Dynamic Kinetic Asymmetric [3+2] Annulation Reactions of Aminocyclopropanes.

Florian de Nanteuil,‡ Eloisa Serrano,‡ Daniele Perrotta and Jerome Waser.

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland.

Supporting Information Placeholder

ABSTRACT: In this communication, we report the first example of dynamic kinetic asymmetric [3+2] annulation reaction of aminocyclopropanes with both enol ethers and aldehydes. Using a copper catalyst and a commercially available bisoxazoline ligand, cyclopentyl- and tetrahydrofurylamines were obtained in 69-97% yield and up to a 98:2 enantiomeric ratio using the same reaction conditions. The method gives access to important enantio-enriched nitrogen building blocks for the synthesis of bioactive compounds.

The combination of nitrogen functionalities and cyclic structures is omnipresent in bioactive compounds. From the ten most sold pharmaceutical products based on small molecules in 2009, nine contain nitrogen atoms embedded in ring systems. Among the multitude of reported nitrogen-rich cyclic scaffolds, tetrahydrofurylamines and cyclopentylamines occupy a privileged position (Figure 1). Tetrahydrofurylamines are especially important in the form of aminosugars, such as aminodeoxyriboses **1**, which are at the core of DNA and many bioactive synthetic nucleoside analogues. Cyclopentylamines are well-represented in bioactive compounds, such as the bicyclic drug Ramipril (**2**) used to treat hypertension and heart diseases.[1] They are also at the core of numerous bioactive natural products, such as the antibiotic Pactamycin (**3**).[2] A stereoselective synthetic access to tetrahydrofuryl- and cyclopentylamines would be consequently highly valuable in order to discover new bioactive compounds.

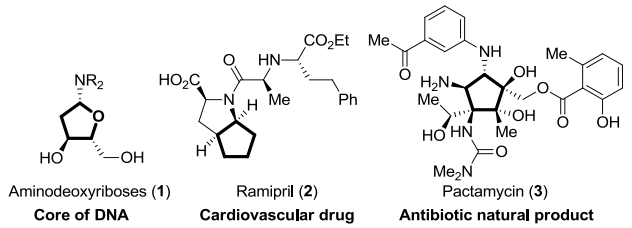
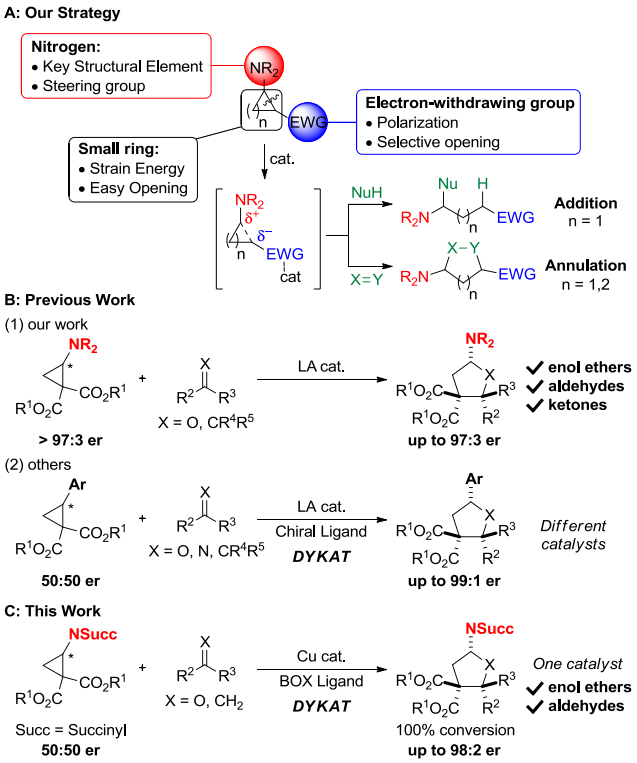


Figure 1: Biomolecules and bioactive compounds containing an amino- tetrahydrofuran or cyclopentane ring.

Since 2010, our group has examined the use of donor-acceptor substituted aminocyclopropanes and aminocyclobutanes for the synthesis of nitrogen-rich molecules (Scheme 1, **A**).[3] This approach is particularly attractive as the nitrogen atom plays a dual role: it is not only an essential structural element of the product, but also a steering group to control regioselective ring opening upon release of ring strain. Despite important progress in the use of donor-acceptor substituted cyclopropanes,[4] only few examples on the use of aminocyclopropanes had been reported prior to our own work.[5] In our hands, the ring-opening of aminocyclopropanes was highly successful for the inter- and intramolecular addition of nucleophiles[3a-c] and the development of new annulation reactions, in particular for the synthesis of cyclopentyl- and tetrahydrofurylamines ((1) in Scheme 1, **B**).[3d-g] The reaction of enol ethers and ketones using a tin catalyst was enantiospecific, whereas the iron-catalyzed annulation of aldehydes gave racemic products.

Scheme 1: General strategy (A), previous work (B) and current work (C) to access nitrogen-rich building blocks.



An approach allowing the complete conversion of easily accessible racemic aminocyclopropanes into enantiopure cyclopentylamines –a dynamic kinetic asymmetric transformation (DYKAT)-[6] would be much more straightforward. Such reactions have been realized for other classes of donor-acceptor cyclopro-

panes in the past,[7] but have never been reported in the case of aminocyclopropanes ((2) in Scheme 1, **B**). Furthermore, each class of substrates asked for the development of a unique catalytic system. The synthesis of cyclopentanes has been especially challenging. Success has been limited to the use of cyclic silyl enol ethers[7h] and indoles[7m] as substrates by Tang and co-workers using a copper catalyst with specifically designed bisoxazoline ligands.

Herein, we would like to report the first successful dynamic kinetic asymmetric annulation of aminocyclopropanes with enol ethers and aldehydes (Scheme 1, **C**). Enantiomeric ratios up to 98:2 could be achieved with complete conversion of the aminocyclopropane starting materials using a simple commercially available bisoxazoline catalyst. In contrast to the only previously reported method for silyl enol ethers,[7h] the transformation was especially successful for non-cyclic alkyl enol ethers. The same catalytic system could then be extended to the reaction of aminocyclopropanes with aldehydes to give tetrahydrofurylamines with up to a 96:4 enantiomeric ratio. To the best of our knowledge, this is the first report of an enantioselective catalytic system working for the synthesis of both cyclopentanes and tetrahydrofurans. The obtained enantiopure chiral building blocks will be highly useful for the synthesis of new nitrogen-rich bioactive compounds.

We started our investigations by studying the annulation reaction between phthalimido-substituted dimethyl ester cyclopropane **4a** and silyl enol ether **5a**, as this transformation had already been studied in our previous work involving enantiospecific reactions (Scheme 2).[3d,8] The catalytic system used in this work ($SnCl_4$ at -78 °C) was not well suited for the development of a dynamic kinetic asymmetric transformation, as it was highly enantiospecific at low temperature and led to decomposition at higher temperature. Consequently, a broad range of other catalysts and chiral ligands were examined. From these studies, copper bisoxazoline complex **7a** emerged as the most promising catalyst, leading to complete conversion of cyclopropane **4a** and formation of the cyclopentylamine **6a** in a 76:24 er and a very good diastereoselectivity (Scheme 2, **A**). Nevertheless, the enantioselectivity observed was still not satisfactory and the yield of the isolated product remained low and variable (0-50%) due to the formation of ring-opening side products resulting from a retro-aldol reaction.

To address these shortcomings, extensive optimization of the reaction conditions, cyclopropane and enol ethers substituents, as well as the catalyst structure was performed (Scheme 2, **B** and **C**).[9] No significant improvement could be obtained by changing solvent, temperature, concentration or catalyst loading. In contrast to what has been observed by Tang and co-workers,[7h] modification of the diester substituents was also not successful. Finally, four parameters were found to be crucial to increase the selectivity and the efficiency of the reaction:

1) Replacing the silyl group on the enol ether by an alkyl group (benzyl) allowed for a significant increase in yield and reproducibility. The higher stability of the carbon-oxygen bond was probably essential to prevent ring-opening side reactions.

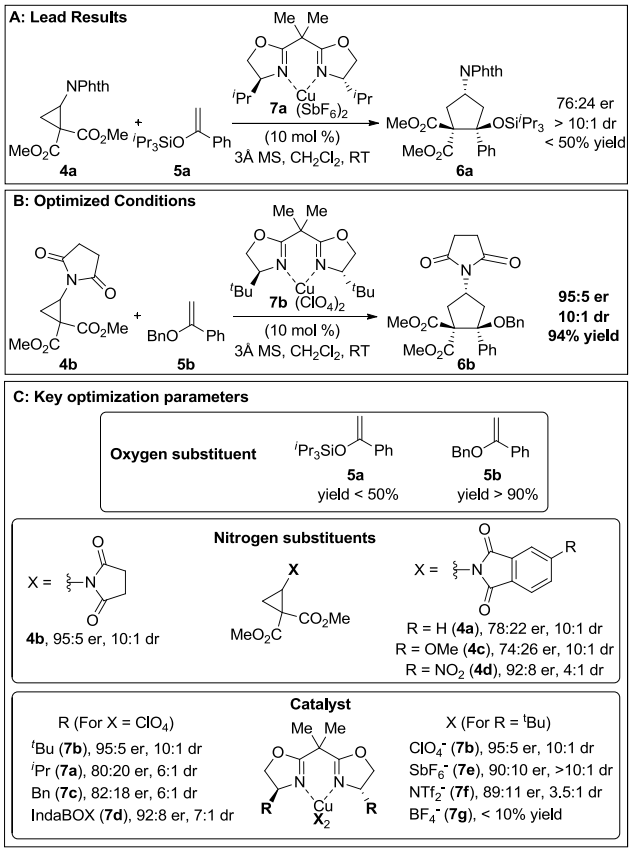
2) The structure of the substituents on the nitrogen was essential to achieve high enantioinduction. The enantiomeric ratio was lower with an electron-donating methoxy substituent on the phthalimide (74:26, cyclopropane **4c**), but increased significantly to 92:8 with a nitro substituent (cyclopropane **4d**). However, this increase of enantioselectivity came at the cost of a lower diastereoselectivity (4:1). On the other hand, replacing the phthalimide group by a succinimide led to the highest enantiomeric ratio (95:5) without compromising the diastereoselectivity.

3) Steric hindrance of the substituent on the ligand was another important factor. Best results were obtained with the commercially available bisoxazoline ligand bearing a bulky *tert*-butyl group.

4) Finally, a strong counteranion effect was observed. The highest enantioinduction was obtained with perchlorate, whereas hexafluoroantimonate led to the highest diastereoselectivity. To obtain high enantioselectivity, it was important to exclude moisture, as the blue copper aqua complex gave lower enantioinduction than the anhydrous green catalyst.

Under the optimized conditions, the desired cyclopentylamine **6b** could finally be obtained in 94% yield and a 95:5 er with good diastereoselectivity (10:1), setting the stage for the investigation of the scope of the reaction (Scheme 1, **B**).

Scheme 2: Lead result (A), optimized reaction conditions (B) and key parameters influencing yield and selectivity of the reaction.

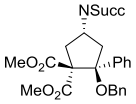
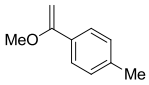
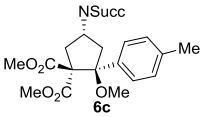
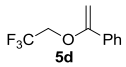
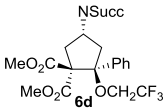
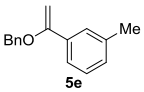
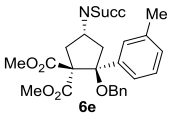
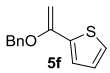
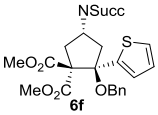
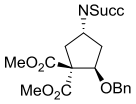
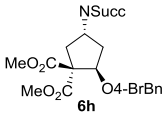
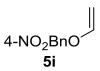
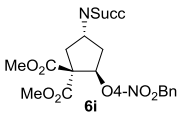


On preparative scale, cyclopentylamine **6b** could be obtained in quantitative yield with a 96:4 er and a 7:1 dr (Table 1, entry 1).Variation of the oxygen substituent was examined first: A methyl enol ether (entry 2) and a more electron-withdrawing trifluoroethyl group (entry 3) both worked in the annulation reaction, but for the latter the diastereoselectivity of the reaction was lost. Variation of the aromatic substituent on the olefin gave comparable enantioinduction for both a *meta* methyl-substituted phenyl ring (entry 4) and a thiophene heterocycle (entry 5). The annulation reaction was not limited to the synthesis of tertiary ethers: unsubstituted benzyl ethers **5g-i** also gave the desired products with useful selectivity (entries 6-8). On a 1 mmol scale, product **6g** was obtained in 80% yield and a 95.5:4.5 er (entry 6).

Achieving high selectivity in DYKAT processes is challenging and the catalytic system often has to be optimized for each class of substrates. Nevertheless, when benzaldehyde (**8a**) was used in the [3+2] annulation process with aminocyclopropane **4b**, the DYKAT process was successful and gave the desired tetrahydrofurylamine **9a** with a 92:8 er and a 13:1 dr (Table 2, entry 1). The annulation reaction was successful for both electron-rich (entries

2 and 3) and electron-poor (entry 4) aromatic aldehydes, as well as for thiophene carboxaldehyde (**8e**) (entry 5). The best enantiomeric ratio (96:4) was observed for the *para*-methoxy substituted benzene ring (entry 2). The reaction was not limited to aromatic aldehydes: both cinnamaldehyde (**8f**) (entry 6) and aliphatic aldehyde **8g** (entry 7) could be used.

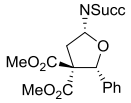
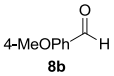
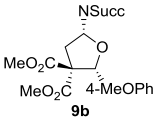
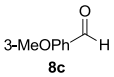
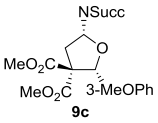
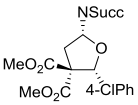
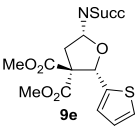
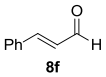
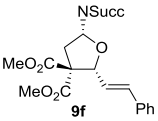
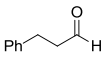
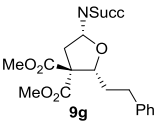
Table 1. Scope of the annulation reaction with enol ethers.[a]

Entry	Enol Ether	Product	Yield[b]/er[c]/dr[d]
1	 **5b**	 **6b**	97% 96:4 er 7:1 dr
2	 **5c**	 **6c**	95% 94.5:5.5 er 20:1 dr
3	 **5d**	 **6d**	88% 95.5:4.5 er[e] 1.5:1 dr
4	 **5e**	 **6e**	99% 95:5 er >20:1 dr
5	 **5f**	 **6f**	94% 94:6 er 8:1 dr
6	 **5g**	 **6g**	96% (80%)[f] 96.5:3.5 (95.5:4.5) er 4:1 (4:1) dr
7	 **5h**	 **6h**	73% 94.5:5.5 er 5:1 dr
8	 **5i**	 **6i**	82% 98:2 er 5:1 dr

[a]Reaction conditions: 0.20 mmol cyclopropane **4b**, 0.40 mmol enol ether **5**, 0.02 mmol catalyst **7b**, 3Å MS in dichloromethane at room temperature, under argon. [b]Yield after purification by column chromatography. [c]Determined by chiral phase HPLC. [d]Determined by analysis of crude ^{1}H NMR. [e]Value for major *anti* diastereoisomer, *syn* diastereoisomer: er = 96.5:3.5. [f]Values in brackets correspond to the results on 1 mmol scale.

The absolute configuration of **6g** was determined by X-ray crystallography (*S* at the center next to the nitrogen atom, Figure 2). Interestingly, the absolute configuration is opposite to the one obtained by Tang and co-workers.[7h,7m] Although further experiments will be required to establish the origin of asymmetric induction, we propose a tentative stereochemical model based on the strong distortion from the square planar geometry in *tert*-butyl-substituted bisoxazoline complexes, which is also apparent in the *bis*-aqua complex of **7b** (Scheme 3).[10] In complex **I**, formed from the *R* enantiomer of cyclopropane **4b**, the distortion moves the cyclopropane to the upper right quadrant, opening a free path for fast attack of the nucleophile and affording the product with the observed absolute configuration. In complex **II** formed from the *S* enantiomer, the attack of the nucleophile is blocked by the *tert*-butyl substituents of the ligand, and is therefore slower.

Table 2. Scope of the annulation reaction with aldehydes.[a]

Entry	aldehyde	Product	Yield[b]/er[c]/dr[d]
1	 **8a**	 **9a**	82% 92:8 er 13:1 dr
2	 **8b**	 **9b**	69% 96:4 er >20:1 dr
3	 **8c**	 **9c**	84% 93:7 er 10:1 dr
4	 **8d**	 **9d**	90% 91:9 er 14:1 dr
5	 **8e**	 **9e**	97% 95:5 er >20:1 dr
6	 **8f**	 **9f**	96% 94:6 er 14:1 dr
7	 **8g**	 **9g**	85% 91.5:8.5 er 13:1 dr

[a]Reaction conditions: 0.20 mmol cyclopropane **4b**, 0.40 mmol aldehyde **8**, 0.02 mmol catalyst **7b**, 3Å MS in dichloromethane at room temperature, under argon. [b]Yield after purification by column chromatography. [c]Determined by chiral phase HPLC. [d]Determined by analysis of crude ^{1}H NMR.

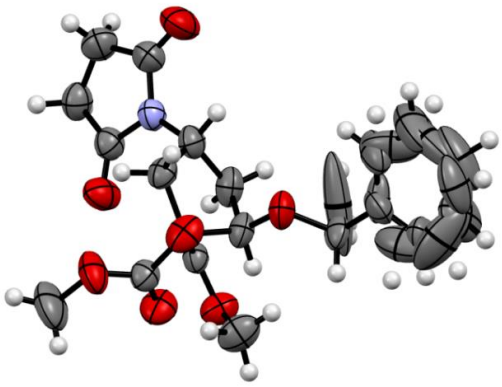
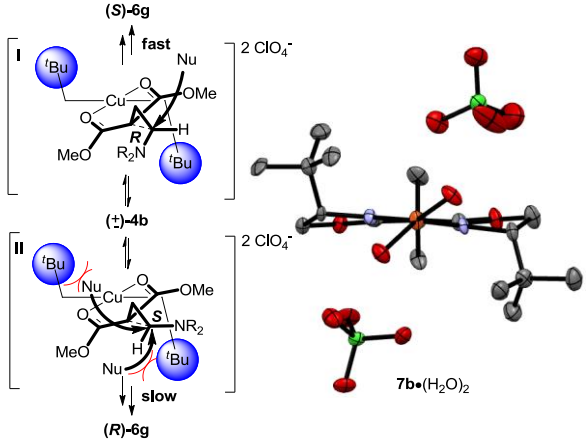


Figure 2: X-ray structure of compound **6g**.[11]

In summary, we have reported the first example of dynamic kinetic asymmetric [3+2] annulation reaction of aminocyclopropanes. The reaction proceeded with high enantioselectivity and diastereoselectivity with a broad range of acyclic alkyl enol ethers and aldehydes using a copper catalyst with a commercially available bisoxazoline ligand. Importantly, the developed catalytic system could be used for both types of substrates without re-optimization. The method is expected to be highly useful for the asymmetric synthesis of nitrogen-rich small organic molecules.

Scheme 3: Stereochemical model for the reaction and X-ray structure of complex 7b•$(H_2O)_2$.[12]



ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

jerome.waser@epfl.ch

Author Contributions

‡These authors contributed equally.

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

We thank F. Hoffmann-La Roche Ltd for an unrestricted research grant and the Swiss National Science Foundation (SNSF, grant number 200021_129874 and 200020_149494) for financial support. We thank Mr. Kurt Schenk of the Institute of the Physics of Biological Systems at EPFL for the X-ray studies.

REFERENCES

(1) Yusuf, S.; Teo, K. K.; Pogue, J.; Dyal, L.; Copland, I.; Schumacher, H.; Ingelheim, B.; Dagenais, G.; Sleight, P.; Anderson, C. *N. Engl. J. Med.* **2008**, *358*, 1547.

(2) (a) Brodersen, D. E.; Clemons, W. M.; Carter, A. P.; Morgan-Warren, R. J.; Wimberly, B. T.; Ramakrishnan, V. *Cell* **2000**, *103*, 1143. (b) Malinowski, J. T.; Sharpe, R. J.; Johnson, J. S. *Science* **2013**, *340*, 180.

(3) Additions: (a) De Simone, F.; Gertsch, J.; Waser, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5767. (b) de Nanteuil, F.; Loup, J.; Waser, J. *Org. Lett.* **2013**, *15*, 3738. (c) Frei, R.; Staedler, D.; Raja, A.; Franke, R.; Sasse, F.; Gerber-Lemaire, S.; Waser, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 13373. Annulations: (d) de Nanteuil, F.; Waser, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 12075. (e) Benfatti, F.; de Nanteuil, F.; Waser, J. *Chem. Eur. J.* **2012**, *18*, 4844. (f) Benfatti, F.; de Nanteuil, F.; Waser, J. *Org. Lett.* **2012**, *14*, 386. (g) de Nanteuil, F.; Waser, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 9009.

(4) (a) Reissig, H. U.; Zimmer, R. *Chem. Rev* **2003**, *103*, 1151. (b) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321. (c) Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051. (d) De Simone, F.; Waser, J. *Synthesis* **2009**, 3353. (e) Lebold, T. P.; Kerr, M. A. *Pure Appl. Chem.* **2010**, *82*, 1797. (f) Mel'nikov, M. Y.; Budynina, E. M.; Ivanova, O. A.; Trushkov, I. V. *Mendeleev Commun.* **2011**, *21*, 293. (g) Schneider, T. F.; Werz, D. B. *Org. Lett.* **2011**, *13*, 1848. (h) Tang, P.; Qin, Y. *Synthesis* **2012**, *44*, 2969.

(5) For selected examples, see: (a) Wenkert, E.; Hudlicky, T.; Showalter, H. D. H. *J. Am. Chem. Soc.* **1978**, *100*, 4893. (b) Ha, J. D.; Lee, J. W.; Blackstock, S. C.; Cha, J. K. *J. Org. Chem.* **1998**, *63*, 8510. (c) Williams, C. M.; de Meijere, A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3699. (d) Larquetoux, L.; Ouhamou, N.; Chiaroni, A.; Six, Y. *Eur. J. Org. Chem.* **2005**, 4654. (e) Madelaine, C.; Six, Y.; Buriez, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 8046. (f) Yang, J.; Wu, H. X.; Shen, L. Q.; Qin, Y. *J. Am. Chem. Soc.* **2007**, *129*, 13794. (g) Zhang, D.; Song, H.; Qin, Y. *Acc. Chem. Res.* **2011**, *44*, 447. For recent examples reported after publication of our work, see: (h) Gharpure, S. J.; Vijayasree, U.; Reddy, S. R. B. *Org. Biomol. Chem.* **2012**, *10*, 1735. (i) Maity, S.; Zhu, M. Z.; Shinabery, R. S.; Zheng, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 222. (j) Rivero, A. R.; Fernandez, I.; Sierra, M. A. *Org. Lett.* **2013**, *15*, 4928. (k) Tejero, R.; Ponce, A.; Adrio, J.; Carretero, J. C. *Chem. Comm.* **2013**, *49*, 10406.

(6) Steinreiber, J.; Faber, K.; Griengl, H. *Chem. Eur. J.* **2008**, *14*, 8060.

(7) DYKAT: (a) Parsons, A. T.; Johnson, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 3122. (b) Parsons, A. T.; Smith, A. G.; Neel, A. J.; Johnson, J. S. *J. Am. Chem. Soc.* **2010**, *132*, 9688. (c) Wales, S. M.; Walker, M. M.; Johnson, J. S. *Org. Lett.* **2013**, *15*, 2558. (d) Trost, B. M.; Morris, P. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 6167. (e) Trost, B. M.; Morris, P. J.; Sprague, S. J. *J. Am. Chem. Soc.* **2012**, *134*, 17823. (f) Mei, L. Y.; Wei, Y.; Xu, Q.; Shi, M. *Organometallics* **2012**, *31*, 7591. (g) Mei, L. Y.; Wei, Y.; Xu, Q.; Shi, M. *Organometallics* **2013**, *32*, 3544. (h) Xu, H.; Qu, J. P.; Liao, S. H.; Xiong, H.; Tang, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 4004. Only the examples based on cyclopropanes as limiting substrates are listed. Kinetic resolutions and other asymmetric transformations: (i) Sibi, M. P.; Ma, Z. H.; Jasperse, C. P. *J. Am. Chem. Soc.* **2005**, *127*, 5764. (j) Kang, Y. B.; Sun, X. L.; Tang, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3918. (k) Zhou, Y. Y.; Wang, L. J.; Li, J.; Sun, X. L.; Tang, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9066. (l) Zhou, Y. Y.; Li, J.; Ling, L.; Liao, S. H.; Sun, X. L.; Li, Y. X.; Wang, L. J.; Tang, Y. *Angew. Chem., Int. Ed.* **2013**, *52*, 1452. (m) Xiong, H.; Xu, H.; Liao, S. H.; Xie, Z. W.; Tang, Y. *J. Am. Chem. Soc.* **2013**, *135*, 7851. (n) Moran, J.; Smith, A. G.; Carris, R. M.; Johnson, J. S.; Krische, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 18618.

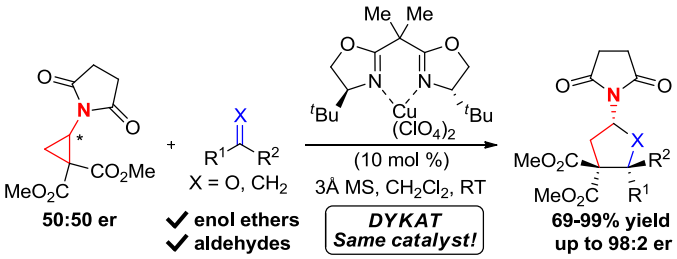
(8) The enol ethers and cyclopropanes used in this study were synthesized using modified reported procedures: Enol ethers: (a) Bosch, M.; Schlaf, M. *J. Org. Chem.* **2003**, *68*, 5225. Cyclopropanes: (b) Bayer, E.; Geckeler, K. *Angew. Chem., Int. Ed.* **1979**, *18*, 533. (c) Baret, N.; Dulcere, J. P.; Rodriguez, J.; Pons, J. M.; Faure, R. *Eur. J. Org. Chem.* **2000**, 1507. (d) Kacprzak, K. *Synth. Commun.* **2003**, *33*, 1499. (e) Wyatt, P.; Hudson, A.; Charmant, J.; Orpen, A. G.; Phetmung, H. *Org. Biomol. Chem.* **2006**, *4*, 2218. (f) Gonzalez-Bobes, F.; Fenster, M. D. B.; Kiau, S.; Kolla, L.; Kolotuchin, S.; Soumeillant, M. *Adv. Synth. Catal.* **2008**, *350*, 813. See Supporting Information for detailed procedures.

(9) For easier comparison, the values given in Scheme 2, **C** have been limited to those obtained when changing a single parameter from the optimized conditions given in Scheme 2, **B**. For the optimization studies, the yields and diastereoselectivities were calculated by NMR and the er by chiral HPLC, see Supporting Information for further details.

(10) (a) Evans, D. A.; Rovis, T.; Kozlowski, M. C.; Tedrow, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 1994. (b) Desimoni, G.; Faita, G.; Jørgensen, K. A. *Chem. Rev* **2011**, *111*, PR284. See also Figure S1 in Supporting Information for a simplified stereochemical model with different complex geometries.

(11) The different atom locations in the benzene region result from the presence of two conformations in the crystal structure.

(12) The hydrogen atoms are omitted for clarity.


Me Me
O
N
O
tBu
Cu
(ClO4)2
tBu
(10 mol %)
3Å MS, CH2Cl2, RT
MeO2C
CO2Me
50:50 er
X = O, CH2
enol ethers
aldehydes
DYKAT
Same catalyst!
MeO2C
R2
R1
69-99% yield
up to 98:2 er

Supporting Information for

Dynamic Kinetic Asymmetric [3+2] Annulation Reactions of Aminocyclopropanes.

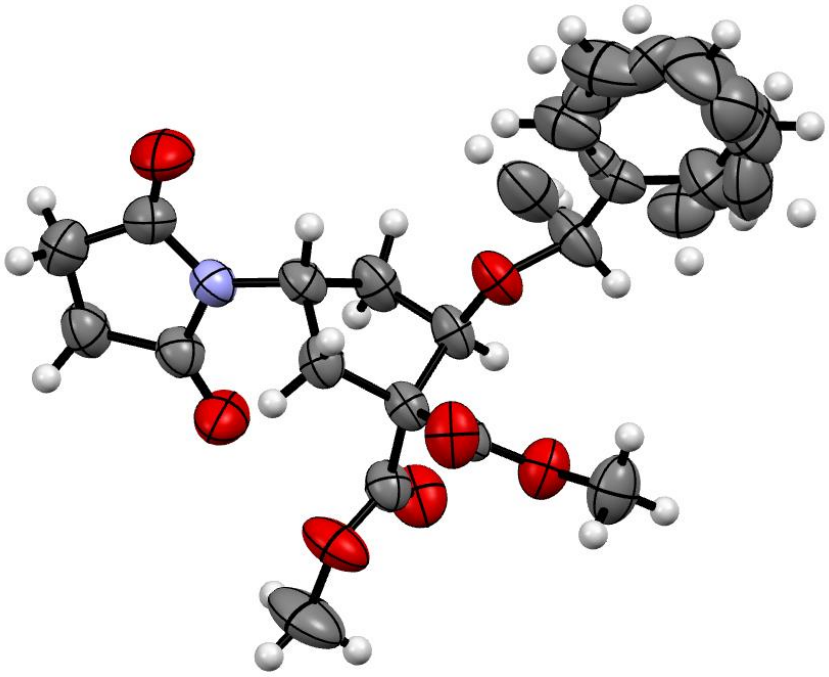
Florian de Nanteuil,‡ Eloisa Serrano,‡ Daniele Perrotta and Jerome Waser.

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne, EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland
jerome.waser@epfl.ch

95 pages

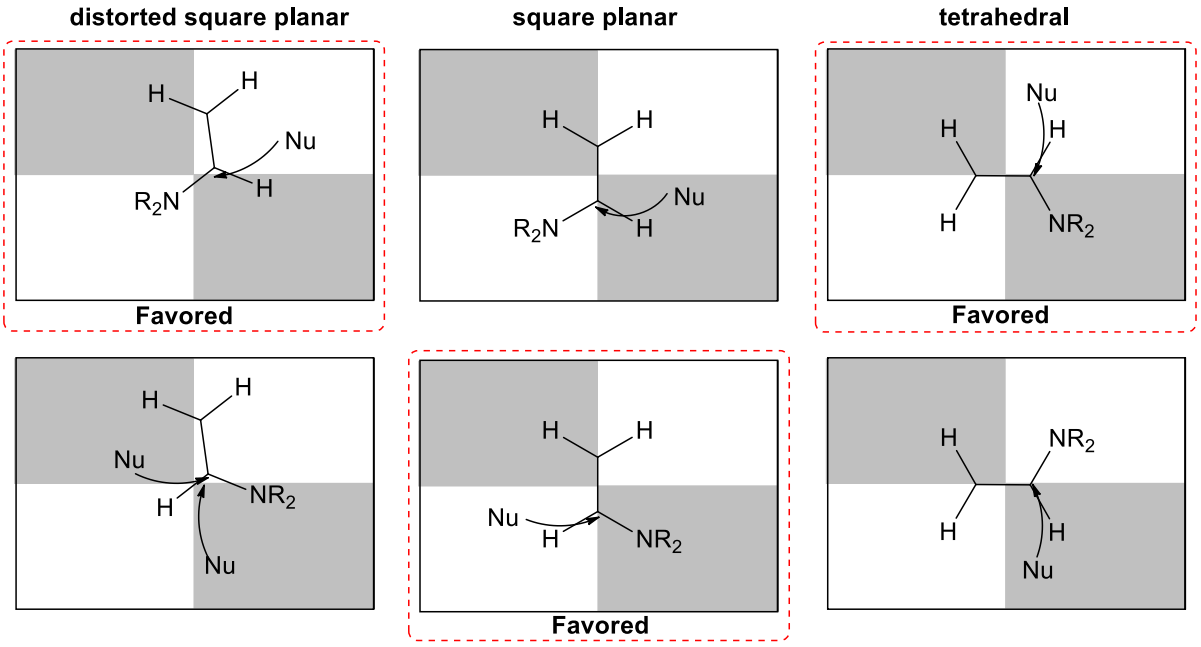
Table of Contents

Figure S1:



X-ray structure of compound **6g**. The different atom locations in the benzene region result from the presence of two conformations in the crystal structure. As the region containing the stereocenters is well-defined, the assignment of the configuration is not disturbed.

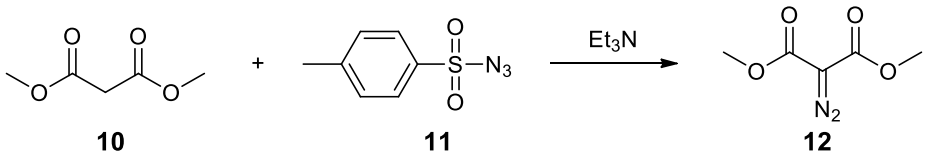
Figure S2:
Simplified stereochemical model for nucleophilic attack on aminocyclopropanes in dependence of the complex geometry. Only the CH_2-CHN bond of the cyclopropane is drawn. The grey quadrants are blocked by the two *tert*-butyl groups of the ligand.



General Methods

All reactions were carried out in oven-dried glassware under nitrogen or argon atmosphere with magnetic stirring, unless stated otherwise. THF, Et_2O, CH_3CN, toluene, hexane and dichloromethane were dried by passage over activated alumina under nitrogen atmosphere (water content < 30 ppm, Karl-Fischer titration) on an Innovative Technology Solvent Delivery System. All chemicals were purchased from Strem, Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å or using aluminium oxide, basic, Brockmann I purchased from Acros, using the solvents indicated as eluent with 0.1-0.5 bar pressure. For flash chromatography, previously distilled technical grade solvents were used. TLC was performed on Merck silica gel 60 F254 TLC glass plates or aluminium plates and visualized with UV light, and by permanganate stain, CAN stain or p-anisaldehyde stain followed by heating. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H- NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in $CDCl_3$, DMSO- d_6, CD_2Cl_2 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm, the internal CD_2Cl_2 signal at 5.31 ppm, or the internal MeOD signal at 3.30 ppm as standard. The data are reported as follows: (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration, interpretation). ^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Brucker DPX- 400 100 MHz spectrometer in $CDCl_3$, DMSO-d_6, CD_2Cl_2 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm, the internal CD_2Cl_2 signal at 53.5 ppm or the internal MeOD signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm-1 (w = weak, m = medium, s = strong, sh = shoulder). High resolution mass spectrometry measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurements were done on a JASCO HPLC system with an AS2055 Autosampler, a PU 2089 Pump, a UV 2075 detector using a CHIRALPAK IC, IB, IF or IA column from DAICEL Chemical. Optical rotations were measured on a polarimeter using a 10 cm cell with a Na 589 nm filter. The specific solvents and concentrations (in g/100 mL) are indicated.

Synthesis of Dimethyl-2-diazomalonate (12)



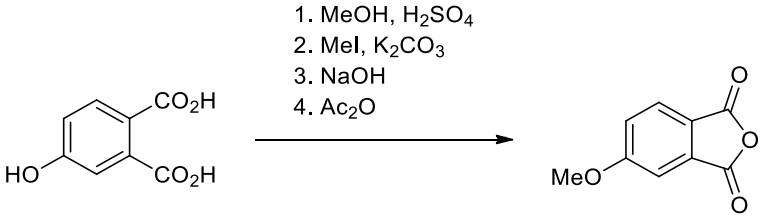
10 11 12

Following a modified procedure,[1] dimethylmalonate (**10**) (7.93 mL, 69.7 mmol, 1.00 eq), triethylamine (10.6 mL, 76.6 mmol, 1.10 eq) and tosyl azide (**11**) (15.1 g, 76.6 mmol, 1.10 eq) were dissolved in acetonitrile (100 mL). The solution was stirred at room temperature for 24 hours. The solution was concentrated under reduced pressure and partitioned between dichloromethane (30 mL) and water (30 mL), the layers were separated and the aqueous layer was extracted with dichloromethane (1 x 20 mL). The organic layers were combined and dried over $MgSO_4$. The crude was first filtered over a plug of silica gel (Hexane/Et_2O 1:1) to remove most of the tosylamide formed during the reaction. Purification by column chromatography (Hexane/Et_2O 90:10 to 80:20) afforded dimethyl-2-diazomalonate (**12**) as yellow oil which solidified under storage at 4 °C (10.4 g, 65.5 mmol, 94 % yield).

R_f 0.32 (1:1 PET/Et2O).
^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.87 (s, 1H, *OCH_3*).
^{13}C NMR (101 MHz, $CDCl_3$) δ: 161.2, 52.4[2]
The characterization data for **12** correspond to the reported values.[1]

Synthesis of N-vinyl-imides

5-Methoxyisobenzofuran-1,3-dione (14)



13 14

Following a modified procedure,[3] a solution of 4-hydroxyphthalic acid (**13**) (2.00 g, 11.0 mmol, 1.00 eq), catalytic sulfuric acid (0.10 mL, 1.9 mmol, 0.17 eq) and MeOH (20.0 mL), was stirred at reflux for 7 hours. under air. The solvent was removed under reduced pressure to afford crude dimethyl 4-hydroxyphthalate. The crude diester was dissolved in acetone (70 mL) and reacted with potassium carbonate (7.40 g, 53.5 mmol, 5.00 eq) at 50 °C for 20 min. Iodomethane (1.47 mL, 23.6 mmol, 2.20 eq) was added, and the mixture was stirred at reflux overnight. K_2CO_3 was removed by filtration and the solvent was removed under reduced pressure to afford a colorless oil.

The crude was dissolved in acetone (16.0 mL) and a 11 M solution of sodium hydroxide, (6.00 mL, 66.0 mmol, 6.20 eq) was added, and the solution was stirred for 6 hours. under air at rt. The solution was then acidified with 2 M HCl to pH 3, and concentrated under reduced

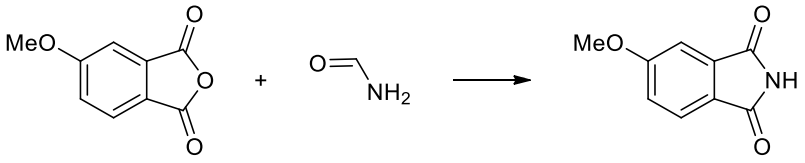
[1] P. Wyatt, A. Hudson, J. Charmant, A. G. Orpen, H. Phetmung, *Org. Biomol. Chem.* **2006**, *4*, 2218-2232.
[2] The diazo carbon could not be detected.
[3] P. H. Mazzocchi, P. Wilson, F. Khachik, L. Klingler, S. Minamikawa, *J. Org. Chem.* 1983, *48*, 2981.

pressure. Then, the crude 4-methoxyphthalic acid was dissolved into acetone (50 mL) and dried over $MgSO_4$, filtered through a plug of cotton wool, and the solvent was removed in vacuo. The crude diacid was partitioned between 2 M NaOH (50 mL) and DCM (50 mL). The organic layer was extracted with NaOH 2 M (50 mL). The combined aqueous phase was cooled down to 0 °C and acidified with 37% HCl % to pH 3. The aqueous layer was then extracted five times with AcOEt (50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford the crude diacid as a light brown solid (1.82 g).

A solution of crude 4-methoxyphthalic acid (1.82 g, 9.28 mmol, 1.00 eq) in acetic anhydride (25.0 mL, 266 mmol, 28.7 eq) was stirred at reflux for 21 hours. Volatiles were removed in vacuo to afford a dark brown solid. The crude was dissolved in DCM (50 mL) and filtered through fritted glass to remove solid impurities. The solution was concentrated under reduced pressure and dried in vacuo to afford the anhydride **14** as a light brown solid (1.62 g, 9.08 mmol, 83% yield over 4 steps)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, 1 H, *J* = 8.5, 0.4 Hz, *Ar*), 7.41 (d, 1 H, *J* = 2.2 Hz, *Ar*), 7.35 (dd, 1 H, *J* = 8.5, 2.3 Hz, *Ar*), 3.98 (s, 3 H, *OMe*).
HRMS (ESI) calcd for $C_9H_7O_4^+$ $[M+H]^+$ 179.0339; found 179.0349.
The ^{1}H NMR data for **14** corresponded to the reported values.[4]

5-Methoxyisoindoline-1,3-dione (16)



14 **15** **16**

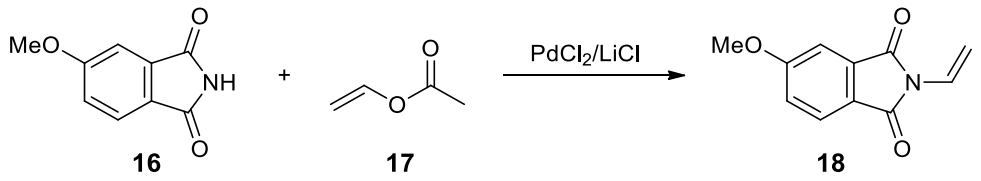
Following a modified procedure,[5] 5-methoxyisobenzofuran-1,3-dione (**14**) (1.58 g, 8.84 mmol, 1.00 eq) and formamide (**15**) (35.0 mL, 880 mmol, 100 eq) were divided between four 20 mL microwave vials sealed with a microwave cap. The mixture was stirred at rt until the product was completely dissolved, then heated 2 times 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 to induce crystallization and cold water (10 mL) was added into each vial. The obtained solid was filtrated over filter paper, washed with water (15 mL) and hexanes (20 mL) and dried under reduced pressure to afford 5-methoxyisoindoline-1,3-dione (**16**) as a beige solid (982 mg, 5.54 mmol, 63% yield) which was used without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, 1 H, *J* = 8.3, 0.4 Hz, *Ar*), 7.59 (br s, 1 H, *NH*), 7.33 (d, 1 H, *J* = 2.2 Hz, *Ar*), 7.20 (dd, 1 H, *J* = 8.3, 2.3 Hz, *Ar*), 3.94 (s, 3 H, *OMe*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.7, 165.0, 135.2, 125.4, 124.5, 120.4, 108.1, 56.2.
HRMS (ESI) calcd for $C_9H_8NO_3^+$ $[M+H]^+$ 178.0499; found 178.0497.

5-Methoxy-2-vinylisoindoline-1,3-dione (18)

[4] N. J. Hinde, C. D. Hall, *J. Chem. Soc., Perkin Trans. 2.* 1998, 1249.

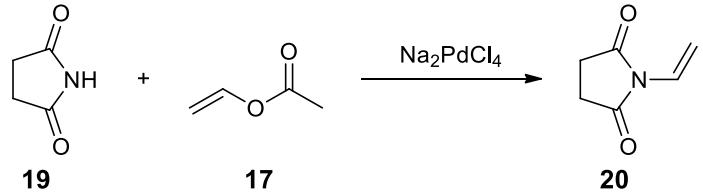
[5] K. Kacprzak, Synth. Commun. 2003, 33, 1499.



Following a modified procedure,[6] 5-methoxyisoindoline-1,3-dione (**16**) (980 mg, 5.53 mmol, 1.00 eq), $PdCl_2$ (98.0 mg, 0.553 mmol, 0.100 eq), LiCl (235 mg, 5.53 mmol, 1.00 eq, weighted in a glovebox) and vinyl acetate (**17**) (13.7 mL, 148 mmol, 26.8 eq) were heated under reflux for 24 hours. The mixture was cooled down to room temperature and diluted with DCM/MeOH 4:1 (20 mL). Activated charcoal was added and the resulting suspension was filtered through a pad of Celite (DCM/MeOH 4:1 100 mL) and concentrated under reduced pressure. Purification by silica gel chromatography (pentane/AcOEt 90:10 to 75:25) afforded 5-methoxy-2-vinylisoindoline-1,3-dione (**18**) as a colorless solid (828 mg, 4.08 mmol, 74% yield).

R_f 0.56 (6:4 Hexane/AcOEt).
M.p. 102.2 - 105.1 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, 1 H, *J* = 8.3 Hz, Ar), 7.32 (d, 1 H, *J* = 2.2 Hz, Ar), 7.17 (dd, 1 H, *J* = 8.3, 2.2 Hz, Ar), 6.83 (dd, 1 H, *J* = 16.4, 9.9 Hz, =C*H*), 6.03 (d, 1 H, *J* = 16.4 Hz, =C*H*), 4.99 (d, 1 H, *J* = 9.9 Hz, =C*H*), 3.93 (s, 3 H, O*Me*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 166.3, 165.1, 134.4, 125.5, 124.0, 123.5, 120.6, 108.2, 104.0, 56.3.
IR 1779 (w), 1720 (s), 1639 (w), 1619 (w), 1493 (w), 1386 (s), 1307 (w), 1295 (w), 1021 (w).
HRMS (ESI) calcd for $C_{11}H_{10}NO_3^+$ $[M+H]^+$ 204.0655; found 204.0662.

1-Vinylpyrrolidine-2,5-dione (20)

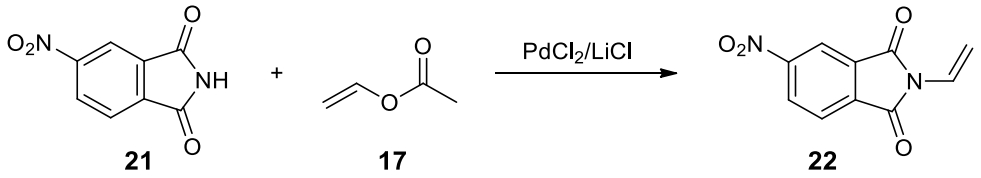


Following a modified procedure,[6] succinimide (**19**) (1.00 g, 10.1 mmol, 1.00 eq), vinyl acetate (**17**) (25.0 mL, 270 mmol, 26.8 eq) and Na_2PdCl_4 (59.0 mg, 0.202 mmol, 2.00 mol%) were heated under reflux for 72 hours. After solvent evaporation, the crude was purified by Biotage (SNAP Cartridge KP-Sil 50 g, 7:3 Hexane/AcOEt) to obtain (**20**) as a yellow solid (1.22 g, 9.78 mmol, 97% yield).

R_f 0.17 (8:2 Hexane/AcOEt). m.p. 47.6 – 48.9 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (dd, 1 H, *J* = 16.4, 9.9 Hz, =*CH*), 6.08 (d, 1 H, *J* = 16.4 Hz, =*CH*), 5.06 (d, 1 H, *J* = 9.9 Hz, =*CH*), 2.72 (s, 4 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 124.3, 106.6, 27.8.
IR 2946 (w), 1707 (s), 1382 (s), 1307 (m), 1222 (s), 1113 (s), 974 (m), 906 (m), 821 (w).
HRMS (ESI) calcd for $C_6H_8NO_2^+$ $[M+H]^+$ 126.0550; found 126.0621.

5-Nitro-2-vinylisoindoline-1,3-dione (22)

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

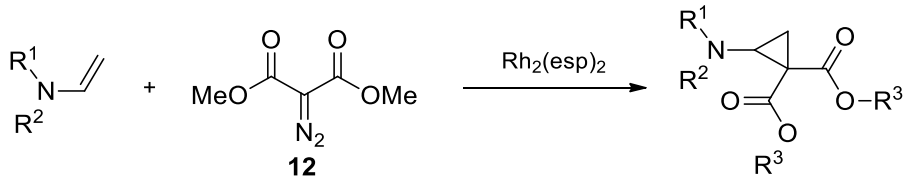


Following a modified procedure,[6] 5-nitrosoindoline-1,3-dione (**21**) (1.00 g, 5.20 mmol, 1.00 eq), $PdCl_2$ (92.0 mg, 0.520 mmol, 0.100 eq), LiCl (0.221 mg, 5.20 mmol, 1.00 eq, weighted in a glovebox) and vinyl acetate (**17**) (12.9 mL, 139 mmol, 26.8 eq) were heated under reflux for 20 hours. The mixture was cooled down to room temperature and the solvent was evaporated under reduced pressure. The crude was purified by column chromatography using silica gel (Hexane/AcOEt 8:2 to 5:5) to afford 5-nitro-2-vinylisoindoline-1,3-dione (**22**) as a bright yellow solid (1.14 g, 5.23 mmol, quantitative yield).

R_f 0.32 (9:1 Pentane/AcOEt).
M.p. 144.3 - 148.6 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (dd, 1 H, *J* = 2.0, 0.5 Hz, *Ar*), 8.63 (dd, 1 H, *J* = 8.1, 2.0 Hz, *Ar*), 8.08 (m, 1 H, *Ar*), 6.88 (dd, 1 H, *J* = 16.4, 9.8 Hz, *CH*-*N*), 6.14 (dd, 1 H, *J* = 16.4, 0.5 Hz, =*CH*$_2$), 5.16 (dd, 1 H, *J* = 9.8, 0.4 Hz, =*CH*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 164.2, 152.1, 136.1, 133.1, 129.8, 125.0, 123.6, 119.2, 106.3.
IR 3101 (w), 3074 (w), 2924 (w), 1709 (s), 1533 (s), 1383 (s), 1341 (s), 1307 (s), 1062 (m), 1024 (s), 915 (s). HRMS (ESI) calcd for $C_{10}H_6N_2O_4$ [M^+] 218.0328; found 218.0355.

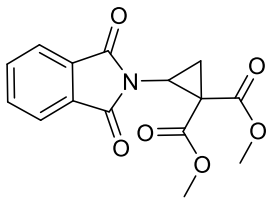
Synthesis of Aminocyclopropanes

General Procedure for the of Synthesis of Aminocyclopropanes



Following a modified procedure,[7] the corresponding N-vinyl-imide (1.00 eq) was dissolved in dry dichloromethane (10.0 mL) and the solution was cooled down to 0 °C with an ice/water bath. Then, bis[rhodium(α,α,α', α'-tetramethyl-1,3-benzenedipropionic acid)] (0.1 mol%) was added in one portion. A solution in dichloromethane (2.0 mL) of dimethyldiazomalonate (**12**) (1.20 eq) was added dropwise over 5 min. After the addition, the mixture was allowed to warm to room temperature and stirred overnight. The solvent is then removed under reduced pressure and the crude is directly purified by column chromatography.

Dimethyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (4a)

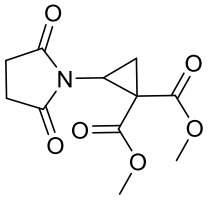


Following the general procedure, **4a** was synthesized starting from N-vinyl-phthalimide (2.50 g, 14.4 mmol, 1.00 eq), dimethyl-diazomalonate (**12**) (2.74 g, 17.3 mmol, 1.20 eq) and bis[rhodium(α,α,α', α'-tetramethyl-1,3-benzenedipropionic acid)] (14.0 mg, 0.0144 mmol, 0.100 mol%). After solvent evaporation, the residue was purified by column chromatography using silica gel (from 8:2 to 6:4 Hexane/AcOEt), to obtain dimethyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**4a**) as a colorless solid (4.03 g, 13.3 mmol, 92% yield).

R_f 0.34 (6:4 Hexane/AcOEt).
M.p. 131.8 – 133.9 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (m, 2 H, *Phth*), 7.75 (m, 2 H, *Phth*), 3.85 (s, 3 H, *OMe*), 3.72 (dd, 1 H, *J* = 8.5, 6.6 Hz, *N-CH*), 3.64 (s, 3 H, *OMe*), 2.73 (dd, 1 H, *J* = 6.5, 6.5 Hz, *CH_2*), 2.06 (dd, 1 H, *J* = 8.5, 6.4 Hz, *CH_2*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 167.8, 166.9, 134.3, 131.4, 123.5, 53.1, 53.0, 34.9, 33.1, 19.6.
IR 2956 (w), 1783 (w), 1727 (s), 1468 (w), 1439 (w), 1399 (m), 1329 (m), 1294 (m), 1222 (m), 1134 (w), 909 (w), 876 (w), 720 (m).
HRMS (ESI) calcd for $C_{15}H_{14}NO_6^+$ $[M+H]^+$ 304.0816; found 304.0811.
The ^{1}H NMR data for **4a** corresponded to the reported values.[8]

Dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (4b)

[7] F. Gonzalez-Bobes, M. D. B. Fenster, S. Kiau, L. Kolla, S. Kolotuchin, M. Soumeillant, *Adv. Synth. Catal.* 2008, *350*, 813.
[8] F. de Nanteuil, J. Loup, J. Waser, *Org. Lett.* **2013**, *15*, 3738.



Following the general procedure, compound **4b** was synthesized starting from N-vinyl-succinimide (**20**) (500 mg, 4.00 mmol, 1.00 eq), dimethyldiazomalonate (**12**) (300 mg, 4.80 mmol, 1.20 eq) and bis[rhodium(α,α,α', α'-tetramethyl-1,3-benzenedipropionic acid)] (3.0 mg, 4.0 μmol, 0.10 mol%). After solvent evaporation, the residue was purified by Biotage (SNAP Cartridge KP-Sil 50 g, 5:5 Hexane/AcOEt), to obtain dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (**4b**) as a yellow solid (801 mg, 3.14 mmol, 79% yield).

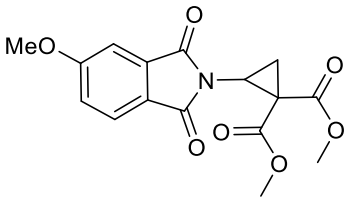
Protocol for the synthesis of enantioenriched 4b:

Following the general procedure, dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (**4b**) was synthesized starting from N-vinylsuccinimide (100 mg, 0.800 mmol, 1.00 eq), dimethyldiazomalonate (152 mg, 0.960 mmol, 1.20 eq) using tetrakis[(S)-(-)-N-(p-dodecylphenylsulfonyl)prolinato]dirhodium(II) (0.8 mg, 8 μmol, 1 mol%). After solvent evaporation, the residue was purified by flash column chromatography on silica gel (1:1 to 3:7 Pentane/AcOEt) to obtain a yellow solid, which was washed two times with MeOH to afford dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate as a white solid (20 mg, 0.078 mmol, 10% yield).

er = 58:42, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 23.2 min; tr2 = 25.8 min.

R_f 0.39 (5:5 Hexane/AcOEt).
M.p. 81.9 – 85.3 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (s, 3 H, *OMe*), 3.68 (s, 3 H, *OMe*), 3.45 (dd, 1 H, *J* = 8.5, 6.5 Hz, *N-CH*), 2.73-2.58 (m, 4 H, O=C-*CH*$_2$), 2.45 (t, 1 H, *J* = 6.5 Hz, *CH*$_2$), 1.93 (dd, 1 H, *J* = 8.5, 6.5 Hz, *CH*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 168.4, 167.2, 53.2, 53.1, 35.1, 32.7, 28.1, 19.7.
IR 2955 (w), 1717 (s), 1439 (w), 1406 (m), 1332 (m), 1296 (m), 1216 (s), 1132 (m), 1079 (w), 910 (s).
HRMS (ESI) calcd for $C_{11}H_{14}NO_6^+$ $[M+H]^+$ 256.0816; found 256.0822.

Dicarboxylate dimethyl 2-(5-methoxy-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (4c)

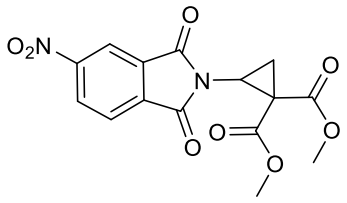


Following the general procedure, compound **4c** was synthesized starting from 5-methoxy-2-vinylisoindoline-1,3-dione (**18**) (0.130 g, 0.640 mmol, 1.00 eq), dimethyldiazomalonate (**12**) (0.121 g, 0.768 mmol, 1.20 eq) and bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] (0.5 mg, 0.6 μmol, 0.1 mol%). After solvent evaporation, the crude was purified by

Biotage (SNAP Cartridge KP-Sil 10 g, 6:4 Hexane/AcOEt), to obtain dicarboxylate dimethyl 2-(5-methoxy-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**4c**) as a colorless solid (176 mg, 0.528 mmol, 83% yield).

R_f 0.15 (8:2 Pentane/AcOEt).
M.p. 113.5 – 117.8 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, 1 H, *J* = 8.3 Hz, *Phth*), 7.27 (d, 1 H, *J* = 2.2 Hz, *Phth*), 7.14 (dd, 1 H, *J* = 8.3, 2.3 Hz, *Phth*), 3.90 (s, 3 H, *OMe*), 3.80 (s, 3 H, *OMe-C=O*), 3.66 (dd, 1 H, *J* = 8.5, 6.6 Hz, *N-CH*), 3.59 (s, 3 H, *OMe-C=O*), 2.68 (t, 1 H, *J* = 6.5 Hz, CH_2), 1.99 (dd, 1 H, *J* = 8.5, 6.4 Hz, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 167.8, 167.6, 167.0, 165.0, 134.1, 125.3, 123.4, 120.4, 108.1, 56.2, 53.2, 53.0, 35.0, 33.2, 19.7.
IR 2955 (w), 1720 (s), 1492 (m), 1437 (m), 1397 (s), 1288 (s), 1133 (m), 1018 (w).
HRMS (ESI) calcd for $C_{16}H_{16}NO_7^+$ $[M+H]^+$ 334.0921; found 334.0915.

Dimethyl 2-(5-nitro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (4d)

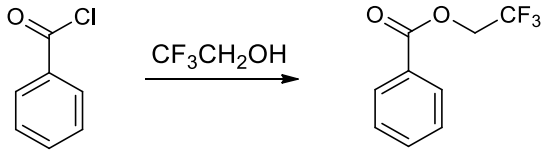


Following the general procedure, compound **4d** was synthesized starting from 5-nitro-2-vinylisoindoline-1,3-dione (**22**) (0.500 g, 2.29 mmol, 1.00 eq), dimethyl diazomalonate (**12**) (0.544 g, 2.75 mmol, 1.20 eq) and bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] (1.7 mg, 2.3 μmol, 0.10 mol%). After solvent evaporation, the crude was purified by Biotage (SNAP Cartridge KP-Sil 50 g, 7:3 Hexane/AcOEt), to obtain Dimethyl 2-(5-nitro-1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**4d**) as a colorless solid (712 mg, 2.04 mmol, 89% yield).

R_f 0.19 (8:2 Pentane/AcOEt).
M.p. 113.0 – 115.8 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (m, 2 H, *Ar*), 8.03 (d, 1 H, *J* = 8.1 Hz, *Ar*), 3.83 (s, 3 H, *OMe*), 3.70 (m, 1 H, *CH-N*), 3.62 (s, 3 H, *OMe*), 2.63 (m, 1 H, CH_2), 2.07 (m, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.1, 165.9, 165.6, 152.0, 135.9, 132.9, 129.6, 124.9, 119.0, 53.3, 53.2, 35.0, 33.1, 19.7.
IR 3110 (w), 2956 (w), 2926 (w), 2853 (w), 1726 (s), 1541 (m), 1400 (m), 1344 (s), 1222 (s), 1130 (m).
HRMS (ESI) calcd for $C_{15}H_{13}N_2O_8^+$ $[M+H]^+$ 349.0666; found 349.0664.

Synthesis of Esters

2,2,2-Trifluoroethyl benzoate (24)

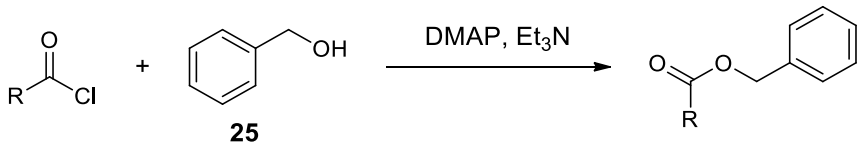


23 **24**

In a 250 mL round bottom flask equipped with a stirring bar, 2,2,2-trifluoroethanol (2.33 mL, 32.3 mmol, 1.00 eq), DMAP (39.5 mg, 0.323 mmol, 0.01 eq) and pyridine (3.14 mL, 38.8 mmol, 1.20 eq) were dissolved in diethyl ether (150 mL) while stirring. A solution of benzoyl chloride (**23**) (5.00 g, 35.6 mmol, 1.10 eq) in diethyl ether (10 mL) was added dropwise to the reaction mixture and the reaction was stirred at room temperature for 12 hours. A saturated $NaHCO_3$ solution (100 mL) was added to the crude mixture. The two layers were separated and the organic layer washed with water (50 mL x 3), dried over $MgSO_4$ and the solvent removed under reduced pressure. 2,2,2-trifluoroethyl benzoate (**24**) was purified by flash column chromatography on silica gel (9:1 to 8:2 Pentane/AcOEt) to obtain a colourless oil (3.50 g, 17.1 mmol, 53 % yield).

R_f 0.8 (9:1 Pentane/Et_2O).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 - 8.07 (m, 2 H, *Ar*), 7.64 - 7.60 (m, 1 H, *Ar*), 7.50 - 7.46 (m, 2 H, *Ar*), 4.71 (q, 2 H, J_{F-H} = 8.4 Hz, CH_2-CF_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 134.0, 130.2, 128.8, 128.5, 123.3 (q, J_{F-C} = 277 Hz), 60.9 (q, J_{F-C} = 37 Hz).
The characterization data for **24** correspond to the reported values[9]

General Procedure for the Synthesis of Benzyl Esters

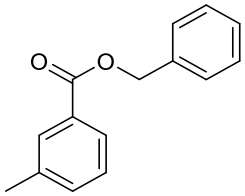


25

In a 250 mL round bottom flask equipped with a stirring bar and a condenser, benzyl alcohol (**25**) (1.00 eq), DMAP (0.01 eq) and triethylamine (1.10 eq) were dissolved in diethyl ether (90 mL) while stirring. A solution of the corresponding acyl chloride (1.20 eq) in diethyl ether (10 mL) was added dropwise to the reaction mixture and the reaction was stirred at reflux for 12 hours. A saturated $NaHCO_3$ solution (100 mL) was added to the crude mixture and stirred for 15 min at room temperature. The two layers were separated and the organic layer was washed with water (50 mL x 3), dried over Na_2SO_4 and the solvent removed under reduced pressure. The esters were purified by flash column chromatography on silica gel (9:1 to 8:2 Pentane/AcOEt).

Benzyl 3-methylbenzoate (26)

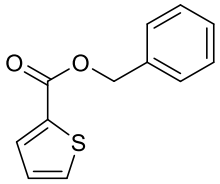
[9] V. Nummert, M. Piirsalu, V. Mäemets, S. Vahur, I. A. Koppel, *J. Phys. Org. Chem*. **2009**, *22*, 1155.



Following the general procedure, compound **26** was synthesized starting from benzyl alcohol (**25**) (1.17 g, 10.8 mmol, 1.00 eq), DMAP (13.0 mg, 0.108 mmol, 0.01 eq), triethylamine (1.66 mL, 11.9 mmol, 1.10 eq) and 3-methylbenzoyl chloride (2.01 g, 13.0 mmol, 1.20 eq). Compound **26** was obtained as a colorless oil (2.37 g, 10.5 mmol, 97% yield).

R_f 0.55 (9:1 Hexane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.88 (m, 2 H, *Ph*), 7.47 – 7.45 (m, 2 H, *Ph*), 7.42 – 7.31 (m, 5 H, *Ph*), 5.37 (s, 2 H, C*H*$_2$), 2.40 (s, 3 H, *Me*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 138.3, 136.3, 133.9, 130.3, 130.2, 128.7, 128.4, 128.3, 128.3, 127.0, 66.8, 21.4.
The characterization data for **26** correspond to the reported values.[10]

Benzyl thiophene-2-carboxylate (27)



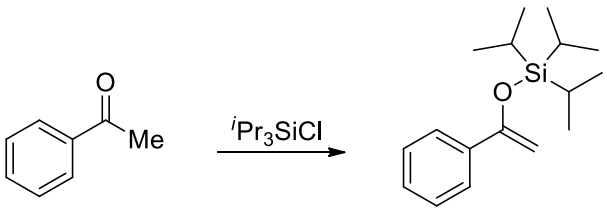
Following the general procedure, compound **27** was synthesized starting from benzyl alcohol (**25**) (1.08 g, 10.0 mmol, 1.00 eq), DMAP (12.2 mg, 0.100 mmol, 0.01 eq), triethylamine (1.54 mL, 11.0 mmol, 1.10 eq) and thiophene-2-carbonyl chloride (1.76 g, 12.0 mmol, 1.20 eq), compound **27** was obtained as a colorless oil (2.09 g, 9.58 mmol, 96% yield).

R_f 0.48 (9:1 Hexane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 - 7.84 (m, 1 H, *Thiophene*), 7.56 (dd, 1 H, *J* = 5.0, 1.2 Hz, *Thiophene*), 7.46 - 7.44 (m, 2 H, *Ph*), 7.42 - 7.33 (m, 3 H, *Ph*), 7.10 (dd, 1 H, *J* = 4.9, 3.8 Hz, *Thiophene*), 5.36 (s, 2 H, C*H*$_2$-Ph).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 135.9, 133.7, 133.7, 132.6, 128.7, 128.4, 128.3, 127.9, 66.8.
The characterization data for **27** correspond to the reported values.[11]

[10] H. Liu , G. Shi , Shulei Pan , Y. Jiang ,Y. Zhang, *Org. Let.* **2013,** *15*, 4098.
[11] M. Ji, X. Wang, Y. N. Lim, Y.-W. Kang, H.-Y. Jang *Eur. J. Org. Chem.* **2013,** *35*, 7881

Synthesis of Enol ethers

Triisopropyl((1-phenylvinyl)oxy)silane (5a)

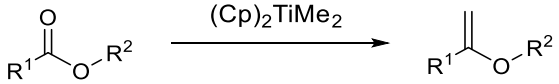


28 **5a**

In an oven-dried flask sealed with a septum and under N_2 atmosphere, acetophenone (**28**) (2.06 g, 17.1 mmol, 1.00 eq) in anhydrous THF (20 mL) is cooled down to -78 °C and a 1.9 M solution of NaHMDS (10.8 mL, 20.5 mmol, 1.20 eq) is added dropwise. The cold bath is removed and the pale yellow solution is stirred for 1 hour at room temperature. The reaction is cooled again to 0 °C and triisopropylsilyl chloride (3.96 g, 20.5 mmol, 1.20 eq) is added dropwise. The reaction is stirred at room temperature for 5 hours and the solvent is directly removed under reduced pressure. The resulting orange oil is purified by plug or by column chromatography on triethylamine-deactivated silica (99% Hexane, 1% Et_3N) to obtain Triisopropyl((1-phenylvinyl)oxy)silane **5a** as a colorless oil (4.7 g, 17 mmol, 99% yield)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.65 (m, 2 H, *Ar*), 7.38-7.29 (m, 3 H, *Ar*), 4.85 (d, 1 H, *J* = 1.8 Hz, C=C*H*$_2$), 4.41 (d, 1 H, *J* = 1.8 Hz, C=C*H*$_2$), 1.39-1.27 (m, 3 H, SiC*H*$(CH_3)_2$), 1.19-1.13 (m, 18 H, SiCH$(CH_3)_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 138.0, 128.2, 128.1, 125.4, 90.0, 18.2, 12.9.
The characterization data for **5a** corresponded to the reported values.[12]

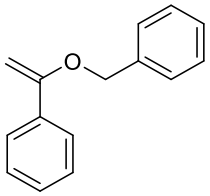
General procedure for the Synthesis of disubstituted Enol Ethers.



Following a slightly modified procedure,[13] a round-bottom flask equipped with a magnetic stirrer was charged with a solution (10 to 15% in toluene) of di(cyclopenta-1,3-dien-1-yl)dimethyltitanium (2.20 eq) in toluene,[14] di(cyclopenta-1,3-dien-1-yl)titanium(IV) chloride (0.060 eq) and the corresponding ester (1.00 eq) under inert atmosphere. The red/orange mixture was heated in the dark to 80 °C for 16 hours, and then cooled to room temperature. Pentane (50 mL) was added to the mixture and the precipitated solids were removed by filtration through a basic alumina plug (Pentane/diethyl ether 9:1, 3 % Et_3N) to afford a yellow oil. The benzyl enol ethers were purified right before use by flash column chromatography using basic alumina (Pentane, 3 % Et_3N).

(1-(Benzyloxy)vinyl)benzene (5b)

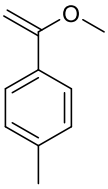
[12] J-F. Zhao, B-H. Tan, T-P. Loh, *Chem. Sci*. 2011, *2*, 349.
[13] J. F. Payack, D. L. Hughes, D. Cai, I. F. Cottrell, T. R. Verhoeven, Org. Synth. 2002, *79*, 19.
[14] The Petasis reagent was synthesised according to J. F. Payack, D. L. Hughes, D. Cai, I. F. Cottrell, T. R. Verhoeven, Org. Synth. 2002, *79*, 19.



Following the general procedure, compound **5b** was synthesized starting from di(cyclopenta-1,3-dien-1-yl)dimethyltitanium (19.1 g of a 10.8% solution in toluene, 9.90 mmol, 2.20 eq), di(cyclopenta-1,3-dien-1-yl)titanium(IV) chloride (67.2 mg, 0.270 mmol, 0.060 eq) and benzyl benzoate (0.955 g, 4.50 mmol, 1.00 eq) to obtain (1-(benzyloxy)vinyl)benzene (**5b**) as a colorless oil (545 mg, 2.59 mmol, 58% yield).

R_f 0.8 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz $CDCl_3$) δ 7.72 (ddd, *J* = 7.5, 3.3, 1.7 Hz, 2 H, *Ar*), 7.59 – 7.29 (m, 8 H, *Ar*), 5.00 (d, *J* = 2.1 Hz, 2 H, O-C*H*$_2$-Ar), 4.79 (t, *J* = 2.8 Hz, 1 H, C*H*=C), 4.36 (t, *J* = 2.5 Hz, 1 H, C*H*=C).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 137.3, 136.5, 128.6, 128.6, 128.3, 127.9, 127.5, 125.6, 83.3, 69.9.
IR 2432 (w), 2407 (w), 1361 (m), 1336 (s), 1161 (m), 1064 (s), 994 (s), 862 (s), 782 (m).
HRMS (ESI) calcd for $C_{15}H_{14}AgO^+$ $[M+Ag]^+$ 317.0090; found 317.0102

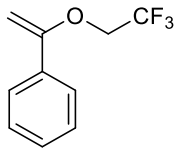
1-(1-Methoxyvinyl)-4-methylbenzene (5c)



Following the general procedure, compound **5c** was synthesized starting from di(cyclopenta-1,3-dien-1-yl)dimethyltitanium (24.2 g of a 12.6% solution in toluene, 14.7 mmol, 2.20 eq), di(cyclopenta-1,3-dien-1-yl)titanium(IV) chloride (99.0 mg, 0.400 mmol, 0.060 eq) and 2,2,2-trifluoroethyl benzoate (1.00 g, 6.66 mmol, 1.00 eq) to obtain 1-(1-methoxyvinyl)-4-methylbenzene (**5c**) as a colorless oil (537 mg, 3.63 mmol, 54% yield).

R_f 0.9 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.45 (m, 2 H, *Ar*), 7.17 (d, *J* = 8.0 Hz, 2 H, *Ar*), 4.64 (dd, *J* = 2.7, 1.0 Hz, 1 H, C=C*H*$_2$), 4.20 (d, *J* = 2.7 Hz, 1 H, C=C*H*$_2$), 3.76 (s, 3 H, O*Me*), 2.38 (s, 3 H, C*H*$_3$Ar).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 138.3, 133.7, 128.9, 128.8, 128.8, 125.3, 125.3, 125.3, 125.3, 81.0, 55.2, 21.2.
IR 2953 (w), 1743 (w), 1706 (w), 1644 (w), 1514 (m), 1303 (s) 1127 (s), 1047 (s), 903 (m), 796 (s).
HRMS (ESI) calcd for $C_{10}H_{12}AgO^+$ $[M+Ag]^+$ 254.9934; found 254.9898.

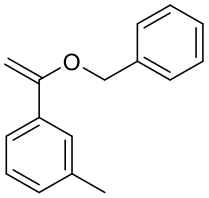
(1-(2,2,2-Trifluoroethoxy)vinyl)benzene (5d)



Following the general procedure, compound **5d** was synthesized starting from di(cyclopenta-1,3-dien-1-yl)dimethyltitanium (18.2 g of a 12.6% solution in toluene, 11.0 mmol, 2.20 eq), di(cyclopenta-1,3-dien-1-yl)titanium(IV) chloride (75.0 mg, 0.300 mmol, 0.060 eq) and 2,2,2-trifluoroethyl benzoate (1.02 g, 5.00 mmol, 1.00 eq) to obtain (1-(2,2,2-trifluoroethoxy)vinyl)benzene (**5d**) as a colorless oil (621 mg, 3.07 mmol, 61% yield).

R_f 0.9 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz $CDCl_3$) δ 7.65 – 7.61 (m, 2 H, *Ar*), 7.39 - 7.36 (m, 3 H, *Ar*), 4.82 (d, *J* = 3.7 Hz, 1 H, C*H*=C), 4.31 – 4.19 (m, 3 H, C*H*=C, CH_2-CF_3).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 135.0, 129.2, 128.4, 125.6, 123.6 (q, *J* = 277 Hz). 84.3, 65.5 (q, *J* = 35.8 Hz).
IR 2374 (w), 1331 (w), 1176 (w), 1047 (s), 966 (s), 818 (m), 801 (m), 656 (s).
HRMS (ESI) calcd for $C_{10}F_3H_{10}O^+$ $[M+H]^+$ 203.0678; found 203.0678.
The NMR data for (XX) corresponded to the reported values.[15]

1-(1-(Benzyloxy)vinyl)-3-methylbenzene (5e)

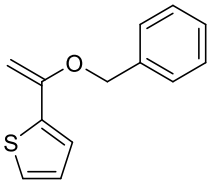


Following the general procedure, compound **5e** was synthesized starting from di(cyclopenta-1,3-dien-1-yl)dimethyltitanium (17.1 g of a 10.7% solution in toluene, 8.80 mmol, 2.20 eq), di(cyclopenta-1,3-dien-1-yl)titanium(IV) chloride (60.0 mg, 0.240 mmol, 0.060 eq) and benzyl 3-methylbenzoate (0.905 g, 4.00 mmol, 1.00 eq) to obtain 1-(1-(benzyloxy)vinyl)-3-methylbenzene (**5e**) as a colorless oil (450 mg, 2.01 mmol, 45% yield).

R_f 0.9 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz $CDCl_3$) δ 7.44 – 7.35 (m, 4 H, *Ph*), 7.31 (t, *J* = 7.5 Hz, 2 H, *Ar*Me), 7.28 – 7.21 (m, 1 H, *Ph*), 7.15 (ddd, *J* = 8.3, 6.1, 1.5 Hz, 1 H, *Ar*Me), 7.05 (d, *J* = 7.5 Hz, 1 H, *Ar*Me), 4.88 (s, 2 H, CH_2-Ph), 4.64 (d, *J* = 2.8 Hz, 1 H, CH_2=C), 4.22 (d, *J* = 2.8 Hz, 1 H, CH_2=C), 2.28 (s, 3 H, *Me*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 137.8, 137.3, 136.5, 129.4, 128.6, 128.2, 127.9, 127.6, 126.3, 122.8, 83.2, 69.9, 21.7.
HRMS (ESI) calcd for $C_{16}H_{17}O^+$ $[M+H]^+$ 225.1274; found 225.1282.

2-(1-(Benzyloxy)vinyl)thiophene (5f)

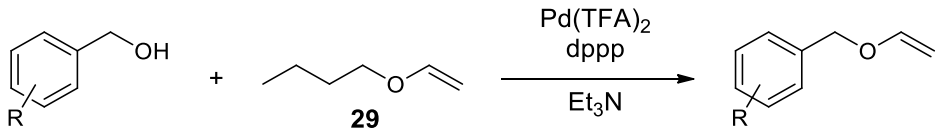
[15] D. Vuluga, J. Legros, B. Crousse, D. Bonnet-Delpon, *Eur. J. Org. Chem.* **2009**, *2009*, 3513.



Following the general procedure, compound **5f** was synthesized starting from di(cyclopenta-1,3-dien-1-yl)dimethyltitanium (17.1 g of a 10.7% solution in toluene, 8.80 mmol, 2.20 eq), di(cyclopenta-1,3-dien-1-yl)titanium(IV) chloride (60.0 mg, 0.240 mmol, 0.060 eq) and benzyl thiophene-2-carboxylate (0.873 g, 4.00 mmol, 1.00 eq) to obtain 2-(1-(benzyloxy)vinyl)thiophene (**5f**) (0.500 g, 4.00 mmol, 58%) as a colorless oil.
Impurities are present in the NMR sample due to degradation of the product during analysis.

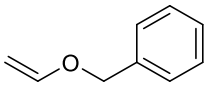
$\mathbf{R}_f$ 0.8 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.35 (m, 6 H, *Ar*), 7.30 (d, *J* = 5.0 Hz, 1 H, *Ar*), 7.07 (dd, *J* = 5.0, 3.7 Hz, 1 H, *Ar*), 5.05 (s, 2 H, *Benzyl*), 4.81 (d, *J* = 2.9 Hz, 1 H, C=C*H*), 4.35 (d, *J* = 3.1 Hz, 1 H, C=C*H*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 140.4, 136.9, 128.6, 127.9, 127.3, 127.3, 125.2, 124.0, 82.7, 69.8.
HRMS (ESI) calcd for $C_{13}H_{13}OS^+$ $[M+H]^+$ 217.0682; found 217.0688.

General Procedure for the Synthesis of Monosubstituted Enol Ethers



Following a slightly modified procedure,[16] palladium(II) trifluoroacetate (0.500 mol%) and 4,7-diphenyl-1,10-phenanthroline (0.500 mol%) were dissolved in 1-(vinyloxy)butane (**29**) (20.0 eq) in an oven-dried 20 mL vial equipped with a stirring bar to obtain a yellow solution. The corresponding alcohol (1.00 eq) and triethylamine (0.0750 eq) were then added to the solution. The flask was sealed with a microwave cap and stirred at 75 °C for 24 hours. The reaction was cooled to room temperature and filtrated through a plug of activated charcoal and eluted with hexane. The solvent was evaporated under reduced pressure to obtain the crude oils that were purified by a short column chromatography using deactivated silica gel (3 % Et_3N) or basic alumina and hexane as eluent.

((Vinyloxy)methyl)benzene (5g)



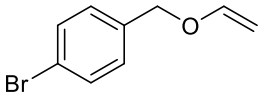
Following the general procedure, compound **5g** was synthesized starting from 1-(vinyloxy)butane (**29**) (12.0 mL, 92.0 mmol, 20.0 eq) and phenylmethanol (500 mg, 4.62 mmol, 1.00 eq) with palladium(II) trifluoroacetate (7.70 mg, 23.0 µmol, 0.500 mol%), 4,7-diphenyl-1,10-phenanthroline (7.70 mg, 23.0 µmol, 0.500 mol%), and triethylamine (35.0 mg, 0.350 mmol, 0.0750 eq). The crude product was purified by a short column chromatography

[16] M. Bosch, M. Schalf, *J. Org. Chem.* 2003, *68*, 5225.

using deactivated silica gel (3 % Et_3N) and hexane as eluent to obtain ((vinyloxy)methyl)benzene (**5g**) as a colorless oil (421 mg, 3.14 mmol, 63% yield).

R_f 0.9 (100 Hexane).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.30 (m, 5 H, *Ph*), 6.57 (dd, 1 H, *J* = 14.3, 6.8 Hz, CH_2=C*H*-O), 4.77 (s, 2 H, C*H*$_2$Ph), 4.31 (dd, 1 H, *J* = 14.3, 1.7 Hz, C*H*$_2$=CH-O), 4.09 (m, 1 H, C*H*$_2$=CH-O).
^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 136.9, 128.5, 128.0, 127.6, 87.4, 70.1.
The characterization data for **5g** corresponded to the reported values.[17]

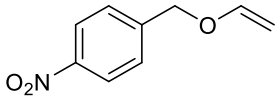
1-Bromo-4-((vinyloxy)methyl)benzene (5h)



Following the procedure described above, compound **5h** was synthesized starting from 1-(vinyloxy)butane (**29**) (14.0 mL, 107 mmol, 20.0 eq) and (4-bromophenyl)methanol (1.00 g, 5.35 mmol, 1.00 eq) with palladium(II) trifluoroacetate (8.9 mg, 27.0 µmol, 0.500 mol%), 4,7-diphenyl-1,10-phenanthroline (8.9 mg, 27.0 µmol,0.500 mol%), and triethylamine (56.0 µmL, 0.401 mmol, 0.075 eq). The crude product was purified by a short column chromatography using basic alumina and hexane as eluent to obtain 1-bromo-4-((vinyloxy)methyl)benzene (**5h**) as a colorless oil (915 mg, 4.29 mmol, 80% yield).

R$_f$ 0.9 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 2 H, *Ar*), 7.23 (d, *J* = 8.3 Hz, 2 H, *Ar*), 6.54 (dd, *J* = 14.3, 6.8 Hz, 1 H, CH_2=C*H*-O), 4.71 (s, 2 H, *CH*$_2$Ar), 4.29 (dd, *J* = 14.3, 2.3 Hz, 1 H, C*H*$_2$=CH-O), 4.10 (dd, *J* = 6.8, 2.3 Hz, 1 H, C*H*$_2$=CH-O).
^{13}C NMR (101 MHz, $CDCl_3$) δ 151.5, 136.1, 131.8, 129.2, 122.0, 87.8, 69.4.
IR 2359 (w), 2316 (w), 1325 (m), 1225 (m), 1091 (m), 993 (s), 895 (m), 847 (m), 684 (s).

1-Nitro-4-((vinyloxy)methyl)benzene (5i)



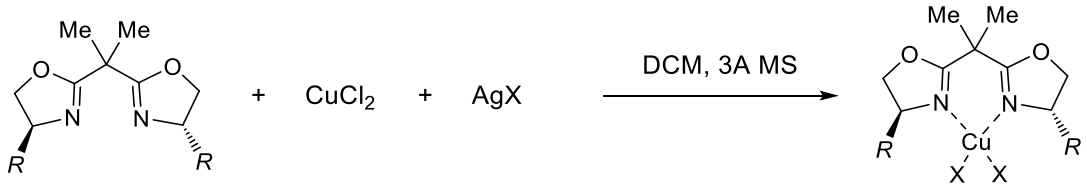
Following the procedure described above, compound **5i** was synthesized starting from 1-(vinyloxy)butane (**29**) (17.0 mL, 131 mmol, 20.0 eq) and (4-nitrophenyl)methanol (1.00 g, 6.53 mmol, 1.00 eq) with palladium(II) trifluoroacetate (10.9 mg, 33.0 µmol, 0.500 mol%) and 4,7-diphenyl-1,10-phenanthroline (10.9 mg, 33.0 µmol, 0.500 mol%),and triethylamine (68.0 µmL, 0.490 mmol, 0.075 eq). The crude product was purified by a short column chromatography using basic alumina and hexane as eluent to obtain 1-nitro-4-((vinyloxy)methyl)benzene (**5i**) as a colorless oil (973 mg, 5.43 mmol, 83% yield).

R_f 0.9 (9:1 Hexane/Et_2O).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (m, 2 H, *Ar*), 7.53 (m, 2 H, *Ar*), 6.57 (dd, 1 H, *J* = 14.3, 6.8 Hz, C*H*=C), 4.87 (s, 2 H, OC*H*$_2$Ar), 4.30 (dd, 1 H, *J* = 14.3, 2.5 Hz, C=C*H*$_2$), 4.16 (dd, 1 H, *J* = 6.8, 2.5 Hz, C=C*H*$_2$).

[17] N-A. Harada, T. Nishikata, H. Nagashima, *Tetrahedron.* 2012, 68, 3243.

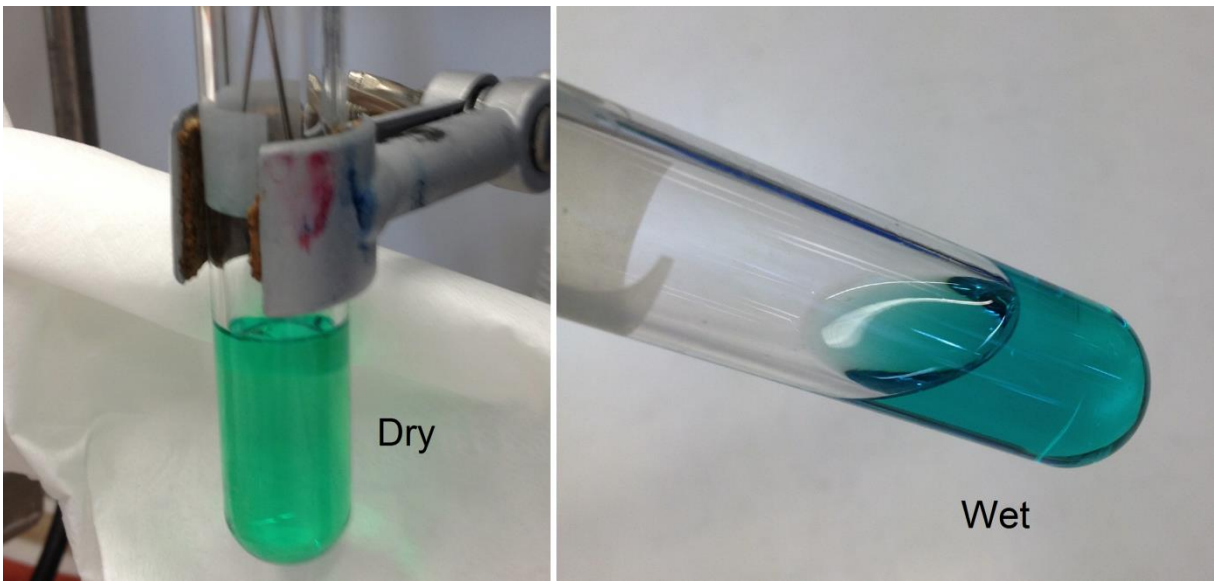
^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1, 147.5, 144.4, 127.6, 123.7, 88.2, 68.5.
The ^{1}H NMR data for **5i** corresponded to the reported values.[18]

Synthesis of cyclopentylamines and tetrahydrofurylamines:



Synthesis of [Cu(BOX)](X)$_2$ 7

Following a modified procedure,[19] an oven-dried Schlenk tube containing a magnetic stirrer was charged with $CuCl_2$ (1.1 mg, 8.0 μmol, 1.0 eq), silver salt (15 μmol, 1.9 eq) and previously activated 3 Å MS in an inert atmosphere (N_2). The flask was sealed with a septum, covered with aluminium foil and removed from the glovebox. Under argon atmosphere,[20] 0.40 mL of a solution of the corresponding BOX ligand (9.6 μmol, 1.2 eq) in dry dichloromethane were added *via* syringe. The mixture was stirred for 3 hours at room temperature and filtrated under Ar into a sealed oven-dried vial using a syringe filter (regenerated cellulose, 0.2 μm), to obtain a bright green solution that was used for the catalysis.[21]



General Procedure for the racemic [3+2] Annulation Reaction:

A. Racemic cyclopentylamines or tetrahydrofurylamines were synthesized using 1 equivalent of cyclopropane with 2 equivalents of enol ether or aldehyde in presence of 20 mol% of scandium triflate in dry DCM at 0 °C. Conversion was followed by TLC and when full conversion was reached, the reaction mixture was filtered on a small silica plug. Purification by Preparative TLC afforded material that was submitted to HPLC.

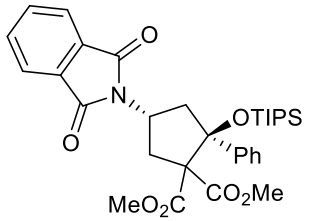
[18] S. Matysiak, H.-P. Fitznar, R. Schnell, W. Pfleiderer, *Helv. Chim. Acta* **1998**, *81*, 1545.
[19] D. A. Evans, G. S. Peterson, J. S. Johnson, D. M. Barnes, K. R. Campos, K. A. Woerpel, *J. Org. Chem.* 1998, *63*, 4541.
[20] Argon from gas cyclinder was used as using central nitrogen supply with Drierite filter gave blue complexes.
[21] Blue complex gave lower er and poorly reproducible results.

B. Racemic cyclopentylamines were synthesized using 1 equivalent of cyclopropane with 2 equivalents of enol ether in presence of 20 mol% of tin tetrachloride in dry DCM at -40°C. Conversion was followed by TLC and when full conversion was reached, the reaction mixture was filtered on a small silica plug. Purification by Preparative TLC afforded material that was submitted to HPLC.

General Procedure for the Screening of Conditions for the Catalytic Asymmetric [3+2] Annulation Reaction:

The corresponding N-protected-aminocyclopropane[22] (40.0 μmol, 1.00 eq) and freshly purified enol ether (50.0 μmol, 1.20 eq) were dissolved in 0.4 mL of dry dichloromethane. The solution was added into a sealed oven-dried vial containing a magnetic stirrer, pre-activated 3 Å MS and 0.4 mL of the solution of the desired complex (0.01 M, 4.00 μmol, 0.1 eq). Dry dichloromethane was used to complete a final volume of 1.0 mL. The mixture was stirred at rt until full conversion was obtained as verified by TLC. The reaction was quenched by addition of 0.3 mL of Et_3N and filtrated through a silica gel plug eluting with 5 mL of a mixture 1:1 Hexane/AcOEt to obtain a yellowish solution. The solvent was evaporated under reduced pressure and the crude analyzed by ^1H NMR and chiral HPLC. The yields indicated in Scheme **2B** was obtained using trimethoxybenzene as internal standard.

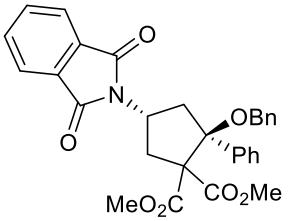
Dimethyl-(2*S*,4*S*)-4-(1,3-dioxoisoindolin-2-yl)-2-phenyl-2-((triisopropylsilyl)oxy) cyclopentane-1,1-dicarboxylate (6a)



Chiralcel IA Hexane/iPrOH 95:5, 0.5 mL/min, λ = 220 nm, tr1 = 19.8 min; tr2 = 21.2 min.
The crude of the reaction using Isopropyl-BOX/$Cu(SbF_6)_2$ complex was analyzed: er = 76:24.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 2 H, *Phth*), 7.80-7.72 (m, 4 H, *Phth* + *Ar*), 7.34-7.25 (m, 3 H, *Ar*), 5.29 (m, 1 H, N-C-*H*), 3.86 (s, 3 H, O*Me*), 3.81 (t, 1 H, *J* = 12.2 Hz, CH_2), 3.47-3.39 (m, 1H, CH_2), 3.42 (s, 3H, O*Me*), 2.91 (dd, 1 H, *J* = 13.7, 8.7 Hz, CH_2), 2.46 (dd, 1 H, *J* = 12.4, 6.2 Hz, CH_2), 1.01-0.92 (m, 21 H, TIPS).
^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 168.7, 168.4, 141.8, 134.1, 132.0, 128.4, 128.0, 127.1, 123.2, 87.6, 70.1, 52.4, 52.1, 47.8, 41.7, 36.2, 18.2, 18.2, 13.7.[23]
The characterization data for **6a** corresponded to the reported values.[24]

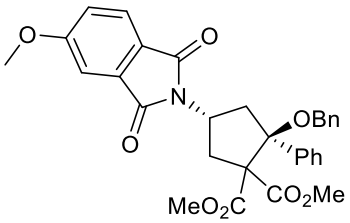
Dimethyl-(2*S*,4*S*)-2-(benzyloxy)-4-(1,3-dioxoisoindolin-2-yl)-2-phenylcyclopentane-1,1-dicarboxylate (30)

[22] Dried by dissolving in benzene then removing the solvent under reduced pressure and drying in high vacuo.
[23] The CH_3 carbons of TIPS are splitting.
[24] F. de Nanteuil, J. Waser, *Angew. Chem. Int. Ed.* **2011**, *50*, 12075.



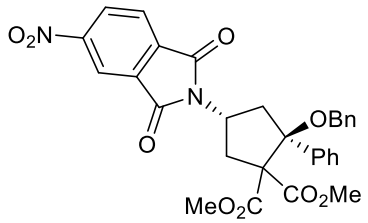
Chiralcel IA Hexane/iPrOH 95:5, 1 mL/min, λ = 254 nm, tr1 = 18.3 min; tr2 = 21.1 min.
The crude of the reaction using *tert*-butyl-BOX/$Cu(ClO_4)_2$ complex was analyzed: er = 78:22.
R_f 0.7 (5:5 Pentane/AcOEt).
M.p. 187.0 – 188.8 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.4, 3.0 Hz, 2 H, *Phth*), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2 H, *Phth*), 7.66 – 7.58 (m, 2 H, *Ar*), 7.42 – 7.27 (m, 8 H, *Ar*), 5.06 (dddd, *J* = 11.6, 10.0, 7.5, 6.2 Hz, 1 H, N-C-*H*), 4.39 (d, *J* = 11.7 Hz, 1 H, C*H*$_2$ Benzyl), 4.08 (d, *J* = 11.7 Hz, 1 H, C*H*$_2$ benzyl), 3.82-3.73 (m, 1 H, C*H*$_2$), 3.76 (s, 3 H, O*Me*), 3.65 – 3.49 (m, 1 H, C*H*$_2$), 3.60 (s, 3 H, O*Me*), 2.88 (dd, *J* = 14.0, 7.5 Hz, 1 H, C*H*$_2$), 2.57 (dd, *J* = 13.1, 6.3 Hz, 1 H, C*H*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 168.5, 168.3, 138.2, 136.5, 134.1, 131.9, 129.2, 128.3, 128.1, 127.3, 127.2, 126.5, 123.3, 89.8, 68.2, 63.5, 52.4, 52.2, 46.4, 36.1, 35.6.
IR 1737 (s), 1712 (s), 1435 (w), 1379 (m), 1259 (w), 1127 (m).
HRMS (ESI) calcd for $C_{30}H_{27}NNaO_7^+$ $[M+Na]^+$ 536.1680; found 536.1667.

Dimethyl-(2*S*,4*S*)-2-(benzyloxy)-4-(5-methoxy-1,3-dioxoisoindolin-2-yl)-2-phenylcyclopentane-1,1-dicarboxylate (31)



Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 220 nm, tr1 = 15.4 min; tr2 = 56.1 min.
The crude of the reaction using *tert*-butyl-BOX/$Cu(ClO_4)_2$ complex was analyzed: er = 74:26.
R_f 0.8 (5:5 Pentane/AcOEt).
M.p. 128.3 – 130.7 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 1 H, *Ar*), 7.67 – 7.58 (m, 2 H, *Ar*), 7.41 – 7.27 (m, 9 H, *Ar*), 7.16 (dd, *J* = 8.3, 2.3 Hz, 1 H, *Ar*), 5.10 – 4.94 (m, 1 H, N-C-*H*), 4.38 (d, *J* = 11.7 Hz, 1H, C*H*$_2$ benzyl), 4.06 (d, *J* = 11.7 Hz, 1H, C*H*$_2$ benzyl), 3.93 (m, 3 H, O*Me*), 3.83-3.71 (m, 1 H, C*H*$_2$), 3.75 (s, 3 H, O*Me*), 3.59 (s, 3 H, O*Me*), 3.57 – 3.47 (m, 1 H, C*H*$_2$), 2.86 (dd, *J* = 14.0, 7.5 Hz, 1 H, C*H*$_2$), 2.55 (dd, *J* = 13.1, 6.3 Hz, 1 H, C*H*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 168.5, 168.1, 168.1, 164.8, 138.2, 136.6, 134.5, 129.2, 128.3, 128.1, 127.3, 127.1, 126.5, 125.0, 123.9, 119.8, 108.0, 89.7, 68.2, 63.4, 56.1, 52.3, 52.2, 46.4, 36.1, 35.6.
IR 1360 (m), 1336 (s), 1263 (w), 1161 (w), 1127 (w), 1116 (w), 1115 (w), 1065 (s), 995 (m), 967 (m), 956 (m), 863 (m), 690 (m), 689 (m).
HRMS (ESI) calcd for $C_{31}H_{29}NNaO_8^+$ $[M+Na]^+$ 566.1785; found 566.1788.

Dimethyl-(2*S*,4*S*)-2-(benzyloxy)-4-(5-nitro-1,3-dioxoisoindolin-2-yl)-2-phenylcyclopentane-1,1-dicarboxylate (32)



Chiralcel IA Hexane/iPrOH 85:15, 1 mL/min, λ = 220 nm, tr1 = 33.4min; tr2 = 36.6 min.
The crude of the reaction using *tert*-butyl-BOX/Cu(ClO_4)$_2$ complex was analyzed: er = 92:8).
R_f 0.8 (5:5 Pentane/AcOEt).
M.p. 95.5 – 98.3 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 – 8.50 (m, 2 H, *Ar*), 8.05 (dd, *J* = 8.1, 0.7 Hz, 1 H, *Ar*), 7.80 – 7.57 (m, 2 H, *Ar*), 7.48 – 7.13 (m, 8 H, *Ar*), 5.06 (tdd, *J* = 7.7, 4.3, 2.2 Hz, 1 H, N-C-*H*), 4.36 (d, *J* = 11.8 Hz, 1 H, C*H*$_2$ benzyl), 4.10 (d, *J* = 11.7 Hz, 1 H, C*H*$_2$ benzyl), 3.84 – 3.67 (m, 1 H, C*H*$_2$), 3.76 (s, 3 H, O*Me*), 3.67 – 3.44 (m, 1 H, C*H*$_2$), 3.60 (s, 3 H, O*Me*), 2.86 (dd, *J* = 14.0, 7.4 Hz, 1 H, C*H*$_2$), 2.60 (dd, *J* = 13.1, 6.3 Hz, 1 H, C*H*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 168.3, 166.1, 165.8, 151.8, 138.0, 136.3, 136.2, 133.3, 129.4, 129.1, 128.4, 128.3, 127.4, 127.3, 126.5, 124.5, 118.7, 89.8, 68.2, 63.6, 52.4, 52.3, 47.2, 36.0, 35.6.
IR 1393 (w), 1345 (s), 1201 (m), 1126 (w), 1115 (w), 1069 (m), 1043 (s), 972 (w), 868 (m), 691 (m).
HRMS (ESI) calcd for $C_{30}H_{26}N_2NaO_9^+$ $[M+Na]^+$ 581.1531; found 581.1540.

General Procedure for the Catalytic Asymmetric [3+2] Annulation Reaction

Dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (**4b**) (51.0 mg, 0.200 mmol, 1.00 eq) and freshly purified enol ether or aldehyde (0.400 mmol, 2.00 eq) were dissolved in 2.0 mL of dry dichloromethane. The solution was added into a sealed oven-dried vial containing a magnetic stirrer, pre-activated 3 Å MS and 2.0 mL of the solution of the copper complex (0.01M, 0.020 mmol, 0.10 eq). Dry dichloromethane was used to complete a final volume of 5.0 mL. The mixture was stirred at rt until full conversion was observed by TLC. The reaction was quenched by addition of 0.5 mL of Et_3N and filtrated through a silica gel plug eluting with 10 mL of a mixture of 3:7 Hexane/AcOEt. The solvent was evaporated under reduced pressure and the crude analyzed by ^{1}H NMR. Purification by column chromatography using pentane/AcOEt (6:4 to 3:7) afforded the product as a mixture of diastereoisomers. In the case of the reaction with enol ether, it was possible to purify the major diastereomer by preparative TLC for characterization and HPLC analysis. For aldehydes, characterization was done directly on the obtained mixture of diastereoisomers.

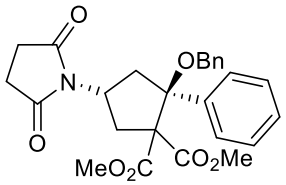
Racemization experiment of cyclopropane 4b

Dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (**4b**) (10 mg, 0.039 mmol, 1.00 eq) was dissolved in 0.5 mL of dry dichloromethane. The solution was added into a sealed oven-dried vial containing a magnetic stirrer, pre-activated 3 Å MS and 2.0 mL of the solution of the copper complex (0.0020 M, 0.0039 mmol, 0.10 eq). Two aliquots (1 mL each) were taken at 30 min and 3 h after the reaction was set up. The aliquots were filtered over a pad of alumina, eluting with AcOEt, and were submitted to chiral HPLC analysis.

er$_{30\ min}$ = 50:50, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 23.9 min; tr2 = 26.8 min.

er$_{3h}$ = 50:50, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 23.7 min; tr2 = 26.4 min.

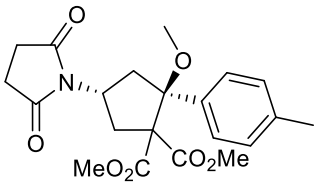
Dimethyl-(2*S*,4*S*)-2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)-2-phenylcyclopentane-1,1-dicarboxylate (6b)



Following the general procedure, using (1-(benzyloxy)vinyl)benzene (**5b**) (84.0 mg, 0.400 mmol, 2.00 eq), dimethyl 2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)-2-phenylcyclopentane-1,1-dicarboxylate (**6b**) (90.3 mg, 0.194 mmol, 97 %) was obtained as a colorless solid.

Crude analysis: *dr* = 7:1 between peaks at 5.01 (*minor*) and 4.67 (*major*).
er$_{major}$ = 96:4, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 18.2 min; tr2 = 24.0 min.
[α]$_D^{25.0}$ -21.0 (c = 0.43, $CHCl_3$).
R$_f$ 0.30 (5:5 Hexane/AcOEt).
M.p. 90.1 – 91.7 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.41 (m, 2 H, *Ar*), 7.32 – 7.13 (m, 8 H, *Ar*), 5.01 – 4.67 (m, 1 H, N-C-*H*), 4.33 (d, *J* = 11.7 Hz, 1H, C*H*$_2$ benzyl), 4.03 (d, *J* = 11.7 Hz, 1H, C*H*$_2$ benzyl), 3.66 (s, 3 H, O*Me*), 3.56 (dd, *J* = 13.1, 11.6 Hz, 1 H, C*H*$_2$), 3.49 (s, 3 H, O*Me*), 3.37 (ddd, *J* = 14.0, 10.3, 0.9 Hz, 1 H, C*H*$_2$), 2.71 (dd, *J* = 13.9, 7.2 Hz, 1 H, C*H*$_2$), 2.63 (s, 4 H, C*H*$_2$ succinimide), 2.38 (dd, *J* = 13.0, 6.4 Hz, 1 H, C*H*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.0, 170.1, 168.3, 138.0, 136.3, 129.1, 128.2, 128.0, 127.1, 127.0, 126.3, 89.6, 68.0, 63.2, 52.2, 52.1, 46.9, 34.9, 34.5, 28.0.
IR 2255 (w), 1738 (w), 1704 (m), 1382 (w), 1260 (w), 1178 (w), 906 (s).
HRMS (ESI) calcd for $C_{26}H_{27}NNaO_7^+$ $[M+Na]^+$ 488.1680; found 488.1687.

Dimethyl-(2S,4S)-4-(2,5-dioxopyrrolidin-1-yl)-2-methoxy-2-(p-tolyl)cyclopentane-1,1-dicarboxylate (6c)

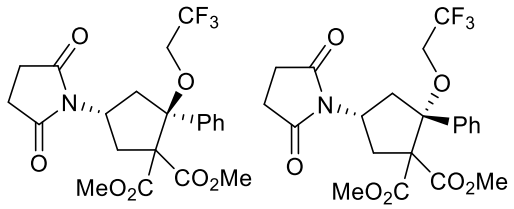


Following the general procedure, using 1-(1-methoxyvinyl)-4-methylbenzene (**5c**) (59.3 mg, 0.400 mmol, 2.00 eq), dimethyl 4-(2,5-dioxopyrrolidin-1-yl)-2-methoxy-2-(p-tolyl)cyclopentane-1,1-dicarboxylate (**6c**) (77.0 mg, 0.191 mmol, 95 %) was obtained as a colorless solid.

Crude analysis: *dr*= 20:1 between peaks at 5.17 (*minor*) and 4.84 (*major*).
er$_{major}$ = 94.5:5.5, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ=220 nm, tr1 = 17.9 min; tr2 = 22.5 min.
[α]$_D^{25.0}$ 15.7 (c = 0.81, $CHCl_3$).

R_f 0.3 (3:7 Pentane/AcOEt).
M.p. 97.5 - 99.0 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.3 Hz, 2 H, *Ar*), 7.13 (d, *J* = 8.1 Hz, 2 H, *Ar*), 4.83 (tt, *J* = 11.0, 6.6 Hz, 1 H, N-C*H*), 3.74 (s, 3 H, O*Me*), 3.58 (s, 3 H, O*Me*), 3.54 – 3.42 (m, 1 H, CH_2), 3.36 (dd, *J* = 14.0, 10.7 Hz, 1 H, CH_2), 2.97 (s, 3 H, *Me*), 2.80 – 2.60 (m, 1 H, CH_2), 2.72 (s, 4 H, CH_2 succinimide), 2.40 – 2.22 (m, 1 H, CH_2), 2.36 (s, 3 H, *Me*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.1, 170.2, 168.5, 137.6, 133.0, 129.3, 127.8, 89.5, 67.7, 52.2, 52.1, 49.5, 46.5, 34.9, 33.8, 28.0, 21.1.
IR 1740 (s), 1703 (s), 1436 (w), 1399 (w), 1382 (m), 1382 (m), 1294 (w), 1276 (w), 1276 (w), 1261 (w), 1178 (m).
HRMS (ESI) calcd for $C_{21}H_{25}NNaO_7^+$ $[M+Na]^+$ 426.1523; found 426.1516.

<u>Dimethyl-(2S,4S)-4-(2,5-dioxopyrrolidin-1-yl)-2-phenyl-2-(2,2,2-trifluoroethoxy)cyclopentane-1,1-dicarboxylate (6d)</u>

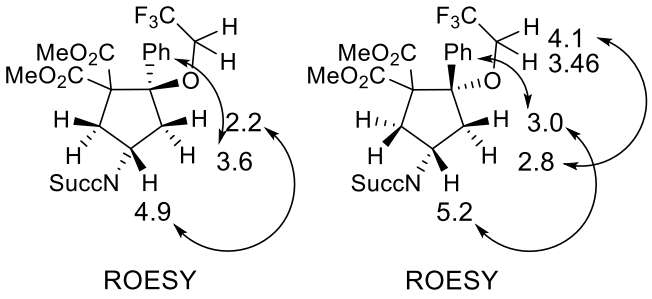


Following the general procedure, using (1-(2,2,2-trifluoroethoxy)vinyl)benzene (**5d**) (81.0 mg, 0.400 mmol, 2.00 eq), dimethyl 4-(2,5-dioxopyrrolidin-1-yl)-2-phenyl-2-(2,2,2-trifluoroethoxy)cyclopentane-1,1-dicarboxylate (**6d**) (80.4 mg, 0.176 mmol, 88 %) was obtained as a colorless oil.

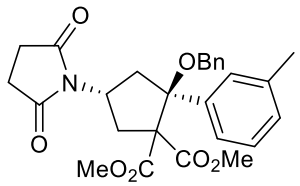
Crude analysis: *dr* = 1.5:1 between peaks at 5.06 (*minor*) and 4.75 (*major*).
<u>*anti*</u>
er = 95.5:4.5, Chiralcel IB Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 14.6 min; tr2 = 17.4 min.
[α]$_D^{25.0}$ 18.9 (c = 0.43, $CHCl_3$).
R_f 0.2 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.43 (m, 2 H, *Ar*), 7.43 – 7.28 (m, 3 H, *Ar*), 4.97 – 4.75 (m, 1 H, N-C*H*), 3.80 (s, 3 H, O*Me*), 3.60 (dd, *J* = 13.4, 11.6 Hz, 1 H, CH_2), 3.56 – 3.44 (m, 1 H, CH_2-CF_3), 3.53 (s, 3 H, O*Me*), 3.43 – 3.30 (m, 2 H, CH_2 + CH_2-CF_3), 2.84 – 2.75 (m, 1 H, CH_2), 2.71 (s, 4 H, CH_2 succinimide), 2.24 (dd, *J* = 13.3, 6.4 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.0, 169.8, 167.7, 135.0, 129.0, 128.7, 127.6, 123.6 (q, *J* = 278 Hz), 90.4, 67.7, 60.50 (q, *J* = 35 Hz), 52.4, 52.3, 46.6, 34.8, 34.6, 28.0.
IR 1808 (m), 1771 (s), 1521 (w), 1520 (w), 1459 (w), 1355 (m), 1256 (s).
HRMS (ESI) calcd for $C_{21}H_{22}F_3NNaO_7^+$ $[M+Na]^+$ 480.1241; found 480.1243.

<u>*syn*</u>
er = 96.5:3.5, Chiralcel IA Hexane/iPrOH 90:10, 1 mL/min, λ = 220 nm, tr1 = 28.6 min; tr2 = 31.1 min.
[α]$_D^{25.0}$ -2.3 (c = 0.39, $CHCl_3$).
R_f 0.3 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.52 (m, 2 H, *Ar*), 7.41 – 7.29 (m, 3 H, *Ar*), 5.20 – 5.06 (m, 1 H, N-C*H*), 4.06 (dq, *J* = 10.2, 8.4 Hz, 1 H, CH_2-CF_3), 3.75 (s, 3 H, *OMe*), 3.61 – 3.40

(m, 1 H, C*H*$_2$ + C*H*$_2$-CF_3), 3.50 (s, 3 H, O*Me*), 3.01 (dd, *J* = 15.1, 11.0 Hz, 1 H, C*H*$_2$), 2.84 – 2.67 (m, 5 H, C*H*$_2$ succinimide + C*H*$_2$), 2.34 (dd, *J* = 12.9, 7.4 Hz, 1 H, C*H*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.1, 169.3, 167.6, 135.2, 129.1, 128.4, 127.6, 124.1 (q, *J* = 278 Hz), 90.7, 70.0, 60.4 (q, *J* = 35 Hz), 52.5, 52.1, 47.4, 36.5, 33.7, 28.0.
IR 1737 (m), 1705 (s), 1447 (w), 1382 (w), 1279 (m), 1256 (w), 1170 (s).
HRMS (ESI) calcd for $C_{21}H_{22}F_3NNaO_7^+$ $[M+Na]^+$ 480.1241; found 480.1237.



Dimethyl-(2*S*,4*S*)-2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)-2-(*m*-tolyl)cyclopentane-1,1-dicarboxylate (6e)

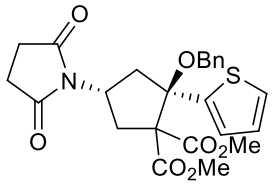


Following the general procedure, using 1-(1-(benzyloxy)vinyl)-3-methylbenzene (**5e**) (90.0 mg, 0.400 mmol, 2.00 eq), dimethyl 2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)-2-(m-tolyl)cyclopentane-1,1-dicarboxylate (**6e**) (96.0 mg, 0.199 mmol, 99%) was obtained as a colorless oil.

Crude analysis: *dr* >20:1.
er = 95:5, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 220 nm, tr1 = 16.2 min; tr2 = 22.1 min.
$[\alpha]_D^{25.0}$ -16.5 (c = 0.44, $CHCl_3$).
R_f 0.25 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 4 H, *Ar*), 7.28 – 7.23 (m, 3 H, *Ar*), 7.20 (t, *J* = 7.7 Hz, 1 H, *Ar*), 7.11 (d, *J* = 7.5 Hz, 1 H, *Ar*), 4.97 – 4.81 (m, 1 H, N-C*H*), 4.31 (d, *J* = 11.7 Hz, 1 H, C*H*$_2$ benzyl), 4.03 (d, *J* = 11.7 Hz, 1 H, C*H*$_2$ benzyl), 3.73 (s, 3 H, O*Me*), 3.65 – 3.55 (m, 1 H, C*H*$_2$), 3.57 (s, 3 H, O*Me*), 3.44 (dd, *J* = 13.9, 10.4 Hz, 1 H, C*H*$_2$), 2.78 (dd, *J* = 13.9, 7.0 Hz, 1 H, C*H*$_2$), 2.70 (s, 4 H, C*H*$_2$ succinimide), 2.45 (dd, *J* = 13.0, 6.5 Hz, 1 H, C*H*$_2$), 2.34 (s, 3 H, *Me*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.1, 170.2, 168.3, 138.2, 136.5, 136.3, 130.0, 128.8, 128.3, 127.1[25], 126.4, 126.2, 89.7, 68.1, 63.3, 52.2, 52.1, 46.9, 35.0, 34.6, 28.0, 21.7.
IR 2924 (w), 1739 (m), 1703 (s), 1435 (w), 1383 (m), 1295 (w), 1259 (w), 1181 (m), 738 (w).
HRMS (ESI) calcd for $C_{27}H_{29}NNaO_7^+$ $[M+Na]^+$ 502.1836; found 502.1845.

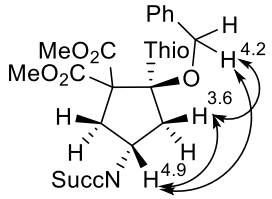
[25] 2 carbon signal overlapping.

Dimethyl-(2*R*,4*S*)-2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)-2-(thiophen-2-yl)cyclopentane-1,1-dicarboxylate (6f)



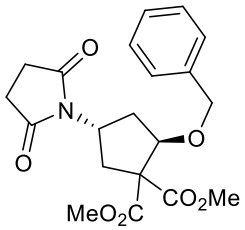
Following the general procedure, using 2-(1-(benzyloxy)vinyl)thiophene (**5f**) (87.0 mg, 0.400 mmol, 2.00 eq), dimethyl 2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)-2-(thiophen-2-yl)cyclopentane-1,1-dicarboxylate (**6f**) (89.1 mg, 0.189 mmol, 94%) was obtained as a colorless oil.

Crude analysis: *dr* = 8:1 between peaks at 5.11 (*minor*) and 4.86 (*major*).
er_{major} = 94:6, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 27.0 min; tr2 = 40.2 min.
[α]$_D^{25.0}$ -11.8 (c = 0.44, $CHCl_3$).
R_f 0.2 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.14 (m, 7 H, *Ar*), 6.97 (dd, *J* = 5.1, 3.6 Hz, 1 H, *Thiophene*), 4.86 (dddd, *J* = 11.9, 10.0, 7.9, 6.3 Hz, 1 H, N-C*H*), 4.33 (d, *J* = 11.4 Hz, 1H, CH_2 *benzyl*), 4.14 (d, *J* = 11.4 Hz, 1H, CH_2 *benzyl*), 3.79 (s, 3 H, O*Me*), 3.63 – 3.52 (m, 1 H, CH_2), 3.60 (s, 3 H, O*Me*), 3.38 (dd, *J* = 13.9, 10.1 Hz, 1 H, CH_2), 2.79 (dd, *J* = 13.9, 7.9 Hz, 1 H, CH_2), 2.70 (s, 4 H, CH_2 succinimide), 2.59 (dd, *J* = 12.9, 6.3 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 177.2, 170.2, 168.5, 141.4, 138.0, 128.9, 128.3, 127.4, 126.9, 126.6, 126.0, 87.7, 68.2, 63.9, 52.5, 52.4, 47.1, 36.8, 34.7, 28.2.
IR 1740 (s), 1704 (s), 1435 (w), 1384 (w), 1270 (w), 1175 (m).
HRMS (ESI) calcd for $C_{24}H_{25}NNaO_7S^+$ $[M+Na]^+$ 494.1244; found 494.1241.



ROESY

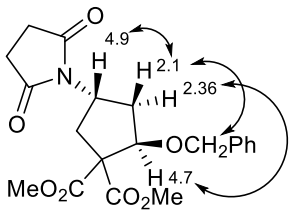
Dimethyl-(2*R*,4*S*)-2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)cyclopentane-1,1-dicarboxylate (6g)



Following the general procedure, using ((vinyloxy)methyl)benzene (**5g**) (53.7 mg, 0.400 mmol, 2.00 eq), dimethyl 2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)cyclopentane-1,1-

dicarboxylate (**6g**) (74.8 mg, 0.192 mmol, 96%) was obtained as a colorless solid. Recrystallized from isopropanol.[26]

Crude analysis: *dr*= 4:1 between peaks at 3.79 (*major*) and 3.75 (*minor*).
er_{major} = 96.5:3.5, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm, tr1 = 27.4 min; tr2 = 37.8 min.
[α]$_D^{25.0}$ -32.7 (c = 0.43, $CHCl_3$).
R_f 0.3 (5:5 Pentane/AcOEt).
M.p. 106.8 – 109.5 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 5 H, *Ar*), 5.03 – 4.82 (m, 1 H, N-C-*H*), 4.75 (dd, *J* = 4.7, 2.7 Hz, 1 H, O-C-*H*), 4.59 (d, *J* = 11.9 Hz, 1H, CH_2 benzyl) 4.49 (d, *J* = 11.9 Hz, 1H, CH_2 benzyl), 3.79 (s, 3 H, O*Me*), 3.68 (s, 3 H, O*Me*), 3.03 (dd, *J* = 14.4, 10.6 Hz, 1 H, CH_2), 2.64 (s, 4 H, *succinimide*), 2.50 – 2.29 (m, 2 H, CH_2), 2.15 (ddd, *J* = 13.4, 8.3, 2.7 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 171.0, 169.0, 138.0, 128.3, 127.6, 127.4, 83.0, 71.7, 65.1, 52.9, 52.7, 48.0, 34.0, 33.3, 28.0.
IR 1737 (m), 1702 (s), 1398 (w), 1397 (w), 1384 (w), 1283 (w), 1262 (w), 1175 (m), 1100 (w).
HRMS (ESI) calcd for $C_{20}H_{24}NO_7^+$ $[M+H]^+$ 390.1547; found 390.1554.



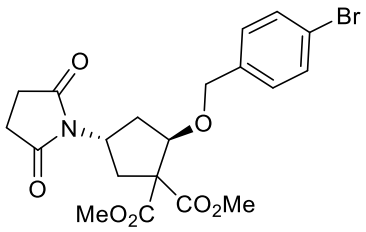
ROESY

Procedure for the Catalytic Asymmetric [3+2] Annulation Reaction on 1 mmol scale:

Dimethyl 2-(2,5-dioxopyrrolidin-1-yl)cyclopropane-1,1-dicarboxylate (**4b**) (255 mg, 1.00 mmol, 1.00 eq) and freshly purified enol ether **5g** (268 mg, 2.00 mmol, 2.00 eq) were dissolved in 10.0 mL of dry dichloromethane. The solution was added into a sealed oven-dried vial containing a magnetic stirrer, pre-activated 3 Å MS and 10.0 mL of the solution of the copper complex (0.01 M, 0.100 mmol, 0.10 eq). Dry dichloromethane was used to complete a final volume of 25.0 mL. The mixture was stirred at rt for 2 hours and full conversion was observed by TLC. The reaction was quenched by addition of 1 mL of Et_3N and filtrated through a silica gel plug eluting with 50 mL of a mixture of 3:7 Hexane/AcOEt. The solvent was evaporated under reduced pressure and the crude analyzed by ^{1}H NMR. Purification by column chromatography using pentane/AcOEt (6:4 to 3:7) afforded dimethyl-2-(benzyloxy)-4-(2,5-dioxopyrrolidin-1-yl)cyclopentane-1,1-dicarboxylate (**6g**) (311 mg, 0.800 mmol, 80%) as a colorless solid.
Crude analysis: *dr*= 4:1 between peaks at 3.03 (*major*) and 3.37 (*minor*).
er_{major} = 95.5:4.5, Chiralcel IA Hexane/iPrOH 80:20, 1 mL/min, λ = 210 nm.

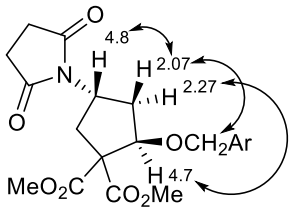
Dimethyl-(2*R*,4*S*)-2-((4-bromobenzyl)oxy)-4-(2,5-dioxopyrrolidin-1-yl)cyclopentane-1,1-dicarboxylate (6h)

[26] Structure is registered in CCDC under the number CCDC 988525



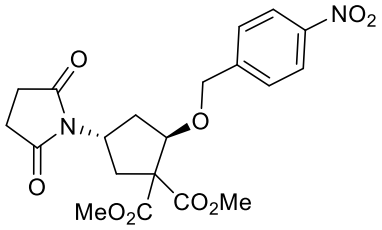
Following the general procedure, using 1-bromo-4-((vinyloxy)methyl)benzene (**5h**) (85.0 mg, 0.400 mmol, 2.00 eq), dimethyl 2-((4-bromobenzyl)oxy)-4-(2,5-dioxopyrrolidin-1-yl)cyclopentane-1,1-dicarboxylate (**6h**) (68.2 mg, 0. 146 mmol, 72.8 %) was obtained as a colorless oil.

Crude analysis: *dr* = 5:1 between peaks at 3.36 (*minor*) and 3.00 (*major*).
er_{major} > 94.5:5.5[27], Chiralcel IB Hexane/iPrOH 80:20, 1 mL/min, λ = 220 nm, tr1 = 26.0 min; tr2 = 29.6 min.
[α]$_D^{25.0}$ -28.9 (c = 0.46, $CHCl_3$).
R_f 0.20 (4:6 Hexane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2 H, *Ar*), 7.13 (d, *J* = 8.3 Hz, 2 H, *Ar*), 4.93 (dtd, *J* = 10.6, 8.7, 6.4 Hz, 1 H, N-C-*H*), 4.75 (dd, *J* = 4.9, 3.0 Hz, 1 H, O-C-*H*), 4.55 (d, *J* = 11.9 Hz, 1H, CH_2 benzyl), 4.44 (d, *J* = 12.1 Hz, 1H, CH_2 benzyl), 3.79 (s, 3 H, O*Me*), 3.68 (s, 3 H, O*Me*), 3.00 (dd, *J* = 14.4, 10.6 Hz, 1 H, CH_2), 2.65 (s, 4 H, CH_2 succinimide), 2.50 – 2.24 (m, 2 H, CH_2), 2.13 (ddd, *J* = 13.5, 8.4, 3.0 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 171.0, 169.0, 137.0, 131.4, 129.0, 121.4, 83.0, 71.0, 65.0, 52.9, 52.7, 47.8, 34.1, 33.4, 28.0.
IR 1739 (m), 1703 (s), 1397 (w), 1383 (w), 1283 (w), 1262 (w), 1261 (w), 1176 (w).
HRMS (ESI) calcd for $C_{20}{}^{79}BrH_{23}NO_7^+$ $[M+H]^+$ 468.0652; found 468.0661.



ROESY

Dimethyl-(2R,4S)-4-(2,5-dioxopyrrolidin-1-yl)-2-((4-nitrobenzyl)oxy)cyclopentane-1,1-dicarboxylate (6i)



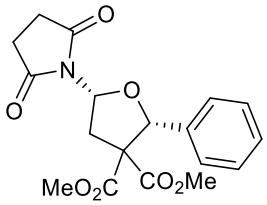
Following the general procedure, using 1-nitro-4-((vinyloxy)methyl)benzene (**5i**) (71.7 mg, 0.400 mmol, 2.00 eq), dimethyl 4-(2,5-dioxopyrrolidin-1-yl)-2-((4-

[27] Due to shoulder in the peaks, separation was not complete (*cf* HPLC spectra).

nitrobenzyl)oxy)cyclopentane-1,1-dicarboxylate (**6i**) (71.0 mg, 0.163 mmol, 82%) was obtained as a colorless solid.

Crude analysis: *dr*= 5:1 between peaks at 4.44 (*minor*) and 4.95 (*major*).
er_{major} = 98:2, Chiralcel IF Hexane/iPrOH 70:30, 1 mL/min, λ=230 nm, tr1 = 49.9 min; tr2 = 67.0 min.
[α]$_D^{25.0}$ -27.1 (c = 0.43, $CHCl_3$).
R_f 0.39 (5:5 Hexane/AcOEt).
M.p. 67.9 – 70.5 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.11 (m, 2 H, *Ar*), 7.46 – 7.39 (m, 2 H, *Ar*), 4.95 (dtd, *J* = 10.5, 8.6, 6.5 Hz, 1 H, N-C*H*), 4.86 – 4.80 (m, 1 H, C*H*O), 4.72 (d, *J* = 13.2 Hz, 1H, CH_2 benzyl), 4.62 (d, *J* = 13.2 Hz, 1H, CH_2 benzyl), 3.80 (s, 3 H, *Me*), 3.70 (s, 3 H, *Me*), 3.00 (dd, *J* = 14.4, 10.5 Hz, 1 H, CH_2), 2.66 (s, 4 H, CH_2 succinimide), 2.45 – 2.34 (m, 2 H, CH_2), 2.19 (ddd, *J* = 13.6, 8.7, 3.6 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 170.8, 168.9, 147.3, 145.5, 127.3, 123.5, 83.4, 70.5, 64.9, 52.9, 52.7, 47.6, 34.0, 33.5, 27.9.
IR 1737 (m), 1703 (s), 1523 (w), 1348 (m), 1284 (w), 1177 (w).
HRMS (ESI) calcd for $C_{20}H_{22}N_2NaO_9^+$ $[M+Na]^+$ 457.1218; found 457.1232.

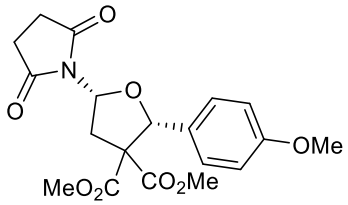
Dimethyl-(2*R*,5*R*)-5-(2,5-dioxopyrrolidin-1-yl)-2-phenyldihydrofuran-3,3(2H)-dicarboxylate (9a)



Following the general procedure, using benzaldehyde (**8a**) (42.4 mg, 0.400 mmol, 2.00 eq), dimethyl 5-(2,5-dioxopyrrolidin-1-yl)-2-phenyldihydrofuran-3,3(2H)-dicarboxylate (**9a**) (59.2 mg, 0. 164 mmol, 82 %) was obtained as a colorless oil.

Crude analysis: *dr* = 13:1 between peaks at 5.35 (*minor*) and 5.78 (*major*).
er_{major} = 92:8, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 18.9 min; tr2 = 24.3 min.
er_{minor} = 92:8, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 11.1 min; tr2 = 13.0 min.
[α]$_D^{25.0}$ 50.9 (c = 0.49, $CHCl_3$).
R_f 0.4 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.5 Hz, 2 H, *Ar*), 7.35 – 7.23 (m, 3 H, *Ar*), 5.78 (m, 2 H, N-C-*H* + Ph-C-*H*), 4.24 – 4.05 (m, 1 H, CH_2), 3.83 (s, 3 H, O*Me*), 3.10 (d, *J* = 1.7 Hz, 3 H, O*Me*), 2.75 (d, *J* = 1.7 Hz, 4 H, CH_2 succinimide), 2.45 – 2.28 (m, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 170.9, 167.8, 137.5, 128.5, 128.0, 127.6, 82.5, 79.6, 65.0, 53.4, 52.3, 33.1, 28.0.
IR 1737 (s), 1715 (s), 1436 (w), 1384 (w), 1275 (m), 1233 (w), 1169 (w).
HRMS (ESI) calcd for $C_{18}H_{20}NO_7^+$ $[M+H]^+$ 362.1234; found 362.1235.

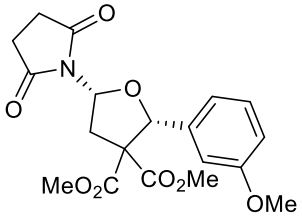
Dimethyl-(2*R*,5*R*)-5-(2,5-dioxopyrrolidin-1-yl)-2-(4-methoxyphenyl)dihydrofuran-3,3(2H)-dicarboxylate (9b)



Following the general procedure, using 4-methoxybenzaldehyde (**8b**) (54.5 mg, 0.400 mmol, 2.00 eq), dimethyl 5-(2,5-dioxopyrrolidin-1-yl)-2-(4-methoxyphenyl)dihydrofuran-3,3(2H)-dicarboxylate (**9b**) (54.1 mg, 0.138 mmol, 69%) was obtained as a colorless oil.

Crude analysis: *dr* > 20:1.
er = 96:4, Chiralcel IC Hexane/iPrOH 80:20, 1 mL/min, λ = 220 nm, tr1 = 34.9 min; tr2 = 38.5 min.
[α]$_D^{25.0}$ 17.8 (c = 0.50, $CHCl_3$).
R_f 0.30 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.38 (m, 2 H, *Ar*), 6.94 – 6.70 (m, 2 H, *Ar*), 5.87 – 5.66 (m, 2 H, N-C-*H* + Ph-C-*H*), 4.14 (dd, *J* = 13.1, 11.0 Hz, 1 H, CH_2), 3.83 (s, 3 H, O*Me*), 3.78 (s, 3 H, O*Me*), 3.17 (s, 3 H, O*Me*), 2.75 (s, 4 H, CH_2 succinimide), 2.35 (dd, *J* = 13.1, 5.1 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 170.9, 167.8, 159.7, 129.7, 128.9, 113.3, 82.3, 79.5, 64.9, 55.2, 53.4, 52.4, 33.0, 28.0.
IR 1732 (s), 1708 (s), 1614 (w), 1516 (w), 1365 (m), 1274 (m), 1250 (s), 1174 (s).
HRMS (ESI) calcd for $C_{19}H_{22}NO_8^+$ $[M+H]^+$ 392.1340; found 392.1346.

Dimethyl-(2*R*,5*R*)-5-(2,5-dioxopyrrolidin-1-yl)-2-(3-methoxyphenyl)dihydrofuran-3,3(2H)-dicarboxylate (9c)

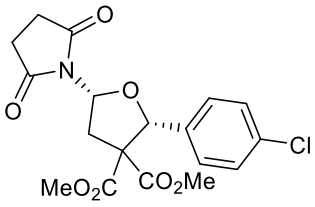


Following the general procedure, using 3-methoxybenzaldehyde (**8c**) (54.5 mg, 0.400 mmol, 2.00 eq), dimethyl 5-(2,5-dioxopyrrolidin-1-yl)-2-(3-methoxyphenyl)dihydrofuran-3,3(2H)-dicarboxylate (**9c**) (65.9 mg, 0.168 mmol, 84 %) was obtained as a colorless oil.

Crude analysis: *dr* = 10:1 between peaks at 6.05 (*minor*) and 5.82 (*major*).
er = 93:7, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 23.8 min; tr2 = 27.2 min.
[α]$_D^{25.0}$ 57.8 (c = 0.47, $CHCl_3$).
R_f 0.4 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.15 (m, 2 H, *Ar*), 7.02 (d, *J* = 7.6 Hz, 1 H, *Ar*), 6.88 – 6.73 (m, 1 H, *Ar*), 5.87 – 5.68 (m, 2 H, N-C-*H* + Ph-C-*H*), 4.15 (dd, *J* = 13.2, 11.1 Hz, 1 H, CH_2), 3.87 – 3.85 (m, 6 H, O*Me* + O*Me*), 3.16 (s, 3 H, O*Me*), 2.75 (s, 4 H, CH_2 succinimide), 2.36 (dd, *J* = 13.1, 5.0 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 170.8, 167.7, 159.5, 139.2, 128.8, 120.1, 115.2, 112.1, 82.5, 79.6, 65.1, 55.4, 53.5, 52.4, 33.0, 28.0.

IR 1736 (s), 1715 (s), 1382 (w), 1276 (m), 1233 (w), 1169 (m), 1048 (w).
HRMS (ESI) calcd for $C_{19}H_{21}NNaO_8^+$ $[M+Na]^+$ 414.1159; found 414.1181.

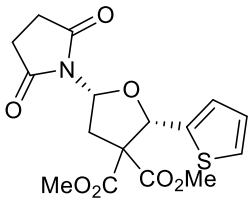
Dimethyl-(2*R*,5*R*)-2-(4-chlorophenyl)-5-(2,5-dioxopyrrolidin-1-yl)dihydrofuran-3,3(2H)-dicarboxylate (9d)



Following the general procedure, using 4-chlorobenzaldehyde (**8d**) (56.2 mg, 0.400 mmol, 2.00 eq), dimethyl 2-(4-chlorophenyl)-5-(2,5-dioxopyrrolidin-1-yl)dihydrofuran-3,3(2H)-dicarboxylate (**9d**) (71.0 mg, 0.179 mmol, 90 %) was obtained as a colorless oil.

Crude analysis: *dr* = 14:1 between peaks at 6.36 (*minor*) and 5.80 (*major*).
er = 91:9, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 19.5 min; tr2 = 47.2 min.
[α]$_D^{25.0}$ 41.8 (c = 0.53, $CHCl_3$).
R_f 0.3 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.2 Hz, 2 H, *Ar*), 7.34 – 7.27 (m, 2 H, *Ar*), 5.84 – 5.70 (m, 2 H, N-C-*H* + Ph-C-*H*), 4.10 (dd, *J* = 13.2, 10.9 Hz, 1 H, C*H*$_2$), 3.84 (d, *J* = 1.2 Hz, 3 H, O*Me*), 3.18 (d, *J* = 1.3 Hz, 3 H, O*Me*), 2.76 (s, 4 H, C*H*$_2$ succinimide), 2.38 (dd, *J* = 13.2, 5.2 Hz, 1 H, C*H*$_2$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.1, 170.7, 167.5, 136.1, 134.3, 129.0, 128.1, 81.8, 79.6, 64.9, 53.5, 52.5, 33.0, 28.0.
IR 1737 (s), 1718 (s), 1659 (w), 1382 (w), 1278 (m), 1231 (m), 1212 (w), 1168 (m).
HRMS (ESI) calcd for $C_{18}ClH_{19}NO_7^+$ $[M+H]^+$ 396.0845; found 396.0844.

Dimethyl-(2*S*,5*R*)-5-(2,5-dioxopyrrolidin-1-yl)-2-(thiophen-2-yl)dihydrofuran-3,3(2H)-dicarboxylate (9e)

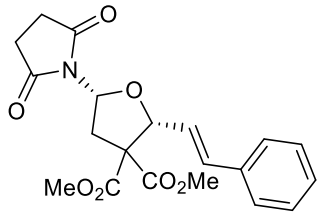


Following the general procedure, using thiophene-2-carbaldehyde (**8e**) (44.9 mg, 0.400 mmol, 2.00 eq), dimethyl 5-(2,5-dioxopyrrolidin-1-yl)-2-(thiophen-2-yl)dihydrofuran-3,3(2H)-dicarboxylate (**9e**) (71.6 mg, 0.195 mmol, 97 %) was obtained as a colorless oil.

Crude analysis: *dr* > 20:1.
er = 95:5, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 24.4 min; tr2 = 31.9 min.
[α]$_D^{25.0}$ 75.3 (c = 0.54, $CHCl_3$).
R_f 0.4 (4:6 Pentane/AcOEt).

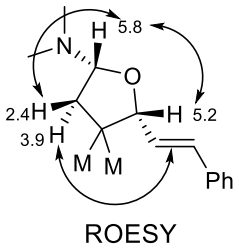
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 2.6 Hz, 2 H, *Ar*), 6.96 (dd, *J* = 5.0, 3.6 Hz, 1 H, *Ar*), 6.03 (s, 1 H, Ar-C-*H*), 5.74 (dd, *J* = 11.1, 4.9 Hz, 1 H, N-C-*H*), 4.22 (dd, *J* = 13.2, 11.1 Hz, 1 H, CH_2), 3.85 (s, 3 H, O*Me*), 3.33 (s, 3 H, O*Me*), 2.74 (s, 4 H, CH_2 succinimide), 2.39 (dd, *J* = 13.2, 4.9 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 170.4, 167.4, 140.1, 127.0, 126.7, 125.9, 79.4, 78.4, 65.2, 53.6, 52.7, 32.2, 28.0.
IR 1736 (s), 1716 (s), 1376 (w), 1279 (w), 1169 (w).
HRMS (ESI) calcd for $C_{16}H_{18}NO_7S^+$ $[M+H]^+$ 368.0799; found 368.0819.

Dimethyl-(2*R*,5*R*)-5-(2,5-dioxopyrrolidin-1-yl)-2-((E)-styryl)dihydrofuran-3,3(2H)-dicarboxylate (9f)



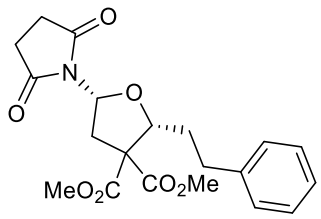
Following the general procedure, using cinnamaldehyde (**8f**) (52.9 mg, 0.400 mmol, 2.00 eq), dimethyl 5-(2,5-dioxopyrrolidin-1-yl)-2-((*E*)-styryl)dihydrofuran-3,3(2H)-dicarboxylate (**9f**) (74.0 mg, 0.191 mmol, 96 %) was obtained as a colorless oil.

Crude analysis: *dr* = 14:1 between peaks at 5.58 (*minor*) and 5.83 (*major*).
er = 94:6, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 30.2 min; tr2 = 56.1 min.
[α]$_D^{25.0}$ 14.8 (c = 0.49, $CHCl_3$).
R_f 0.4 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 2 H, *Ar*), 7.30 (dd, *J* = 8.4, 6.5 Hz, 2 H, *Ar*), 7.24 (m, 3 H, *Ar*), 6.76 – 6.51 (m, 2 H, C*H* olefin), 5.83 (dd, *J* = 10.2, 5.9 Hz, 1 H, N-C-*H*), 5.25 (dd, *J* = 5.3, 3.1 Hz, 1 H, O-C-*H*), 3.95 (dd, *J* = 13.3, 10.2 Hz, 1 H, CH_2), 3.85 (s, 3 H, O*Me*), 3.61 (s, 3 H, O*Me*), 2.72 (s, 4 H, CH_2 succinimide), 2.49 (dd, *J* = 13.3, 6.0 Hz, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.3, 170.0, 167.2, 136.2, 134.5, 128.6, 128.1, 126.9, 125.2, 83.0, 80.0, 64.8, 53.5, 53.0, 32.0, 28.0.
IR 1739 (s), 1717 (s), 1435 (w), 1276 (m), 1231 (m), 1219 (w), 1169 (m).
HRMS (ESI) calcd for $C_{20}H_{22}NO_7^+$ $[M+H]^+$ 388.1391; found 388.1388.



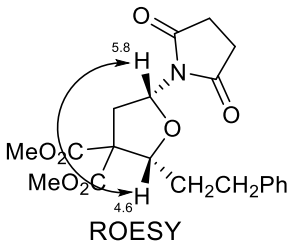
ROESY

Dimethyl-(2*R*,5*R*)-5-(2,5-dioxopyrrolidin-1-yl)-2-phenethyldihydrofuran-3,3(2H)-dicarboxylate (9g)

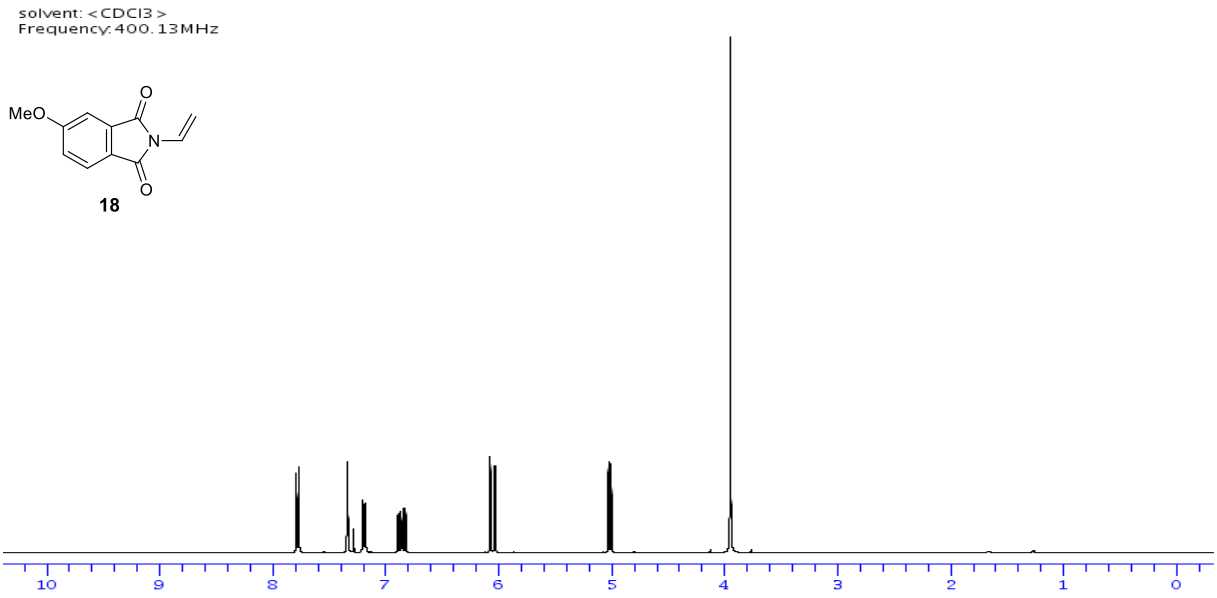


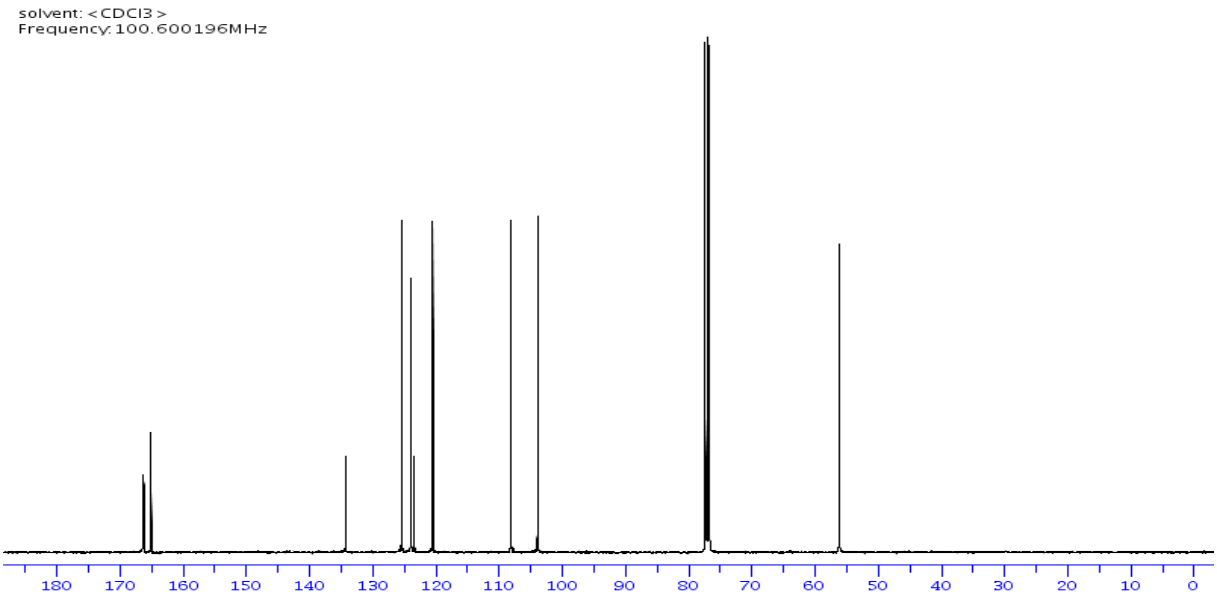
Following the general procedure, using 3-phenylpropanal (**8g**) (53.7 mg, 0.400 mmol, 2.00 eq), dimethyl 5-(2,5-dioxopyrrolidin-1-yl)-2-phenethyldihydrofuran-3,3(2H)-dicarboxylate (**9g**) (65.9 mg, 0.169 mmol, 85 %) was obtained as a colorless oil.

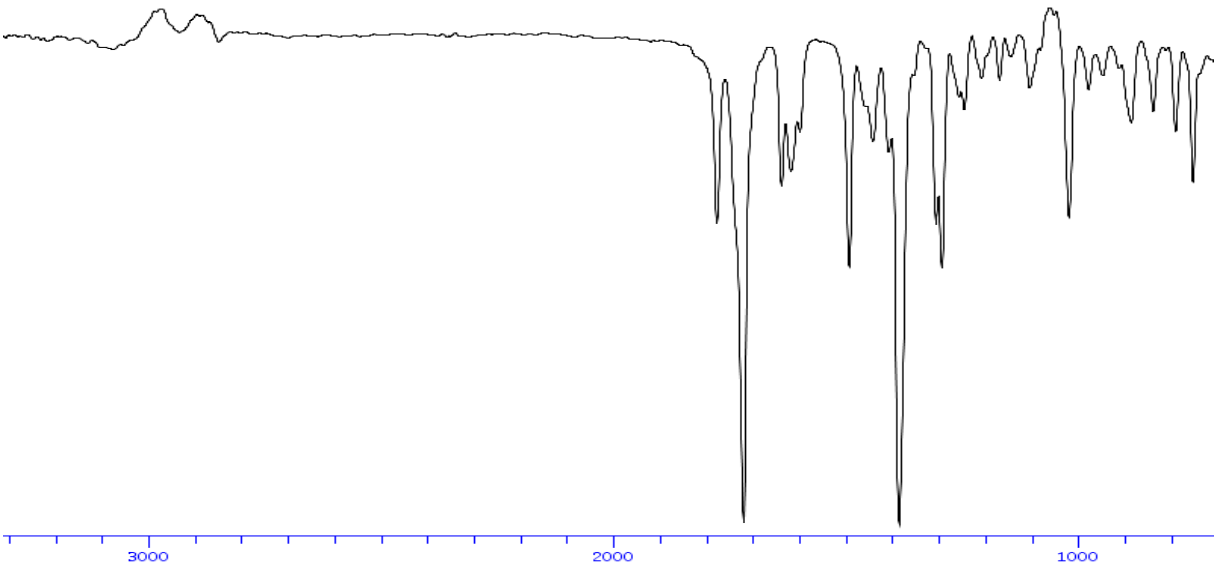
Crude analysis: *dr* = 13:1 between peaks at 6.15 (*minor*) and 5.79 (*major*).
er = 91.5:8.5, Chiralcel IA Hexane/iPrOH 70:30, 1 mL/min, λ = 210 nm, tr1 = 10.3 min; tr2 = 18.5 min.
[α]$_D^{25.0}$ 21.6 (c = 0.42, $CHCl_3$).
R_f 0.4 (4:6 Pentane/AcOEt).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.07 (m, 5 H, *Ar*), 5.79 (dd, *J* = 10.0, 6.1 Hz, 1 H, N-C-*H*), 4.65 (dd, *J* = 11.4, 2.7 Hz, 1 H, O-C-*H*), 3.83 (s, 3 H, O*Me*), 3.79 – 3.73 (m, 1 H, CH_2 THF), 3.76 (s, 3 H, O*Me*), 2.85 (ddd, *J* = 14.7, 10.5, 4.8 Hz, 1 H, CH_2), 2.76 (s, 4 H, CH_2 succinimide), 2.57 (ddd, *J* = 13.6, 10.1, 6.3 Hz, 1 H, CH_2), 2.48 (dd, *J* = 13.2, 6.1 Hz, 1 H, CH_2 THF), 2.37 – 2.24 (m, 1 H, CH_2), 1.79 – 1.53 (m, 1 H, CH_2).
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 170.3, 167.9, 141.8, 128.6, 128.3, 125.8, 80.8, 79.5, 63.6, 53.4, 53.0, 33.4, 32.3, 32.2, 28.0.
IR 1736 (s), 1712 (s), 1436 (w), 1371 (w), 1274 (m), 1168 (m), 1041 (w).
HRMS (ESI) calcd for $C_{20}H_{23}NNaO_7^+$ $[M+Na]^+$ 412.1367; found 412.1349.

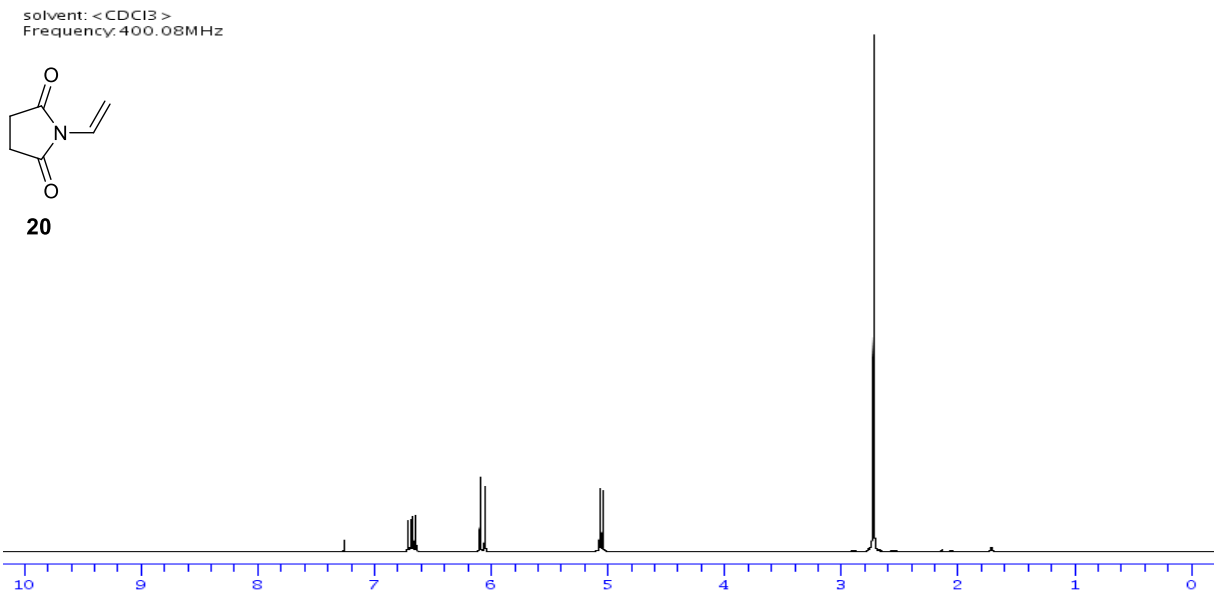


Spectra

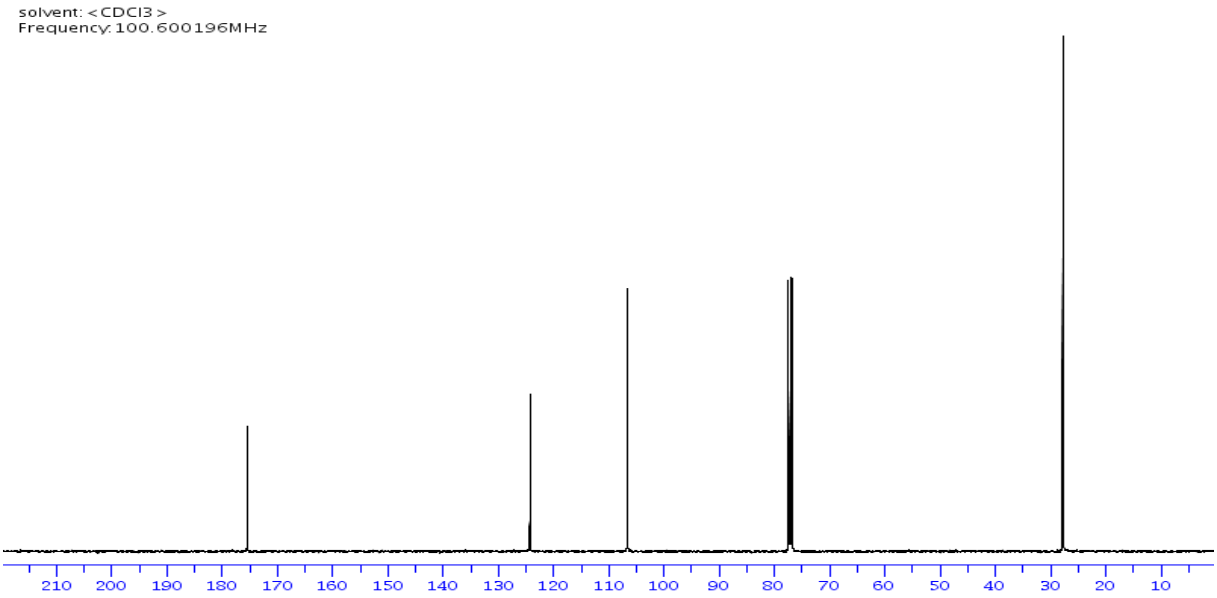

solvent: <CDCl3>
Frequency: 400.13MHz
MeO
O
N
O
18
10
9
8
7
6
5
4
3
2
1
0

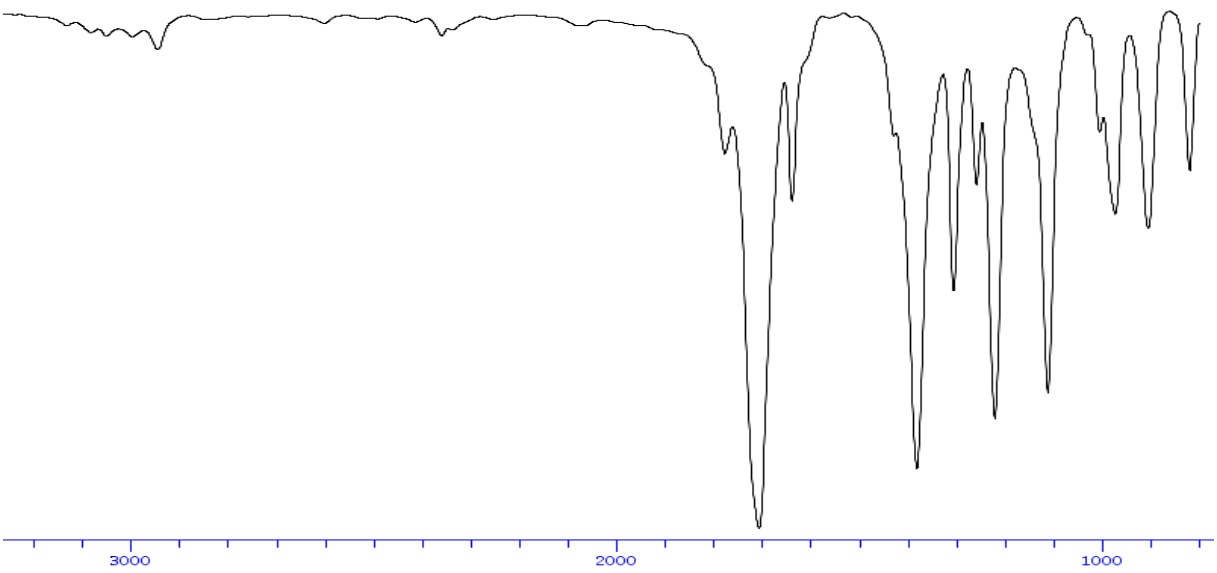

solvent: <CDCl3>
Frequency: 100.600196MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


3000
2000
1000

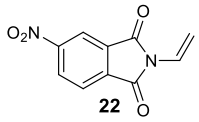

solvent: <CDCl3 >
Frequency: 400.08MHz
O
N
O
10
9
8
7
6
5
4
3
2
1
0

20

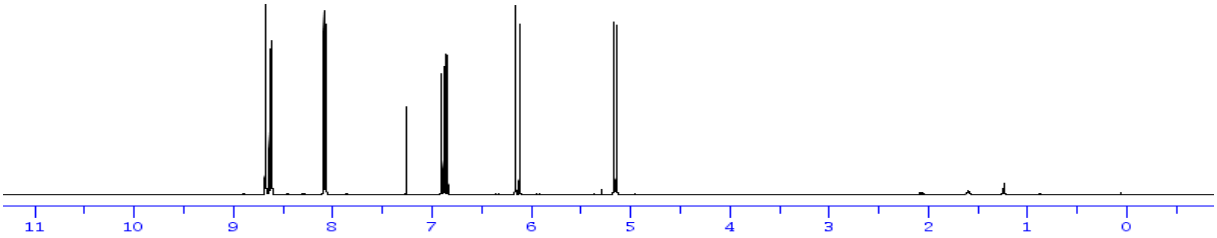

solvent: <CDCl3 >
Frequency: 100.600196MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


3000
2000
1000

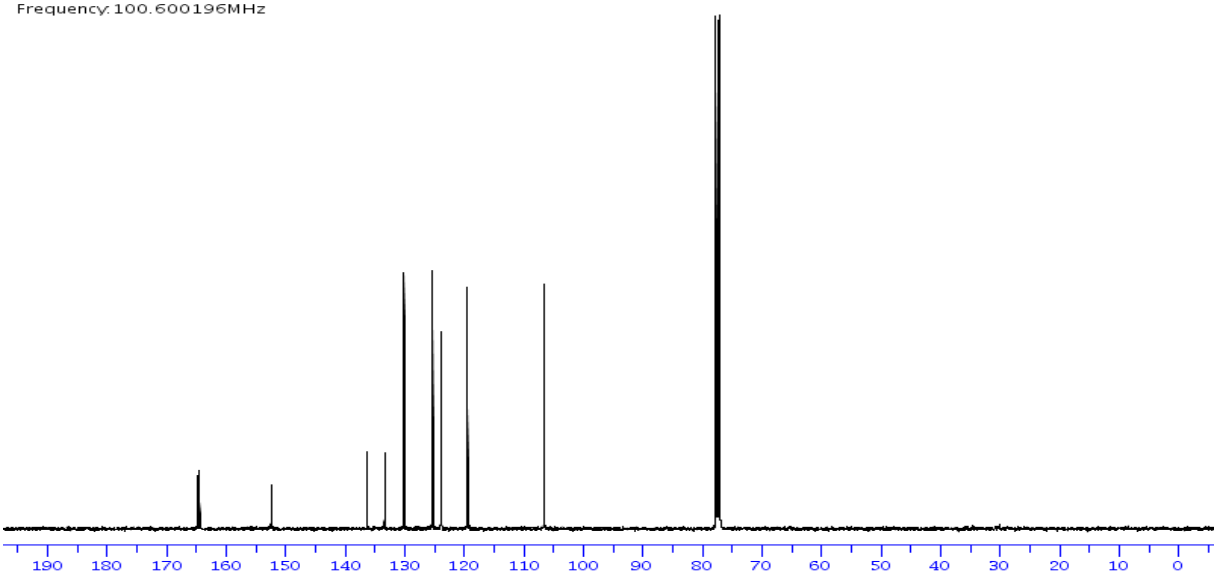
solvent: <CDCl3>
Frequency: 400.08MHz

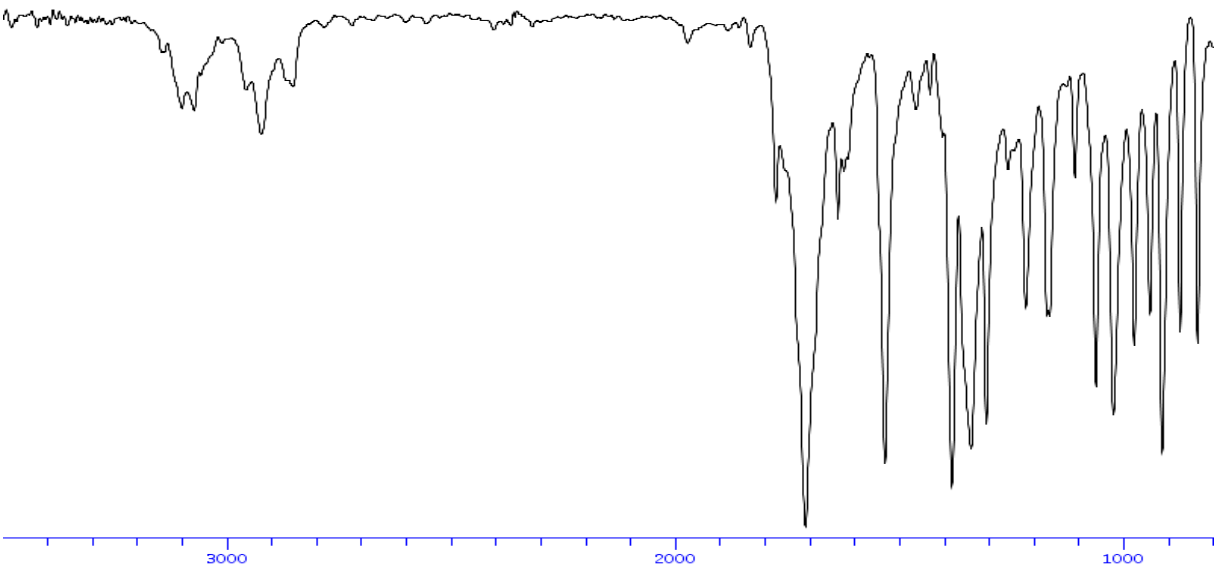


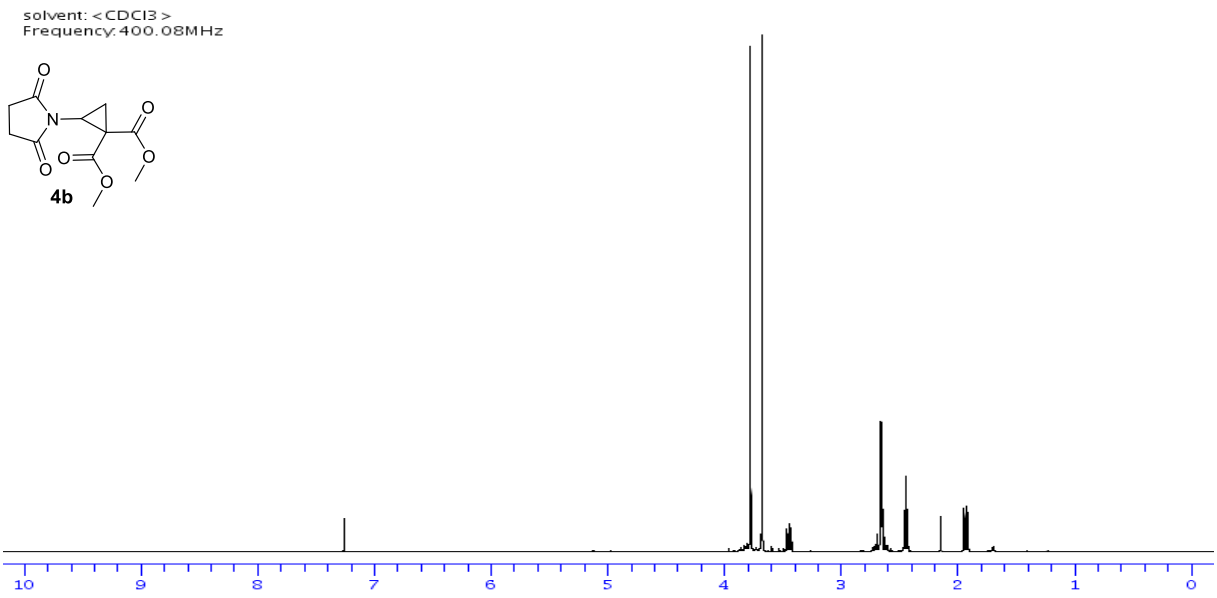
22

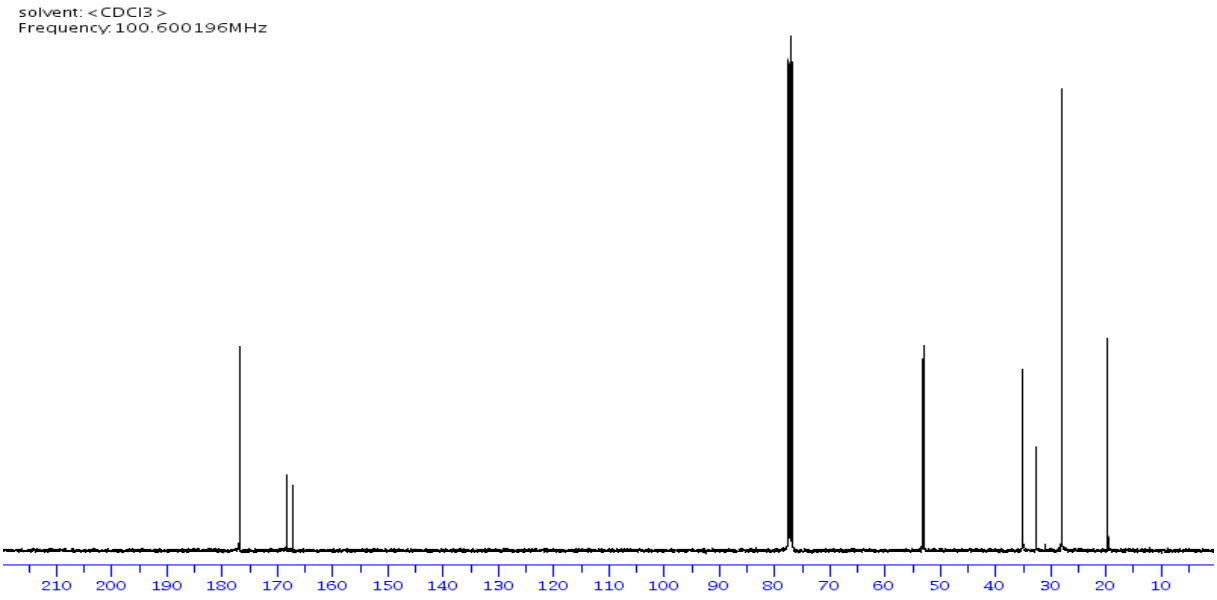


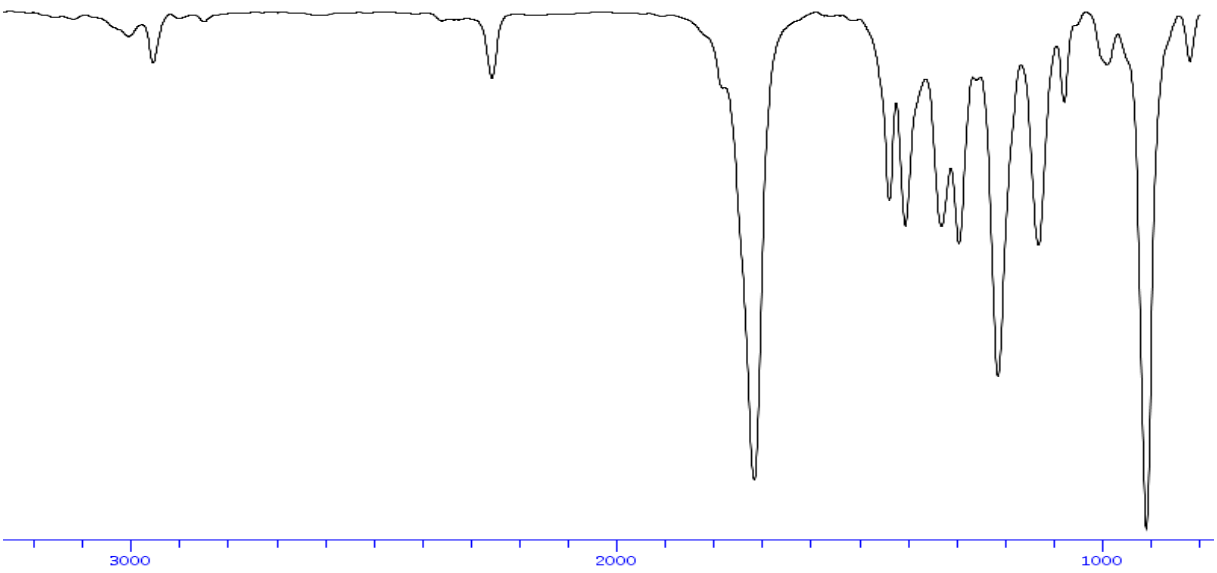
solvent: <CDCl3>
Frequency: 100.600196MHz

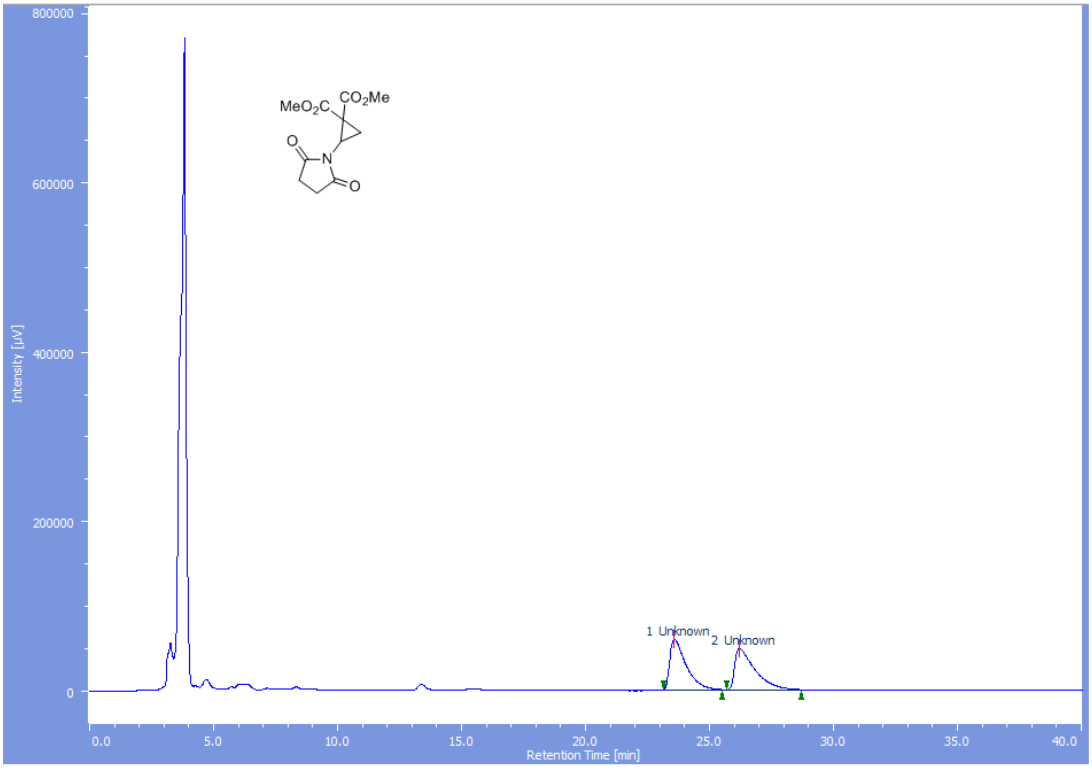




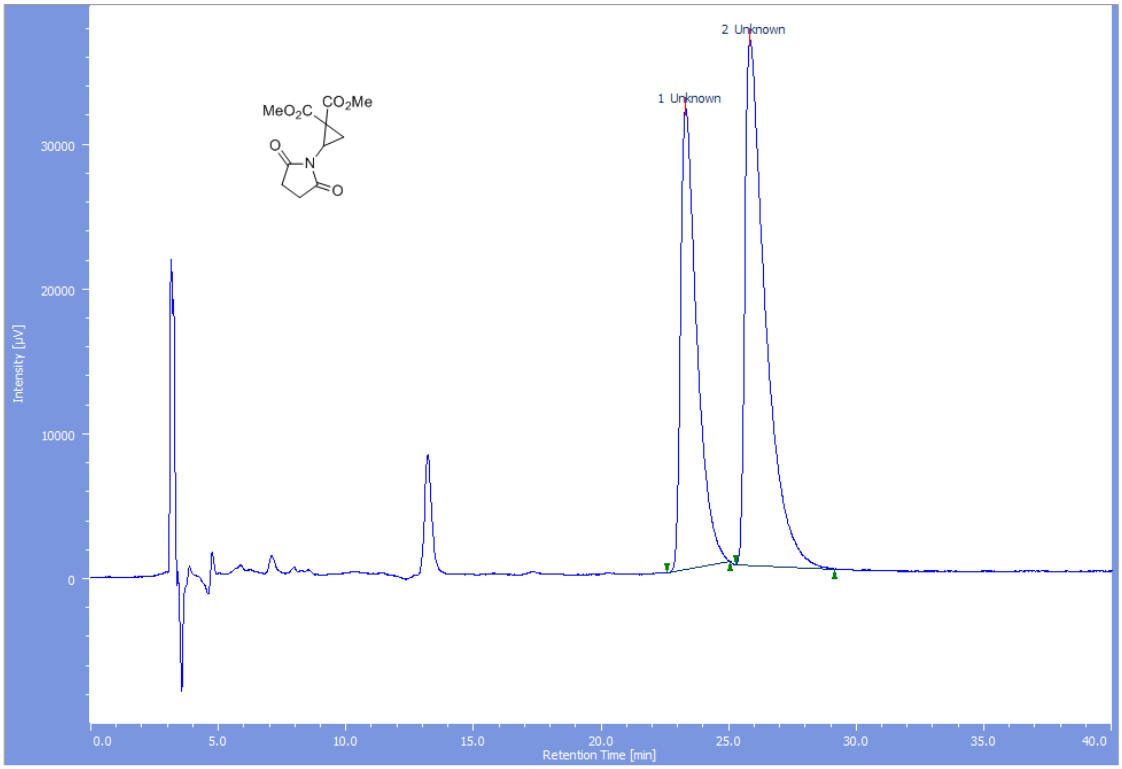

solvent: <CDCl3 >
Frequency: 400.08MHz
O
N
O
O
O
O
O
4b
10
9
8
7
6
5
4
3
2
1
0


solvent: <CDCl3 >
Frequency: 100.600196MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

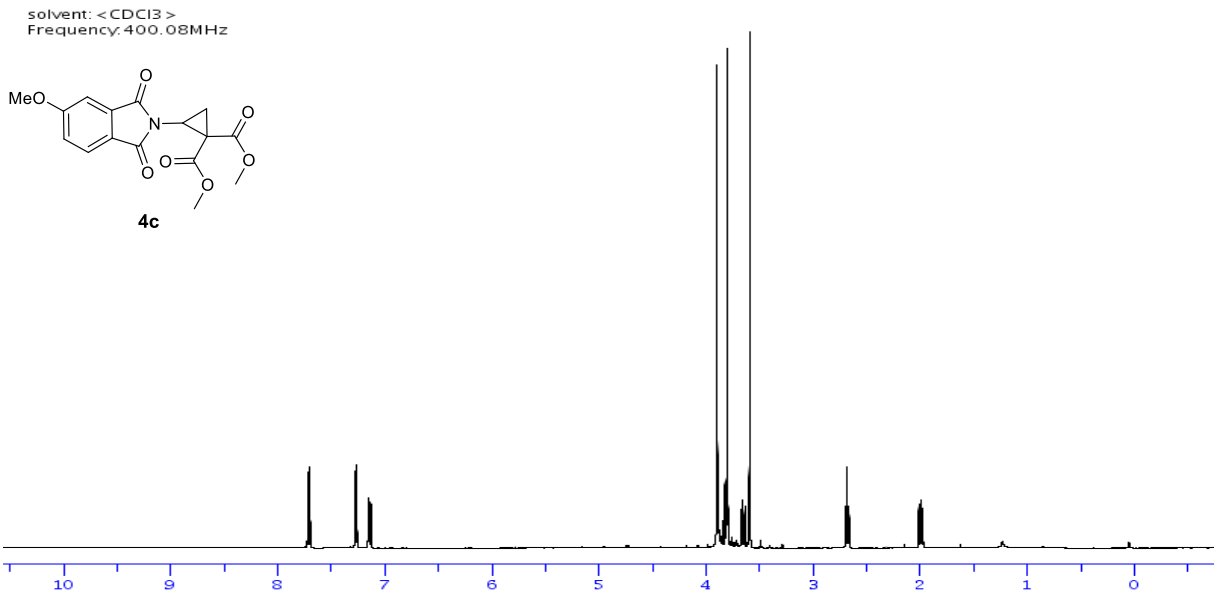

3000
2000
1000



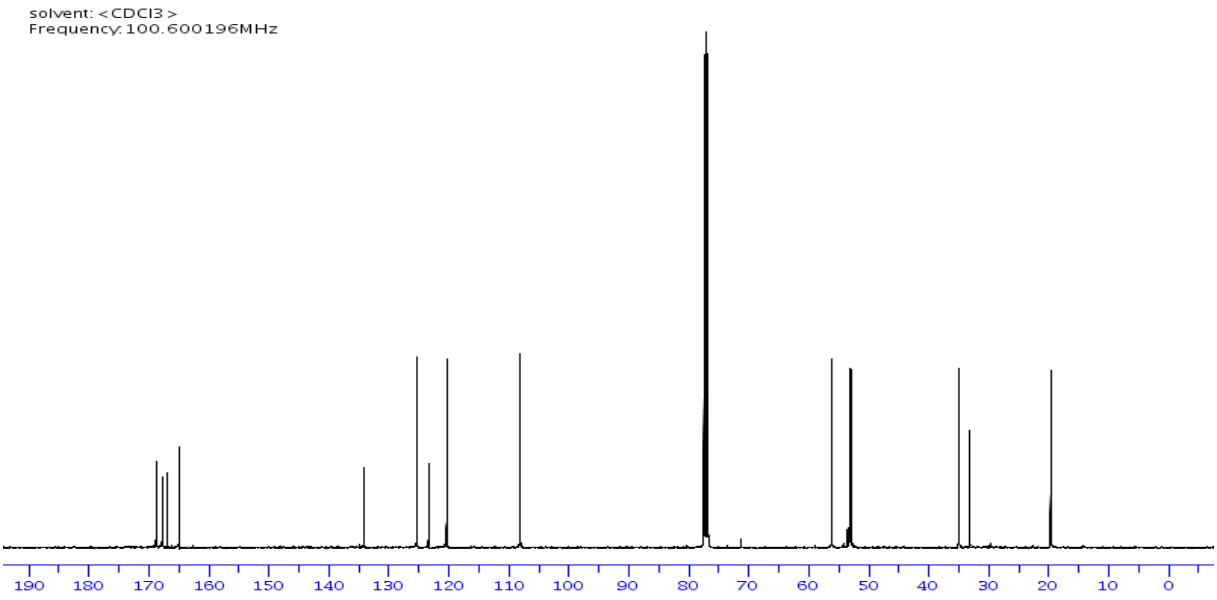
#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	23.557	2726543	59555	49.885	55.051	23.107	25.500	23.107	25.500	Manual
2	Unknown	26.180	2739107	48626	50.115	44.949	25.680	28.680	25.680	28.680	Manual

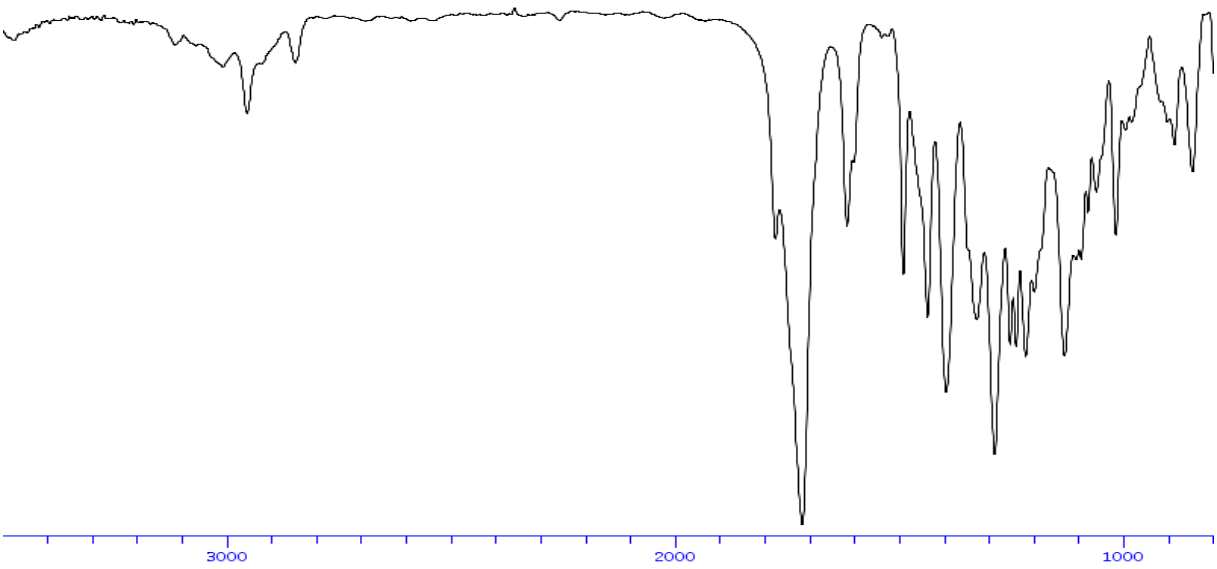


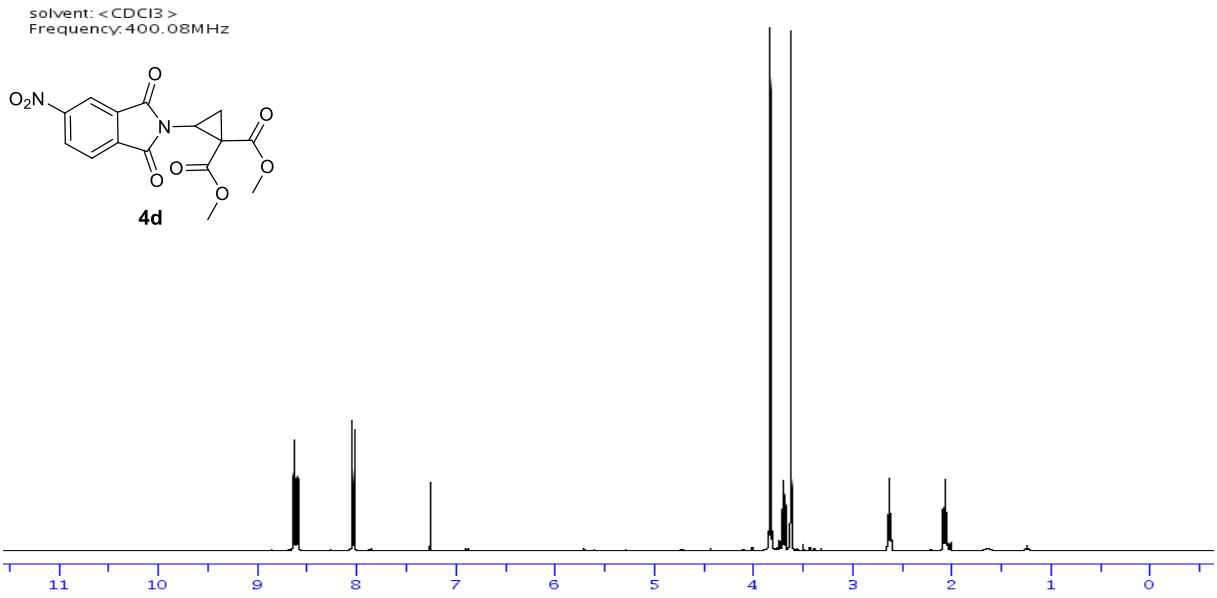
#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	23.293	1414043	31904	41.218	46.759	22.570	25.037	22.570	25.037	Manual
2	Unknown	25.810	2016605	36326	58.782	53.241	25.250	29.143	25.250	29.143	Manual

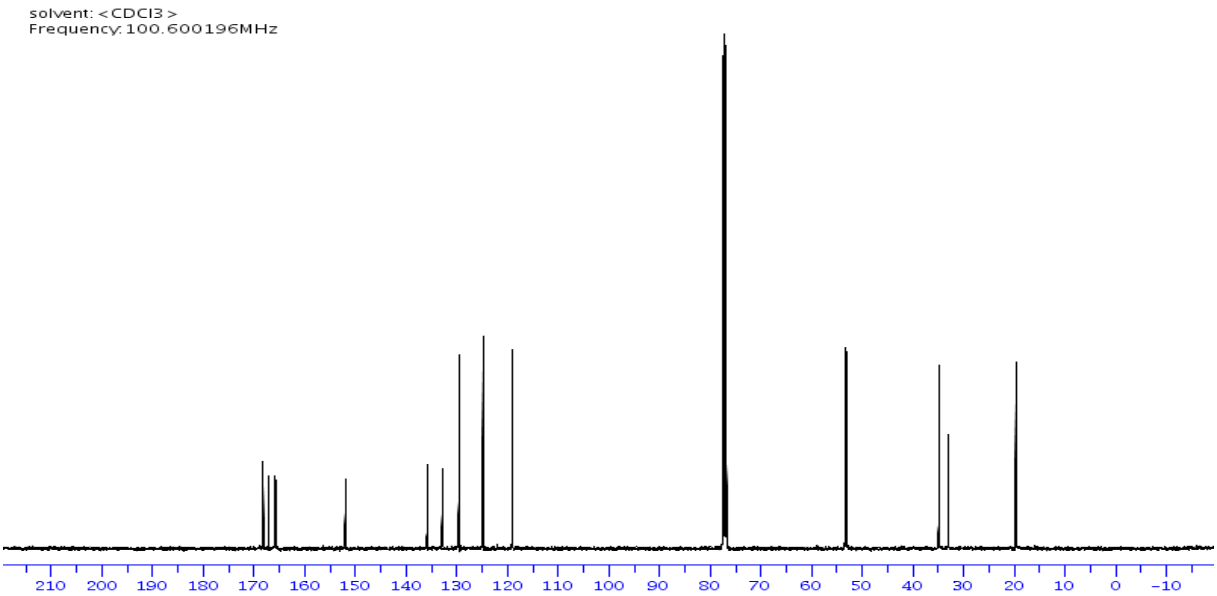

solvent: <CDCl3 >
Frequency: 400.08MHz
MeO
O
N
O
O
O
O
O
O
10
9
8
7
6
5
4
3
2
1
0

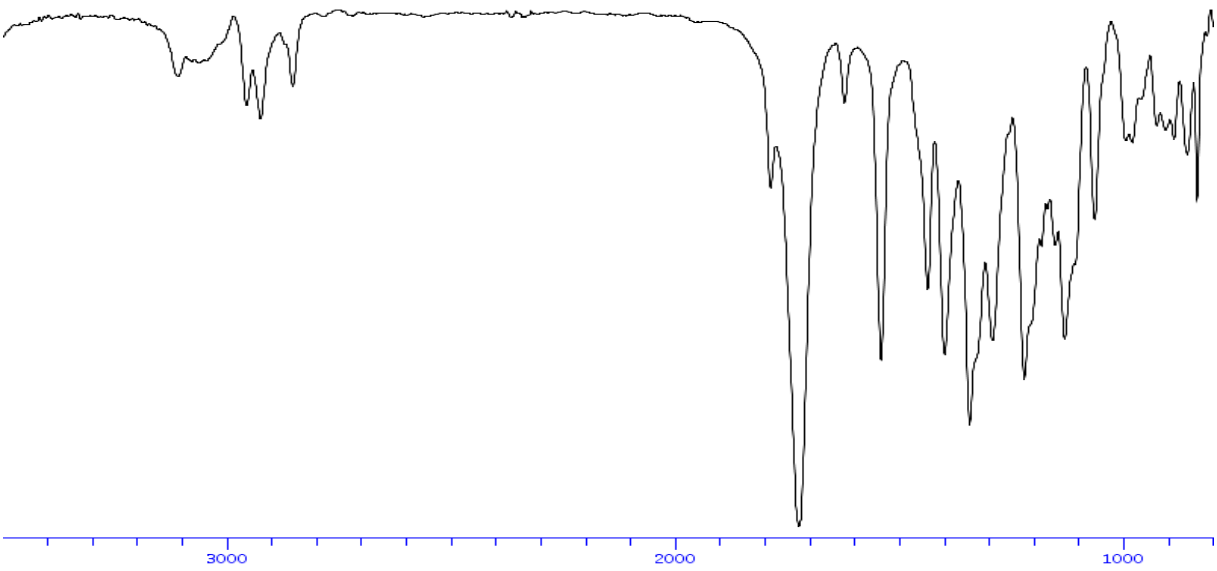
4c

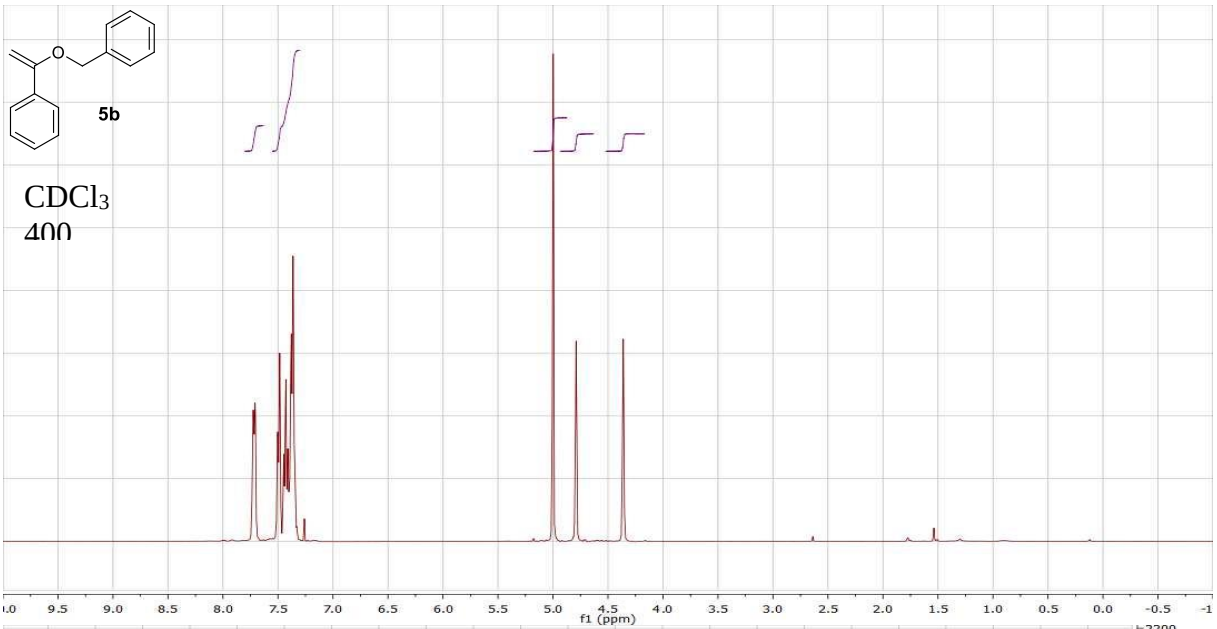

solvent: <CDCl3 >
Frequency: 100.600196MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

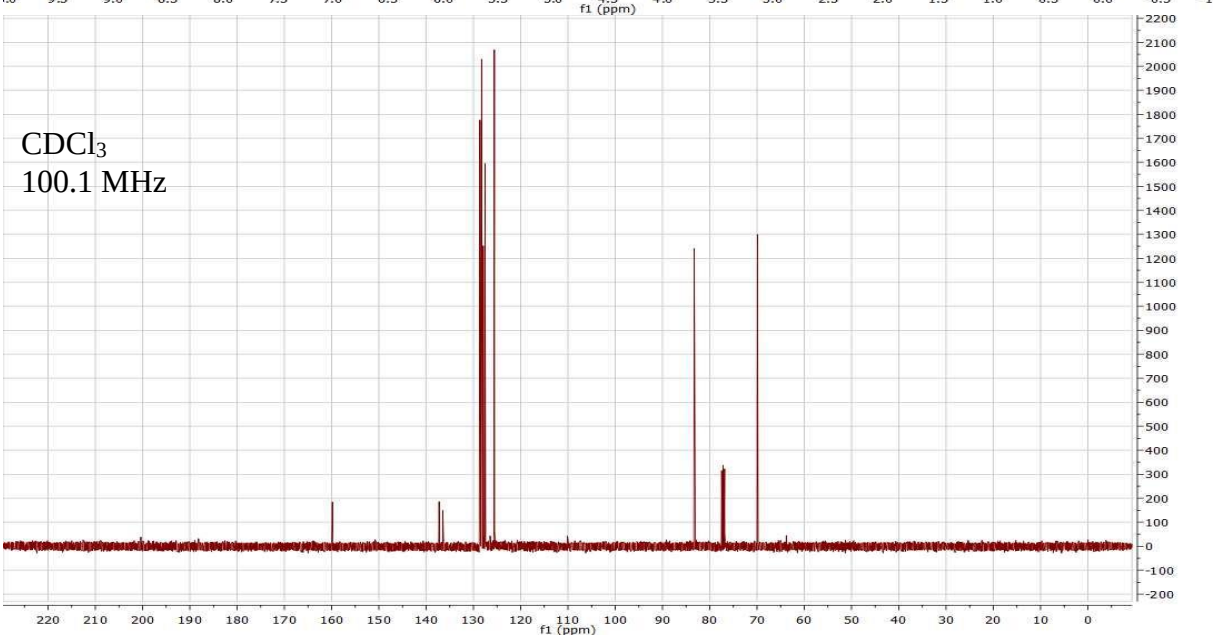

3000
2000
1000

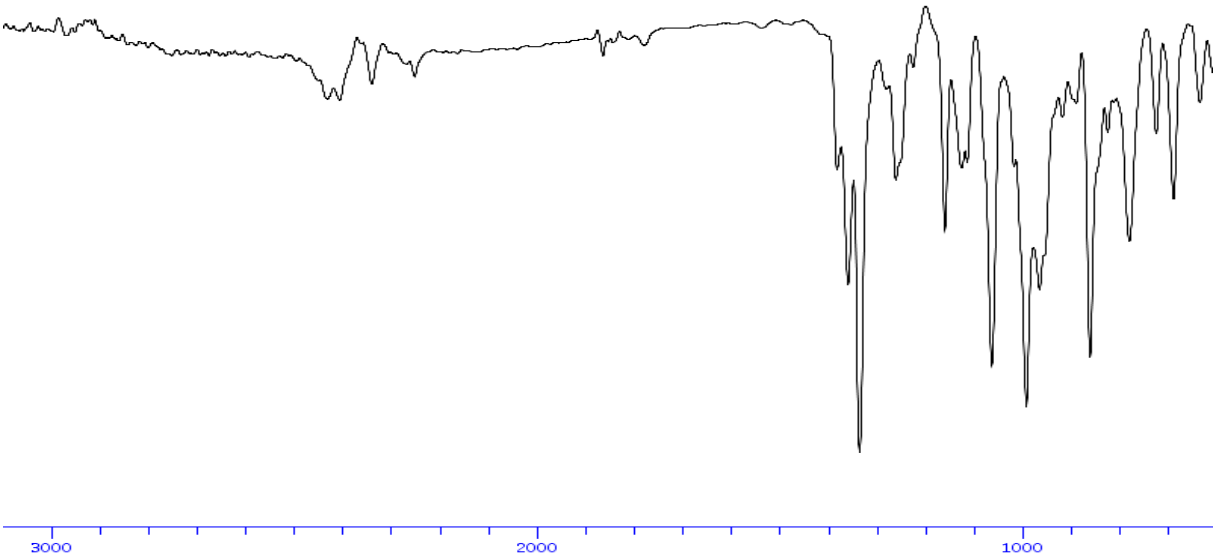

solvent: <CDCl3 >
Frequency: 400.08MHz
O2N
O
N
O
O
O
O
O
4d
11
10
9
8
7
6
5
4
3
2
1
0

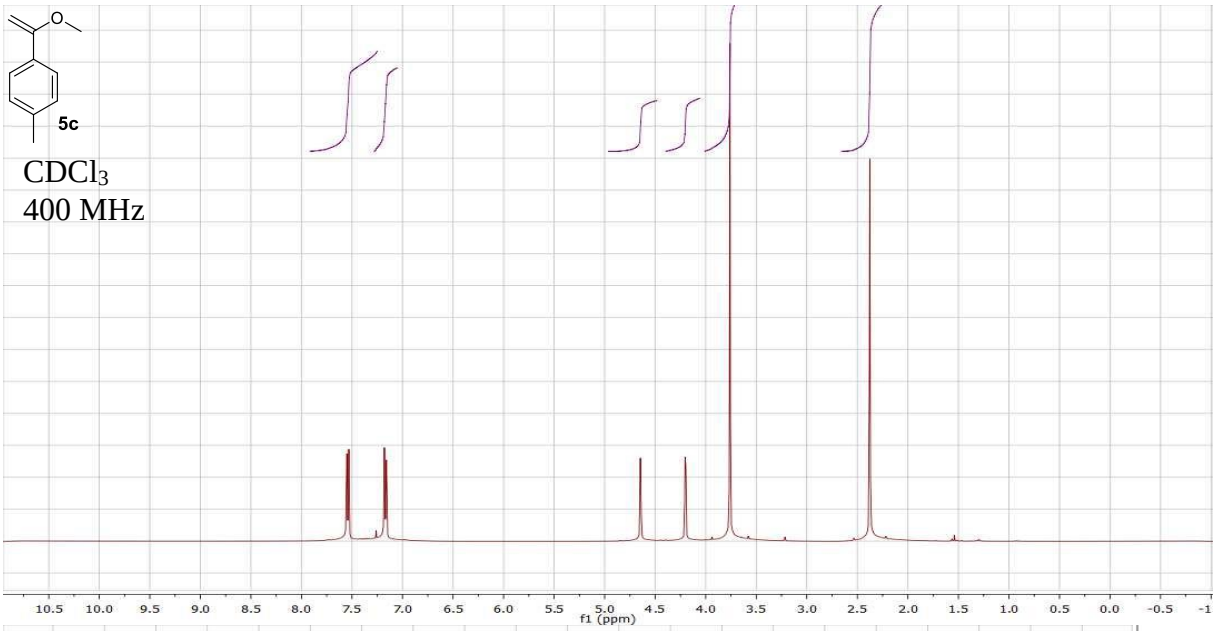

solvent: <CDCl3 >
Frequency: 100.600196MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

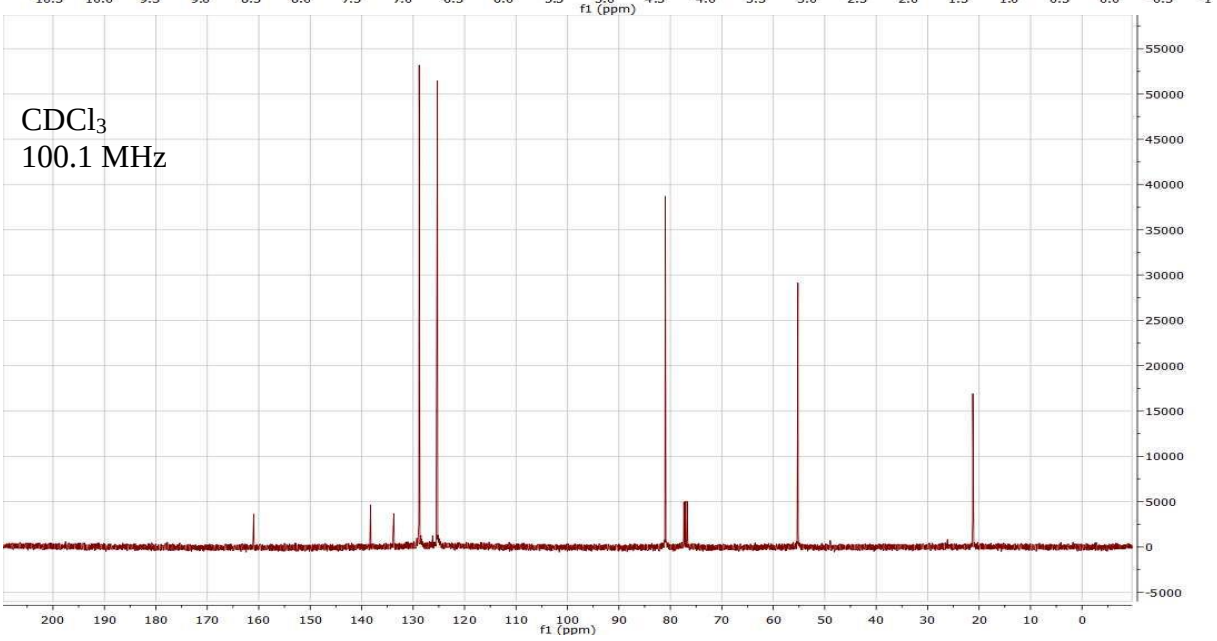

3000
2000
1000

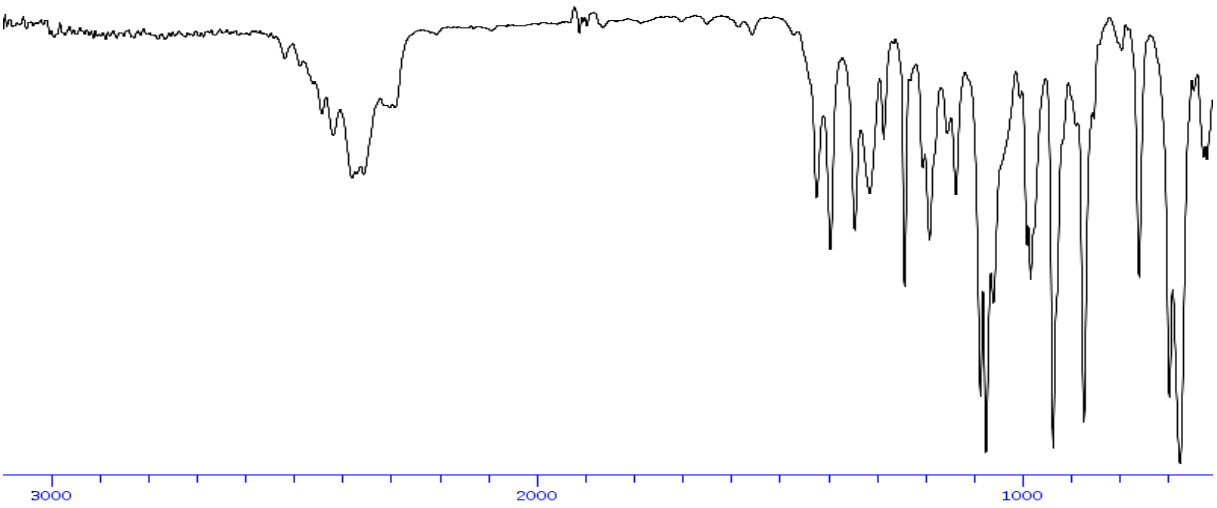

5b
CDCl3
400
f1 (ppm)

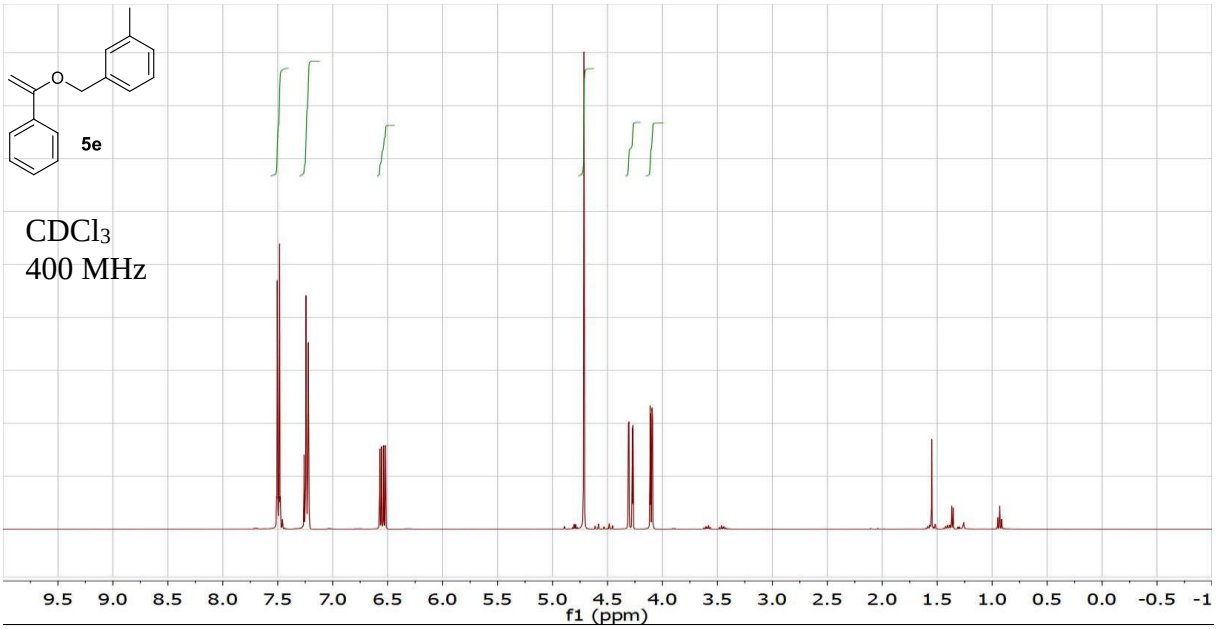

CDCl3
100.1 MHz
f1 (ppm)

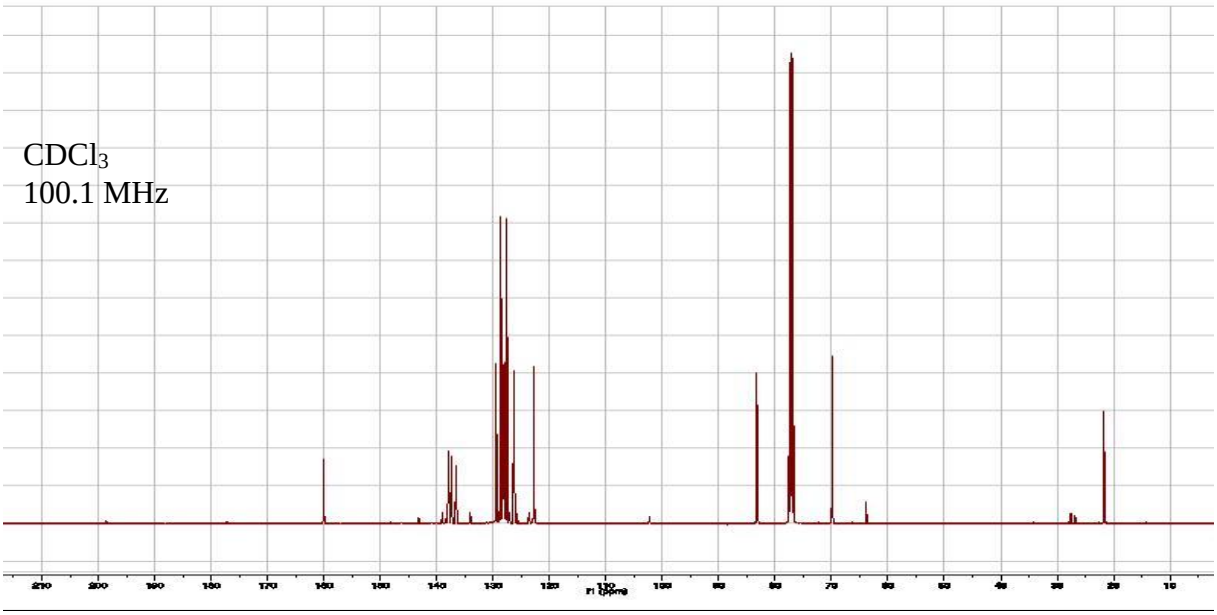

3000
2000
1000

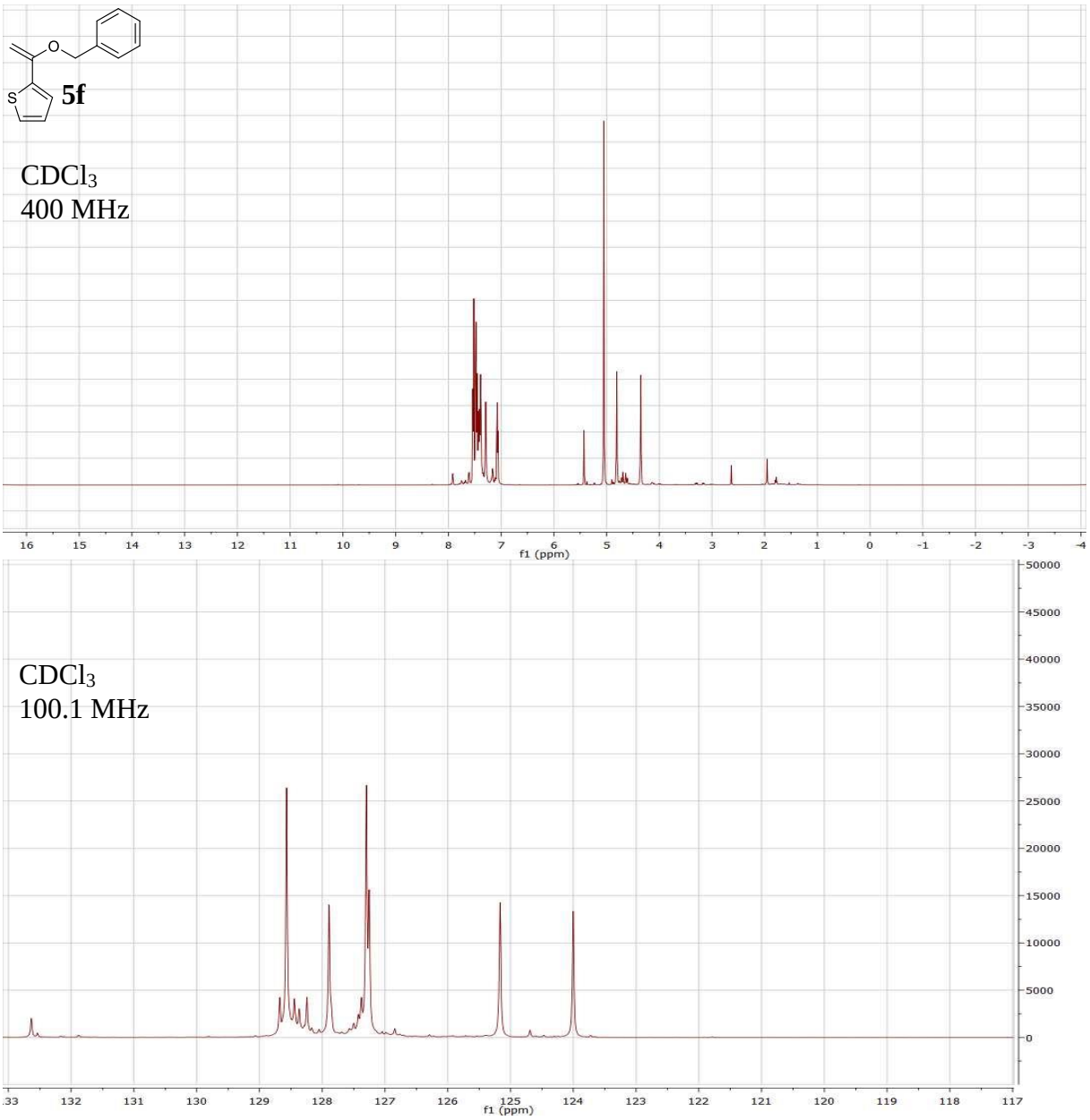

5c
CDCl3
400 MHz
f1 (ppm)

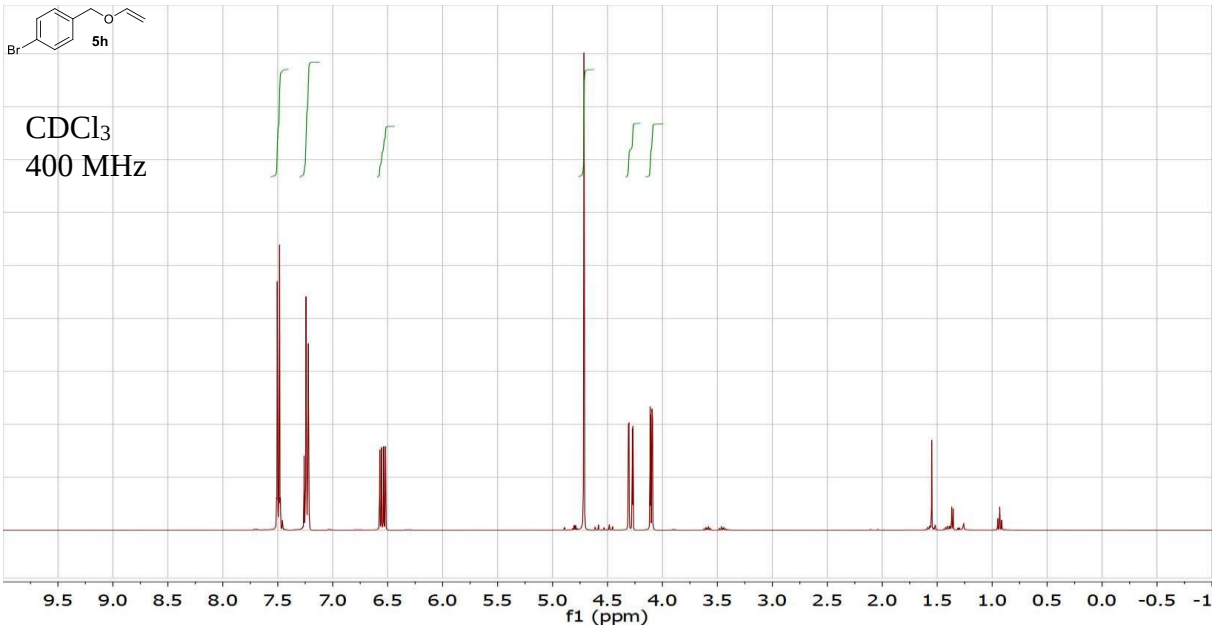

CDCl3
100.1 MHz
f1 (ppm)

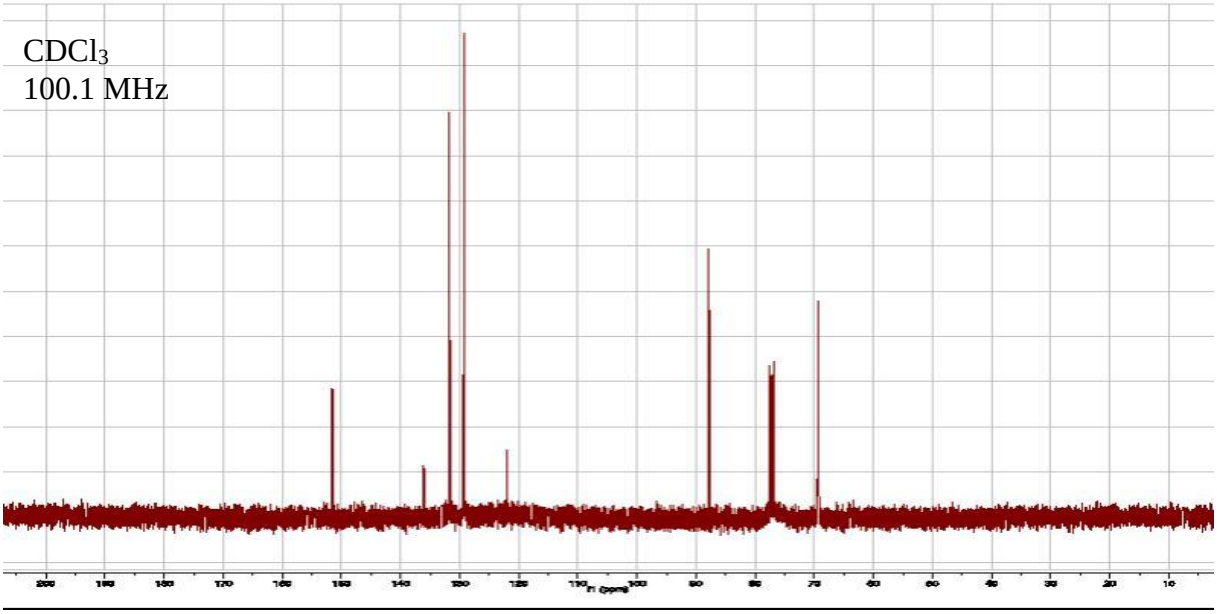

3000
2000
1000

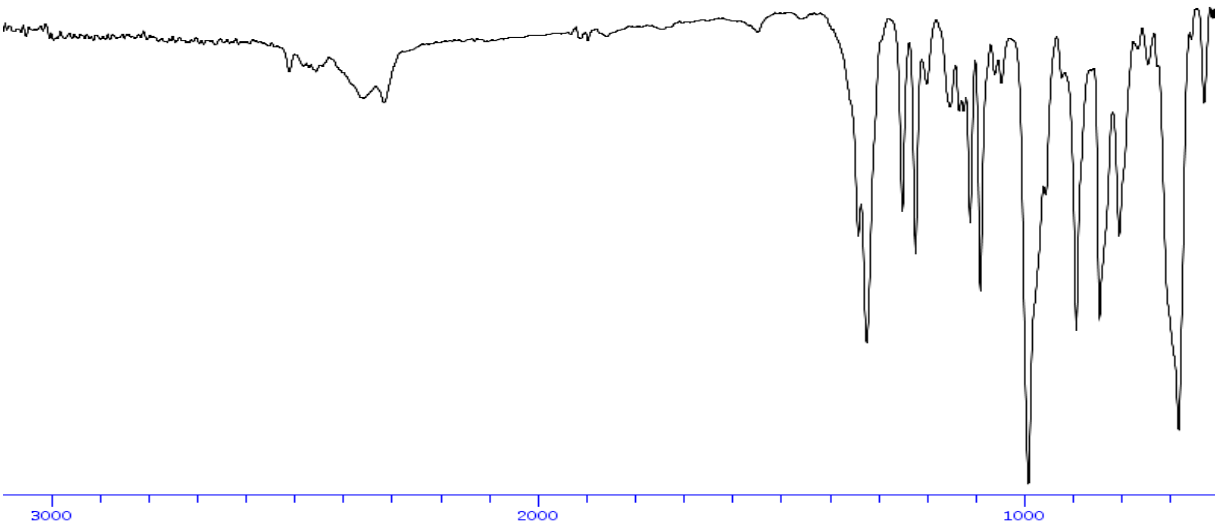

5e
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

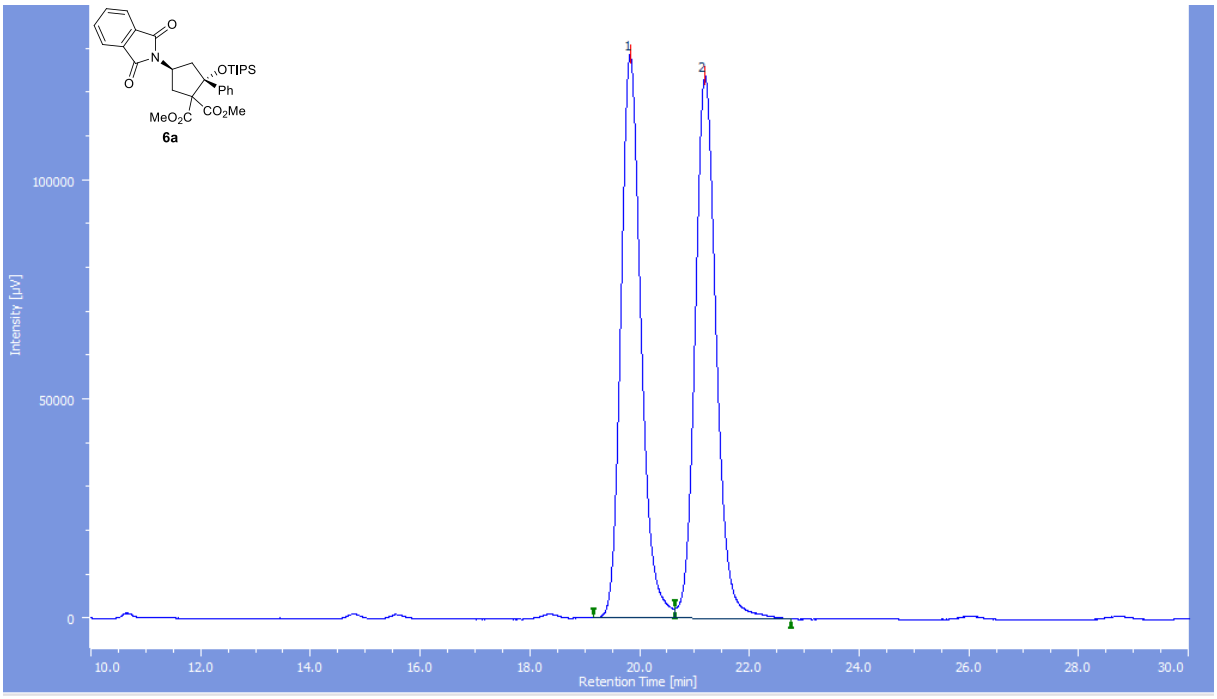

CDCl3
100.1 MHz


5f
CDCl3
400 MHz
f1 (ppm)
CDCl3
100.1 MHz
f1 (ppm)

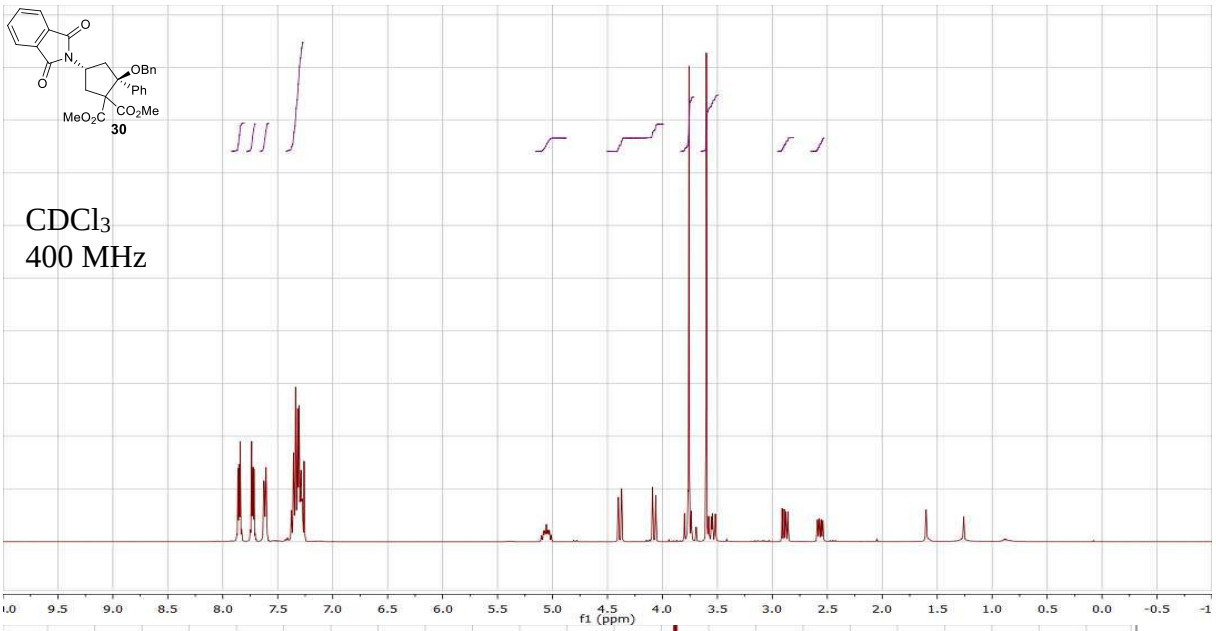

Br
5h
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

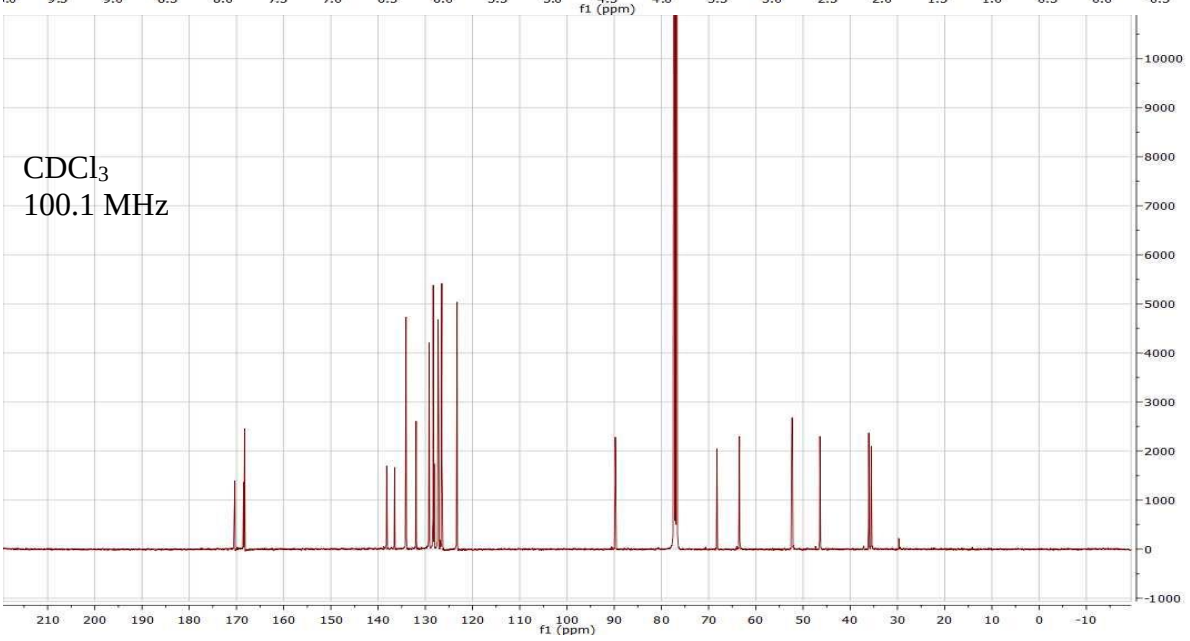

CDCl3
100.1 MHz

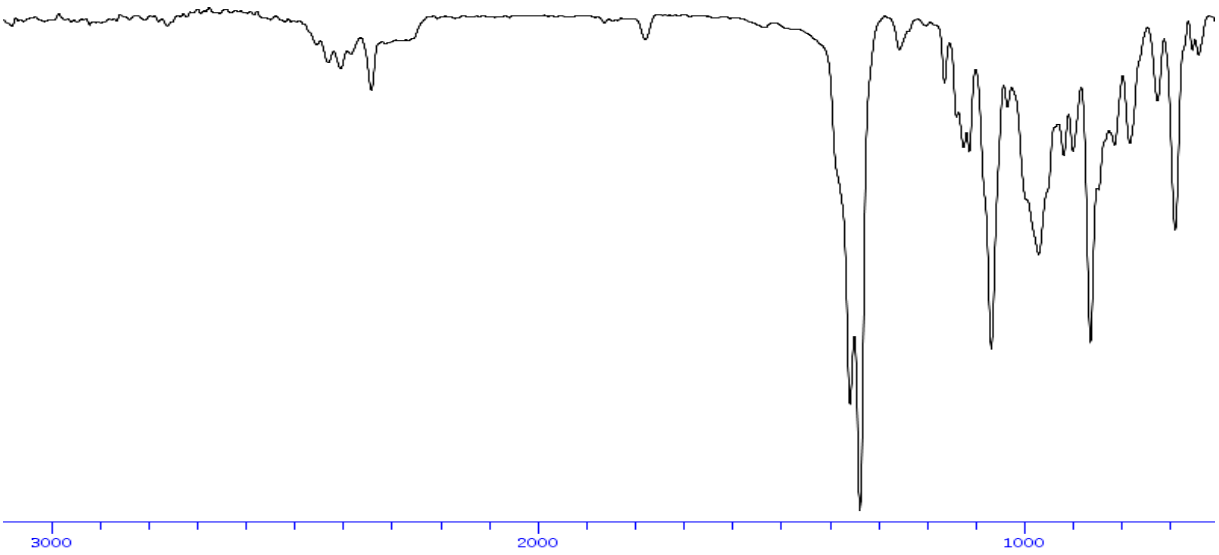

3000
2000
1000

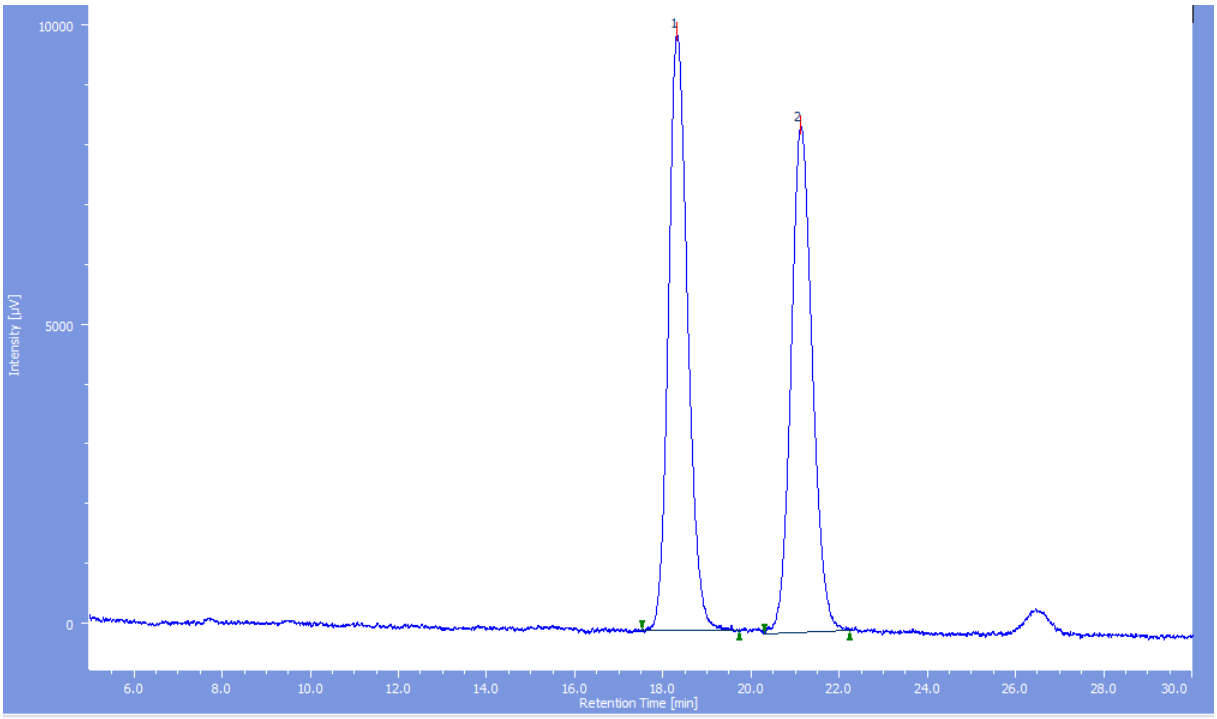


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	19.817	3260458	128165	49.594	50.903	N/A	14839	2.057	1.221	
2	Unknown	3	21.183	3313874	123618	50.406	49.097	N/A	15465	N/A	1.132	

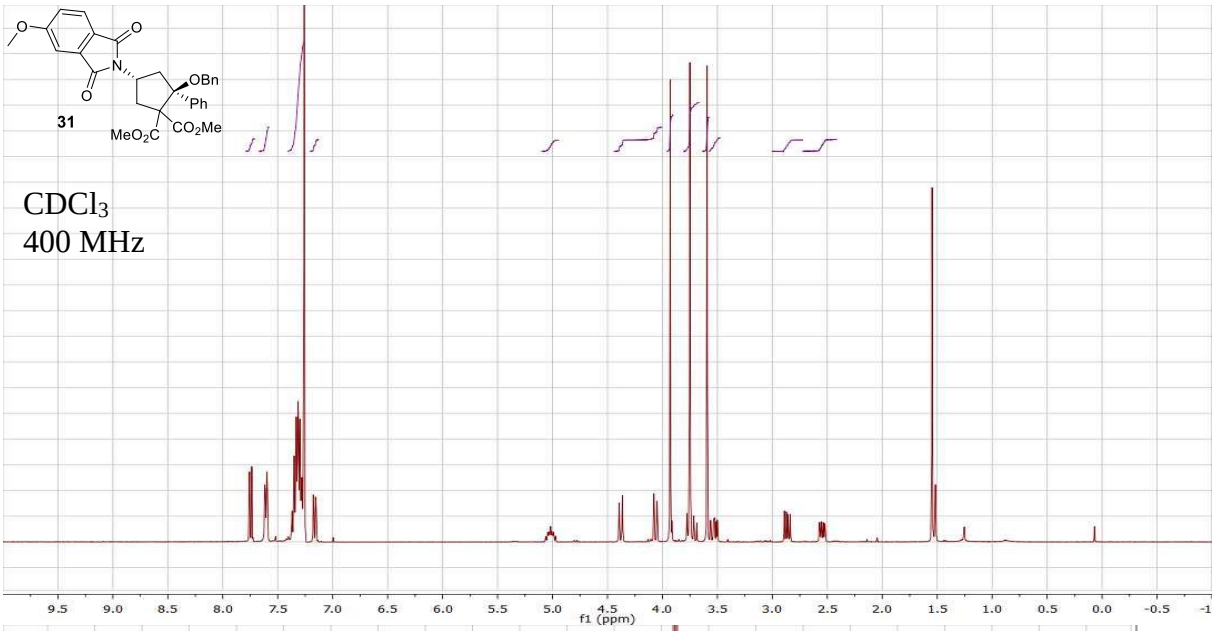

OBn
Ph
CO2Me
MeO2C
30
CDCl3
400 MHz
f1 (ppm)

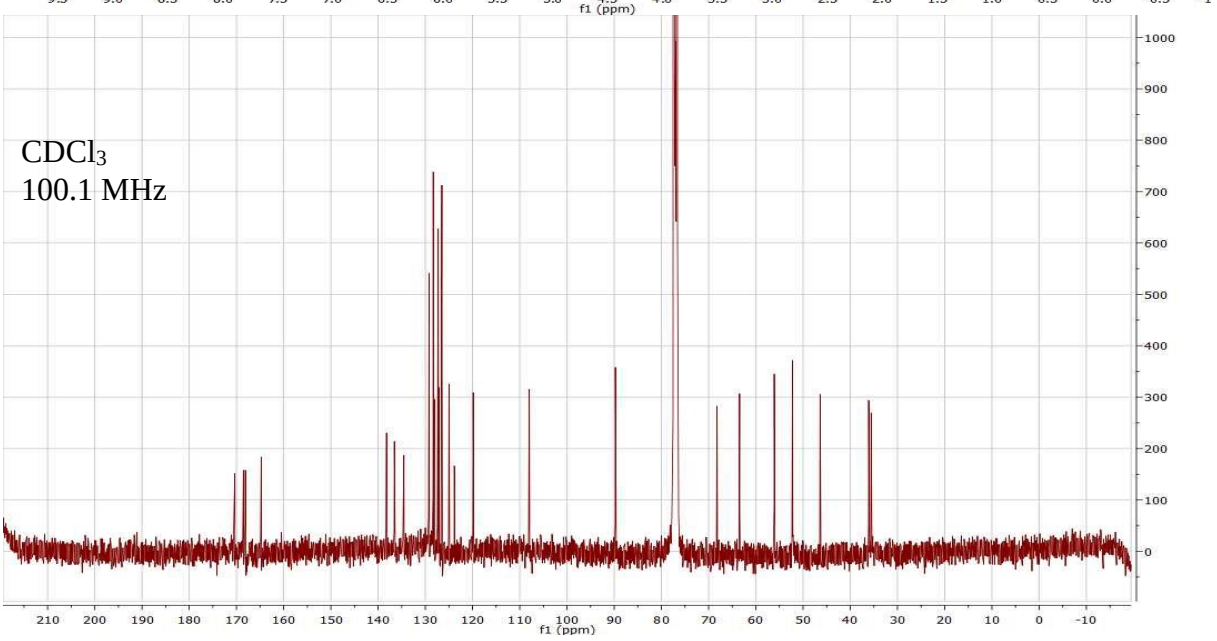

CDCl3
100.1 MHz
f1 (ppm)

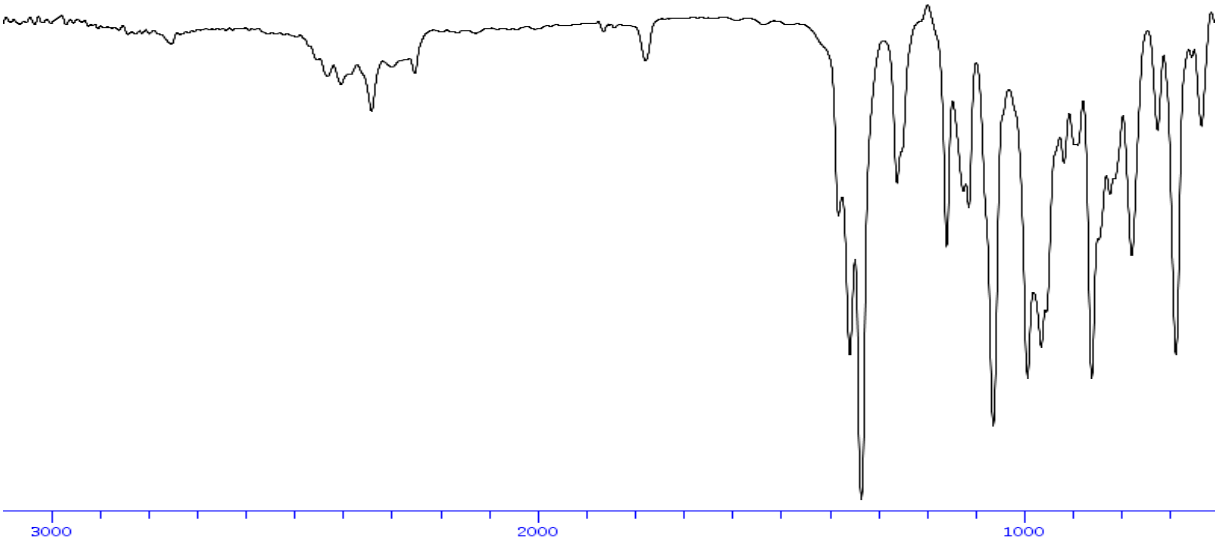

3000
2000
1000

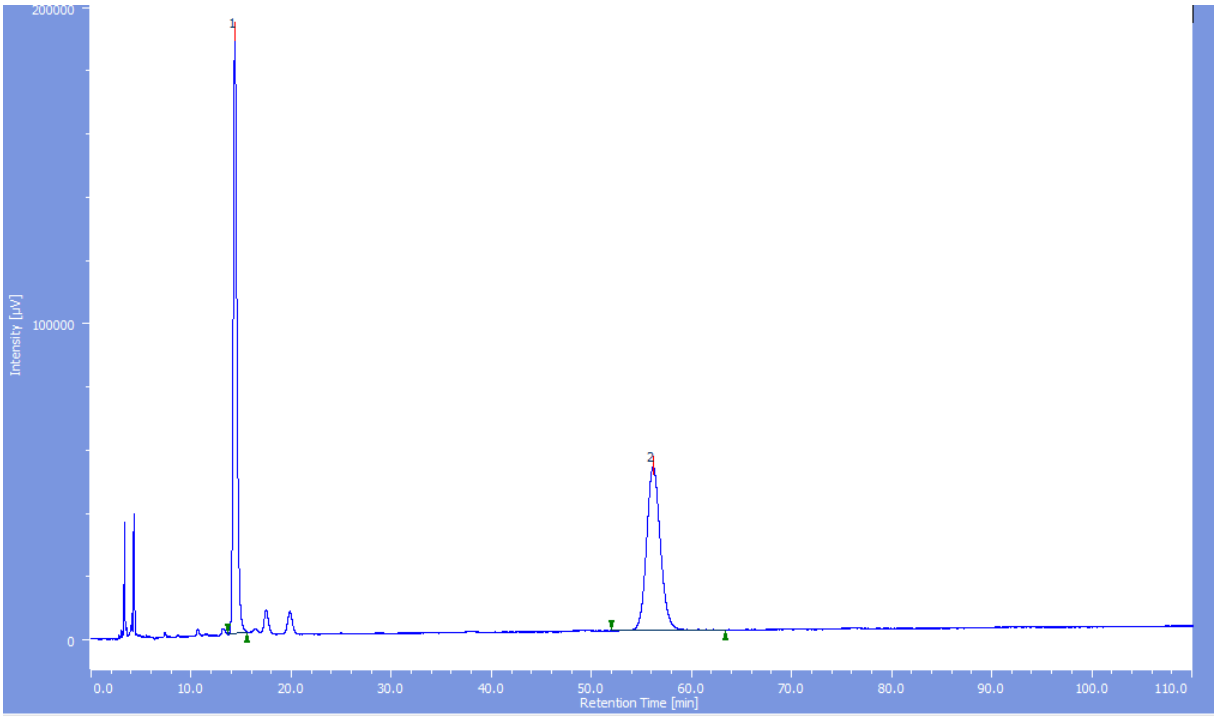


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	18.300	302146	9986	51.599	54.155	N/A	8814	3.419	1.190	
2	Unknown	1	21.107	283421	8454	48.401	45.845	N/A	9497	N/A	1.135	

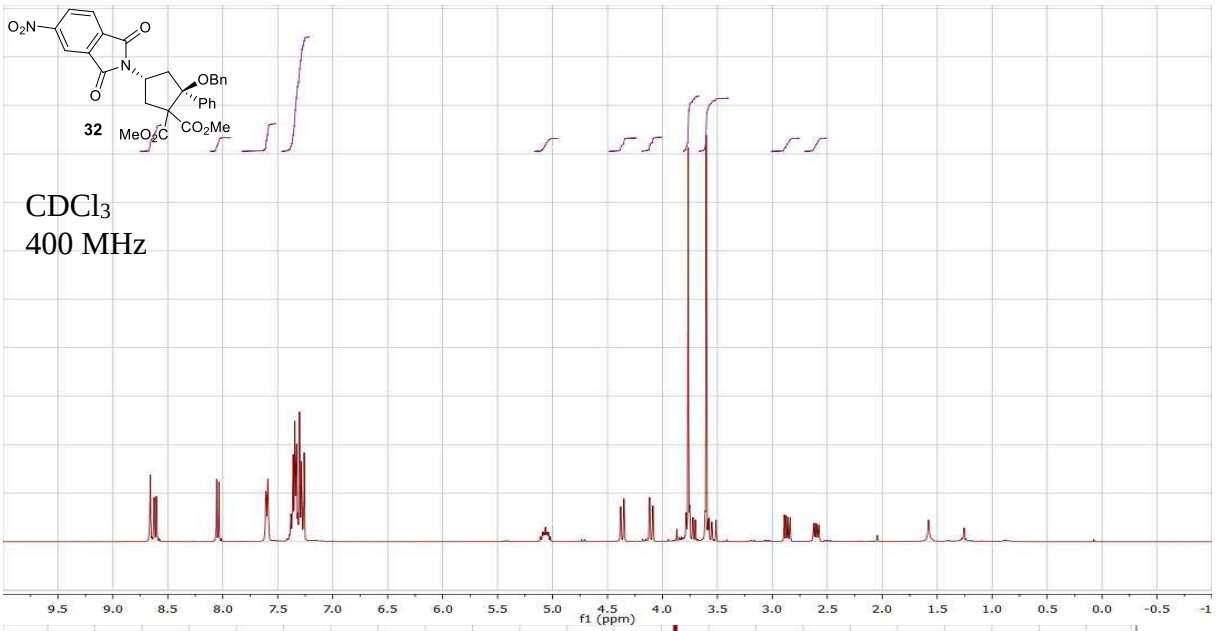

31
OBn
Ph
CO2Me
MeO2C
CDCl3
400 MHz
f1 (ppm)

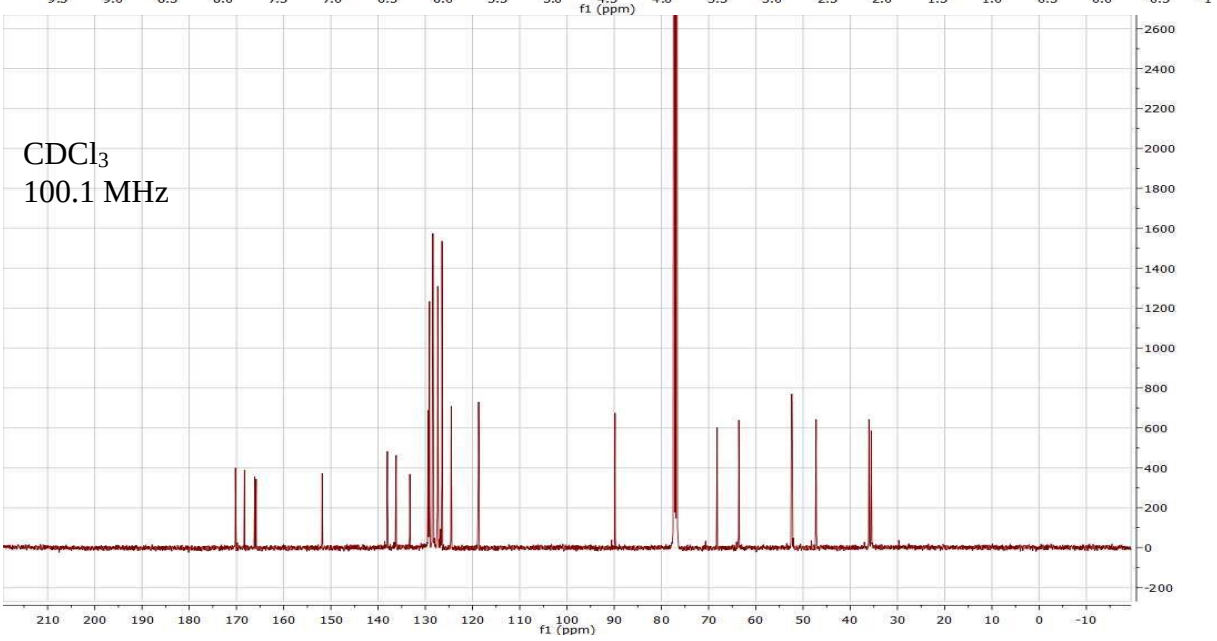

CDCl3
100.1 MHz
f1 (ppm)

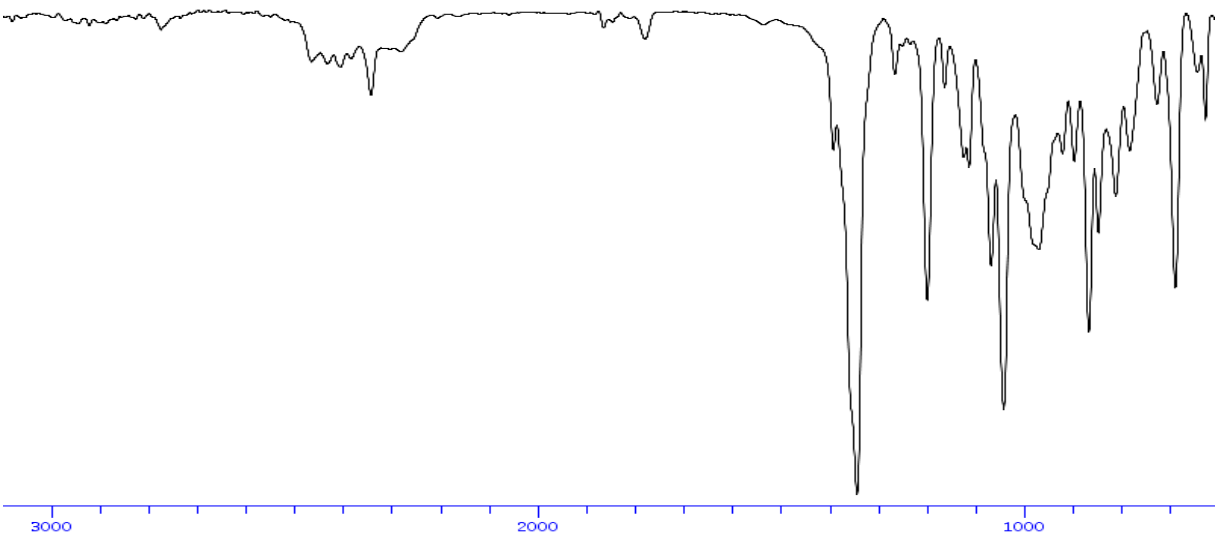

3000
2000
1000

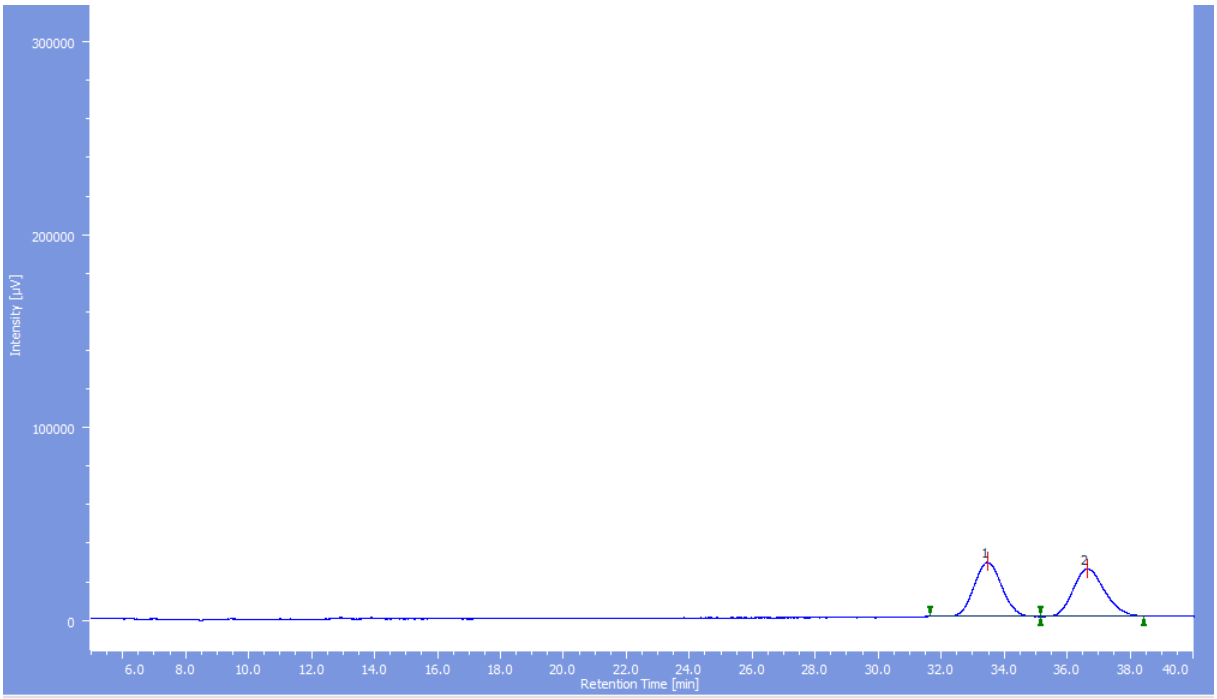


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	14.353	4826606	189777	49.349	78.563	N/A	7862	26.889	1.255	
2	Unknown	3	56.103	4953865	51785	50.651	21.437	N/A	8280	N/A	1.125	

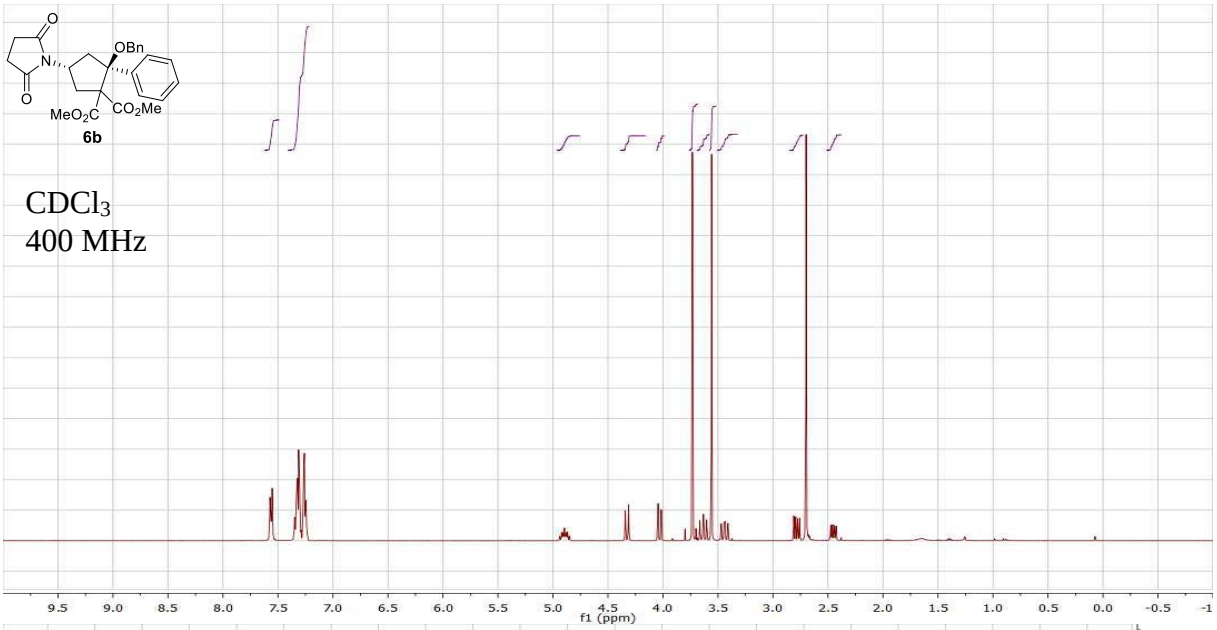

O2N
O
N
O
OBn
Ph
CO2Me
MeO2C
32
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

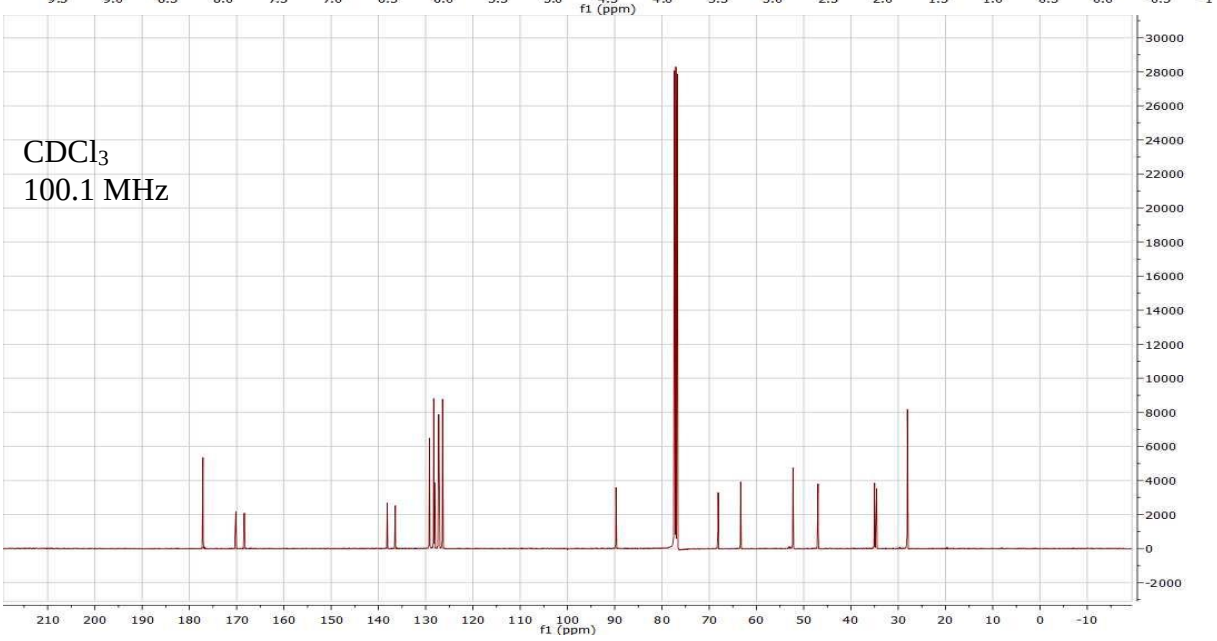

CDCl3
100.1 MHz
2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

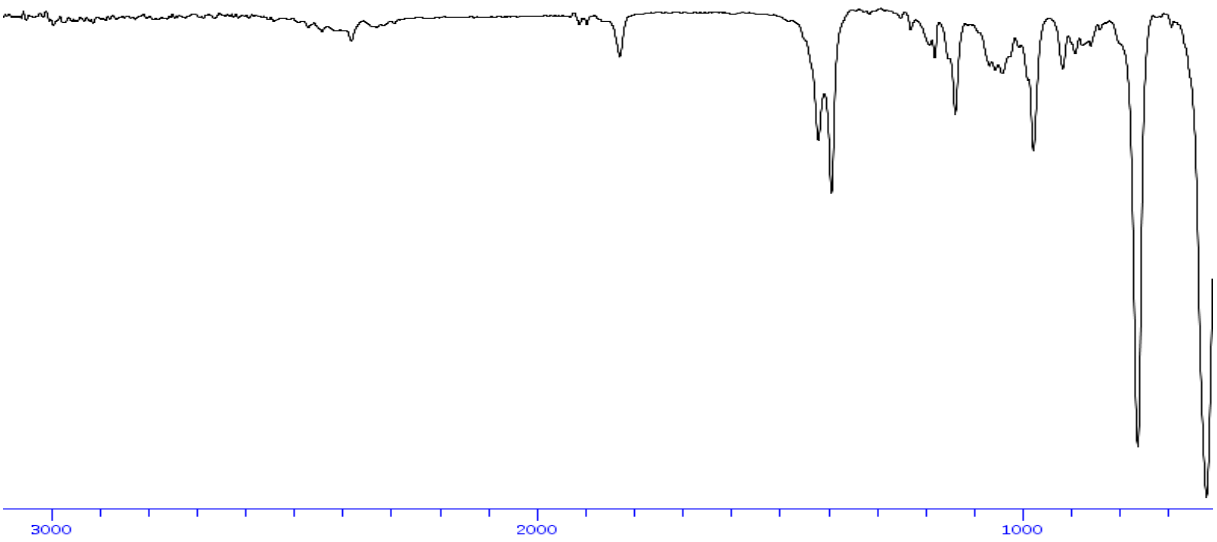

3000
2000
1000

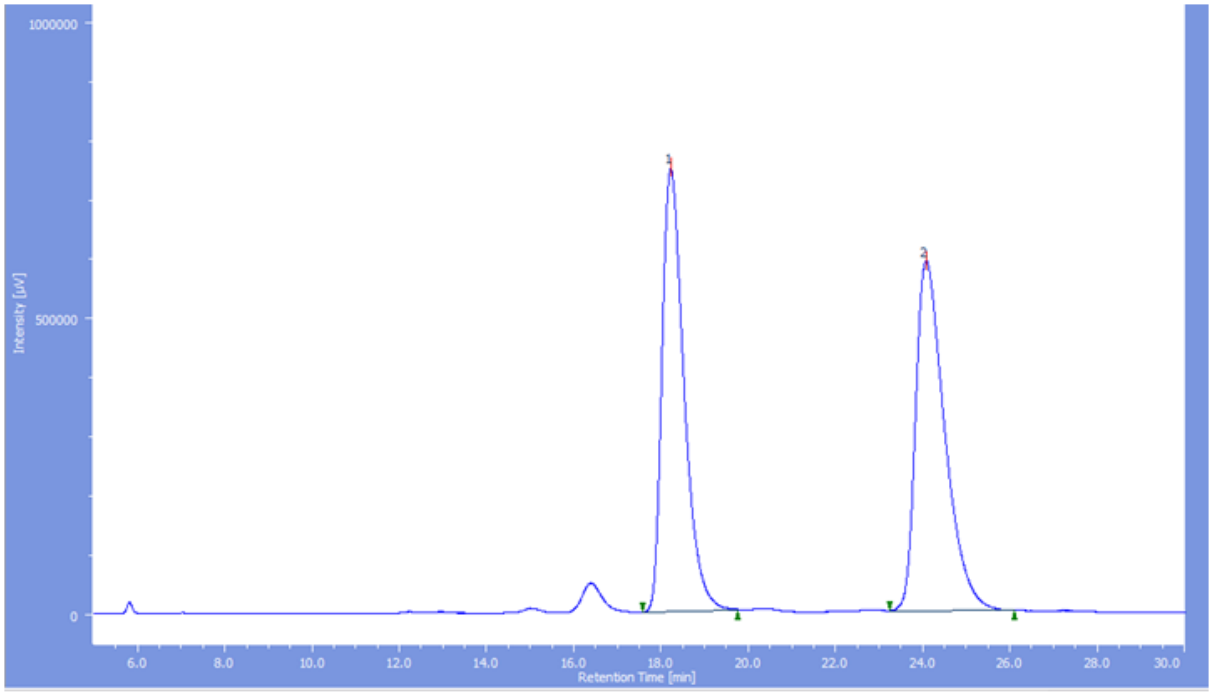


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	33.443	1680251	27955	50.132	53.290	N/A	6869	1.842	1.073	
2	Unknown	3	36.597	1671409	24504	49.868	46.710	N/A	6472	N/A	1.210	

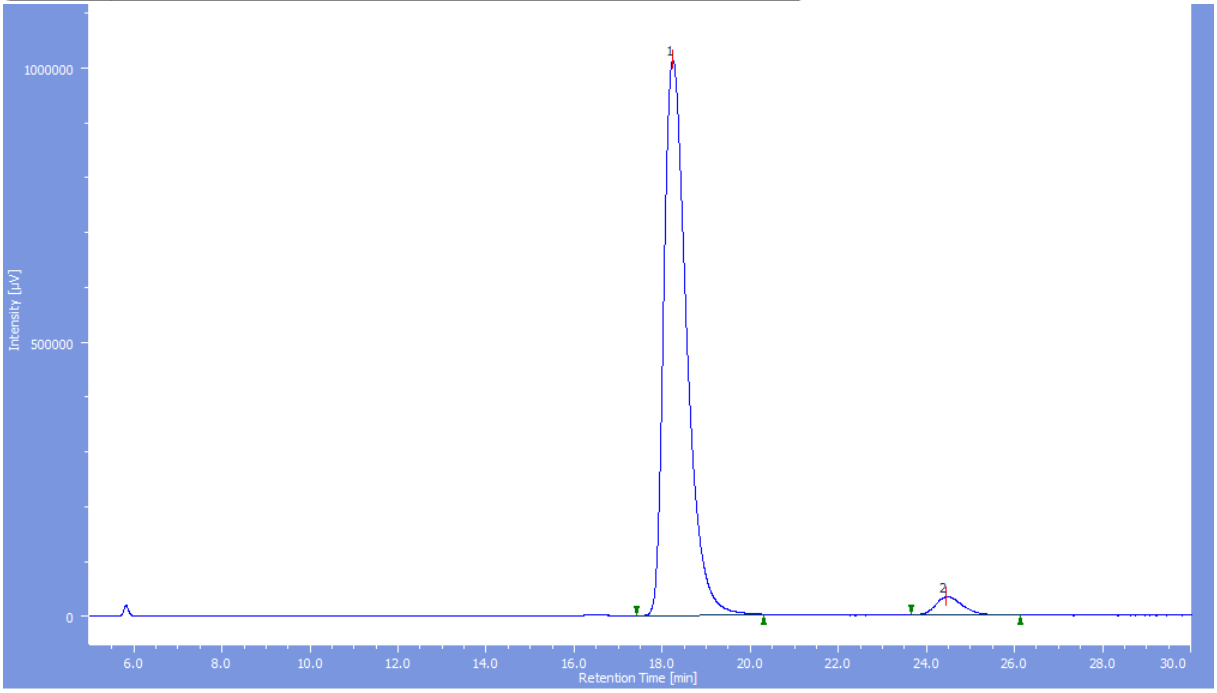

O
N
O
OBn
MeO2C
CO2Me
6b
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


CDCl3
100.1 MHz
30000 28000 26000 24000 22000 20000 18000 16000 14000 12000 10000 8000 6000 4000 2000 0 -2000
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)

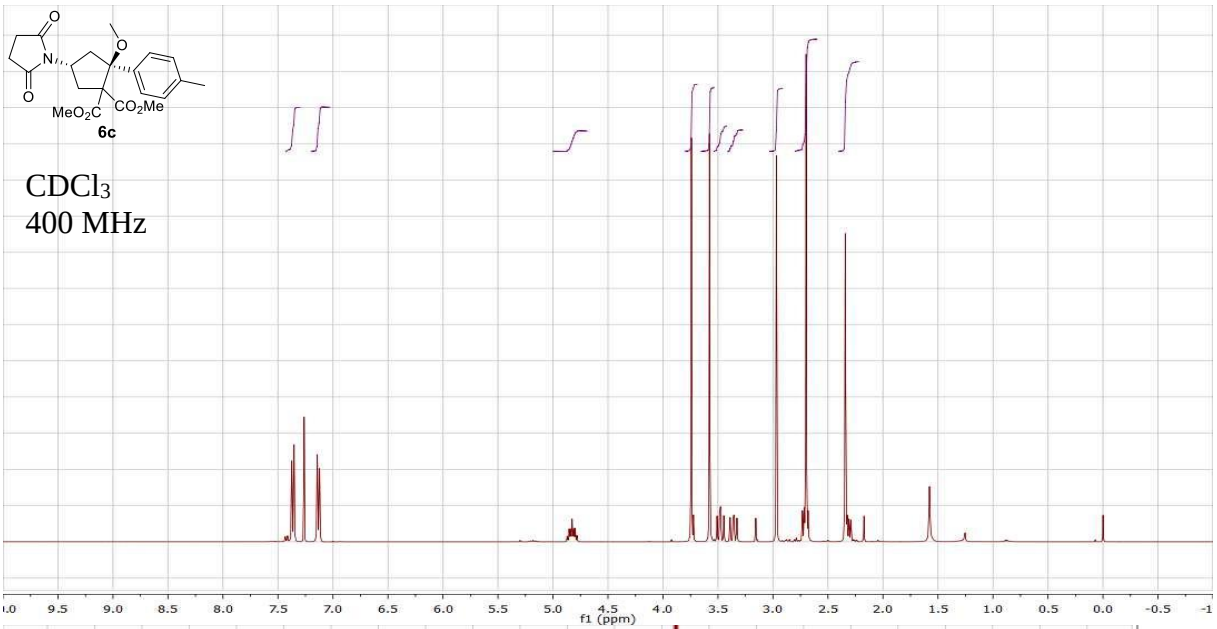

3000
2000
1000

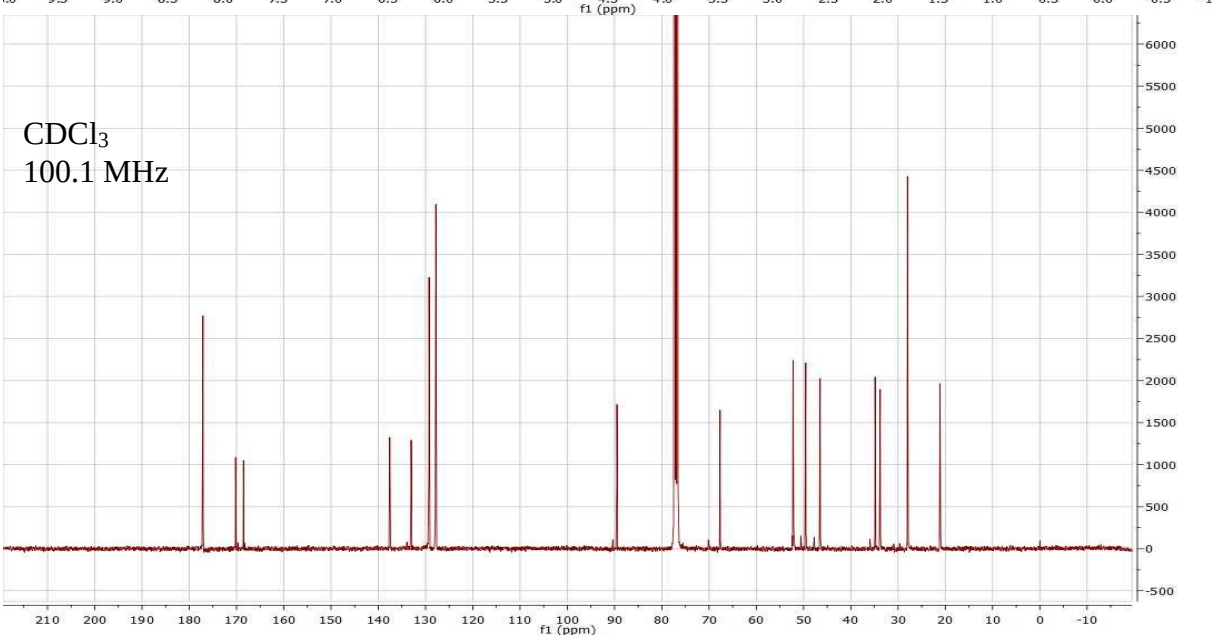


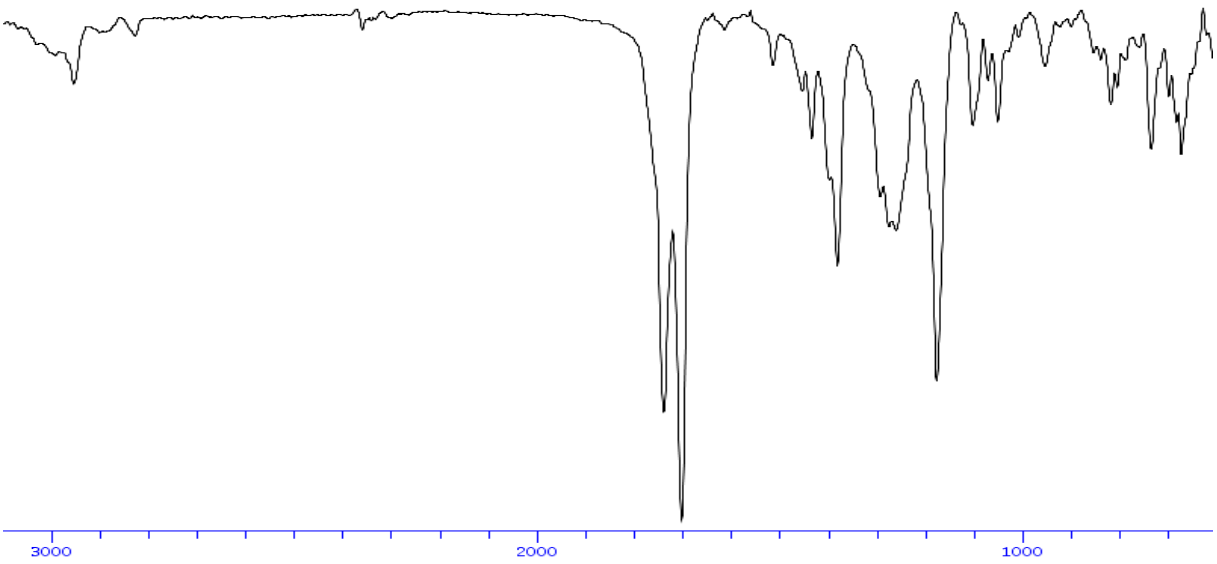
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	18.213	26081531	748330	48.846	55.902	N/A	6590	5.621	1.490	
2	Unknown	1	24.063	27314128	590321	51.154	44.098	N/A	6548	N/A	1.609	

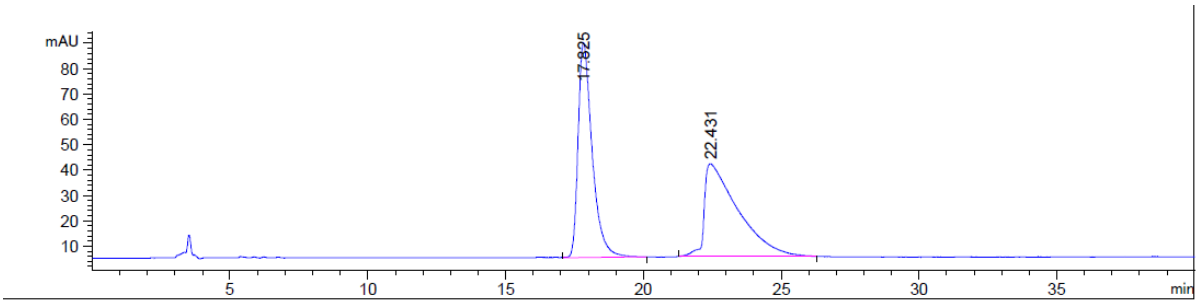


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	18.223	36342909	1010847	96.169	96.779	N/A	6246	6.136	1.543	
2	Unknown	1	24.423	1447791	33642	3.831	3.221	N/A	7830	N/A	1.330	

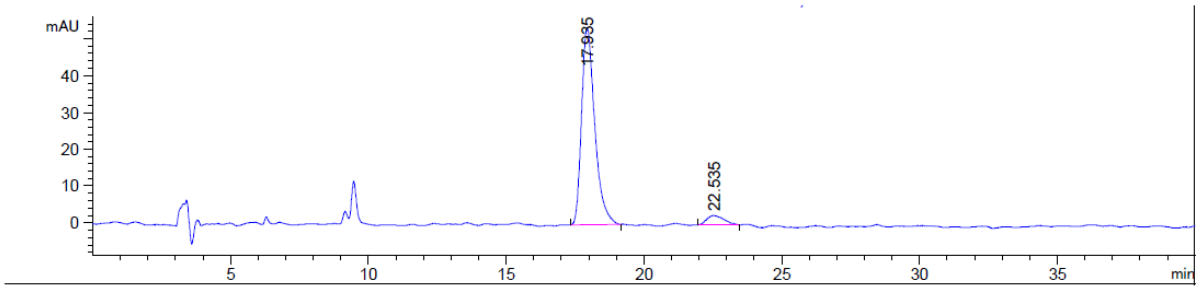

MeO2C
CO2Me
6c
CDCl3
400 MHz
f1 (ppm)


CDCl3
100.1 MHz
f1 (ppm)

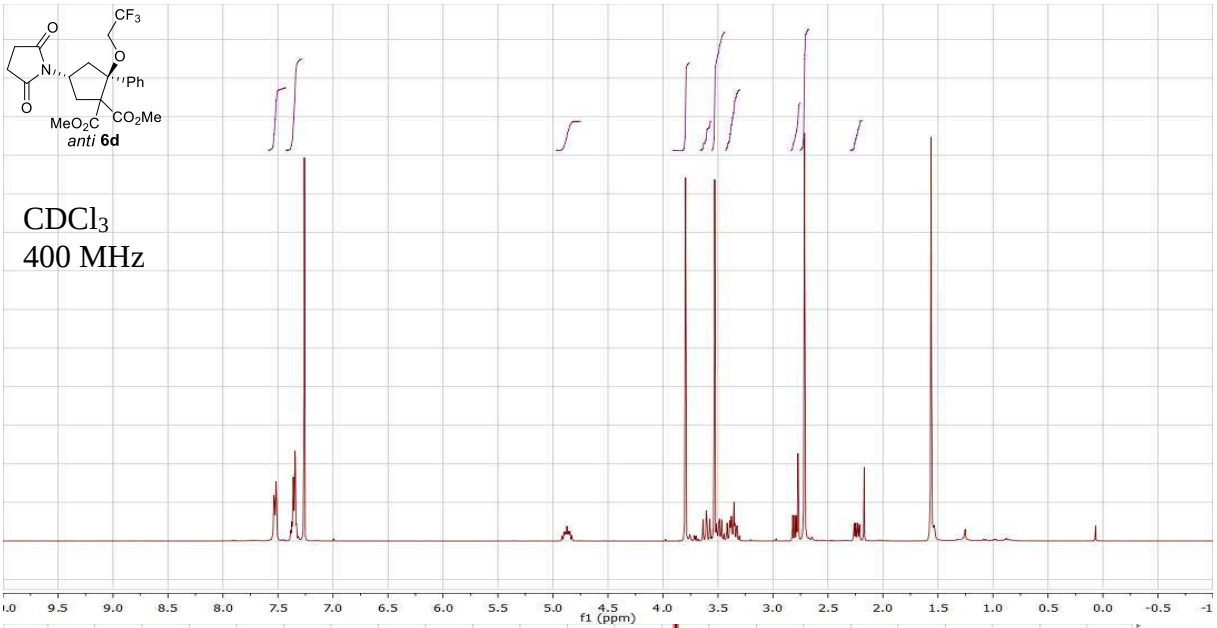

3000
2000
1000

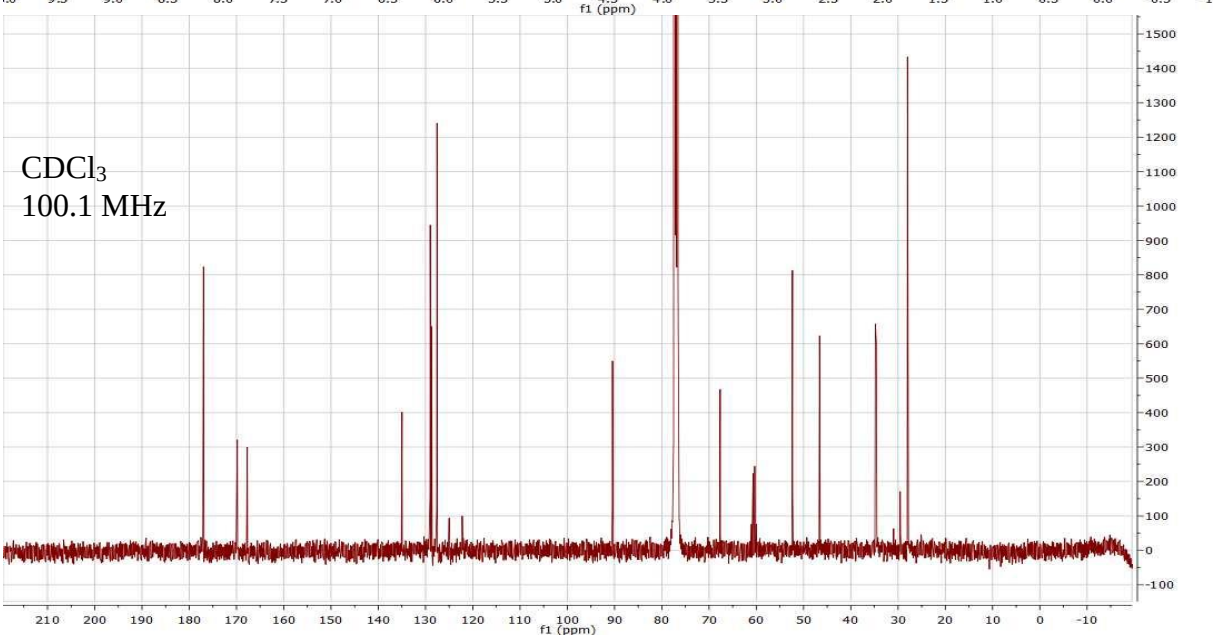


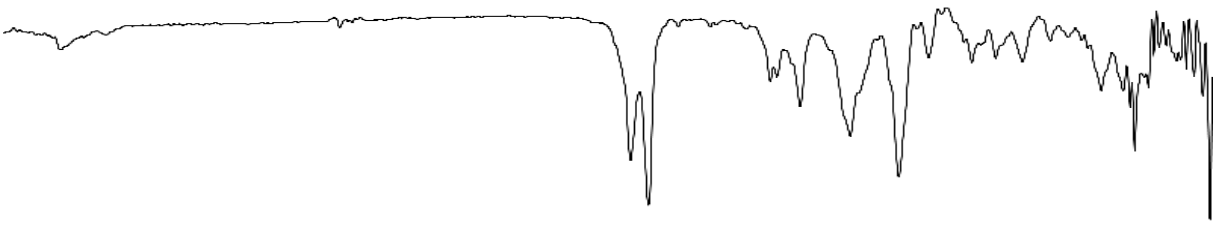
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.825	BB	0.5313	2998.75903	84.64332	49.1939
2	22.431	BB	1.0975	3097.02979	36.44181	50.8061



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.934	BB	0.5147	1377.40356	40.91861	94.5825
2	22.511	MM	0.7362	78.89477	1.78616	5.4175

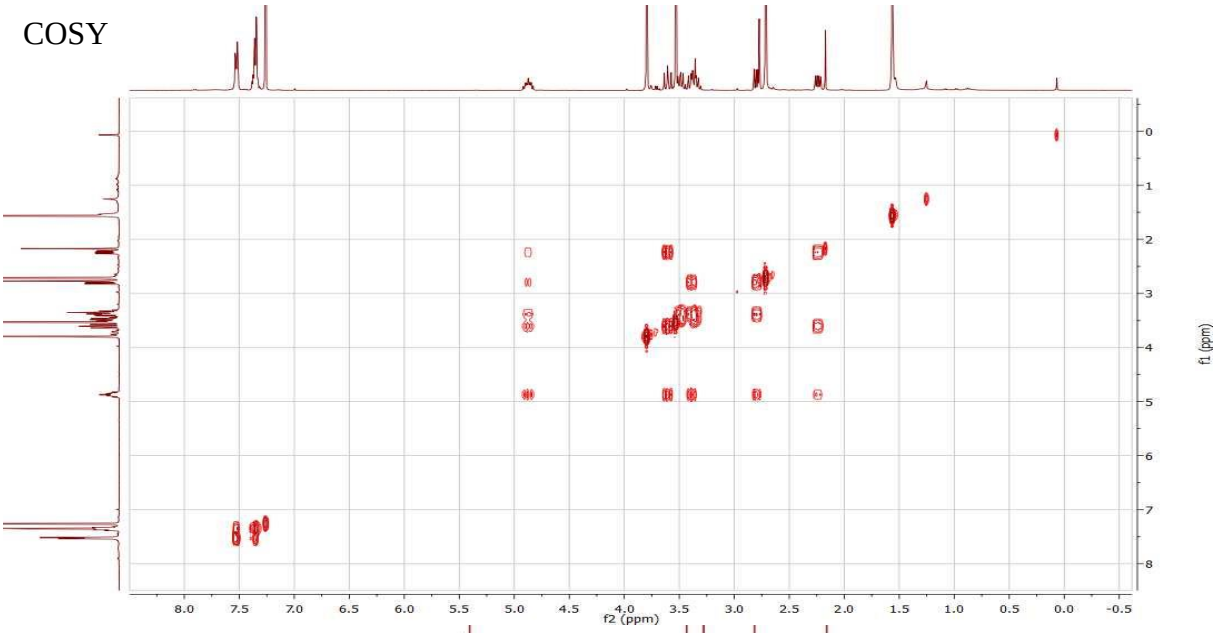

CF3
O
N
O
O
Ph
MeO2C
CO2Me
anti 6d
CDCl3
400 MHz
f1 (ppm)


CDCl3
100.1 MHz
f1 (ppm)

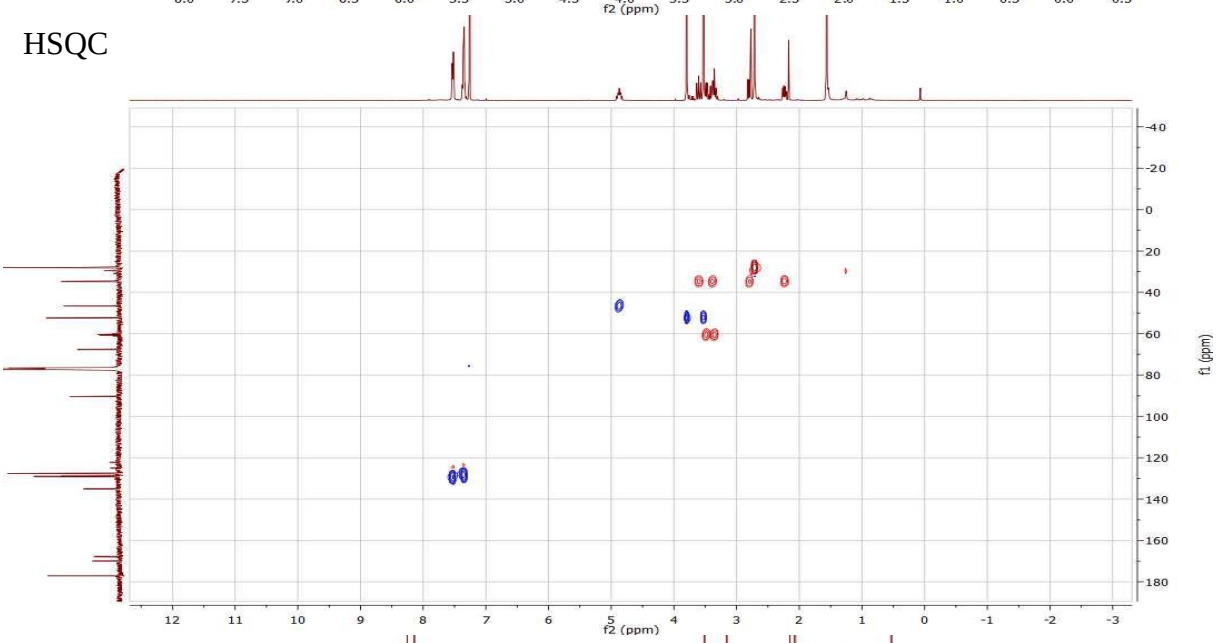



3000
2000
1000

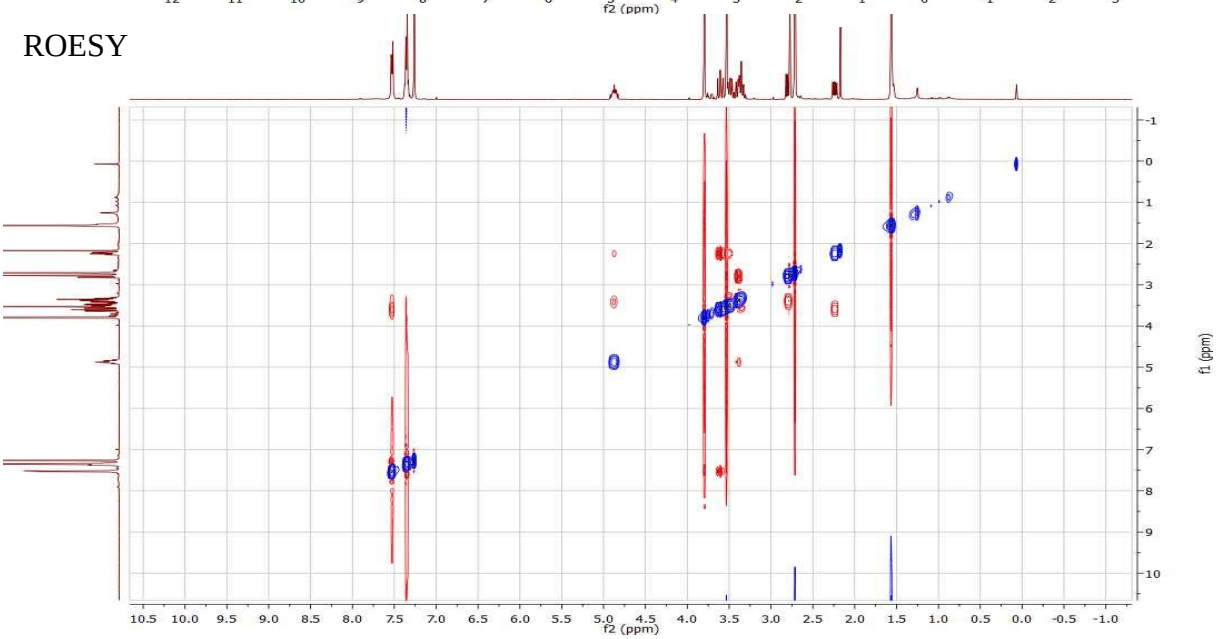
COSY

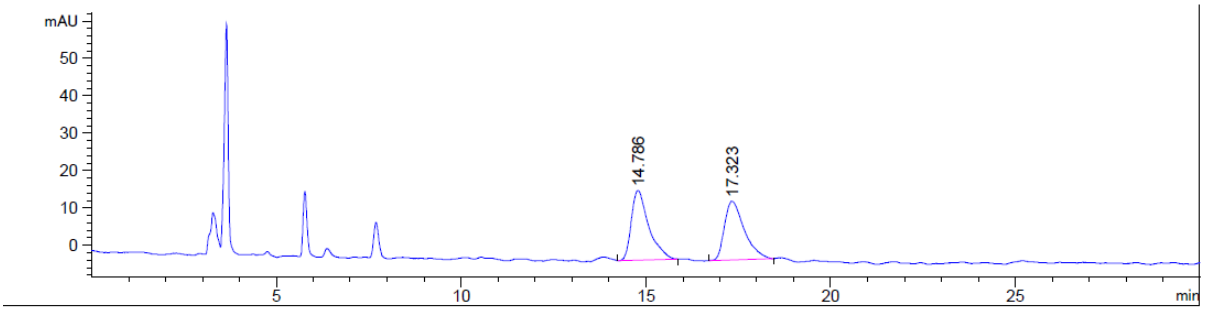


HSQC

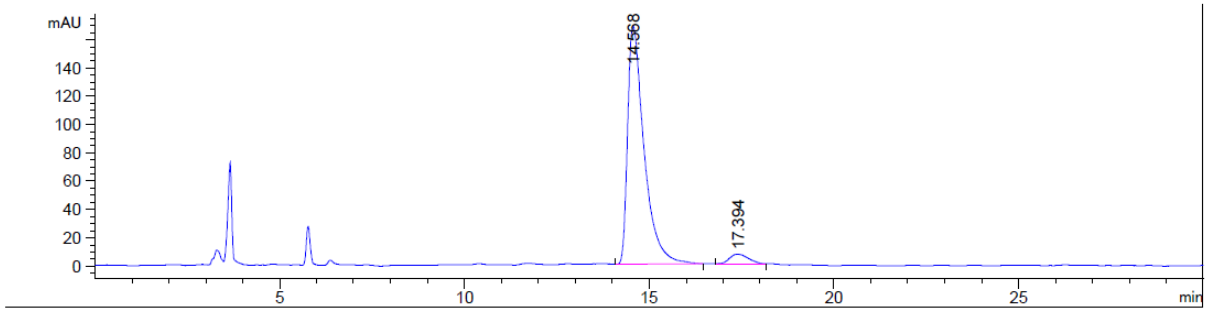


ROESY

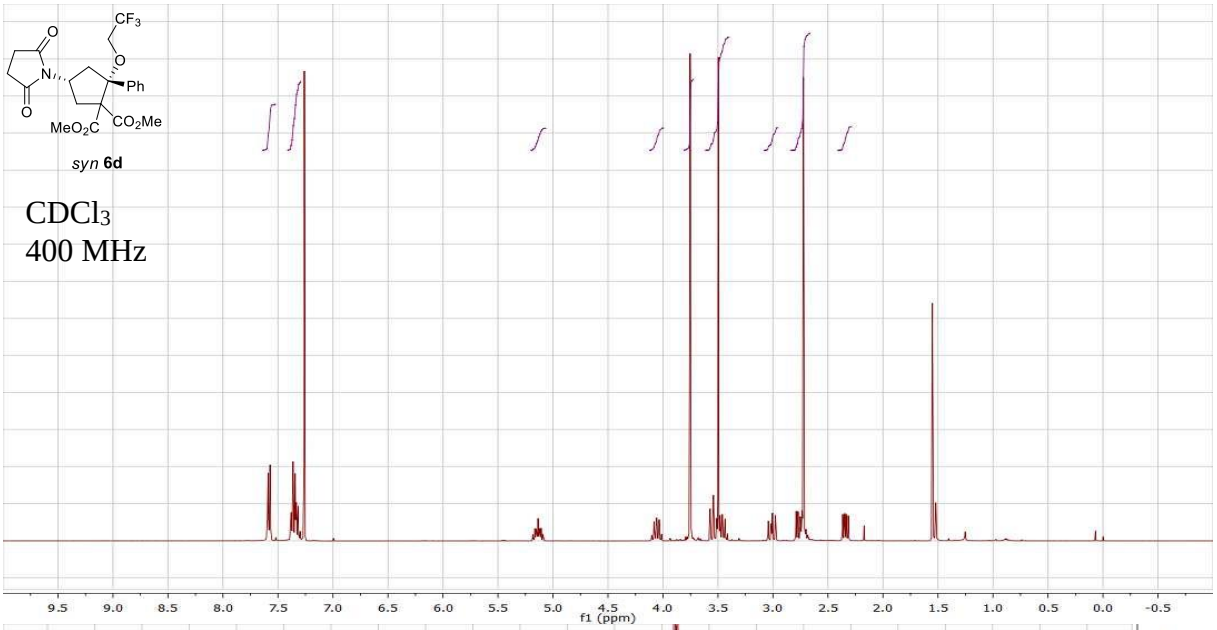


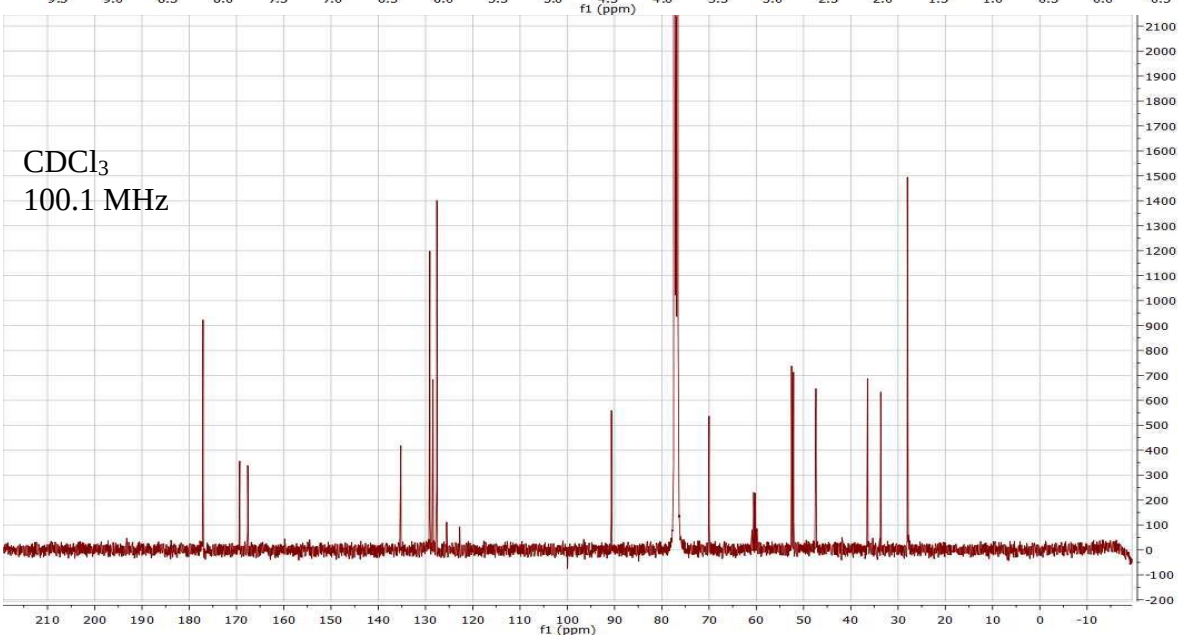


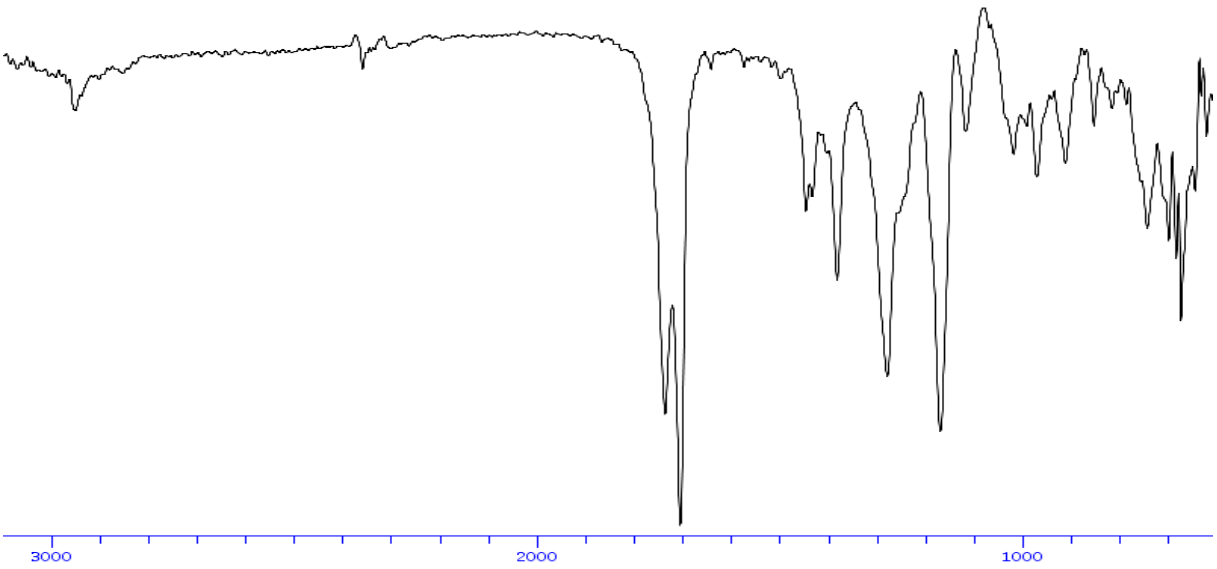
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.786	BB	0.4799	612.02264	18.69464	51.2501
2	17.323	BB	0.4927	582.16473	15.69609	48.7499



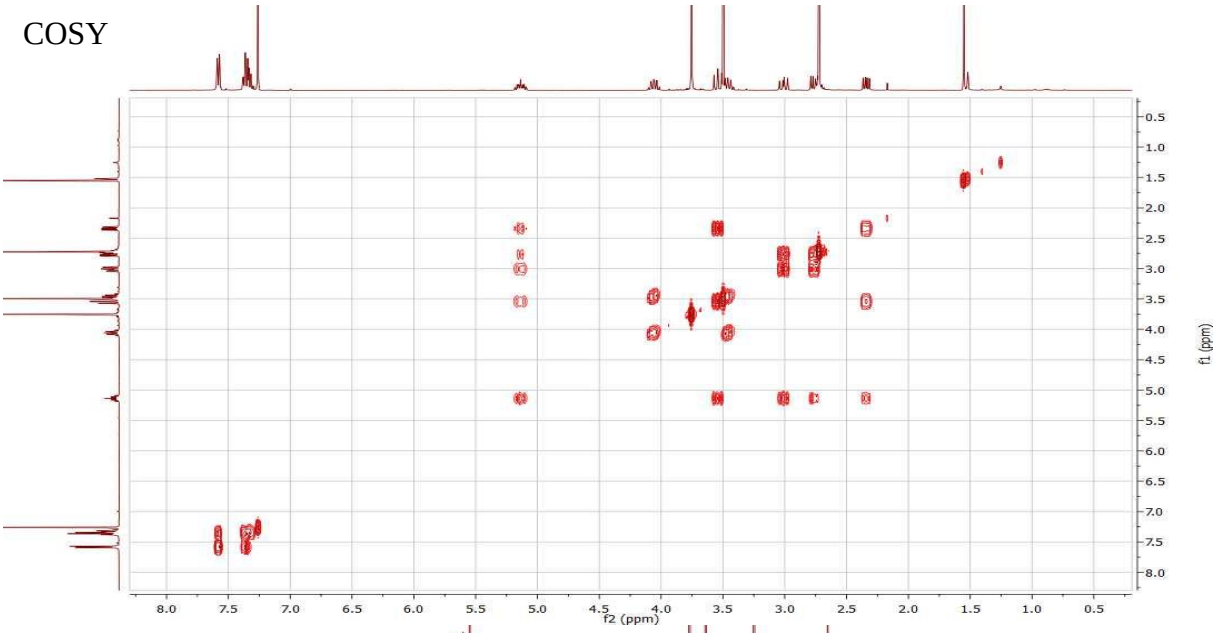
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.568	BB	0.4647	5242.71924	168.62868	95.6216
2	17.394	BB	0.4666	240.05623	6.82068	4.3784


CF3
O
N
O
O
Ph
MeO2C
CO2Me
syn 6d
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

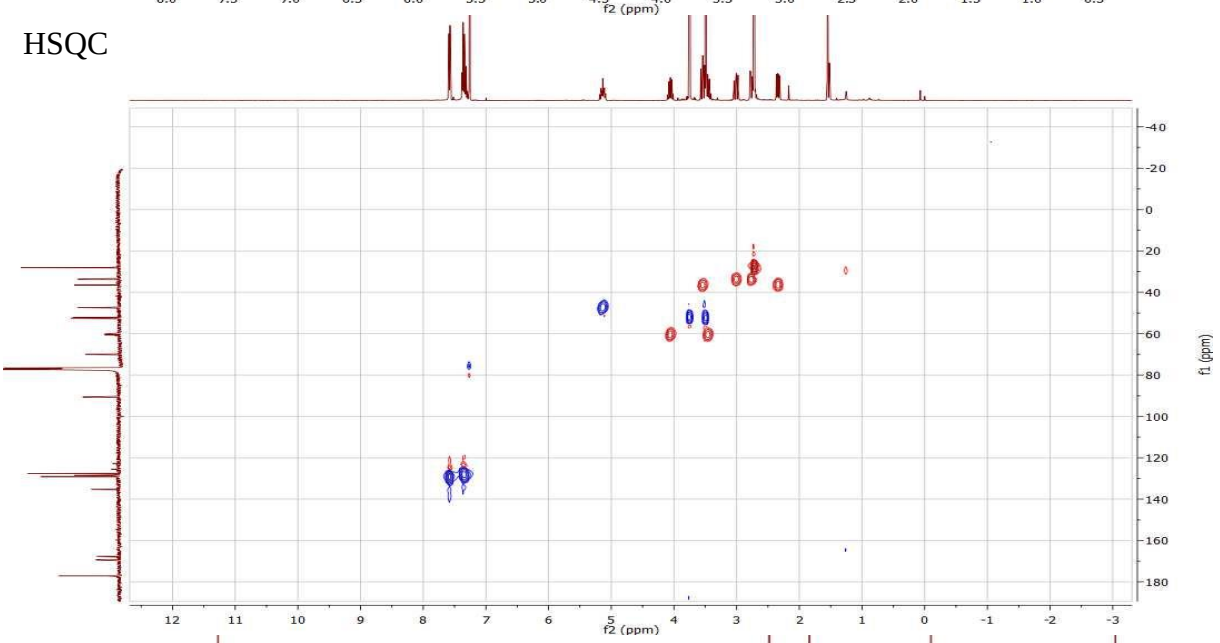

CDCl3
100.1 MHz
2100 2000 1900 1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100 -200
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


3000
2000
1000

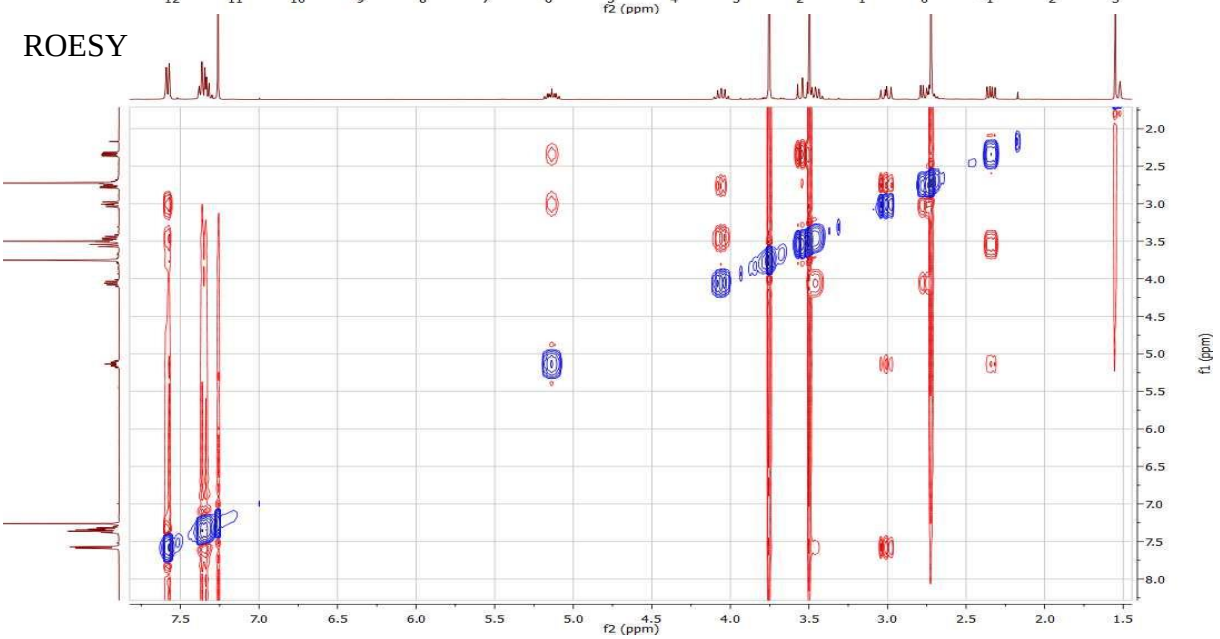
COSY

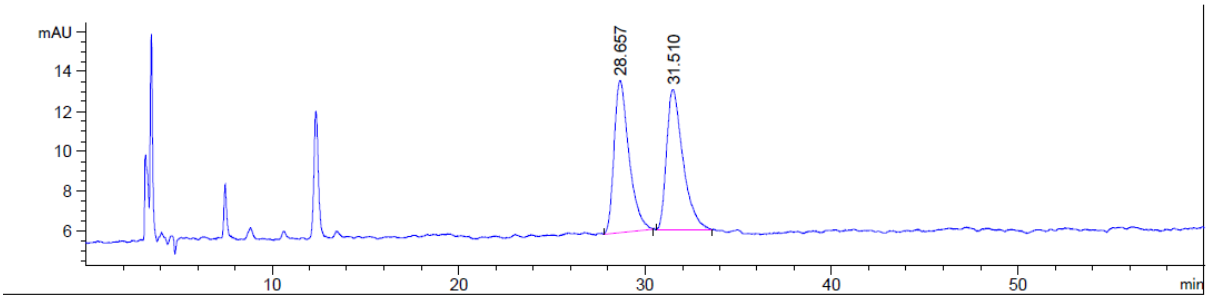


HSQC

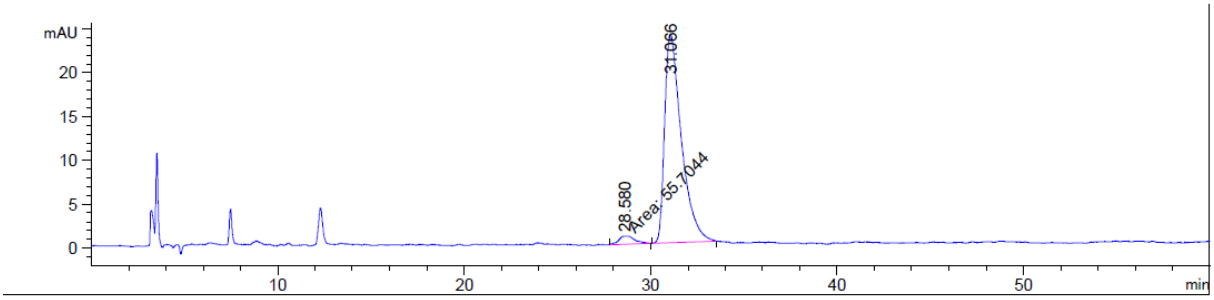


ROESY

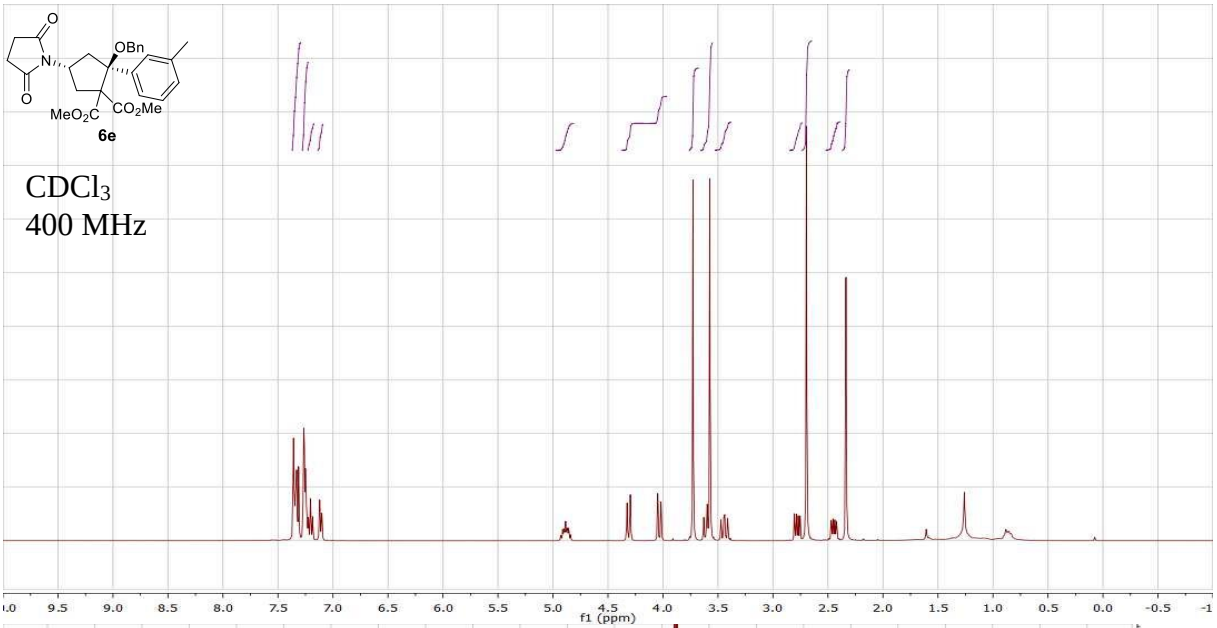


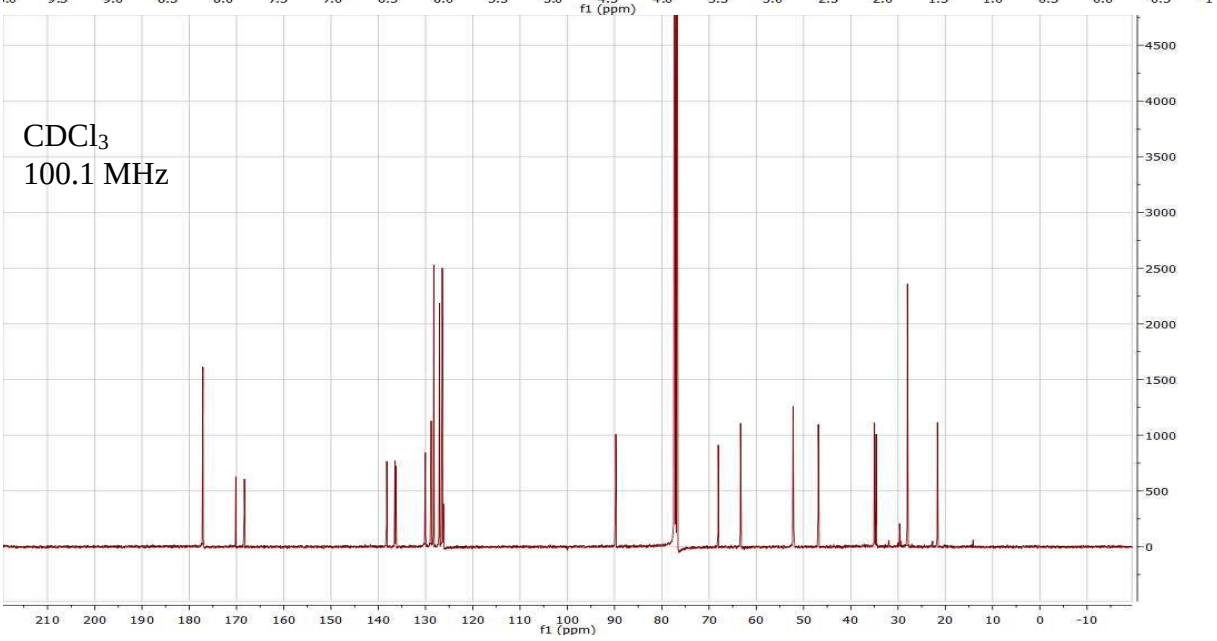


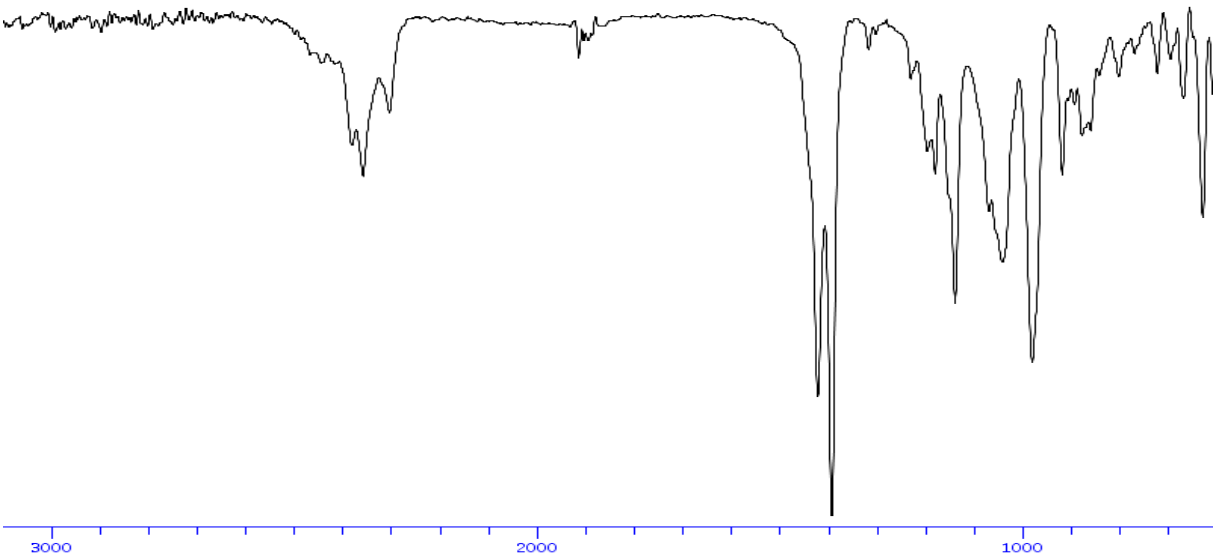
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.667	BB	0.6863	872.56097	16.10004	49.5524
2	31.501	BB	0.7222	888.32397	14.59279	50.4476

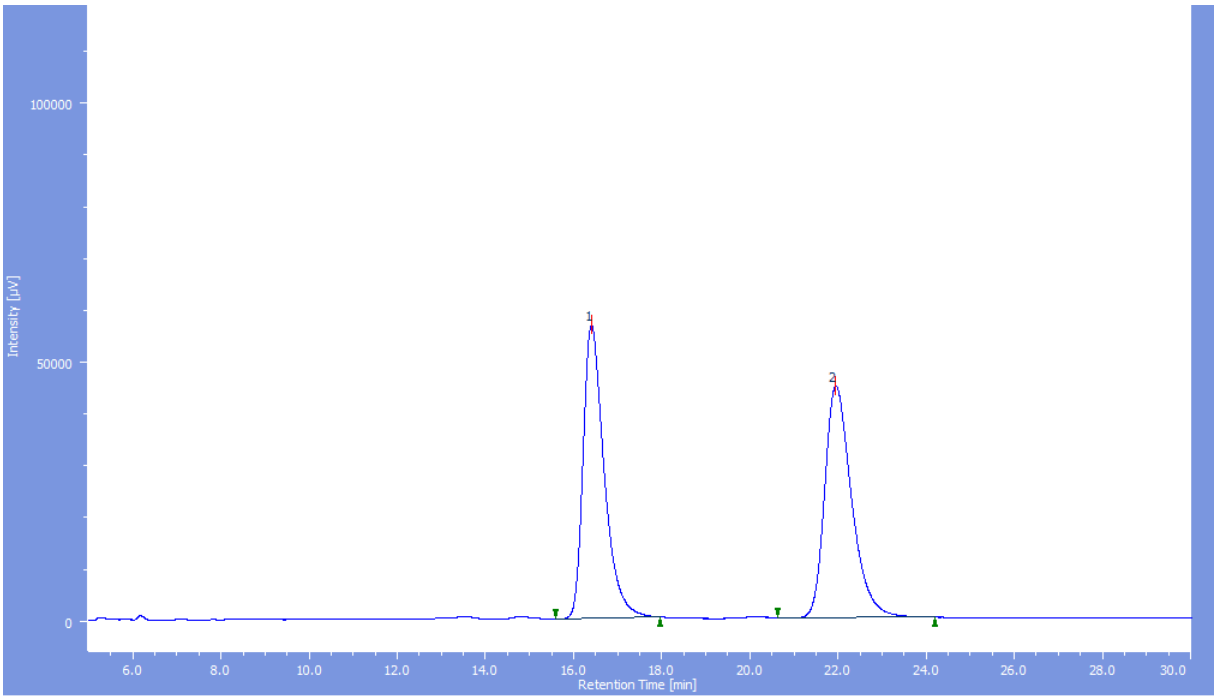


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.580	MM	0.9864	55.70440	9.41187e-1	3.6138
2	31.066	BB	0.8913	1485.72107	23.76870	96.3862

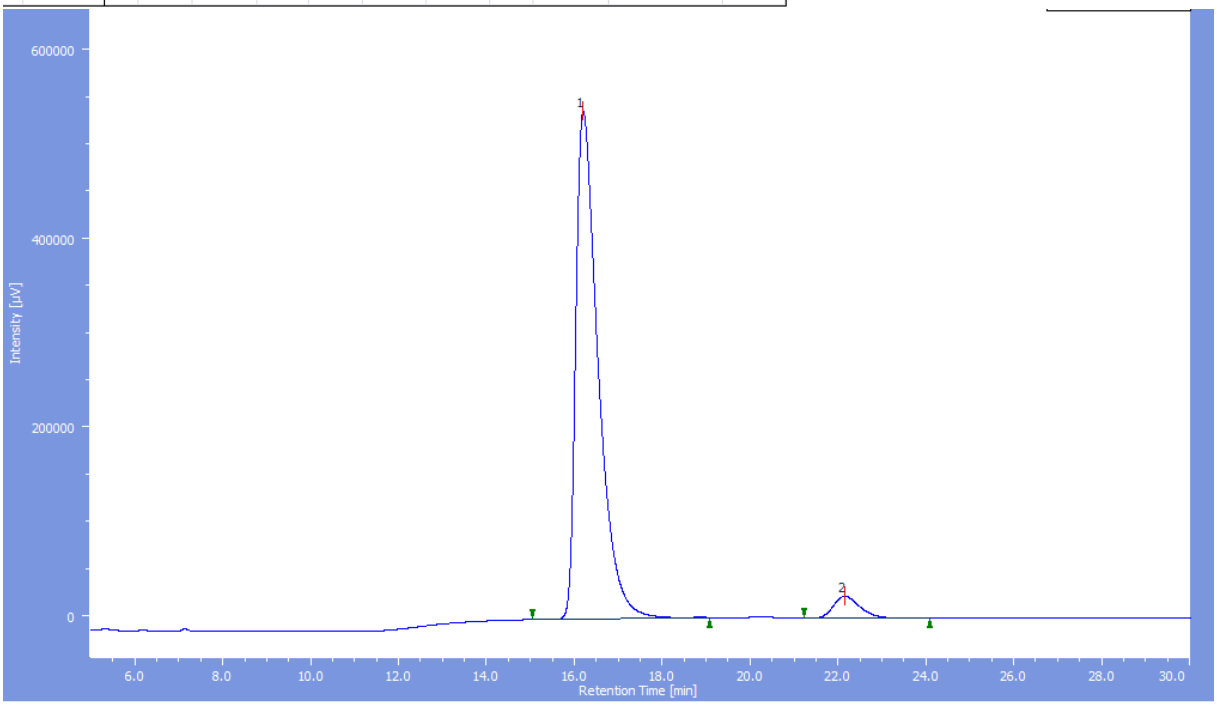

OBn
N
O
O
MeO2C
CO2Me
6e
CDCl3
400 MHz
f1 (ppm)


CDCl3
100.1 MHz
f1 (ppm)

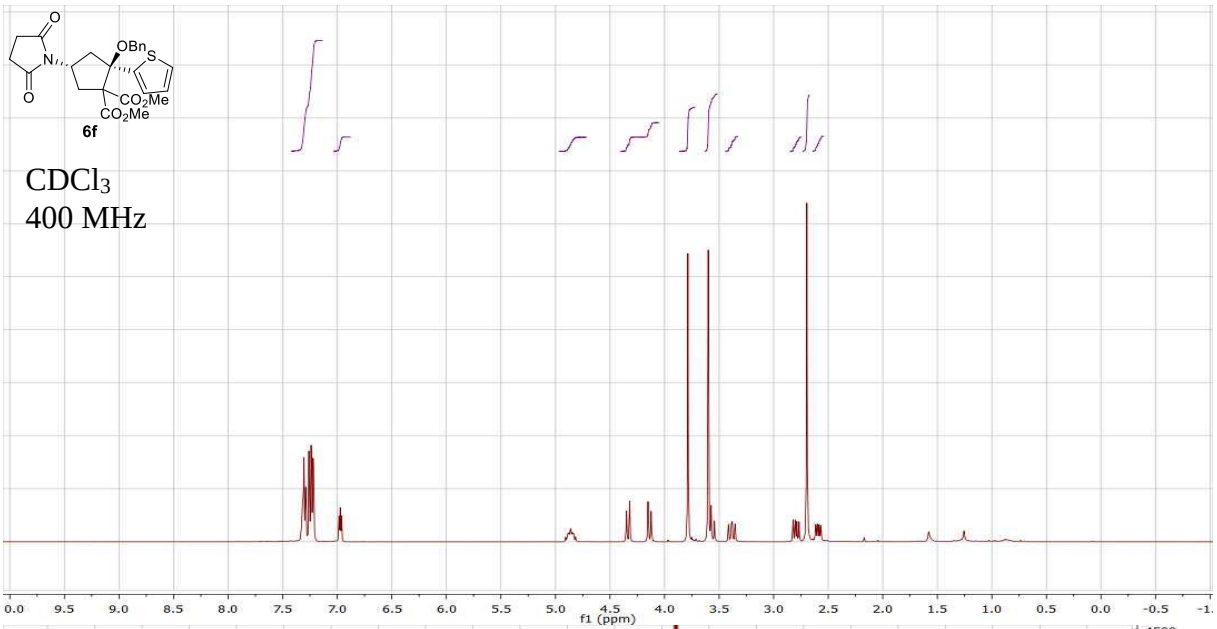

3000
2000
1000

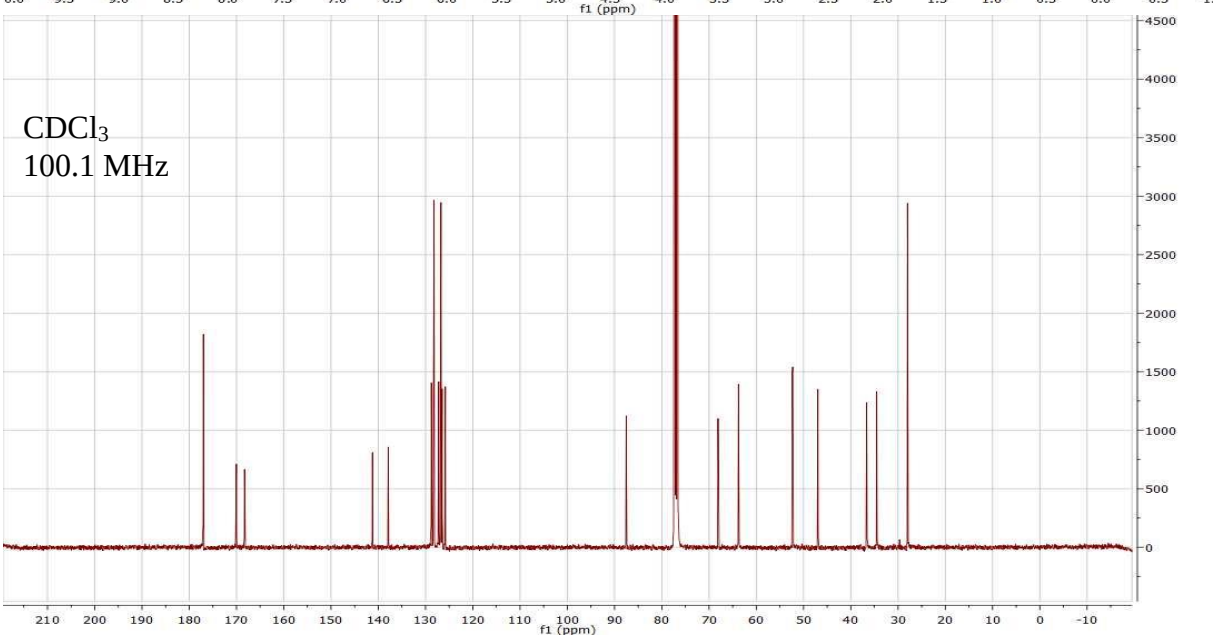


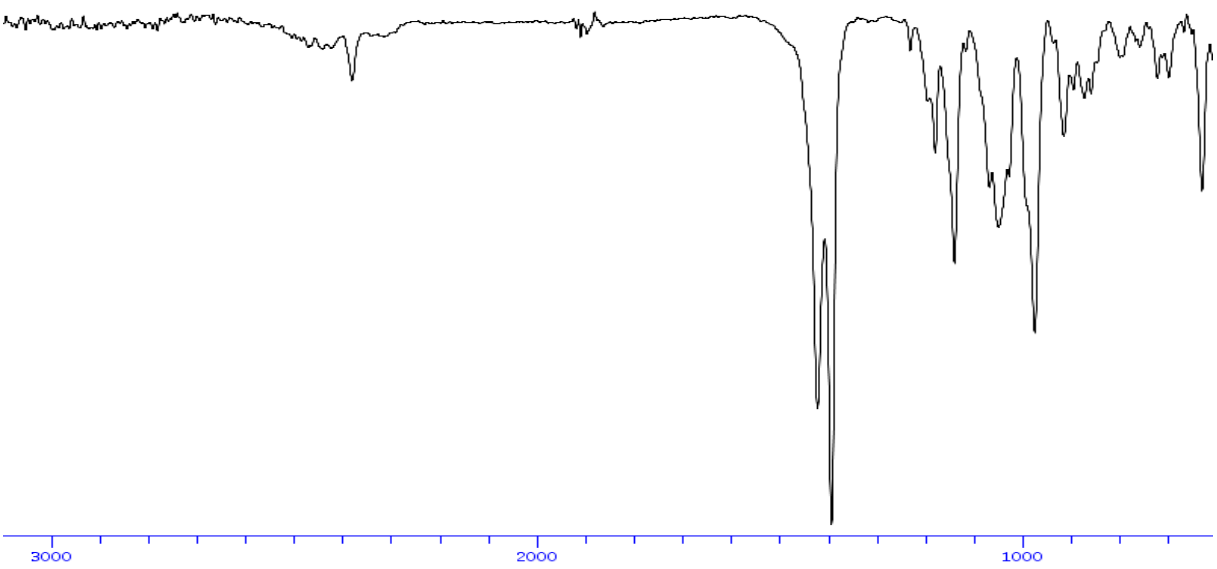
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	16.393	1876402	56520	49.778	55.841	N/A	6121	5.790	1.491	
2	Unknown	2	21.933	1893120	44696	50.222	44.159	N/A	6592	N/A	1.374	



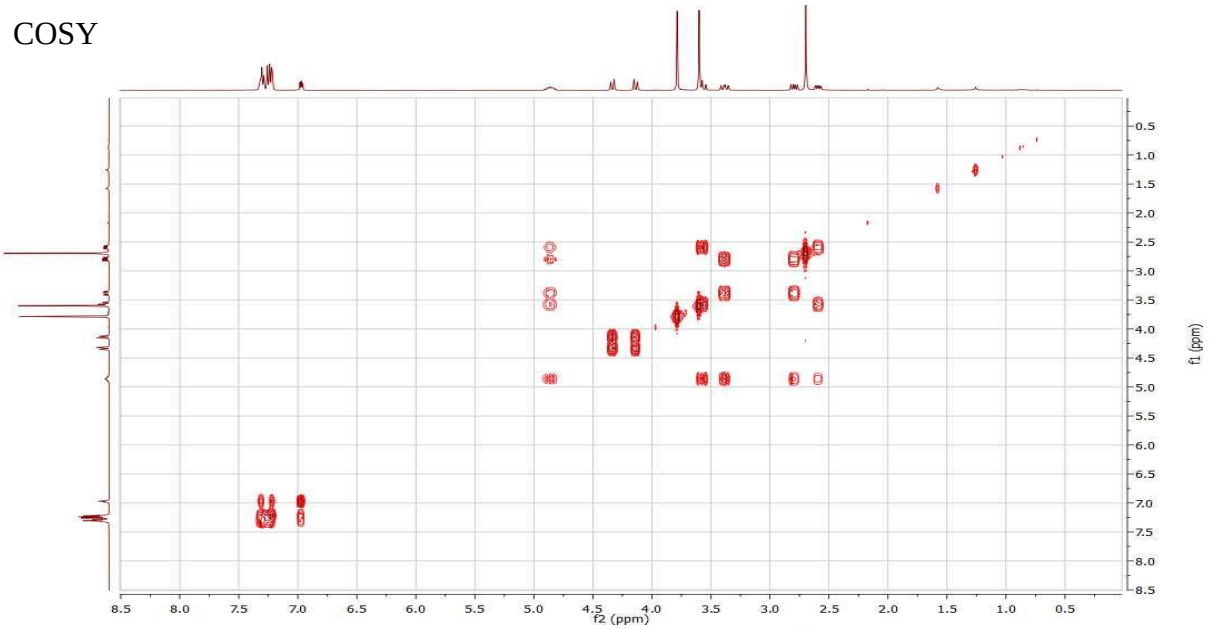
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	16.193	18944684	537147	95.057	95.842	N/A	5291	6.010	1.863	
2	Unknown	2	22.140	985224	23301	4.943	4.158	N/A	6558	N/A	1.273	


OBn
S
N
O
O
CO2Me
CO2Me
6f
CDCl3
400 MHz
f1 (ppm)

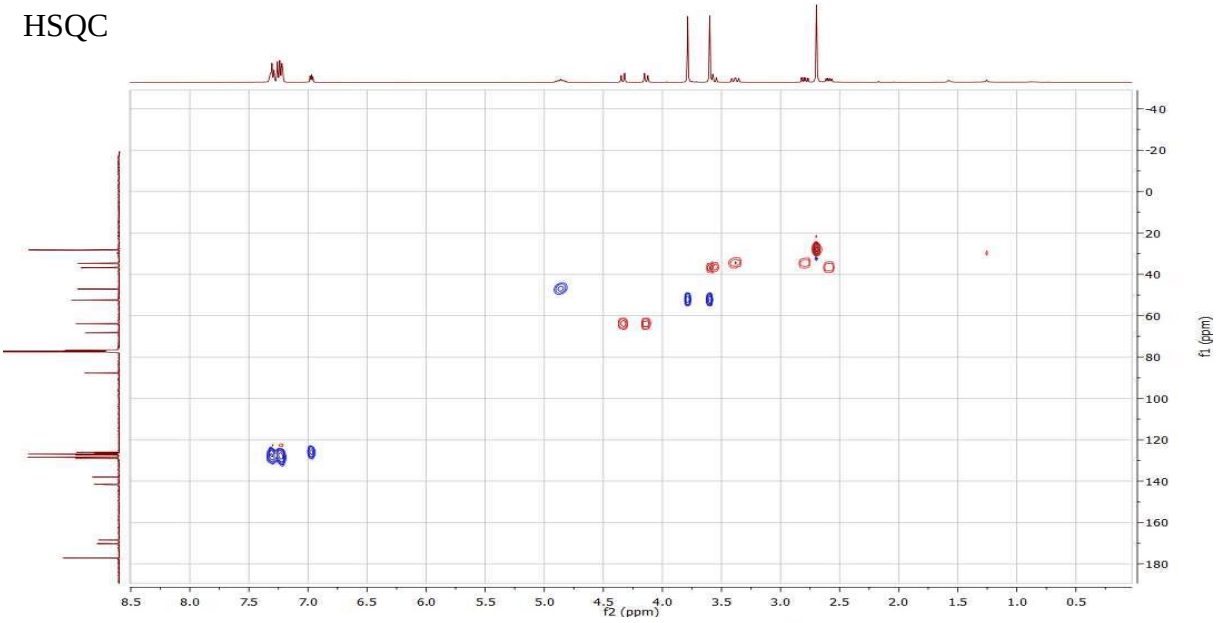

CDCl3
100.1 MHz
f1 (ppm)


3000
2000
1000

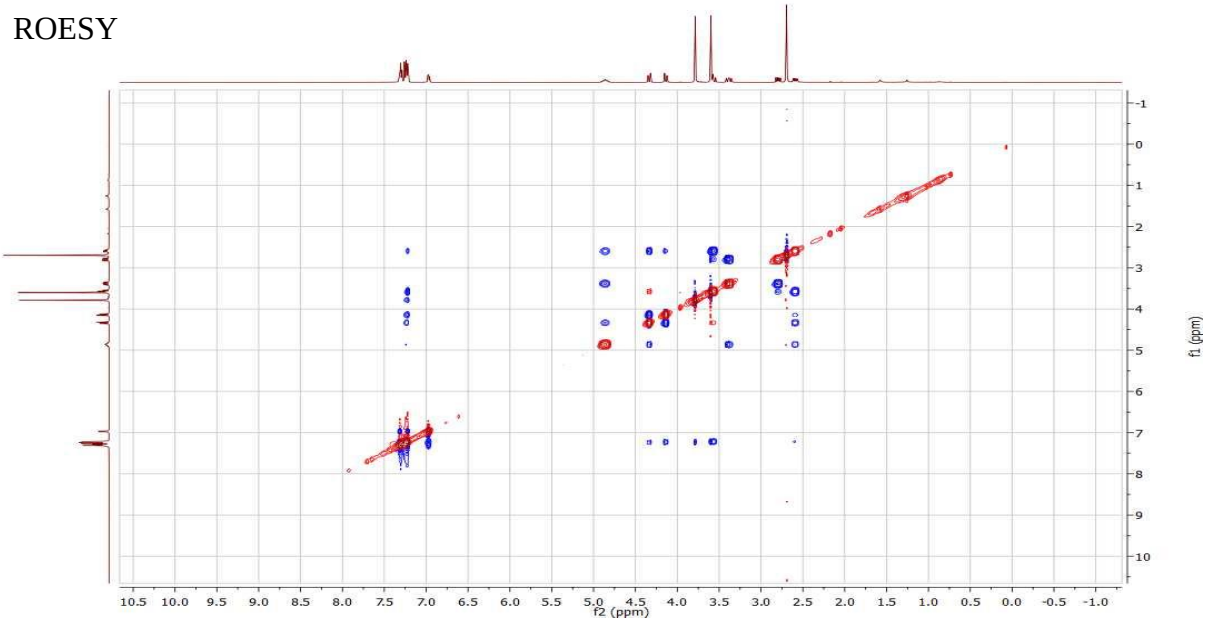
COSY

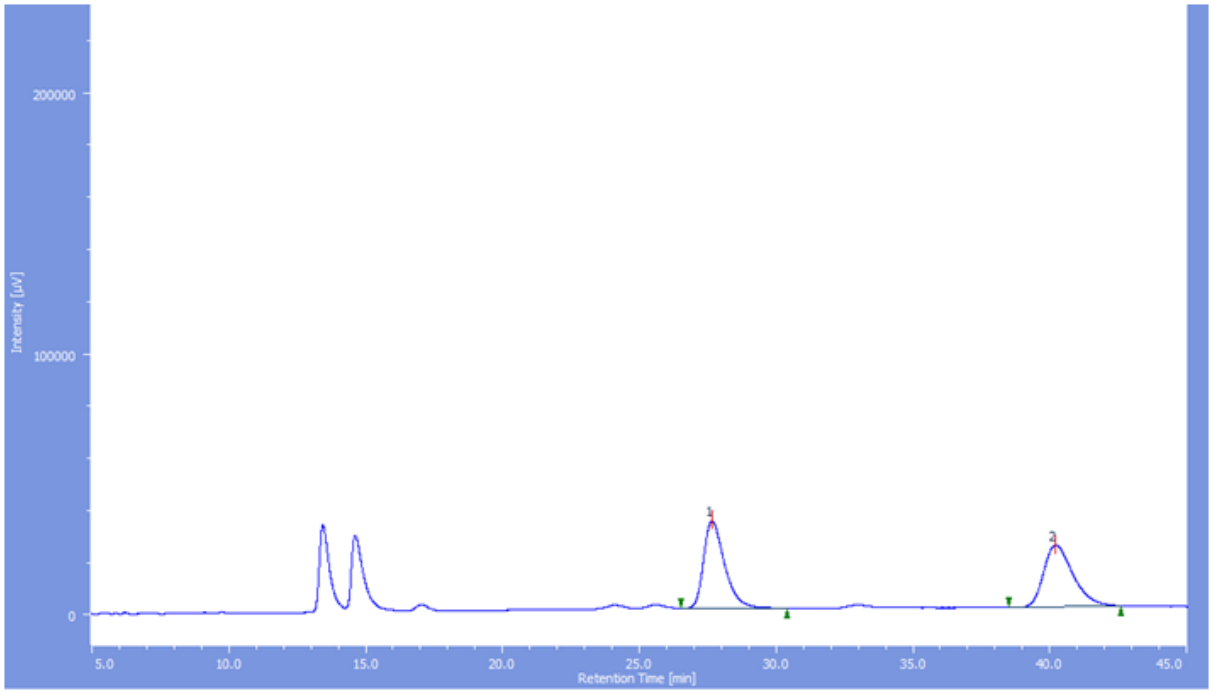


HSQC

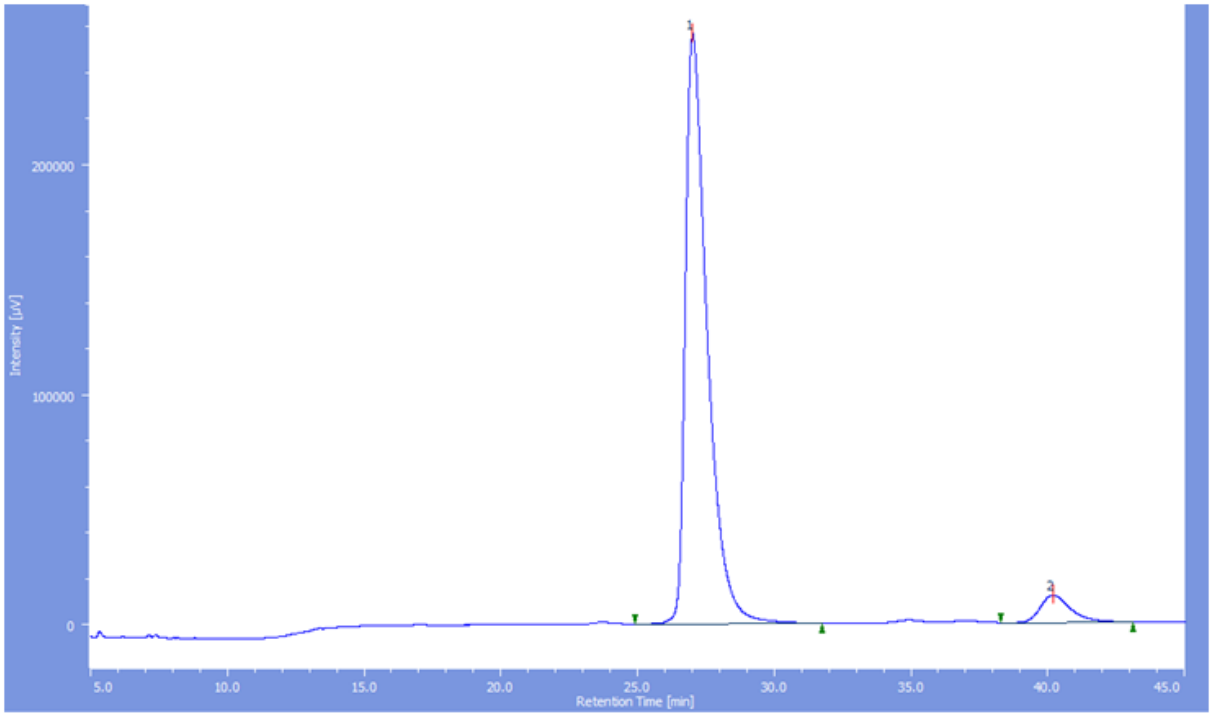


ROESY

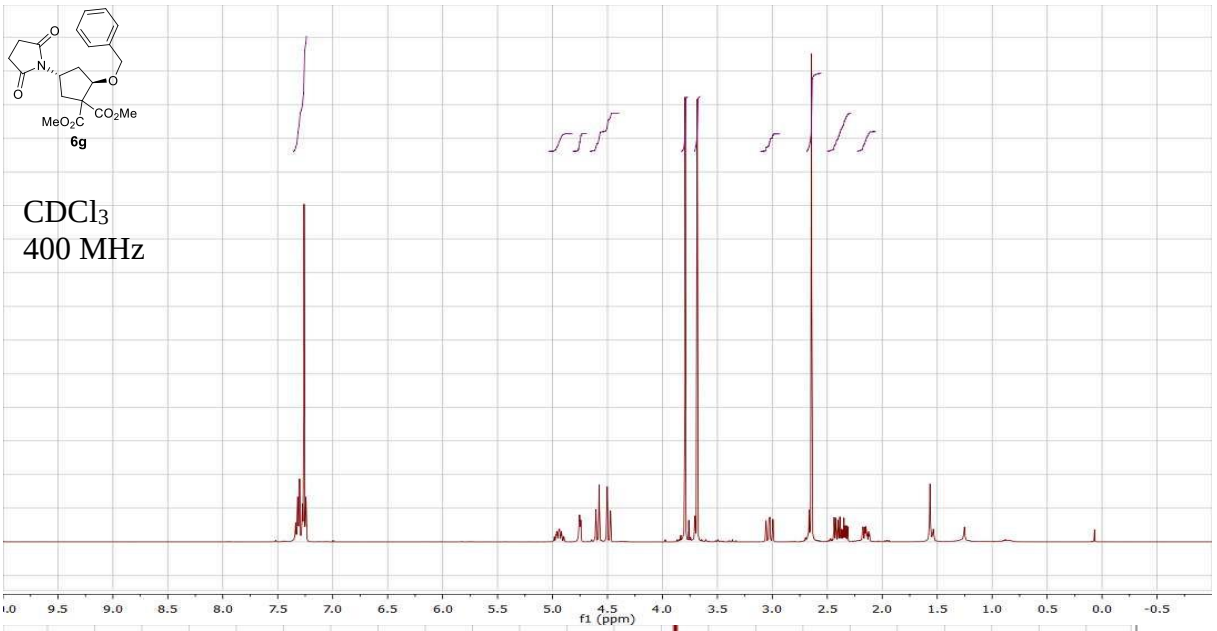


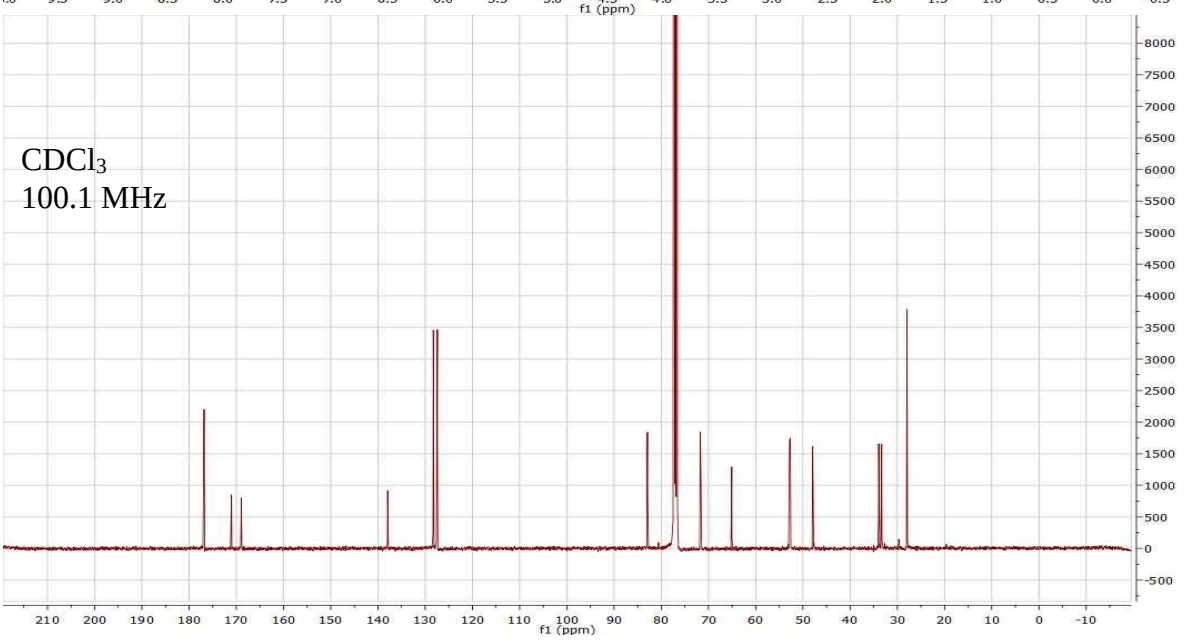


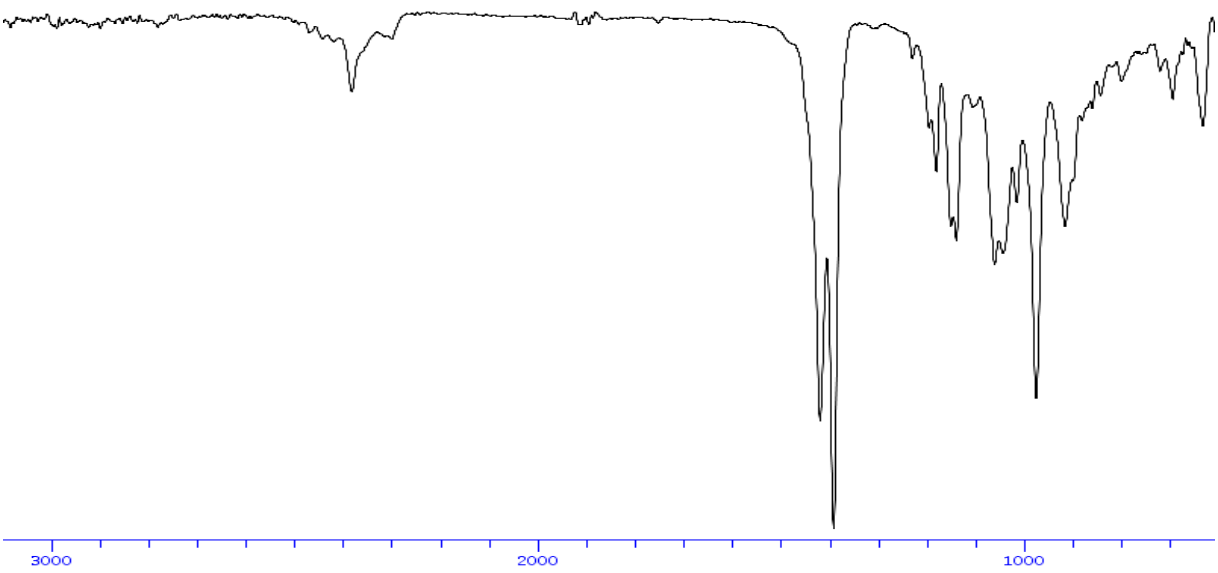
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	27.633	1784129	33537	50.217	58.621	N/A	6712	7.678	1.458	
2	Unknown	1	40.177	1768714	23673	49.783	41.379	N/A	6958	N/A	1.392	



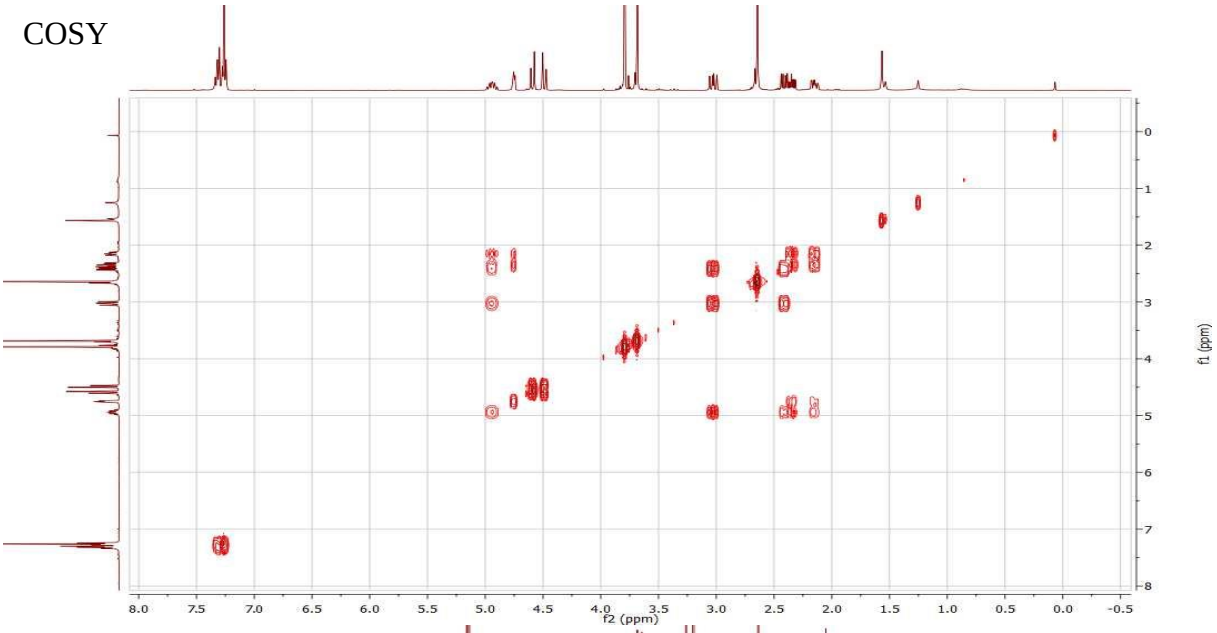
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	26.997	14213770	255962	93.933	95.569	N/A	6098	7.950	1.830	
2	Unknown	1	40.163	918106	11868	6.067	4.431	N/A	6869	N/A	1.481	


MeO2C
CO2Me
6g
CDCl3
400 MHz
f1 (ppm)

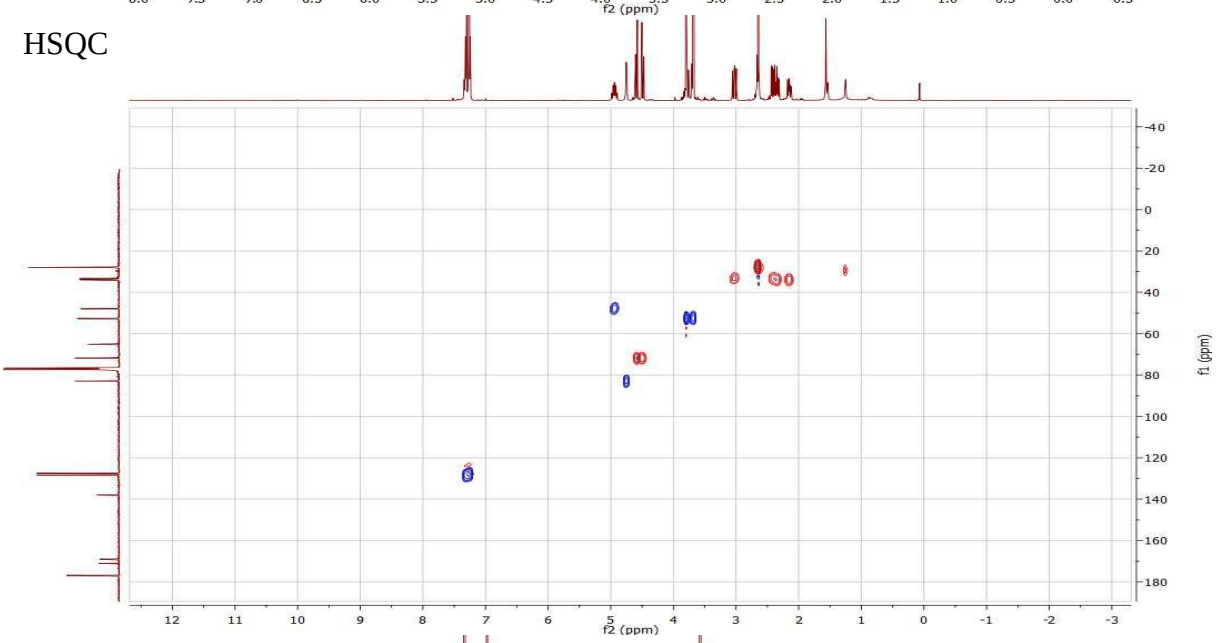

CDCl3
100.1 MHz
f1 (ppm)


3000
2000
1000

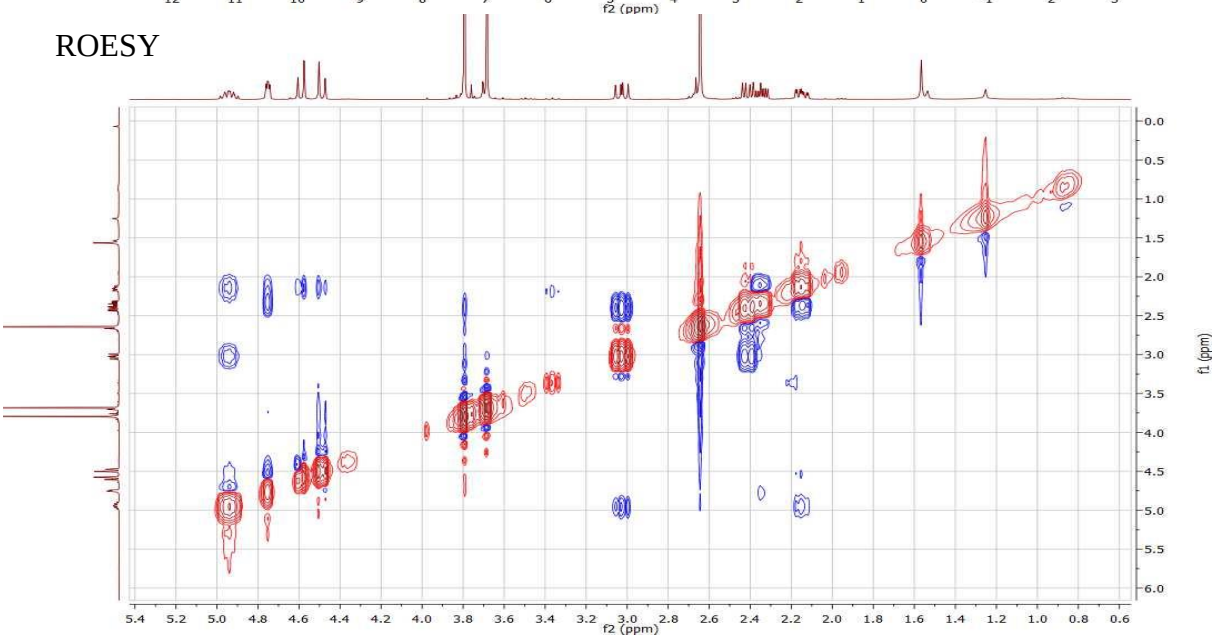
COSY

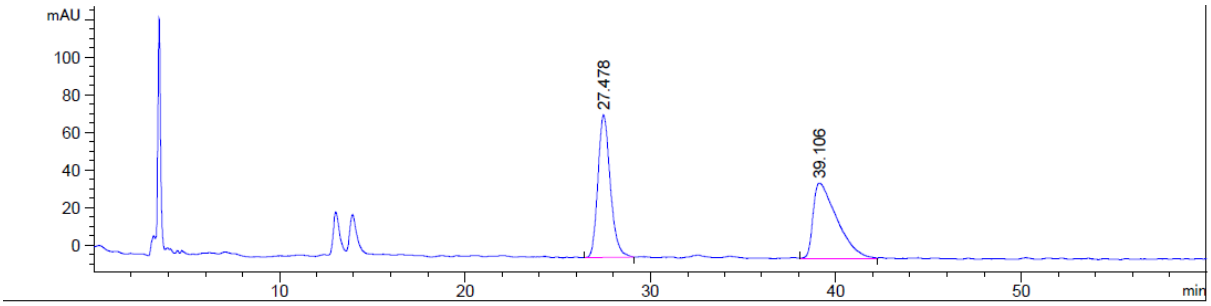


HSQC

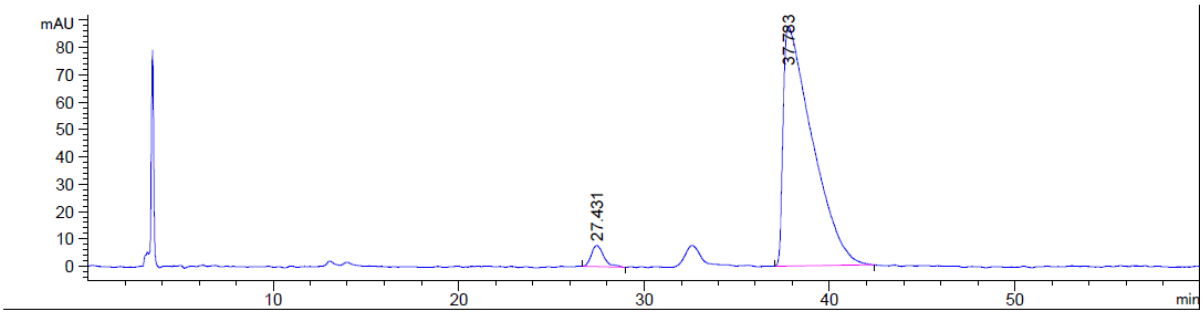


ROESY

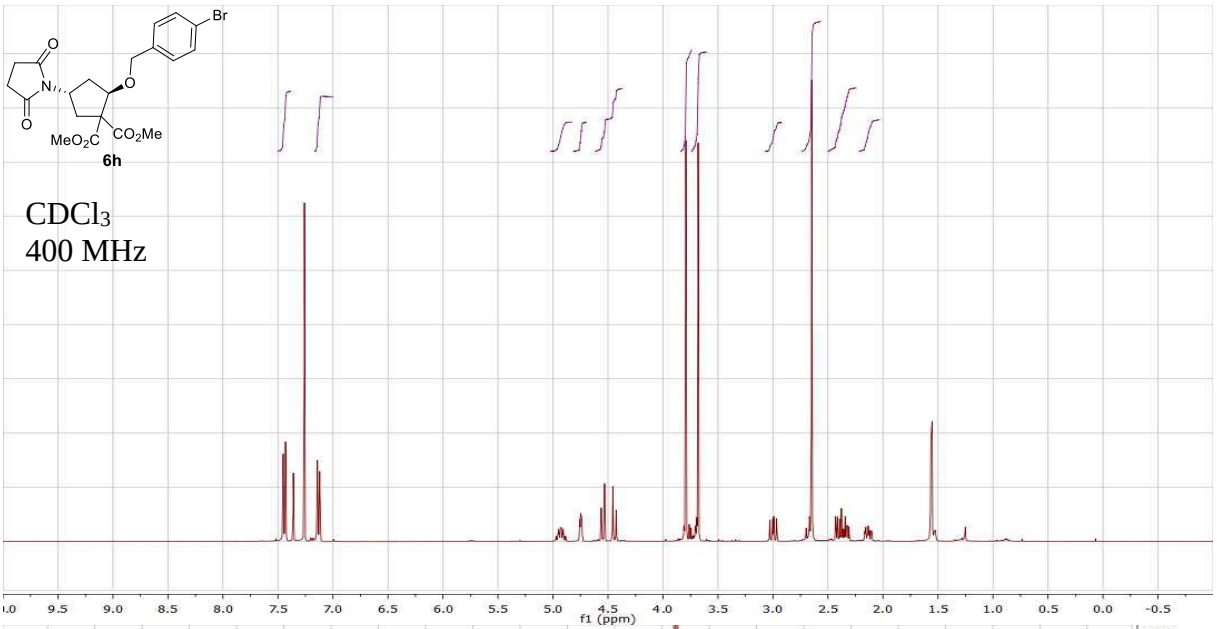


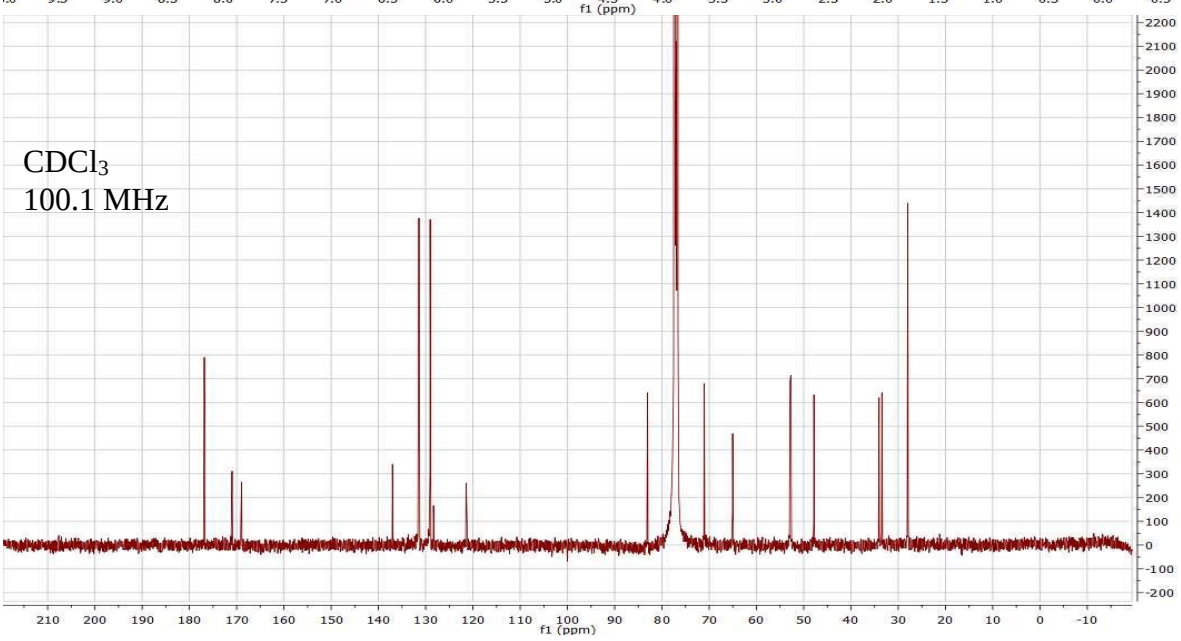


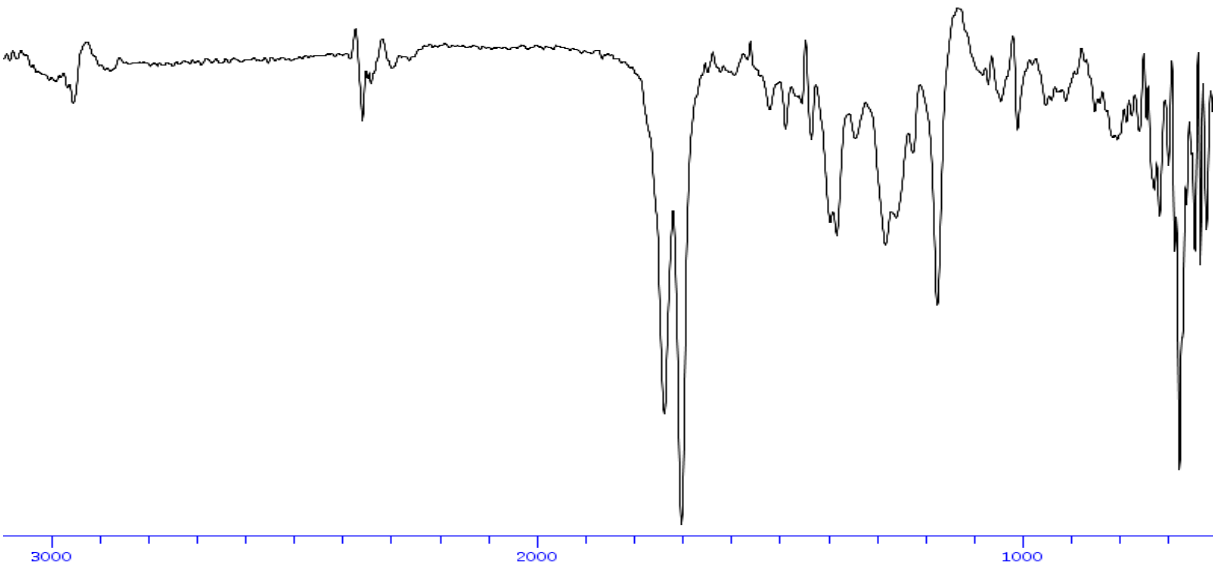
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.478	BB	0.7066	3530.93970	75.91951	49.9681
2	39.106	BB	1.1410	3535.45459	40.00510	50.0319



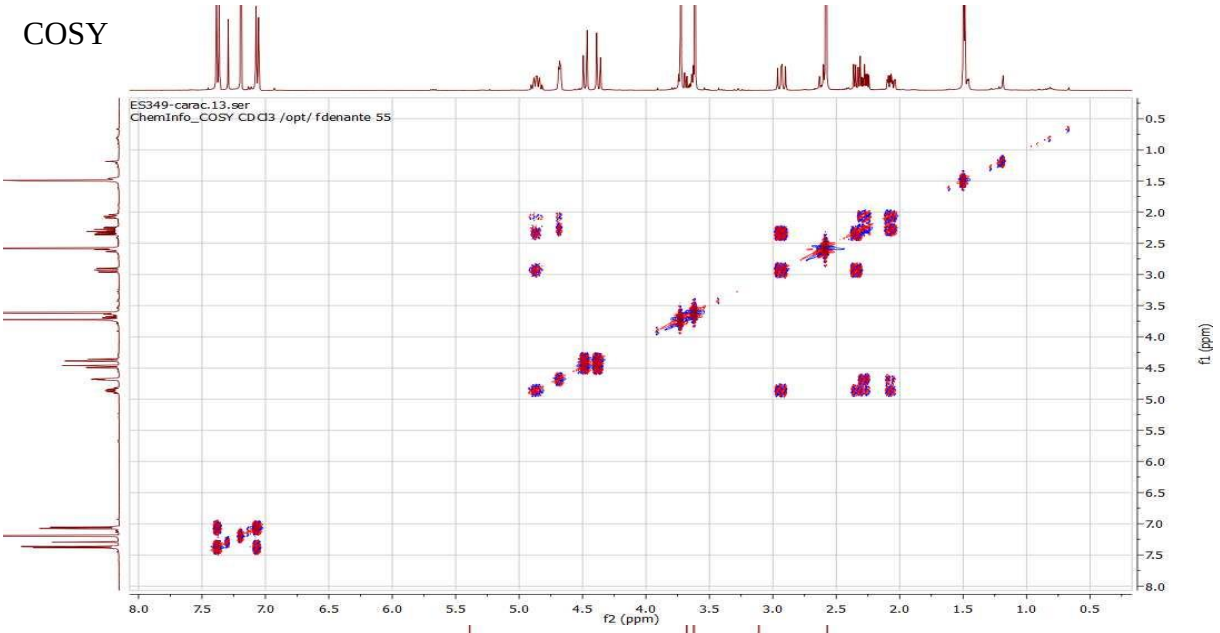
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.431	BB	0.5551	359.82034	7.72933	3.6369
2	37.783	BB	1.4007	9533.67578	87.39443	96.3631


Br
O
N
O
O
O
MeO2C
CO2Me
6h
CDCl3
400 MHz
f1 (ppm)

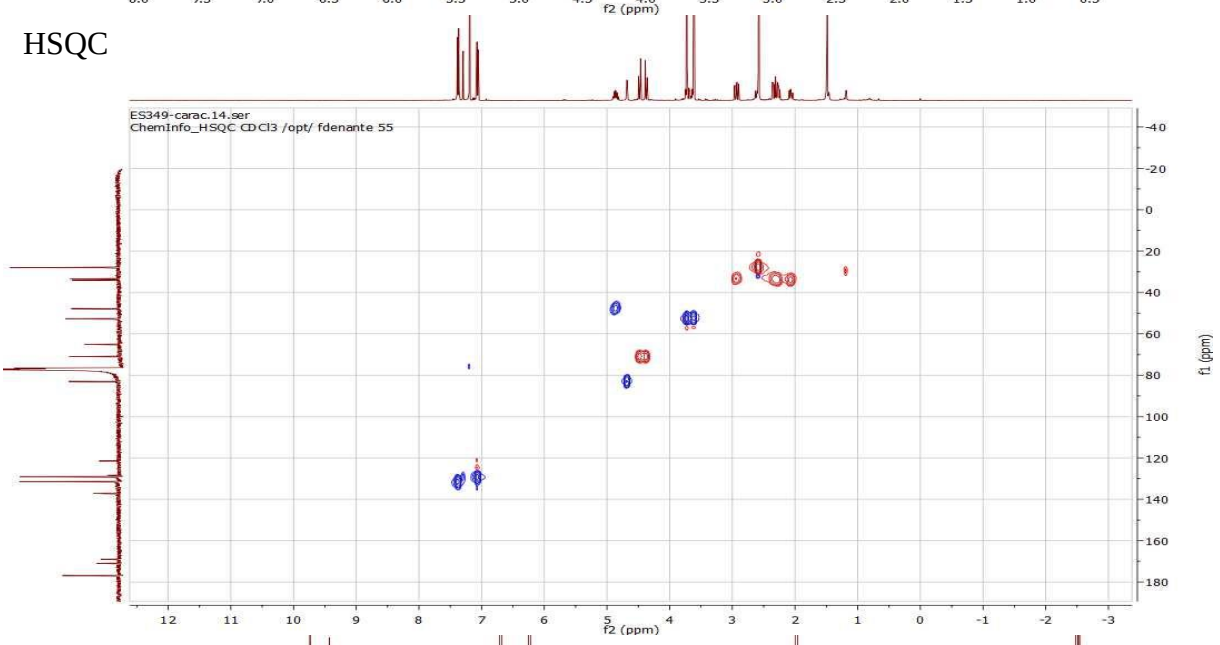

CDCl3
100.1 MHz
f1 (ppm)


3000
2000
1000

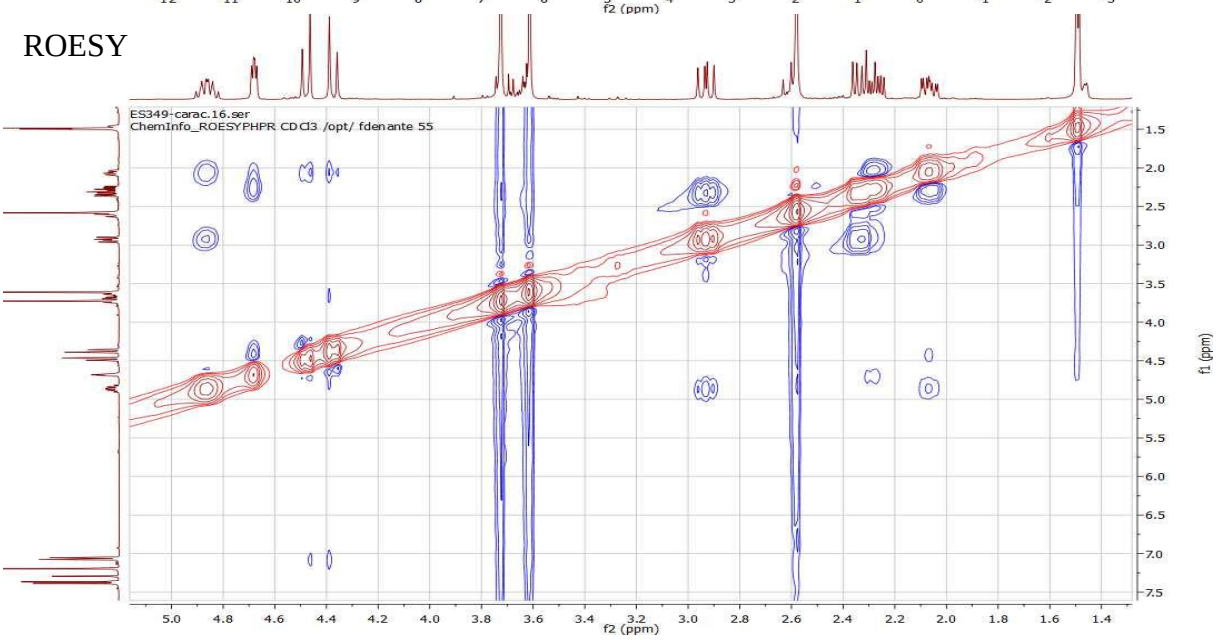
COSY

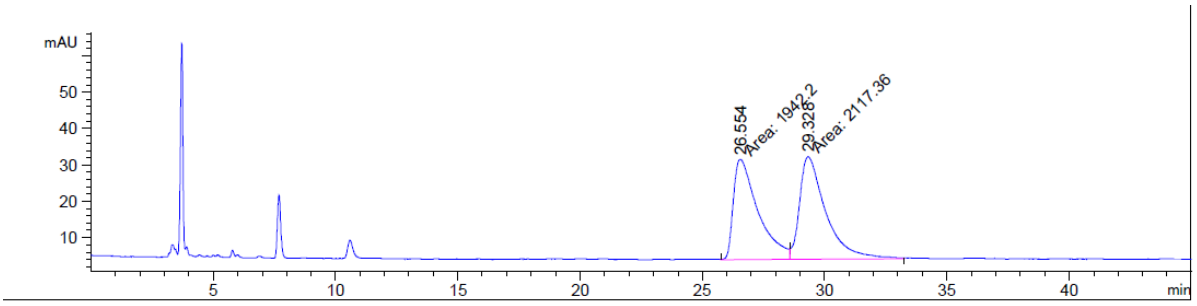


HSQC

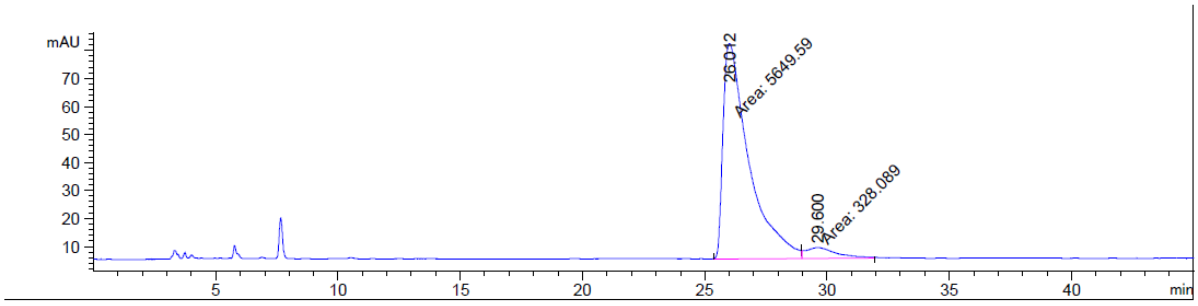


ROESY

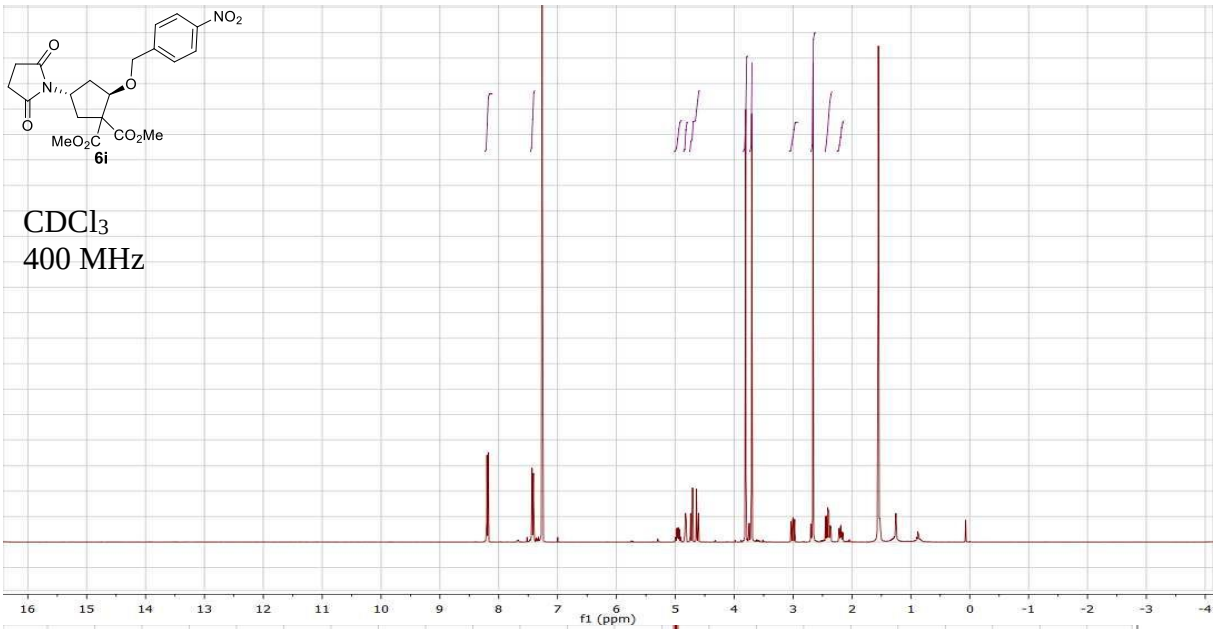


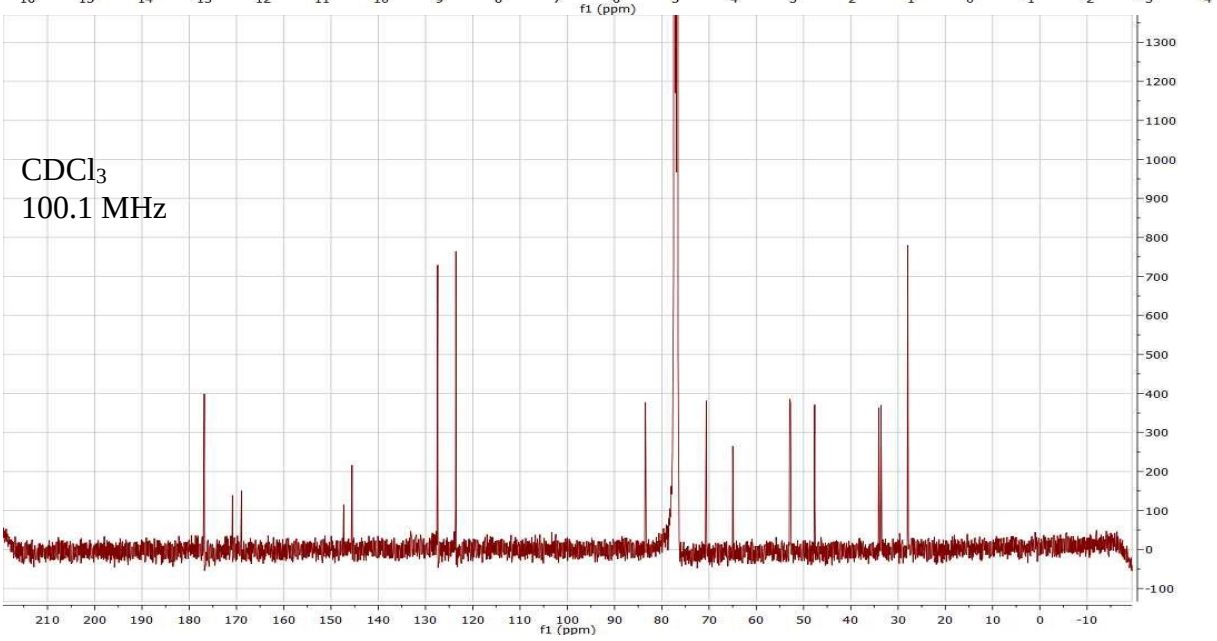


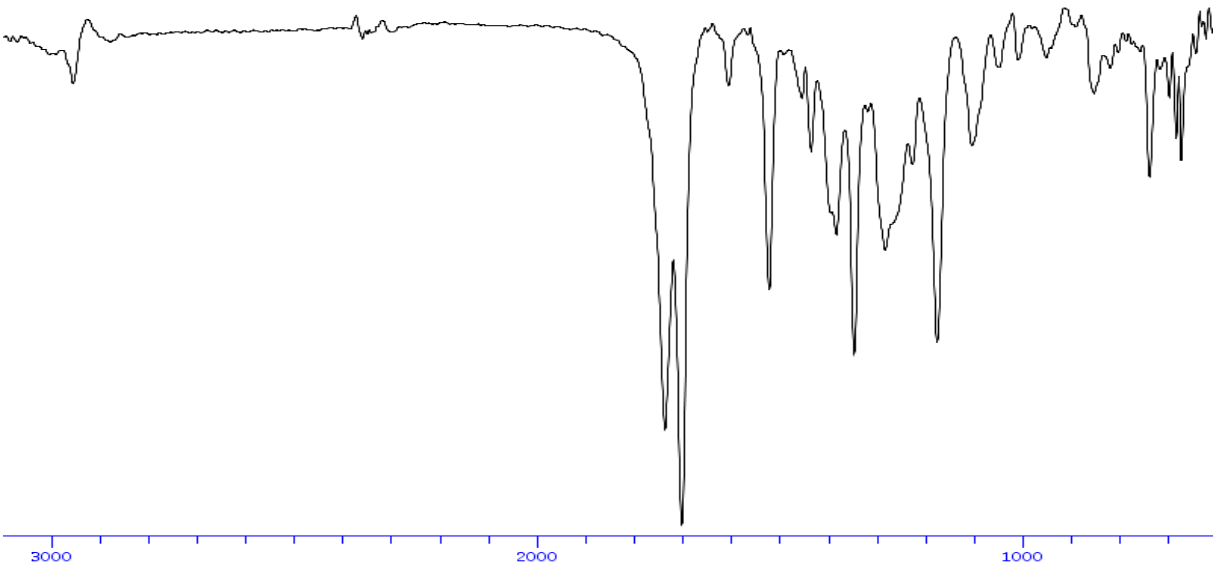
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.554	MF	1.1738	1942.19519	27.57736	47.8425
2	29.328	FM	1.2503	2117.36304	28.22524	52.1575



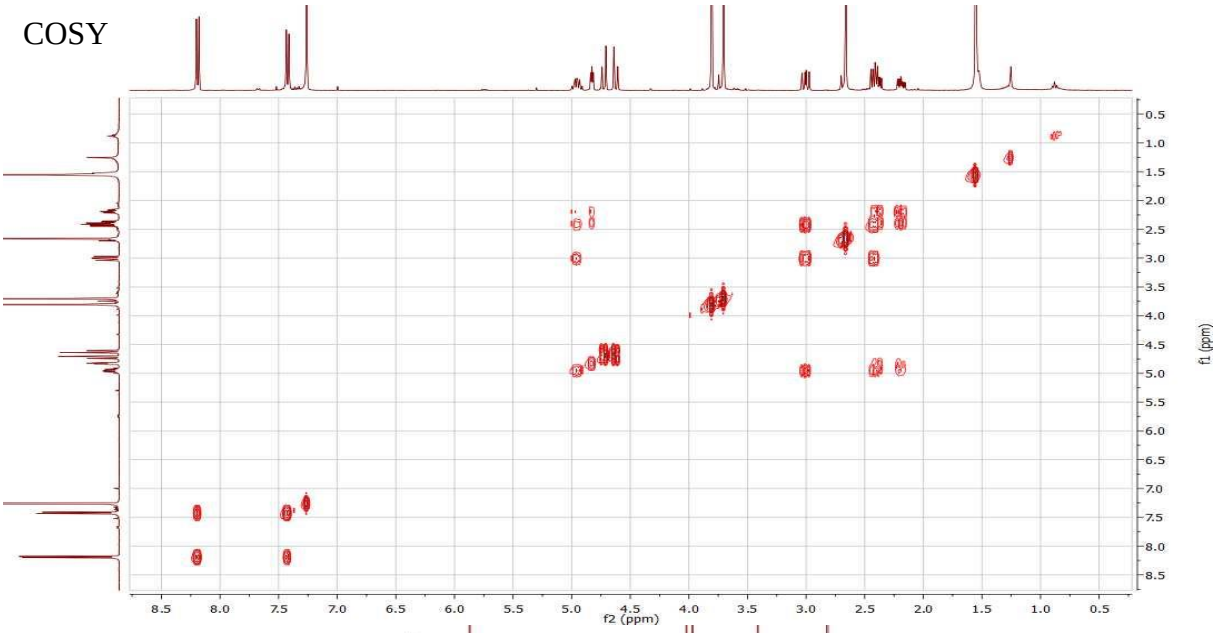
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.012	MF	1.2226	5649.59229	77.01463	94.5114
2	29.600	FM	1.4142	328.08899	3.86652	5.4886


NO2
O
N
O
O
MeO2C
CO2Me
6i
CDCl3
400 MHz
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

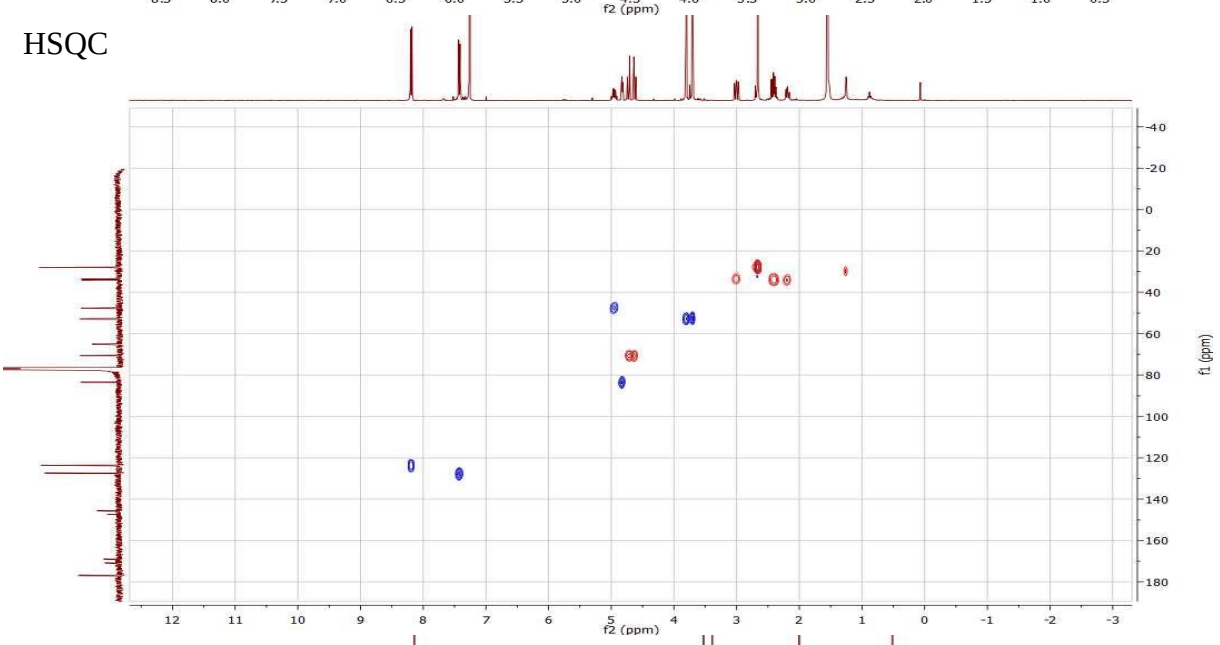

CDCl3
100.1 MHz
1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


3000
2000
1000

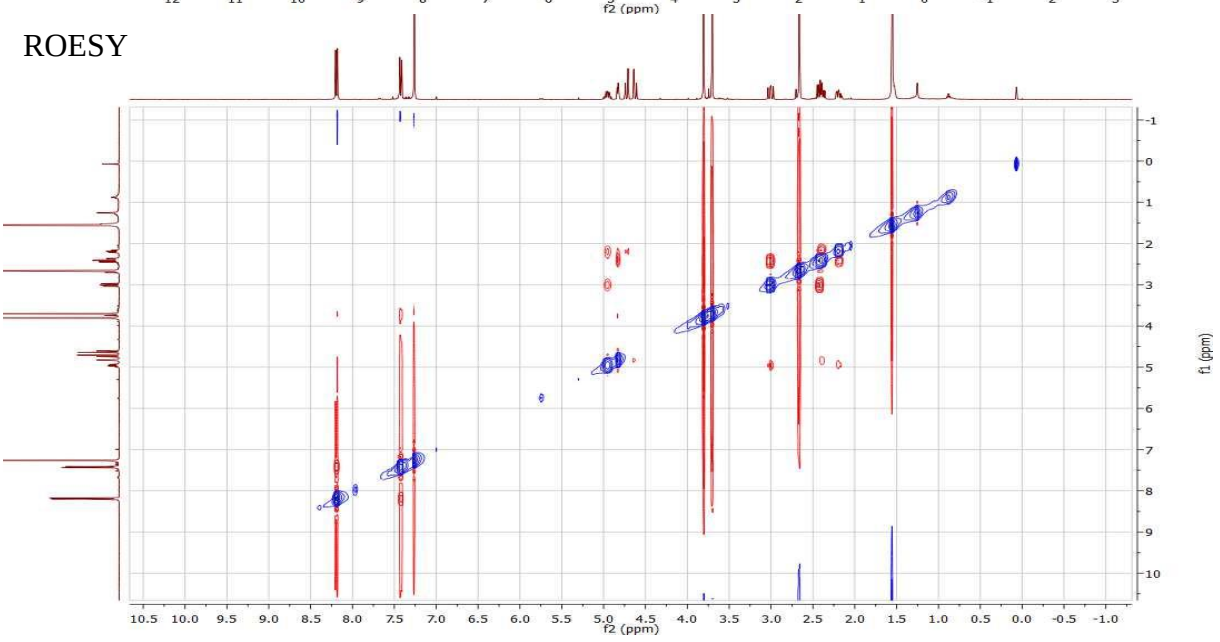
COSY

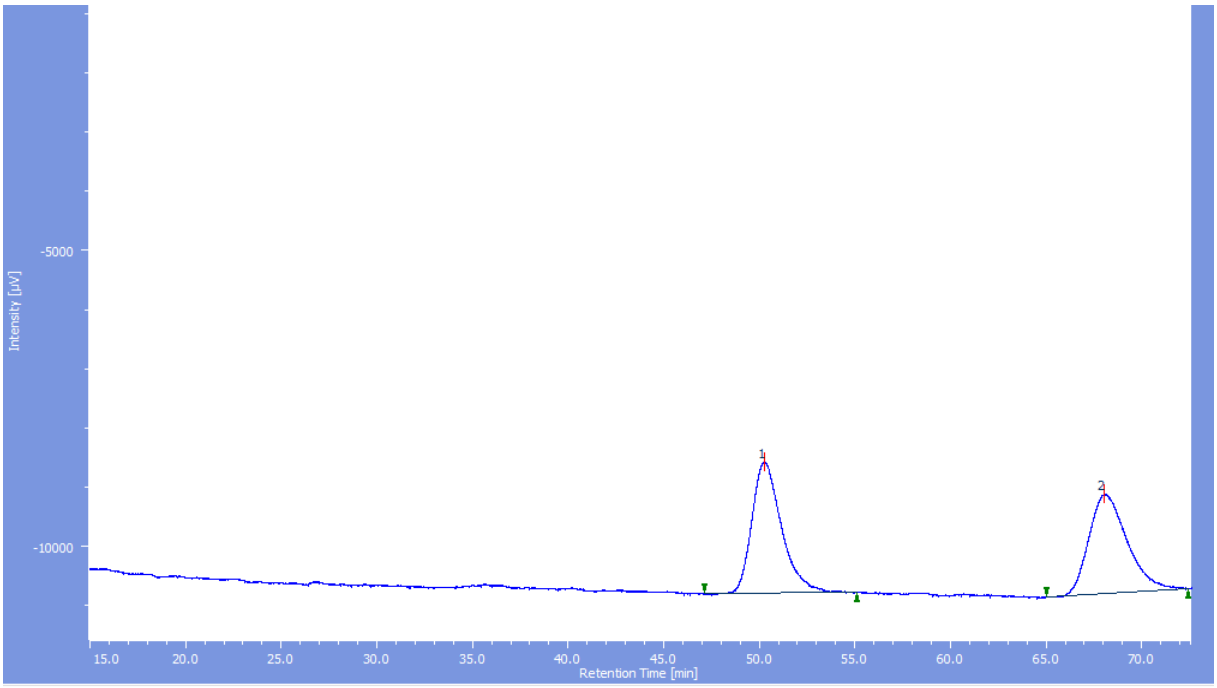


HSQC

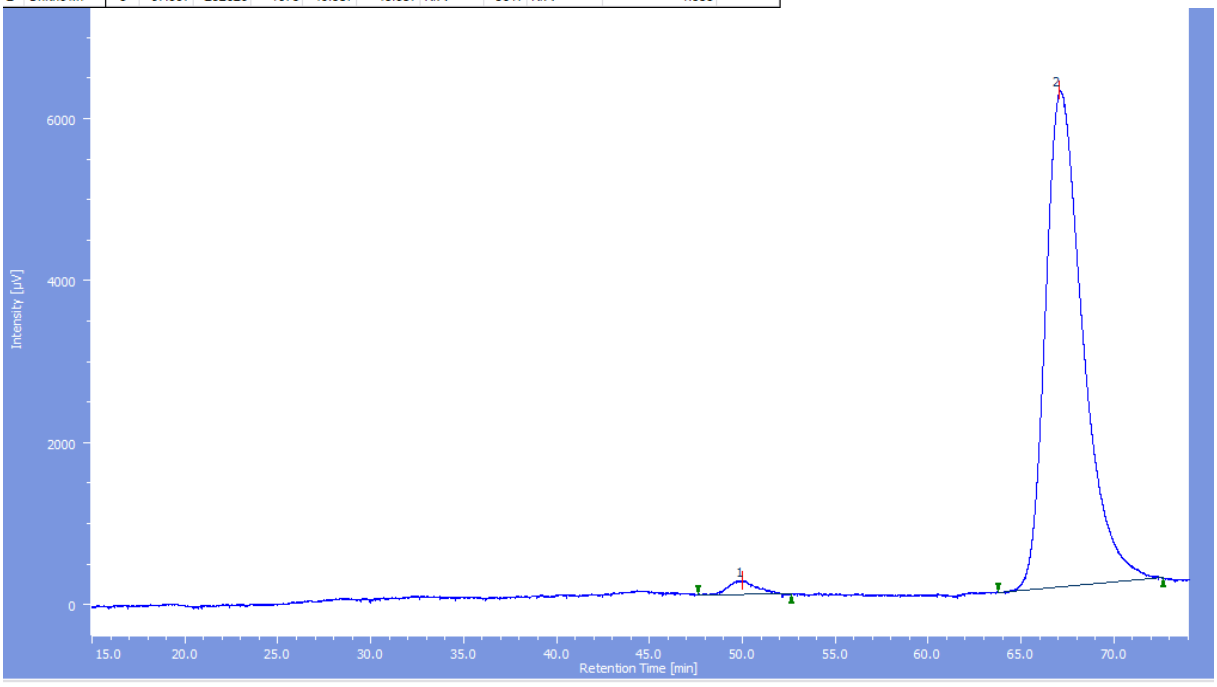


ROESY

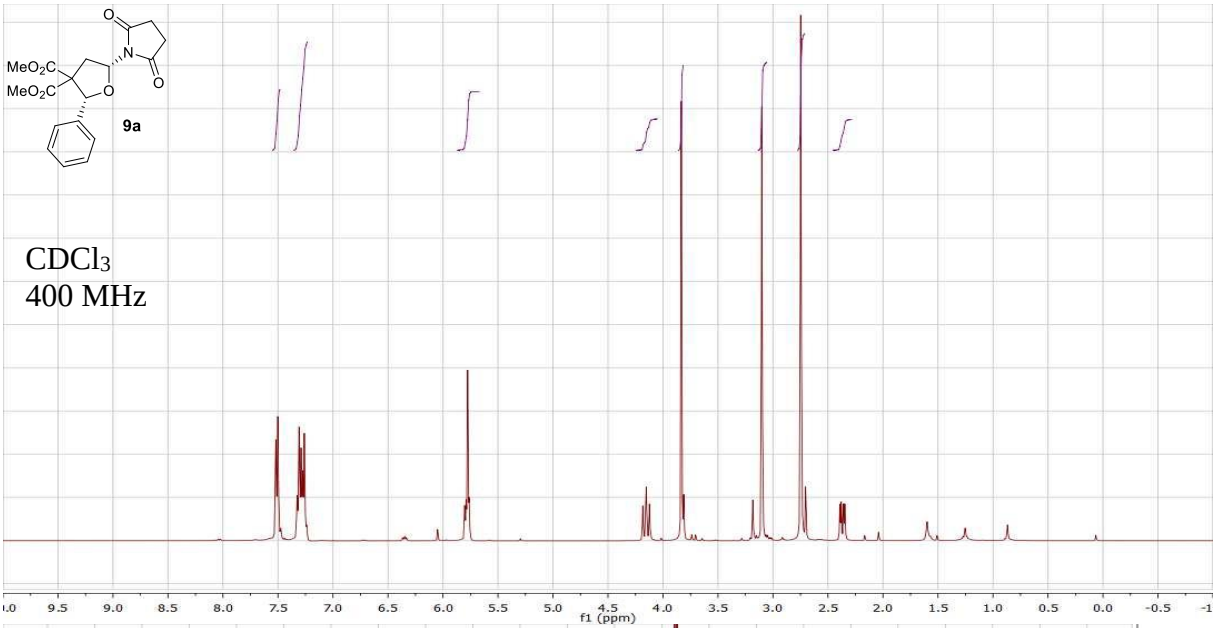


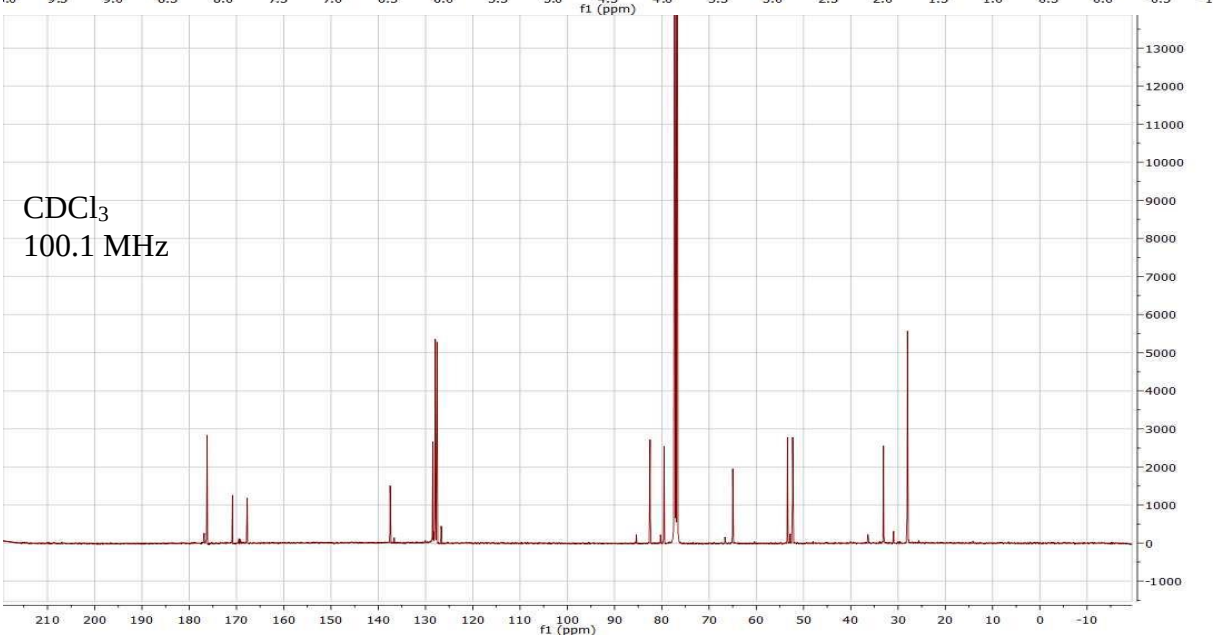


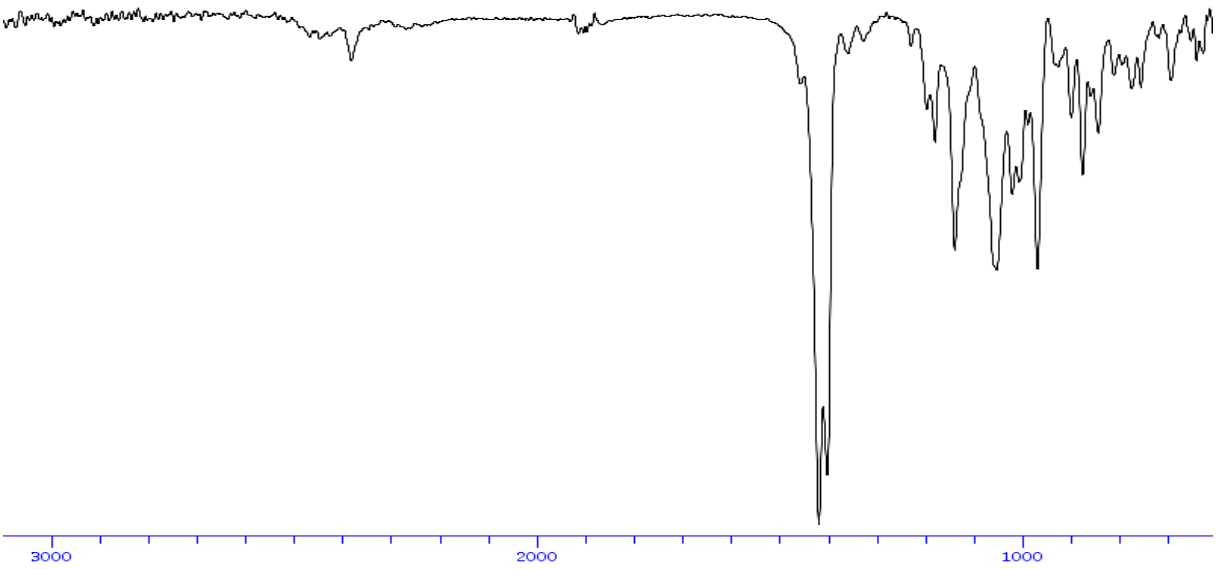
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	50.227	238399	2213	50.613	56.943	N/A	5359	5.591	1.362	
2	Unknown	3	67.997	232620	1673	49.387	43.057	N/A	5617	N/A	1.353	

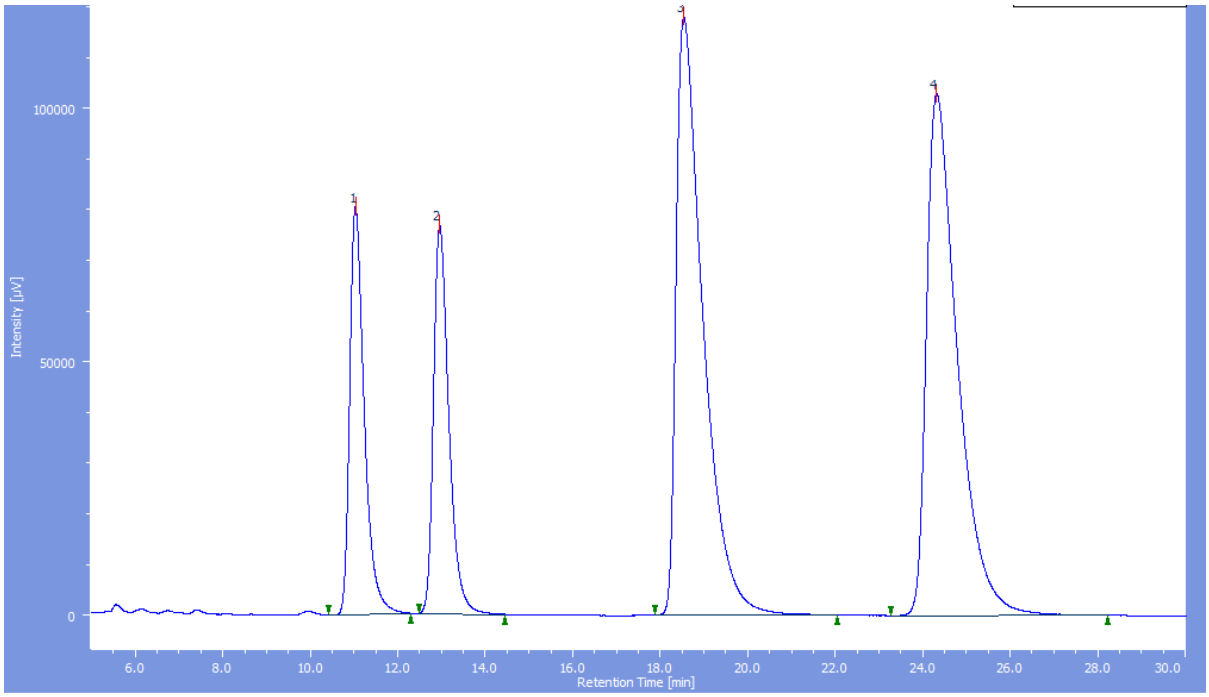


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	3	49.943	16773	165	1.925	2.631	N/A	5073	5.391	1.139	
2	Unknown	3	67.027	854577	6112	98.075	97.369	N/A	5705	N/A	1.492	

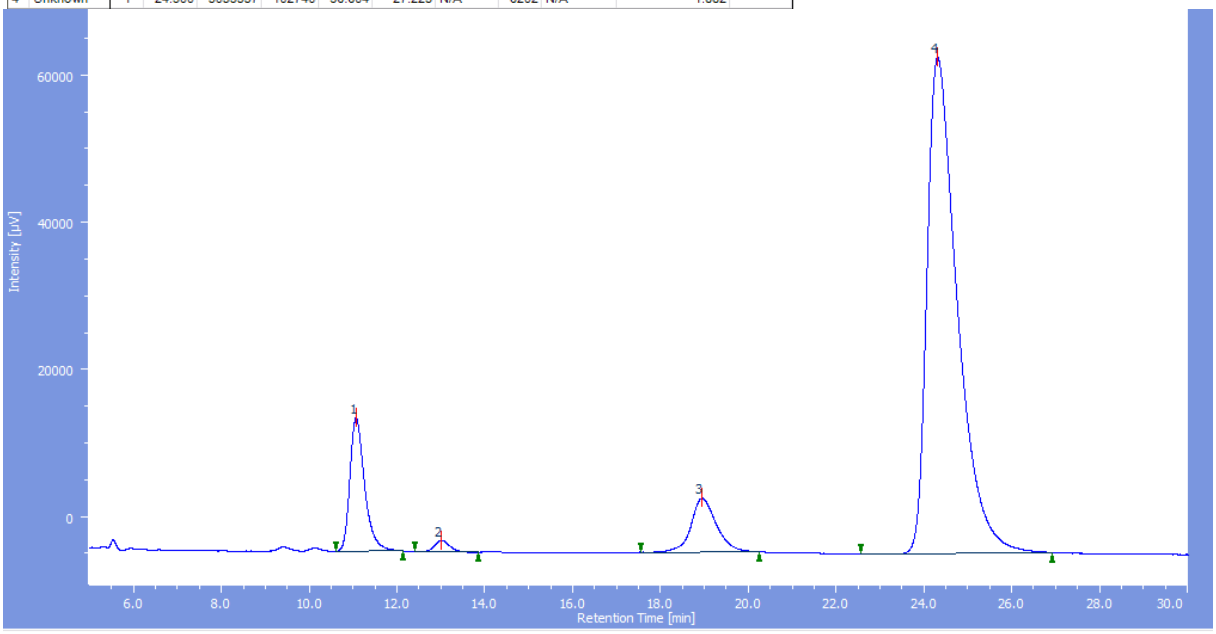

MeO2C
MeO2C
O
N
O
O
9a
CDCl3
400 MHz
f1 (ppm)


CDCl3
100.1 MHz
f1 (ppm)

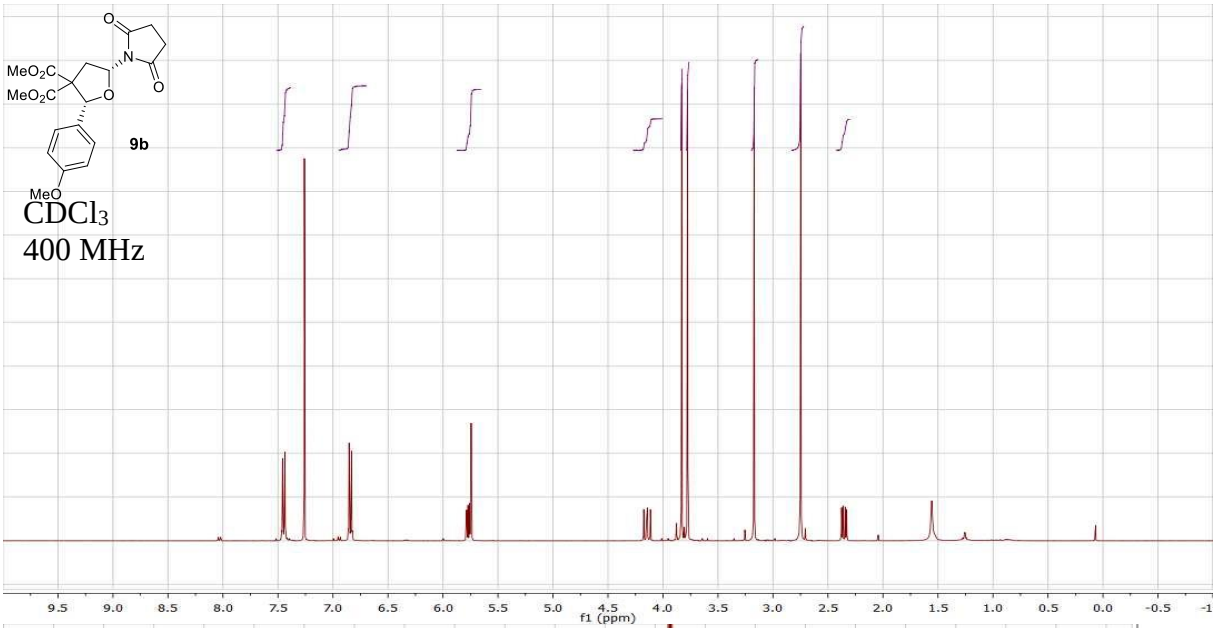

3000
2000
1000

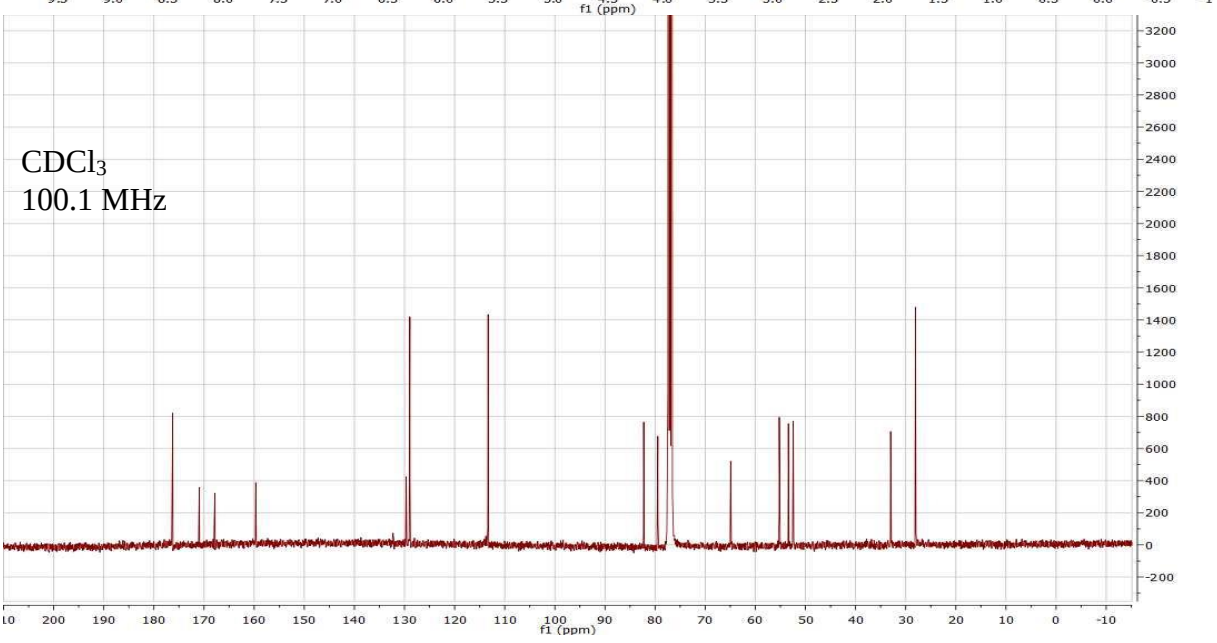


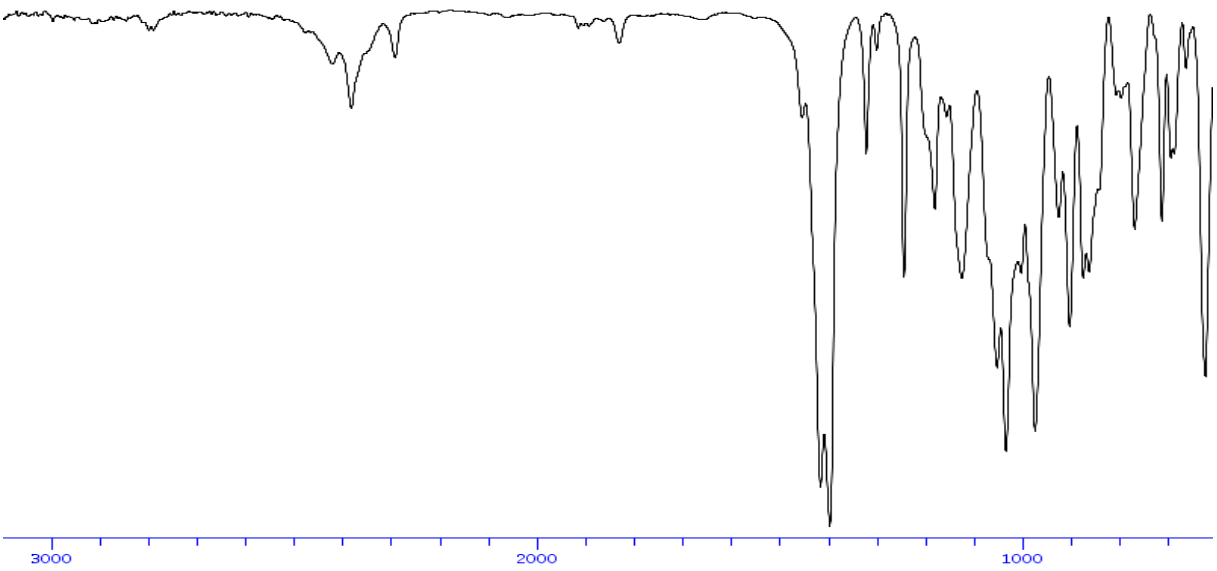
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	11.027	1855962	80274	13.443	21.271	N/A	5813	3.227	1.519	
2	Unknown	1	12.950	1859283	76498	13.467	20.271	N/A	7057	6.635	1.428	
3	Unknown	1	18.527	5037285	117867	36.486	31.233	N/A	4807	5.027	2.254	
4	Unknown	1	24.300	5053557	102740	36.604	27.225	N/A	6202	N/A	1.882	

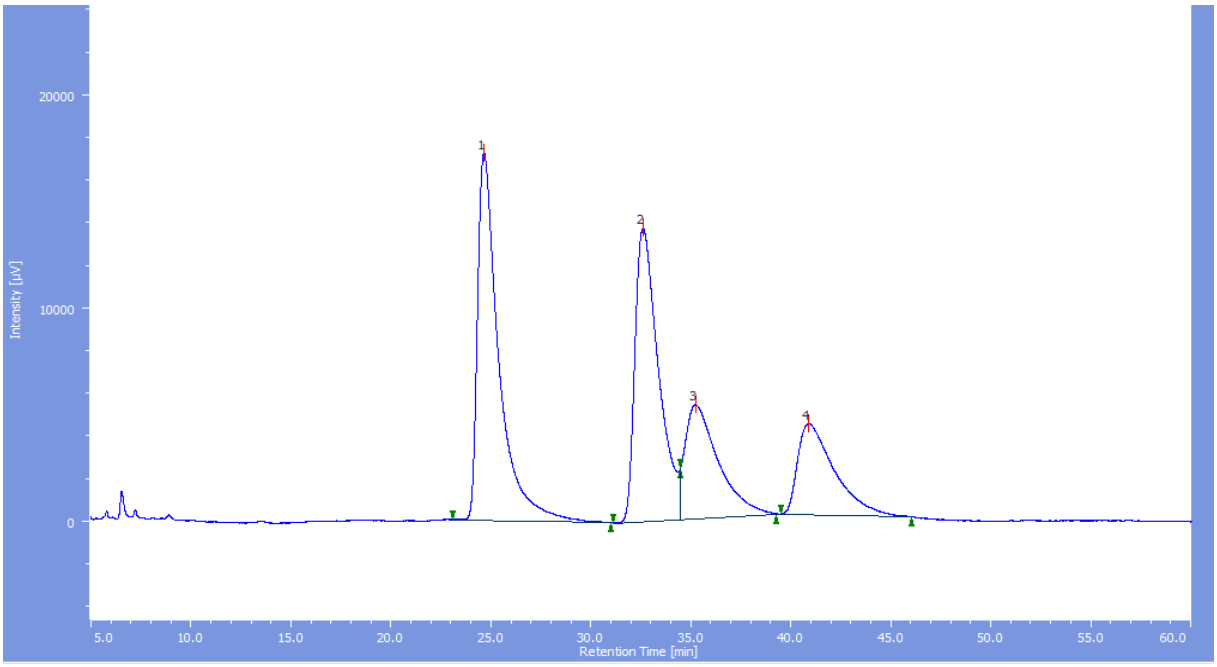


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	11.063	422957	18100	10.645	19.213	N/A	5701	3.276	1.390	
2	Unknown	1	13.007	35254	1537	0.887	1.632	N/A	7430	7.438	1.192	
3	Unknown	1	18.937	293798	7281	7.394	7.729	N/A	5794	4.873	1.111	
4	Unknown	1	24.293	3221193	67290	81.073	71.427	N/A	6460	N/A	1.722	

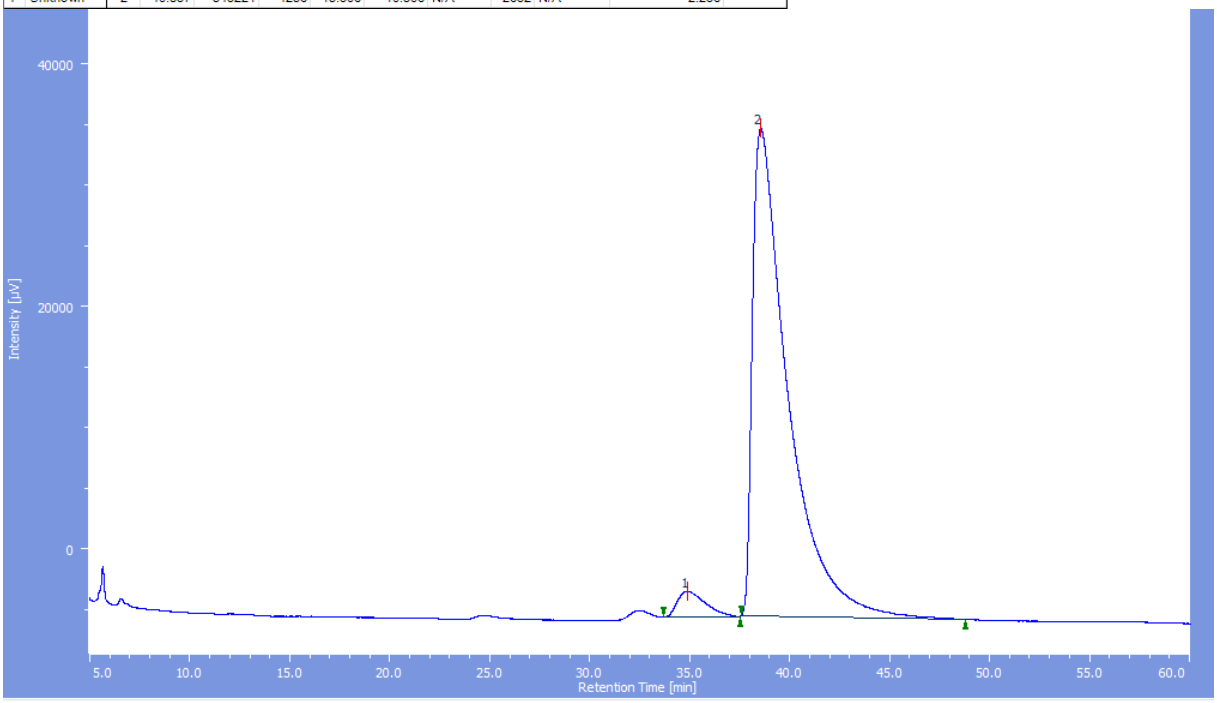

MeO2C
MeO2C
O
N
O
O
MeO
9b
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


CDCl3
100.1 MHz
3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

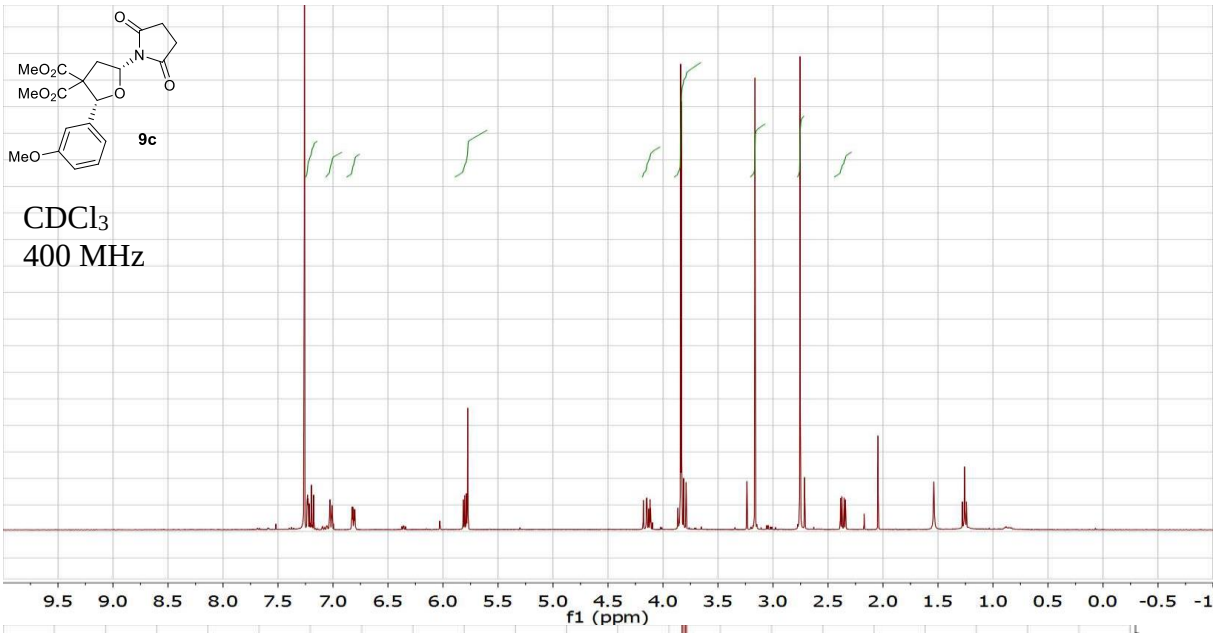

3000
2000
1000

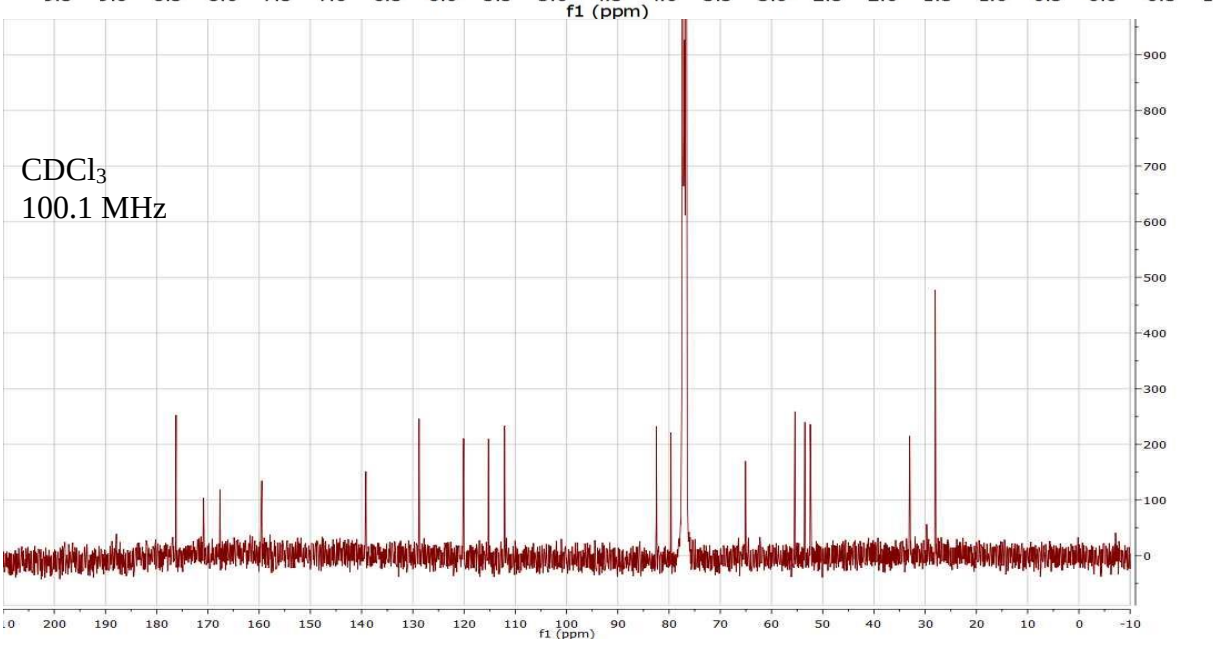


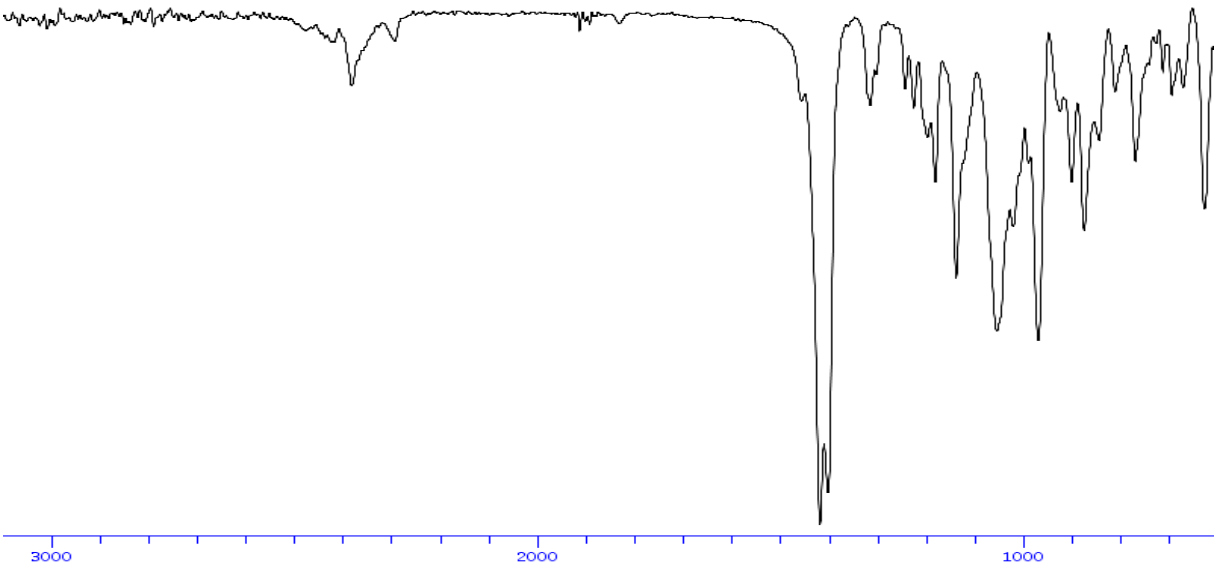
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	24.637	1269238	17192	35.763	42.441	N/A	3385	4.188	2.388	
2	Unknown	2	32.573	1123447	13735	31.655	33.907	N/A	3824	1.024	N/A	
3	Unknown	2	35.207	613163	5325	17.277	13.146	N/A	2130	1.811	N/A	
4	Unknown	2	40.837	543221	4256	15.306	10.506	N/A	2632	N/A	2.236	

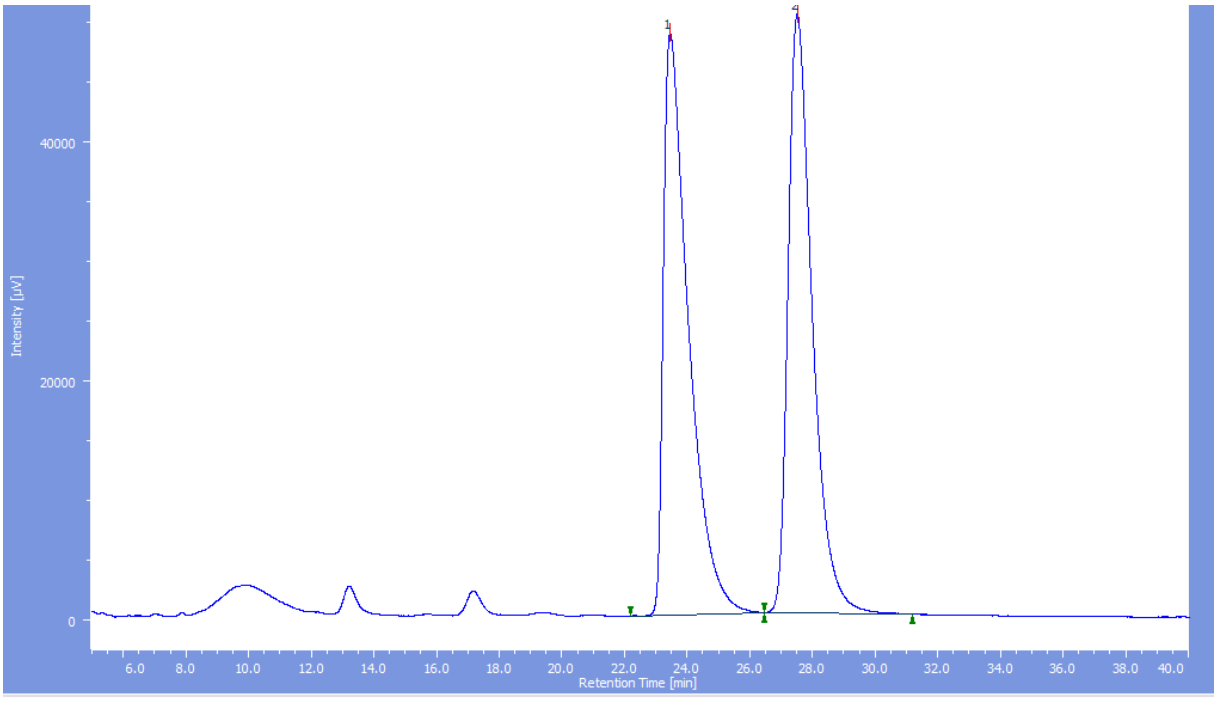


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	2	34.850	205375	2118	3.991	5.011	N/A	2836	1.339	1.611	
2	Unknown	2	38.533	4940943	40143	96.009	94.989	N/A	2828	N/A	3.228	

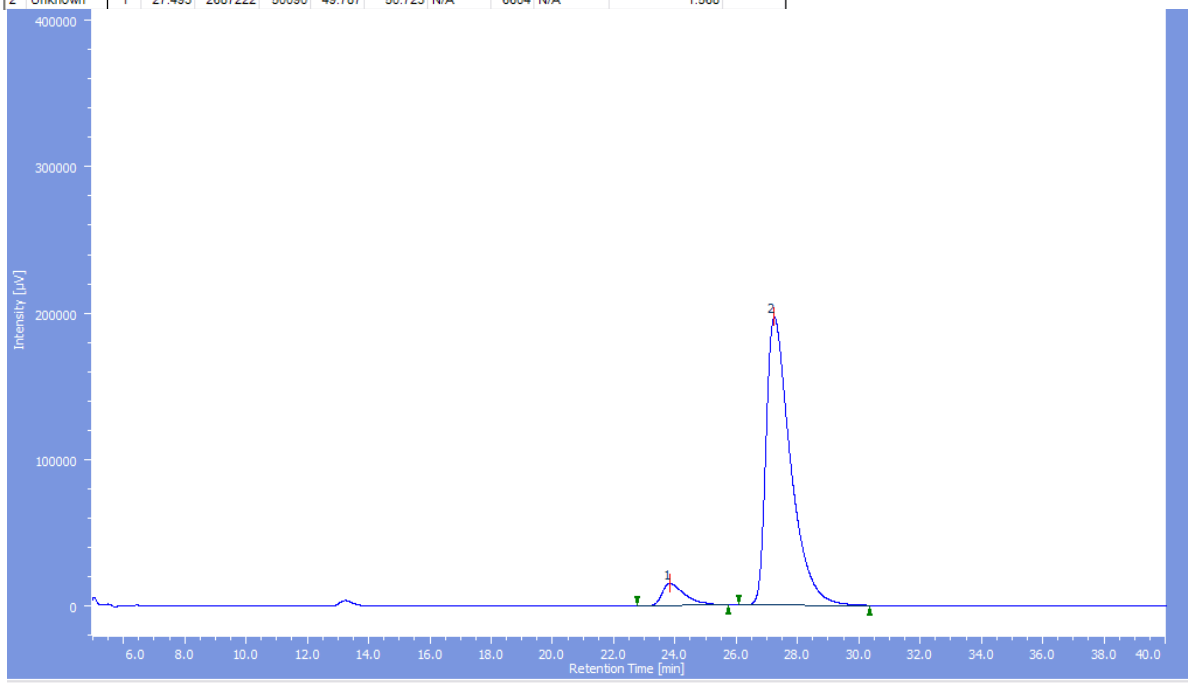

MeO2C
MeO2C
MeO
9c
CDCl3
400 MHz
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


CDCl3
100.1 MHz
900 800 700 600 500 400 300 200 100 0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

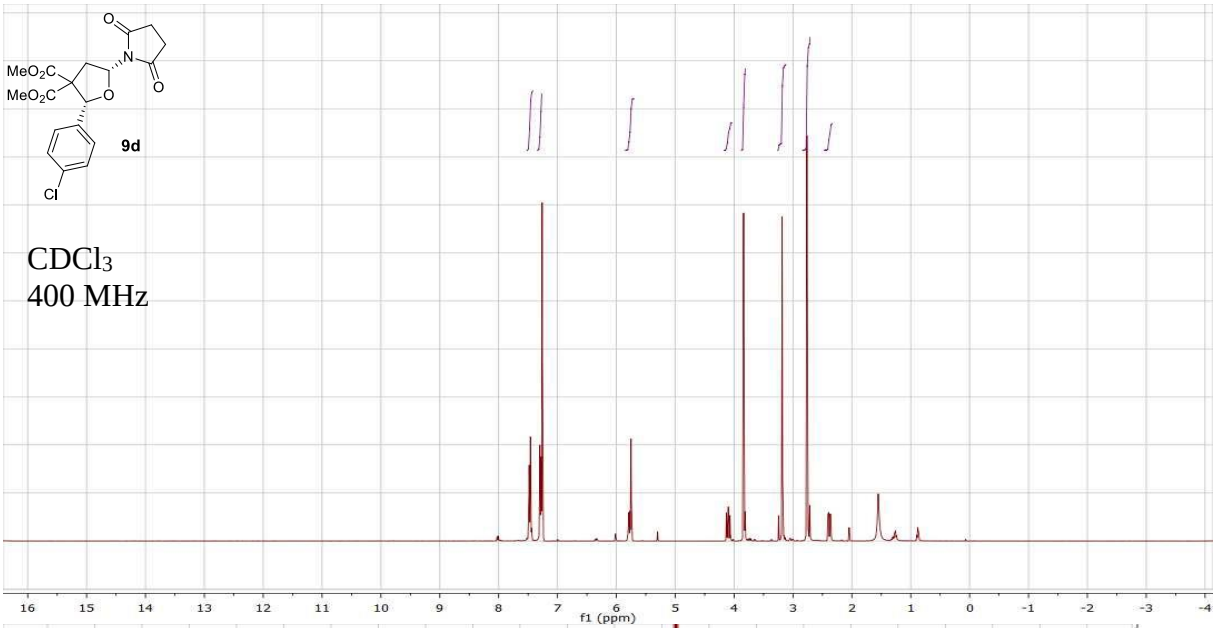

3000
2000
1000

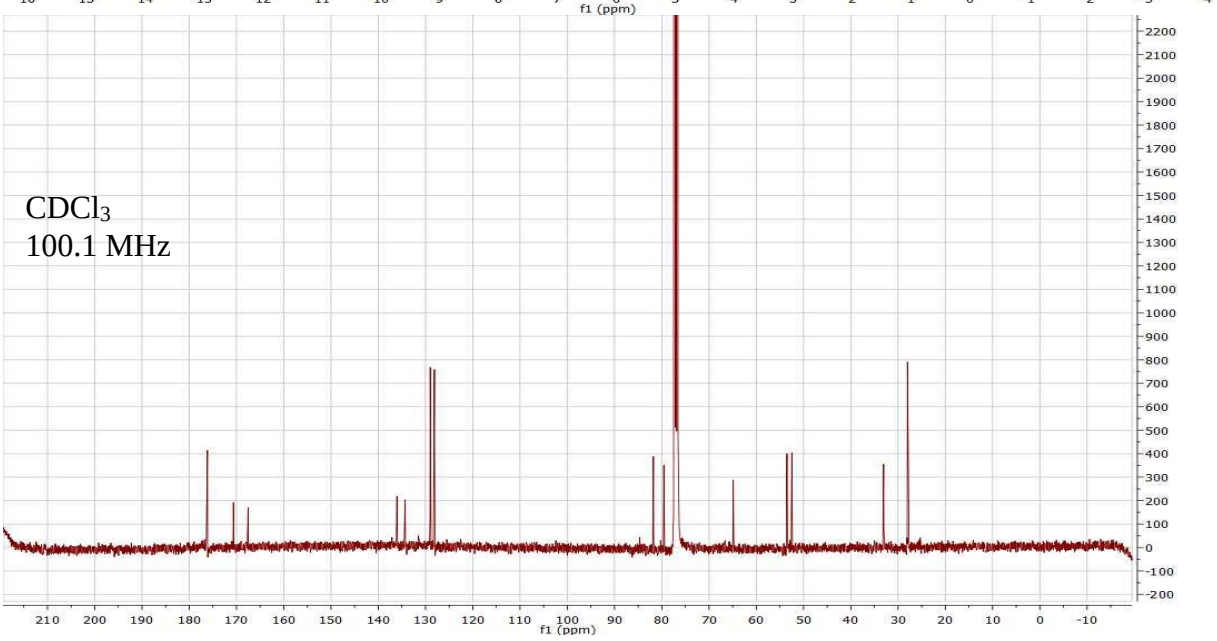


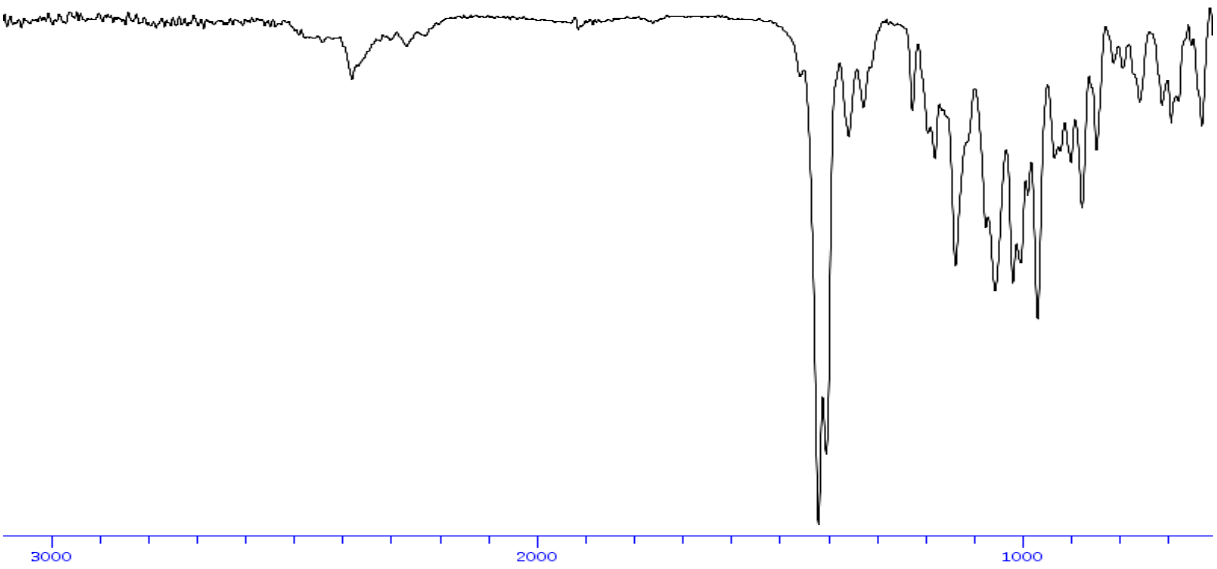
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	23.440	2710250	48661	50.213	49.277	N/A	4512	2.957	2.431	
2	Unknown	1	27.493	2687222	50090	49.787	50.723	N/A	6604	N/A	1.568	

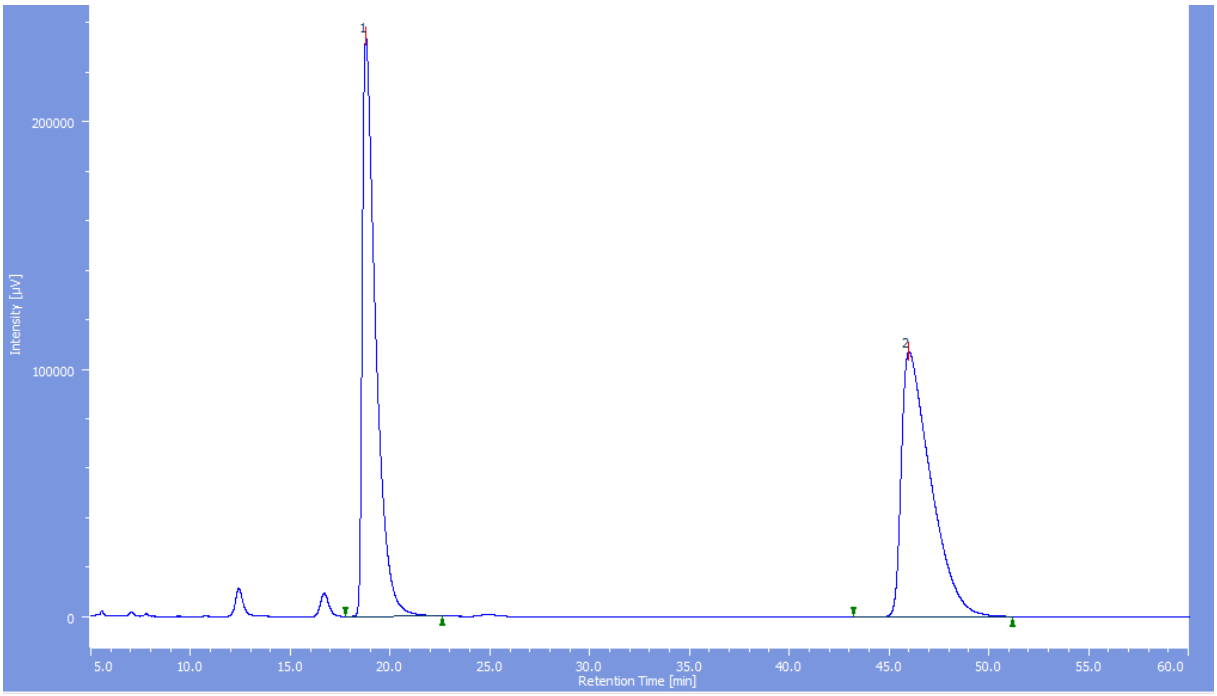


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	23.817	801970	15066	6.893	7.123	N/A	5145	2.510	1.812	
2	Unknown	1	27.220	10831934	196451	93.107	92.877	N/A	6130	N/A	1.838	

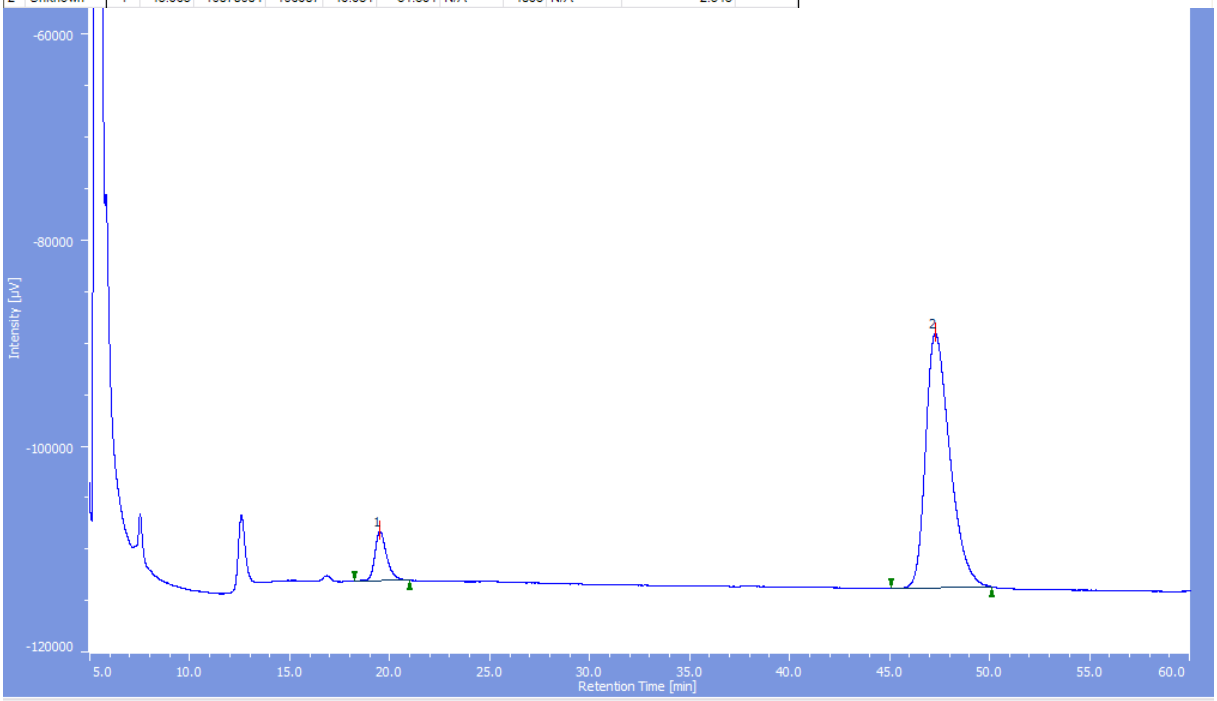

MeO2C
MeO2C
O
N
O
O
Cl
9d
CDCl3
400 MHz
f1 (ppm)


CDCl3
100.1 MHz
f1 (ppm)

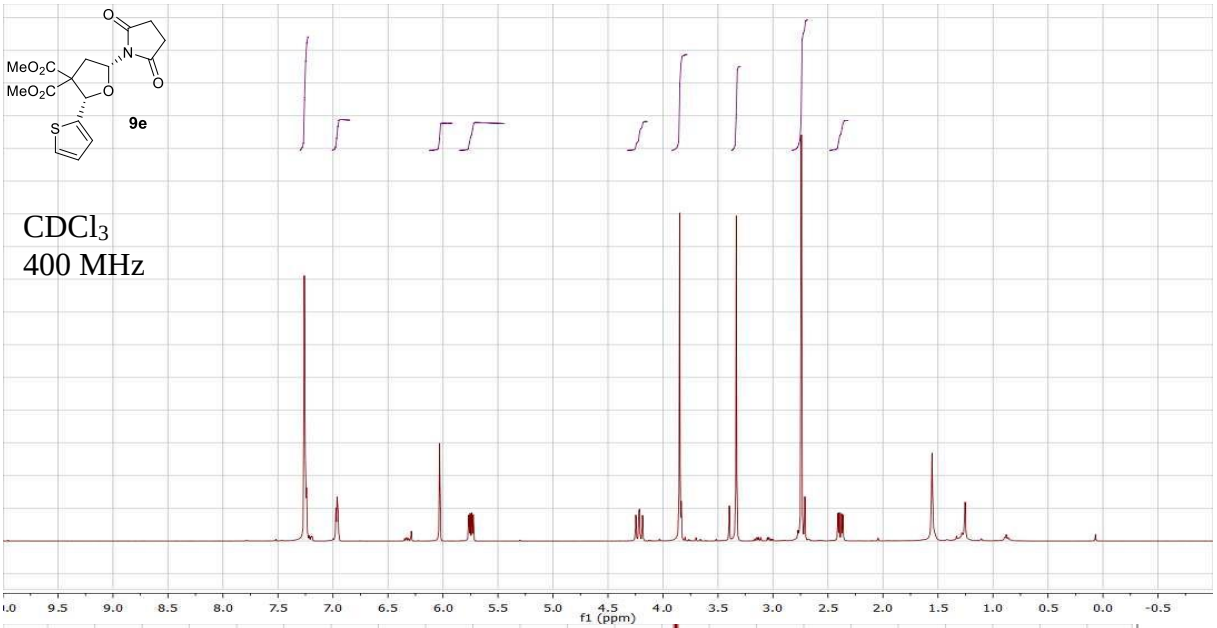

3000
2000
1000

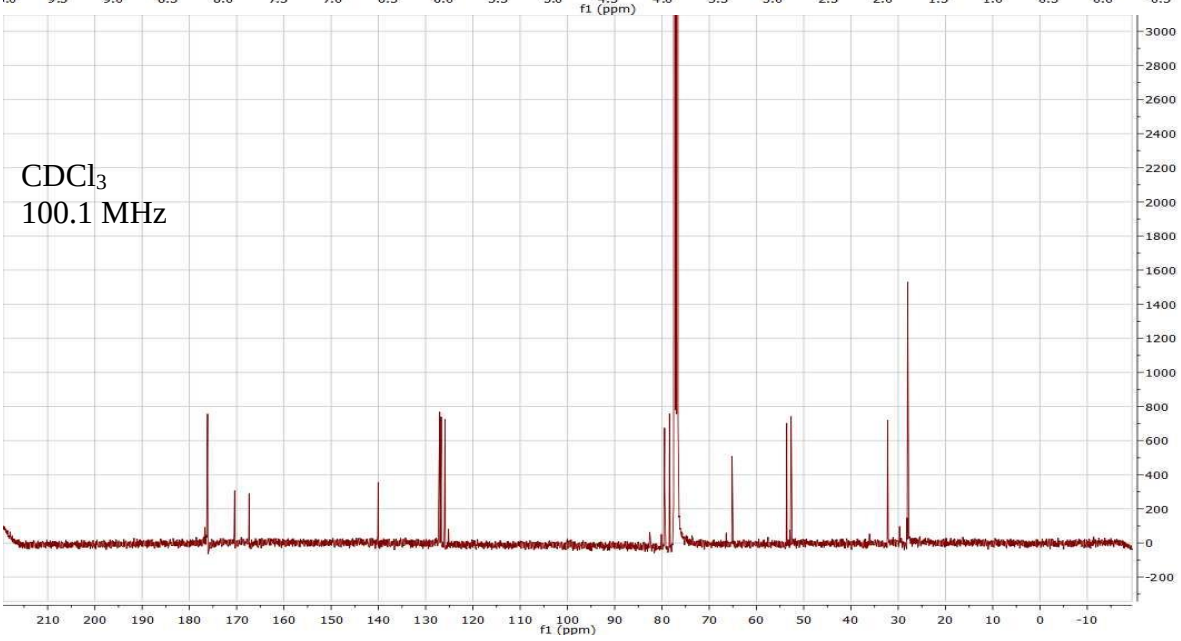


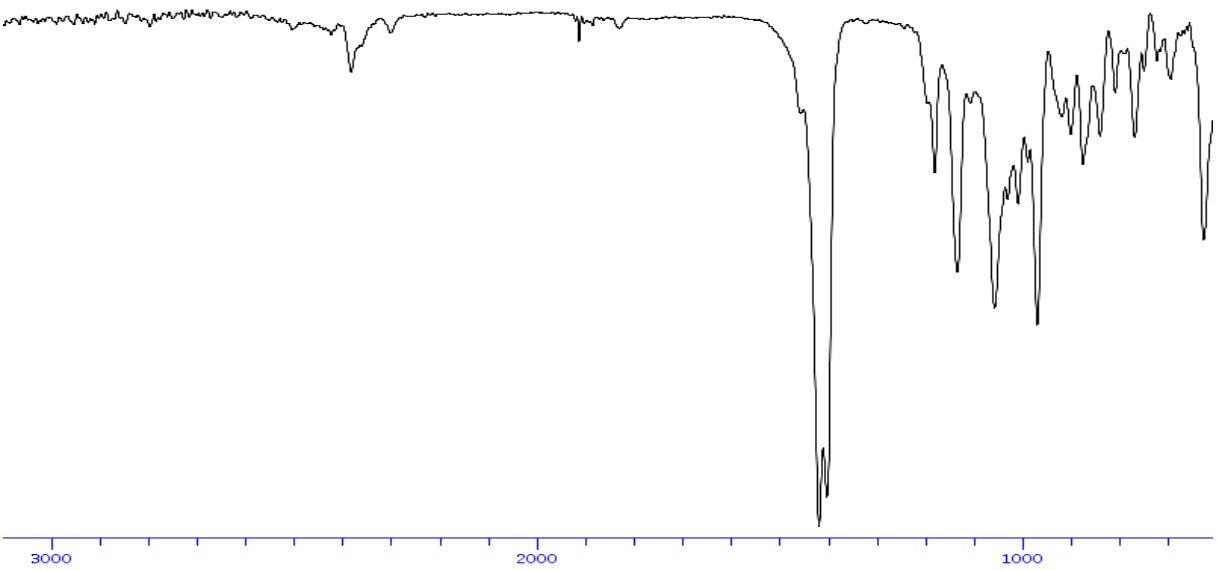
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	18.770	10899246	233837	50.049	68.609	N/A	4202	14.402	2.497	
2	Unknown	1	45.963	10878084	106987	49.951	31.391	N/A	4893	N/A	2.343	

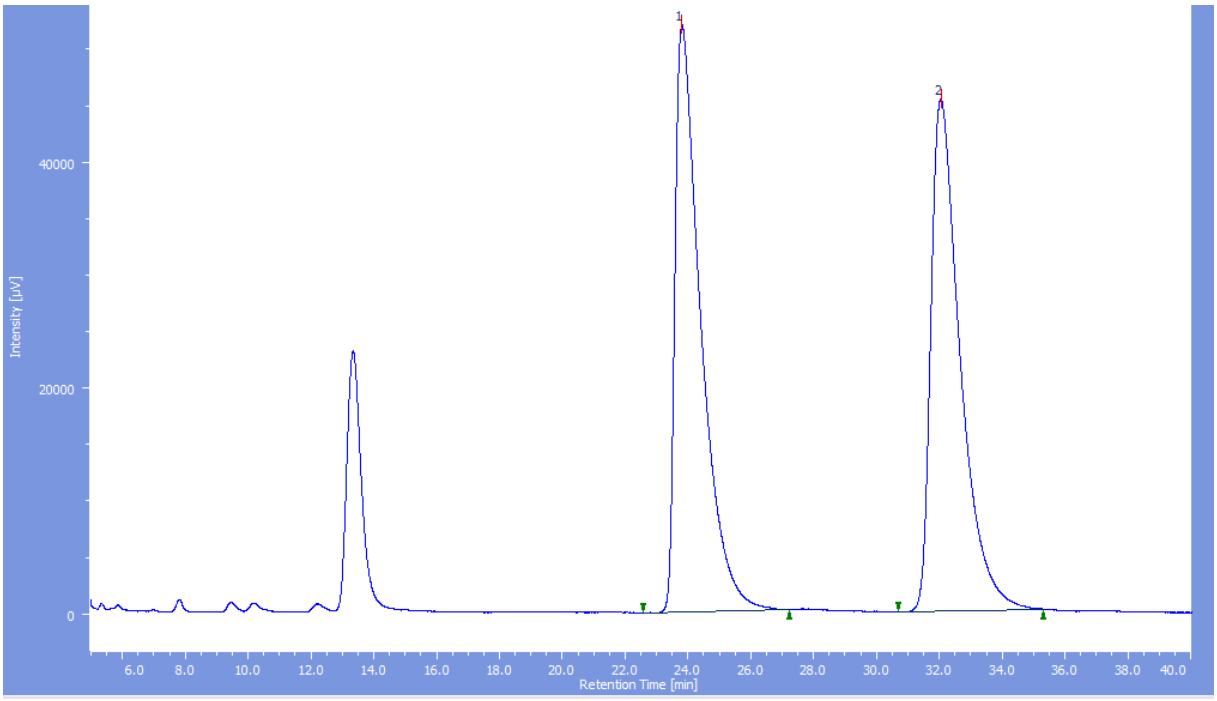


#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	19.487	199549	4809	8.771	16.309	N/A	5746	17.365	1.335	
2	Unknown	1	47.250	2075445	24679	91.229	83.691	N/A	7532	N/A	1.392	

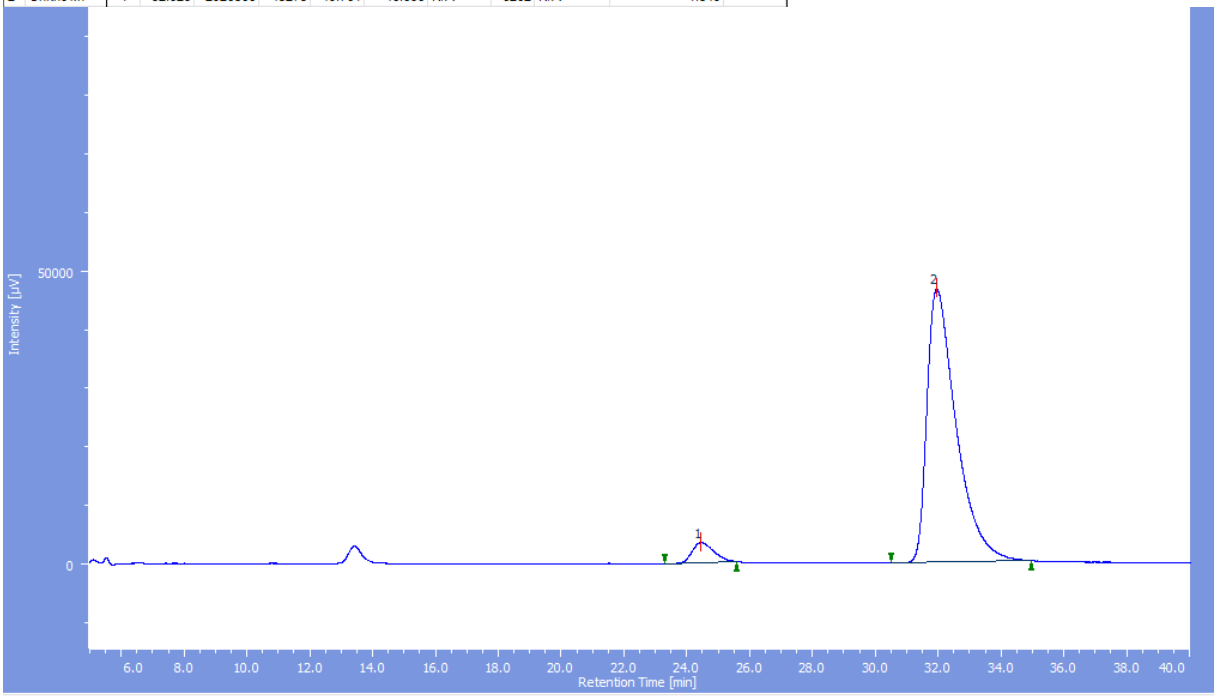

MeO2C
MeO2C
O
N
O
O
S
9e
CDCl3
400 MHz
f1 (ppm)


CDCl3
100.1 MHz
f1 (ppm)

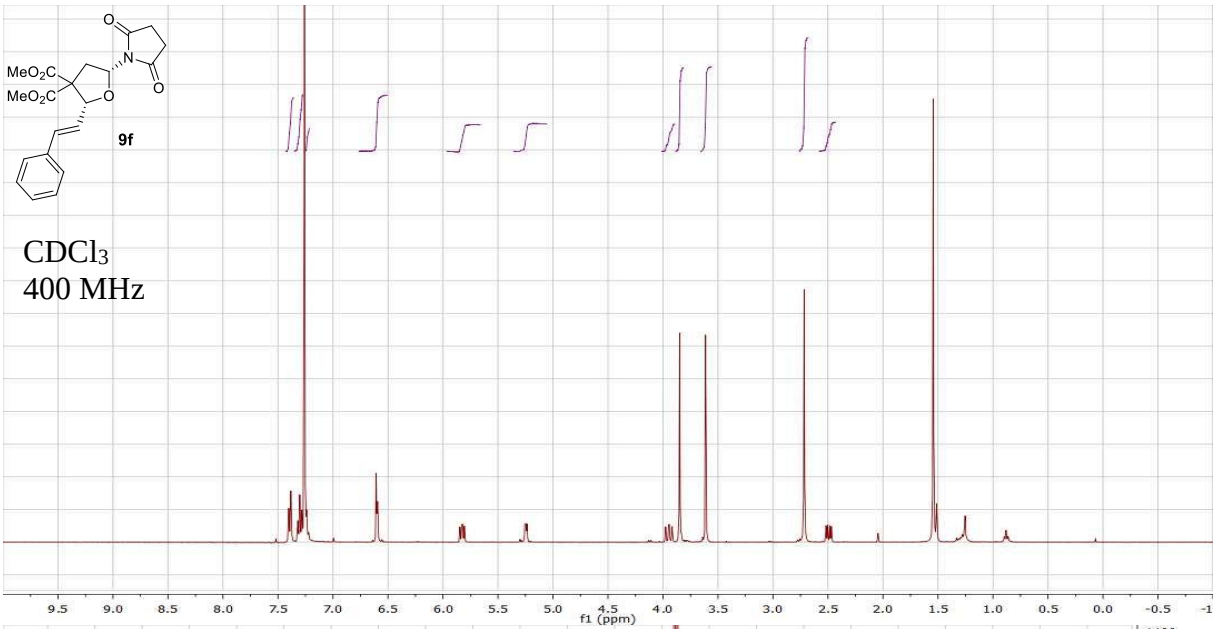

3000
2000
1000

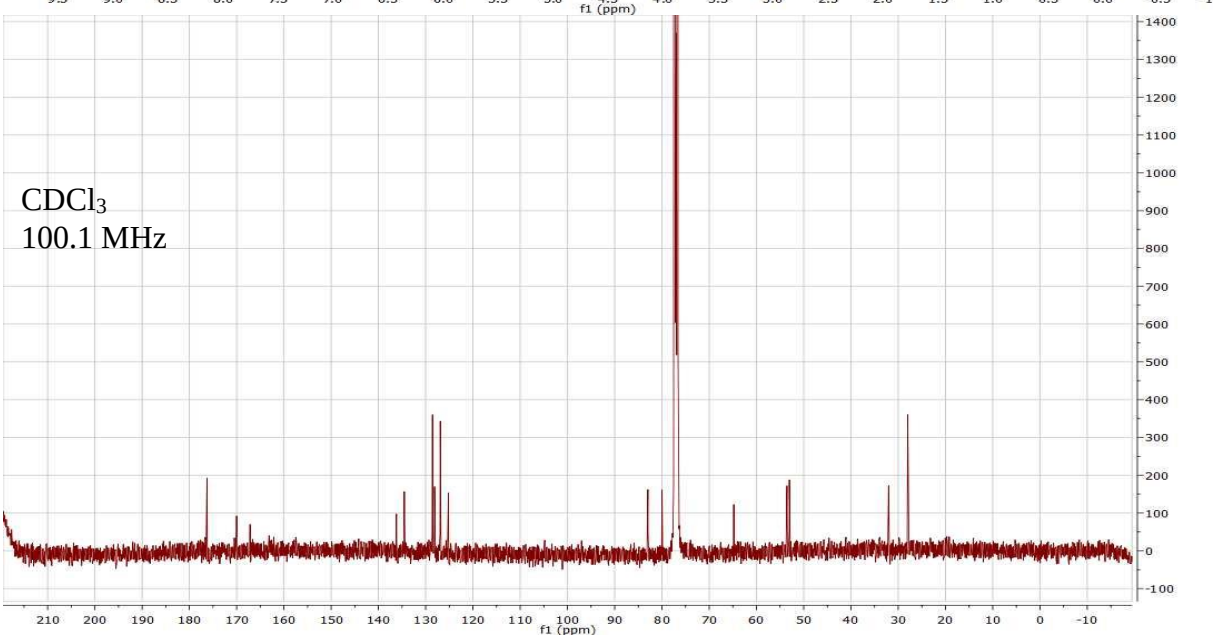


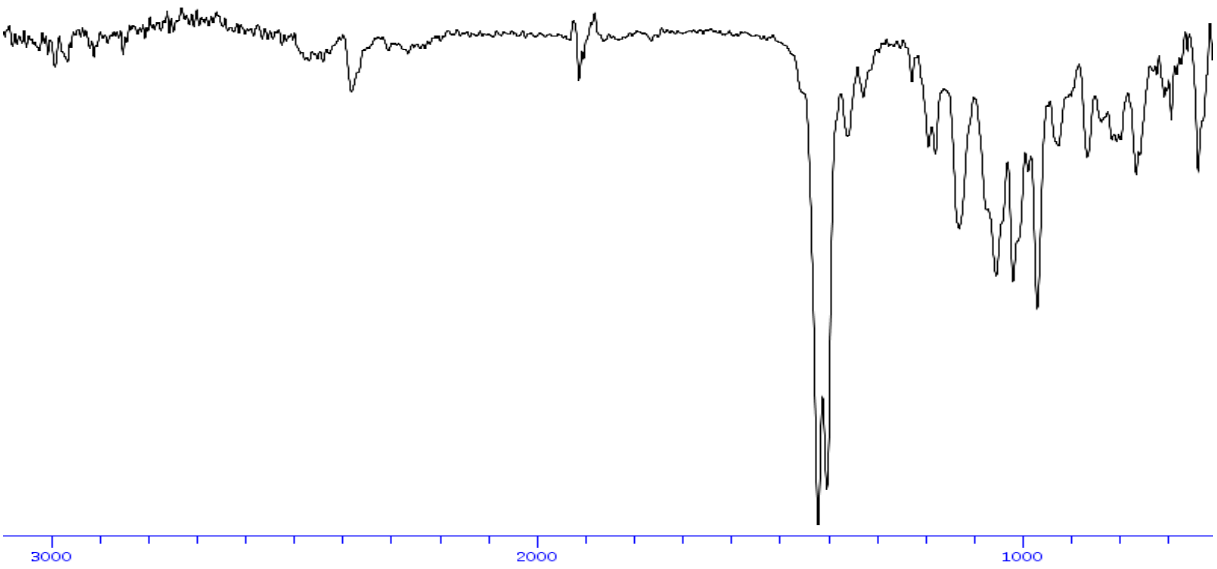
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	23.793	2954924	51868	50.239	53.394	N/A	4473	5.426	2.417	
2	Unknown	1	32.023	2926866	45275	49.761	46.606	N/A	6262	N/A	1.849	



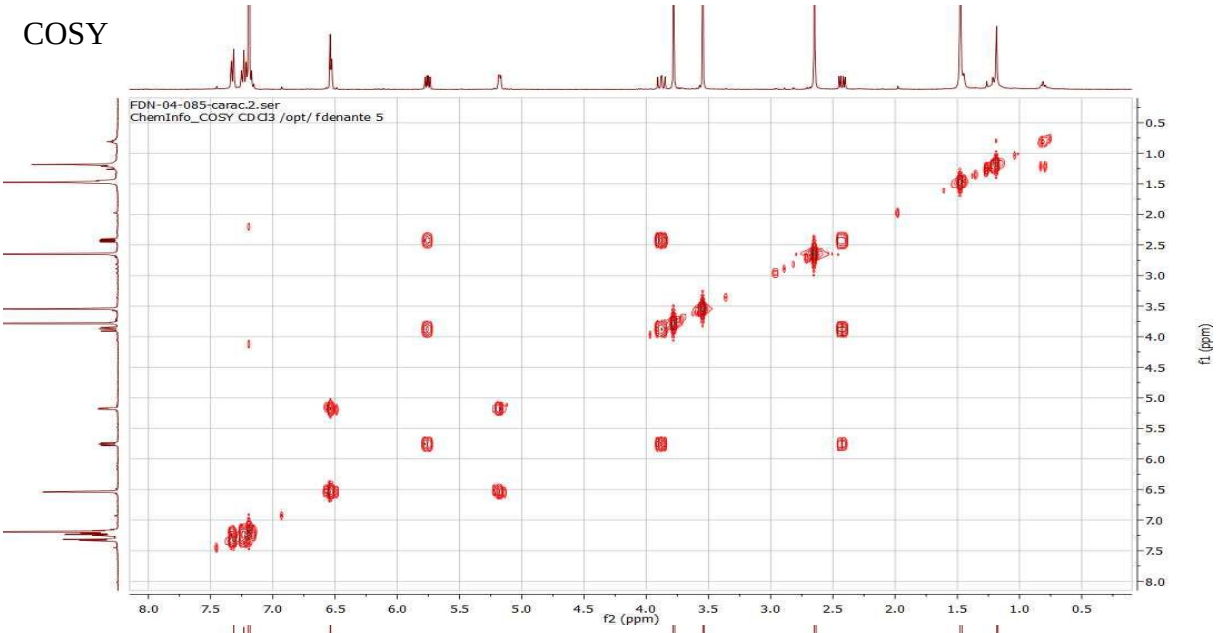
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	24.440	163597	3410	5.152	6.812	N/A	5898	5.191	1.332	
2	Unknown	1	31.937	3011808	46651	94.848	93.188	N/A	6193	N/A	1.839	


MeO2C
MeO2C
O
N
O
O
9f
CDCl3
400 MHz
f1 (ppm)

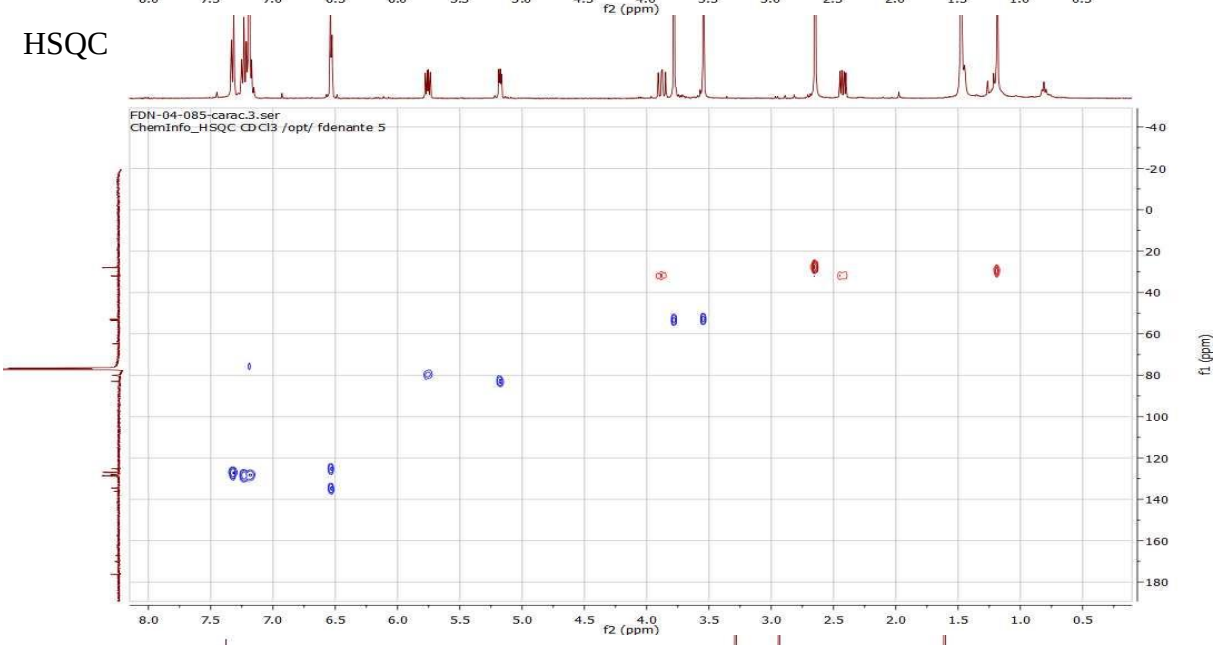

CDCl3
100.1 MHz
f1 (ppm)


3000
2000
1000

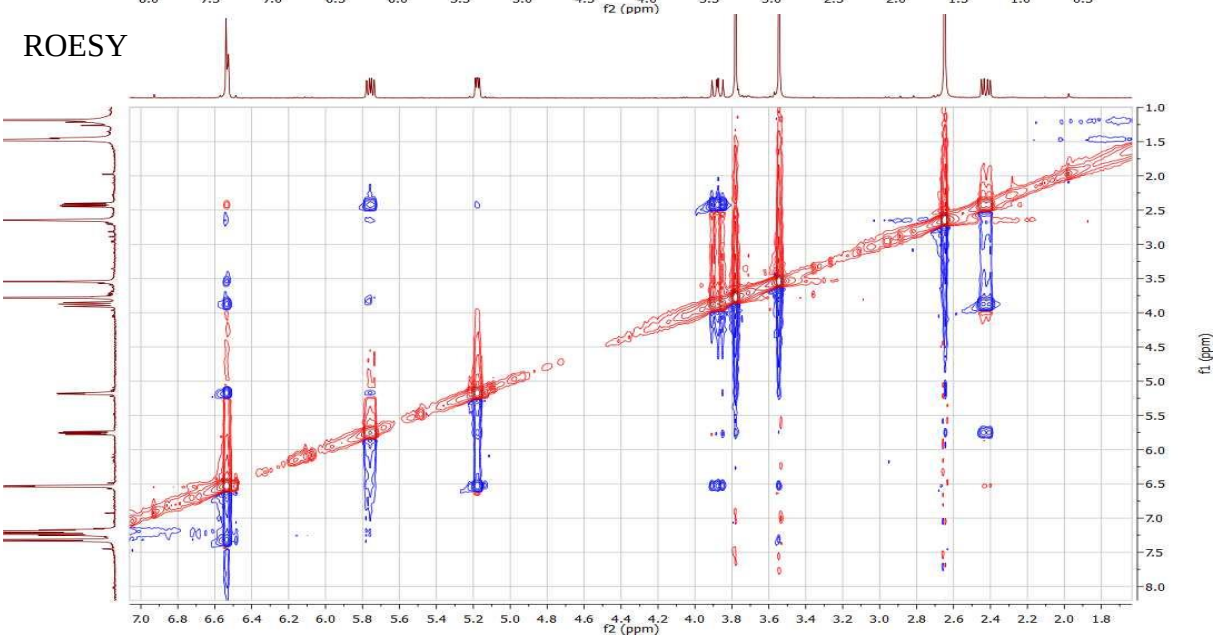
COSY

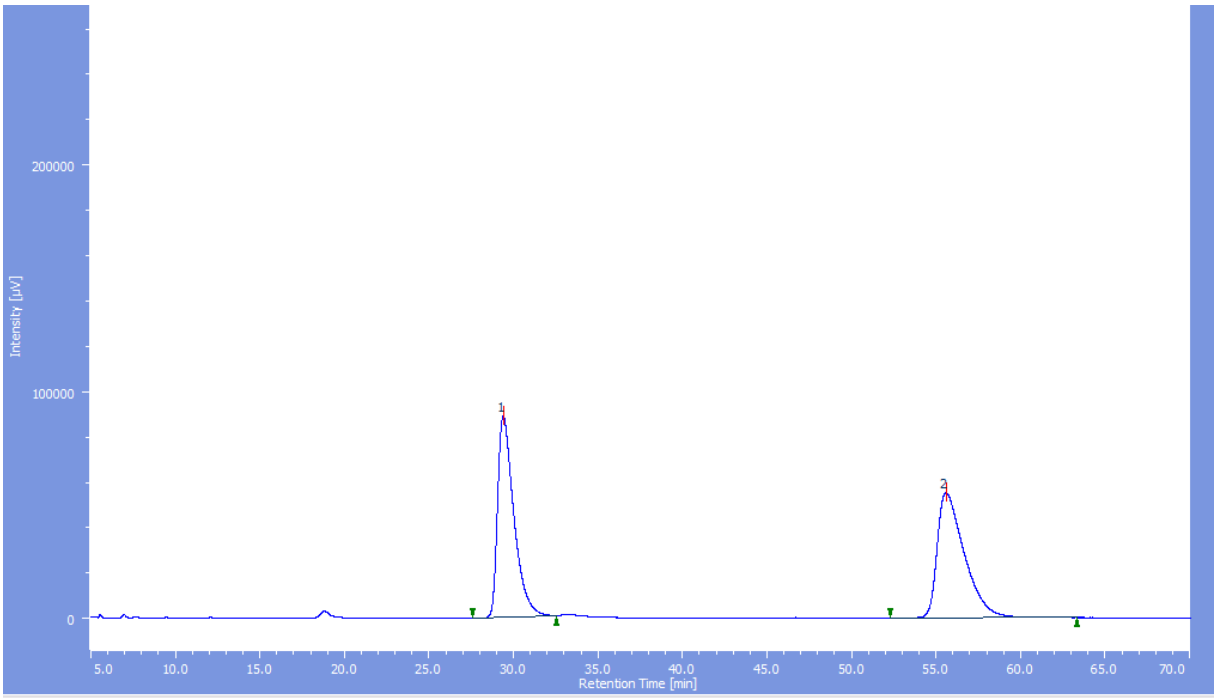


HSQC

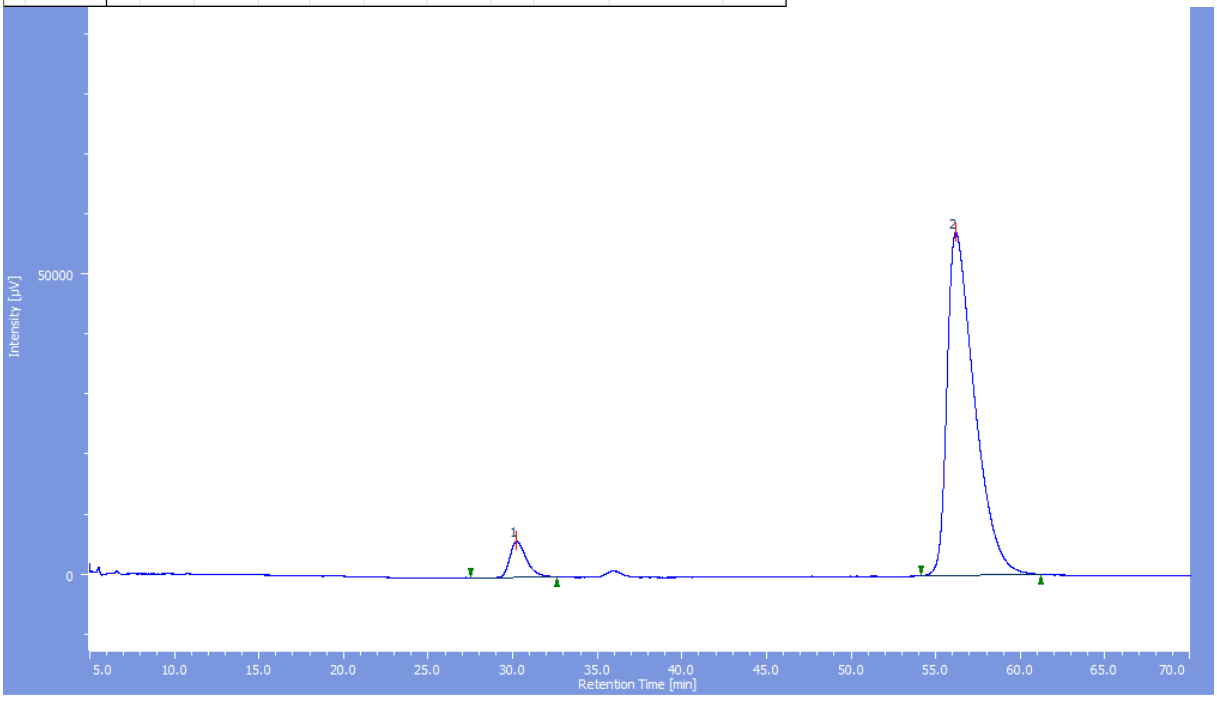


ROESY

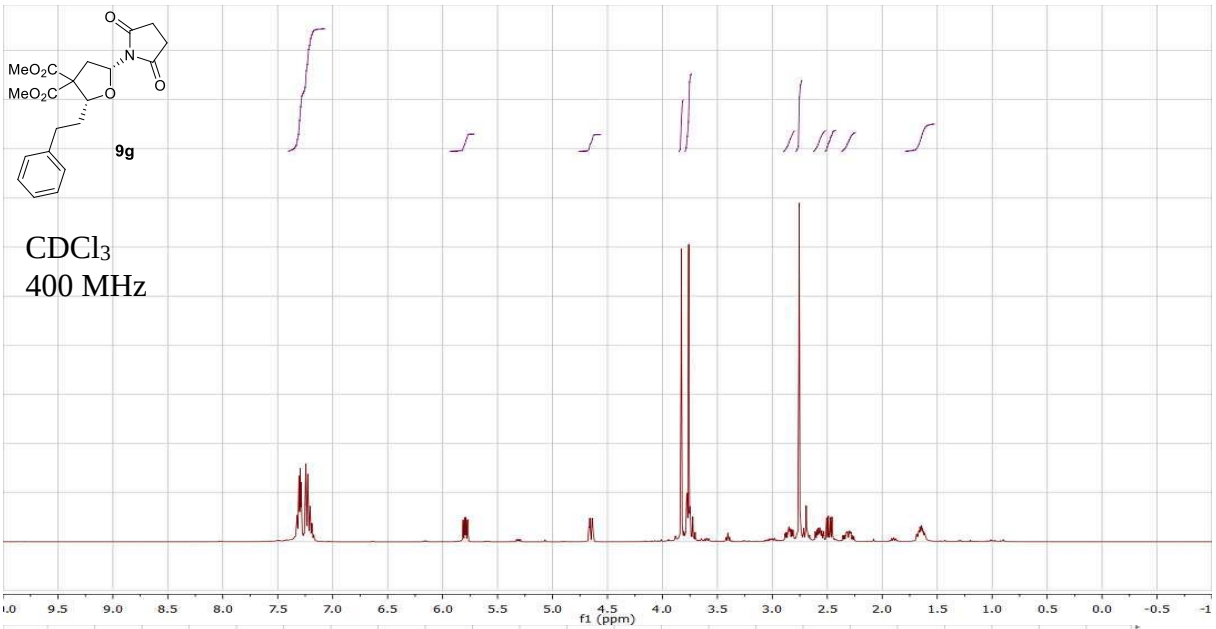


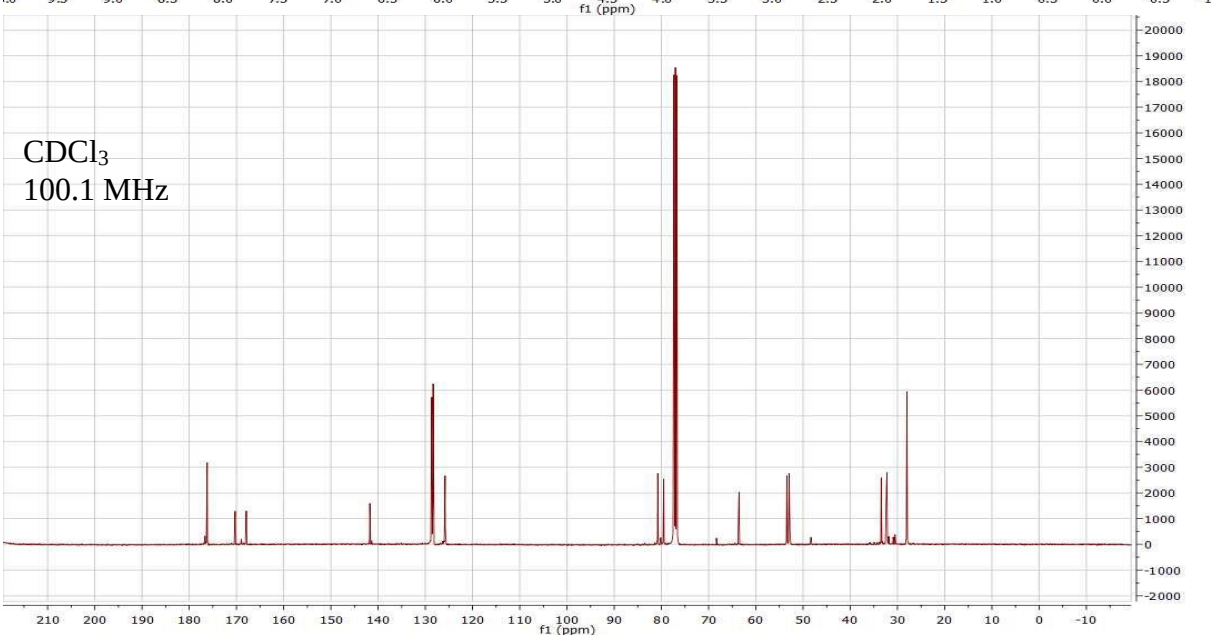


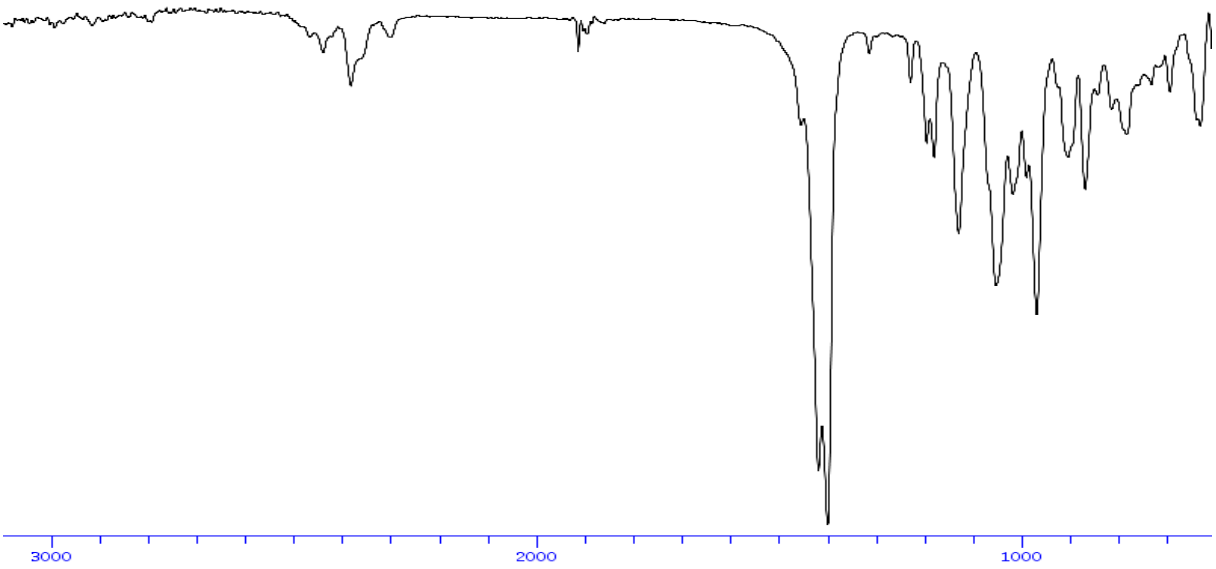
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	29.370	5899150	88363	49.004	61.571	N/A	4789	11.550	1.773	
2	Unknown	1	55.537	6138926	55151	50.996	38.429	N/A	6095	N/A	1.817	



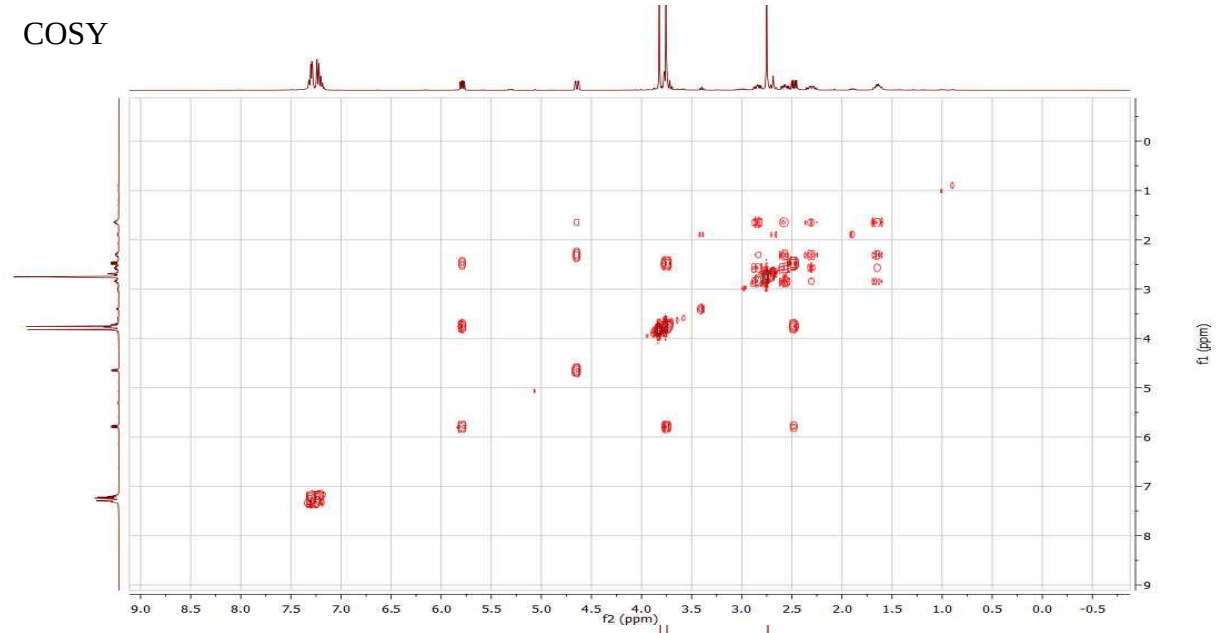
#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	30.197	403999	6029	5.932	9.564	N/A	5000	11.318	1.410	
2	Unknown	1	56.130	6406274	57012	94.068	90.436	N/A	6050	N/A	1.828	


MeO2C
MeO2C
O
N
O
O
9g
CDCl3
400 MHz
f1 (ppm)

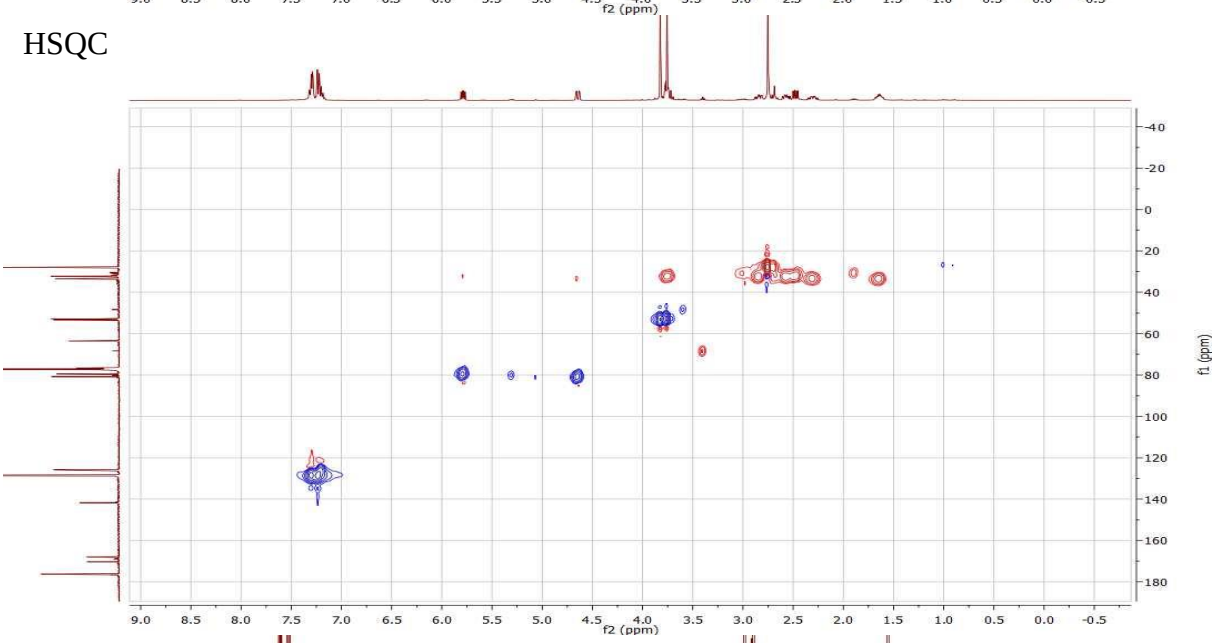

CDCl3
100.1 MHz
f1 (ppm)


3000
2000
1000

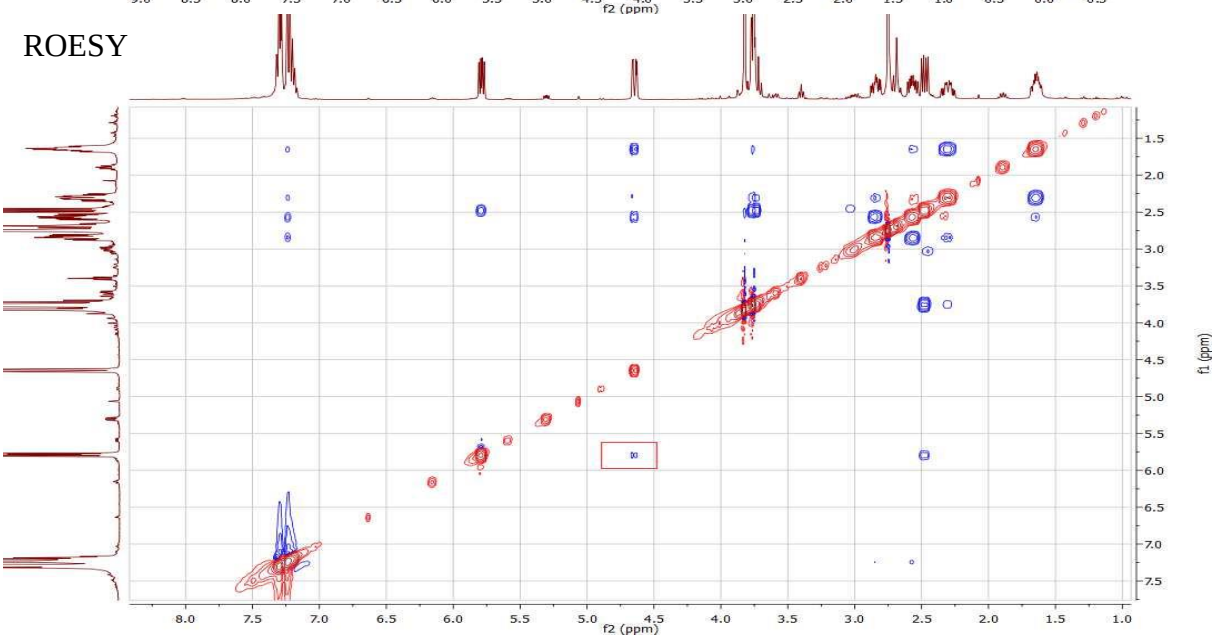
COSY

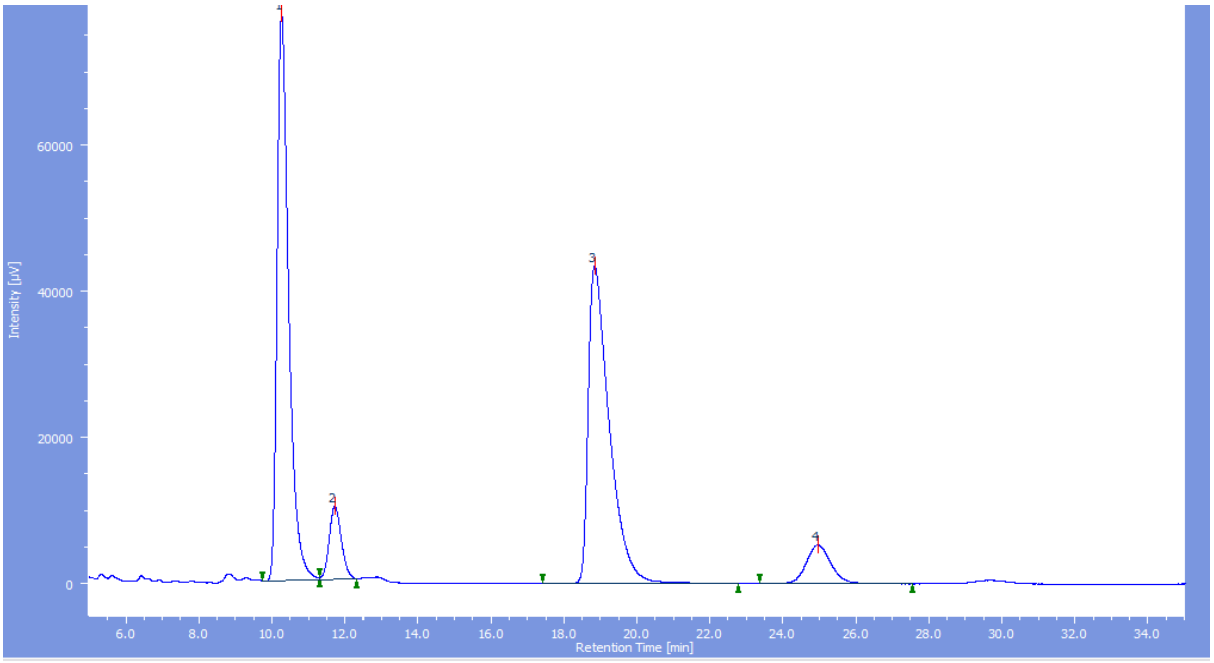


HSQC

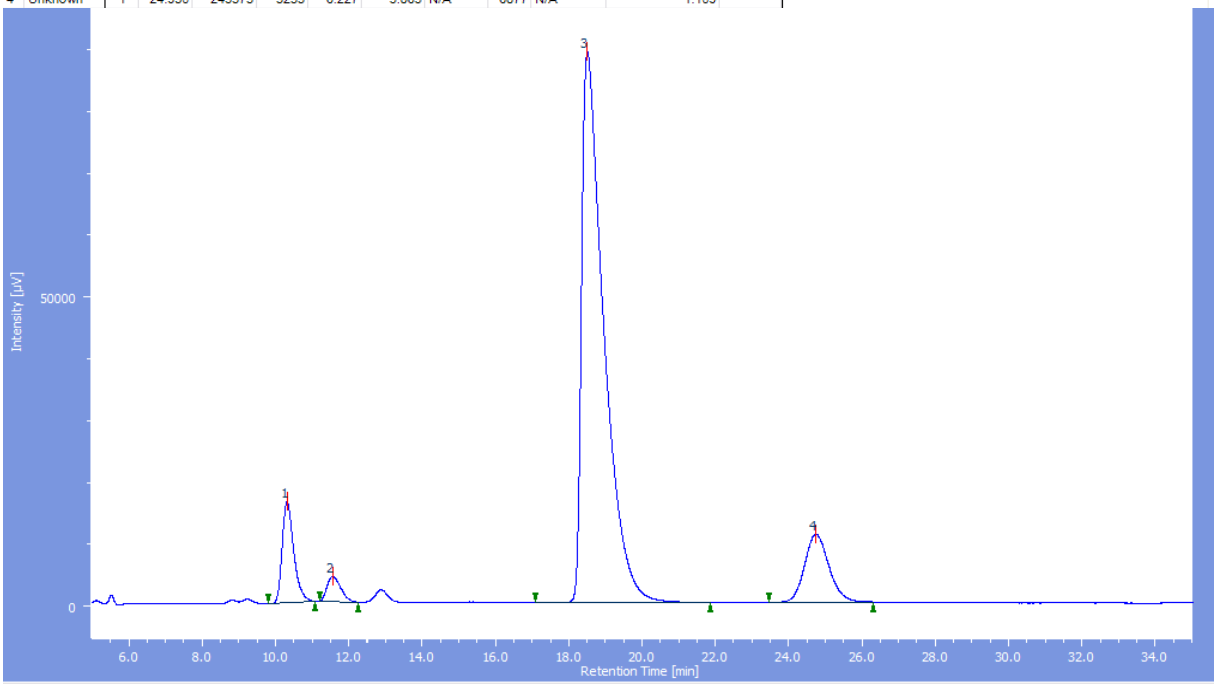


ROESY





#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	10.260	1706133	77391	43.615	56.892	N/A	5546	2.526	1.565	
2	Unknown	1	11.717	230477	9976	5.892	7.334	N/A	5995	8.872	1.131	
3	Unknown	1	18.827	1731603	43411	44.266	31.912	N/A	5650	5.568	2.066	
4	Unknown	1	24.950	243575	5255	6.227	3.863	N/A	6877	N/A	1.109	



#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	10.310	359218	16311	7.653	13.558	N/A	5437	1.968	1.393	
2	Unknown	1	11.550	105285	4051	2.243	3.367	N/A	4305	7.927	1.353	
3	Unknown	1	18.493	3728090	88990	79.421	73.966	N/A	4941	5.563	2.523	
4	Unknown	1	24.717	501513	10960	10.684	9.110	N/A	6891	N/A	1.163	