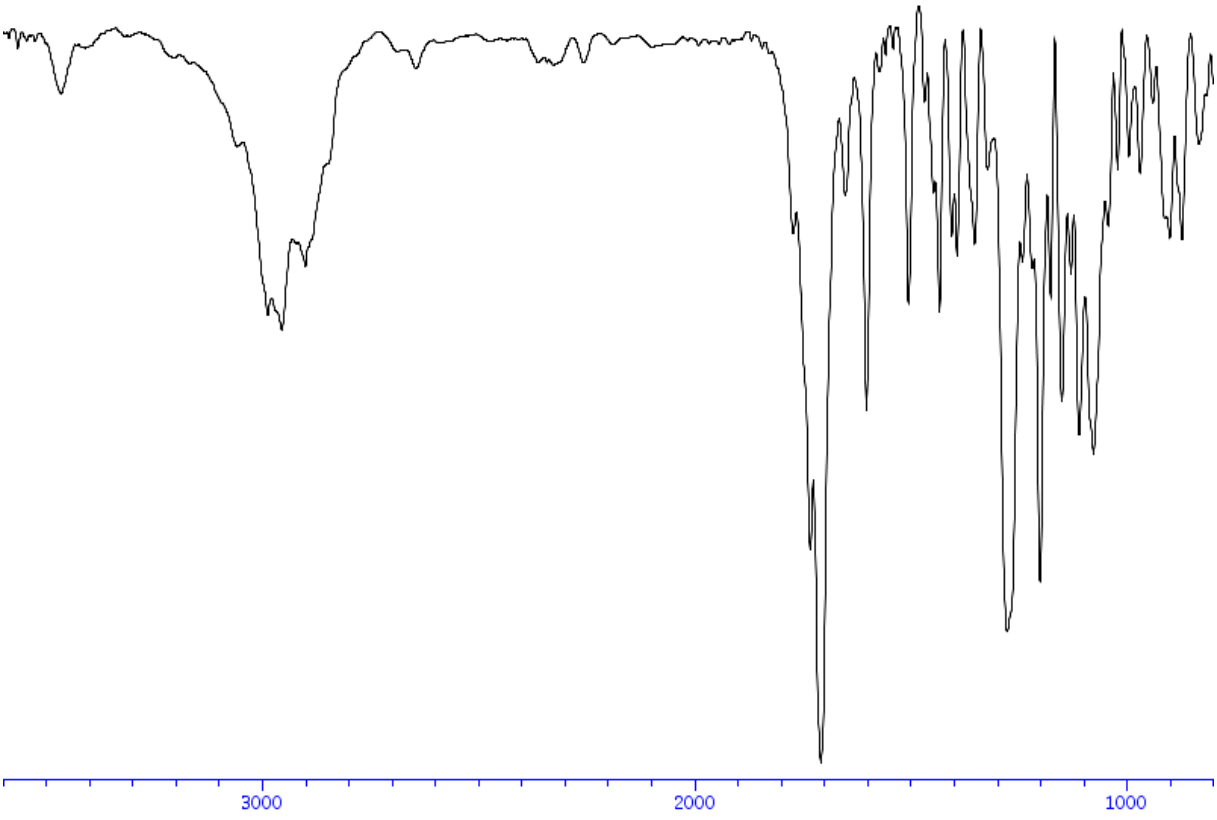




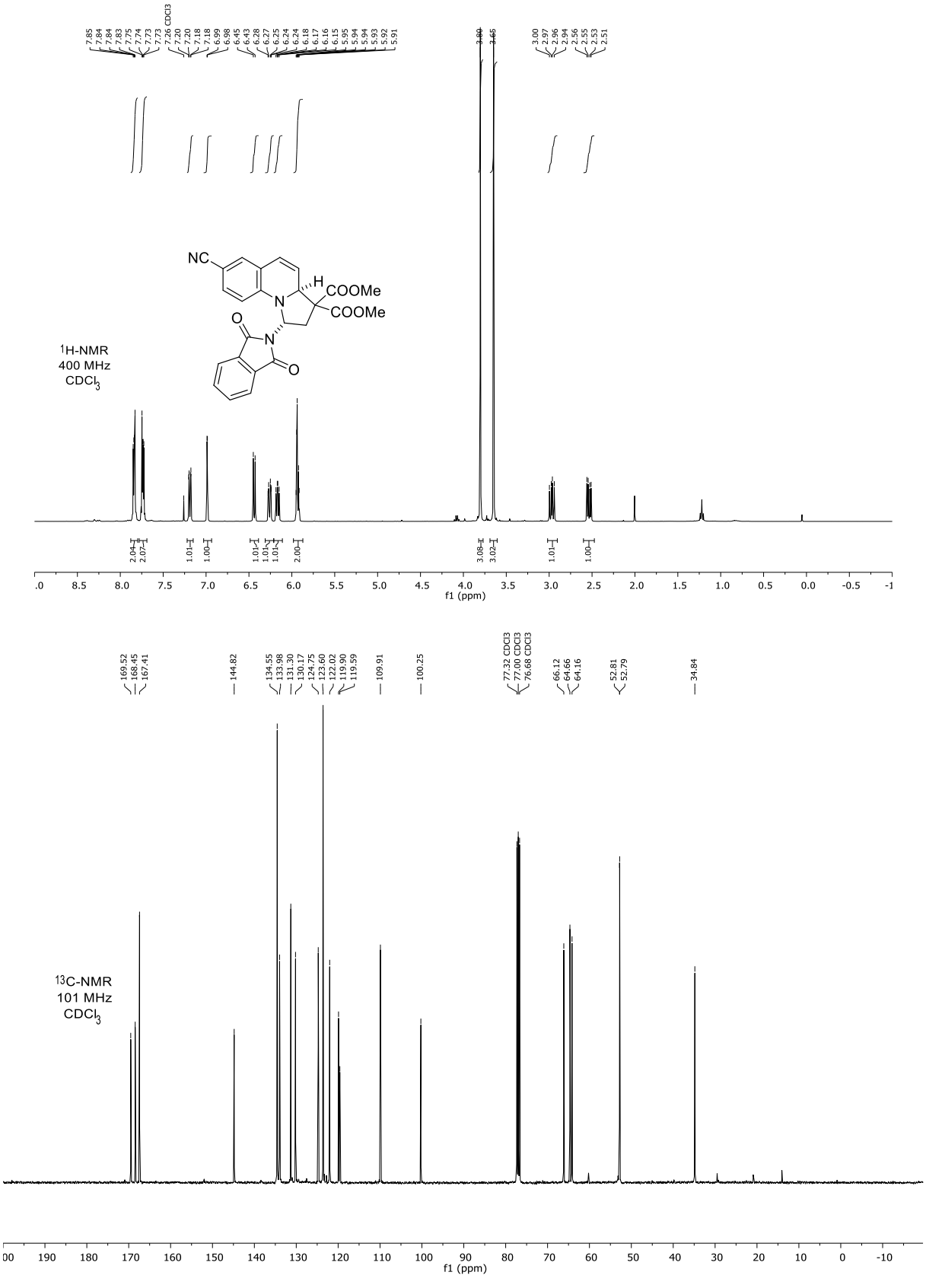
***anti*-Trimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3,7(3a*H*)-tricarboxylate** (**29**).

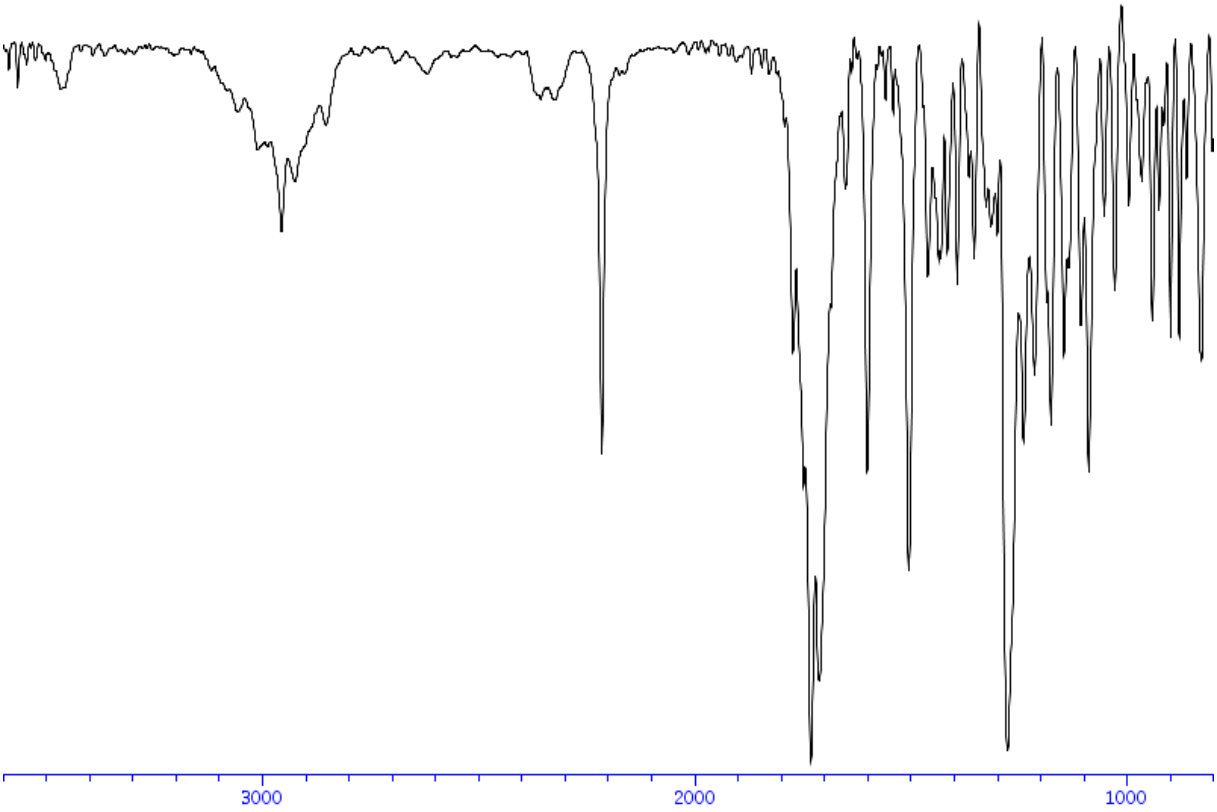



169.67
168.73
167.52
166.75
145.39
134.45
131.83
131.47
128.54
125.81
123.56
120.81
119.52
118.99
109.17
77.32 CDCl3
76.68 CDCl3
66.50
64.90
64.32
52.78
52.74
51.50
35.05
13C-NMR
101 MHz
CDCl3
f1 (ppm)

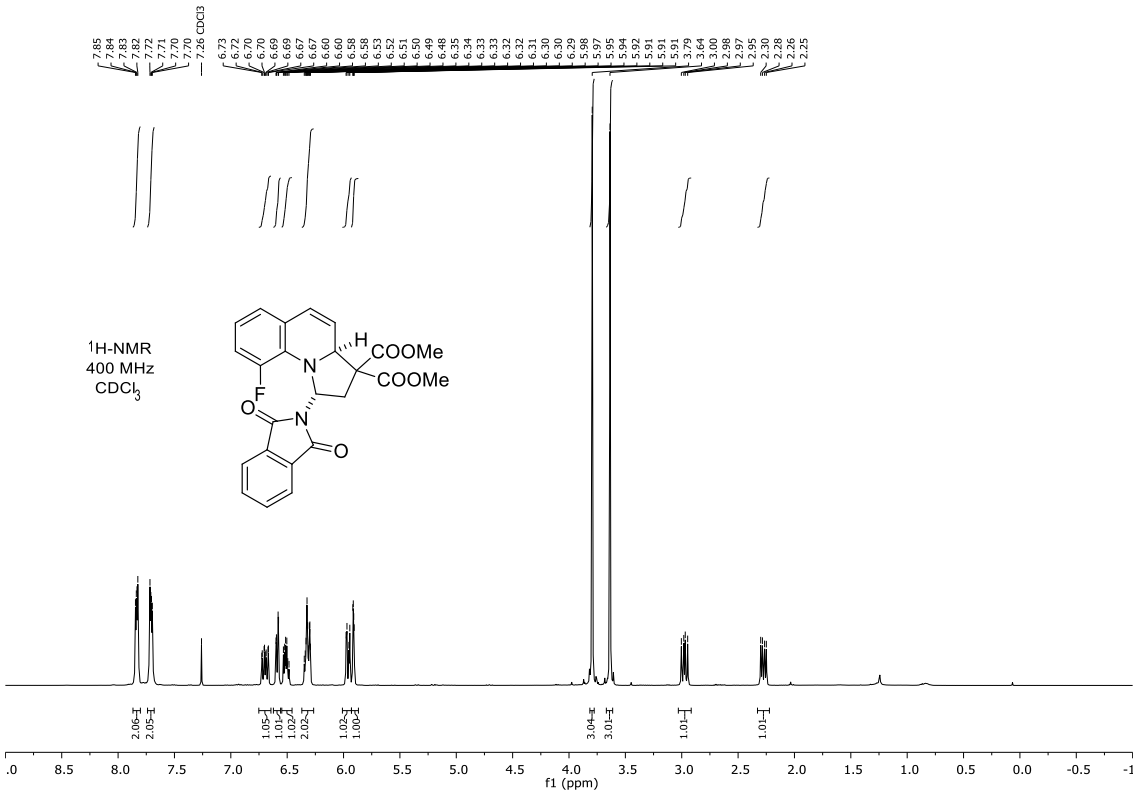

3000
2000
1000

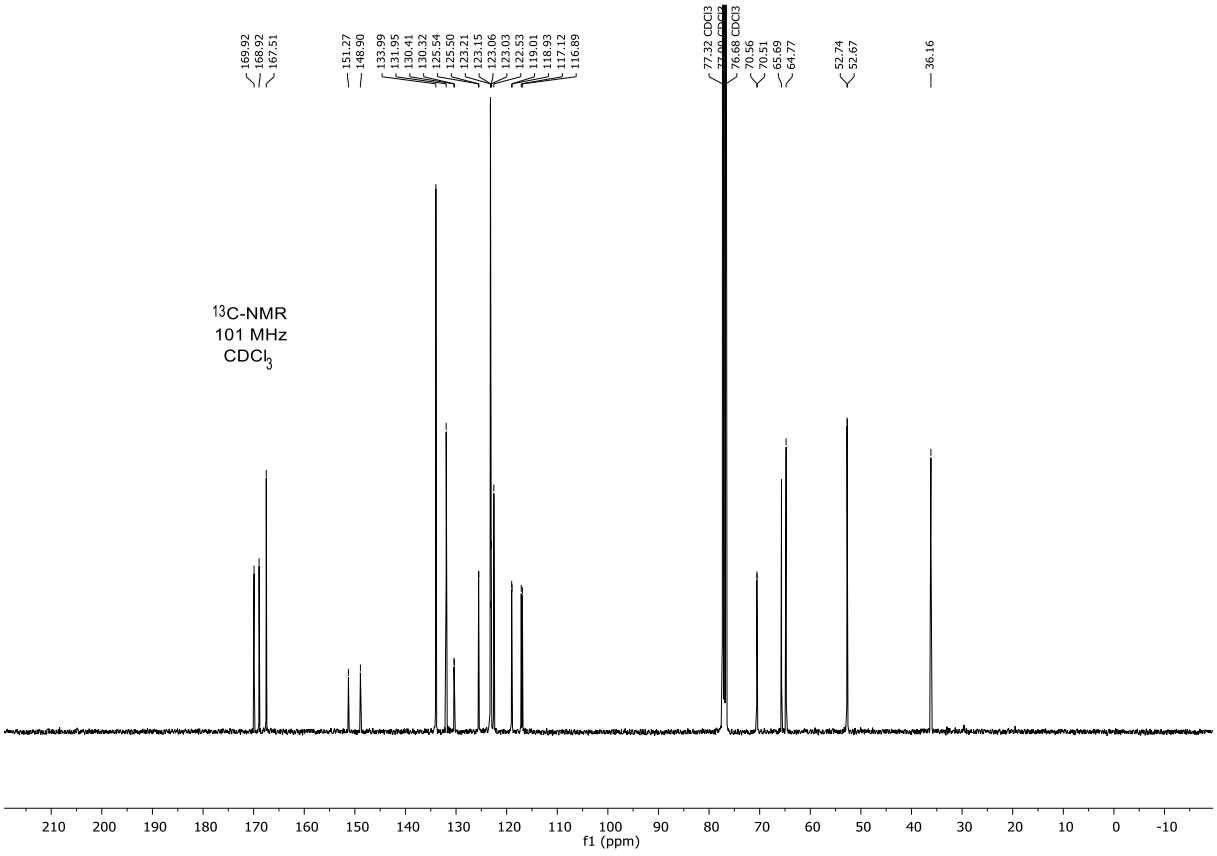
***anti*-Dimethyl 7-cyano-1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate** (**30**).

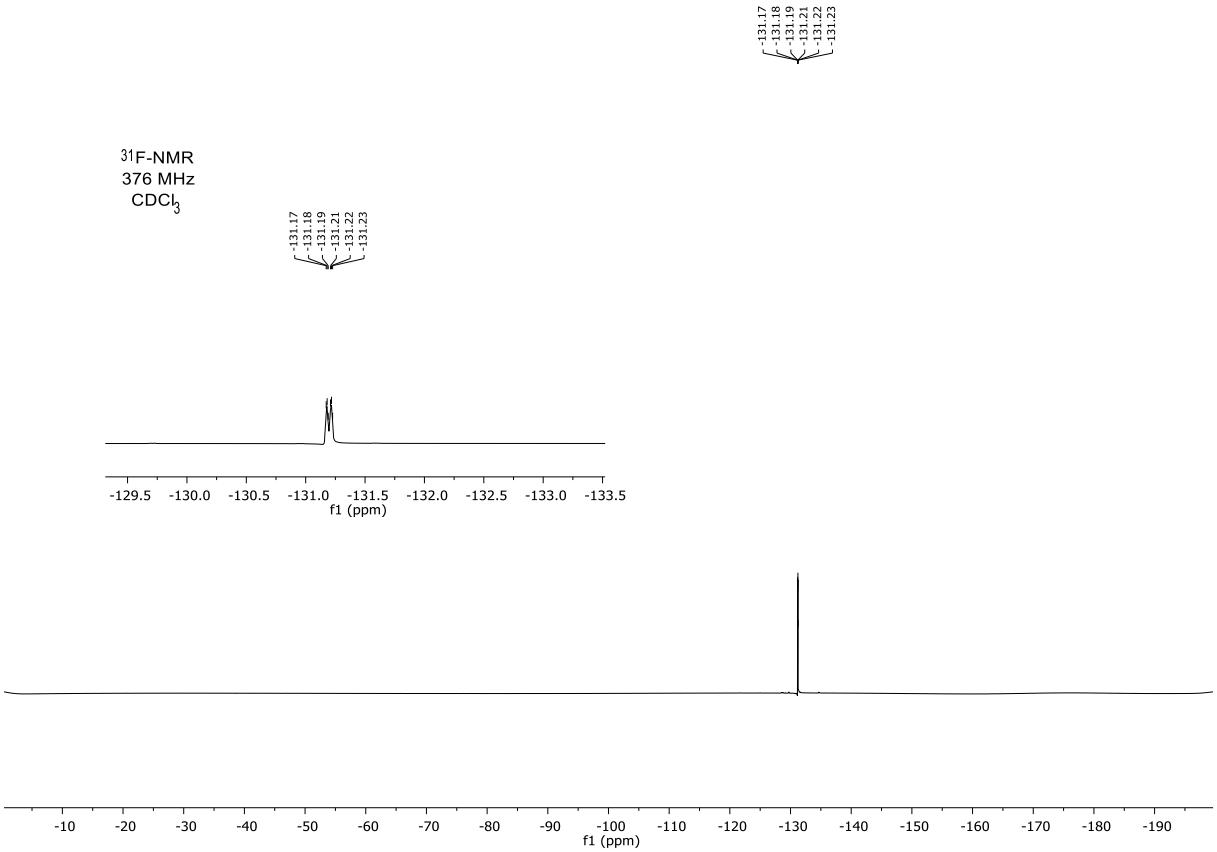


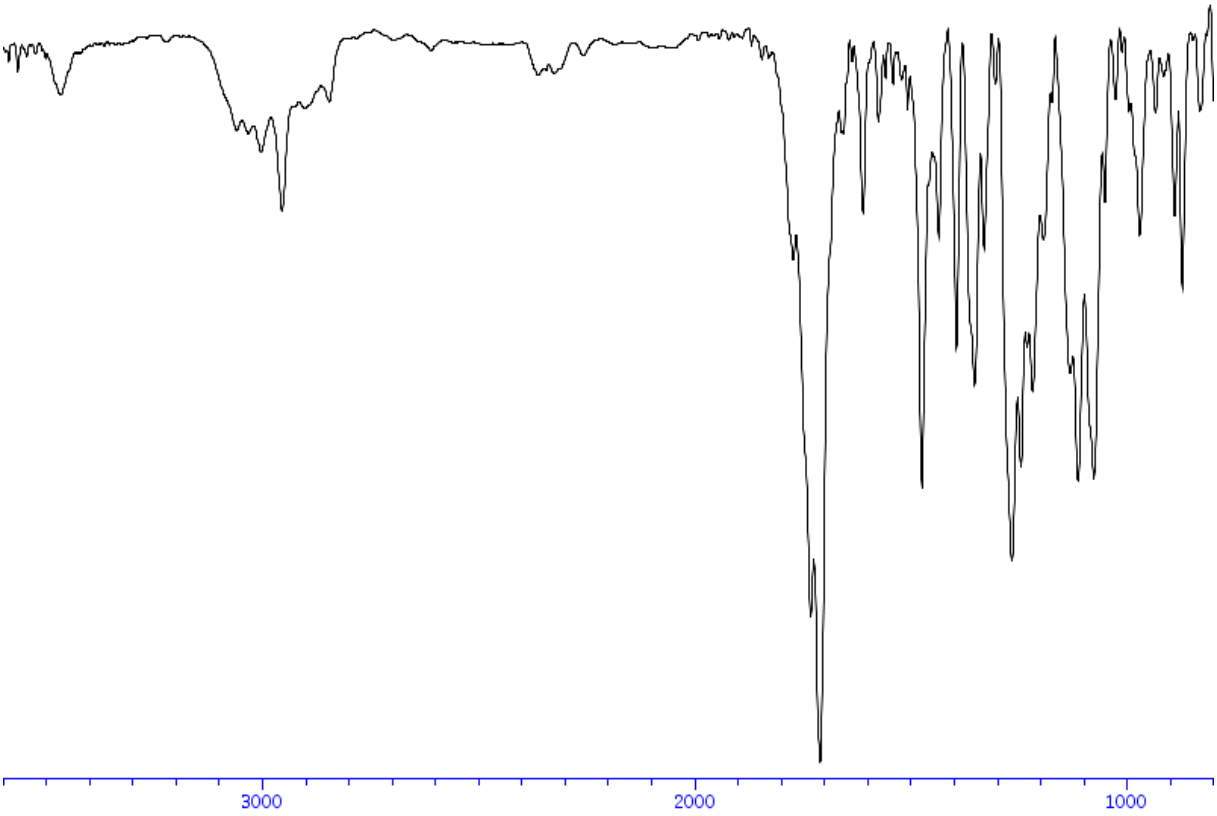


***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-9-fluoro-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (31).**

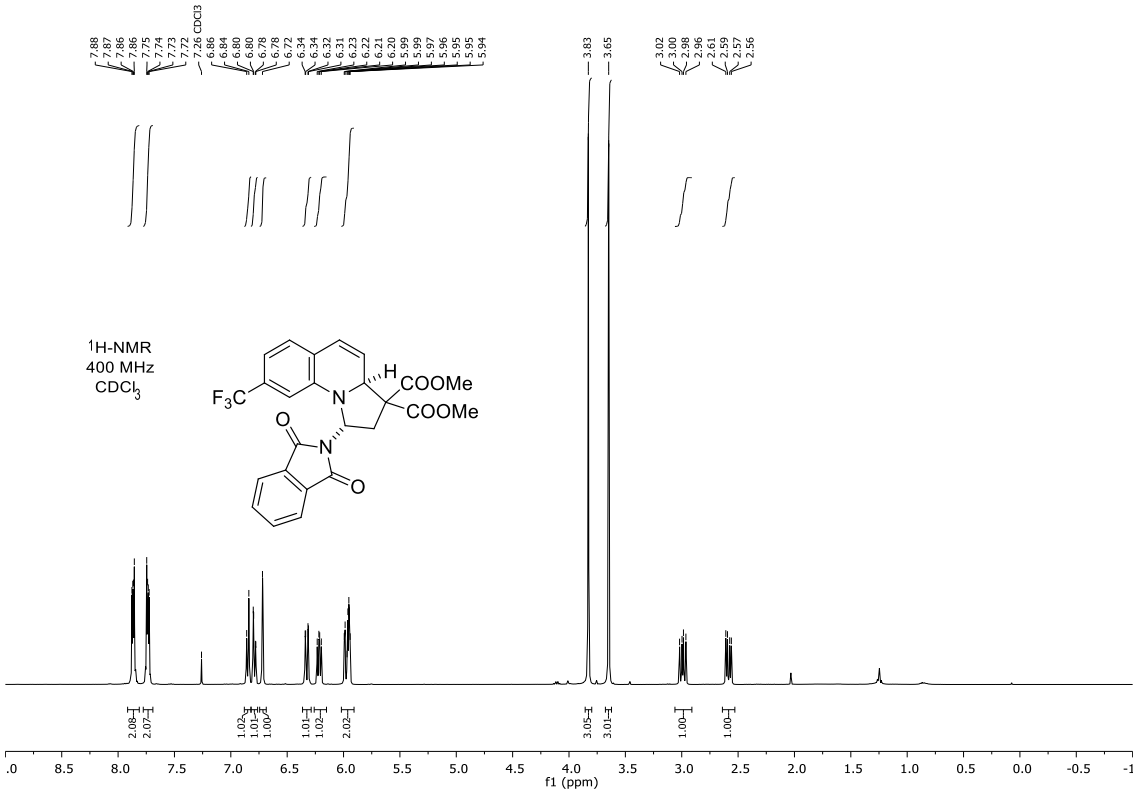


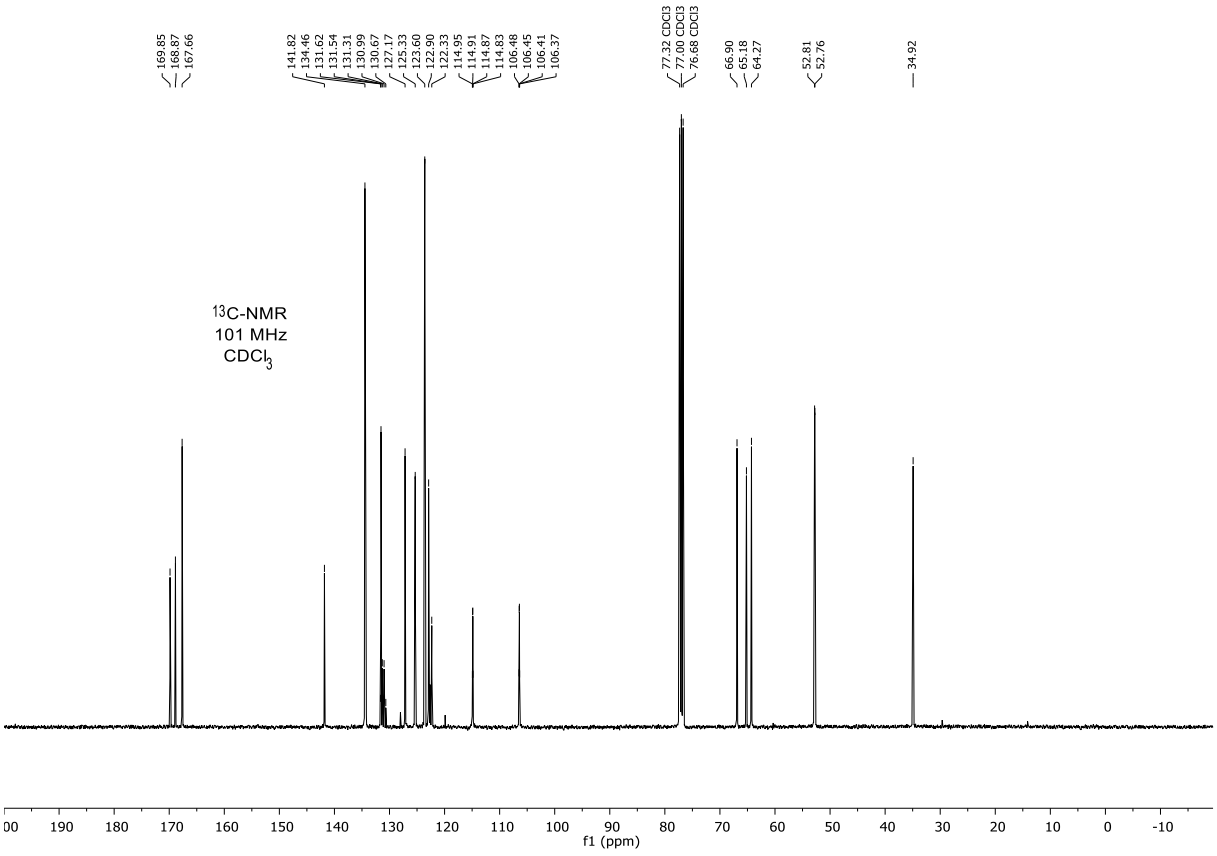

169.92
168.92
167.51
151.27
148.90
133.99
131.95
130.41
130.32
125.54
125.50
123.21
123.15
123.06
123.03
122.53
119.01
118.93
117.12
116.89
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
70.56
70.51
65.69
64.77
52.74
52.67
36.16
13C-NMR
101 MHz
CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

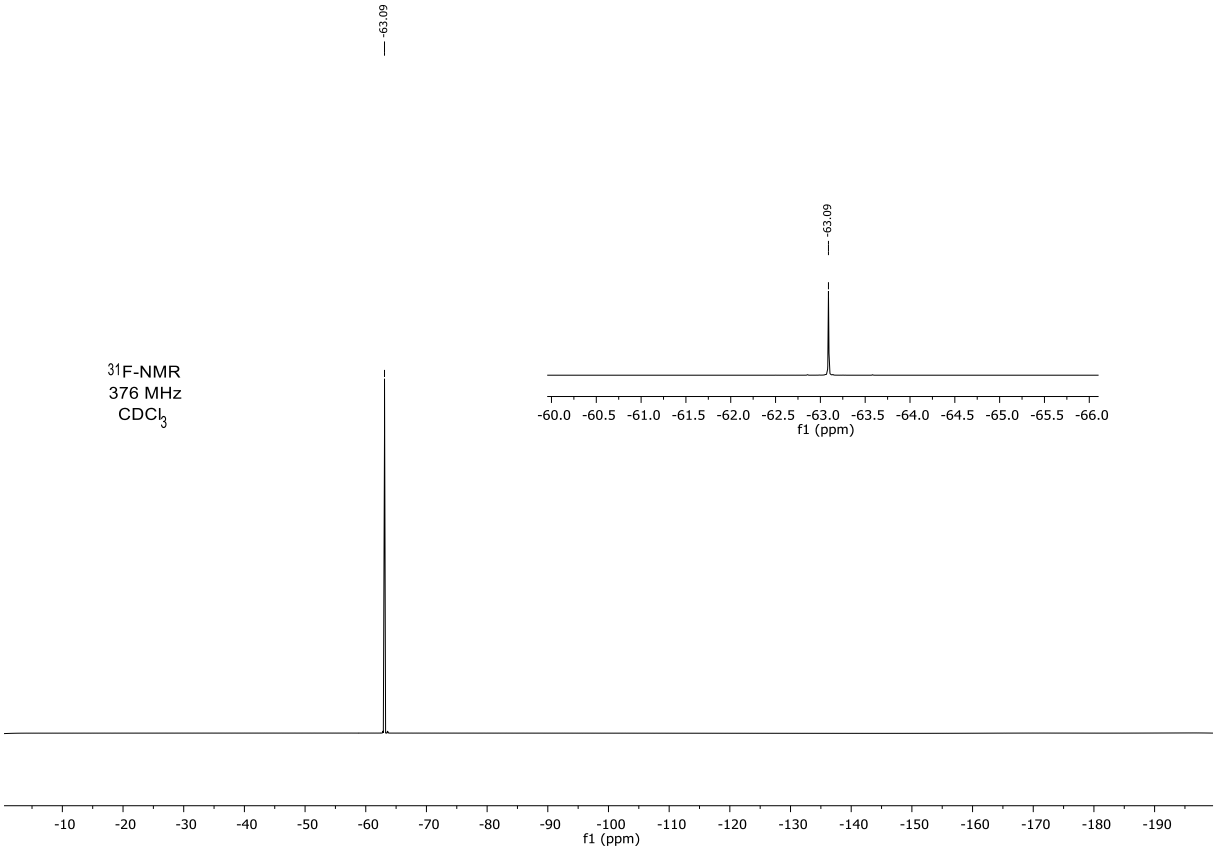

-131.17
-131.18
-131.19
-131.21
-131.22
-131.23
31F-NMR
376 MHz
CDCl3
-129.5 -130.0 -130.5 -131.0 -131.5 -132.0 -132.5 -133.0 -133.5
f1 (ppm)
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

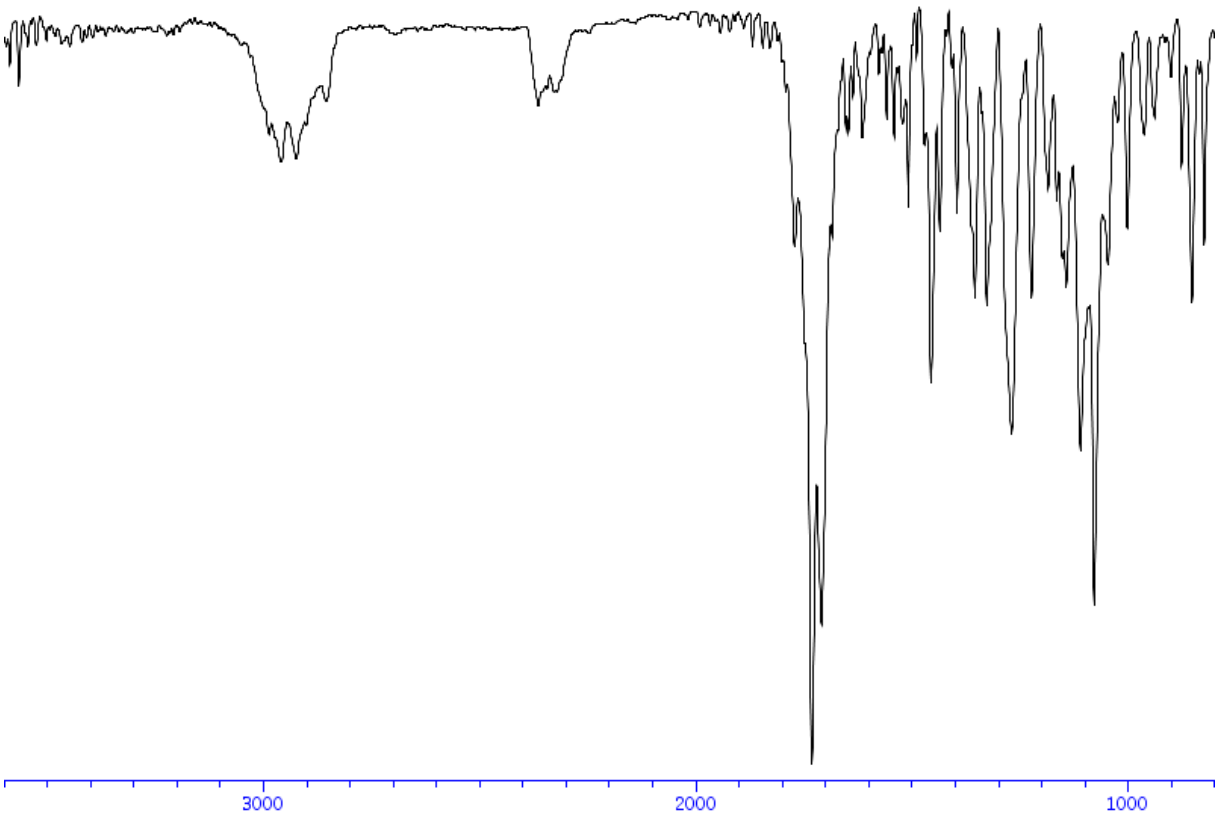


***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-8-(trifluoromethyl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (32).**

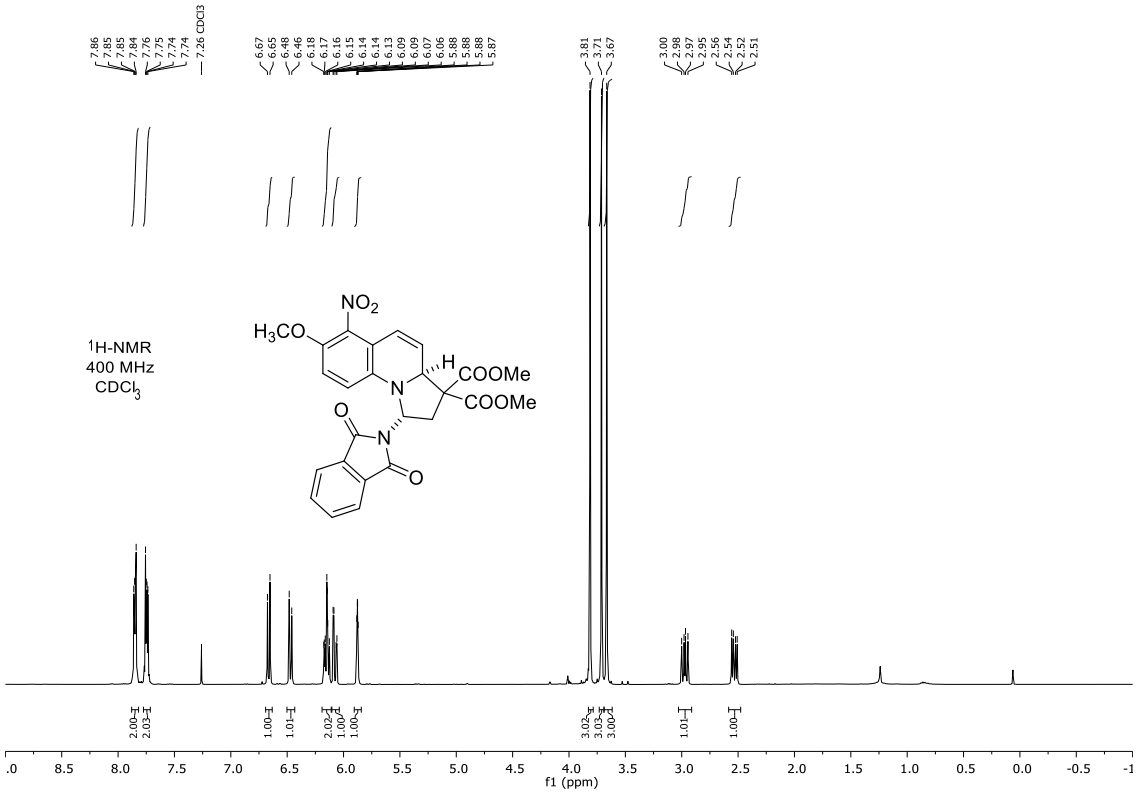


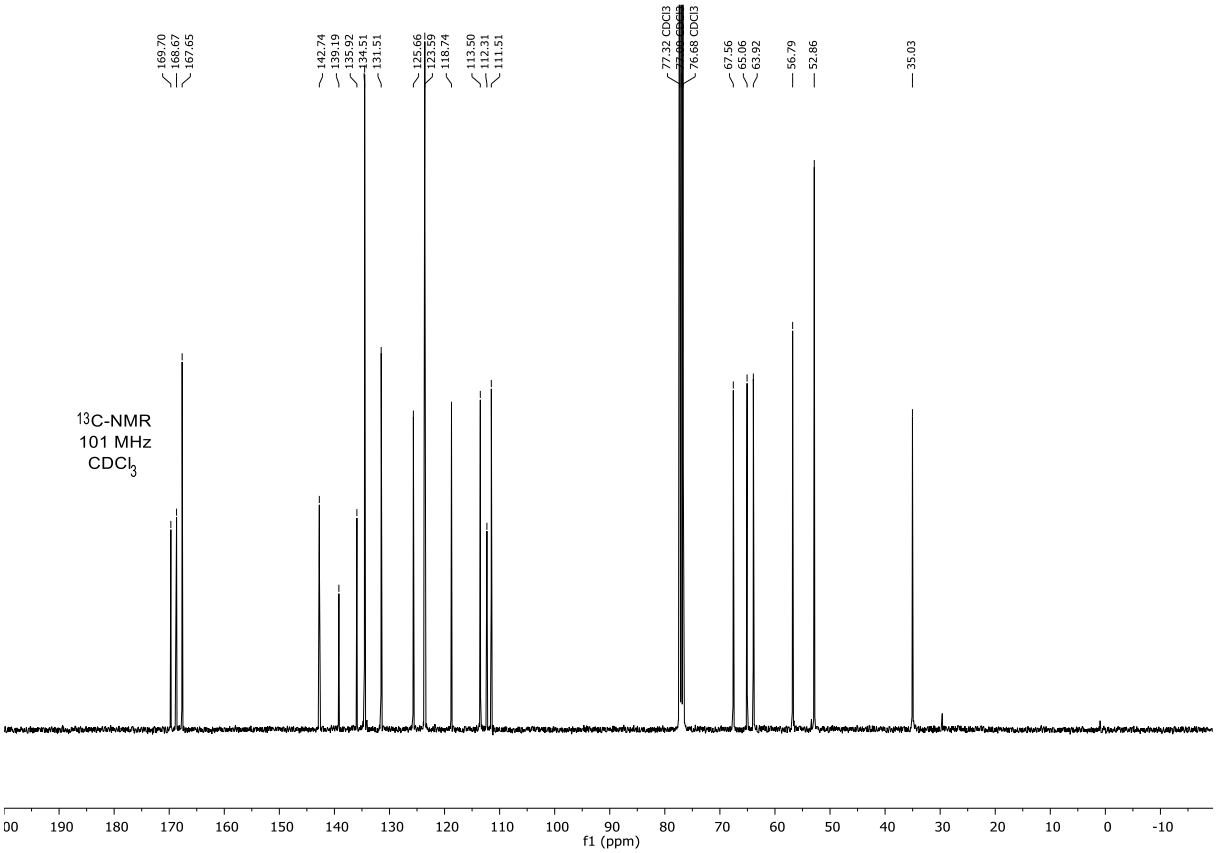

169.85
168.87
167.66
141.82
134.46
131.62
131.54
131.31
130.99
130.67
127.17
125.33
123.60
122.90
122.33
114.95
114.91
114.87
114.83
106.48
106.45
106.41
106.37
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
66.90
65.18
64.27
52.81
52.76
34.92
13C-NMR
101 MHz
CDCl3
f1 (ppm)

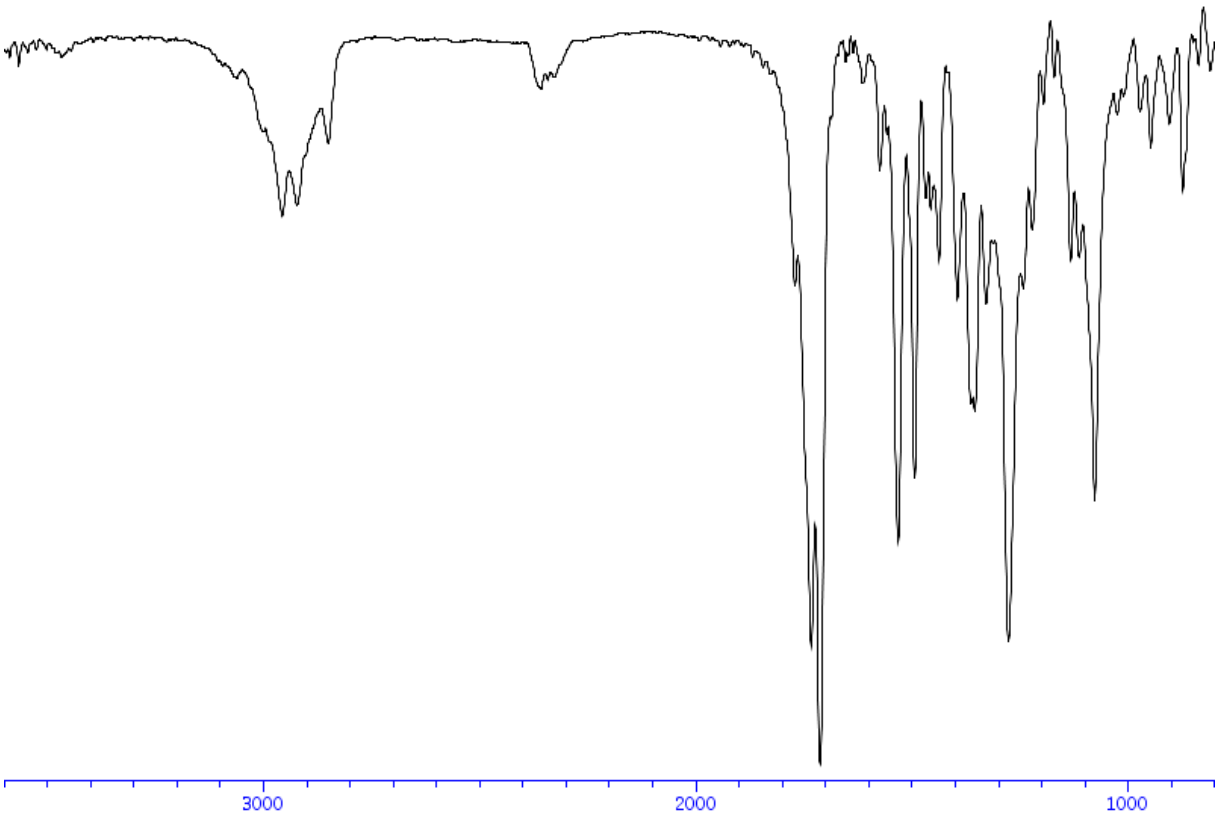

-63.09
-63.09
31F-NMR
376 MHz
CDCl3
f1 (ppm)
f1 (ppm)



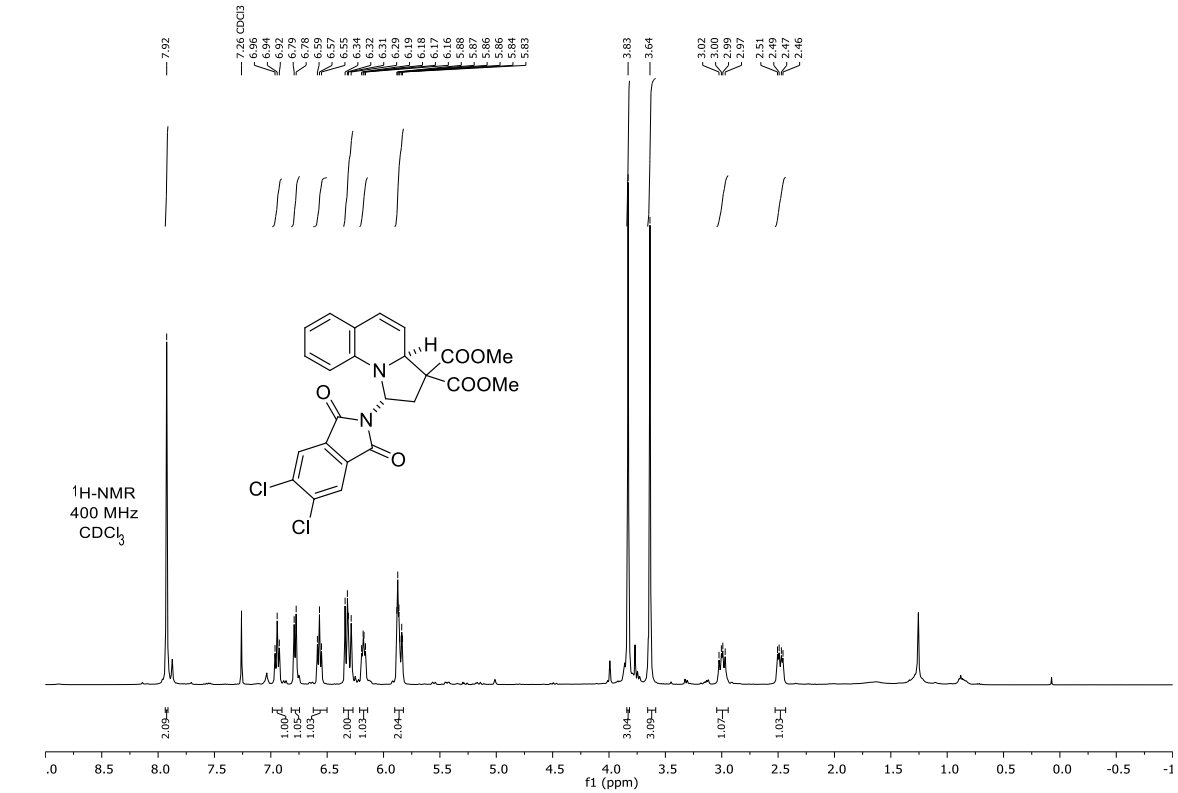
***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-7-methoxy-6-nitro-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (34).**

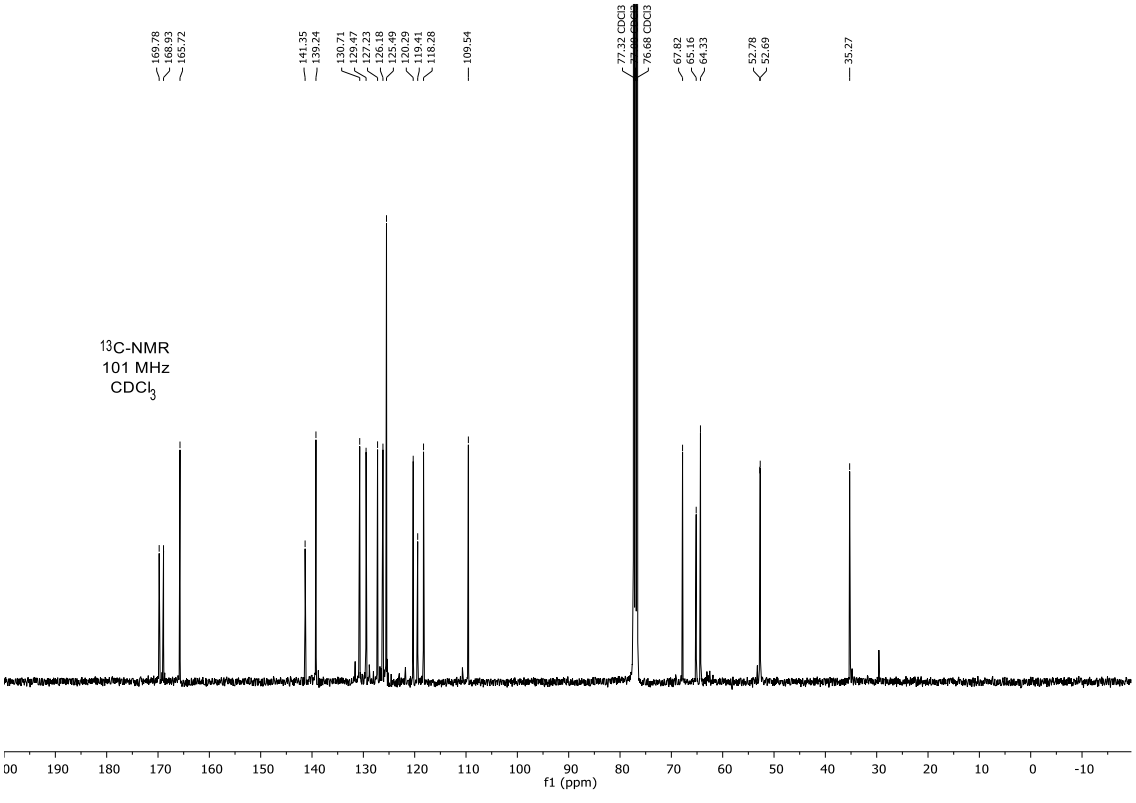


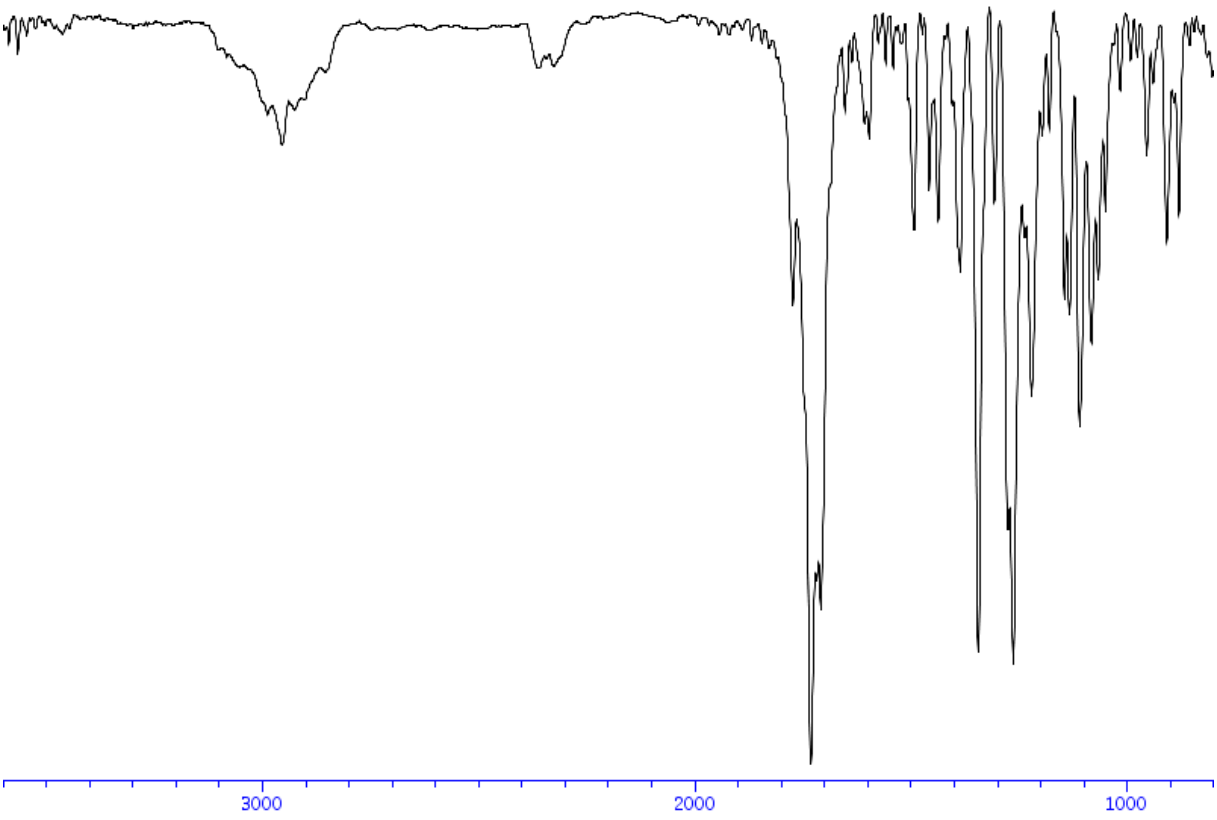

169.70
168.67
167.65
142.74
139.19
135.92
134.51
131.51
125.66
123.59
118.74
113.50
112.31
111.51
77.32 CDCl3
76.68 CDCl3
67.56
65.06
63.92
56.79
52.86
35.03
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

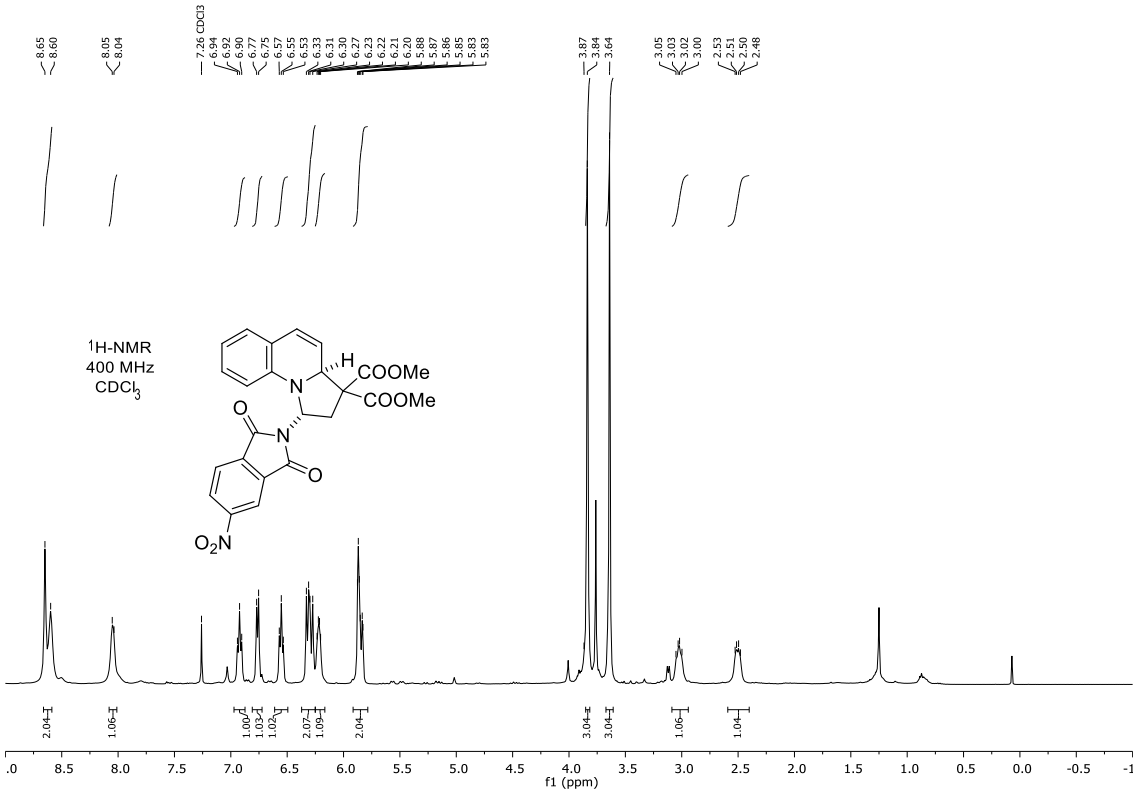
***anti*-Dimethyl 1-(5,6-dichloro-1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (35).**

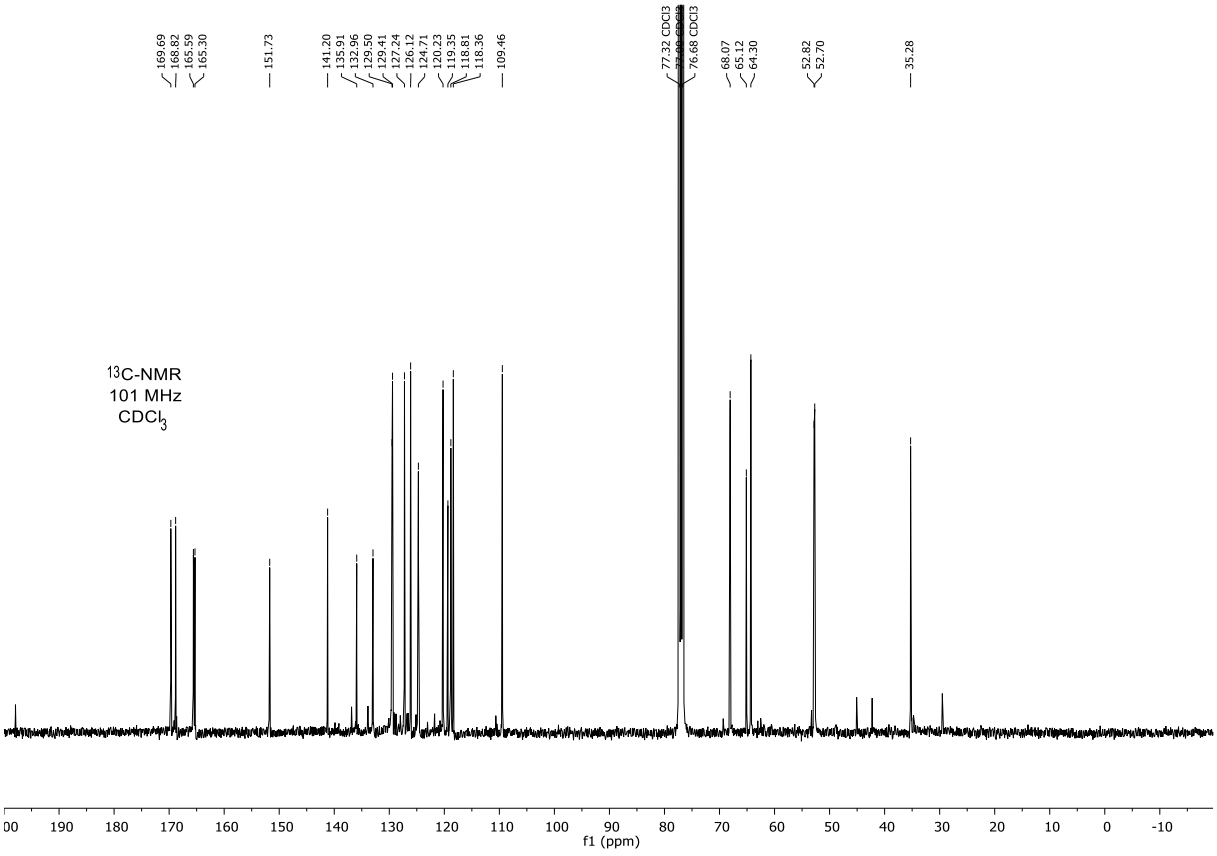


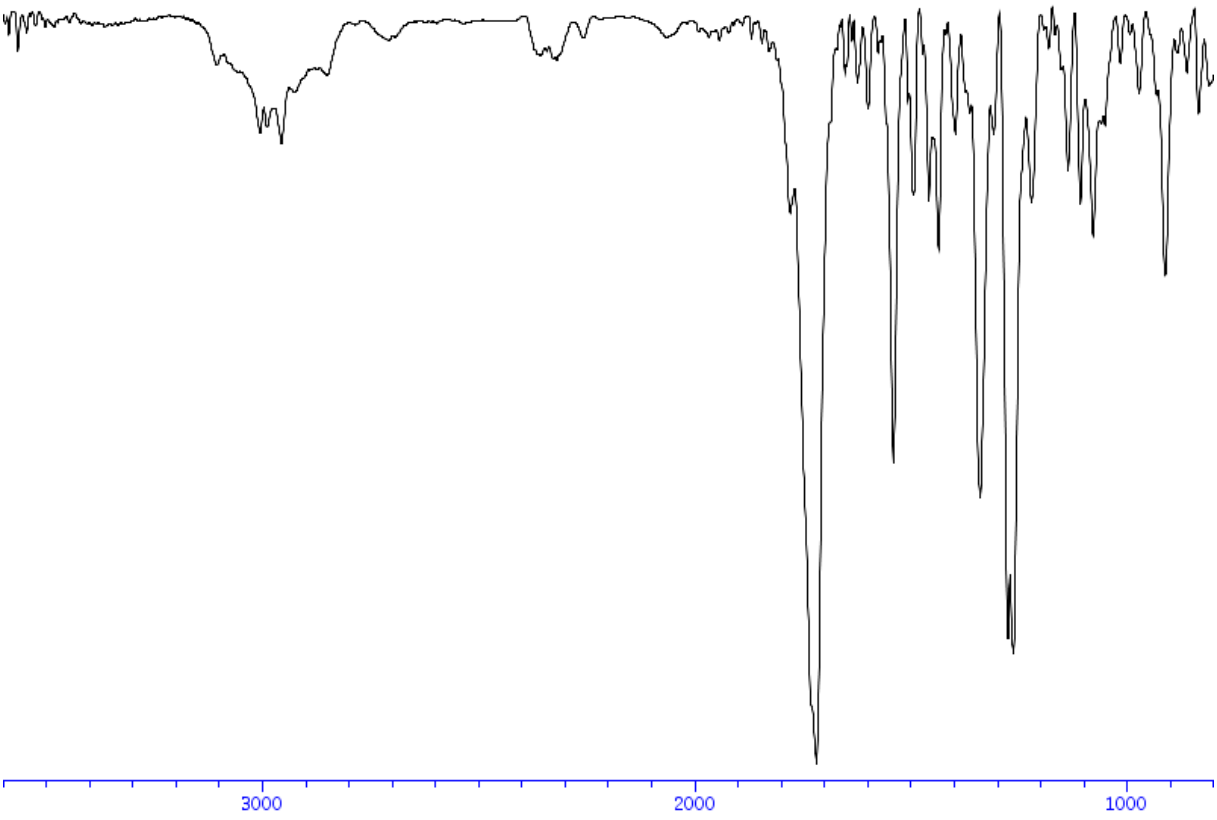




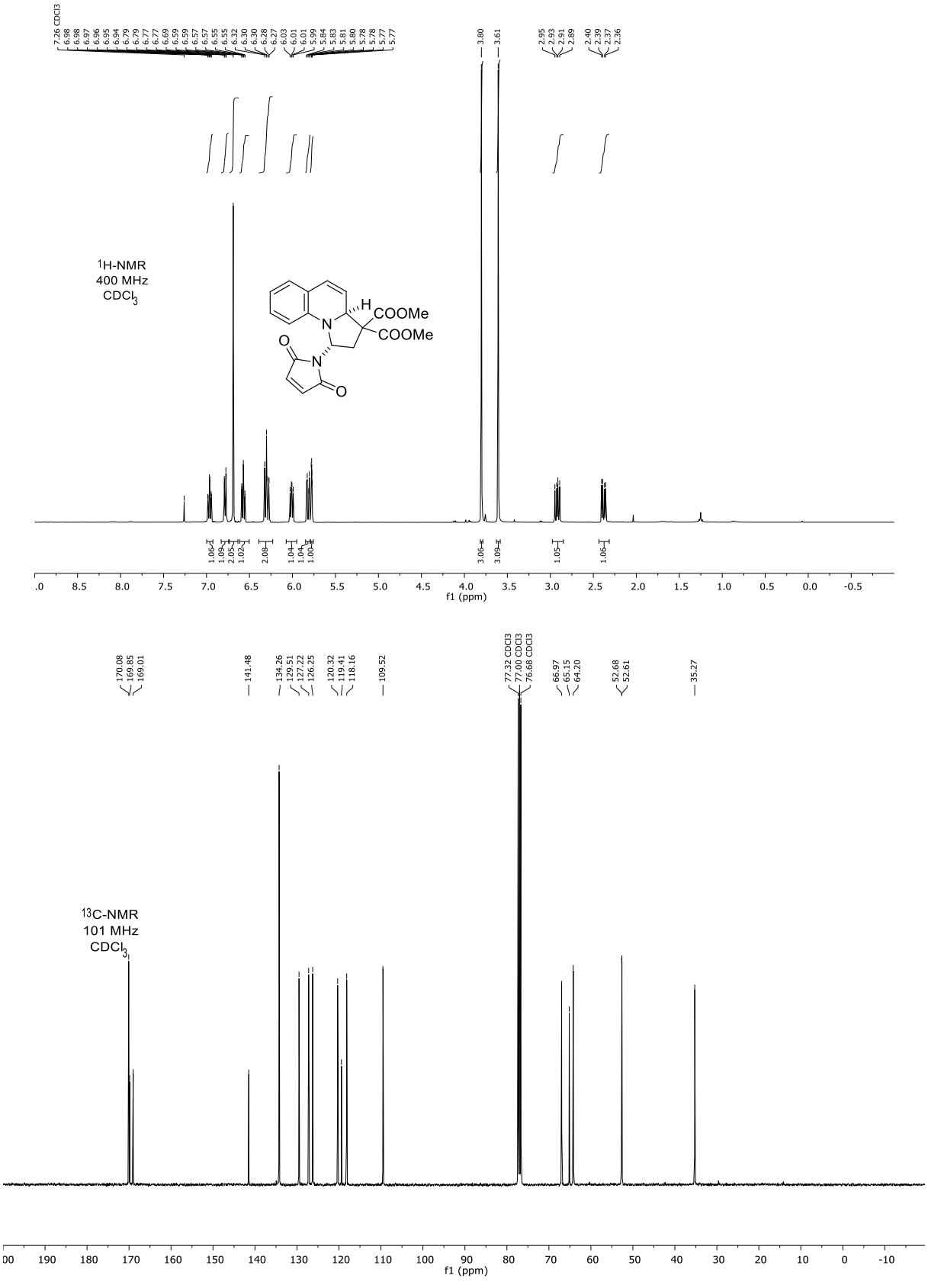
***anti*-Dimethyl 1-(5-nitro-1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (36).**

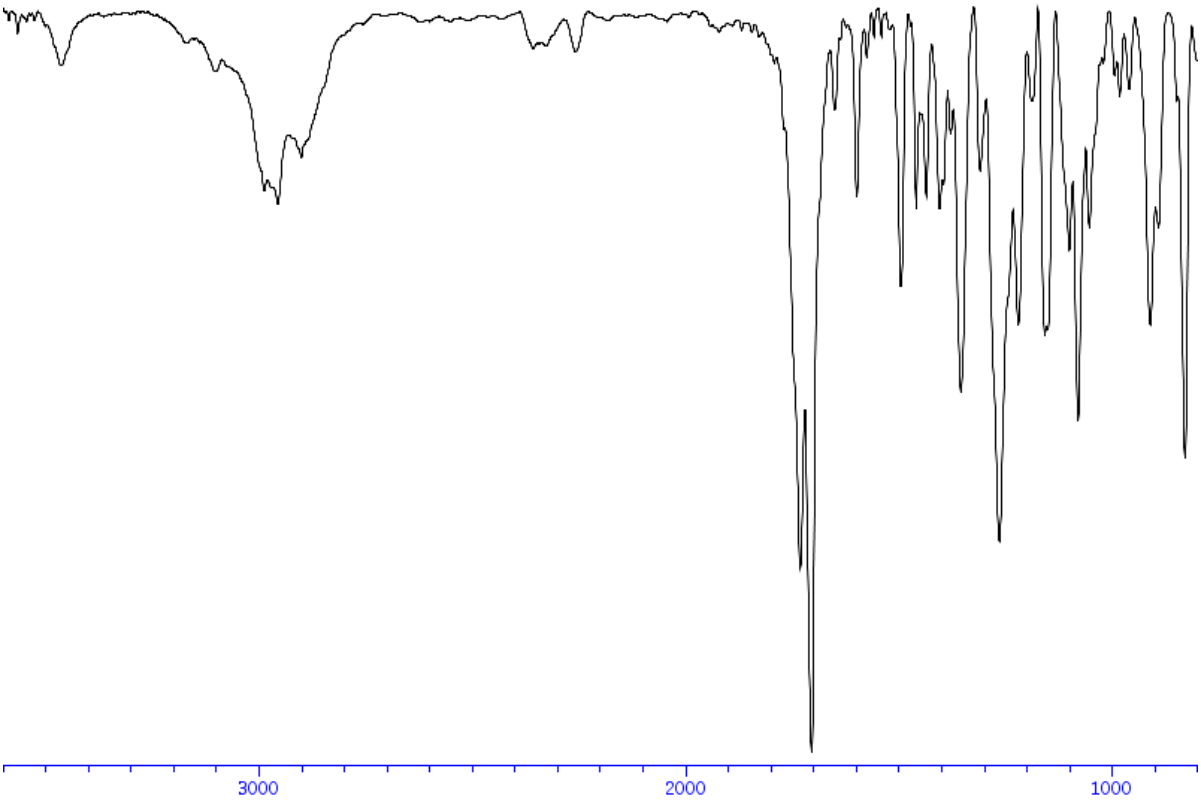



169.69
168.82
165.59
165.30
151.73
141.20
135.91
132.96
129.50
129.41
127.24
126.12
124.71
120.23
119.35
118.81
118.36
109.46
77.32 CDCl3
76.68 CDCl3
68.07
65.12
64.30
52.82
52.70
35.28
13C-NMR
101 MHz
CDCl3
f1 (ppm)

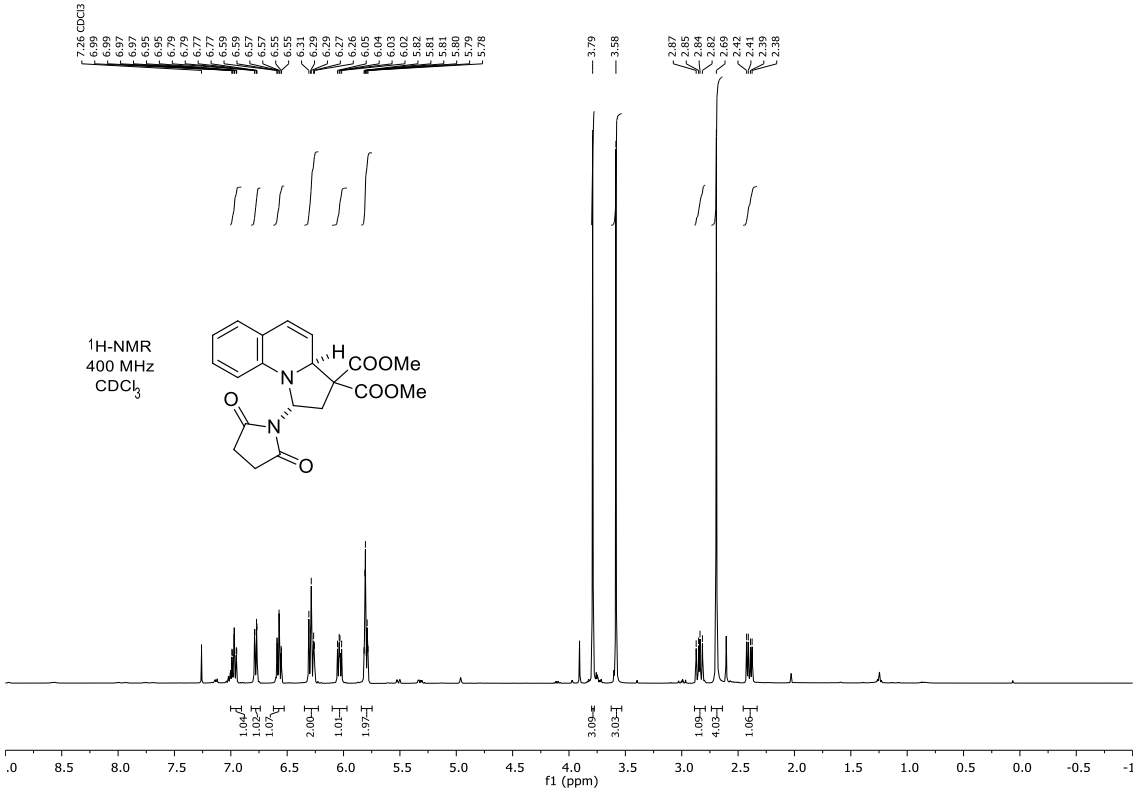

3000
2000
1000

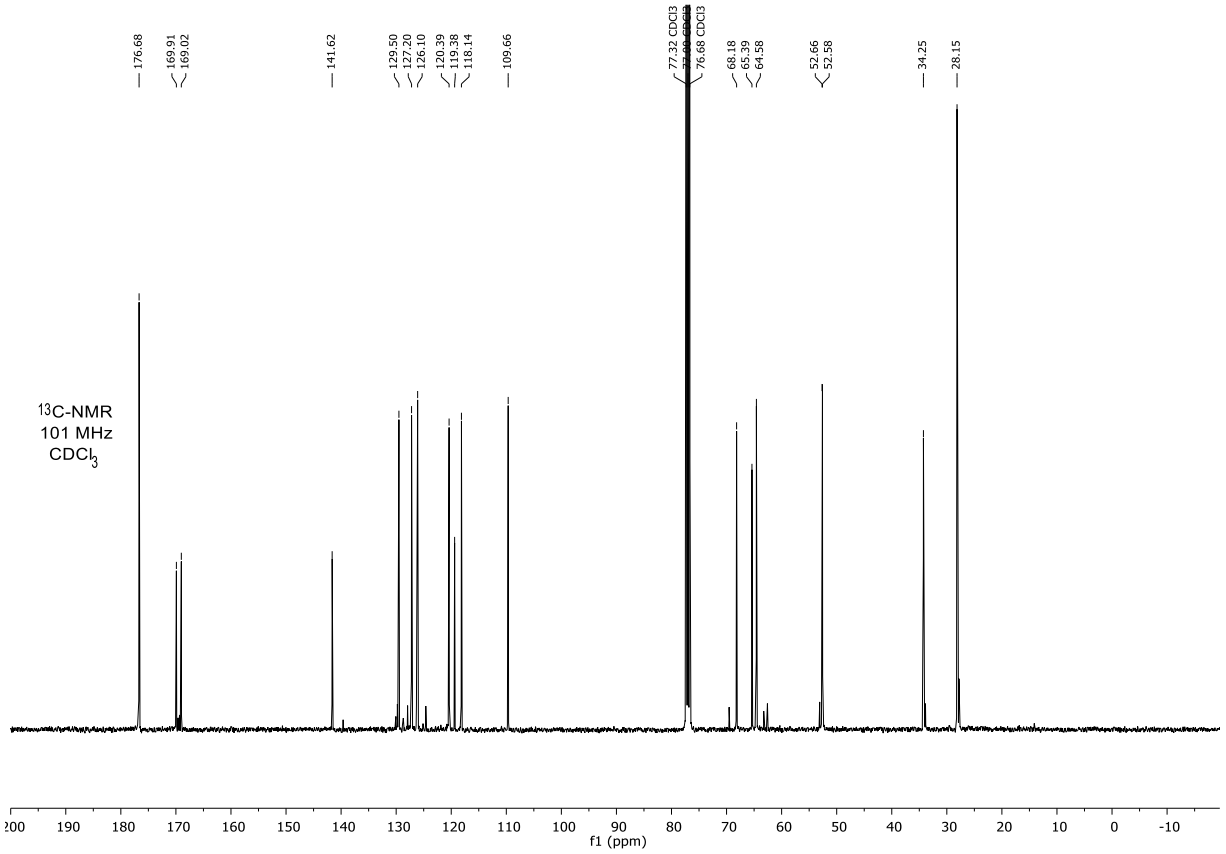
***anti*-Dimethyl 1-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (37).**

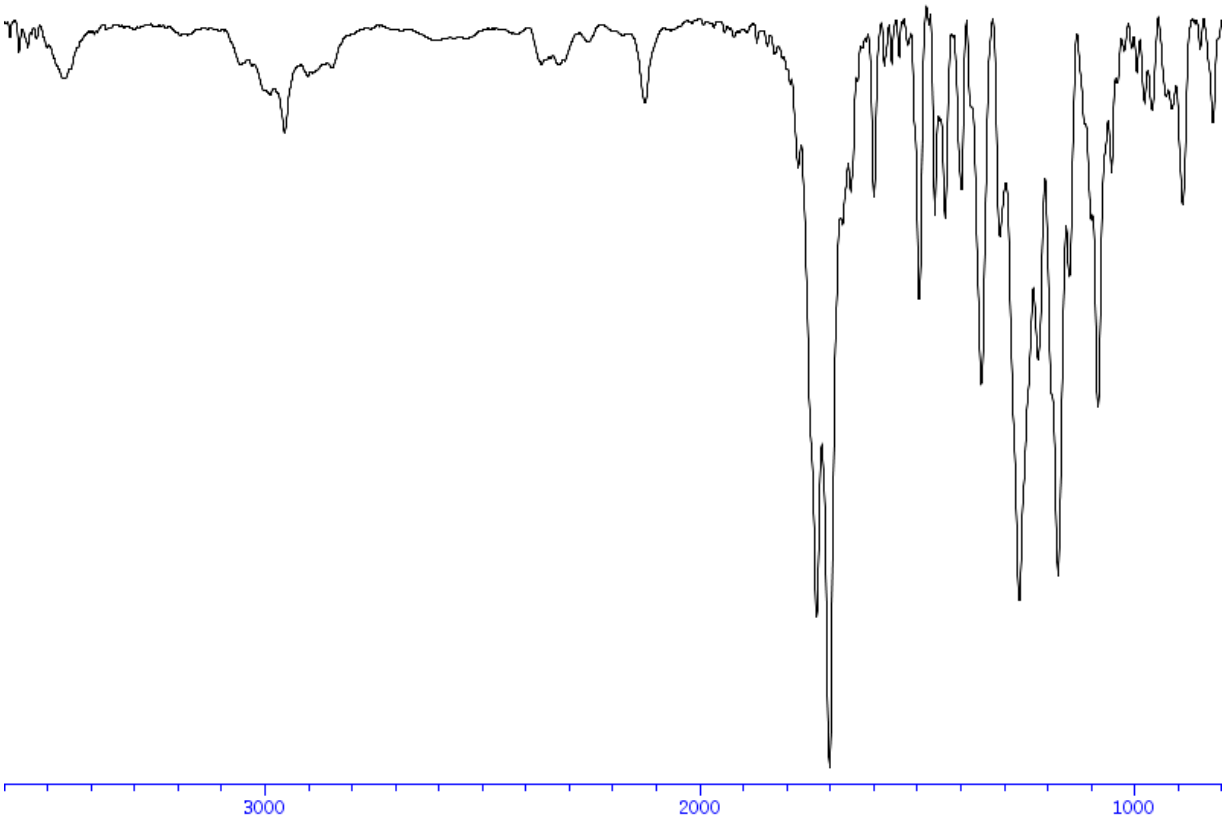




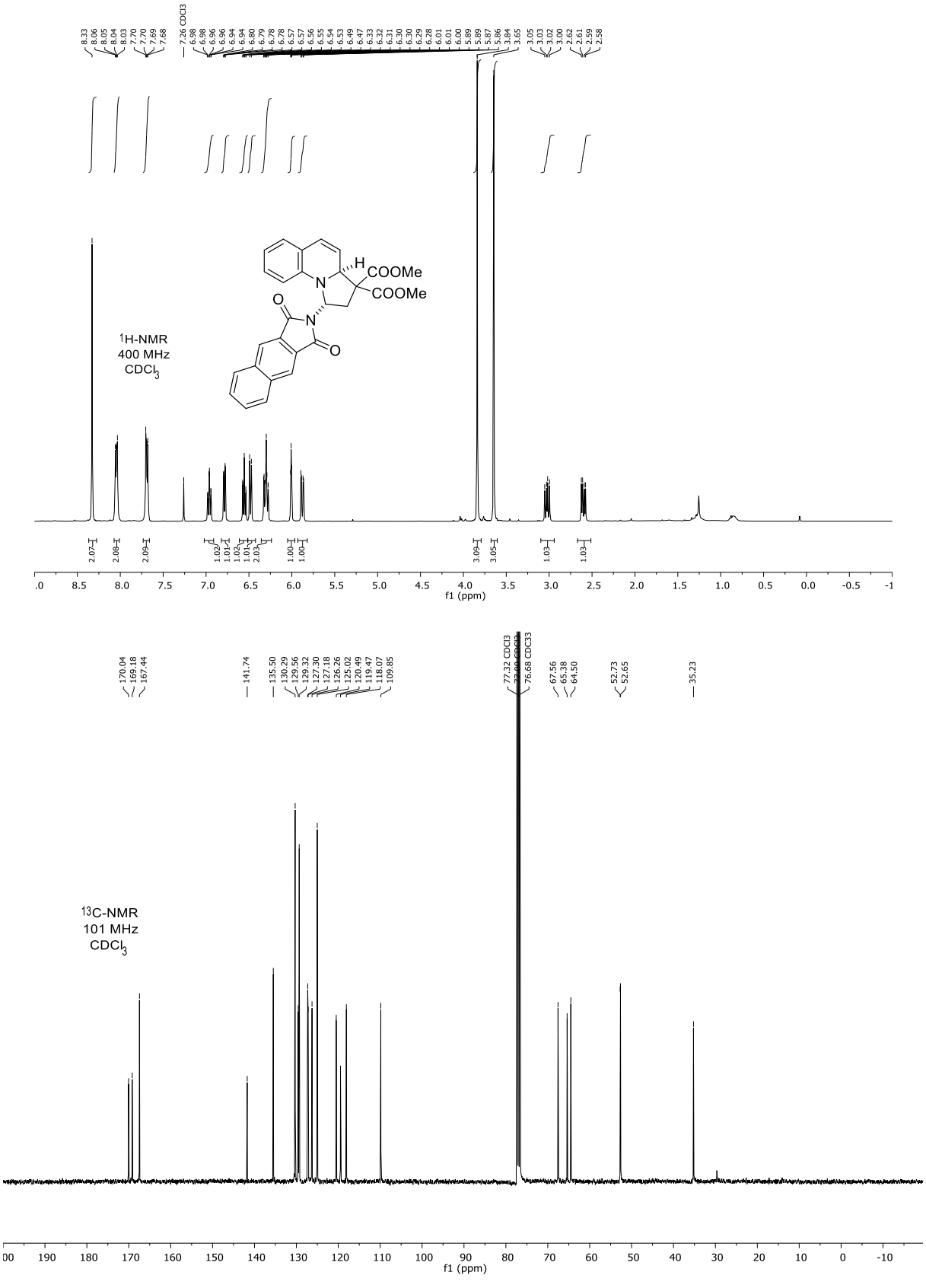
***anti*-Dimethyl 1-(2,5-dioxopyrrolidin-1-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (38).**

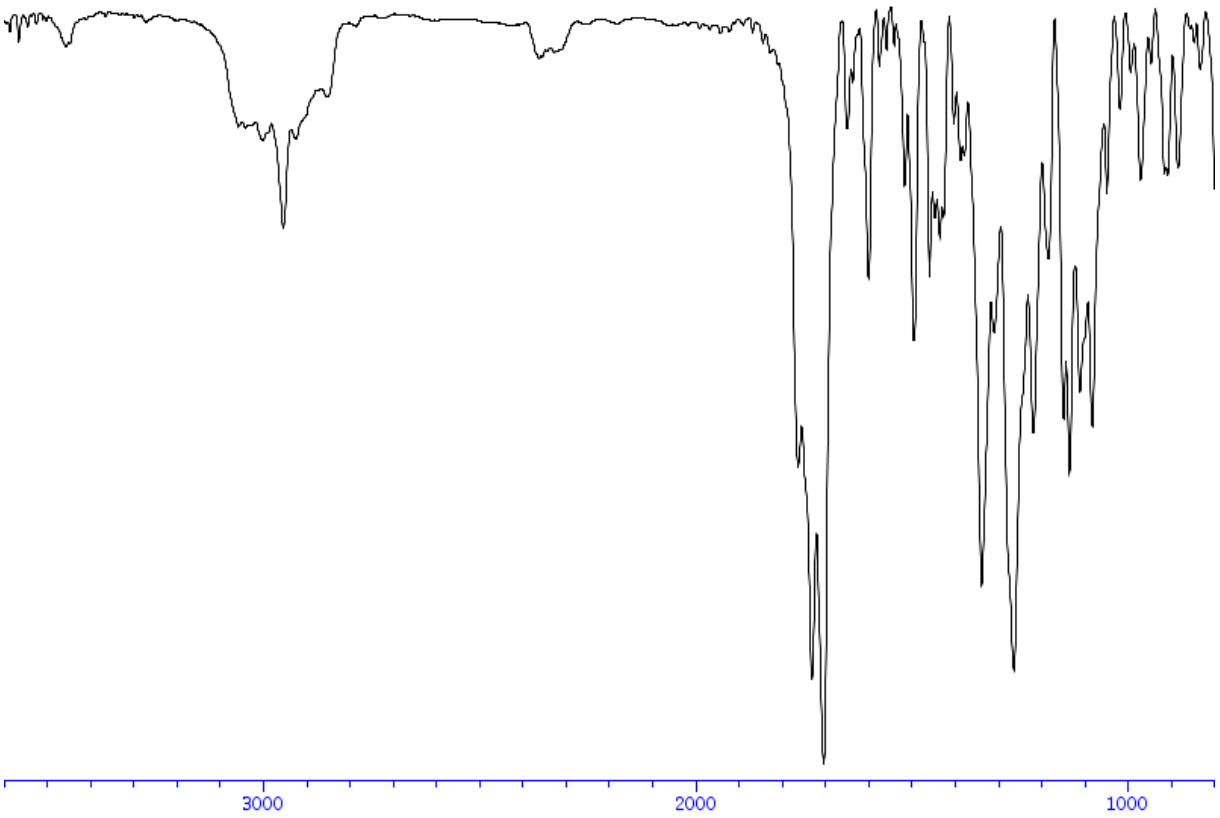



176.68
169.91
169.02
141.62
129.50
127.20
126.10
120.39
119.38
118.14
109.66
77.32 CDCl3
76.68 CDCl3
68.18
65.39
64.58
52.66
52.58
34.25
28.15
13C-NMR
101 MHz
CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

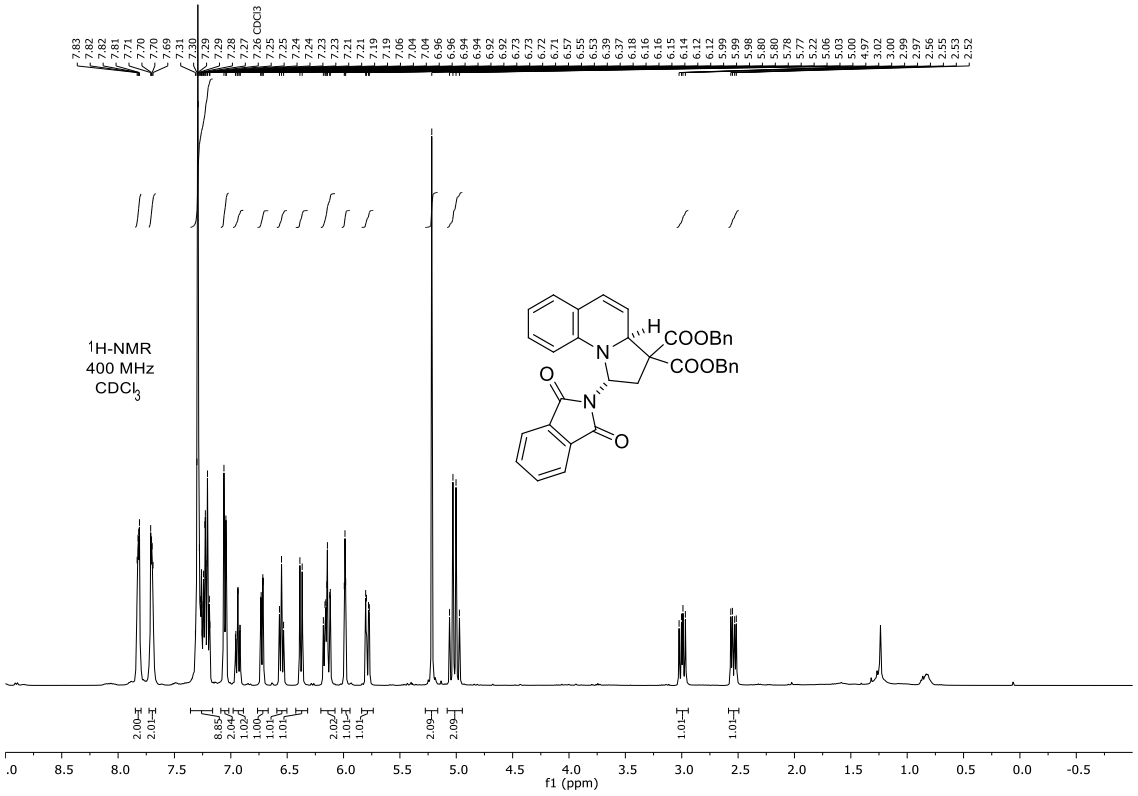

3000
2000
1000

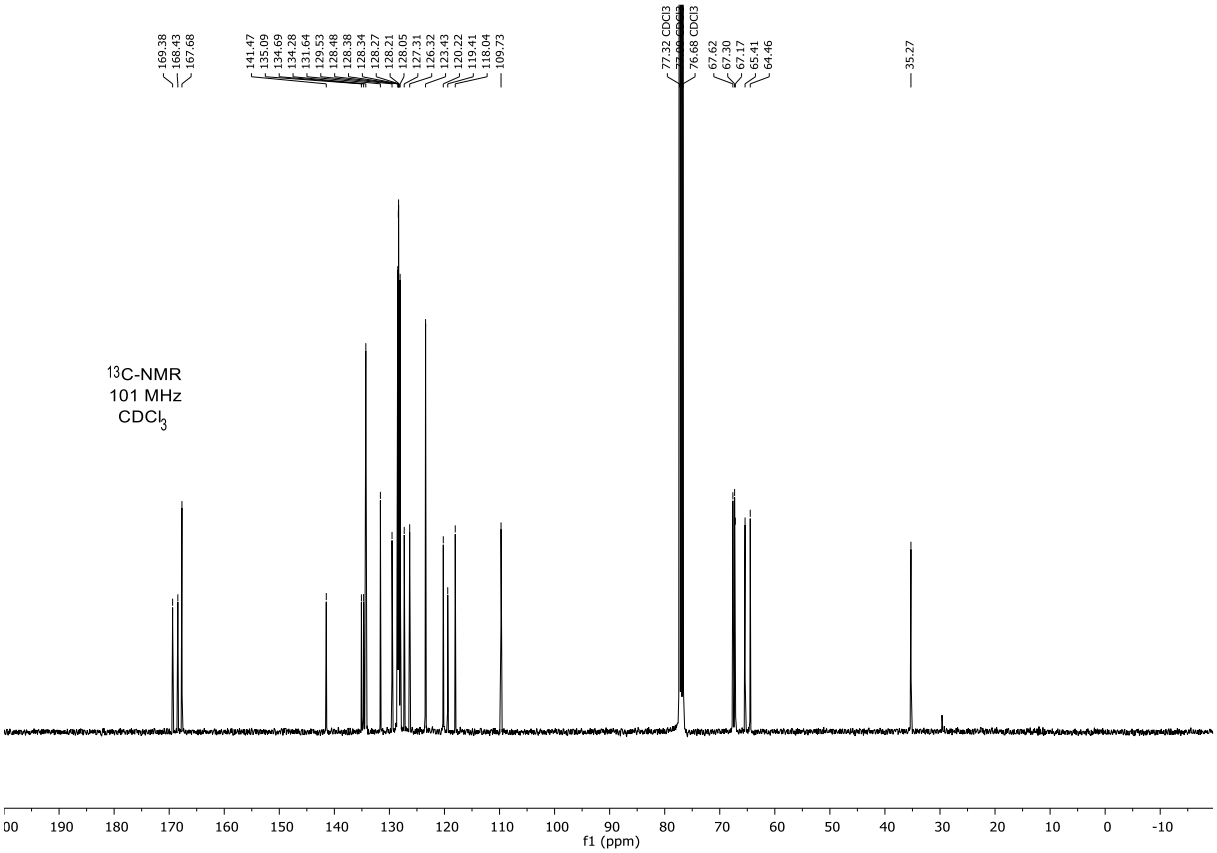
***anti*-Dimethyl 1-(1,3-dioxo-1H-benzo[f]isoindol-2(3H)-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (39).**

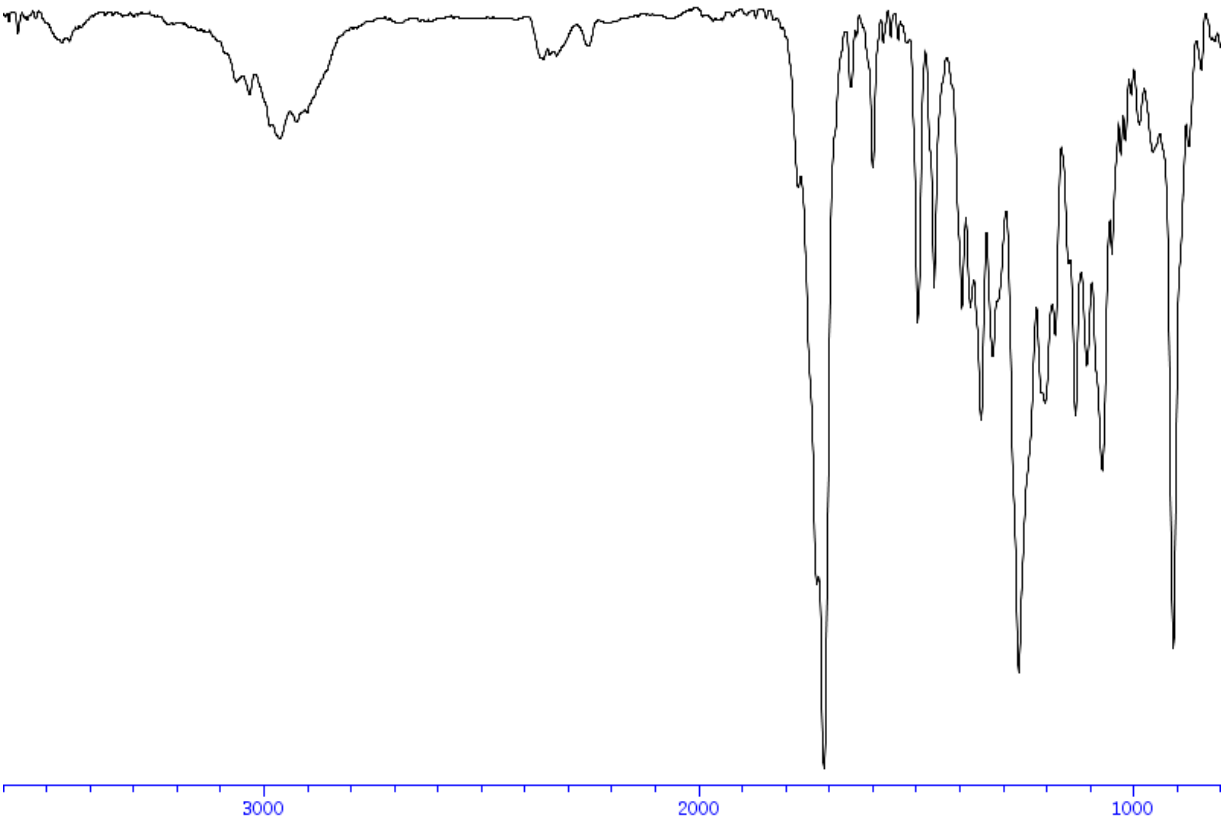




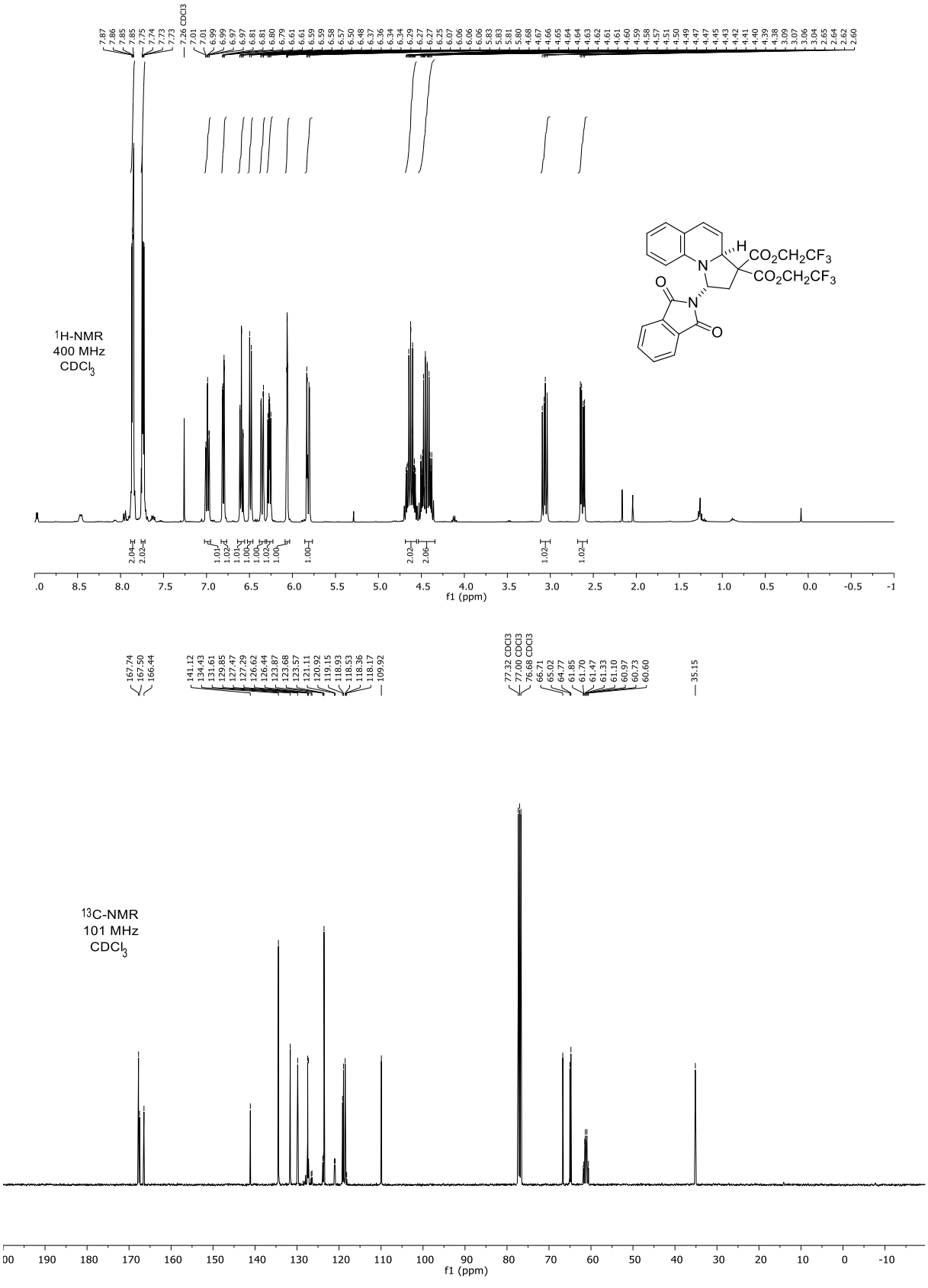
***anti*-Dibenzyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (40).**

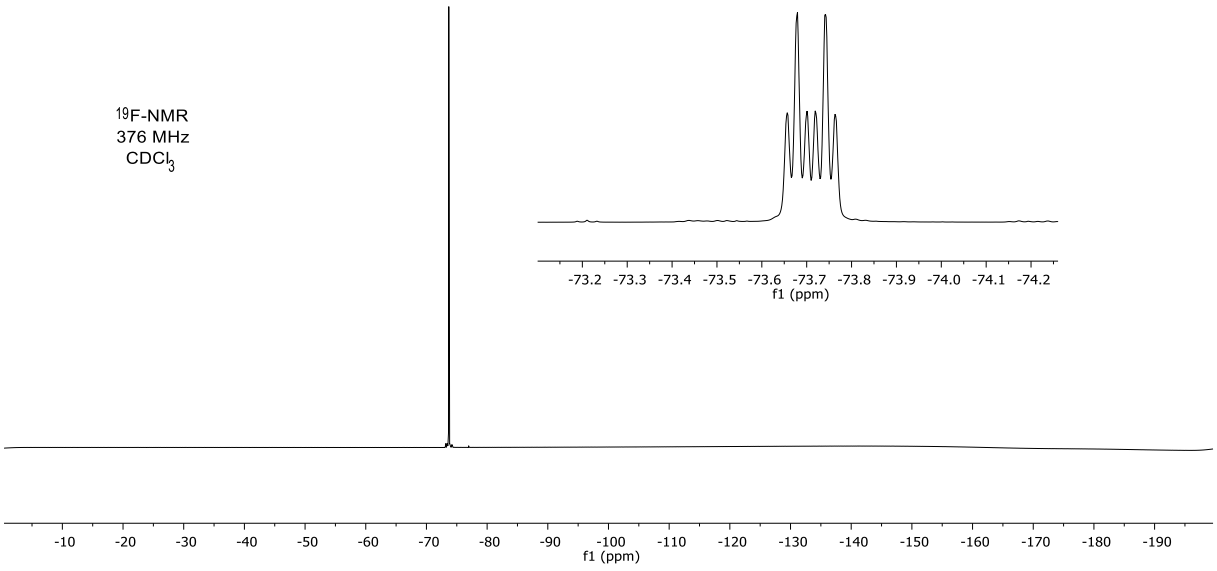


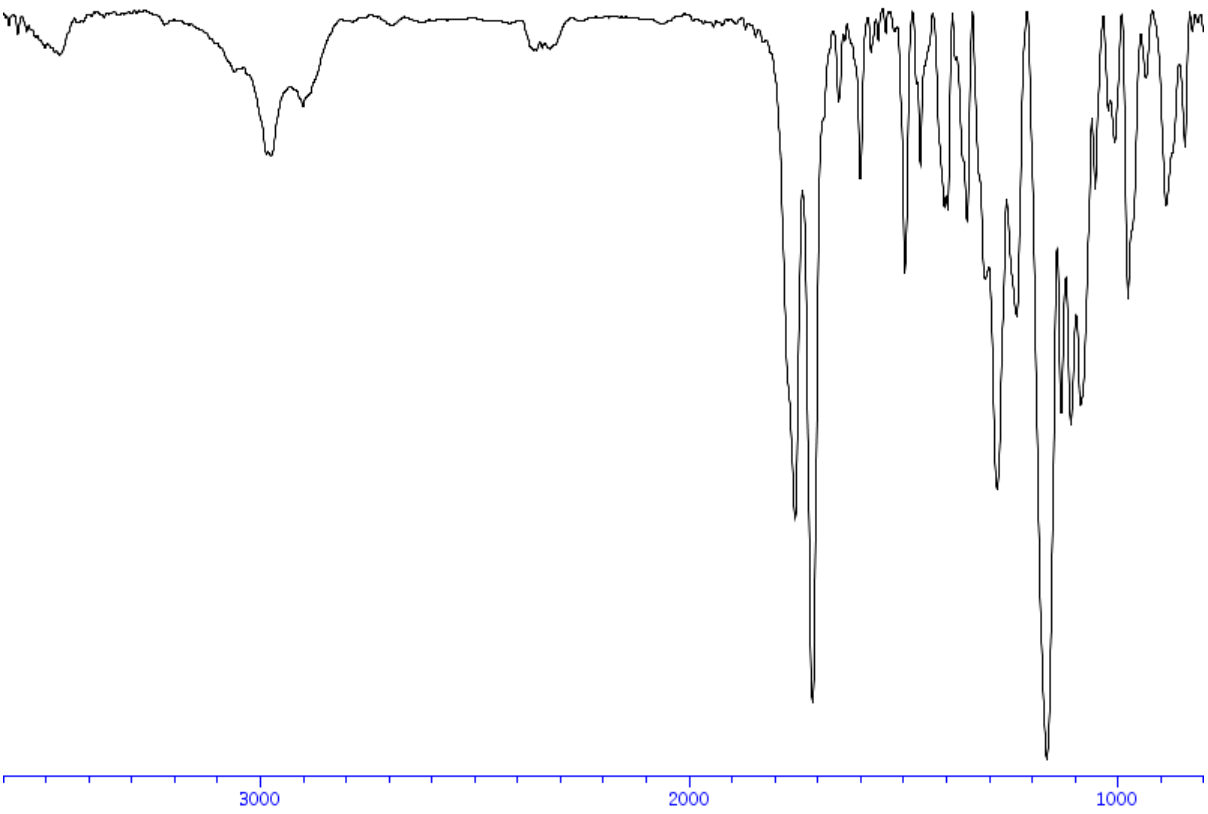

169.38
168.43
167.68
141.47
135.09
134.69
134.28
131.64
129.53
128.48
128.38
128.34
128.27
128.21
127.05
127.31
126.32
123.43
120.22
119.41
118.04
109.73
77.32 CDCl3
76.68 CDCl3
67.62
67.30
67.17
65.41
64.46
35.27
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

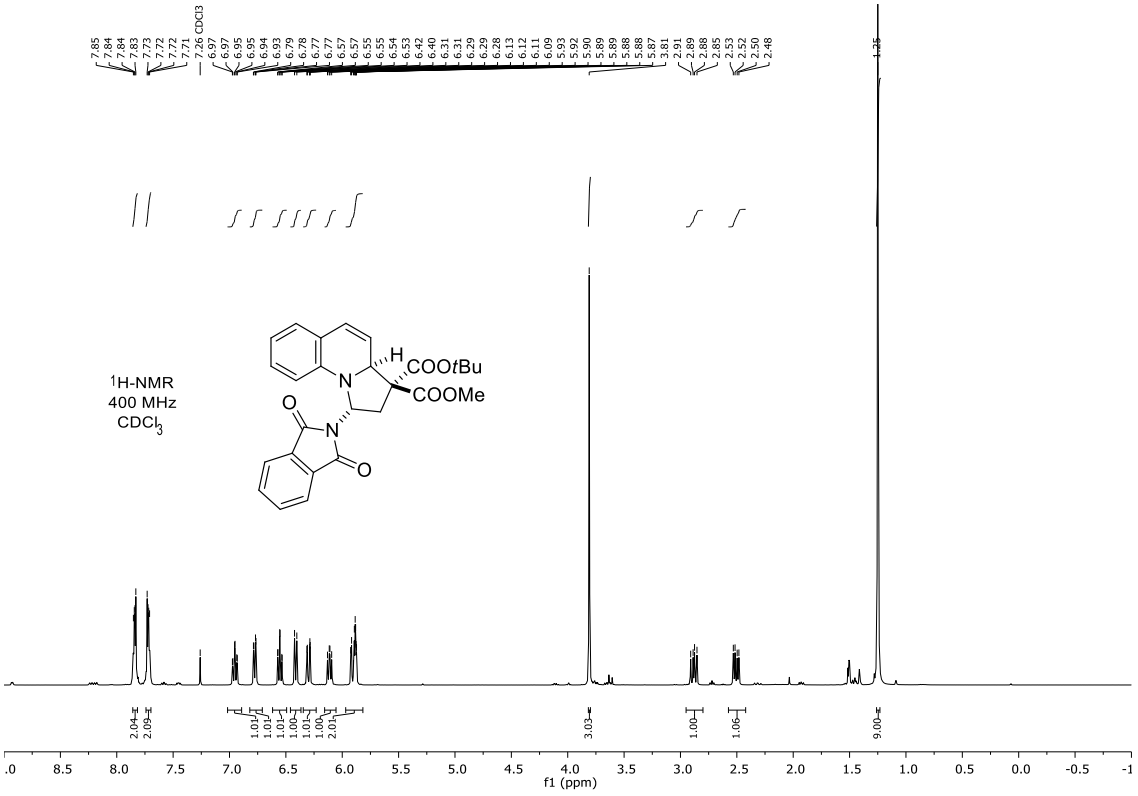
***anti-bis*(2,2,2-Trifluoroethyl) 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (41).**

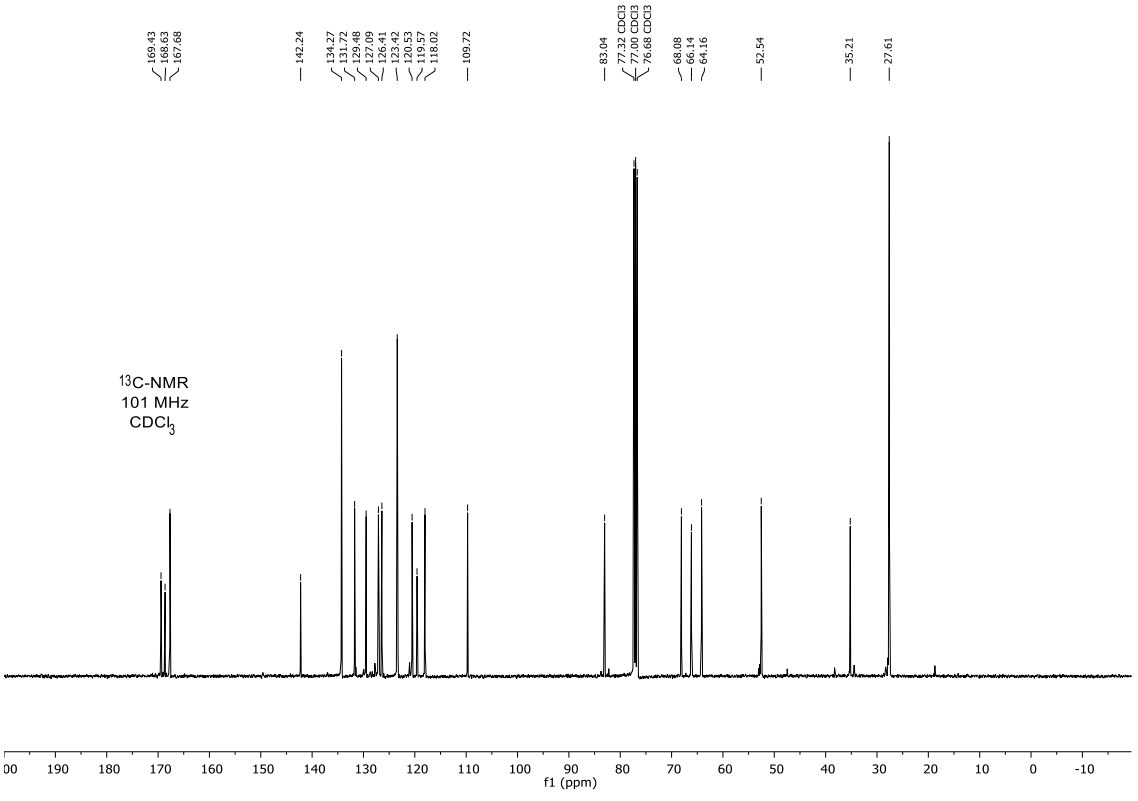


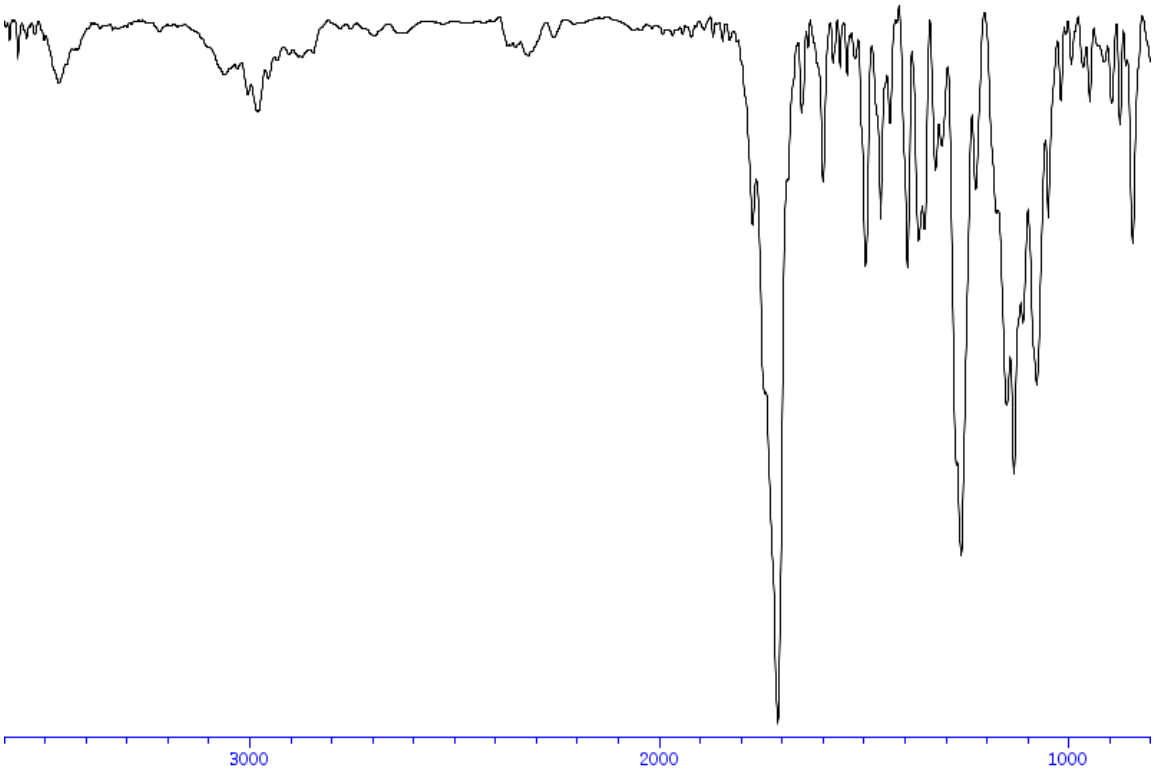

19F-NMR
376 MHz
CDCl3
-73.2 -73.3 -73.4 -73.5 -73.6 -73.7 -73.8 -73.9 -74.0 -74.1 -74.2
f1 (ppm)
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


3000
2000
1000

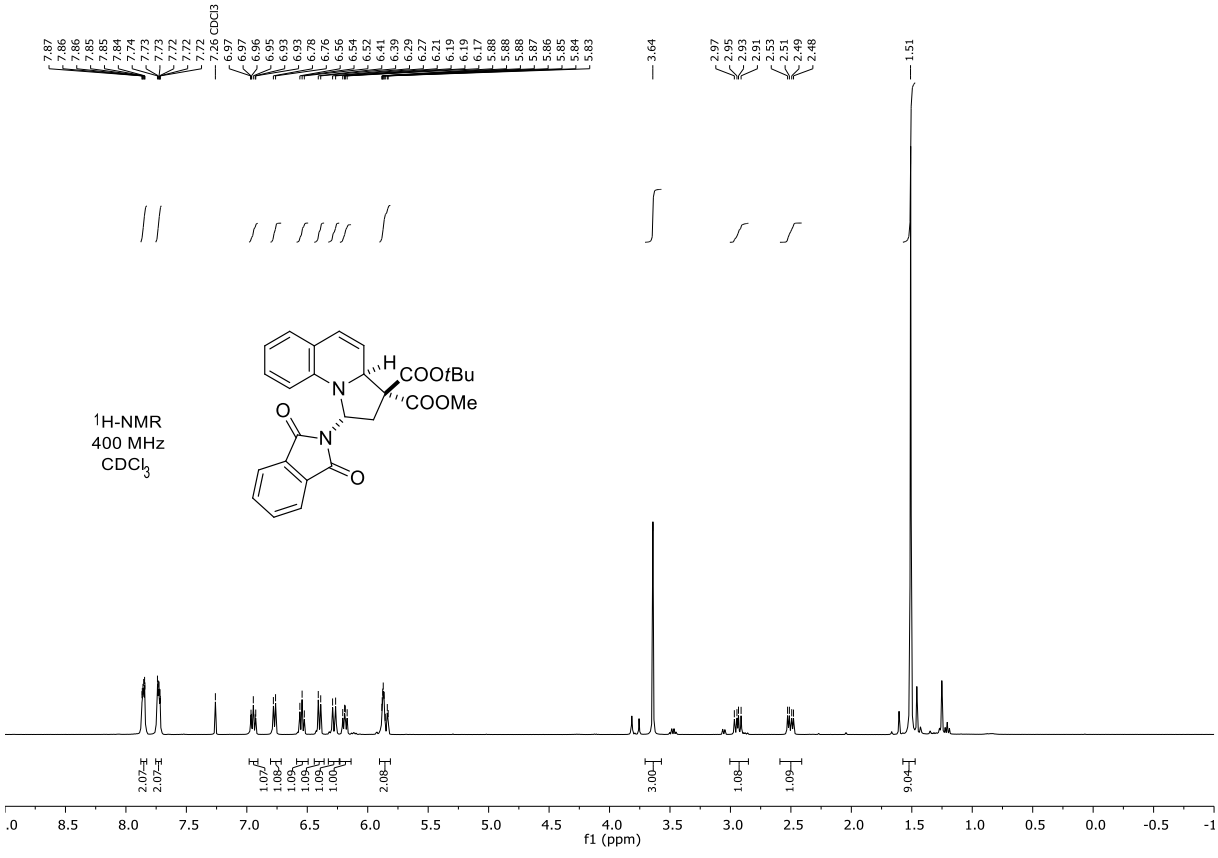
***(1R,3S,3aR)*-3-*tert*-Butyl 3-methyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (42a).**

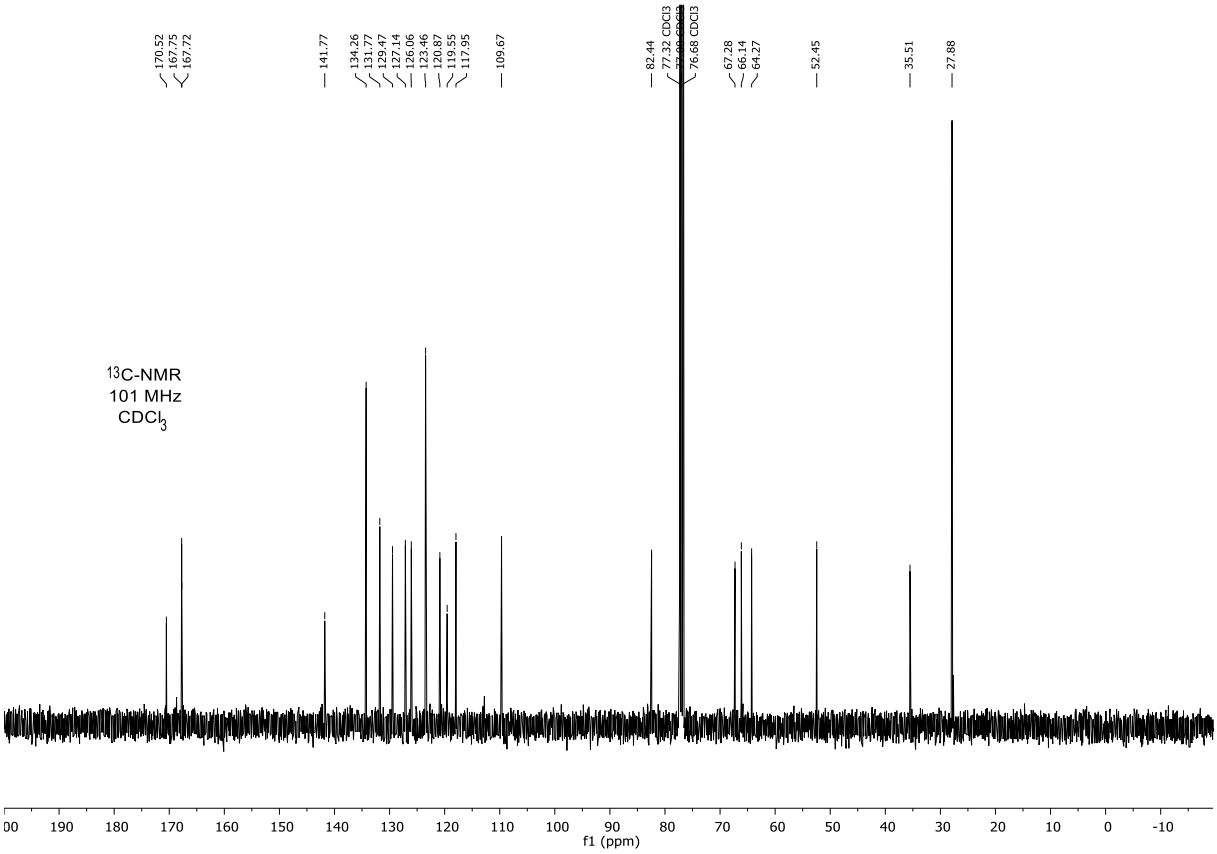


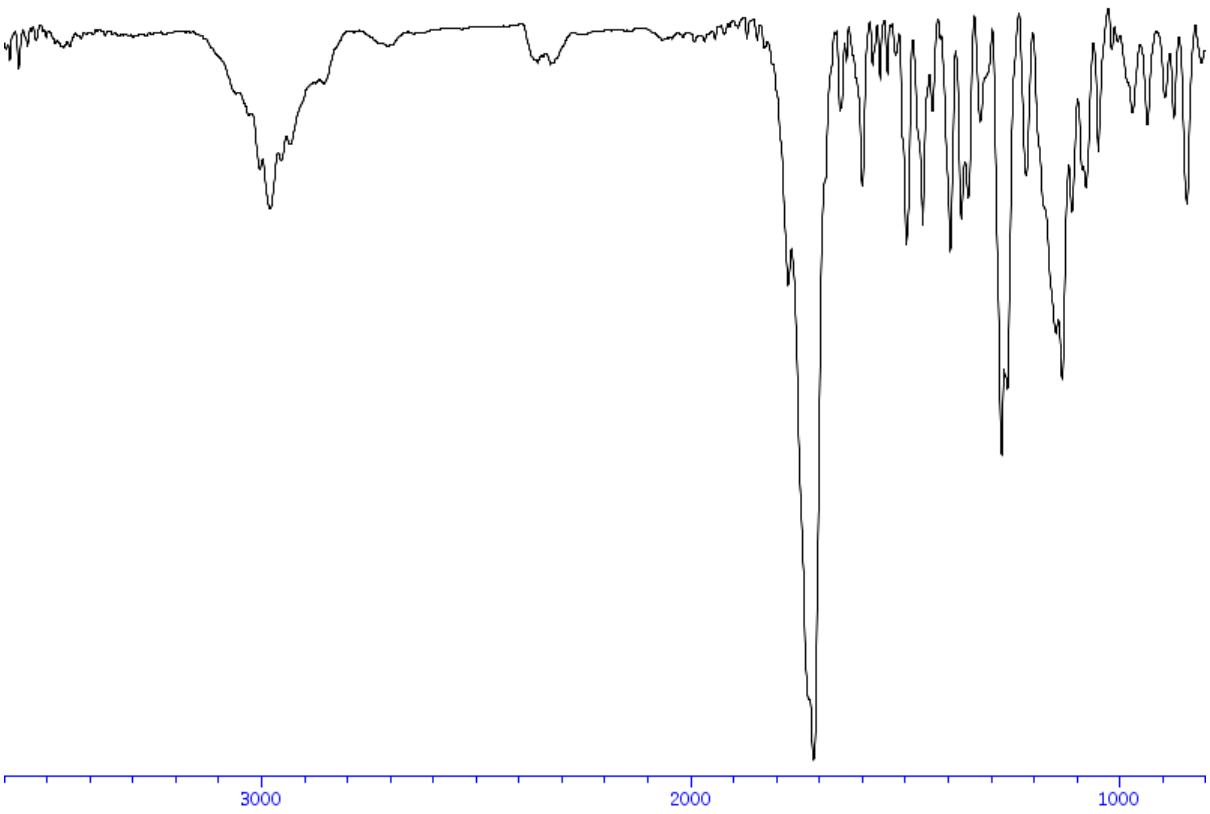




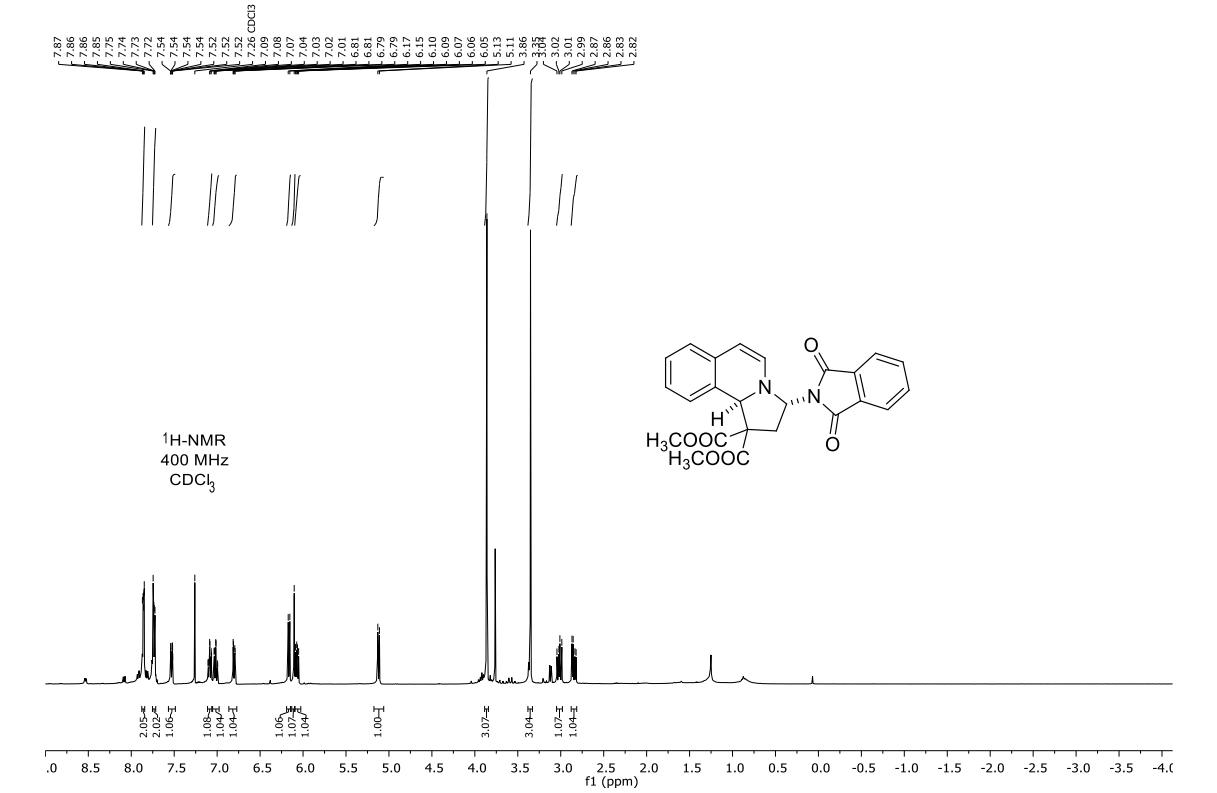
(1*R*,3*R*,3a*R*)-3-*tert*-Butyl 3-methyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**42b**).

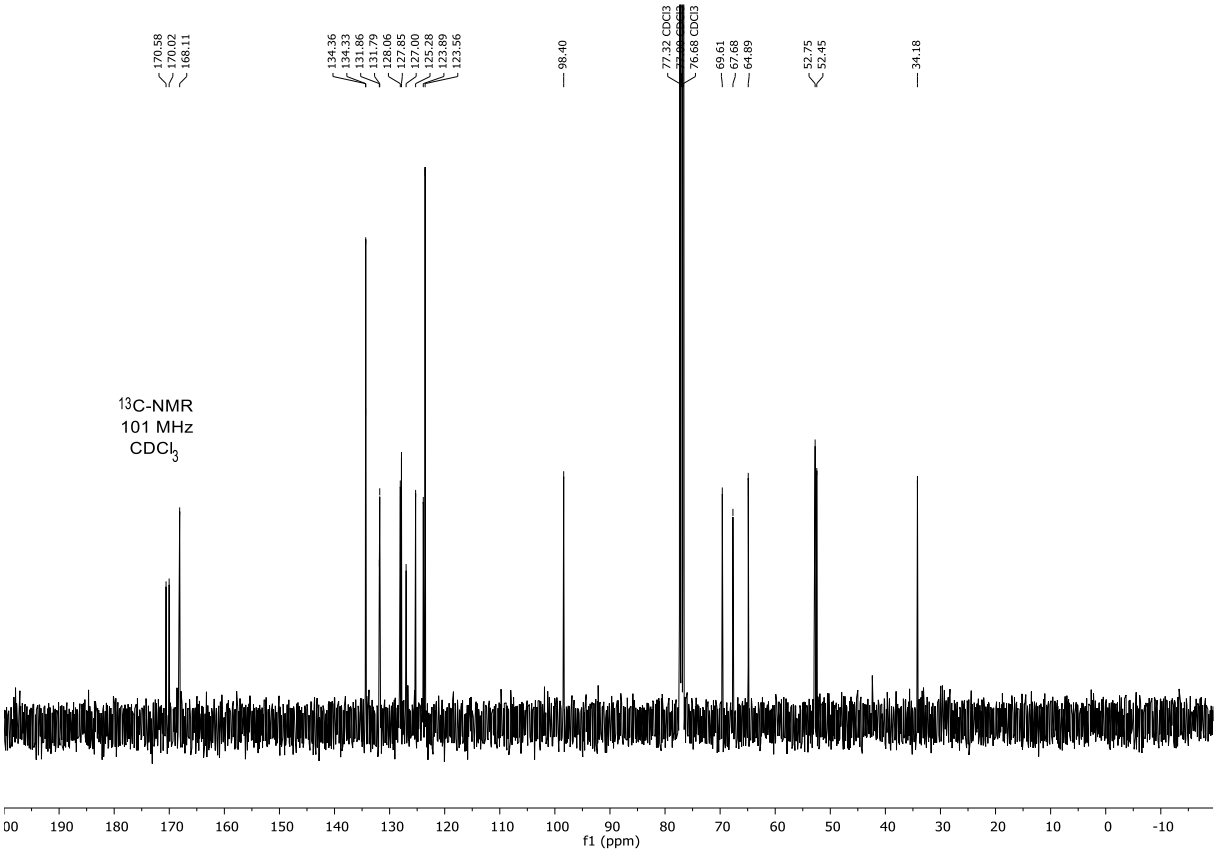


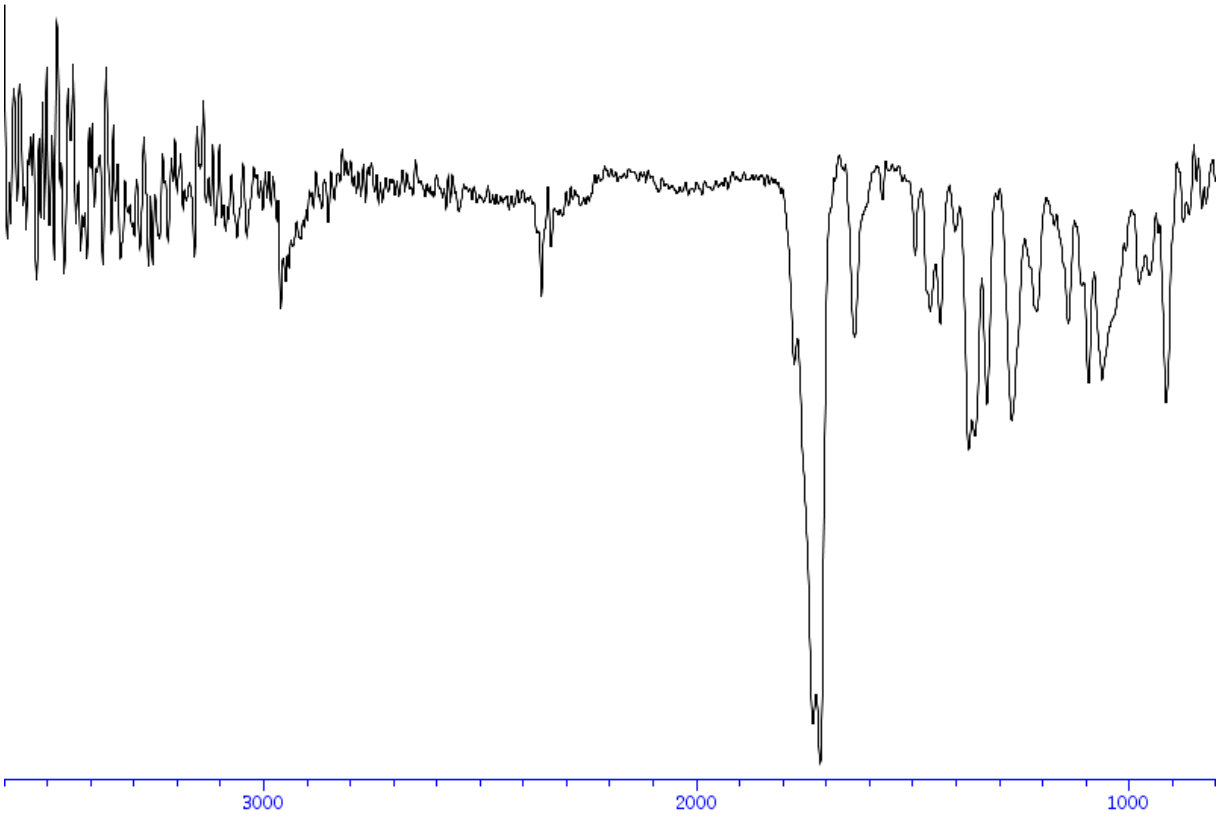

170.52
167.75
167.72
141.77
134.26
131.77
129.47
127.14
126.06
123.46
120.87
119.55
117.95
109.67
82.44
77.32 CDCl3
76.68 CDCl3
67.28
66.14
64.27
52.45
35.51
27.88
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

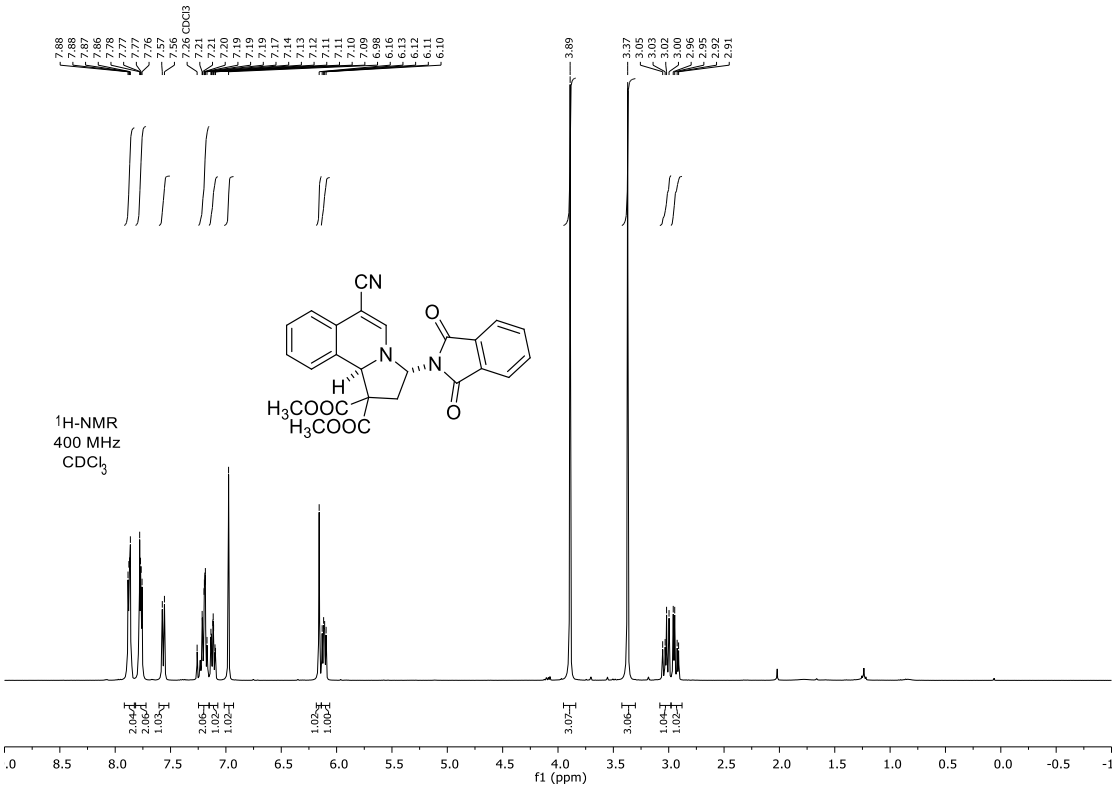
***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydropyrrolo[2,1-a]isoquinoline-1,1(10b*H*)-dicarboxylate (43).**

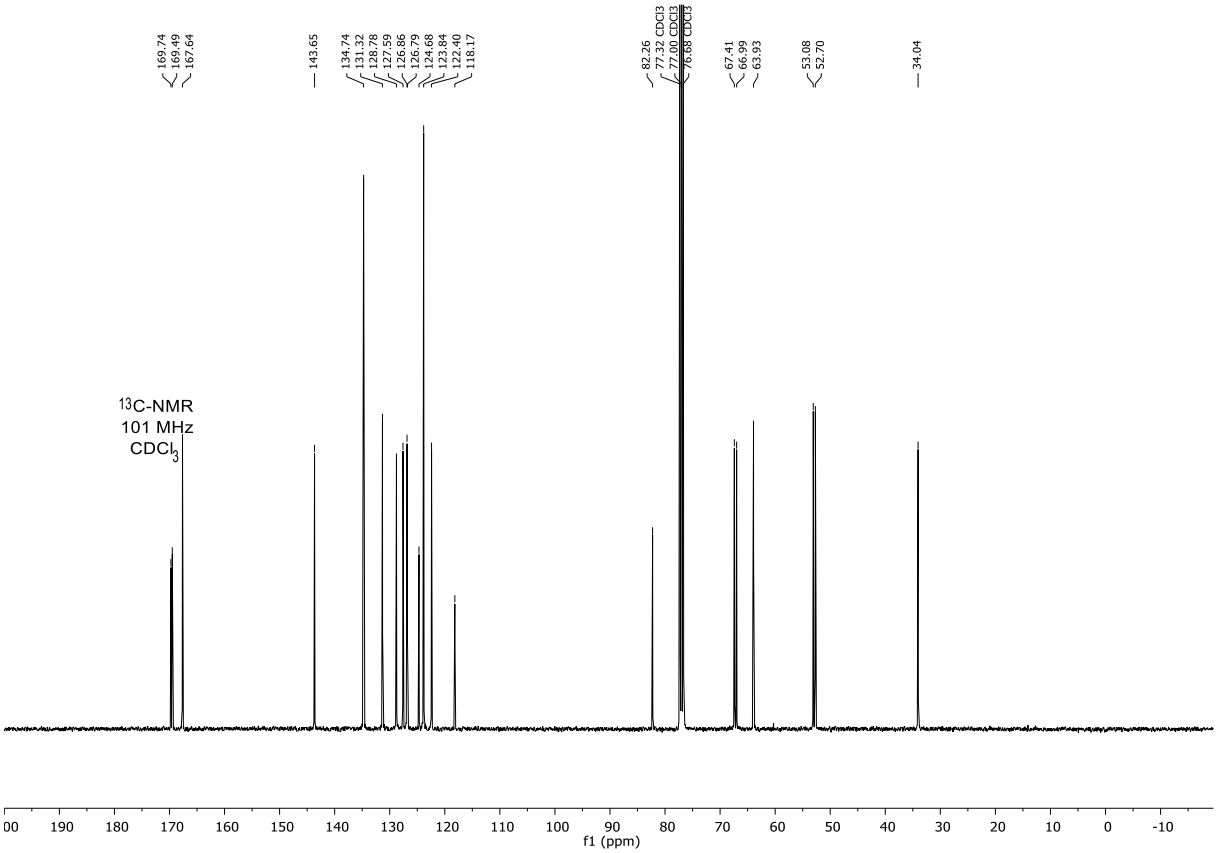


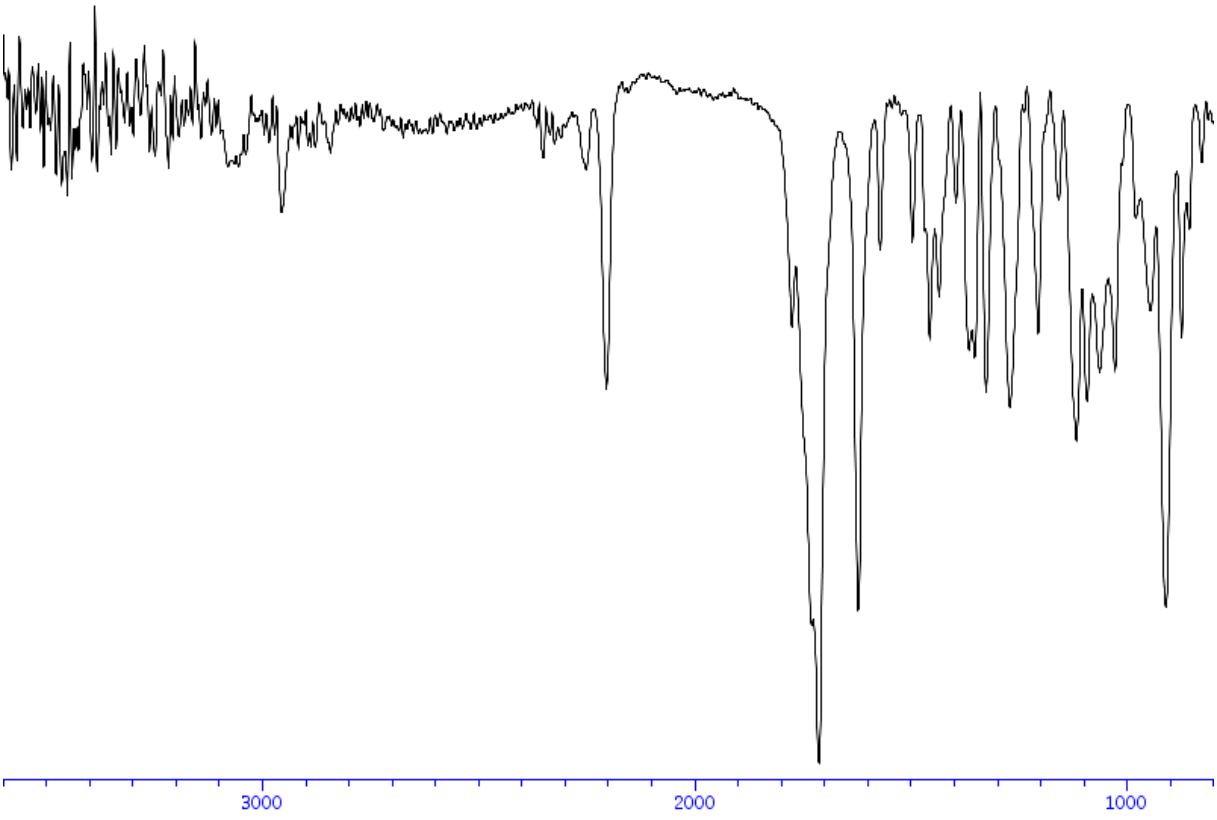




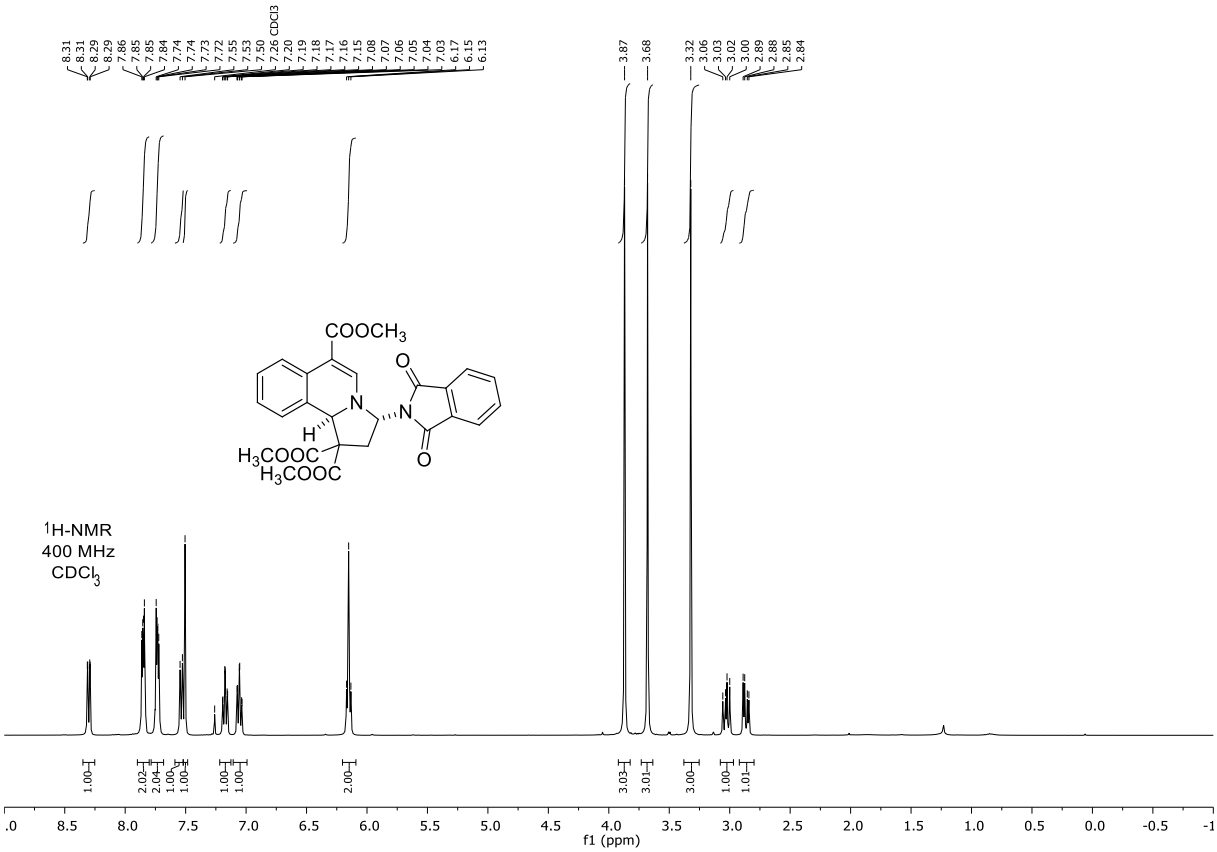
***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydropyrrolo[2,1-a]isoquinoline-1,1(10b*H*)-dicarboxylate (44).**

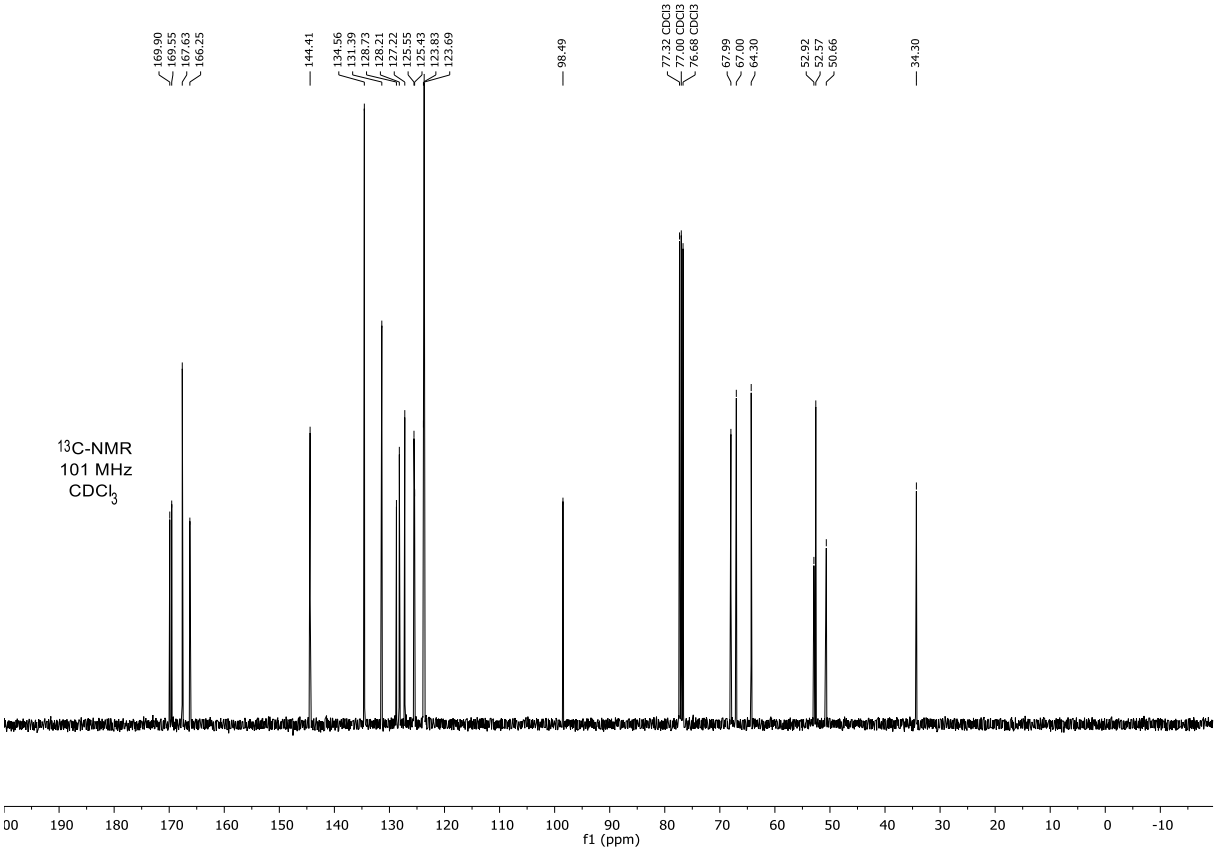


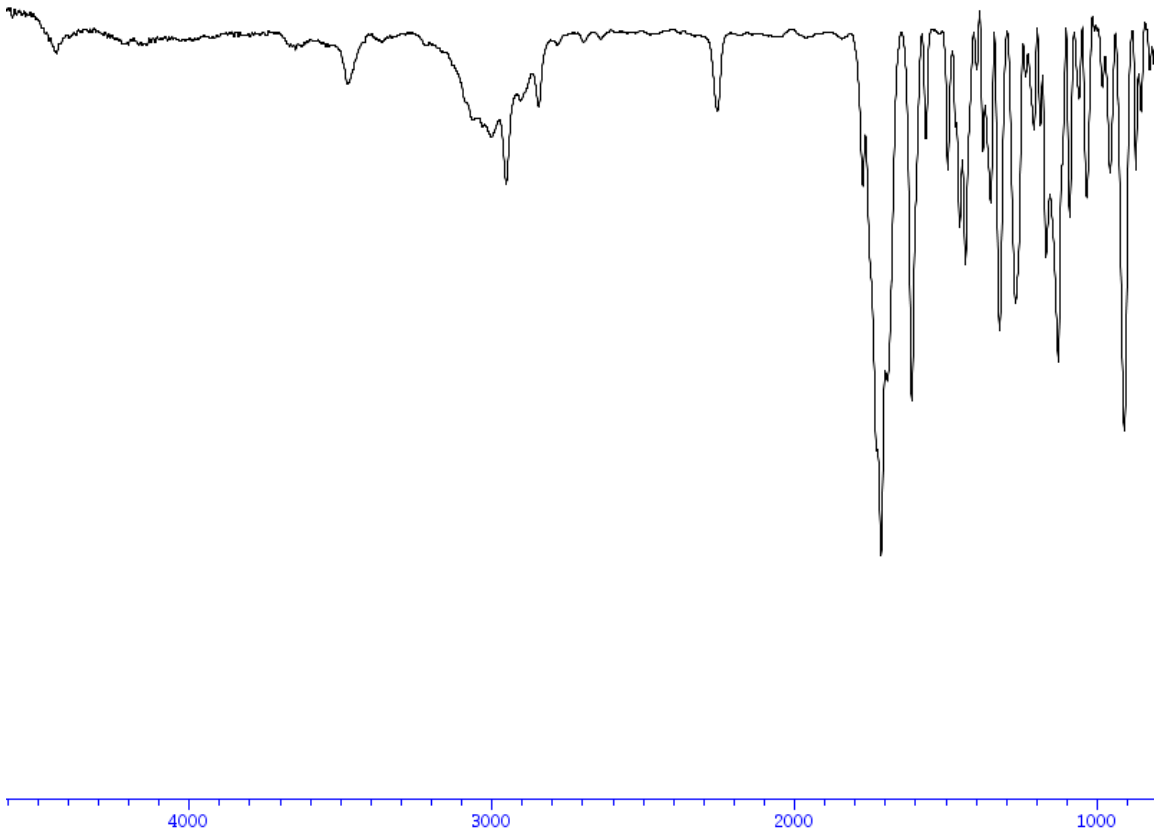

169.74
169.49
167.64
143.65
134.74
131.32
128.78
127.59
126.86
126.79
124.68
123.84
122.40
118.17
82.26
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
67.41
66.99
63.93
53.08
52.70
34.04
13C-NMR
101 MHz
CDCl3
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


3000
2000
1000

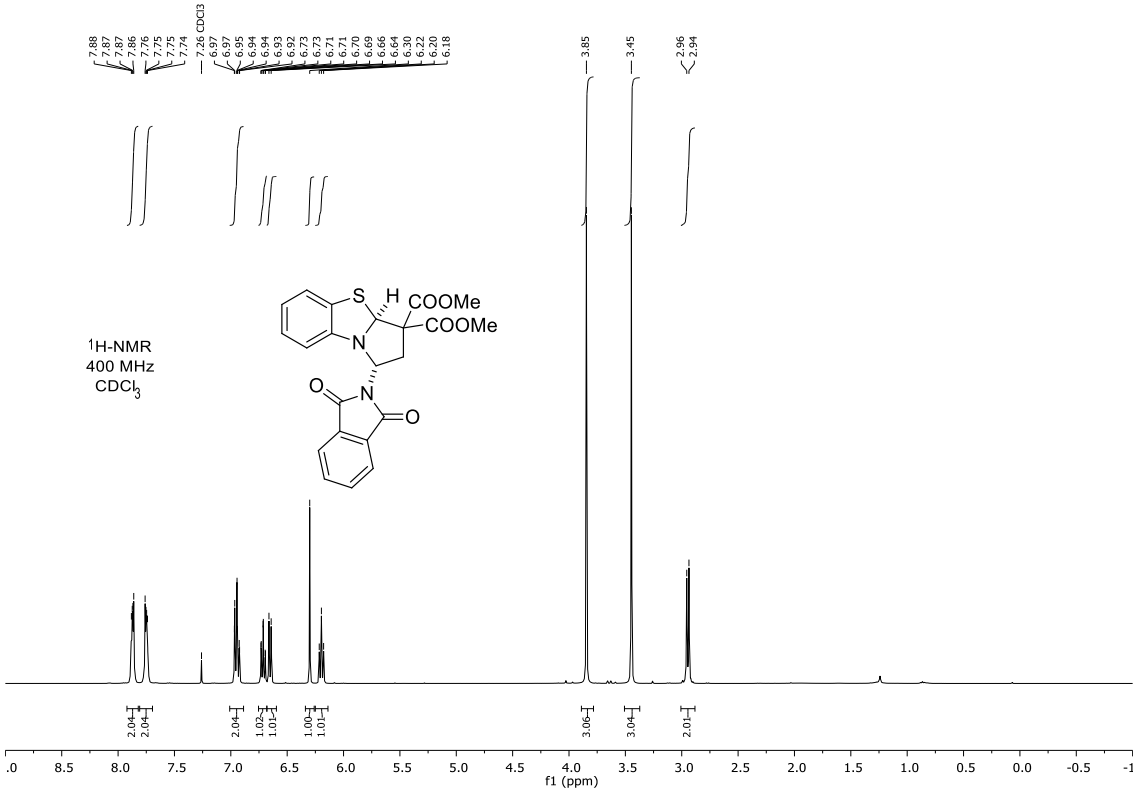
***anti*-Trimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydropyrrolo[2,1-a]isoquinoline-1,1,6(10b*H*)-tricarboxylate** (**45**).

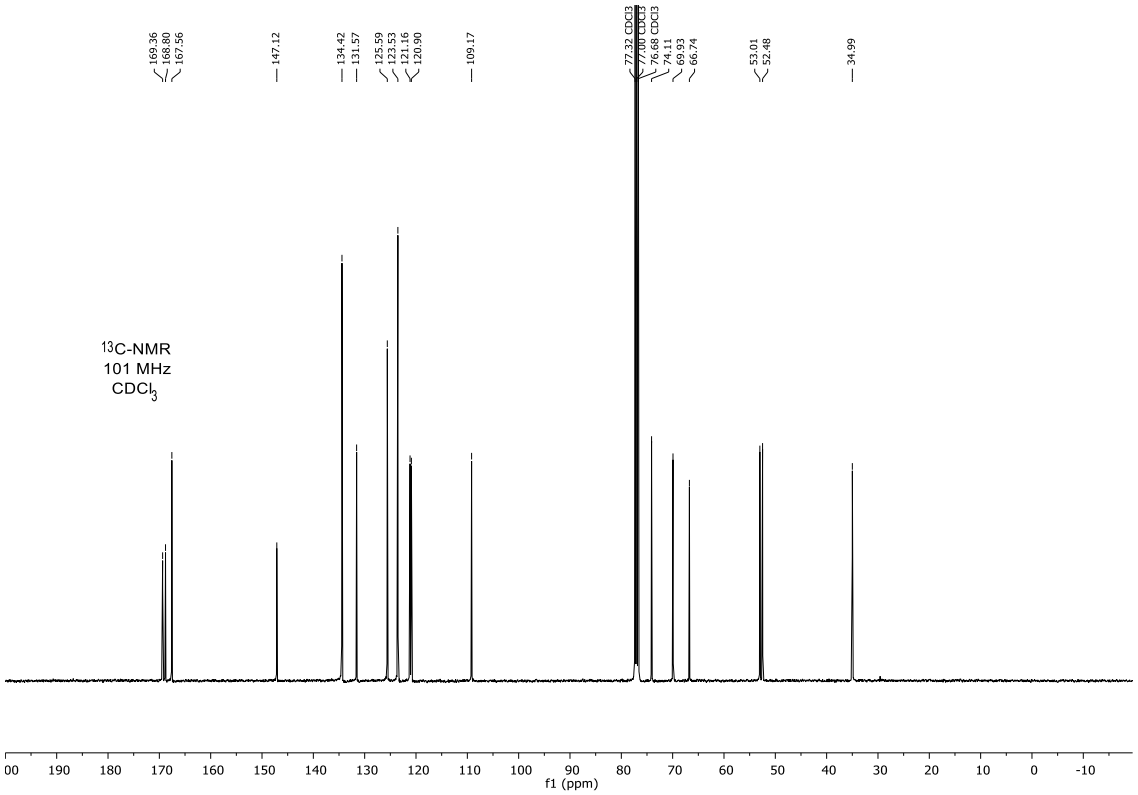


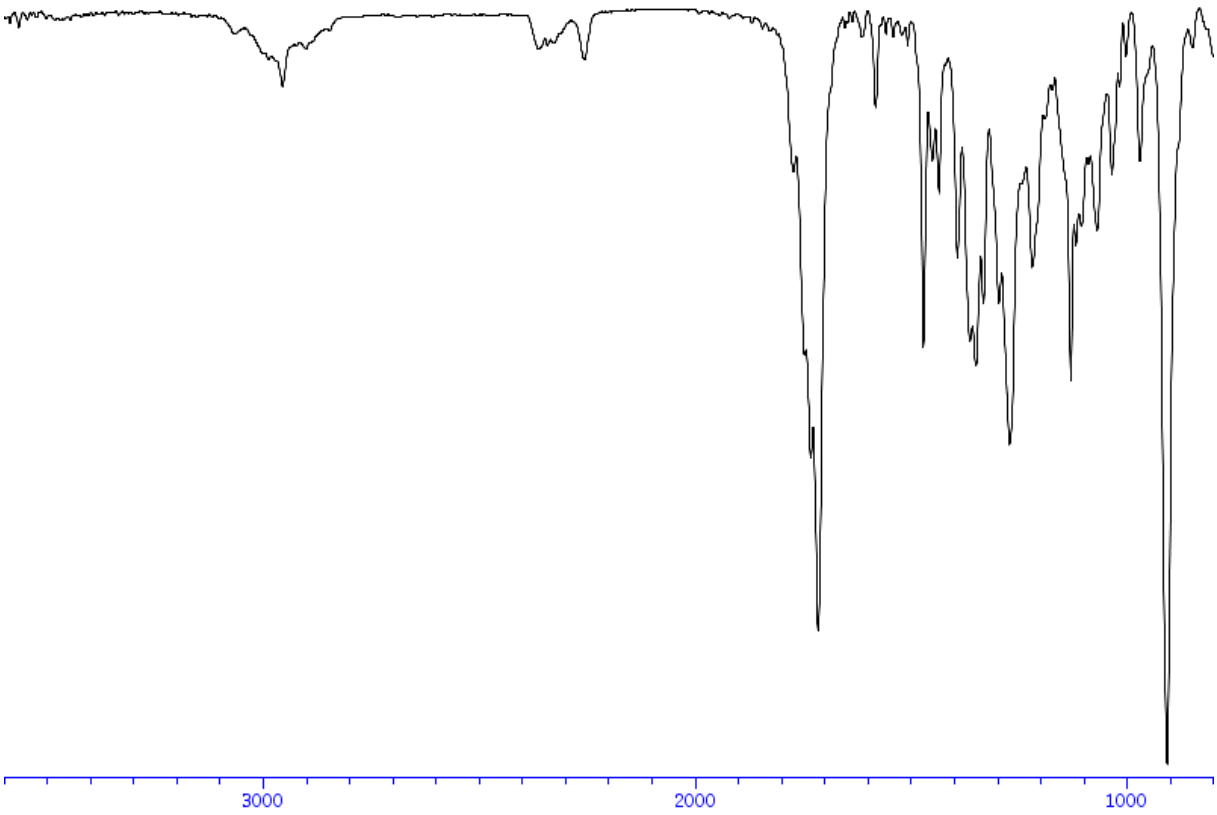




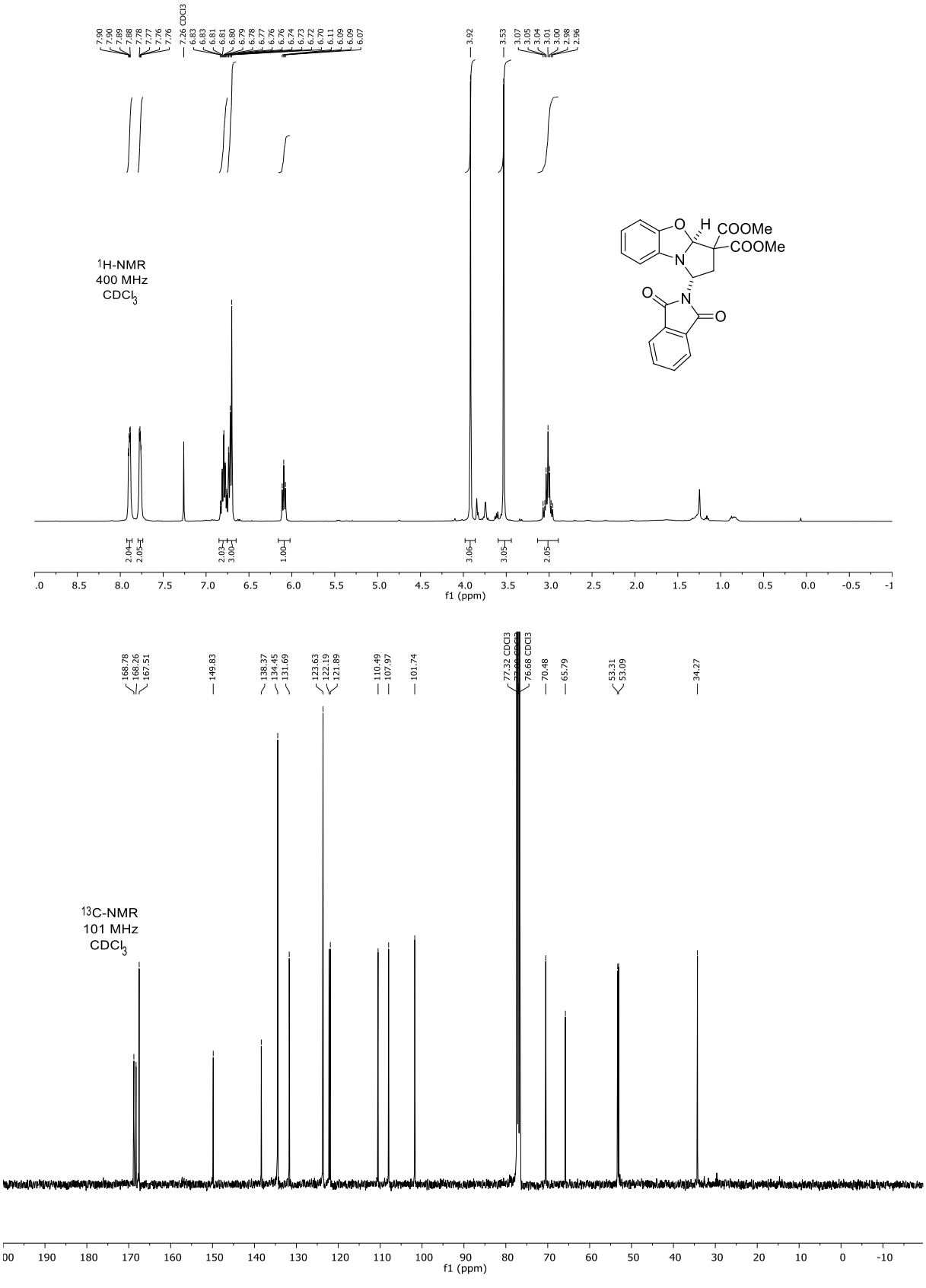
***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydrobenzo[d]pyrrolo[2,1-b]thiazole-3,3(3a*H*)-dicarboxylate** (**46**).

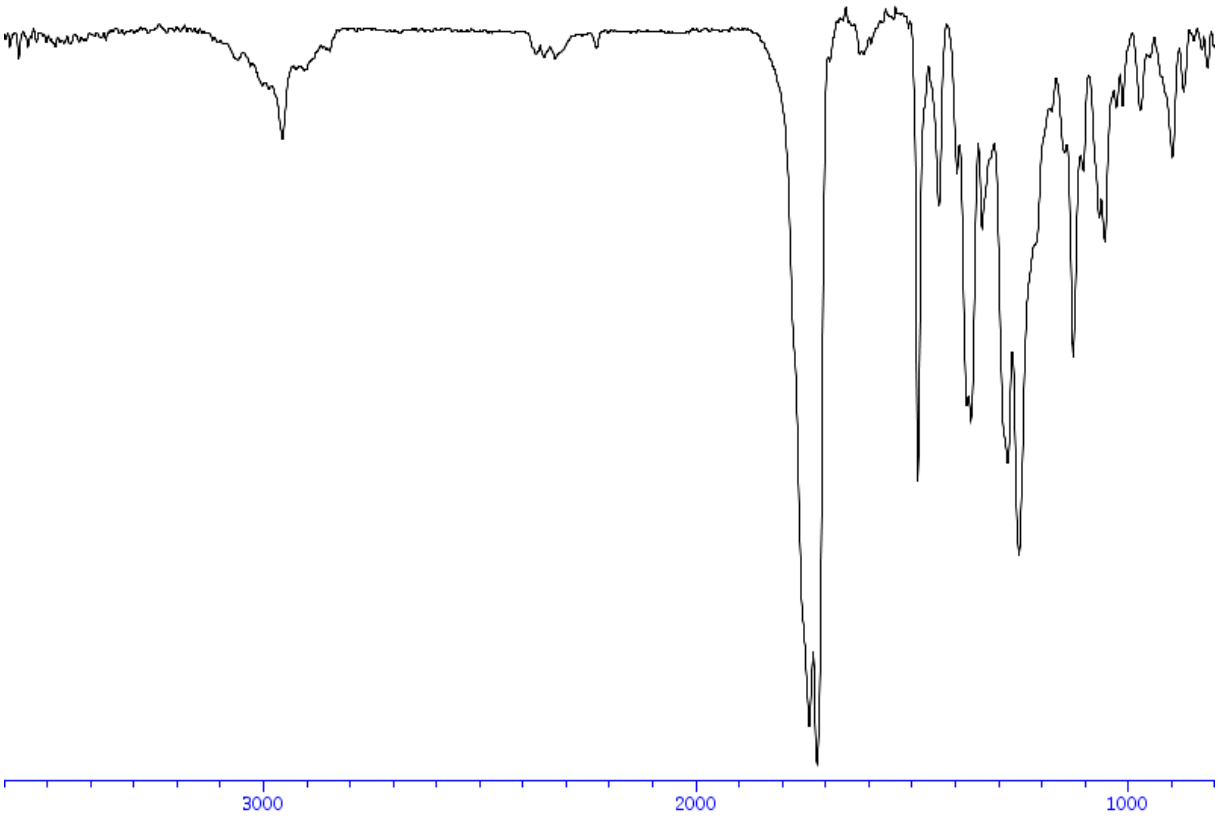



169.36
168.80
167.56
147.12
134.42
131.57
125.59
123.53
121.16
120.90
109.17
77.23 CDCl3
77.00 CDCl3
76.68 CDCl3
74.11
69.93
66.74
53.01
52.48
34.99
13C-NMR
101 MHz
CDCl3
f1 (ppm)

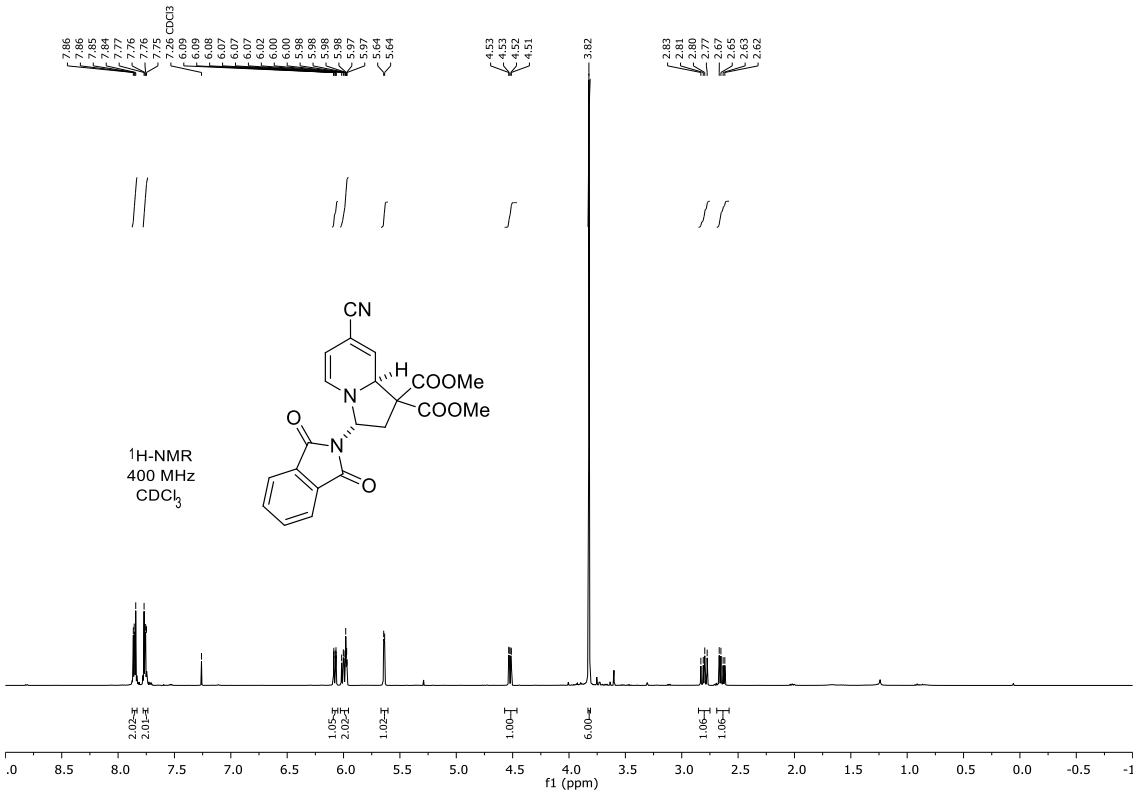

3000
2000
1000

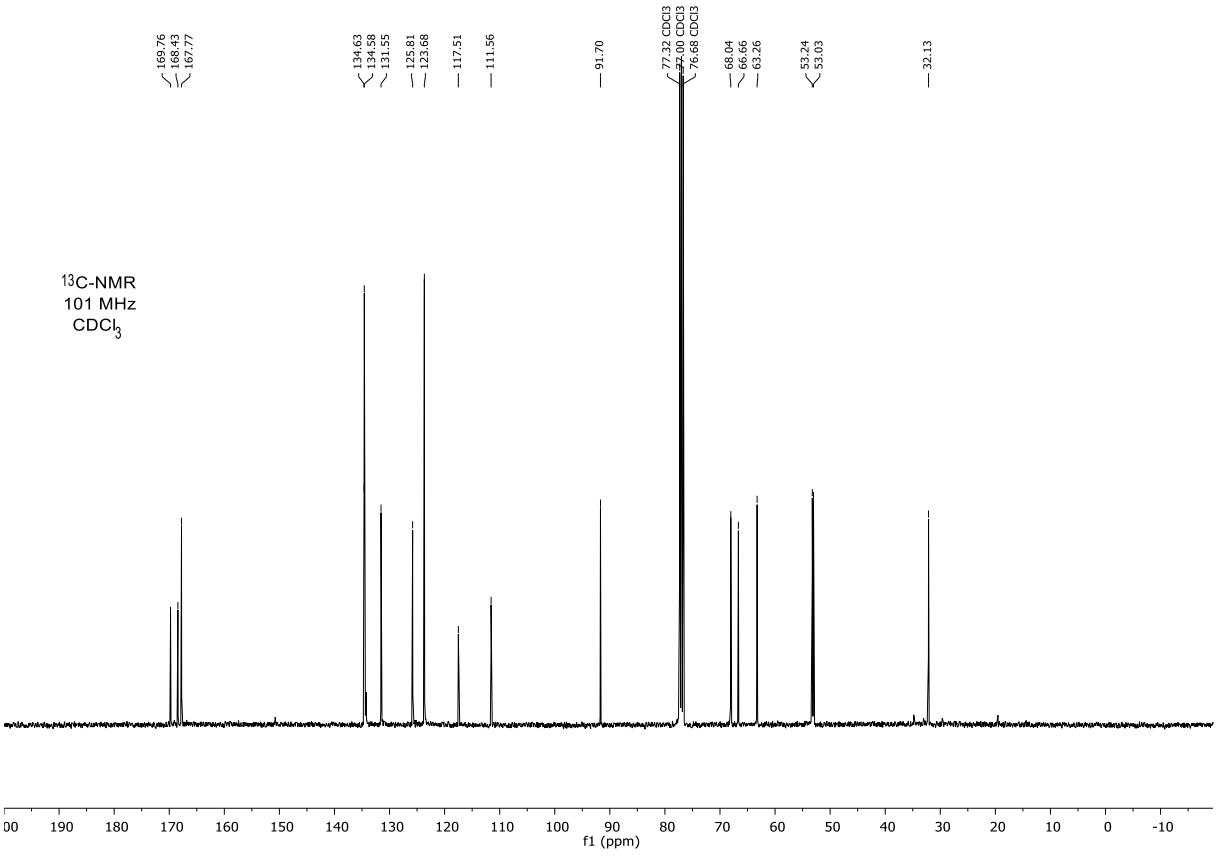
***anti*-Dimethyl 1-(1,3-dioxoisoindolin-2-yl)-1,2-dihydrobenzo[d]pyrrolo[2,1-b]oxazole-3,3(3a*H*)-dicarboxylate** (**47**).

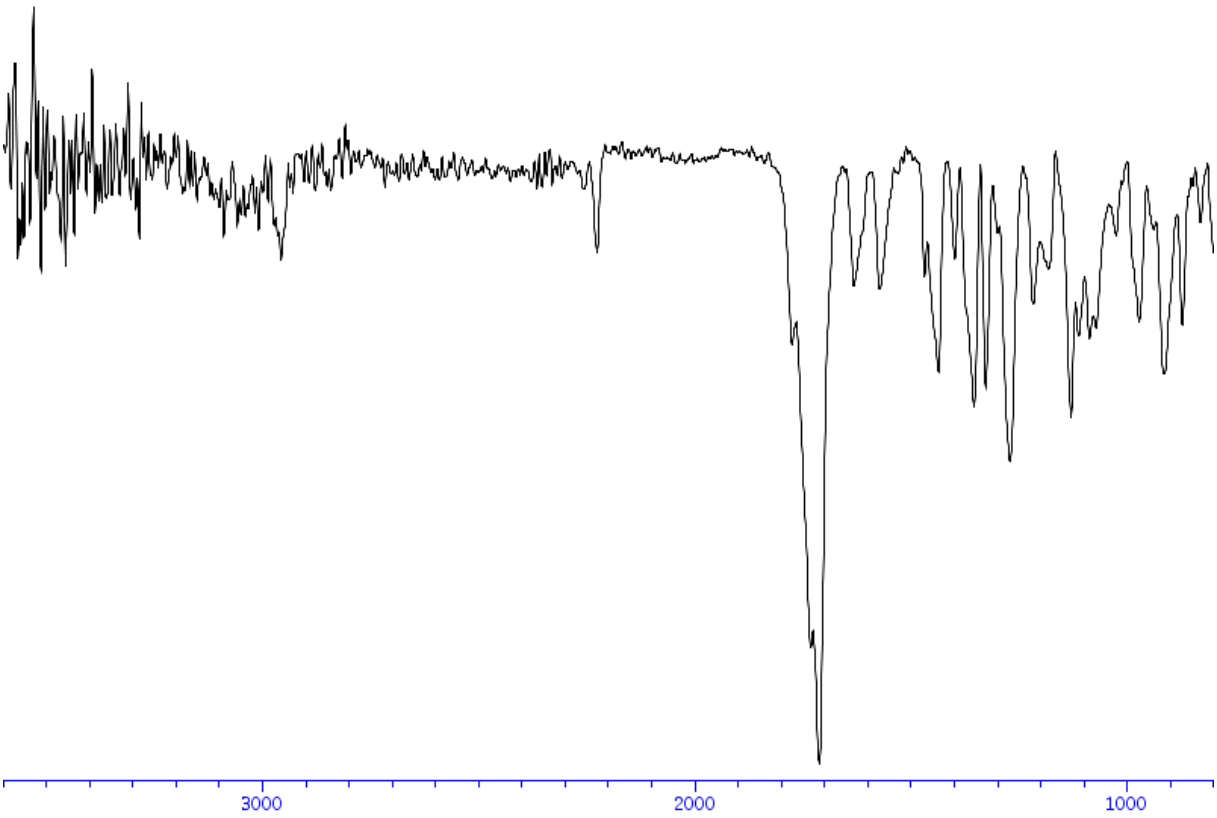




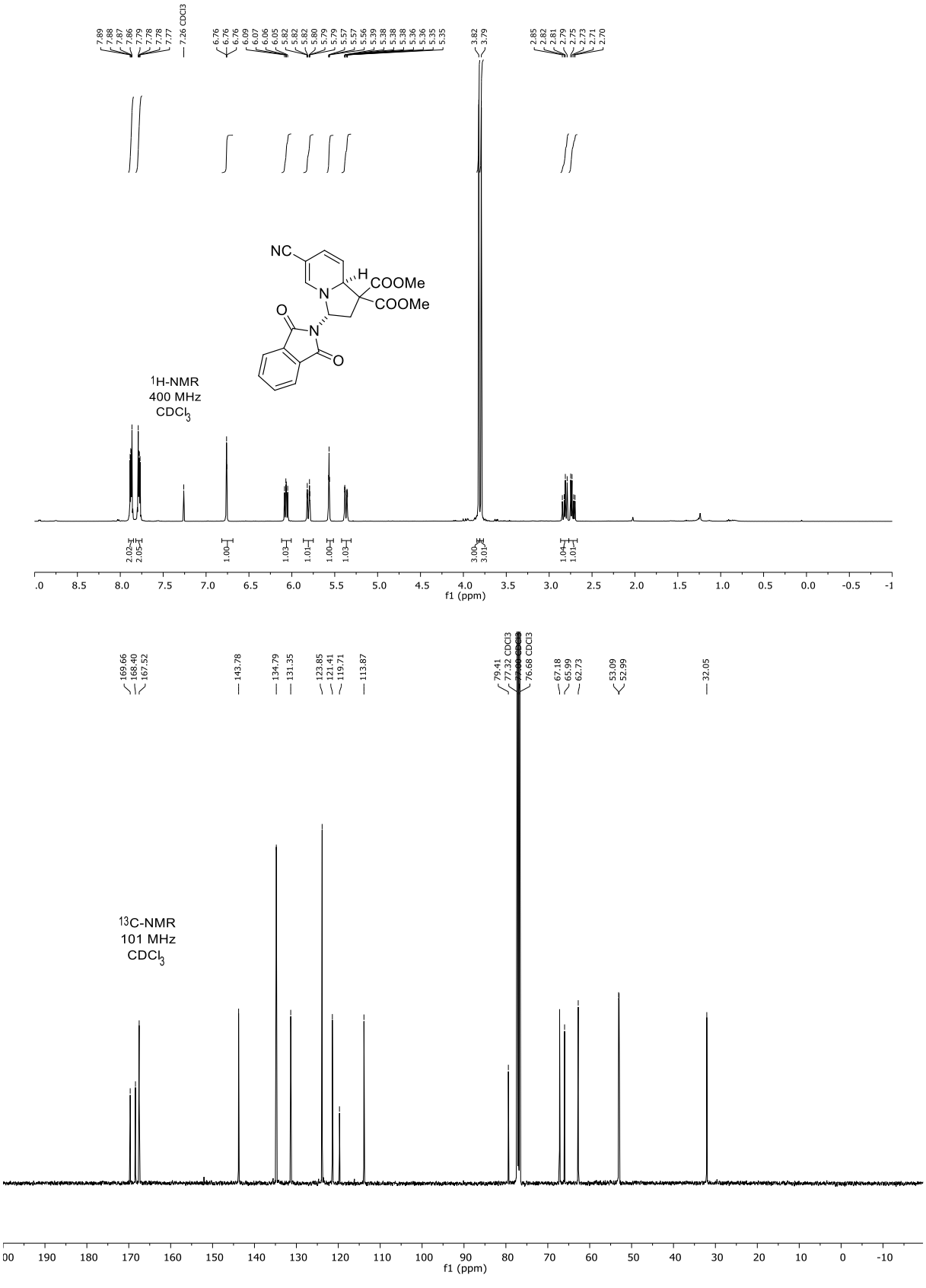
***anti*-Dimethyl 7-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (48).**

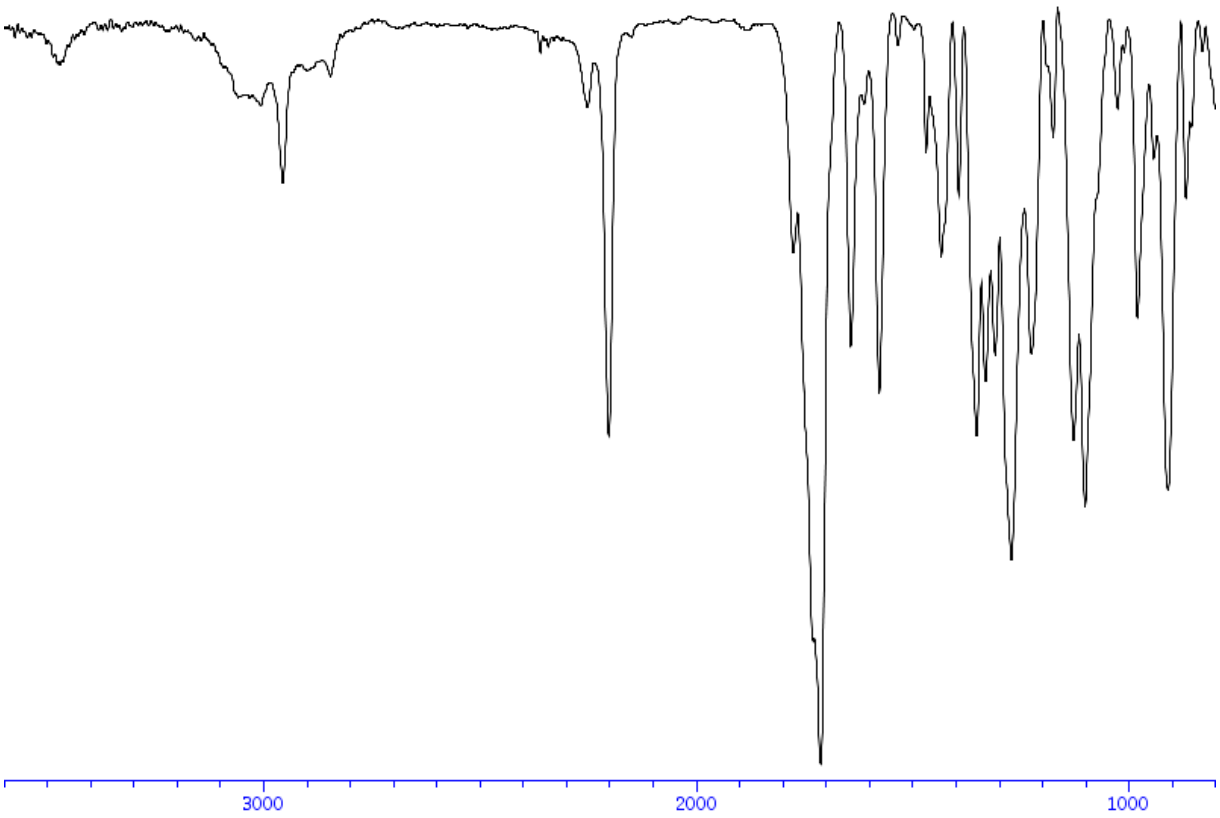



169.76
168.43
167.77
134.63
134.58
131.55
125.81
123.68
117.51
111.56
91.70
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
68.04
66.66
63.26
53.24
53.03
32.13
13C-NMR
101 MHz
CDCl3
f1 (ppm)

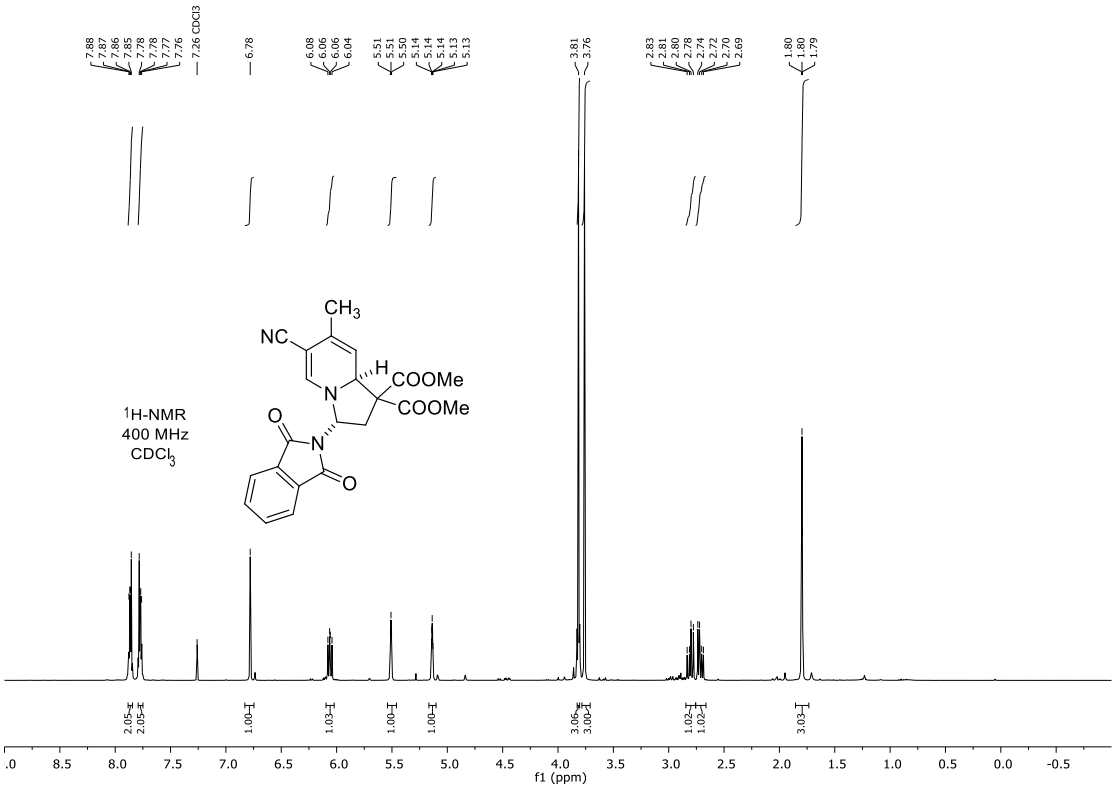

3000
2000
1000

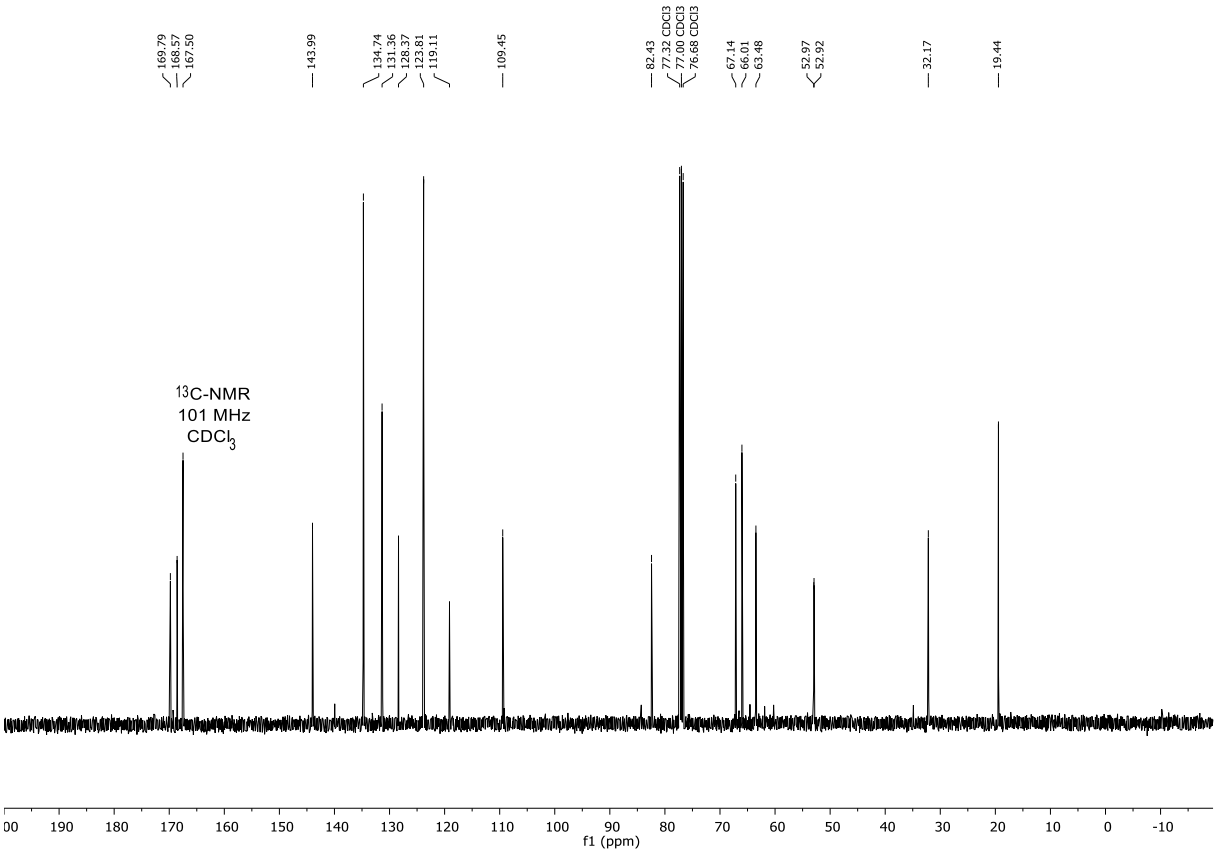
***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (49).**

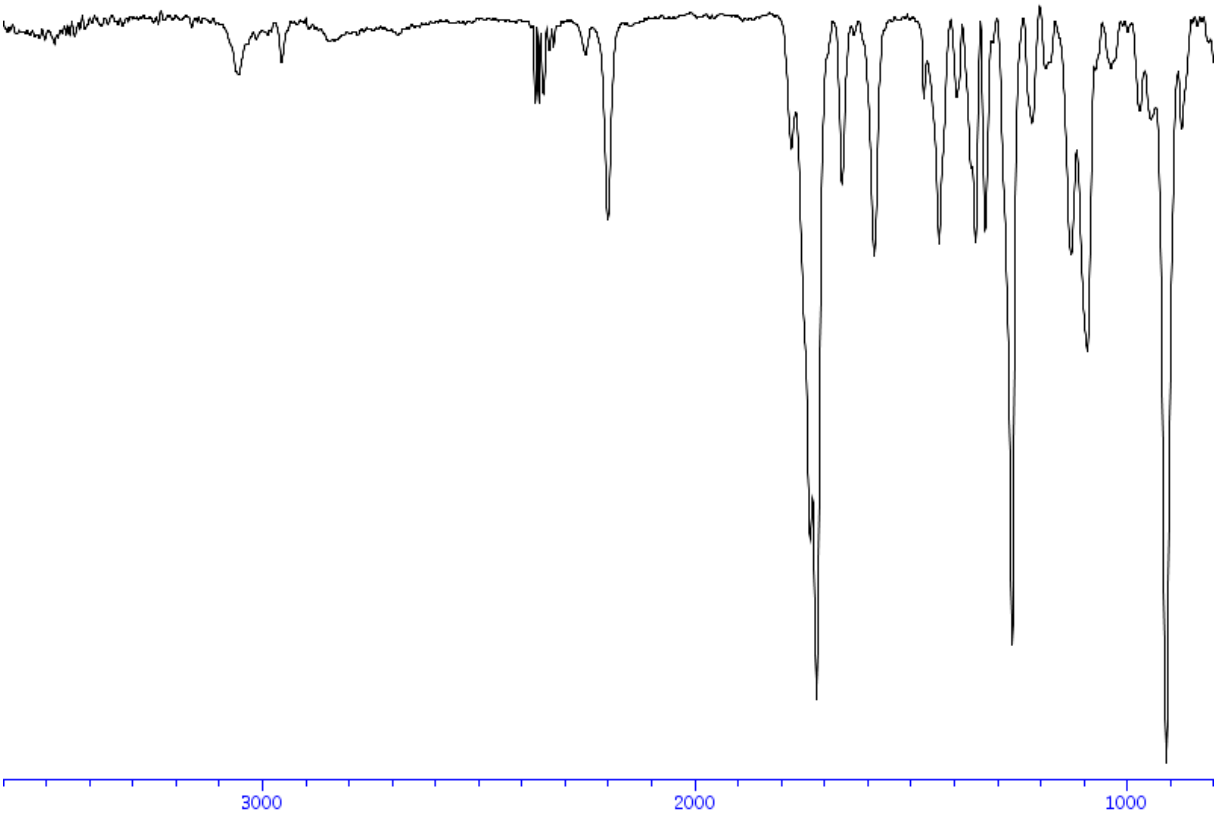




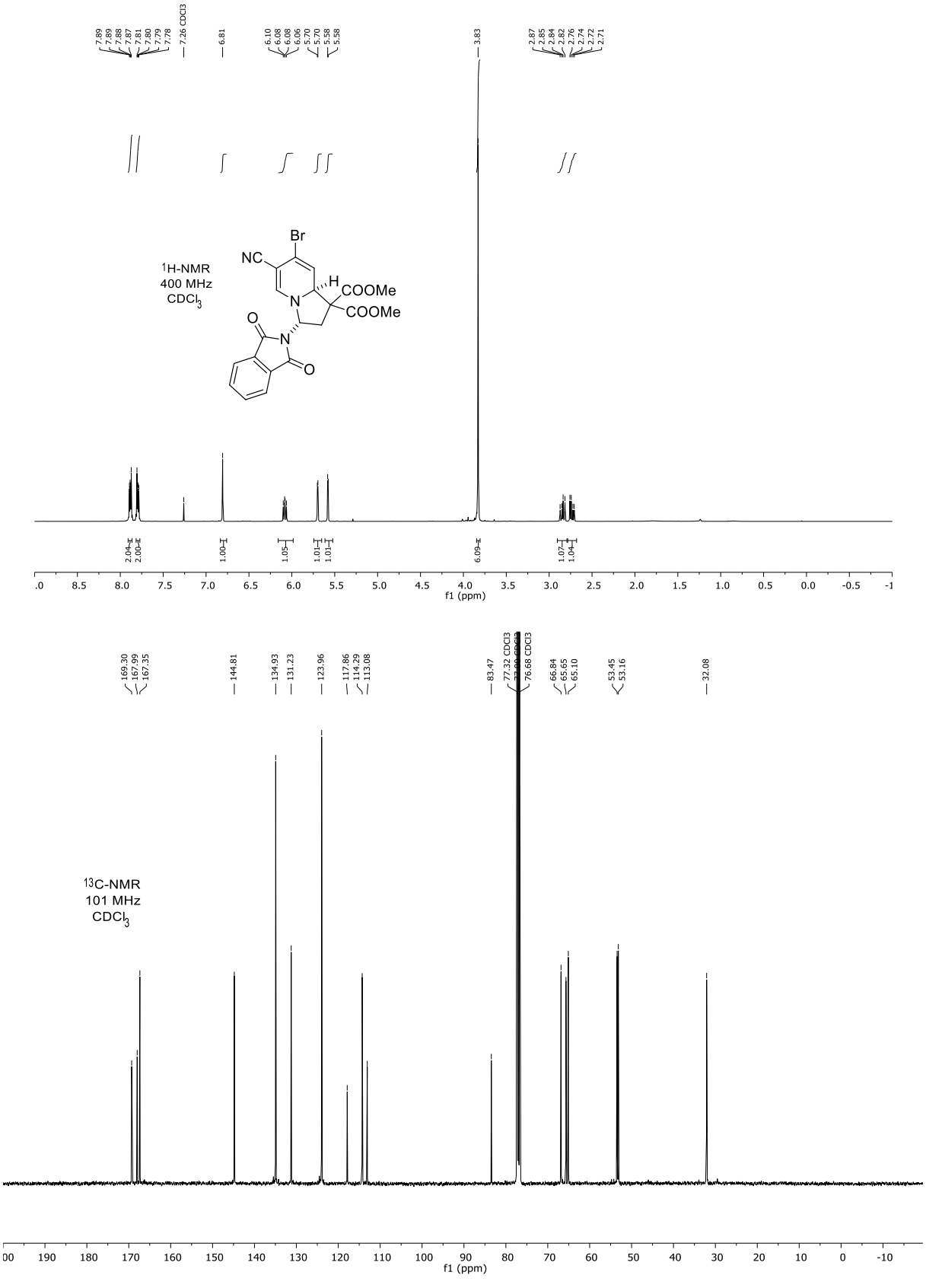
***anti*-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-7-methyl-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (50).**

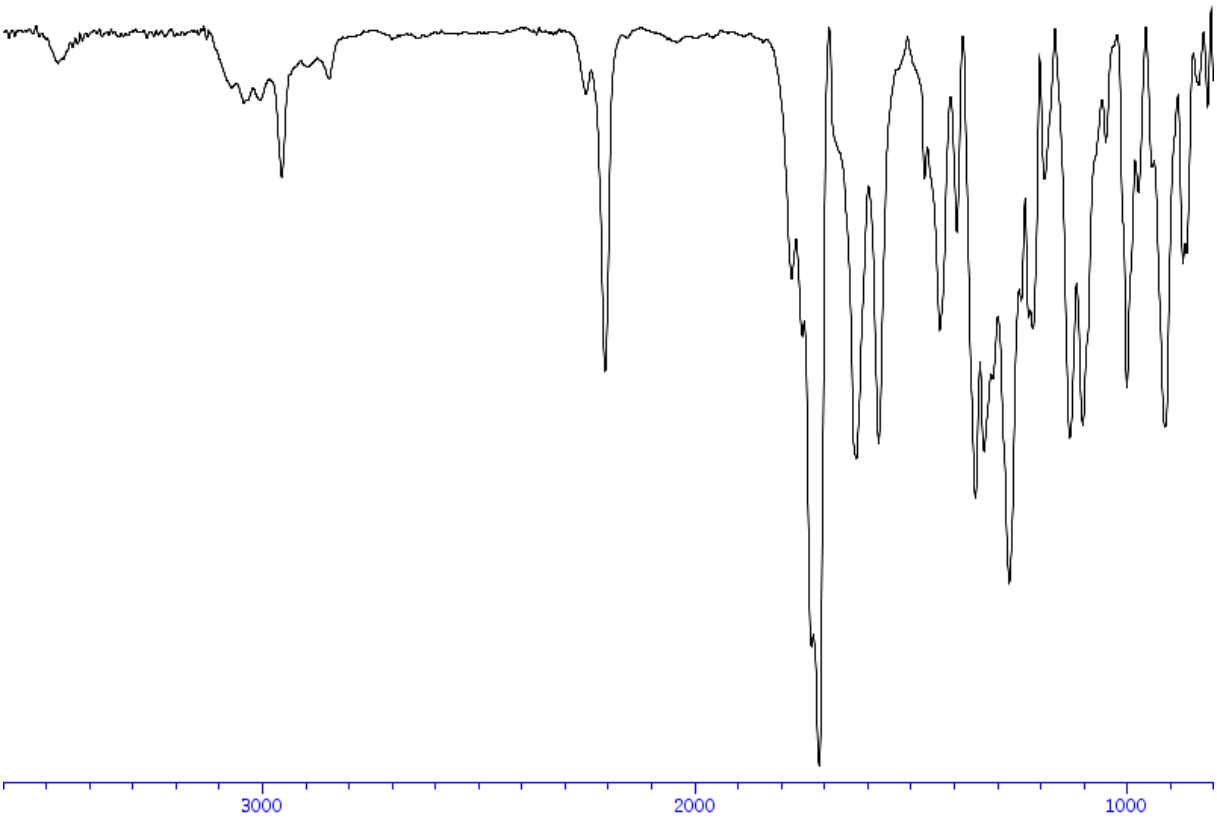



169.79
168.57
167.50
143.99
134.74
131.36
128.37
123.81
119.11
109.45
82.43
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
67.14
66.01
63.48
52.97
52.92
32.17
19.44
13C-NMR
101 MHz
CDCl3
f1 (ppm)

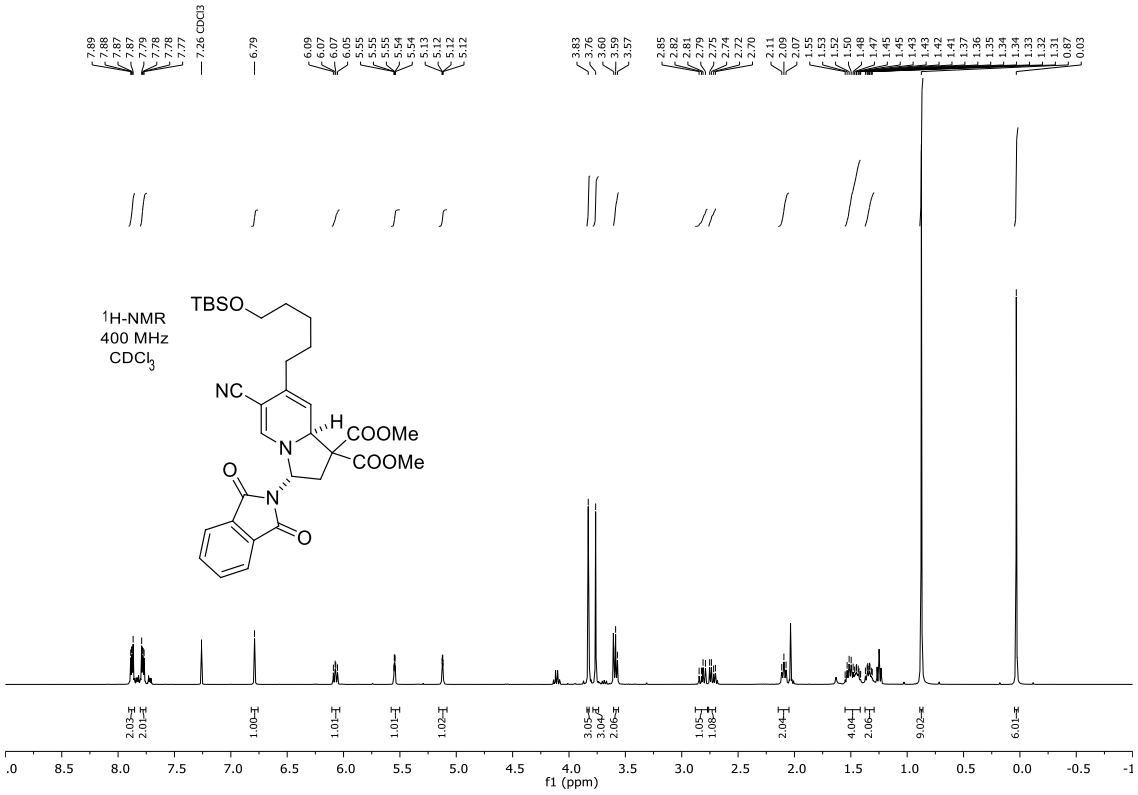

3000
2000
1000

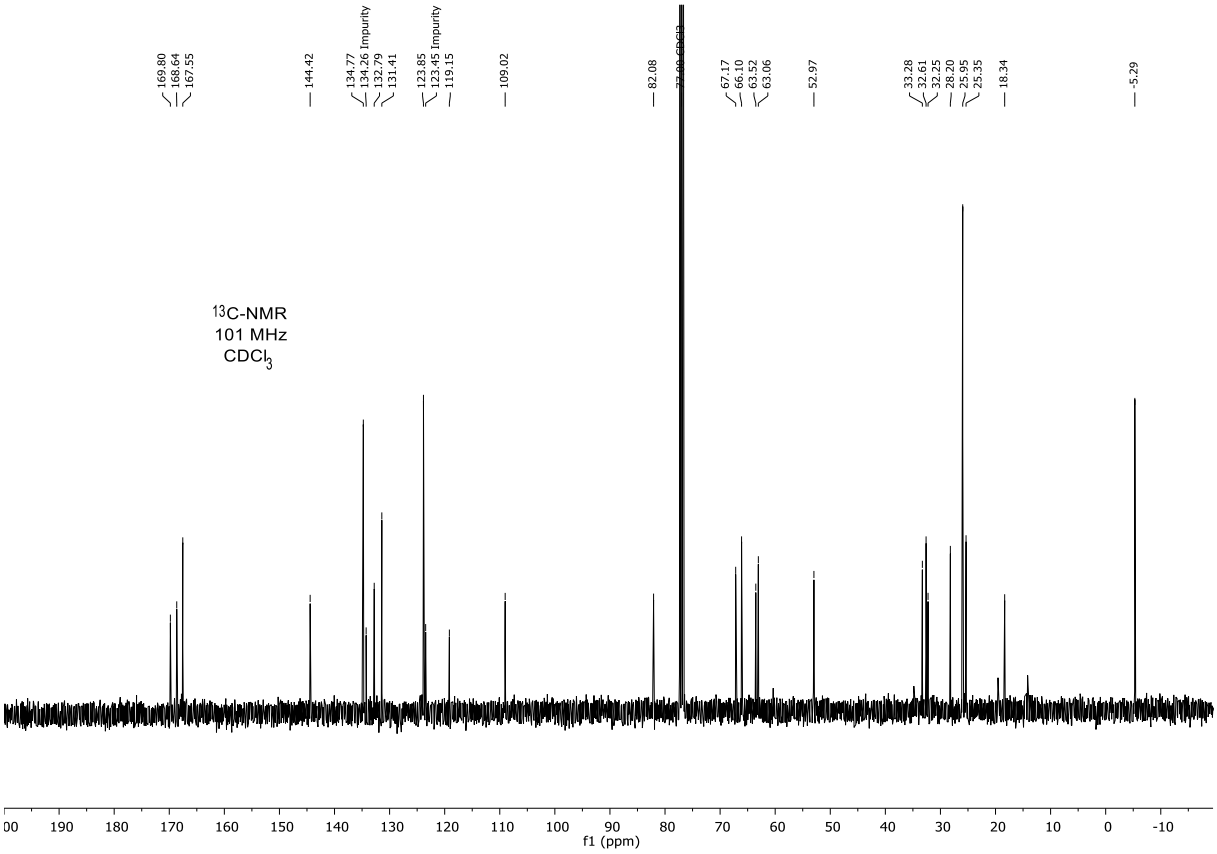
***anti*-Dimethyl 7-bromo-6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (51).**

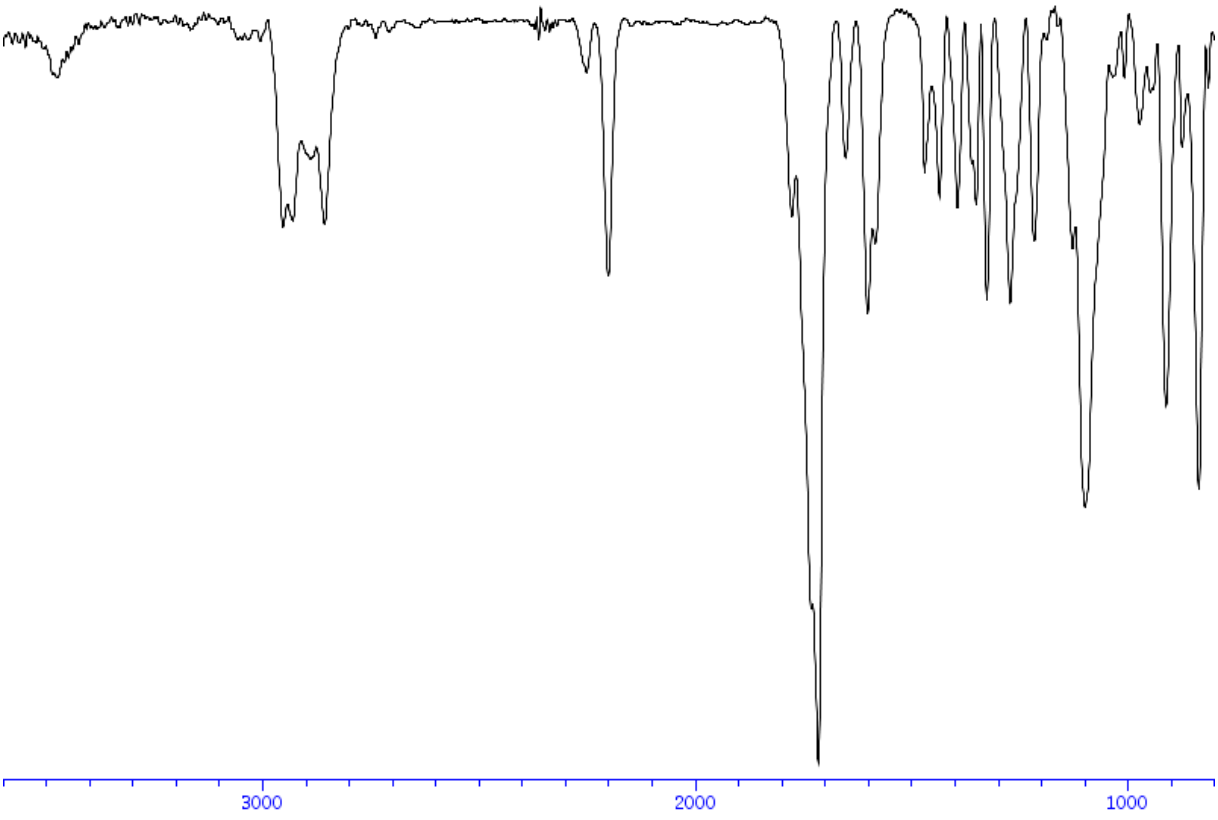




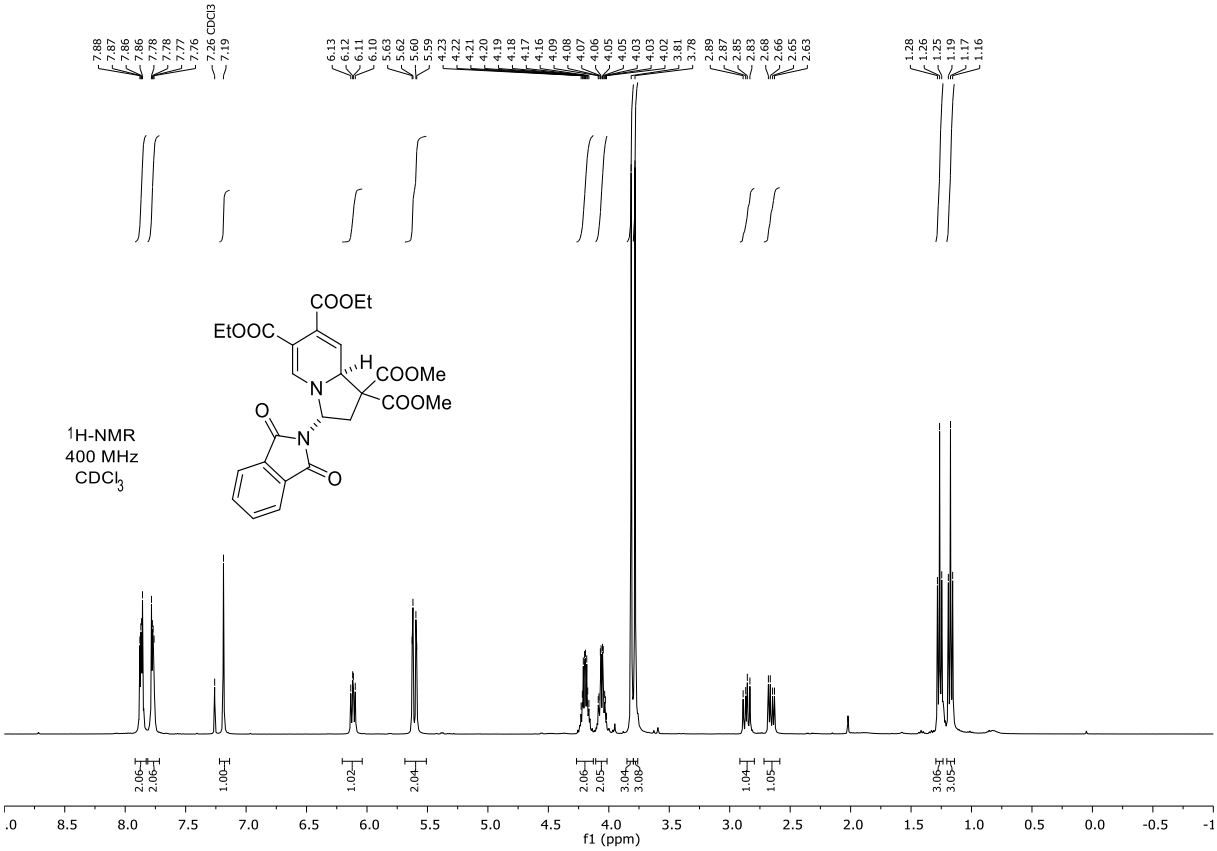
***anti*-Dimethyl 7-(5-((*tert*-butyldimethylsilyl)oxy)pentyl)-6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (52).**

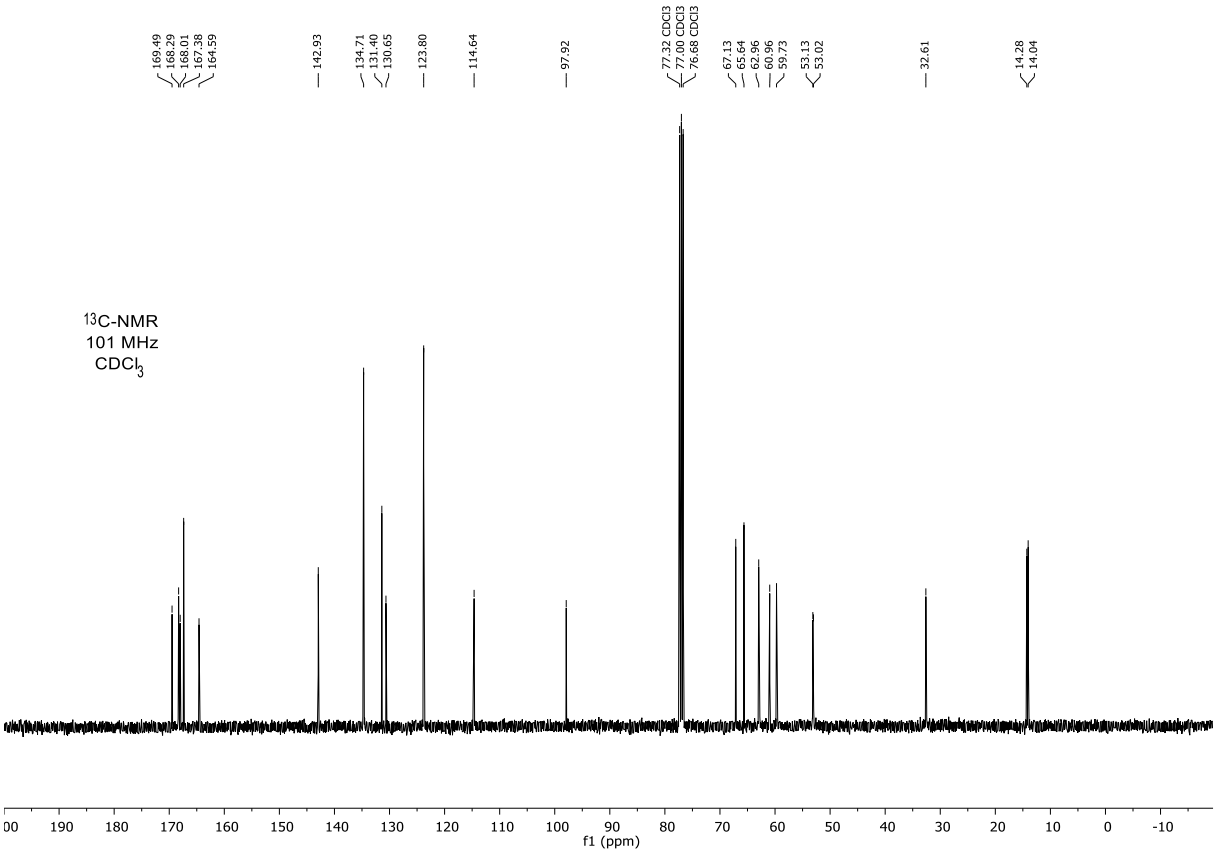


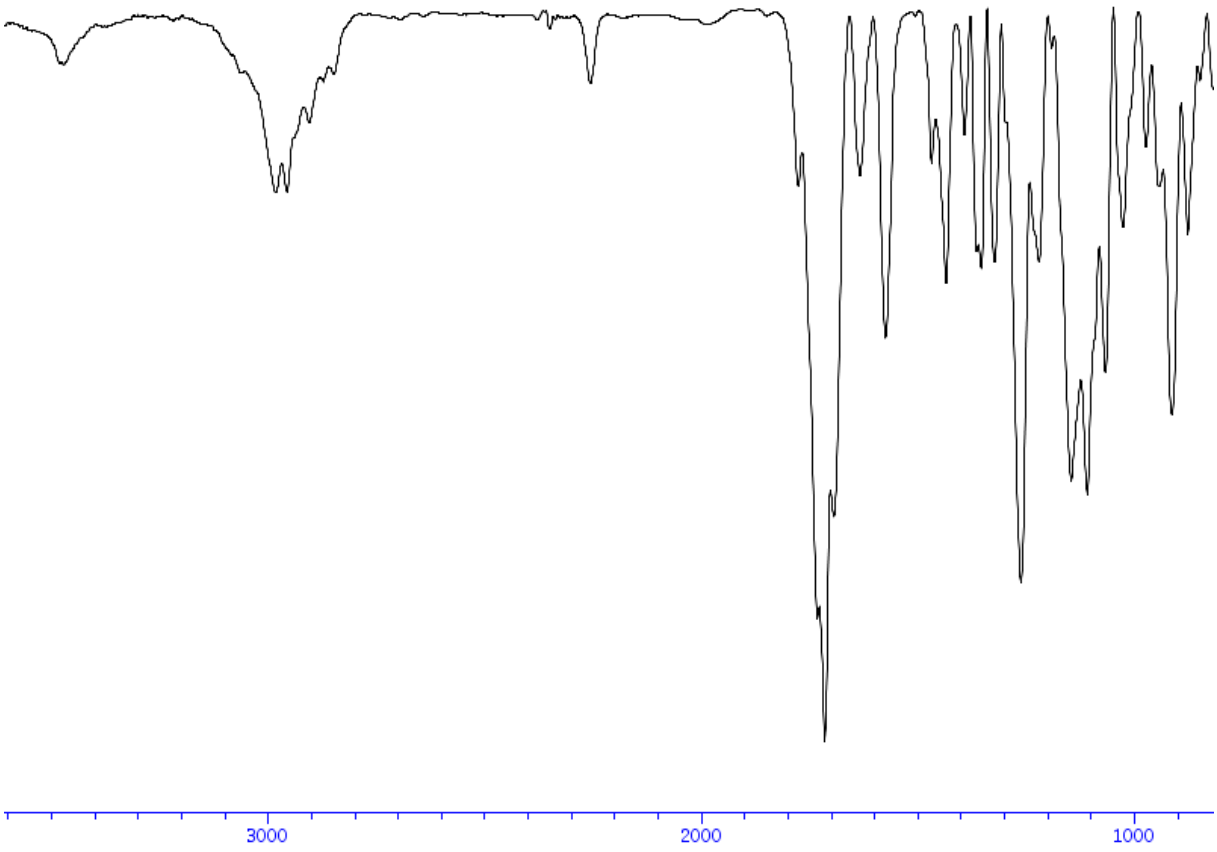

169.80
168.64
167.55
144.42
134.77
134.26 Impurity
132.79
131.41
123.85
123.45 Impurity
119.15
109.02
82.08
77.00 CDCl3
67.17
66.10
63.52
63.06
52.97
33.28
32.61
32.25
28.20
25.95
25.35
18.34
-5.29
13C-NMR
101 MHz
CDCl3
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


3000
2000
1000

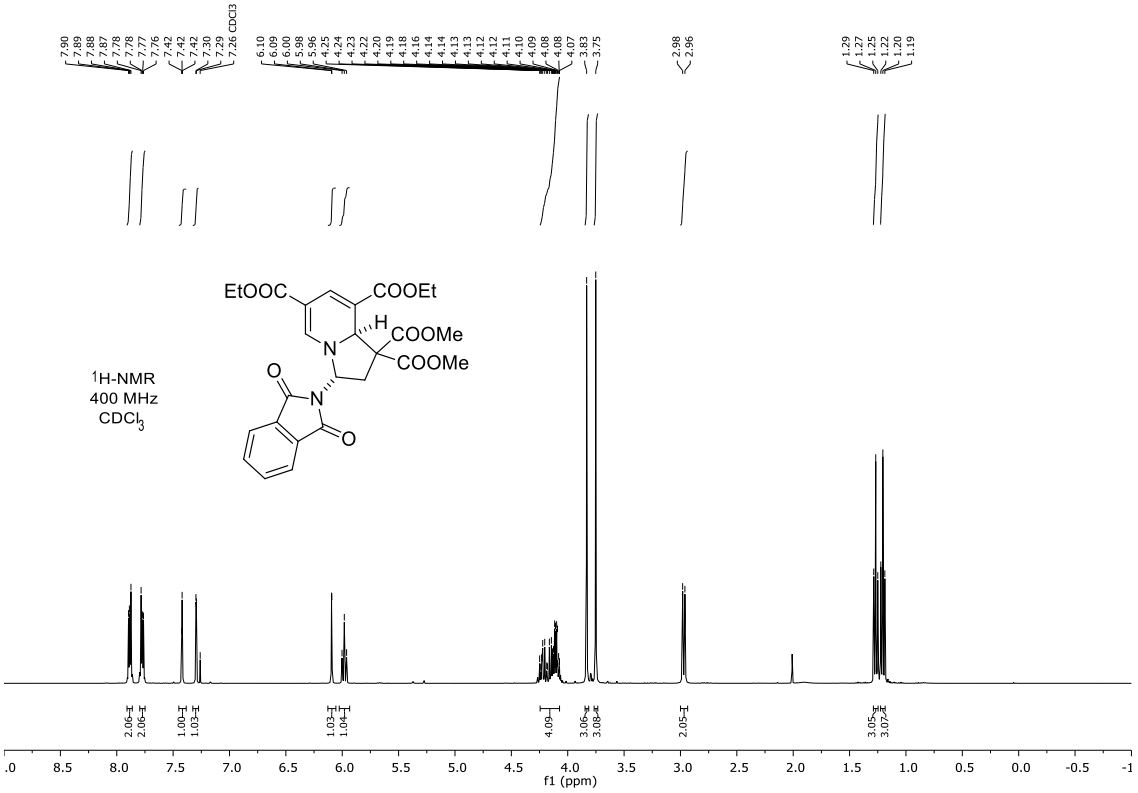
***anti*-6,7-Diethyl 1,1-dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6,7(8a*H*)-tetracarboxylate** (**54**).

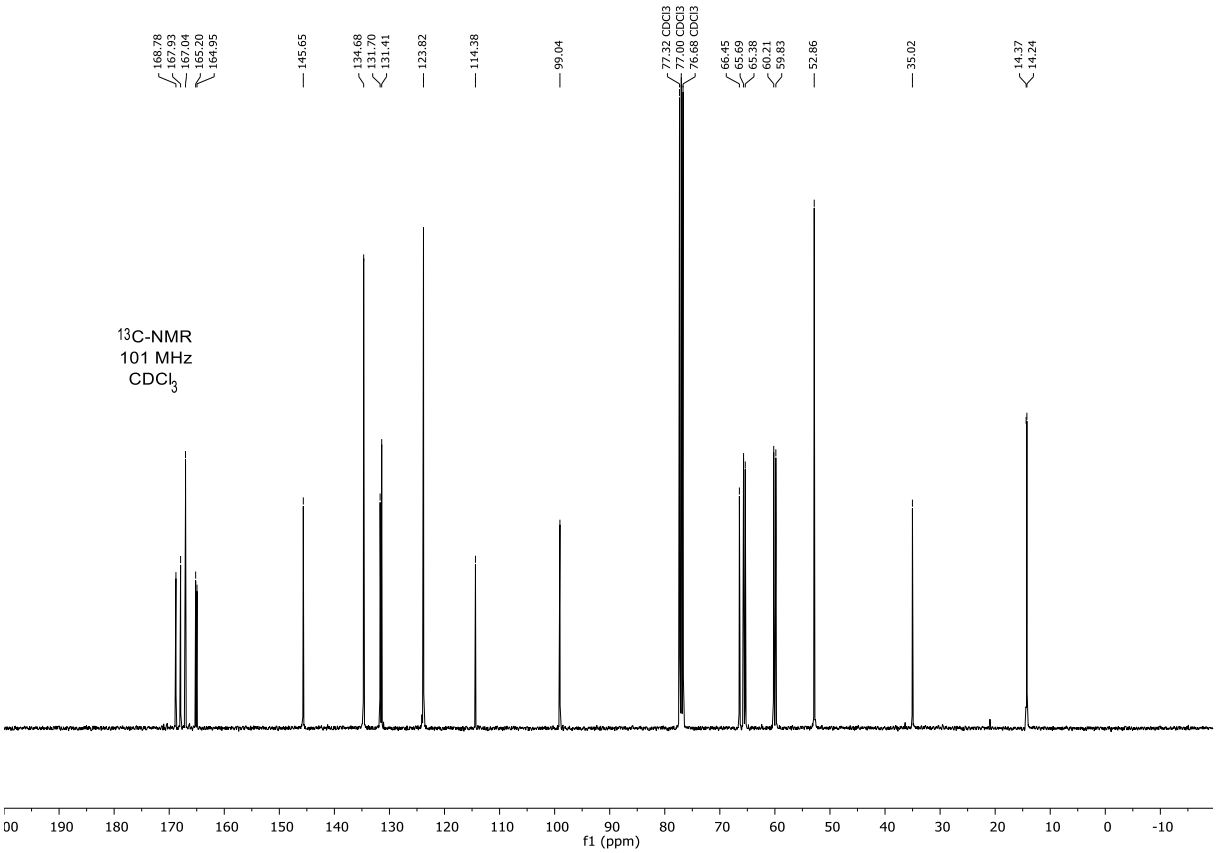


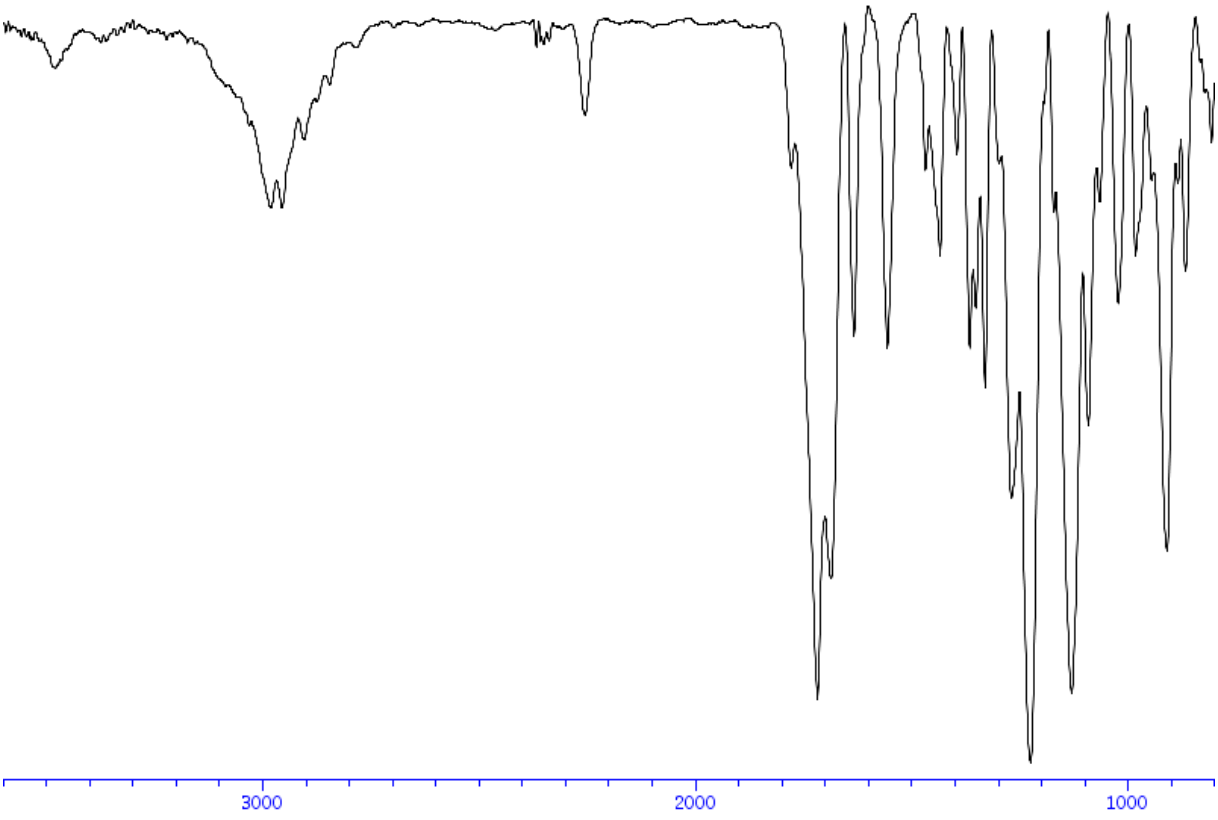




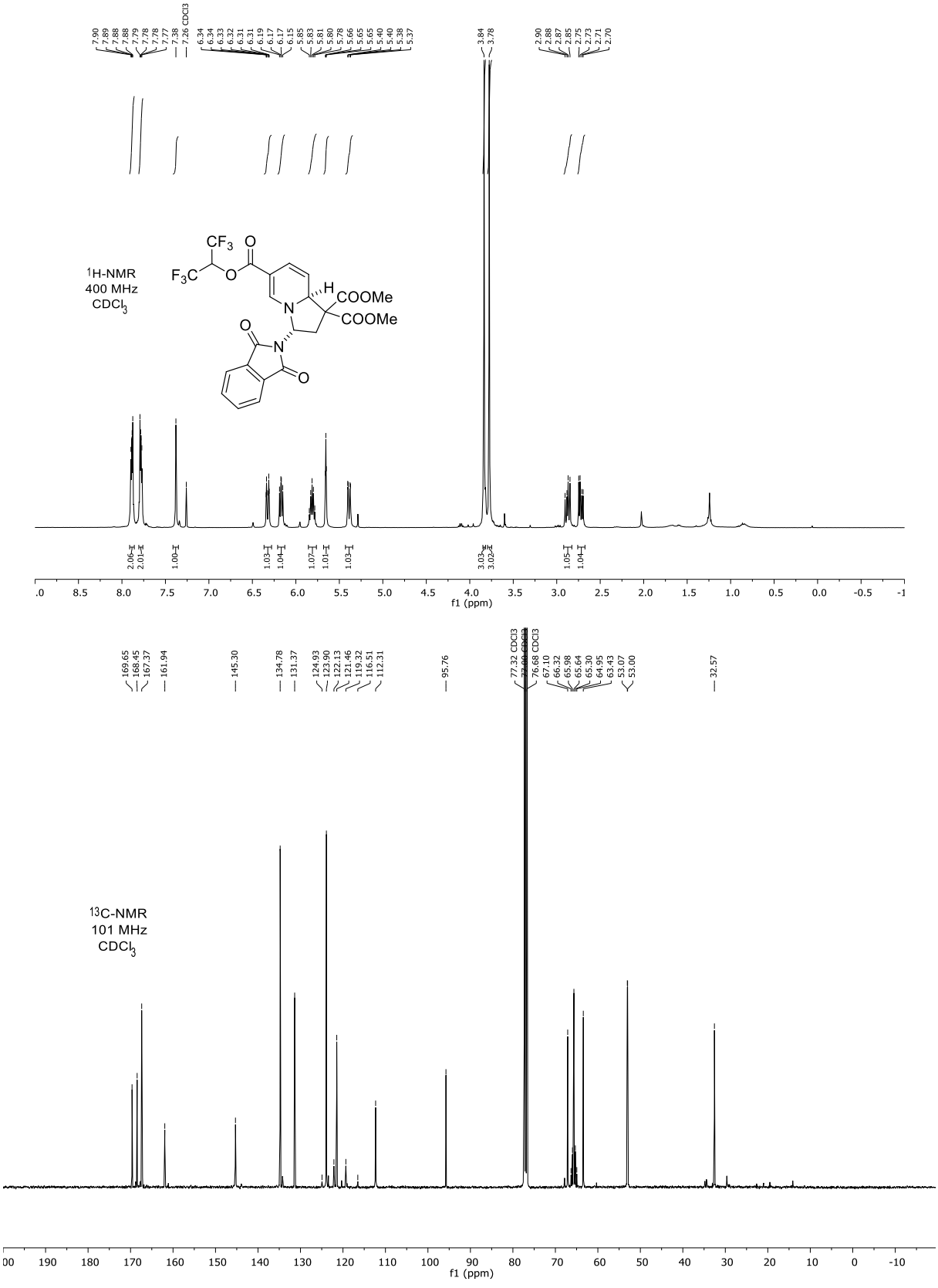
***anti*-6,8-Diethyl 1,1-dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6,8(8a*H*)-tetracarboxylate** (**55**).

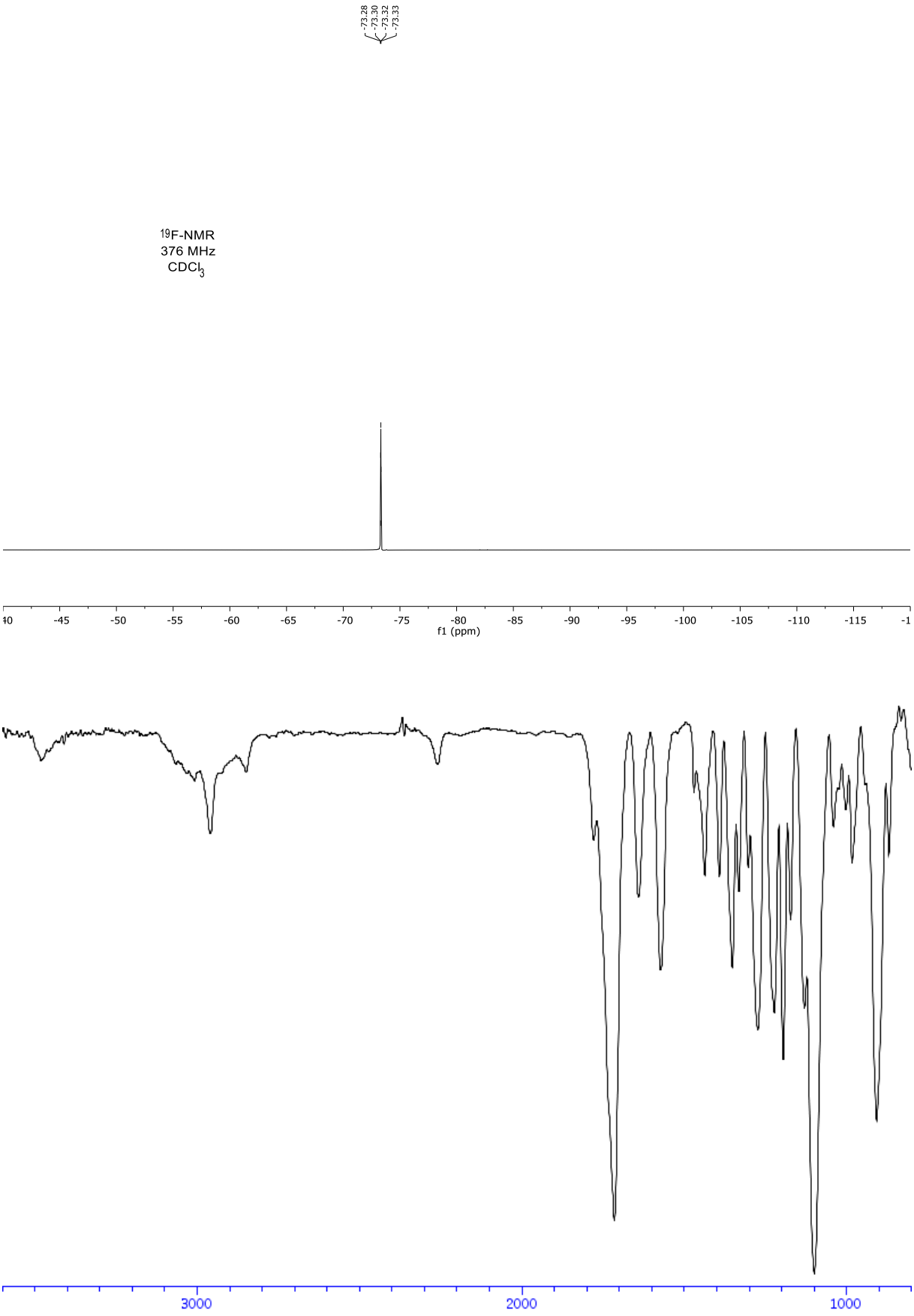



168.78
167.93
167.04
165.20
164.95
145.65
134.68
131.70
131.41
123.82
114.38
99.04
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
66.45
65.98
65.38
60.21
59.83
52.86
35.02
14.37
14.24
13C-NMR
101 MHz
CDCl3
f1 (ppm)

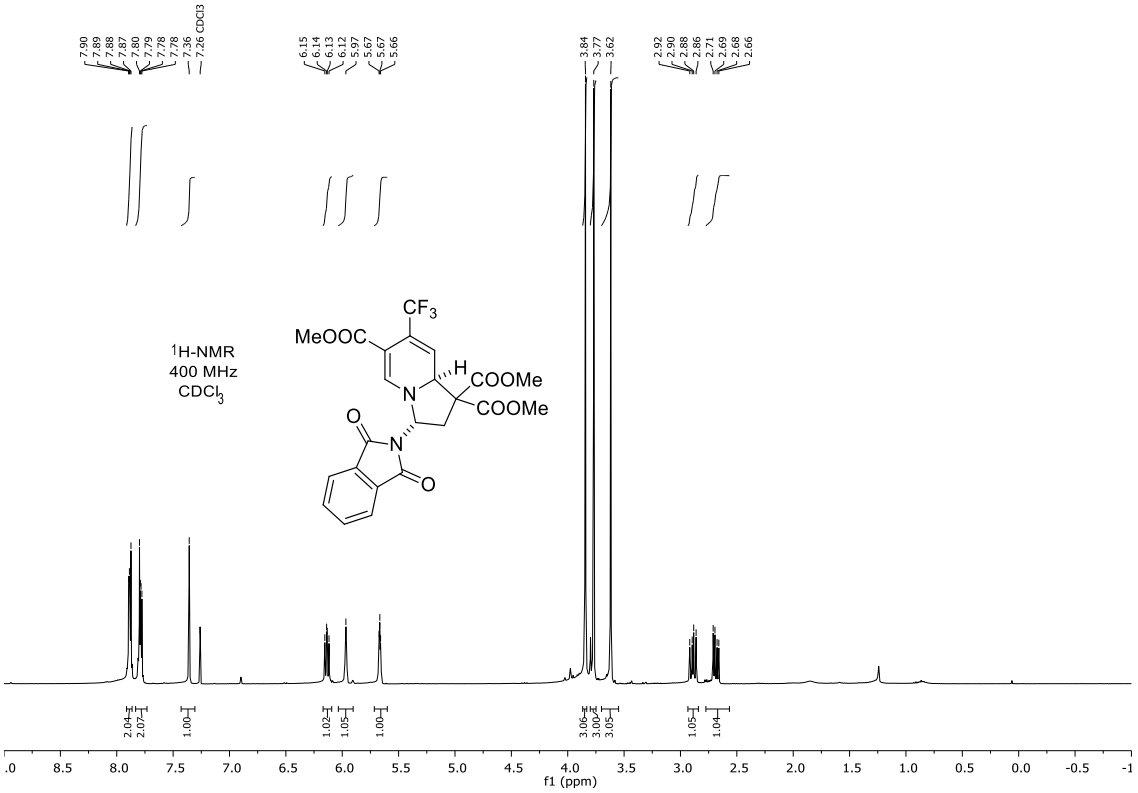

3000
2000
1000

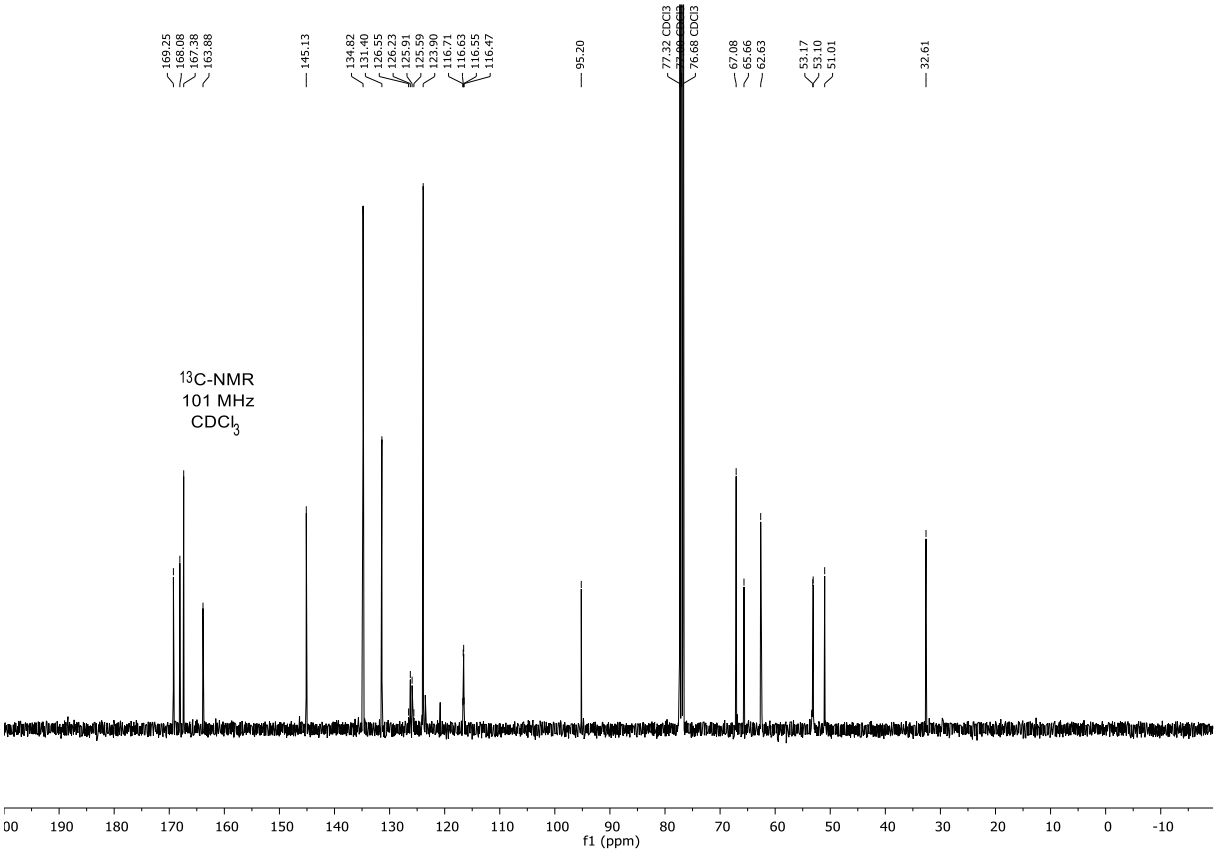
***anti*-6-(1,1,1,3,3,3-Hexafluoropropan-2-yl) 1,1-dimethyl 3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6(8a*H*)-tricarboxylate** (**56**).

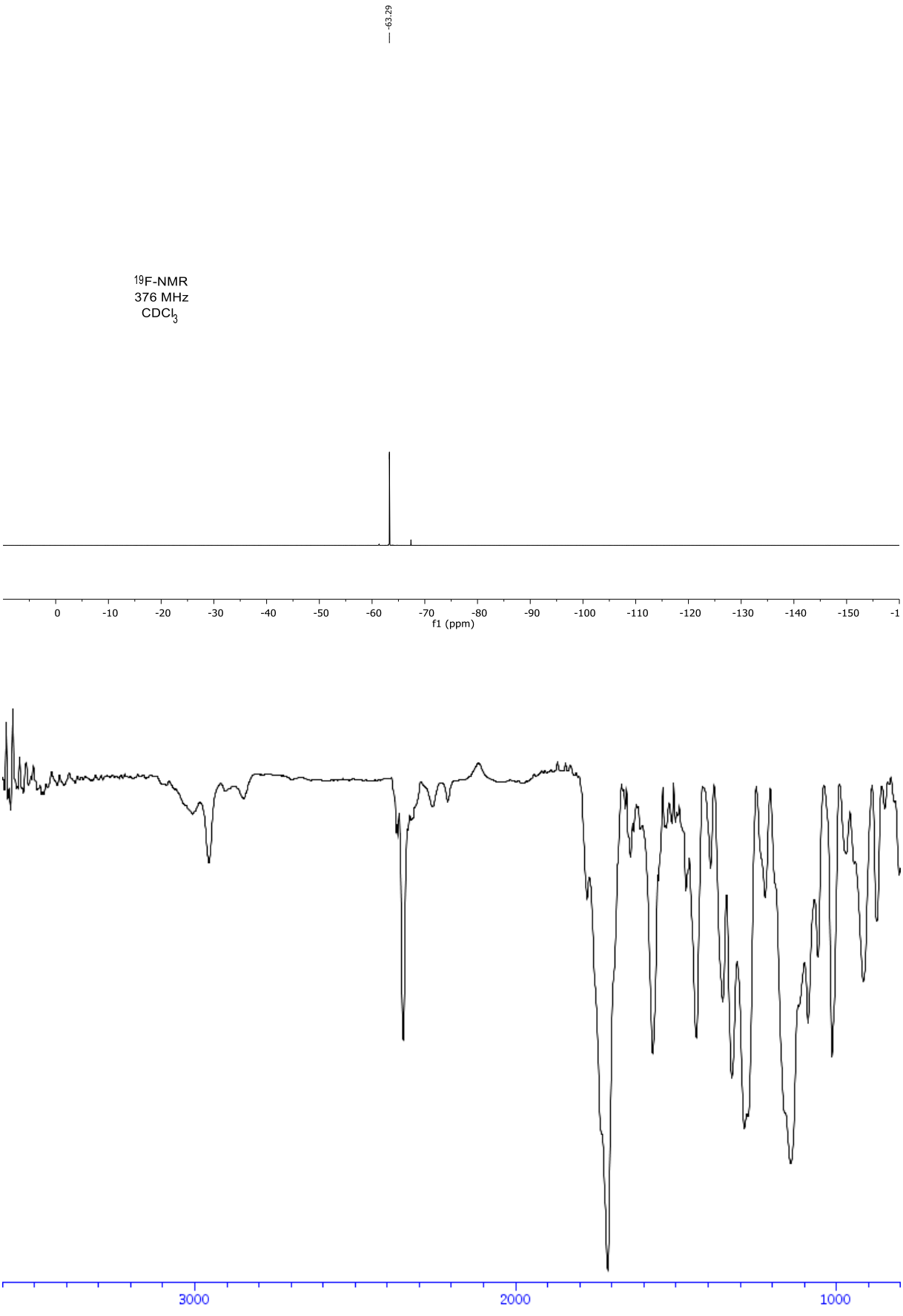



-73.28
-73.30
-73.32
-73.33
19F-NMR
376 MHz
CDCl3
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
f1 (ppm)
3000
2000
1000

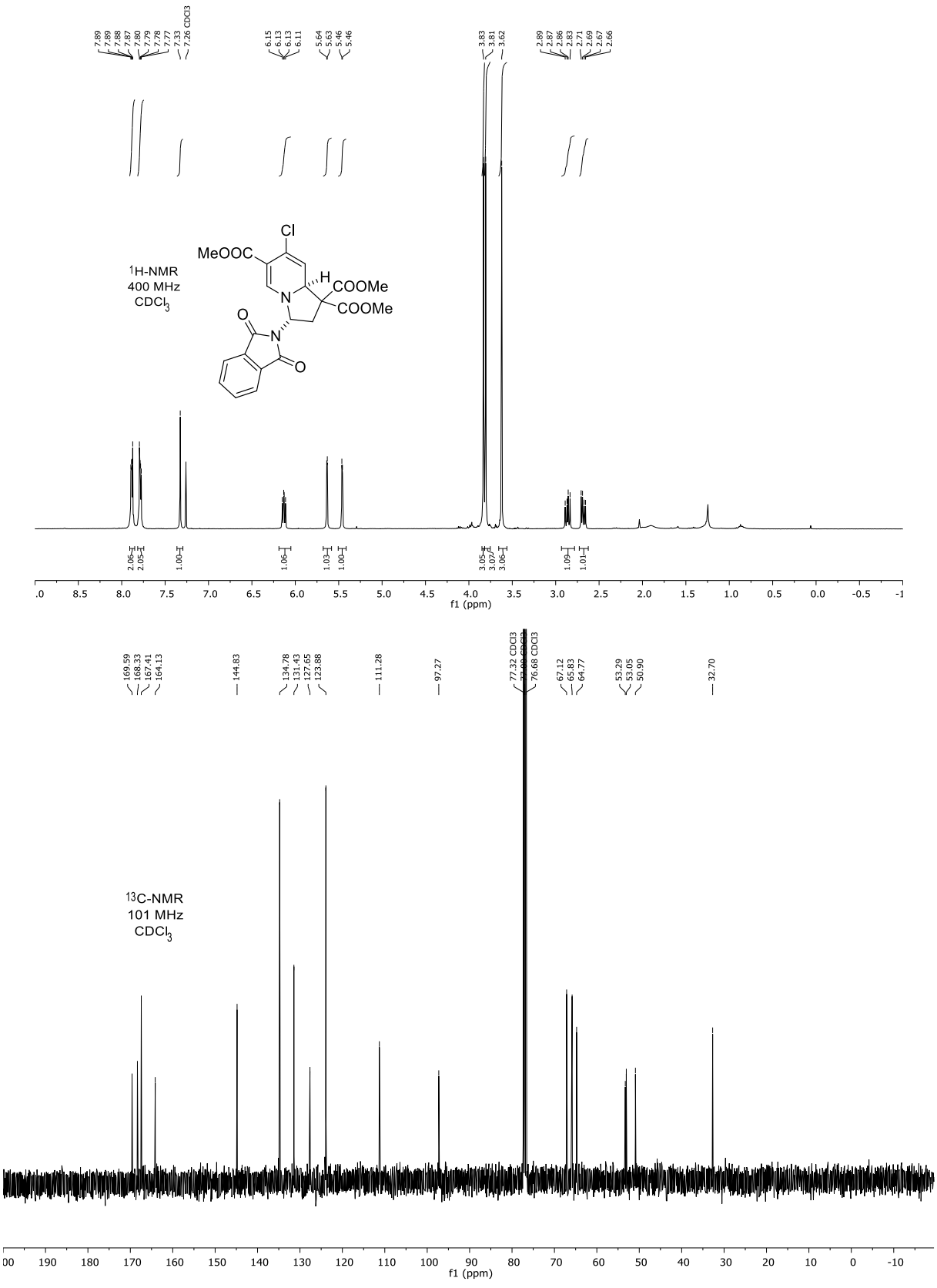
***anti*-Trimethyl 3-(1,3-dioxoisoindolin-2-yl)-7-(trifluoromethyl)-2,3-dihydroindolizine-1,1,6(8a*H*)-tricarboxylate (57).**

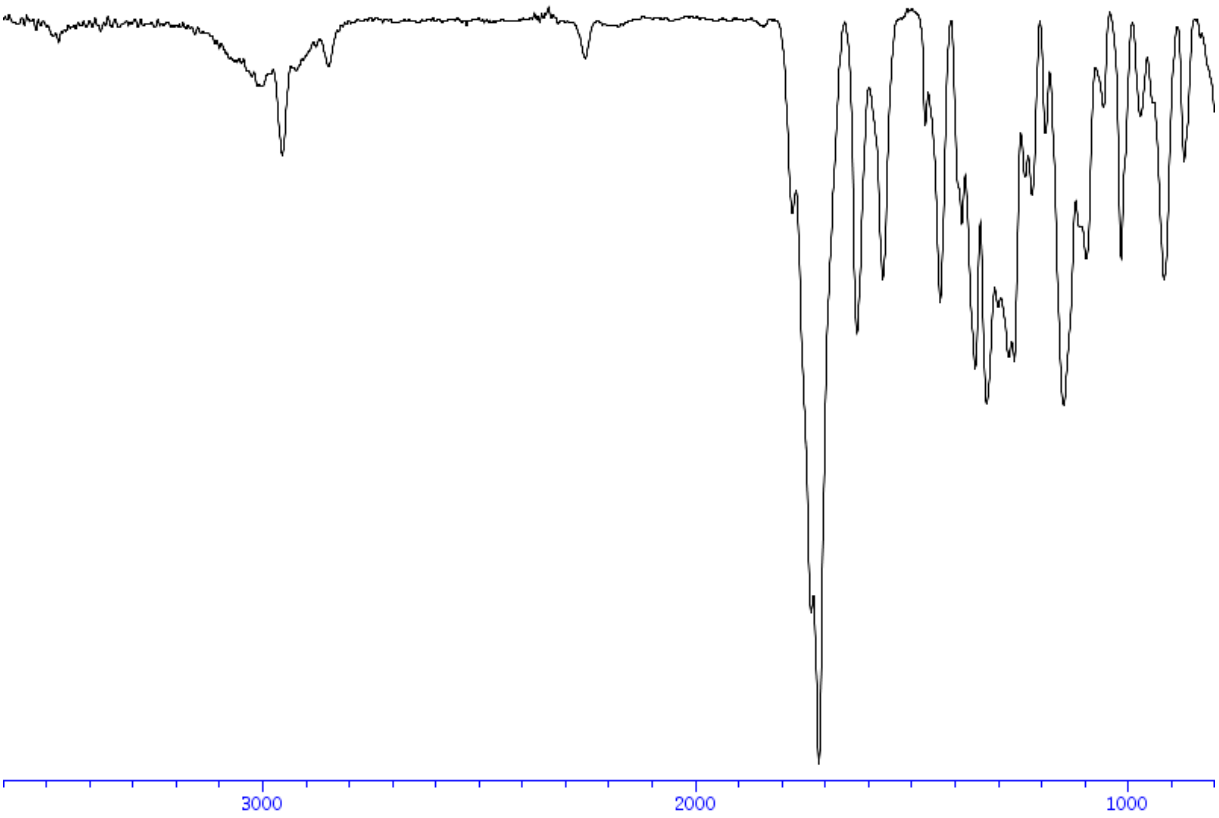




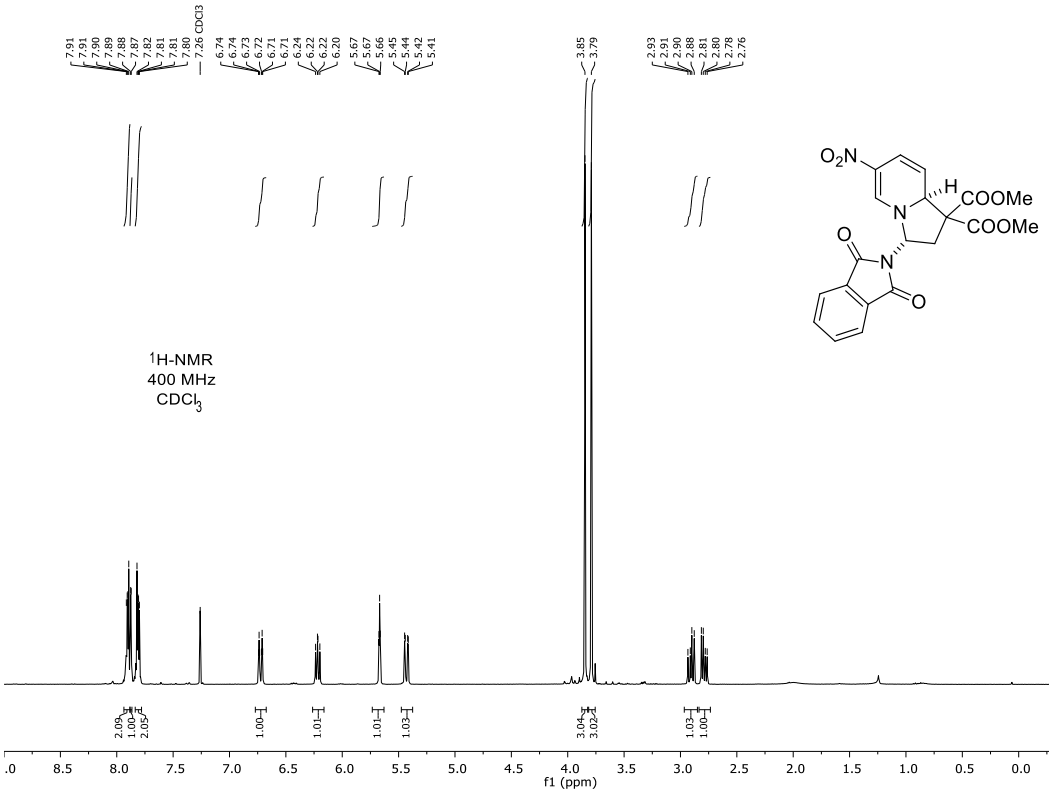

— -63.29
19F-NMR
376 MHz
CDCl3
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)
3000
2000
1000

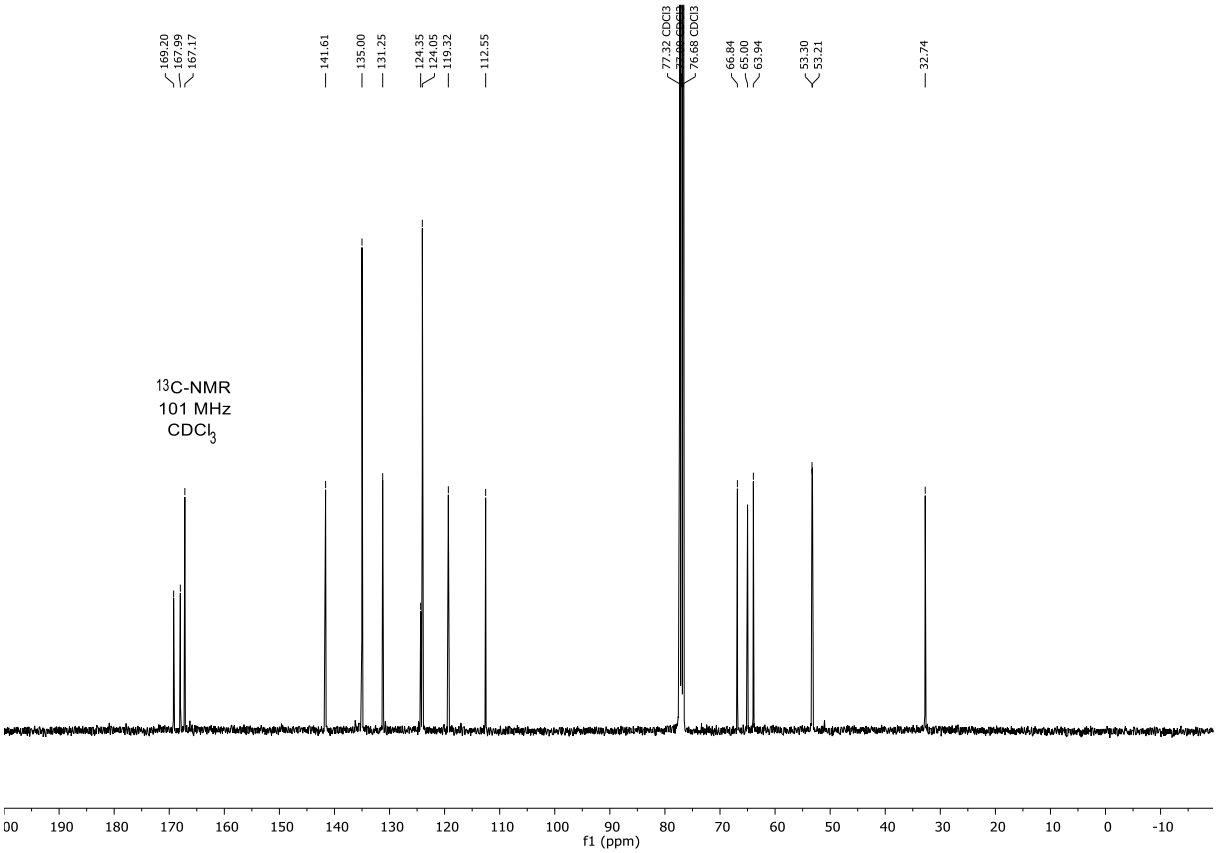
***anti*-Trimethyl 7-chloro-3-(1,3-dioxoisoindolin-2-yl)-2,3-dihydroindolizine-1,1,6(8a*H*)-tricarboxylate (58).**

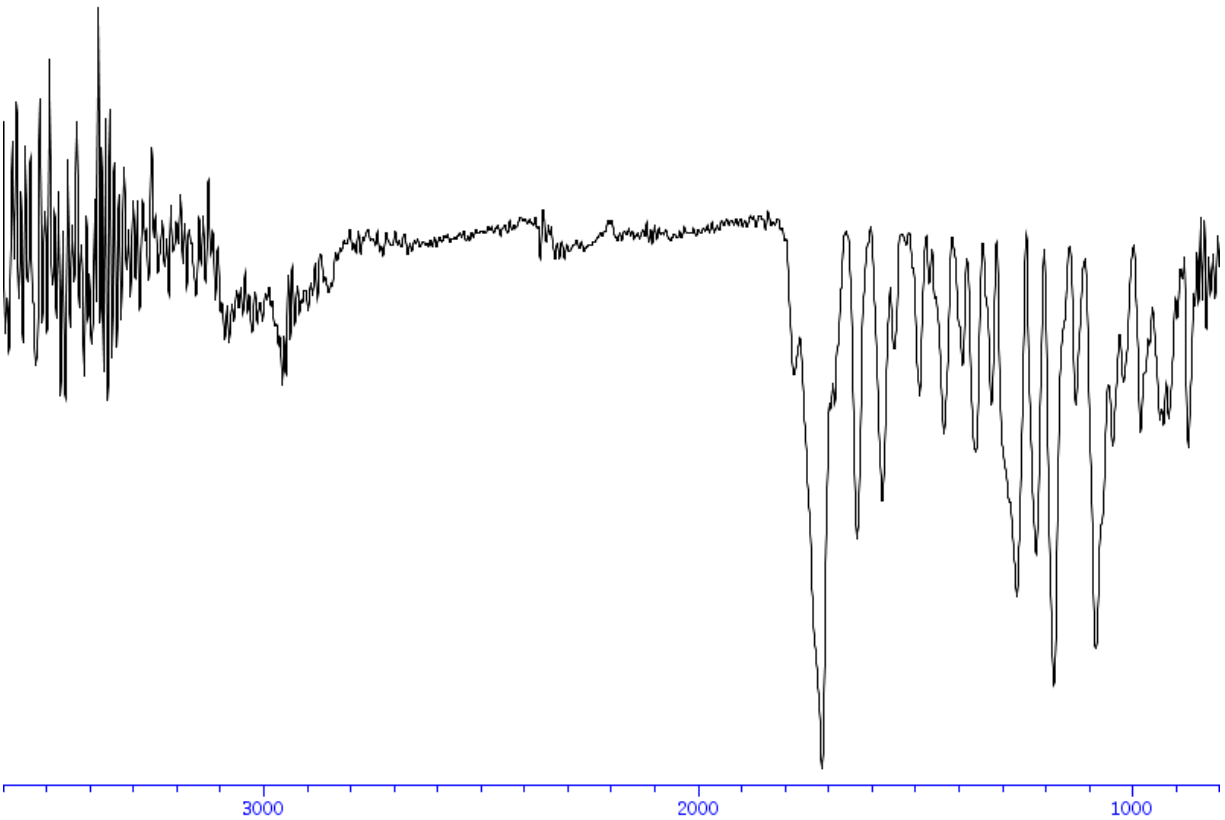




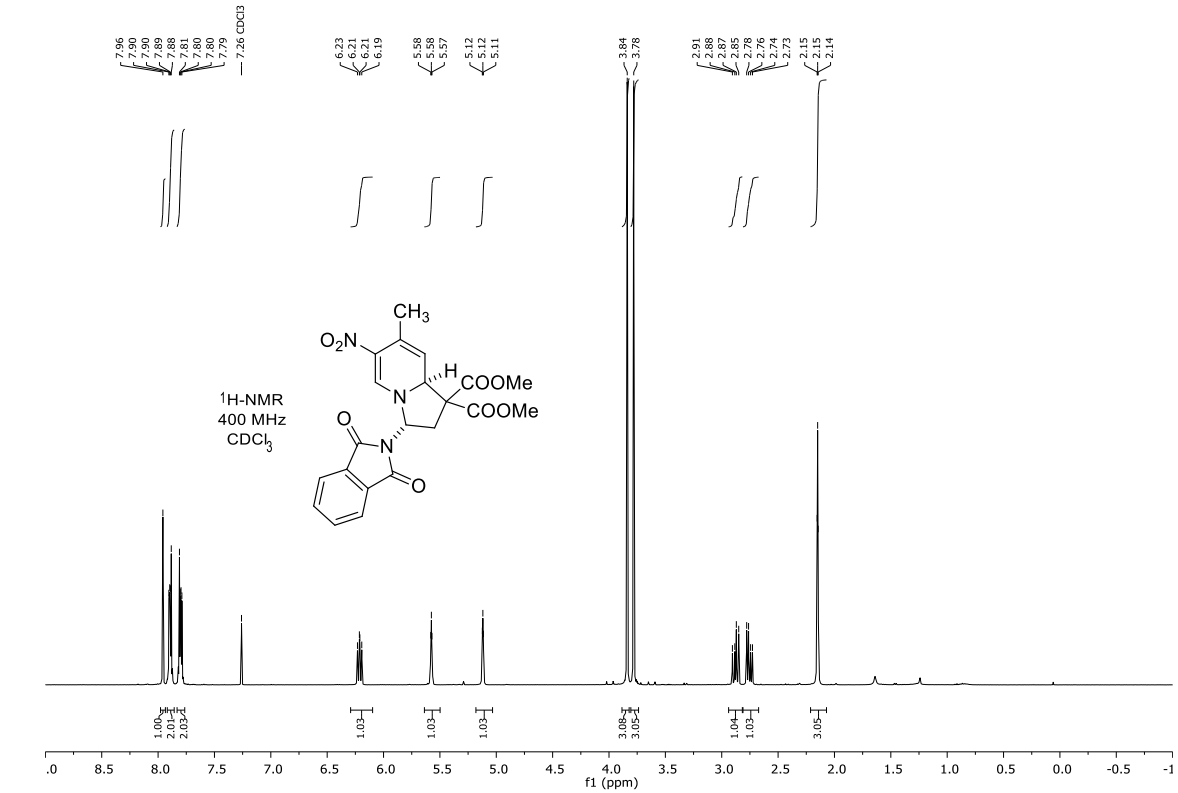
***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-6-nitro-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (59).**

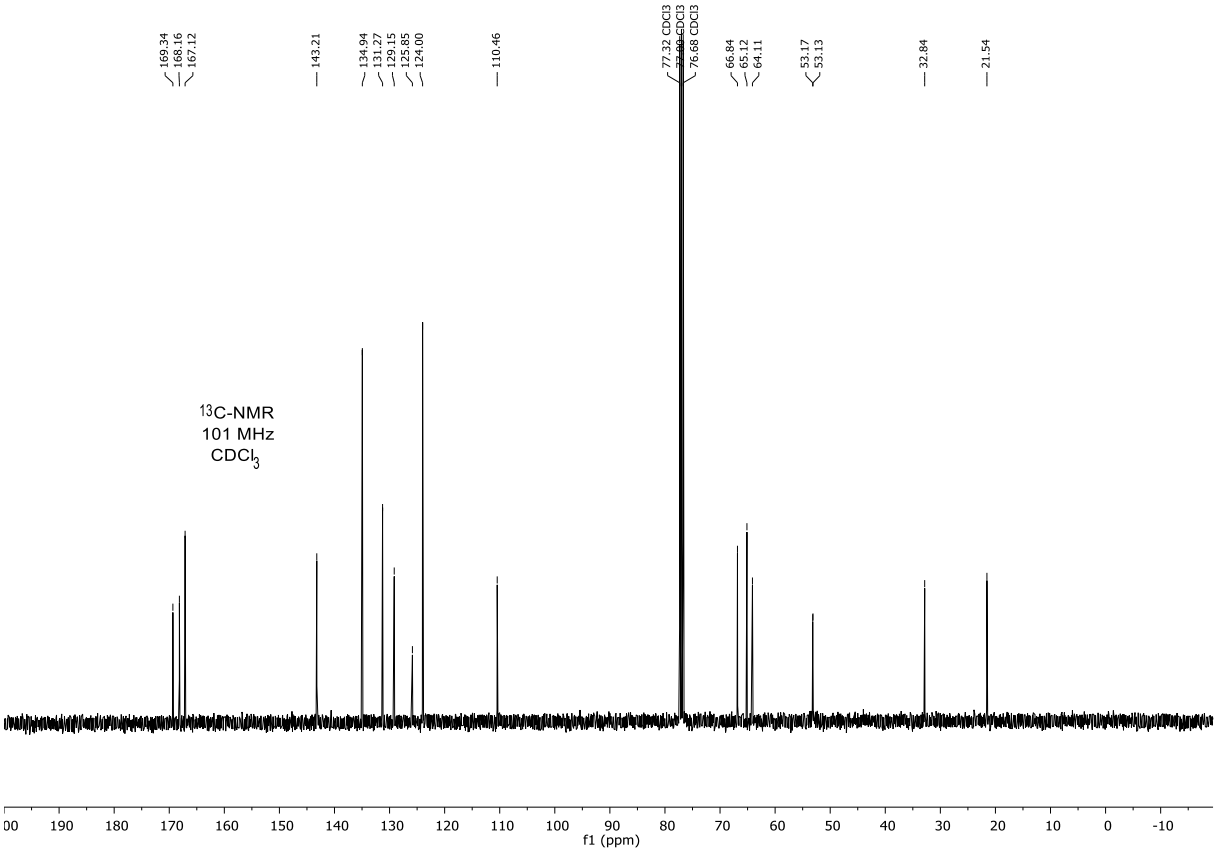


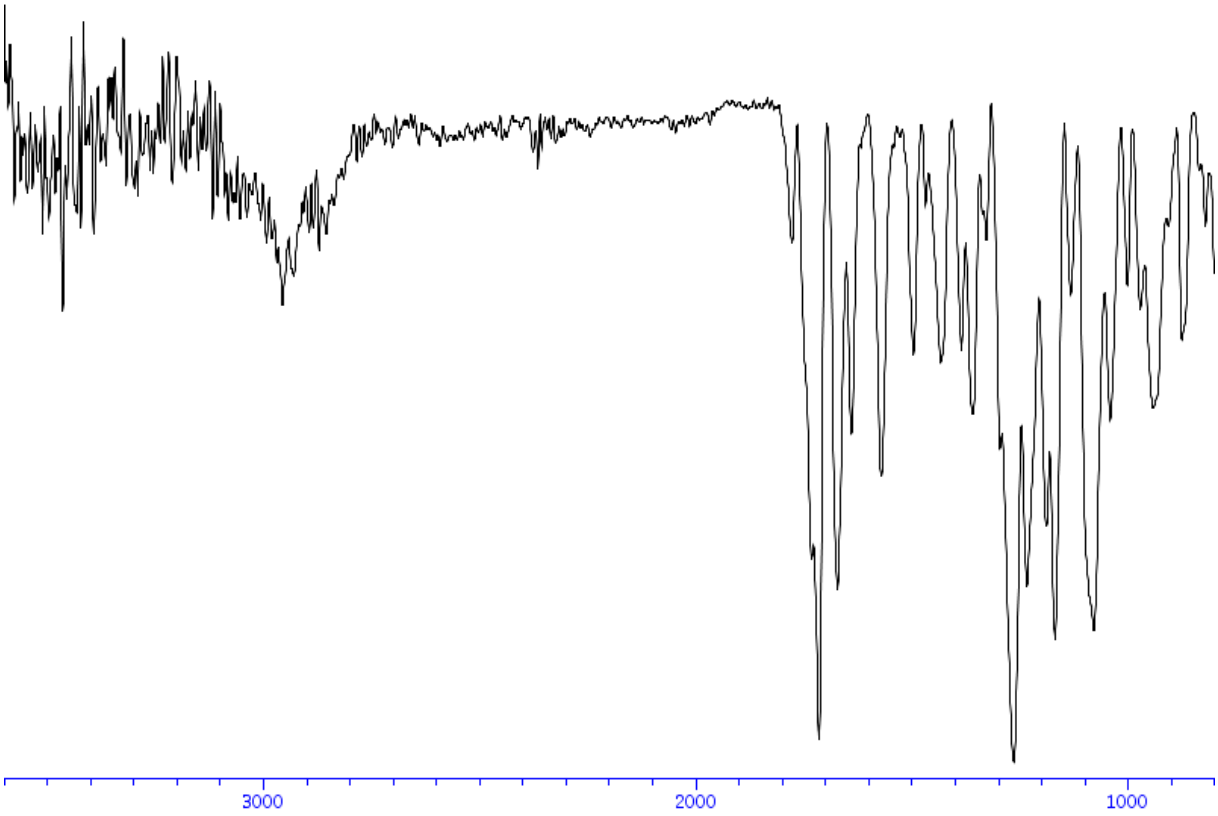

169.20
167.99
167.17
141.61
135.00
131.25
124.35
124.05
119.32
112.55
77.32 CDCl3
76.68 CDCl3
66.84
65.00
63.94
53.30
53.21
32.74
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

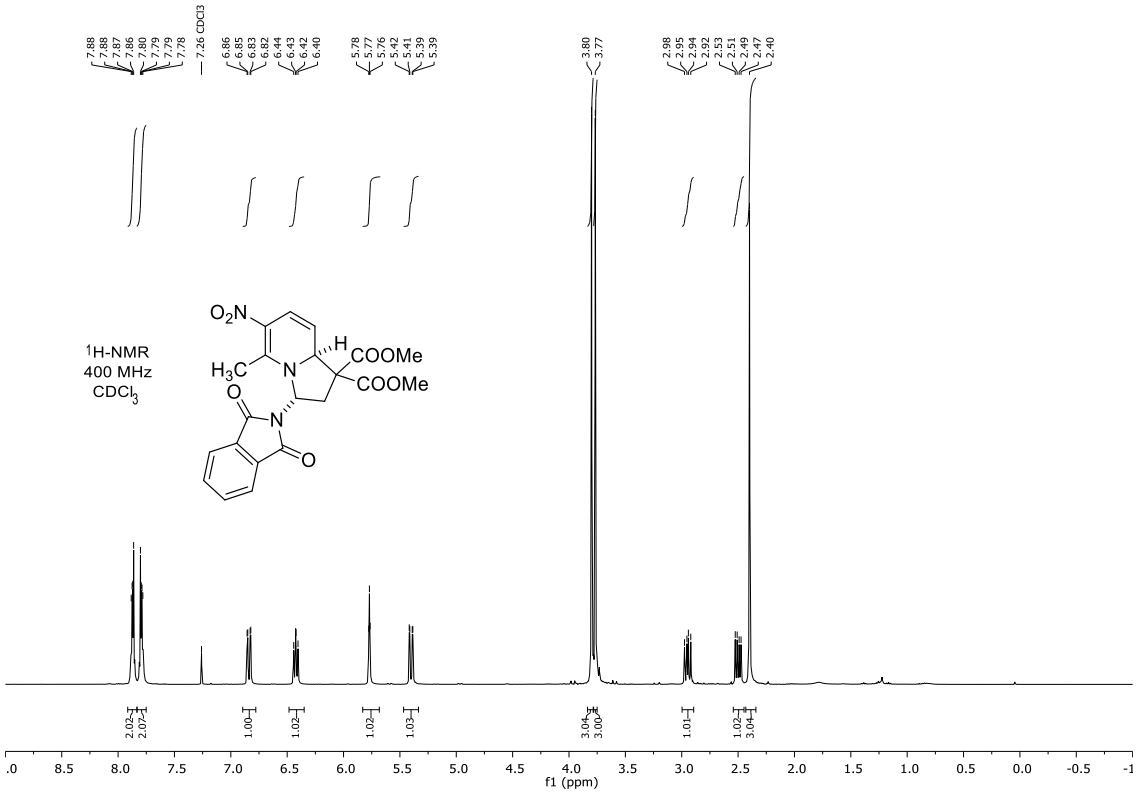
***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-7-methyl-6-nitro-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (60).**

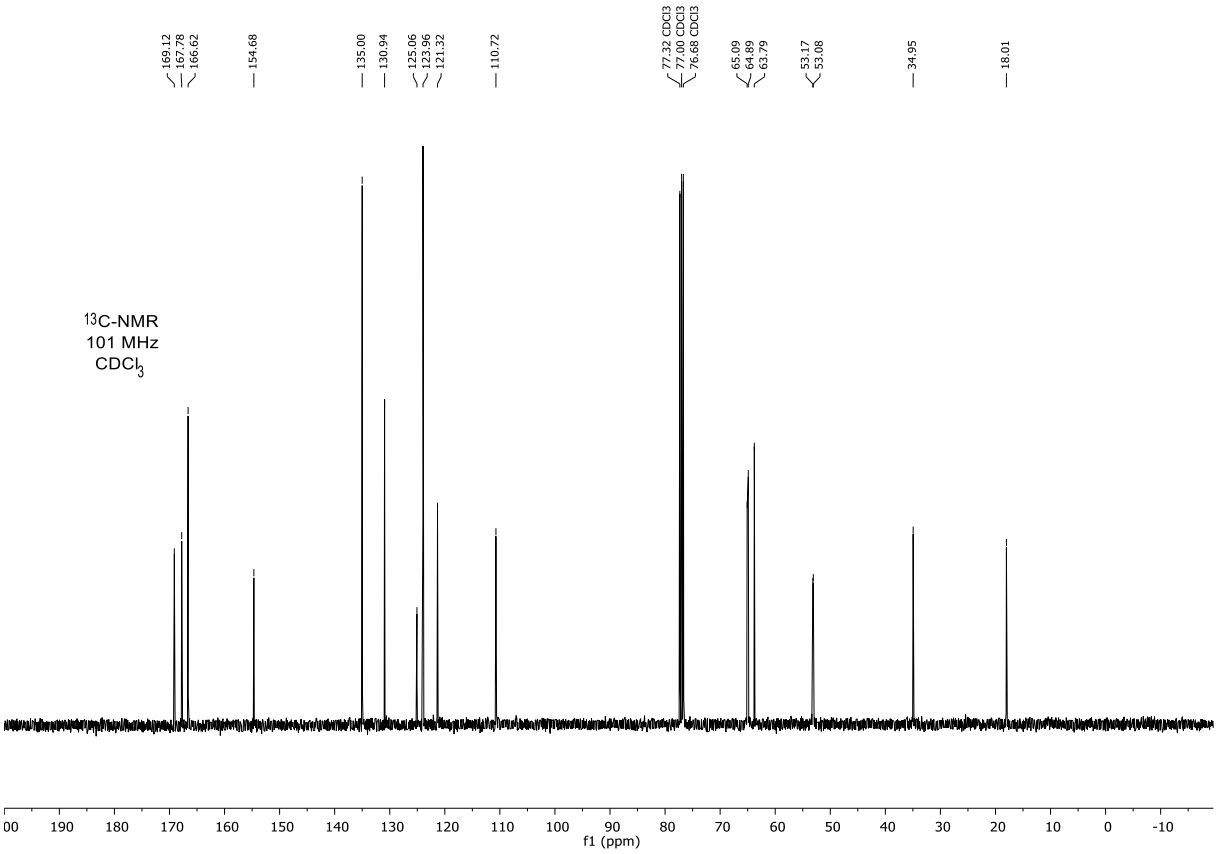


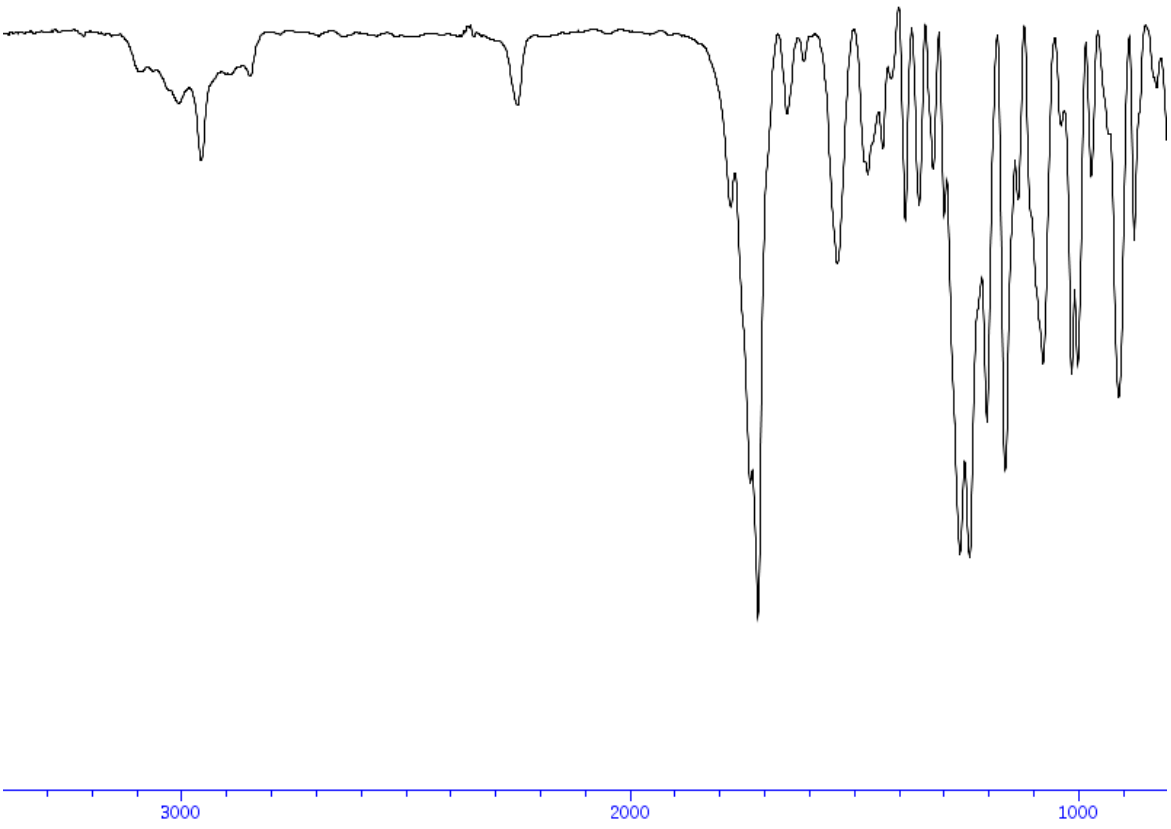




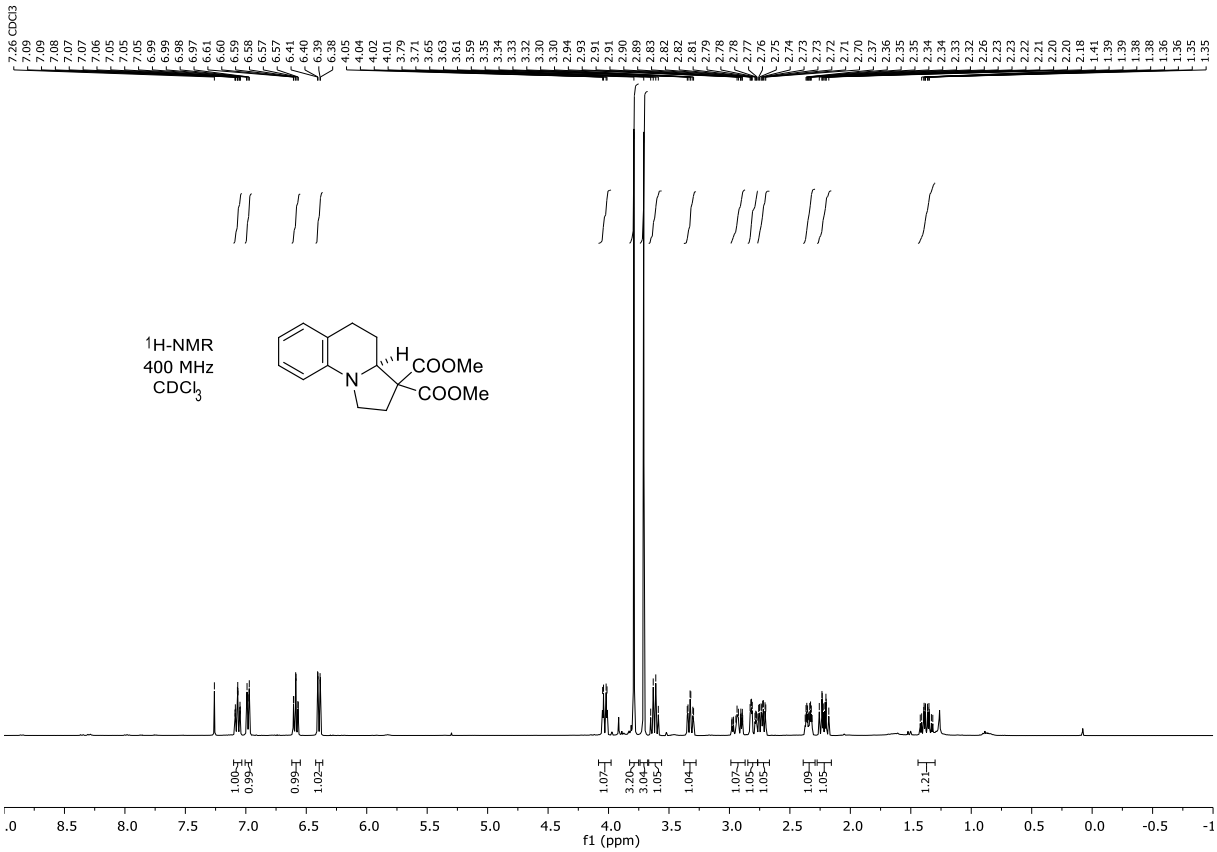
***anti*-Dimethyl 3-(1,3-dioxoisoindolin-2-yl)-5-methyl-6-nitro-2,3-dihydroindolizine-1,1(8a*H*)-dicarboxylate (61).**

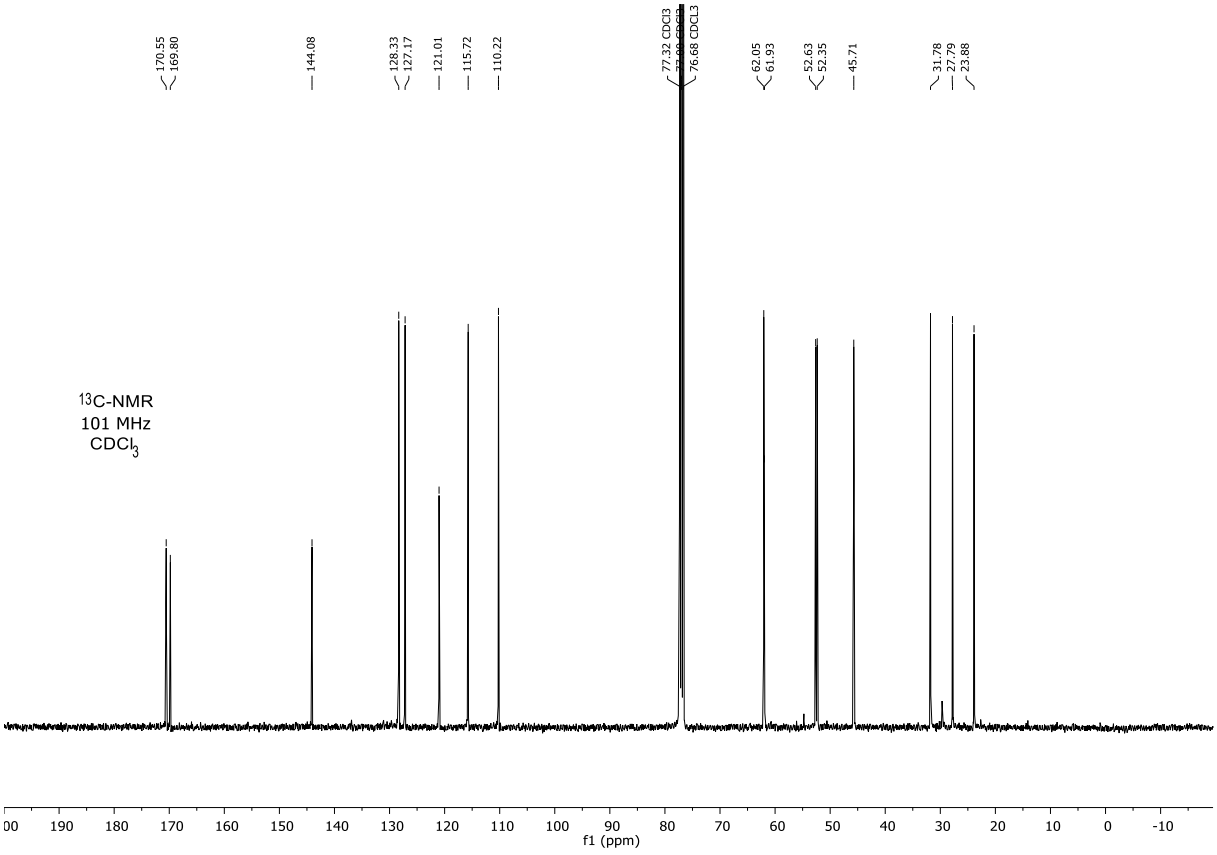


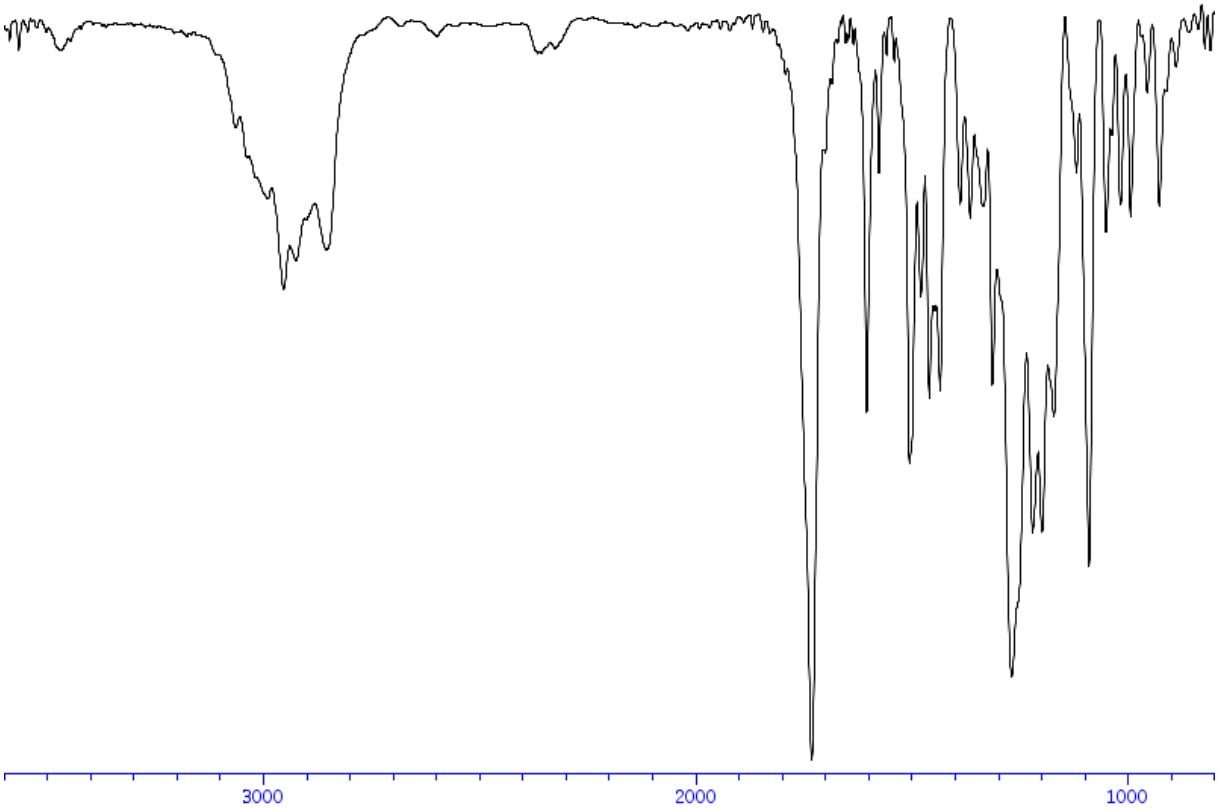

169.12
167.78
166.62
154.68
135.00
130.94
125.06
123.96
121.32
110.72
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
65.09
64.89
63.79
53.17
53.08
34.95
18.01
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

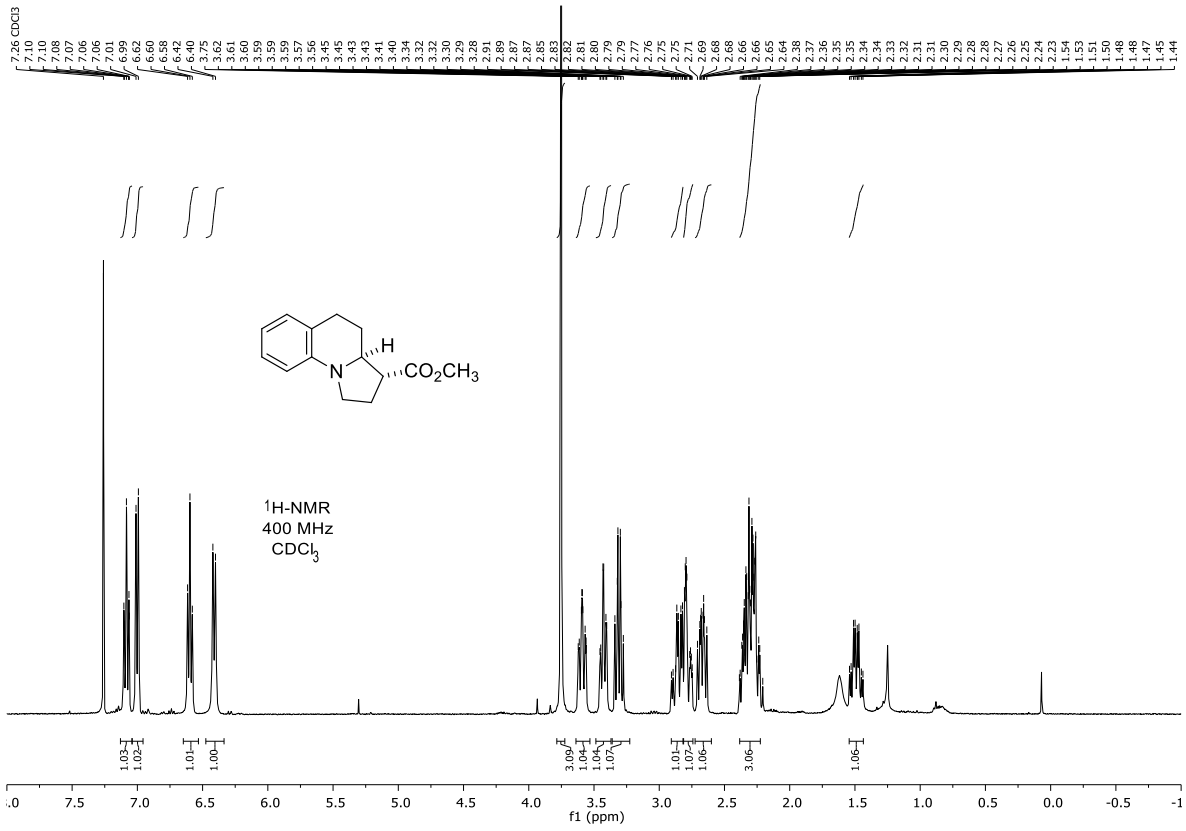
Dimethyl 1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**SI-75**).

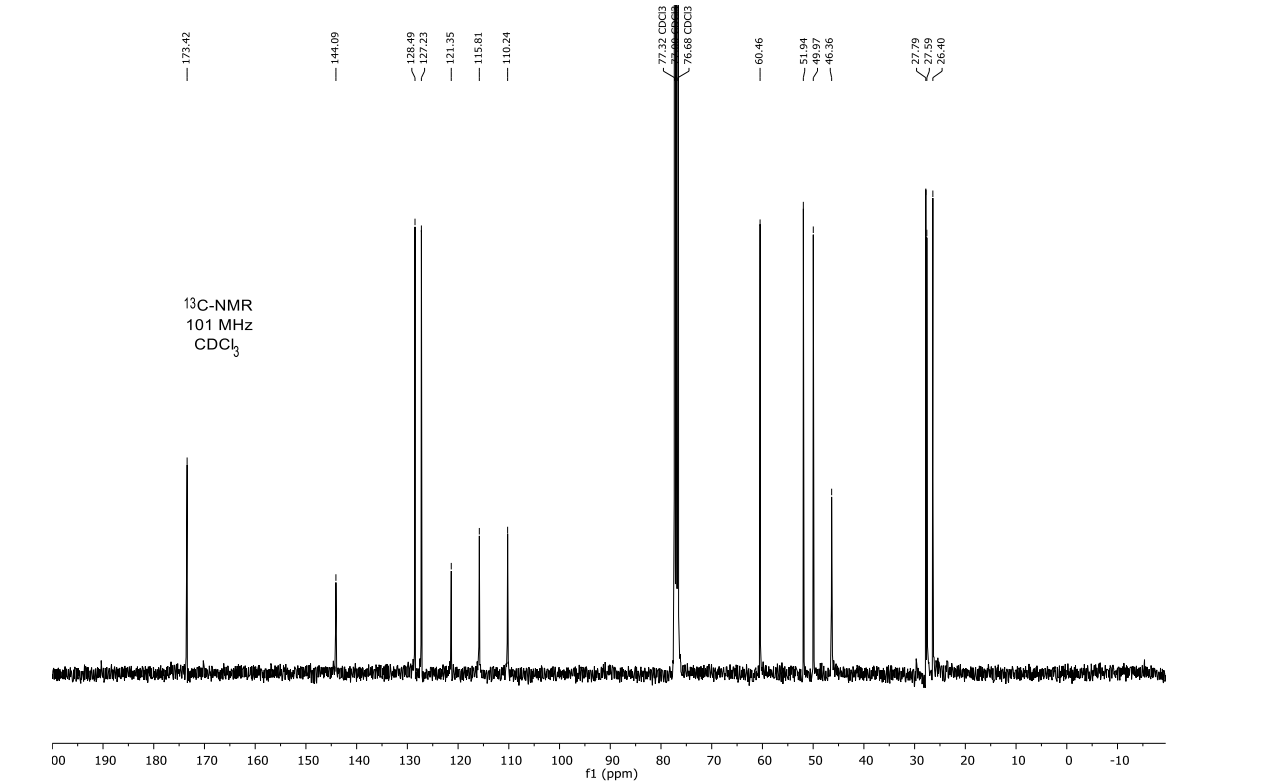


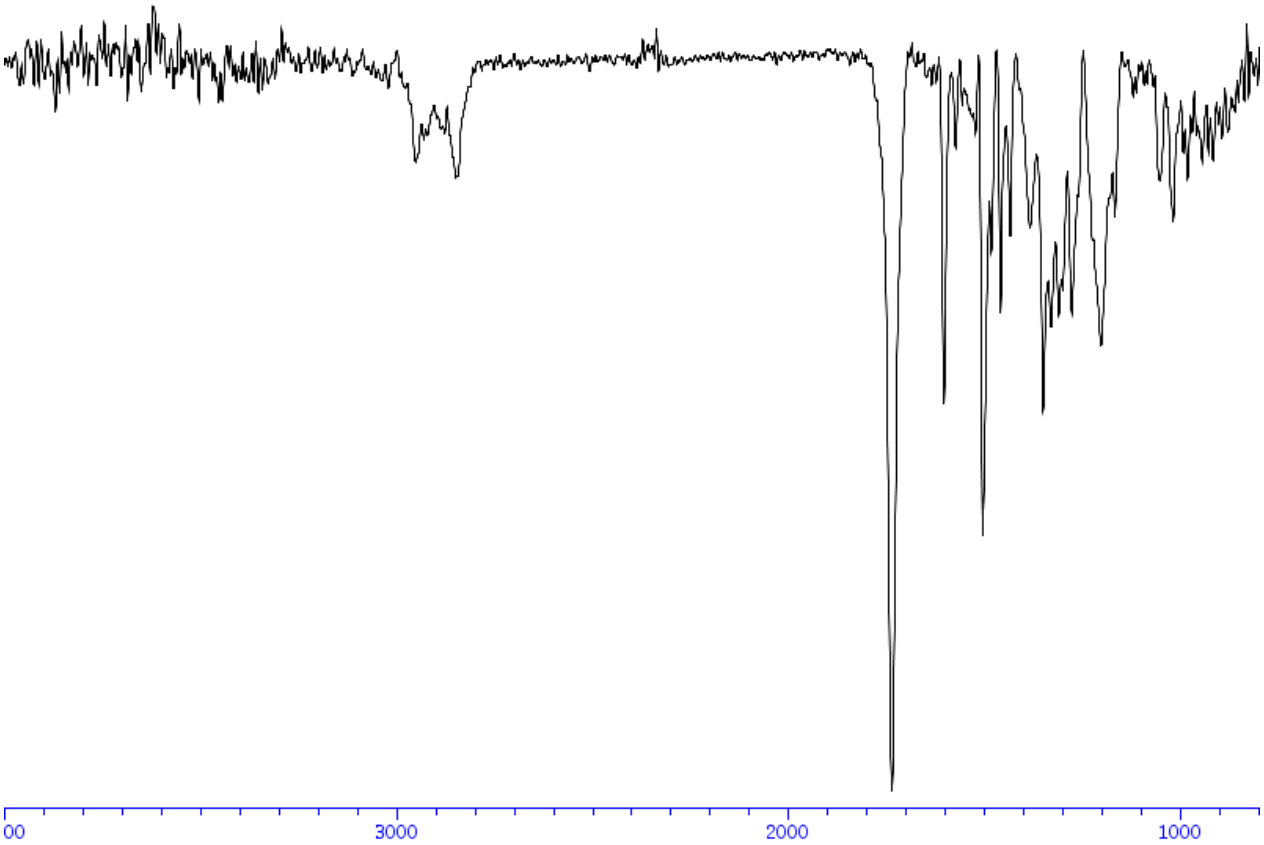




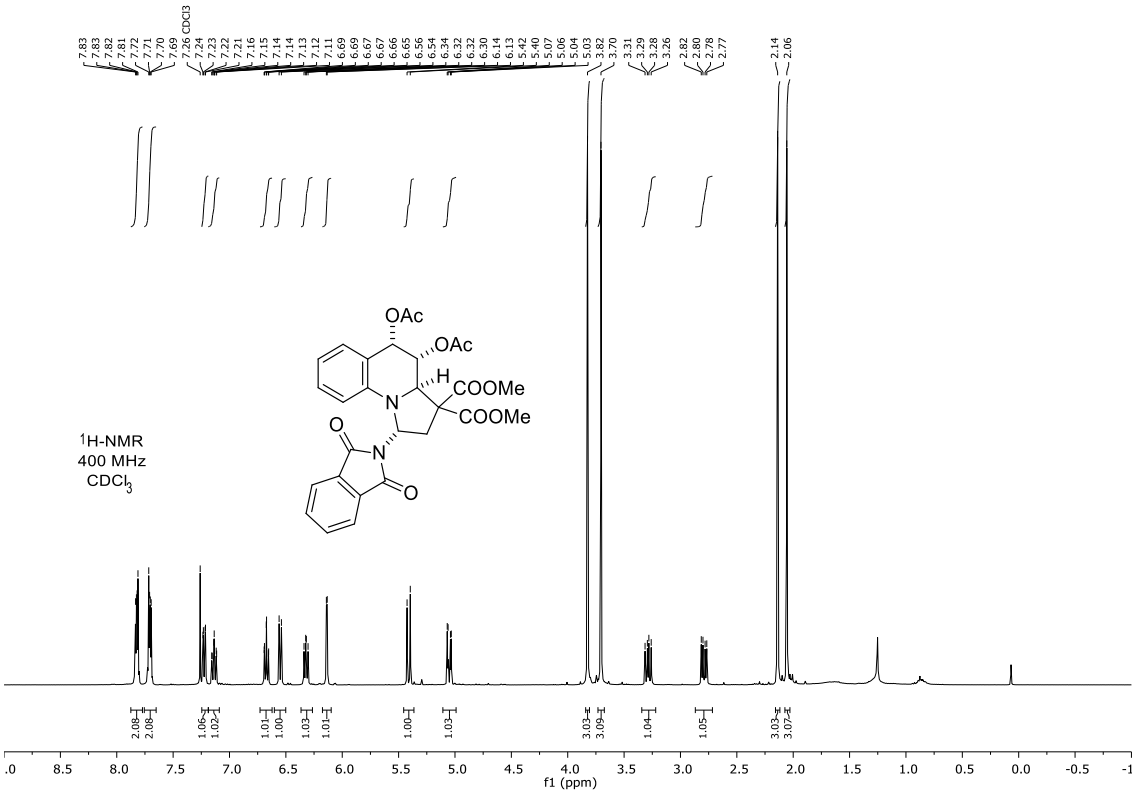
(3*S*,3a*R*)-methyl 1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinoline-3-carboxylate (62).

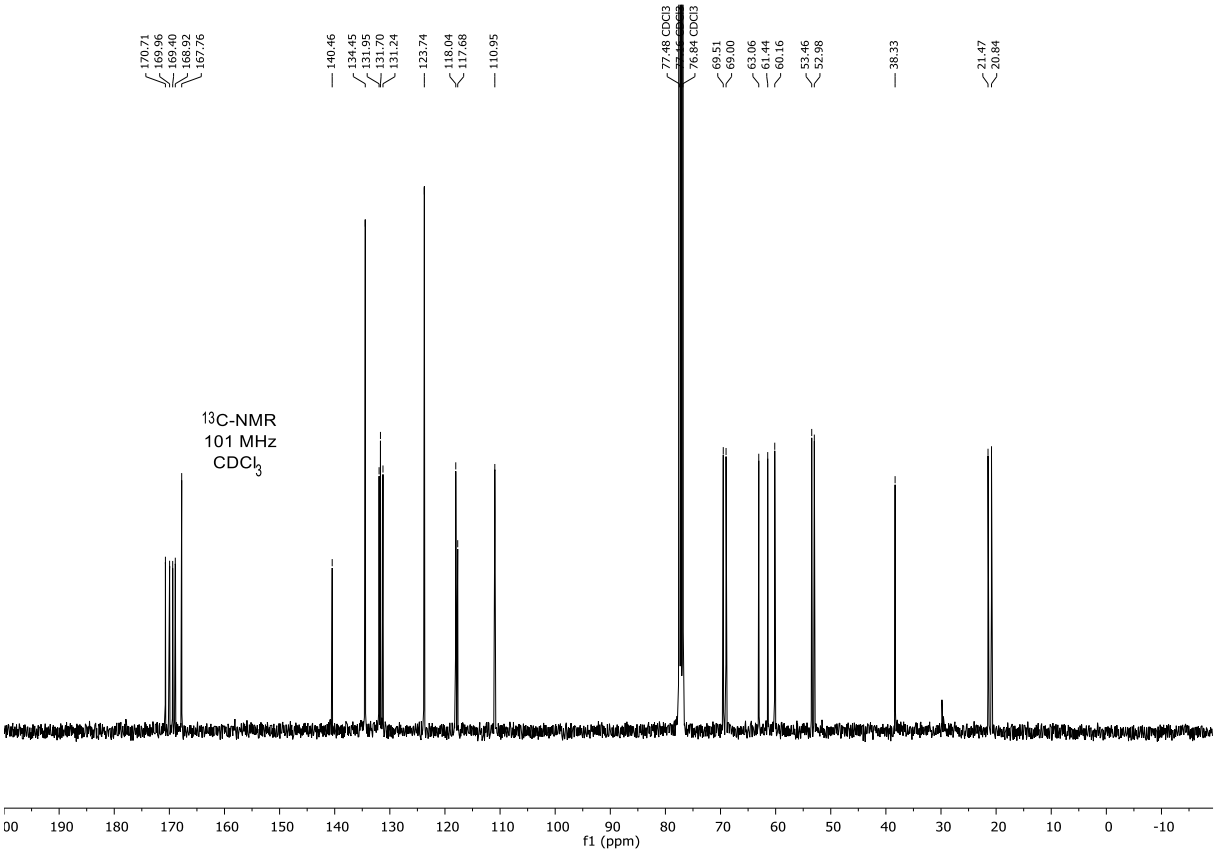


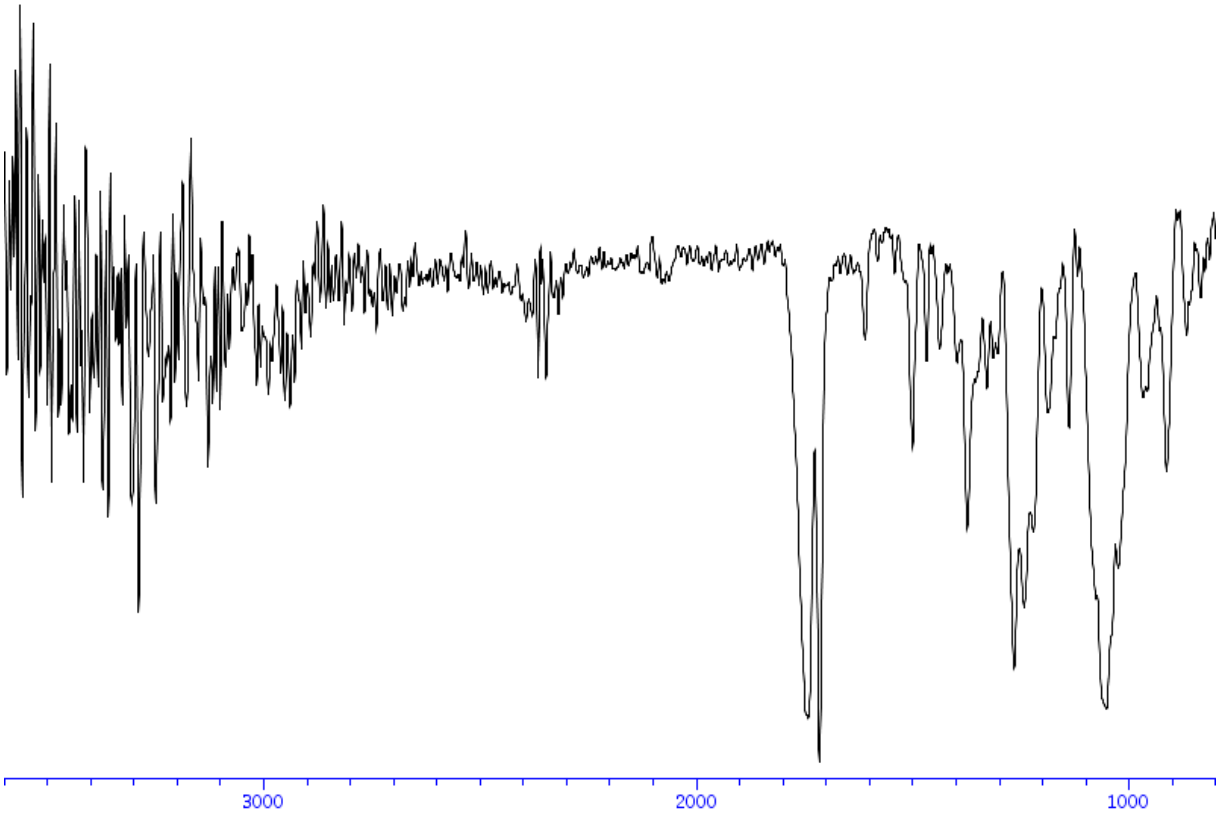

173.42
144.09
128.49
127.23
121.35
115.81
110.24
77.32 CDCl3
76.68 CDCl3
60.46
51.94
49.97
46.36
27.79
27.59
26.40
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000

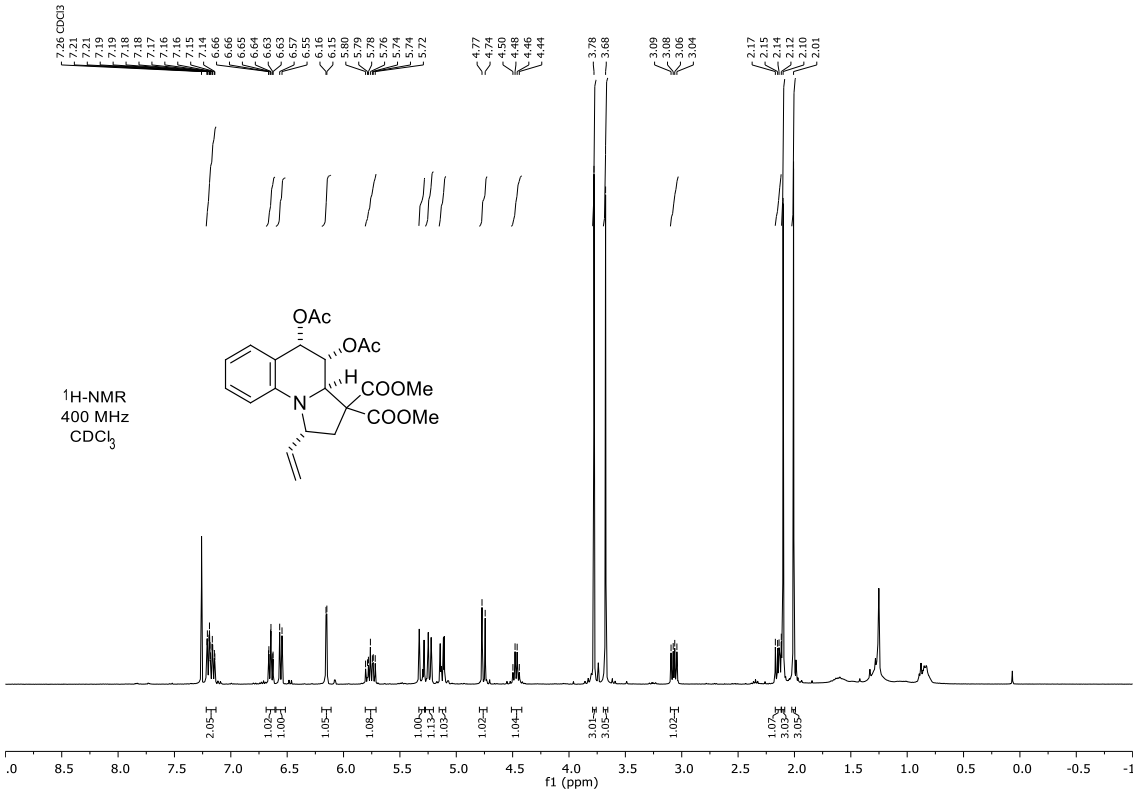
(1*R*,3a*S*,4*S*,5*R*)-Dimethyl 4,5-diacetoxy-1-(1,3-dioxoisoindolin-2-yl)-1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**SI-76**).

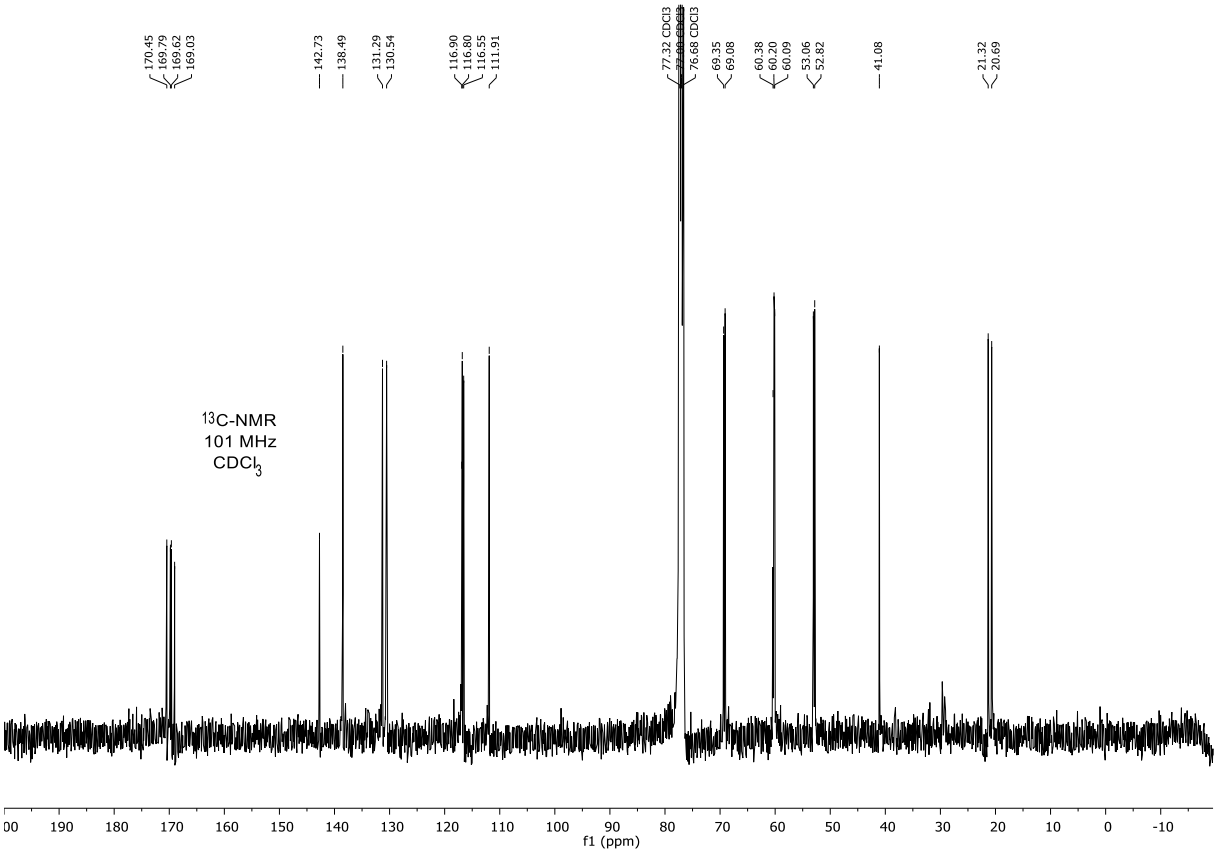


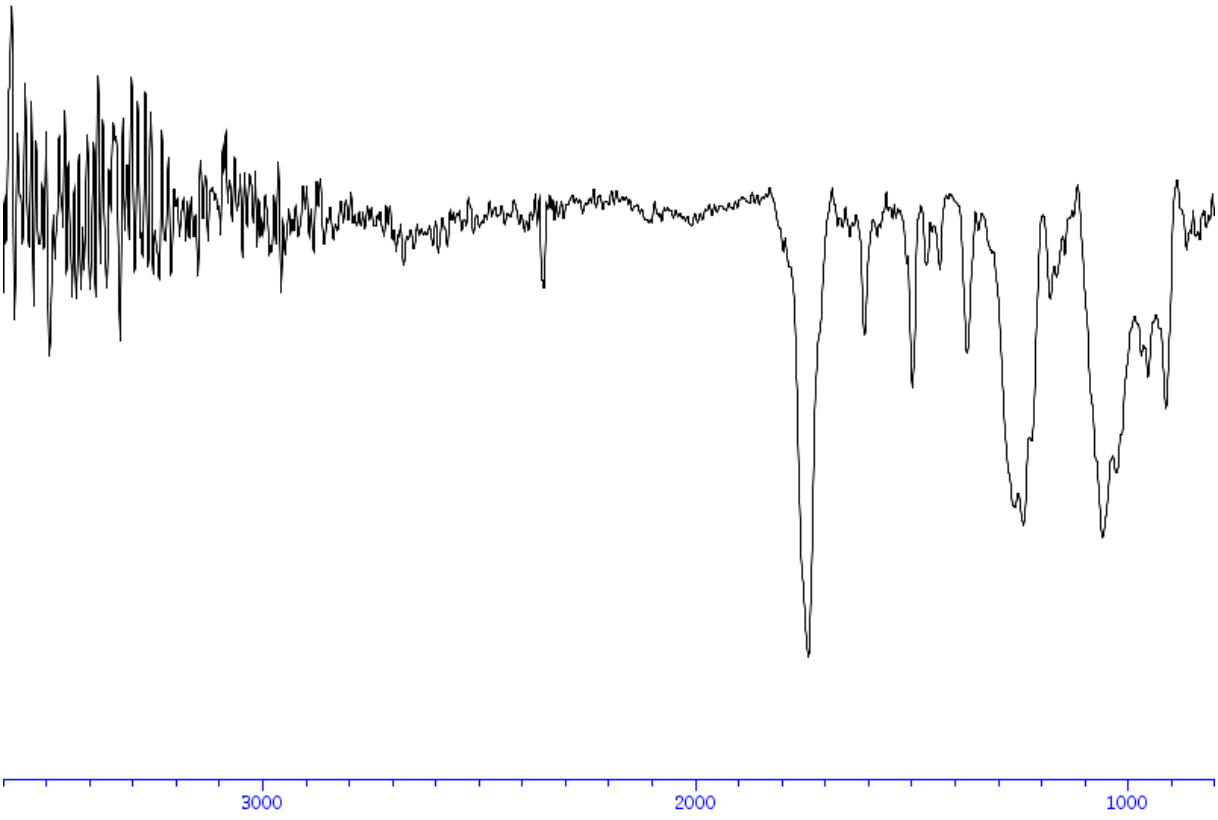




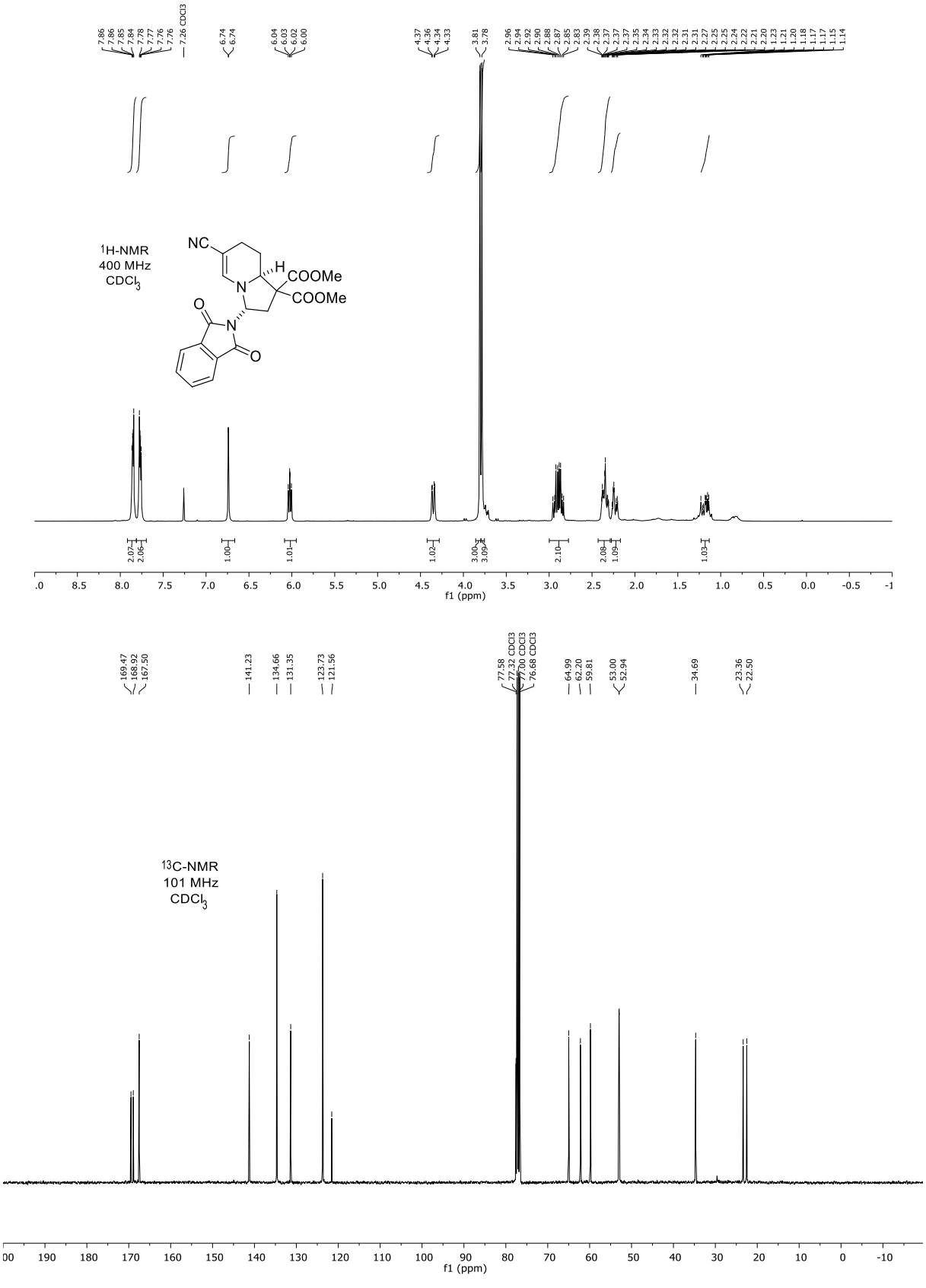
(1*S*,3a*S*,4*S*,5*R*)-Dimethyl 4,5-diacetoxy-1-vinyl-1,2,4,5-tetrahydropyrrolo[1,2-a]quinoline-3,3(3a*H*)-dicarboxylate (**63**).

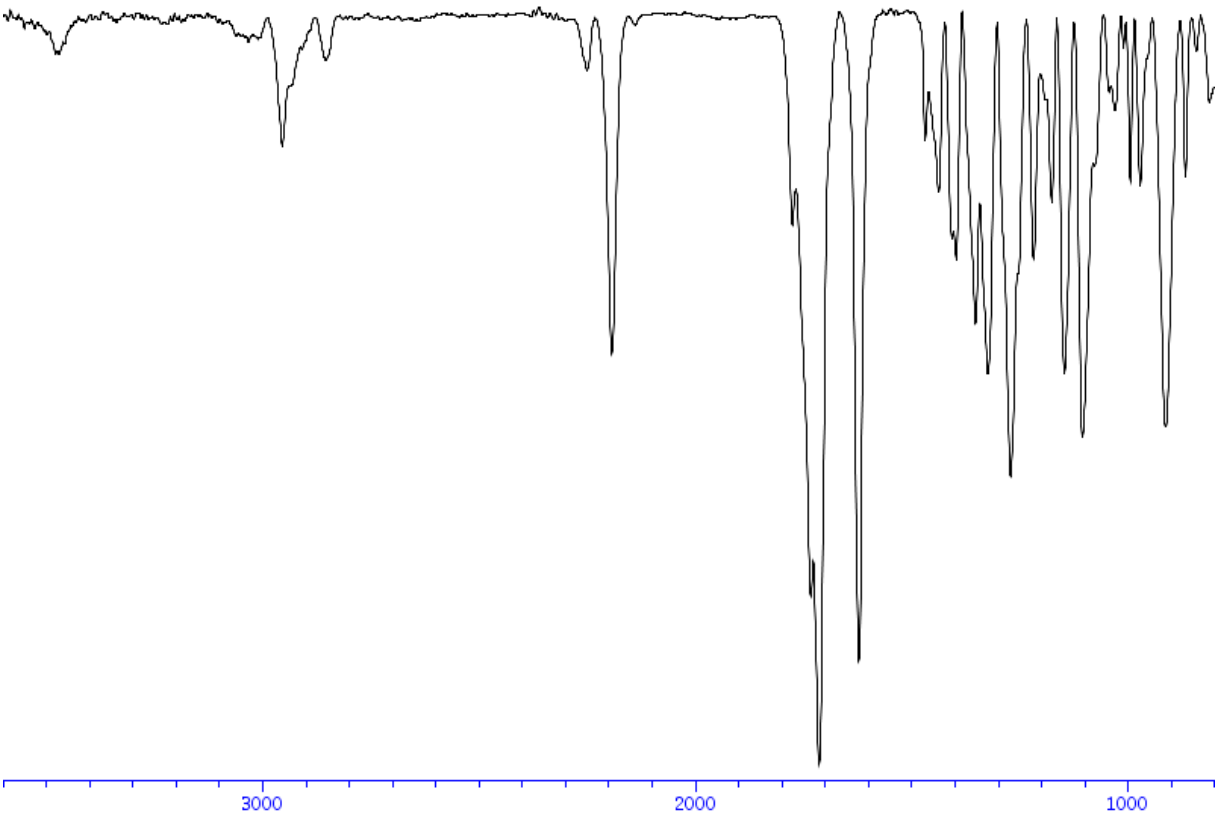



170.45
169.79
169.62
169.03
142.73
138.49
131.29
130.54
116.90
116.80
116.55
111.91
77.32 CDCl3
76.68 CDCl3
69.35
69.08
60.38
60.20
60.09
53.06
52.82
41.08
21.32
20.69
13C-NMR
101 MHz
CDCl3
f1 (ppm)

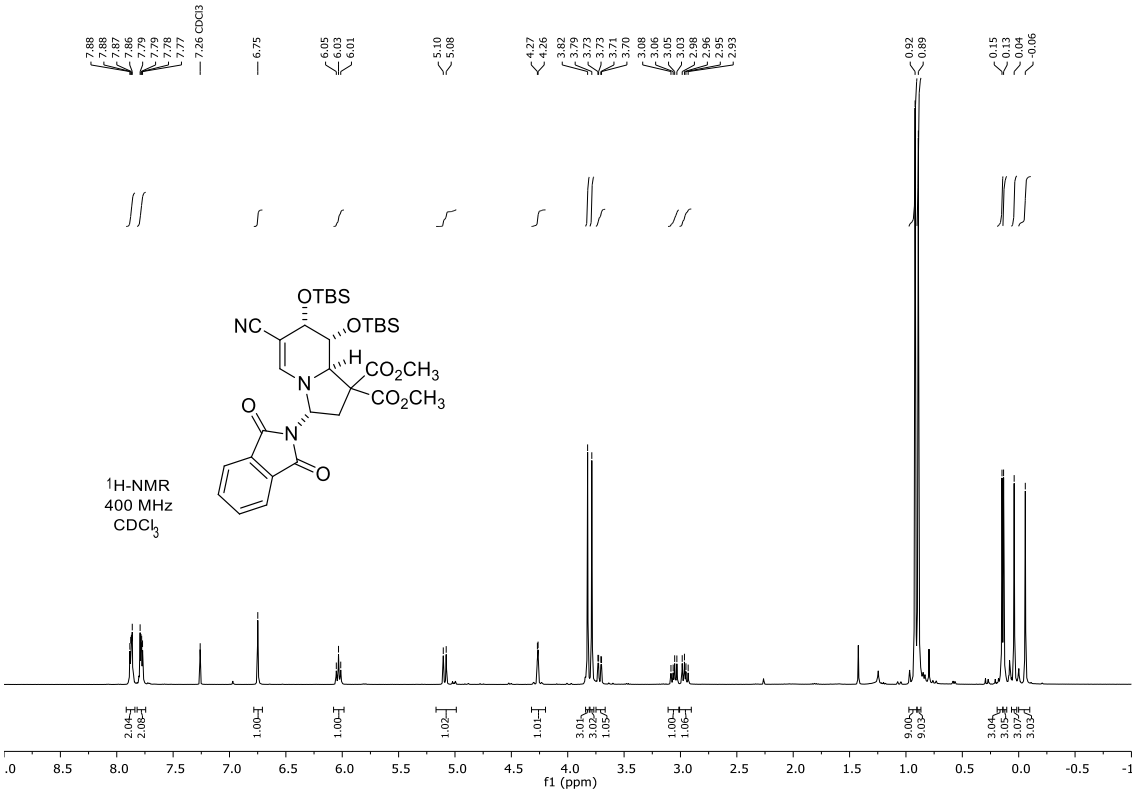

3000
2000
1000

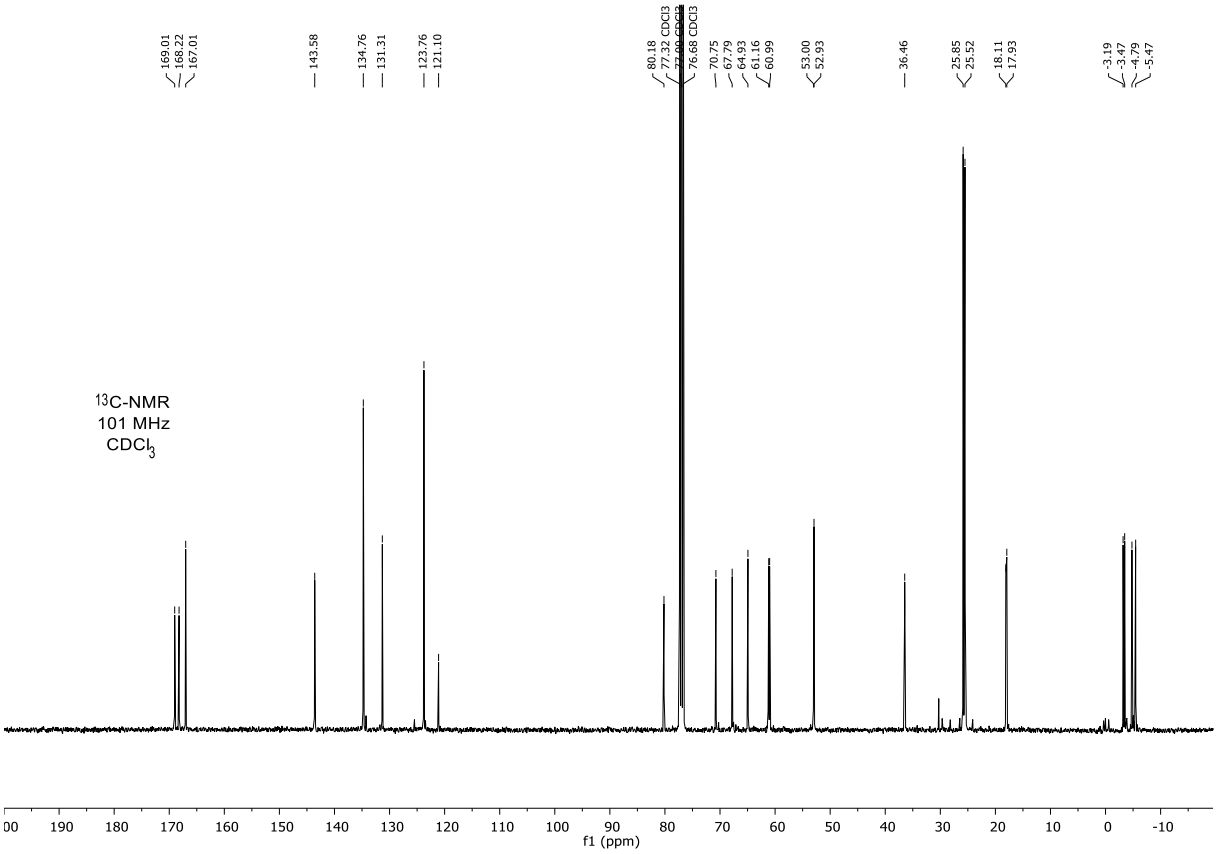
(3*R*,8a*R*)-Dimethyl 6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3,8,8a-tetrahydroindolizine-1,1(7*H*)-dicarboxylate (**64**).

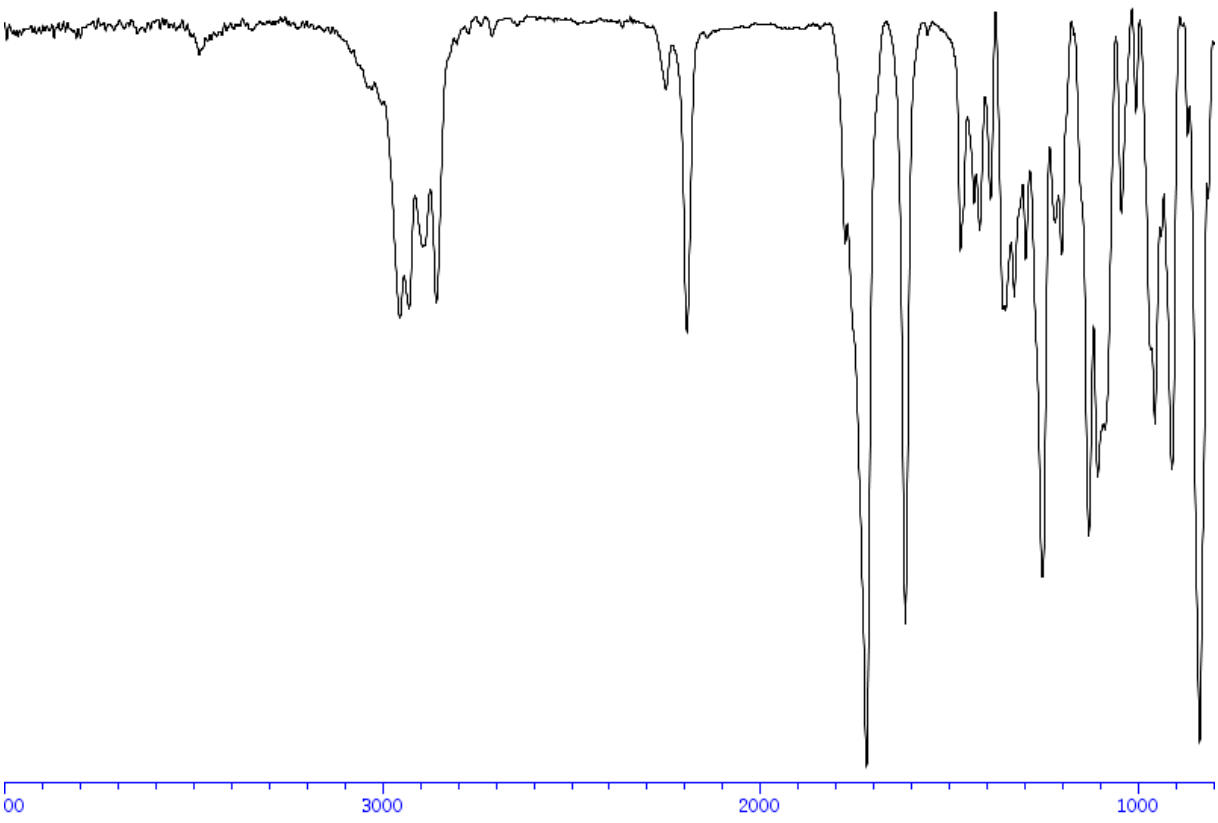




(3*R*,7*R*,8*S*,8a*S*)-Dimethyl 7,8-bis((*tert*-butyldimethylsilyl)oxy)-6-cyano-3-(1,3-dioxoisoindolin-2-yl)-2,3,8,8a-tetrahydroindolizine-1,1(7*H*)-dicarboxylate (**65**).




169.01
168.22
167.01
143.58
134.76
131.31
123.76
121.10
80.18
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
70.75
67.79
64.93
61.16
60.99
53.00
52.93
36.46
25.85
25.52
18.11
17.93
-3.19
-3.47
-4.79
-5.47
13C-NMR
101 MHz
CDCl3
f1 (ppm)


3000
2000
1000