Iron-Catalysed [3+2] Annulation of Aminocyclopropanes with Aldehydes: Stereoselective Synthesis of Aminotetrahydrofurans

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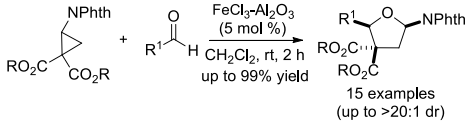
ABSTRACT



The first method for the [3+2] annulation of donor-acceptor aminocyclopropanes with aldehydes is reported. The reaction is catalyzed by iron trichloride on alumina in yields up to 99% and with excellent *cis* selectivities (up to >20:1), and represents a stereoselective and atom economic access to valuable 2-aminotetrahydrofurans, which constitute the core of DNA and RNA.

Donor-acceptor (D-A) cyclopropanes represent versatile three-carbons zwitterionic synthons,[1] and are widely used to assemble carbocycles and heterocycles by means of [3+n] annulation reactions.[2] Among them, the [3+2] reaction with olefins,[3] carbonyls[4] and imines[5] represents a valuable tool for the convergent synthesis of cyclopentanes, tetrahydrofurans[6] and pyrrolidines, respectively.

The annulation of D-A cyclopropanes with carbonyl compounds in particular has been hampered for a long time by modest diastereoselectivity and the need of stoichiometric amounts of a strong Lewis acid (*i.e.* TiX_4,

(1) For reviews on D-A cyclopropanes, see: (a) Reissig, H.-U.; Zimmer, R. *Chem. Rev* **2003**, *103*, 1151. (b) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321. (c) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev* **2007**, *107*, 3117. (d) De Simone, F.; Waser, J. *Synthesis* **2009**, *2009*, 3353. Theoretical study: (e) Schneider, T. F.; Werz, D. B. *Org. Lett.* **2011**, *13*, 1848.

(2) (a) Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051. (b) Lebold, T. P.; Kerr, M. A. *Pure Appl. Chem.* **2010**, *82*, 1797. (c) Agrawal, D.; Yadav, V. K. *Chem. Comm.* **2008**, 6471. (d) Ivanova, O. A.; Budynina, E. M.; Chagarovskiy, A. O.; Trushkov, I. V.; Melnikov, M. Y. *J. Org. Chem* **2011**, *76*, 8852.

(3) Selected examples with silyl enol ethers: (a) Komatsu, M.; Suehiro, I.; Horiguchi, Y.; Kuwajima, I. *Synlett* **1991**, 771. (b) Qu, J.-P.; Deng, C.; Zhou, J.; Sun, X.-L.; Tang, Y. *J. Org. Chem* **2009**, *74*, 7684. With enamines: (c) Dolfini, J. E.; Menich, K.; Corliss, P. *Tetrahedron Lett.* **1966**, 4421. (d) Berkowitz, W. F.; Grenetz, S. C. *J. Org. Chem.* **1976**, *41*, 10. With indoles: (e) England, D. B.; Kuss, T. D. O.; Keddy, R. G.; Kerr, M. A. *J. Org. Chem* **2001**, *66*, 4704. (f) Bajtos, B.; Yu, M.; Zhao, H.; Pagenkopf, B. L. *J. Am. Chem. Soc.* **2007**, *129*, 9631. With allyl silanes (g) Sugita, Y.; Yamadoi, S.; Hosoya, H.; Yokoe, I. *Chem. Pharm. Bull.* **2001**, *49*, 657. (h) Sapeta, K.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 2081.

(4) Perspective article: (a) Campbell, M. J.; Johnson, J. S.; Parsons, A. T.; Pohlhaus, P. D.; Sanders, S. D. *J. Org. Chem.* **2010**, *75*, 6317. Pioneering examples: (b) Reissig, H.-U. *Tetrahedron Lett.* **1981**, *22*, 2981. (c) Shimada, S.; Hashimoto, Y.; Sudo, A.; Hasegawa, M.; Saigo, K. *J. Org. Chem.* **1992**, *57*, 7126. (d) Shimada, S.; Hashimoto, Y.; Nagashima, T.; Hasegawa, M.; Saigo, K. *Tetrahedron* **1993**, *49*, 1589. (e) Shimada, S.; Hashimoto, Y.; Saigo, K. *J. Org. Chem.* **1993**, *58*, 5226. (f) Sugita, Y.; Kawai, K.; Yokoe, I. *Heterocycles* **2000**, *53*, 657. (g) Sugita, Y.; Kawai, K.; Yokoe, I. *Heterocycles* **2001**, *55*, 135. (h) Han, Z.; Uehira, S.; Tsuritani, T.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2001**, *57*, 987.

(5) Selected examples: (a) Alper, P. B.; Meyers, C.; Lerchner, A.; Siegel, D. R.; Carreira, E. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 3186. (b) Carson, C. A.; Kerr, M. A. *J. Org. Chem* **2005**, *70*, 8242. (c) Kang, Y.-B.; Tang, Y.; Sun, X.-L. *Org. Biomol. Chem.* **2006**, *4*, 299. (d) Parsons, A. T.; Smith, A. G.; Neel, A. J.; Johnson, J. S. *J. Am. Chem. Soc.* **2010**, *132*, 9688.

(6) For a review on the synthesis of tetrahydrofurans, see: Wolfe, J. P.; Hay, M. B. *Tetrahedron* **2007**, *63*, 261.

SnX_4).[7] In the last decade, this transformation has been the focus of a renewed research effort. In particular, Johnson and co-workers developed catalytic methods for the highly stereoselective synthesis of tetrahydrofurans (THFs) using Lewis acids (*i.e.* $Sn(OTf)_2$, $Hf(OTf)_4$) under mild conditions.[8]

In the [3+2] annulation with aldehydes and ketones, D-A cyclopropanes bearing oxygen donor group(s) were most frequently exploited,[4b-g,8e] but the use of aryl,[4a,8a,c] alkenyl,[8b,d] alkyl,[4a,8d] and silylmethyl[2c] donors has also been documented. To the best of our knowledge, this transformation has never been reported using D-A cyclopropanes substituted with a nitrogen-containing donor group instead.[9] In fact, aminocyclopropanes are generally underrepresented in annulation and cyclization reactions,[10] despite the abundance of synthetic methods for their preparation.[11]

The development of [3+2] annulations of aminocyclopropanes with aldehydes would constitute an important progress in the field, as this reaction allows the one-pot, atom-economic assembly of 2-aminotetrahydrofurans, a common motif in "evolutionarily selected" molecules such as nucleosides, as well as in synthetic drugs such as AZT (**1**)[12] (Figure 1).

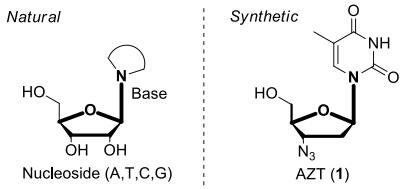


Figure 1. Bioactive natural and synthetic compounds containing an aminotetrahydrofuran core.

(7) Only two catalytic methods were reported before 2005 : refs 4f-g.

(8) Enantiospecific annulation: (a) Pohlhaus, P. D.; Johnson, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 16014. (b) Pohlhaus, P. D.; Sanders, S. D.; Parsons, A. T.; Li, W.; Johnson, J. S. *J. Am. Chem. Soc.* **2008**, *130*, 8642. DyKAT: (c) Parsons, A. T.; Johnson, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 3122. With quaternary sterocenters: (d) Smith, A. G.; Slade, M. C.; Johnson, J. S. *Org. Lett.* **2011**, *13*, 1996. Recently, an example of intramolecular annulation was also reported by Wang and co-workers: (e) Xing, S., Li, Y., Li, Z., Liu, C., Ren, J. and Wang, Z. *Angew. Chem., Int. Ed.* **2011**, doi: 10.1002/anie.201106368.

(9) For reviews on aminocyclopropanes, see: (a) Gnad, F.; Reiser, O. *Chem. Rev* **2003**, *103*, 1603. (b) Brackmann, F.; de Meijere, A. *Chem. Rev* **2007**, *107*, 4493.

(10) Intermolecular: (a) Wimalasena, K.; Wickman, Heang B.; Mahindaratne, Mathew P. D. *Eur. J. Org. Chem.* **2001**, *2001*, 3811. (b) Tanguy, C.; Bertus, P.; Szymoniak, J.; Larionov, O. V.; de Meijere, A. *Synlett* **2006**, *2006*, 2339. Intramolecular: (c) Lee, H. B.; Sung, M. J.; Blackstock, S. C.; Cha, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 11322. (d) Larquetoux, L.; Ouhamou, N.; Chiaroni, A.; Six, Y. *Eur. J. Org. Chem.* **2005**, *2005*, 4654. (e) Mangelinckx, S.; De Kimpe, N. *Synlett* **2006**, *2006*, 0369. Applications in total synthesis: (f) Zhang, D.; Song, H.; Qin, Y. *Acc. Chem. Res.* **2011**, *44*, 447. (g) De Simone, F.; Waser, J. *Synlett* **2011**, *2011*, 589.

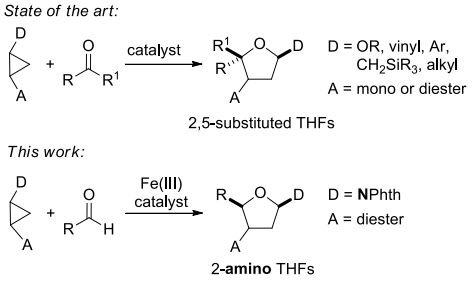
(11) Recent examples: (a) Faler, C. A.; Joullié, M. M. *Org. Lett.* **2007**, *9*, 1987. (b) Song, Z. L.; Lu, T.; Hsung, R. P.; Al-Rashid, Z. F.; Ko, C. H.; Tang, Y. *Angew. Chem. Int. Ed.* **2007**, *46*, 4069. (c) Valenta, P.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2010**, *132*, 14179, and references therein.

(12) (a) Mitsuya, H.; Yarchoan, R.; Broder, S. *Science* **1990**, *249*, 1533. (b) Basavapathruni, A.; Anderson, K. S. *The FASEB Journal* **2007**, *21*, 3795.

It is well-known that nucleosides and their mimetics[13] are widespread as therapeutic agents for the treatment of cancer, infections and viral diseases. Therefore the 2-aminotetrahydrofuran core may be rightly considered as a privileged scaffold for drug discovery.

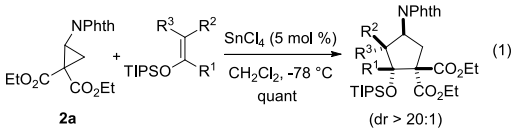
Herein, we describe the first catalytic method for the [3+2] annulation of donor-acceptor aminocyclopropanes with aldehydes affording 2-aminotetrahydrofurans with excellent diastereoselectivity (Scheme 1).

Our group has been interested in the use of D-A cyclopropanes (D = NPg or aryl, Pg = protecting group) as precursors of reactive intermediates in cyclization reactions onto electron-rich olefins or heterocycles.[14] In particular, we made use of aminocyclopropanes as acyl iminium precursors in the synthesis of natural alkaloids.[14b]



Scheme 1. [3+2] annulation of D-A aminocyclopropanes with aldehydes.

In 2011, we decided to investigate the use of more convergent annulation reactions of aminocyclopropanes for the efficient synthesis of carbo- and hetero- cycles. As a result of these efforts, we reported the first catalytic, enantiospecific [3+2] annulation between silyl enol ethers and D-A aminocyclopropane **2a** to give cyclopentylamines (Eq. 1).[15]



(1)

The fine-tuning of the D-A substituents on **2a** was required to reach an optimal compromise between stability and reactivity. We found that the combination of phthalimide as weak donor group and a *gem*-diester as acceptor to be ideal. As an extension to our work, we were wondering if phthaloyl aminocyclopropane **2a** could

(13) Herdewijn, P., *Modified Nucleosides: in Biochemistry, Biotechnology and Medicine*; Wiley-VCH, Weinheim, 2008.

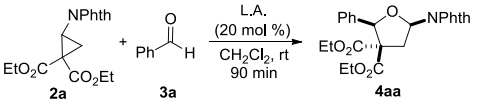
(14) (a) De Simone, F.; Andrès, J.; Torosantucci, R.; Waser, J. *Org. Lett.* **2009**, *11*, 1023. (b) De Simone, F.; Gertsch, J.; Waser, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5767.

(15) De Nanteuil, F.; Waser, J. *Angew. Chem. Int. Ed.* **2011,** *50*, 12075. Aminocyclopropane **2a** can be synthesised in multi-grams scale *via* rhodium-catalysed cyclopropanation of commercially available vinylphthalimide with diethyl diazomalonate.

be exploited in the [3+2] reaction with other partners, such as carbonyls.

We decided to examine first the reaction of D-A aminocyclopropane **2a** with benzaldehyde (**3a**). In contrast to the results obtained with enol ethers, the use of tin tetrachloride (Eq. 1) was not ideal, since a low yield was observed at rt, while irreproducible results were obtained at -78 °C (Table 1, entries 1-2). We consequently decided to screen a more extended selection of Lewis acids. Pleasingly, all Lewis acids tested, except $Yb(OTf)_3$ (entry 3, Table 1), were competent catalysts for the activation of aminocyclopropane **2a**, affording 2-amino tetrahydrofuran **4aa** in excellent diastereoselectivity in favour of the *cis* isomer (entries 4-11). Employing $In(OTf)_3$, a trace of the *trans* isomer could be identified in the crude ^1H NMR spectrum (dr = 19:1, entry 4), otherwise only the 2,5-*cis* tetrahydrofuran[16] was detected. Cyclopropane **2a** was completely consumed after 90 minutes in all cases, except for $Cu(OTf)_2$ (entry 5).

Table 1. Screening of Lewis Acids[a]



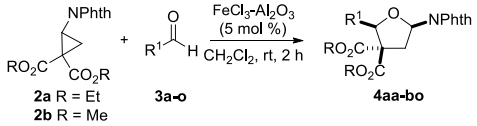
entry	Lewis acid	yield (%)[b]	dr (*cis*:*trans*)[c]
1[d]	$SnCl_4$	46	>20:1
2	$SnCl_4$	70-100	>20:1
3	$Yb(OTf)_3$	n.r.	-
4	$In(OTf)_3$	72	19:1
5[e]	$Cu(OTf)_2$	50	>20:1
6	$InCl_3$	74	>20:1
7	AuCl	91	>20:1
8	$Sn(OTf)_2$	82	>20:1
9	$Hf(OTf)_4$	100	>20:1
10	$Sc(OTf)_3$	100	>20:1
11	$FeCl_3$-Al_2O_3	100	>20:1

[a] Reaction conditions: 1.0 equiv **2a**, 1.5 equiv **3a**, 20 mol % of Lewis acid, 0.1 M in dichloromethane. [b] Yield was determined via ^1H NMR spectroscopy using hexamethyldisiloxane as internal standard. [c] Determined by ^1H NMR spectroscopy on the crude raction mixture. [d] Performed at -78 °C. [e] Only 50% conversion of **2a** was observed.

The effect of the counteranion was studied in the case of indium salts, and it proved negligible (triflate *vs.* chloride, entry 4 *vs.* 6). When the formation of 5-membered ring **4aa** was not quantitative (entries 1-2, 4-8), the crude ^1H NMR spectrum showed the presence of by-products, most likely derived from decomposition of the Lewis acid-activated aminocyclopropane **2a**. The cleanest reactions were observed with $Hf(OTf)_4$, $Sc(OTf)_3$ and $FeCl_3$-Al_2O_3 (entries 9-11).[17] We selected the latter as catalyst to continue our studies due to its low cost and toxicity.[18] Although the efficiency of iron catalysts in promoting cycloaddition and ring expansion reactions is well established,[19] this represents the first example of iron-catalyzed [3+2] annulation of D-A cyclopropanes.

Next, the scope of the reaction with D-A aminocyclopropanes **2a** and **2b** was explored, using 5 mol % of iron(III) chloride on alumina, and 1.5 equiv. of aldehydes **3a-o** at room temperature (Table 2).

Table 2. Scope of Aldehydes **3a-o** in the [3+2] Annulation with Aminocyclopropanes **2a-b**[a]



entry	R	R'	yield (%)	dr[b,c] (*dr*)[d]
1(**4aa**)	Et	Ph (**3a**)	94	>20:1
2(**4ba**)	Me	Ph (**3a**)	95	>20:1
3(**4ab**)	Et	4-$MeOC_6H_4$ (**3b**)	97	6:1
4(**4bc**)	Me	2-$MeOC_6H_4$ (**3c**)	83	5:1
5(**4bd**)	Me	2-thienyl (**3d**)	84	5:1
6(**4ab**)[e]	Et	4-$MeOC_6H_4$ (**3b**)	98	9:1(*>20:1*)
7(**4bc**)[e]	Me	2-$MeOC_6H_4$ (**3c**)	92	17:1 (*>20:1*)
8(**4bd**)[e]	Me	2-thienyl (**3d**)	89	>20:1
9(**4be**)	Me	4-ClC_6H_4 (**3e**)	91	>20:1
10(**4bf**)	Me	4-$NO_2C_6H_4$ (**3f**)	71	>20:1
11(**4bg**)	Me	(*E*)-CH=CHPh (**3g**)	94	2.5:1
12(**4bg**)[e]	Me	(*E*)-CH=CHPh (**3g**)	95	10:1(*>20:1*)
13(**4ah**)	Et	(*E*)-$CH=CHC_3H_7$ (**3h**)	99	10:1(*>20:1*)
14(**4bh**)	Me	(*E*)-$CH=CHC_3H_7$ (**3h**)	95	7:1(*>20:1*)
15(**4ai**)	Et	*n*-Pr (**3i**)	94	9:1(*>20:1*)
16(**4bl**)	Me	CH_2CH_2Ph (**3l**)	89	>20:1
17(**4am**)	Et	*i*-Pr (**3m**)	99	7:1
18(**4an**)	Et	Cyclohexyl (**3n**)	90	7:1
19(**4bo**)	Me	*t*-Bu (**3o**)	92	9:1(*>20:1*)

[a] Standard reaction conditions: 0.2 mmol **2a-b**, 1.5 equiv **3a-o**, 5 mol % of $FeCl_3$-Al_2O_3 , 0.1 M in dichloromethane. [b] Expressed as *cis*:*trans*. [c] Determined by ^1H NMR spectroscopy on the crude raction mixture. [d] Obtained after one single recrystallization (see Supporting Informations). [e] Reaction run at -10 °C.

In general, excellent yields were obtained in short reaction time (2 hours),[20] while employing aldehydes with diverse steric and electronic properties. No difference in reactivity/selectivity was observed between the ethyl diester **2a** and the methyl diester **2b** in the reaction with benzaldehyde (**3a**) (entry 1 *vs.* 2). The electron-rich *para*-

(16) 2,5-relative stereochemistry was assigned on the basis of x-ray diffraction analysis performed on compound **4ab**, and extended to the other compounds of the serie on the basis of the regularity in their NMR spectra (see Figure 3 and supporting information for details).

(17) Iron trichloride gave comparable results, but the alumina-supported reagent was preferred because it is easier to handle and known to be a scavenger of adventitious traces of water and acid. For examples on the use of $FeCl_3$-Al_2O_3, see: a) Tietze, L. F.; Beifuss, U. *Synthesis* **1988**, *5*, 359. b) Tietze, L. F.; Beifuss, U.; Antel, J.; Sheldrick, G. M. *Angew. Chem., Int. Ed.* **1988**, *27*, 703.

(18) In the last decade, a revival of iron catalysis in organic synthesis was observed, due to the abundance and versatility of this environmentally benign metal. See for example: *Iron Catalysis Fundamentals and Applications;* Plietker, B., Ed.; Topics in Organometallic Chemistry; Springer-Verlag: Berlin Heidelberg, 2011; Vol. 33.

(19) (a) Hilt, G.; Janikowski, J. *Iron Catalysis in Organic Chemistry: Reactions and Applications*, Wiley-VCH, Weinheim, 2008, Chapter 9. (b) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev* **2004**, *104*, 6217.

(20) Two hours was the chosen standard time to have full conversion. When completion was reached in shorter time, the prolonged stirring with the catalyst at rt caused no erosion in yield or dr.

and *ortho*- anisaldehydes (**3b-c)** and thiophene-2-carboxaldehyde (**3d**) displayed modest stereoselectivities at rt (up to 6:1 *cis*:*trans*; entries 3-5), nevertheless increased dr's were obtained at a lower temperature (up to >20:1 *cis*:*trans*, entries 6-8). Interestingly, no detrimental effect on yield and stereoselectivity of *ortho vs*. *para* substituent was observed with anisaldehyde **3c** *vs.* **3b** (entries 6-7). In all cases, the two isomers could not be separated by flash chromatography. However, the pure *cis* isomer could be obtained by means of a single recrystallization, except for products **4am** and **4an.** The x-ray diffraction analysis performed on aminotetrahydrofuran **4ab** allowed the unambiguous attribution of the 2,5-*cis* relative stereochemistry (Figure 2).

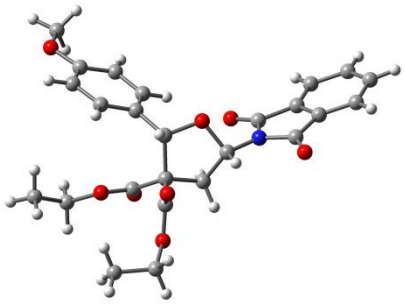
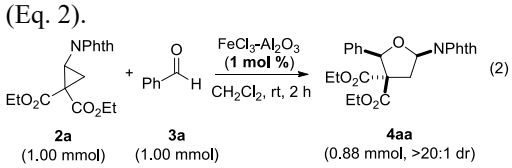


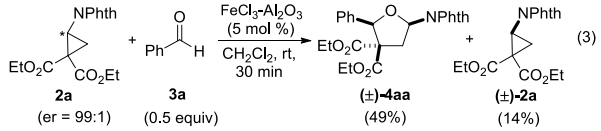
Figure 2. X-ray structure of aminotetrahydrofuran **4ab**.

The annulation reaction was not limited to aromatic aldehydes, and a good yield was also obtained in the case of cinnamyl aldehyde (**4bg**), albeit with a low diastereoselectivity (entry 11). Once again, the *cis*-selectivity could be increased by lowering the temperature to -10 °C (entry 12). The reaction was also successful for unsaturated aldehyde **3h**, both with aminocyclopropanes **2a** and **2b** (entries 13 and 14). Aliphatic aldehydes are generally challenging substrates for Lewis acids-catalyzed reactions, as they are prone to undergo aldol side reactions. Gratifyingly, this was not an issue under our mild reaction conditions, and aliphatic aldehydes with linear (entries 15-16), or branched (entries 17-19) substituents afforded the corresponding amino tetrahydrofurans in outstanding yields (89-99%) and good diastereoselectivities (up to >20:1 *cis*:*trans*).

As a further evidence of the efficiency of our methodology, the reaction of aminocyclopropane **2a** with an equimolar amount of benzaldehyde (**3a**) in the presence of 1 mol % loading of iron catalyst, afforded compound **4aa** in 88% yield and excellent dr on a 1 mmol scale (Eq. 2).



To gain more knowledge on the mechanism of our [3+2] annulation, enantioenriched **2a** (er = 99:1)[21] was reacted with **3a** under the standard reaction conditions (Eq. 3). We had found in our previous work that the reaction of enantiopure aminocyclopropane **2a** with silyl enol ethers was enantiospecific with all the olefins tested,[15] indicating most probably the formation of a tight, configurationally stable ion pair between the cyclopropane and the tin catalyst. In contrast, the iron-catalysed annulation of **2a** with benzaldehyde (**3a**) at rt resulted in a complete loss of the stereochemical information, as tetrahydrofuran **4aa** was isolated in a racemic form.[8b,22] This evidence suggests that, upon Lewis acid activation, the aminocyclopropane undergoes fast racemization *via* an open, zwitterionic species. While the result hampers the synthesis of enantioenriched amino THFs, it is a potential starting point for the development of a dynamic kinetic asymmetric transformation (DyKAT).[8c,23]



In summary, we have developed the first iron (III) catalysed [3+2] annulation of aminocyclopropanes with aldehydes, affording aminotetrahydrofurans in excellent yields (71-99%) and diasteroselectivities (up to >20:1 dr). This protocol represents an atom-economic, stereoselective route to unprecedented structures, that share a aminotetrahydrofuran motif of utmost value, due to its presence in DNA and RNA. The exploration of the synthetic potential of the aminotetrahydrofurans,[24] the development of an asymmetric version of the reaction, as well as its extension to ketones are currently under investigation in our laboratories.

Acknowledgment We thank the European Commission (Marie Curie IEF fellowship to F.B., grant number 253274) and the Swiss National Science Foundation (SFN, grant number 200021_129874) for financial support. Dr. Rosario Scopelliti (EPFL) is acknowledged for the X-ray studies.

Supporting Information Available: Experimental details, characterization data and X-rays diffraction analysis.

(21) Obtained by preparative HPLC separation on chiral stationary phase (see supporting information for details).

(22) Sapeta, K.; Kerr, M. A. *J. Org. Chem* **2007**, *72*, 8597.

(23) (a) Pellissier, H. *Chirality from dynamic kinetic resolution*; RSC Publishing: Cambridge, 2011. (b) Steinreiber, J. ; Faber, K.; Griengl, H. *Chem. Eur. J.* **2008**, *14*, 8060.

(24) The ring opening of phthalimide with amines was accomplished, but the cleavage of the second C-N bond could not yet be achieved due to the instability of the resulting free aminotetrahydrofuran. As alternative strategies, the use of modified aminocyclopropanes or the substitution of the phthalimide with nucleophiles will be investigated in the future for the synthesis of nucleoside analogues.

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List of Abbreviations

Ac	acetyl
DCM	dichloromethane
dr	diastereomeric ratio
eq	equivalent
ESI	Electrospray Ionization
Et	ethyl
h	hours
hept	heptet
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectra
iPr	isopropyl
M	molar mol/L
Me	methyl
Mp	melting point
MS	Mass Spectrometry
NMR	Nuclear Magnetic Resonance
Ph	phenyl
Phth	phthaloyl
R_f	Retention Factor
rt	room temperature
TMS	trimethylsilyl

1 Experimental procedures

1.1 General Methods

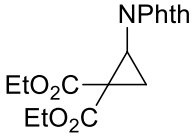
All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. CH_2Cl_2 was dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 30 ppm, Karl-Fischer titration). All chemicals were purchased from 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, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plastic plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. 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 chloroform-d, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration; interpretation). ^{13}C-NMR spectra were recorded with 1H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, all signals are reported in ppm with the internal chloroform signal at 77.0 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). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurement were done on a JASCO HPLC system with an AS2055 Autosampler, a PU 2089 Pump, a UV 2075 detector and a SEDEX 85 (SEDERE) detector using a CHIRALPAK IC, IB or IA column from DAICEL Chemical Industries Ltd. HPLC grade solvents from Sigma-Aldrich were used. The aldehydes used in this study are all

commercially available and were used as received. Iron trichloride on alumina was prepared according to a reported procedure.[1]

1.2 Preparation of amino cyclopropanes 2a-b

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

Following a reported procedure[2], a two-neck flask equipped with a nitrogen inlet was loaded with 14 mg (0.018 mmol, 0.1 mol %) of bis[rhodium(α,α,α',α'-tetramethyl-1,3-benzenedipropionic acid)] inside the glove box, then the flask was sealed with a rubber septum and evacuated from the glove box. A solution of *N*-vinyl-phthalimide (3.0 g, 18 mmol, 1 eq) in 30 mL of dry dichloromethane was added to the flask and the resulting green suspension was cooled down to 0°C with an ice/water bath. A solution of diethyl-2-diazomalonate[3] (4.0 g, 21 mmol, 1.2 eq) in 20 mL of dichloromethane was added over five minutes. When the addition was complete, the reaction was allowed to warm to room temperature. After 5 h at room temperature, the solvent was removed under reduced pressure and the crude was directly purified by column chromatography (SiO_2, 9/1 to 7/3 (*n*-hexane: AcOEt). 5.4 g (16 mmol, 90 % yield) of **2a** as a colorless solid were obtained.



2a

R_f 0.36 (*n*-hex/EtOAc 6/4);

Mp 93 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 2 H, *Phth*), 7.74 (m, 2 H, *Phth*), 4.30 (m, 2 H, *OCH₂*), 4.07 (m, 2 H, *OCH₂*), 3.71 (dd, 1 H, *J* = 8.5, 6.6 Hz, *N-C-H*), 2.74 (t, 1 H, *J* = 6.5 Hz, *CH₂*), 2.02 (dd, 1 H, *J* = 8.5, 6.4 Hz, *CH₂*), 1.34 (t, 3 H, *J* = 7.1 Hz, *CH₃*), 1.12 (t, 3 H, *J* = 7.1 Hz, *CH₃*);

^{13}C NMR (101 MHz, CDCl3) δ 168.2, 167.8, 166.4, 134.3, 131.6, 123.4, 62.0, 61.8, 34.7, 33.5, 19.2, 14.1, 13.8;

IR 2985 (w), 2938 (w), 2907 (w), 1783 (m), 1719 (s), 1614 (w), 1393 (s), 1321 (m), 1218 (s), 1133 (m), 719 (s);

HRMS (ESI) calcd for $C_{17}H_{18}NO_6^+$ $[M+H]^+$ 332.1129; found 332.1135.

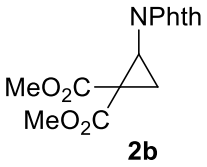
HPLC analysis: Chiracel IA (0.46 x 25 cm): 85:15 (hexane: *i*-PrOH), flow 1.0mL/min. t_1: 9.0 min, t_2: 11.2 min.

[1] Tietze, L. F.; Beifuss, U. *Synthesis* **1988**, *5*, 359.
[2] De Nanteuil, F.; Waser, J. *Angew. Chem., Int. Ed.* **2011**, doi: 10.1002/anie.201106255.
[3] P. Wyatt, A. Hudson, J. Charmant, A. G. Orpen, H. Phetmung, *Org. Biomol. Chem.* **2006**, *4*, 2218

Preparative HPLC: Chiracel IA (20 x 250 mm), 85:13.5:1.5 (hexane: AcOEt: *i*-PrOH), flow 10 mL/min. t_1 = 18 min, $[\alpha]_D^{25}$ 115 (er: 98:2, *c* 1.0, $CHCl_3$), t_2 = 24 min, $[\alpha]_D^{25}$ -115 (er: 98:2, *c* 1.0, $CHCl_3$).

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

Following the same procedure described above, using 2.5 g (14 mmol, 1 eq) of *N*-vinyl-phthalimide, 2.5 g (15 mmol, 1.1 eq) of dimethyl-2-diazomalonate and 10.9 mg (0.014 mmol, 0.1 mol %) of bis[rhodium(α,α,α',α'-tetramethyl-1,3-benzenedipropionic acid)], 3.40 g (11.2 mmol, 78 % yield) of **2b** were isolated as a colorless solid.



2b

R_f 0.27 (*n*-hex/EtOAc 6/4);

Mp 124-125 °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, 1H, *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 304.0804.

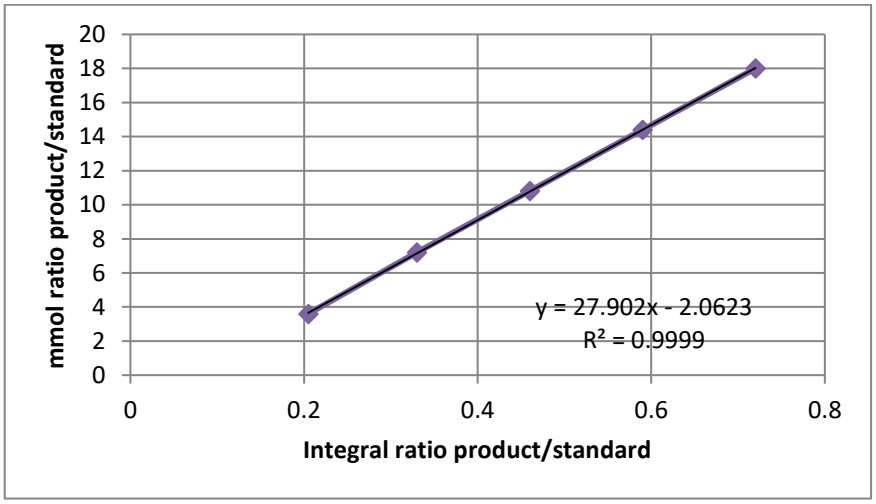
1.3 Standard procedure for the screening of Lewis acids

All the reactions were carried out under nitrogen in glass vials equipped with rubber septa and Teflon-coated stir bars. The Lewis acid (4 μmol, 20 mol %) was added to the vial in the glove box, followed by a solution of aminocyclopropane **2a** (20 μmol, 6.6 mg, 1 equiv.) and benzaldehyde **3a** (30 μmol, 3 μL, 1.5 equiv.) in anhydrous dichloromethane (0.1 M, 0.2 mL) was added under nitrogen. The mixture was stirred for 90 min at the indicated temperature, and then it was diluted with dichloromethane (0.5 mL) and flushed through a short plug of silica gel. The solvent was removed in vacuo, then a ^{1}H-NMR sample was prepared by dissolving the crude mixture in $CDCl_3$ (0.7 mL) and a standard hexamethyldisiloxane solution (0.01 M, 0.111 mL) was added. The ^{1}H-NMR yield was calculated according to the following calibration curve.

^{1}H-NMR calibration curve

Hexamethyldisiloxane (4.3 μL, 0.02 mmol) was dissolved in $CDCl_3$ (2.0 mL), to give a 0.01 M standard solution. Compound **4aa** (11.8 mg, 0.03 mmol) was dissolved in $CDCl_3$ (0.7 mL), then the following volumes of standard 0.01 M solution were added: 150 μL for sample A (1.50 μmol); 188 μL for sample B (1.88 μmol); 250 μL for sample C (2.50 μmol); 375 μL for sample D (3.75 μmol) ; 750 μL for sample E (7.50 μmol) .

^{1}H NMR spectra were acquired for solution A-E, and the ratios between the integrals of the signal at δ 6.00 (dd, 1 H, *J* = 11.0, 5.2 Hz, CHNPhth) of **4aa** and the signal at δ 0.06 (s, 1 H, TMS) of hexamethyldisiloxane were determined. These experimental ratios were plotted vs. the ratios mmol **4aa** / mmol hexamethyldisiloxane to give the calibration graph.



1.4 Standard procedure for the iron-catalysed [3+2] annulation of amino cyclopropanes with aldehydes

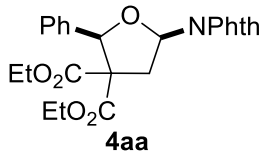
A two-neck flask equipped with a nitrogen inlet was loaded with $FeCl_3$-Al_2O_3 (10 μmol, 10 mg, 5 mol %) inside the glove box, then the flask was sealed with a rubber septum and evacuated from the glove box. The iron catalyst was stirred in 1 mL of anhydrous dichloromethane, before adding a solution of aminocyclopropane **2a-b** (0.20 mmol, 60-66 mg, 1 equiv.) and aldehyde **3a-o** (1.5 equiv.) in anhydrous dichloromethane (1 mL). The mixture was stirred under nitrogen for 2 h at rt (or -10° C for **4ab**, **4bc**, **4bd** and **4bg**), then it was diluted with dichloromethane (2 mL) and flushed through a short plug of silica gel, eluting with EtOAc (5 mL). The solvent was removed *in vacuo*, affording the crude reaction mixture, which was submitted to ^{1}H NMR analysis to determine the dr before purification via flash chromatography (SiO_2, 8/2 to 1/1 (*n*-hexane: AcOEt)).

2 Scope of the reaction

Diethyl dihydro-5-(1,3-dioxoisoindolin-2-yl)-2-phenylfuran-3,3(2H)-dicarboxylate (4aa)

Flash chromatography afforded the title compound (82 mg, 0.19 mmol, 94% yield) as a colorless solid, as a single diastereoisomer (dr > 20:1).

When the reaction was performed on 1 mmol scale of **2a** (331 mg), with 1 eq. of benzaldehyde (102 μL, 1 mmol) and 1 mol % of $FeCl_3$-Al_2O_3 (10 mg, 10 μmol), 385 mg of product **4aa** (0.88 mmol, 88 % yield) were obtained.



4aa

R_f 0.58 (*n*-hex/EtOAc 6/4);

Mp 103-105 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.79 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.58 (d, 2 H, *J* = 7.0 Hz, Ph), 7.37-7.23 (m, 3 H), 6.00 (dd, 1 H, *J* = 11.0, 5.2 Hz, *CH*NPhth), 5.84 (s, 1 H, *CH*Ph), 4.45-4.22 (m, 3 H, O*CH*$_2$CH$_3$ + *CH*$_2$CHNPhth), 3.78-3.67 (m, 1 H, O*CH*$_2$CH$_3$), 3.54-3.43 (m, 1 H, O*CH*$_2$CH$_3$), 2.52 (dd, 1 H, *J* = 13.2, 5.2 Hz, *CH*$_2$CHNPhth), 1.33 (t, 3 H, *J* = 7.1 Hz, OCH$_2$*CH*$_3$), 0.84 (t, 3 H, *J* = 7.1 Hz, OCH$_2$*CH*$_3$);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 167.4, 137.8, 134.5, 131.8, 128.4, 128.0, 127.8, 123.8, 82.3, 79.1, 65.0, 62.4, 61.7, 34.2, 14.0, 13.4;

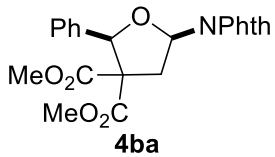
IR 2983 (w), 2934 (w), 1783 (w), 1725 (s), 1469 (w), 1380 (m), 1370 (m), 1338 (w), 1297 (w), 1266 (m), 1233 (w), 1205 (w), 1194 (w), 1140 (m), 1113 (w), 1078 (w), 1026 (w), 916 (w), 868 (w), 757 (w), 721 (m), 703 (w), 658 (w);

HRMS (ESI) calcd for $C_{24}H_{24}NO_7^+$ $[M+H]^+$ 438.1547; found 438.1547.

HPLC analysis: Chiracel IA: 85:15 (hexane: *i*-PrOH), flow 1.0 mL/min. t_1:13.5 min; t_2: 24.0 min

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-phenyldihydrofuran-3,3(2H)-dicarboxylate (4ba)

Flash chromatography afforded the title compound (78 mg, 0.19 mmol, 95% yield) as a colorless solid, as a single diastereoisomer (dr > 20:1).



4ba

R_f 0.52 (*n*-hex/EtOAc 6/4);

Mp 170-173 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, 2 H, *J* = 5.5, 2.9 Hz, Phth), 7.79 (dd, 2 H, *J* = 5.5, 2.9 Hz, Phth), 7.57 (d, 2 H, *J* = 7.2 Hz, Ph), 7.38-7.20 (m, 3 H, Ph), 5.99 (dd, 1 H, *J* = 11.0, 5.2 Hz, *CH*NPhth), 5.85 (s, 1 H, *CH*Ph), 4.28 (dd, 1 H, *J* = 13.2, 11.0

Hz, *CH*$_2$CHNPhth), 3.88 (s, 3 H, OCH$_3$), 3.15 (s, 3 H, OCH$_3$), 2.53 (dd, 1 H, *J* = 13.2, 5.2 Hz, *CH*$_2$CHNPhth);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 167.8, 167.2, 137.5, 134.5, 131.6, 128.3, 127.8, 127.4, 123.7, 82.3, 79.1, 65.0, 53.4, 52.3, 34.0;

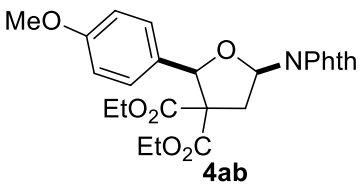
IR 3067 (w), 3034 (w), 3010 (w), 2954 (w), 1781 (m), 1781 (m), 1720 (s), 1612 (w), 1498 (w), 1469 (w), 1457 (w), 1436 (m), 1365 (m), 1338 (m), 1272 (s), 1233 (m), 1208 (m), 1137 (s), 1116 (m), 1077 (m), 1054 (m), 1022 (m), 973 (m), 914 (m), 870 (m), 756 (m), 721 (s), 703 (s), 659 (m);

HRMS (ESI) calcd for $C_{22}H_{20}NO_7^+$ $[M+H]^+$ 410.1234; found 410.1238.

Diethyl dihydro-2-(4-methoxyphenyl)-5-(1,3-dioxoisoindolin-2-yl)furan-3,3(2H)-dicarboxylate (4ab)

Flash chromatography afforded the title compound (90 mg, 0.19 mmol, 97% yield) as a colorless solid, as an inseparable mixture of diastereoisomers; dr = 6:1 determined by integration of ^{1}H NMR signals: *δminor* 6.53 (dd), *δmajor* 5.96 ppm (dd).

When the reaction was performed at -10 °C, 91 mg (0.195 mmol, 98% yield) of the title compound were isolated (dr = 9:1). Recrystallization from *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).



4ab

R$_f$ 0.79 (*n*-hex/EtOAc 6/4);

Mp 122-124 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.77 (dd, 2 H, *J* = 5.5, 2.9 Hz, Phth), 7.52 (d, 2 H, *J* = 8.8 Hz, Ar), 6.87 (d, 2 H, *J* = 8.8 Hz, Ar), 5.96 (dd, 1 H, *J* = 11.1, 5.1 Hz *CH*NPhth), 5.81 (s, 1 H, *CH*O), 4.43-4.21 (m, 3 H, O*CH*$_2$CH$_3$ + *CH*$_2$CHNPhth), 3.79 (s, 3H, OCH$_3$), 3.82-3.71 (m, 1 H, O*CH*$_2$CH$_3$), 3.61-3.49 (m, 1 H, O*CH*$_2$CH$_3$), 2.49 (dd, 1 H, *J* = 13.2, 5.1 Hz, *CH*$_2$CHNPhth), 1.31 (t, 3 H, *J* = 7.1 Hz, OCH$_2$*CH*$_3$), 0.88 (t, 3 H, *J* = 7.1 Hz, OCH$_2$*CH*$_3$);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 167.6, 167.4, 159.7, 134.4, 131.8, 130.0, 129.1, 123.7, 113.3, 82.0, 79.0, 64.9, 62.3, 61.7, 55.3, 34.1, 14.1, 13.5;

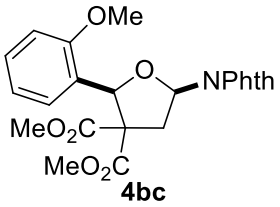
IR 2982 (w), 2938 (w), 1782 (w), 1722 (s), 1615 (w), 1516 (m), 1468 (w), 1369 (m), 1338 (w), 1299 (w), 1266 (m), 1251 (m), 1233 (w), 1206 (w), 1193 (w), 1179 (w), 1138 (m), 1112 (w), 1077 (w), 1054 (m), 1027 (m), 914 (w), 867 (w), 847 (w), 843 (w), 721 (m), 706 (w), 653 (w);

HRMS (ESI) calcd for $C_{25}H_{26}NO_8^+$ $[M+H]^+$ 468.1653; found 468.1670.

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-(2-methoxyphenyl)dihydrofuran-3,3(2H)-dicarboxylate (4bc)

Flash chromatography afforded the title compound (73 mg, 0.17 mmol, 83% yield) as a colorless solid, as an inseparable mixture of diastereoisomers; dr = 5:1 determined by integration of ^{1}H NMR signals: *δminor* 6.46-6.53 (m), *δmajor* 6.02 ppm (dd).

When the reaction was performed at -10 °C, 81 mg (0.18 mmol, 92% yield) of the title compound were isolated (dr = 17:1). Recrystallization from *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).



4bc

Rf 0.34 (*n*-hex/EtOAc 6/4);

Mp 168-170 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.80-7.69 (m, 3 H, Phth + Ar), 7.24 (t, 1 H, *J* = 8.2 Hz, Ar), 6.99 (t, 1 H, *J* = 7.5 Hz, Ar), 6.82 (d, 1 H, *J* = 8.2 Hz, Ar), 6.29 (s, 1 H, *CH*O), 6.02 (dd, 1 H, *J* = 10.6, 5.3 Hz, *CH*NPhth), 4.23 (dd, 1 H, *J* = 13.1, 10.6 Hz, *CH$_2$*CHNPhth), 3.87 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.20 (s, 3H, OCH_3), 2.49 (dd, 1 H, *J* = 13.1, 5.3 Hz, *CH$_2$*CHNPhth);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 164.2, 163.4, 153.3, 131.9, 129.3, 126.9, 126.1, 124.1, 121.6, 118.6, 108.4, 78.7, 76.5, 64.7, 56.5, 54.2, 53.2, 36.9;

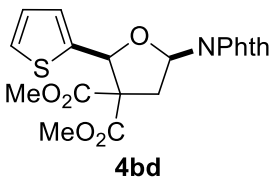
IR 3013 (w), 2951 (w), 2838 (w), 1780 (w), 1732 (s), 1718 (s), 1603 (w), 1495 (w), 1462 (w), 1435 (w), 1376 (s), 1270 (s), 1199 (m), 1137 (s), 1072 (m), 1052 (s), 1021 (s), 974 (m), 944 (w), 891 (w), 871 (m), 761 (m), 721 (s), 656 (m);

HRMS (ESI) calcd for $C_{23}H_{22}NO_8^+$ $[M+H]^+$ 440.1340; found 440.1342.

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-(thiophen-2-yl)dihydrofuran-3,3(2H)-dicarboxylate (4bd)

Flash chromatography afforded the title compound (70 mg, 0.17 mmol, 84% yield) as a colorless solid, as an inseparable mixture of diastereoisomers; dr = 5:1 determined by integration of ^{1}H NMR signals: *δminor* 6.52 (dd), *δmajor* 5.94 ppm (dd).

When the reaction was performed at -10 °C, 74 mg (0.18 mmol, 89% yield) of the title compound were isolated (dr > 20:1).



4bd

Rf 0.44 (*n*-hex/EtOAc 6/4);

Mp 188-190 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, 2 H, *J* = 5.5, 3.0 Hz, Phth), 7.79 (dd, 2 H, *J* = 5.5, 3.0 Hz, Phth), 7.30-7.24 (m, 2 H, thiophene),

6.99 (dd, 1 H, *J* = 5.0, 3.6 Hz, thiophene), 6.10 (s, 1 H, *CH*O), 5.94 (dd, 1 H, *J* = 11.1, 5.0 Hz, *CH*NPhth), 4.33 (dd, 1 H, *J* = 13.2, 11.1 Hz, CH_2CHNPhth), 3.89 (s, 3 H, OCH_3), 3.38 (s, 3 H, OCH_3), 2.53 (dd, 1 H, *J* = 13.2, 5.0 Hz, CH_2CHNPhth);

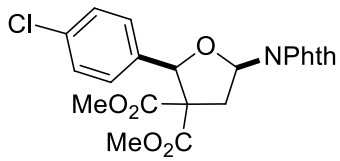
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 167.4, 167.2, 140.3, 134.5, 131.6, 126.8, 126.6, 125.8, 123.7, 79.0, 78.3, 65.2, 53.5, 52.6, 33.1;

IR 2954 (w), 1782 (w), 1722 (s), 1436 (w), 1371 (s), 1278 (m), 1244 (m), 1202 (w), 1136 (m), 1076 (w), 1039 (w), 1019 (m), 973 (w), 914 (w), 884 (w), 869 (w), 798 (w), 721 (m);

HRMS (ESI) calcd for $C_{20}H_{18}NO_7S^+$ $[M+H]^+$ 416.0799; found 416.0810.

Dimethyl 2-(4-chlorophenyl)-5-(1,3-dioxoisoindolin-2-yl)dihydrofuran-3,3(2H)-dicarboxylate (4be)

Flash chromatography afforded the title compound (81 mg, 0.18 mmol, 91% yield) as a colorless solid, as a single diastereoisomer (dr > 20:1).



4be

R_f 0.50 (*n*-hex/EtOAc 6/4);

Mp 173-175 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.79 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.52 (d, 2 H, *J* = 8.5 Hz, Ar), 7.32 (d, 2 H, *J* = 8.5 Hz, Ar), 5.97 (dd, 1 H, *J* = 10.9, 5.2 Hz, *CH*NPhth), 5.81 (s, 1 H, *CH*O), 4.22 (dd, 1 H, *J* = 13.3, 10.9 Hz, CH_2CHNPhth), 3.88 (s, 3 H, OCH_3), 3.22 (s, 3 H, OCH_3), 2.53 (dd, 1 H, *J* = 13.3, 5.2 Hz, CH_2CHNPhth);

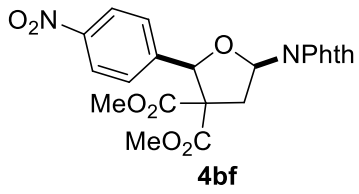
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 167.7, 167.3, 136.2, 134.6, 134.3, 131.7, 129.0, 128.2, 123.8, 81.7, 79.2, 65.0, 53.6, 52.6, 34.0;

IR 2954 (w), 1783 (m), 1734 (s), 1721 (s), 1612 (w), 1598 (w), 1491 (w), 1470 (w), 1436 (w), 1436 (w), 1377 (s), 1274 (m), 1234 (m), 1234 (m), 1208 (m), 1208 (m), 1138 (m), 1118 (w), 1107 (w), 1077 (m), 1056 (m), 1056 (m), 1026 (m), 1015 (m), 973 (w), 913 (w), 913 (w), 870 (w), 844 (w), 798 (w), 722 (s), 661 (w), 653 (w);

HRMS (ESI) calcd for $C_{22}ClH_{19}NO_7^+$ $[M+H]^+$ 444.0845; found 444.0857.

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-(4-nitrophenyl)dihydrofuran-3,3(2H)-dicarboxylate (4bf)

Flash chromatography afforded the title compound (65 mg, 0.14 mmol, 71% yield) as a colorless solid, as a single diastereoisomer (dr > 20:1).



4bf

R$_f$ 0.36 (*n*-hex/EtOAc 6/4);

Mp 178-181 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, 2 H, *J* = 8.8 Hz, Ar), 7.95 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.82 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.78 (d, 2 H, *J* = 8.8 Hz, Ar), 6.02 (dd, 1 H, *J* = 10.8, 5.4 Hz, *CH*NPhth), 5.91 (s, 1 H, *CH*O), 4.20 (dd, 1 H, *J* = 13.4, 10.8 Hz, *CH$_2$*CHNPhth), 3.90 (s, 3 H, OCH_3), 3.23 (s, 3 H, OCH_3), 2.60 (dd, 1 H, *J* = 13.4, 5.4 Hz, *CH$_2$*CHNPhth);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 167.5, 167.3, 147.9, 145.0, 134.7, 131.6, 128.6, 123.9, 123.1, 81.3, 79.4, 65.1, 53.7, 52.6, 34.2;

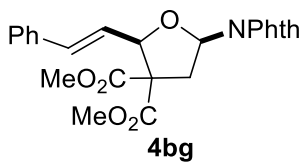
IR 2955 (w), 1782 (m), 1736 (s), 1609 (w), 1524 (m), 1471 (w), 1458 (w), 1436 (w), 1377 (s), 1351 (m), 1276 (m), 1247 (w), 1234 (w), 1209 (w), 1139 (m), 1112 (w), 1075 (m), 1058 (w), 1028 (w), 974 (w), 913 (m), 893 (w), 869 (m), 724 (s), 700 (w), 686 (w), 673 (m), 667 (w), 652 (w), 639 (w), 631 (w), 614 (w), 604 (w);

HRMS (ESI) calcd for $C_{22}H_{19}N_2O_9^+$ $[M+H]^+$ 455.1085; found 455.1083.

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-((*E*)-styryl)dihydrofuran-3,3(2H)-dicarboxylate (4bg)

Flash chromatography afforded the title compound (82 mg, 0.19 mmol, 94% yield) as a colorless solid, as an inseparable mixture of diastereoisomers; dr = 2.5:1 determined by integration of ^{1}H NMR signals: *δminor* 6.43 (dd), *δmajor* 6.02 ppm (dd).

When the reaction was performed at -10 °C, 83 mg (0.19 mmol, 95% yield) of the title compound were isolated (dr = 10:1). Recrystallization from *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).



4bg

R$_f$ 0.47 (*n*-hex/EtOAc 6/4);

Mp 188-190 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, 2 H, *J* = 5.5, 3.0 Hz, Phth), 7.77 (dd, 2 H, *J* = 5.5, 3.0 Hz, Phth), 7.44 (d, 2 H, *J* = 8.6 Hz, Ph), 7.36-7.23 (m, 3 H, Ph), 6.67-6.64 (m, 2 H, CH=CH), 6.02 (dd, 1 H, *J* = 10.3, 5.9 Hz, *CH*NPhth), 5.31 (dd, 1 H, *J* = 4.7, 3.6 Hz, C*H*O), 4.09 (dd, 1 H, *J* = 13.4, 10.3 Hz, *CH$_2$*CHNPhth), 3.90 (s, 3 H, OCH_3), 3.66 (s, 3 H, OCH_3), 2.64 (dd, 1 H, *J* = 13.4, 5.9 Hz, *CH$_2$*CHNPhth);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 167.4, 167.3, 136.3, 134.5, 134.4, 131.7, 128.6, 128.1, 126.9, 125.4, 123.7, 82.8, 79.6, 64.9, 53.6, 53.1, 33.0;

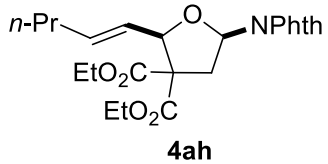
IR 3028 (w), 2955 (w), 1781 (w), 1718 (s), 1451 (w), 1436 (m), 1371 (m), 1355 (m), 1333 (m), 1273 (s), 1227 (m), 1208 (m), 1133 (m), 1110 (m), 1090 (m), 1075 (m), 1041 (m), 1018 (m), 1007 (m), 969 (m), 910 (m), 893 (w), 864 (m), 720 (s), 695 (m), 651 (m);

HRMS (ESI) calcd for $C_{24}H_{22}NO_7^+$ $[M+H]^+$ 436.1391; found 436.1370.

Diethyl 5-(1,3-dioxoisoindolin-2-yl)-2-((*E*)-pent-1-en-1-yl)dihydrofuran-3,3(2H)-dicarboxylate (4ah)

Flash chromatography afforded the title compound (86 mg, 0.20 mmol, 99% yield) as a sticky wax, as an inseparable mixture of diastereoisomers; dr = 10:1 determined by integration of ^{1}H NMR signals: *δminor* 6.45 (dd), *δmajor* 5.11 ppm (d).

Recrystallization from *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).



4ah

R$_f$ 0.63 (*n*-hex/EtOAc 6/4);

Mp 118-120 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.75 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 5.96-5.74 (m, 3 H, CH=CH + *CH*NPhth), 5.11 (d, 1 H, *J* = 8.9, Hz, *CH*O), 4.41-4.08 (m, 4 H, O*CH$_2$*CH$_3$), 4.00 (dd, 1 H, *J* = 13.3, 10.5 Hz, *CH$_2$*CHNPhth), 2.53 (dd, 1 H, *J* = 13.3, 5.8 Hz, *CH$_2$*CHNPhth), 2.09-1.95 (m, 2 H, *CH$_2$*CH=CH), 1.46-1.35 (m, 2 H, CH$_2$*CH$_2$*CH$_3$), 1.32 (t, 3 H, *J* = 7.1 Hz, OCH$_2$*CH$_3$*), 1.25 (t, 3 H, *J* = 7.1 Hz, OCH$_2$*CH$_3$*), 0.90 (t, 3 H, *J* = 7.3 Hz, CH$_2$CH$_2$*CH$_3$*);

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 167.4, 167.0, 136.8, 134.4, 131.8, 126.2, 123.5, 82.7, 79.2, 64.4, 62.3, 61.8, 34.3, 32.9, 22.1, 14.0, 13.7;[4]

IR 2963 (w), 2934 (w), 2874 (w), 1783 (w), 1723 (s), 1467 (w), 1368 (s), 1298 (m), 1263 (s), 1230 (m), 1206 (m), 1126 (m), 1097 (m), 1042 (m), 1021 (m), 992 (m), 975 (m), 928 (w), 919 (w), 720 (s), 673 (w), 672 (w);

HRMS (ESI) calcd for $C_{23}H_{28}NO_7^+$ $[M+H]^+$ 430.1860; found 430.1861.

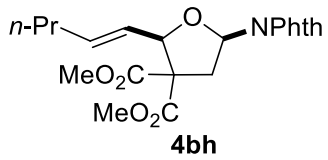
Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-((*E*)-pent-1-en-1-yl)dihydrofuran-3,3(2H)-dicarboxylate (4bh)

Flash chromatography afforded the title compound (76 mg, 0.19 mmol, 95% yield) as a colorless solid, as an inseparable mixture of diastereoisomers; dr = 7:1 determined by integration of ^{1}H NMR signals: *δminor* 6.32 (dd), *δmajor* 5.10 ppm (d).

Recrystallization from *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).

R$_f$ 0.50 (*n*-hex/EtOAc 6/4);

[4] Two methyl carbons are overlapping.



4bh

Mp 160-161 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 7.75 (dd, 2 H, *J* = 5.5, 3.1 Hz, Phth), 5.95-5.74 (m, 3 H, CH=CH + *CH*NPhth), 5.10 (d, 1 H, *J* = 8.8, Hz, *CH*O), 4.00 (dd, 1 H, *J* = 13.3, 10.4 Hz, *CH*$_2$CHNPhth), 3.86 (s, 3 H, OCH_3), 3.72 (s, 3 H, OCH_3), 2.55 (dd, 1 H, *J* = 13.3, 5.8 Hz, *CH*$_2$CHNPhth), 2.10-1.95 (m, 2 H, *CH*$_2$CH=CH), 1.46-1.30 (m, 2 H, CH_2*CH*$_2$$CH_3$), 0.89 (t, 3 H, *J* = 7.3 Hz, CH_2CH_2*CH*$_3$);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 167.5, 167.4, 137.0, 134.4, 131.7, 126.1, 123.6, 82.8, 79.3, 64.5, 53.4, 52.8, 34.3, 32.9, 22.2, 13.7;

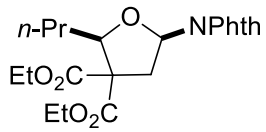
IR 2957 (w), 2932 (w), 2872 (w), 1777 (w), 1733 (s), 1712 (s), 1463 (w), 1454 (w), 1435 (w), 1376 (m), 1363 (m), 1343 (w), 1268 (s), 1233 (m), 1208 (m), 1129 (m), 1103 (m), 1078 (m), 1057 (w), 1040 (m), 1017 (m), 1006 (m), 975 (m), 962 (m), 908 (m), 879 (m), 863 (m), 802 (w), 723 (s), 707 (m), 687 (w), 658 (w);

HRMS (ESI) calcd for $C_{21}H_{24}NO_7^+$ $[M+H]^+$ 402.1547; found 402.1540.

Diethyl 5-(1,3-dioxoisoindolin-2-yl)-2-propyldihydrofuran-3,3(2H)-dicarboxylate (4ai)

Flash chromatography afforded the title compound (81 mg, 0.19 mmol, 94% yield) as a sticky wax, as an inseparable mixture of diastereoisomers; dr = 9:1 determined by integration of ^{1}H NMR signals: *δminor* 6.29 (dd), *δmajor* 5.91 ppm (dd).

Recrystallization from *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).



4ai

R$_f$ 0.63 (*n*-hex/EtOAc 6/4);

Mp 82-85 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, 2 H, *J* = 5.6, 3.2 Hz, Phth), 7.77 (dd, 2 H, *J* = 5.6, 3.2 Hz, Phth), 5.91 (dd, 1 H, *J* = 10.2, 6.0 Hz, *CH*NPhth), 4.66 (dd, 1 H, *J* = 10.8, 2.3 Hz, *CH*O), 4.40-4.20 (m, 4 H, O*CH*$_2$$CH_3$), 3.89 (dd, 1 H, *J* = 13.4, 10.2 Hz, *CH*$_2$CHNPhth), 2.55 (dd, 1 H, *J* = 13.4, 6.0 Hz, *CH*$_2$CHNPhth), 2.03-1.91 (m, 1 H, *n*-Pr), 1.58-1.37 (m, 3 H, *n*-Pr), 1.34 (t, 3 H, *J* = 7.0 Hz, OCH_2*CH*$_3$), 1.33 (t, 3 H, *J* = 7.3 Hz, CH_2CH_2*CH*$_3$), 0.94 (t, 3 H, *J* = 7.0 Hz, OCH_2*CH*$_3$);

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 167.9, 167.3, 134.4, 131.9, 123.6, 80.8, 78.9, 63.6, 62.2, 61.9, 33.6, 33.3, 19.3, 14.0, 13.8;[5]

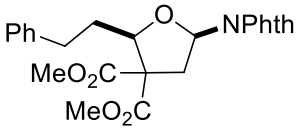
IR 2963 (w), 2938 (w), 2874 (w), 1781 (w), 1721 (s), 1469 (w), 1369 (m), 1296 (m), 1263 (s), 1228 (m), 1192 (m), 1145 (m), 1120 (m), 1092 (m), 1070 (m), 1037 (m), 1017 (m), 876 (w), 862 (w), 720 (s), 677 (w), 656 (w);

[5] Two methyl carbons are overlapping.

HRMS (ESI) calcd for $C_{21}H_{26}NO_7^+$ $[M+H]^+$ 404.1704; found: 404.1713.

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-2-phenethyldihydrofuran-3,3(2H)-dicarboxylate (4bj)

Flash chromatography afforded the title compound (77 mg, 0.18 mmol, 89% yield) as a transparent oil, as an inseparable mixture of diastereoisomers; dr = 20:1 determined by integration of ^{1}H NMR signals: *δminor* 6.33 (dd), *δmajor* 5.97 ppm (dd).



4bj

R$_f$ 0.51 (*n*-hex/EtOAc 6/4);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, 2 H, *J* = 5.3, 3.0 Hz, Phth), 7.79 (dd, 2 H, *J* = 5.3, 3.0 Hz, Phth), 7.37-7.02 (m, 5 H, Ph), 5.97 (dd, 1 H, *J* = 10.0, 6.1 Hz, *CH*NPhth), 4.68 (dd, 1 H, *J* = 11.2, 2.6 Hz, *CH*O), 3.90 (dd, 1 H, *J* = 13.2, 9.9 Hz, *CH$_2$*CHNPhth), 3.85 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 2.93-2.80 (m, 1 H, CH_2Ph), 2.67-2.54 (m, 2 H, *CH$_2$*CHNPhth+ CH_2Ph), 2.43-2.28 (m, 1 H, *CH$_2$*CH_2Ph), 1.80-1.67 (m, 1 H, *CH$_2$*CH_2Ph);

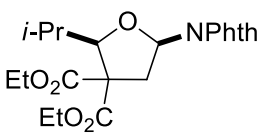
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 168.1, 167.3, 141.8, 134.4, 131.8, 128.7, 128.3, 125.8, 123.7, 80.5, 79.1, 63.6, 53.4, 52.9, 33.6, 33.2, 32.2;

IR 3028 (w), 2954 (w), 1780 (w), 1720 (s), 1468 (w), 1456 (w), 1436 (w), 1370 (m), 1333 (w), 1263 (m), 1229 (m), 1205 (m), 1134 (m), 1090 (m), 1074 (m), 1046 (m), 1016 (m), 999 (w), 973 (m), 943 (w), 914 (m), 876 (w), 796 (w), 720 (s), 702 (m), 684 (w), 673 (m), 658 (w), 630 (w);

HRMS (ESI) calcd for $C_{24}H_{24}NO_7^+$ $[M+H]^+$ 438.1547; found 438.1549.

Diethyl 5-(1,3-dioxoisoindolin-2-yl)-2-isopropyldihydrofuran-3,3(2H)-dicarboxylate (4ak)

Flash chromatography afforded the title compound (80 mg, 0.20 mmol, 99% yield) as a transparent oil, as an inseparable mixture of diastereoisomers; dr = 7:1 determined by integration of ^{1}H NMR signals: *δminor* 6.25 (pseudo t), *δmajor* 5.82 ppm (dd).



4ak

Rf 0.59 (*n*-hex/EtOAc 6/4);

^{1}H NMR (*cis*+*trans* mixture, 400 MHz, $CDCl_3$) δ 7.89 (dd, 2 H, *J* = 5.6, 3.0 Hz, Phth), 7.76 (dd, 2 H, *J* = 5.6, 3.0 Hz, Phth), 6.25 (pseudo t, 1 H_{trans}, *J* = 7.3 Hz, *CH*NPhth), 5.82 (dd, 1 H_{cis}, *J* = 9.8, 6.1 Hz, *CH*NPhth), 4.77 (d, 1 H_{trans}, *J* = 8.2 Hz, *CH*O), 4.38-4.21 (m, 5 H, O*CH$_2$*CH_3 + *CH_{cis}*O), 3.89 (dd, 1 H*cis*, *J* = 13.2, 9.8 Hz, *CH$_2$*CHNPhth), 3.13-3.04 (m, 2 H_{trans}, *CH$_2$*CHNPhth), 2.60 (dd, 1 H*cis*, *J* = 13.2, 6.1 Hz, *CH$_2$*CHNPhth), 2.31 (hept, 1 H_{cis}, *J*

= 6.7 Hz, *i*Pr), 1.88-1.76 (m, 1 H_{trans}, *i*Pr), 1.37-1.28 (m, 6 H, OCH_2CH_3), 1.05 (d, 3 H_{trans}, *J* = 6.7 Hz, *i*Pr), 0.98 (d, 3 H, *J* = 6.7 Hz, *i*-Pr), 0.95 (d, 3 H, *J* = 6.7 Hz, *i*Pr);

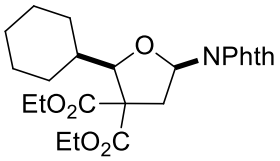
^{13}C NMR (101 MHz, $CDCl_3$, *cis* isomer) δ 170.8, 168.7, 167.3, 134.4, 131.8, 123.6, 86.6, 78.2, 62.3, 62.2, 61.9, 35.6, 29.6, 20.2, 18.8, 14.0, 13.9;

IR 2983 (w), 2939 (w), 2909 (w), 2908 (w), 2876 (w), 1781 (w), 1720 (s), 1612 (w), 1470 (w), 1447 (w), 1369 (s), 1329 (m), 1298 (m), 1262 (m), 1231 (m), 1192 (m), 1141 (m), 1117 (m), 1092 (m), 1044 (m), 1026 (m), 1017 (m), 1006 (m), 952 (w), 868 (w), 796 (w), 720 (s), 654 (w), 635 (w);

HRMS (ESI) calcd for $C_{21}H_{26}NO_7^+$ $[M+H]^+$ 404.1704; found 404.1698.

Diethyl 2-cyclohexyl-5-(1,3-dioxoisoindolin-2-yl)dihydrofuran-3,3(2H)-dicarboxylate (4al)

Flash chromatography afforded the title compound (79 mg, 0.18 mmol, 90% yield) as a transparent oil, as an inseparable mixture of diastereoisomers; dr = 7:1 determined by integration of ^{1}H NMR signals: *δminor* 6.25 (pseudo t), *δmajor* 5.81 ppm (dd).



4al

R_f 0.60 (*n*-hex/EtOAc 6/4);

^{1}H NMR (*cis*+*trans* mixture, 400 MHz, $CDCl_3$) δ 7.89 (dd, 2 H, *J* = 5.6, 2.9 Hz, Phth), 7.76 (dd, 2 H, *J* = 5.6, 2.9 Hz, Phth), 6.25 (pseudo t, 1 H_{trans}, *J* = 7.3 Hz, *CH*NPhth), 5.81 (dd, 1 H_{cis}, *J* = 9.6, 6.2 Hz, *CH*NPhth), 4.81 (d, 1 H_{trans}, *J* = 8.2 Hz, *CH*O), 4.36-4.20 (m, 5 H, OCH_2CH_3 + $CH_{cis}O$), 3.86 (dd, 1 H*cis*, *J* = 13.2, 9.6 Hz, CH_2CHNPhth), 3.08 (pseudo d, 2 H_{trans}, *J* = 7.3 Hz, CH_2CHNPhth), 2.60 (dd, 1 H*cis*, *J* = 13.2, 6.2 Hz, CH_2CHNPhth), 2.04-1.93 (m, 1 H, cyclohexyl), 1.89-1.77 (m, 1 H, cyclohexyl), 1.77-1.52 (m, 4 H, cyclohexyl), 1.34 (t, 3 H, *J* = 7.1 Hz, OCH_2CH_3), 1.31 (t, 3 H, *J* = 7.1 Hz, OCH_2CH_3), 1.27-1.03 (m, 5 H, cyclohexyl);

^{13}C NMR (101 MHz, $CDCl_3$, *cis* isomer) δ 170.9, 168.9, 167.3, 134.3, 131.8, 123.6, 85.8, 78.1, 62.1, 61.8, 39.2, 36.0, 30.4, 28.7, 26.2, 26.1, 25.9, 13.9, 14.0; [6]

IR 2981 (w), 2936 (w), 1782 (w), 1720 (s), 1468 (w), 1452 (w), 1368 (m), 1303 (m), 1258 (m), 1218 (m), 1195 (m), 1139 (m), 1115 (m), 1090 (m), 1073 (m), 1015 (m), 914 (m), 873 (m), 763 (m), 720 (s), 651 (m);

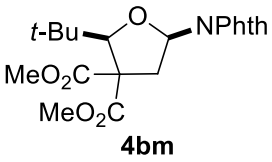
HRMS (ESI) calcd for $C_{24}H_{30}NO_7^+$ $[M+H]^+$ 444.2017; found 444.2019.

Dimethyl 2-(tert-butyl)-5-(1,3-dioxoisoindolin-2-yl)dihydrofuran-3,3(2H)-dicarboxylate (4bm)

[6] Two carbons are overlapping.

Flash chromatography afforded the title compound (72 mg, 0.19 mmol, 92% yield) as a transparent sticky oil, as an inseparable mixture of diastereoisomers; dr = 9:1 determined by integration of ^{1}H NMR signals: *δminor* 6.28 (dd), *δmajor* 5.67 ppm (dd).

Crystallization in *i*PrOH afforded analytically pure *cis* isomer (dr > 20:1).



4bm

R$_f$ 0.53 (*n*-hex/EtOAc 6/4);

Mp 171-173 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, 2 H, *J* = 5.3, 3.0 Hz, Phth), 7.77 (dd, 2 H, *J* = 5.3, 3.0 Hz, Phth), 5.67 (dd, 1 H, *J* = 10.8, 5.4 Hz, *CH*NPhth), 4.49 (s, 1 H, *CH*O), 4.10 (dd, 1 H, *J* = 13.0, 10.8 Hz, *CH$_2$*CHNPhth), 3.84 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 2.50 (dd, 1 H, *J* = 13.0, 5.4 Hz, *CH$_2$*CHNPhth), 1.02 (s, 9H, *t*Bu);

^{13}C NMR (101 MHz, $CDCl_3$) 171.6, 169.5, 167.4, 134.4, 131.8, 123.7, 88.3, 77.8, 61.4, 53.3, 52.7, 36.2, 34.7, 26.5;

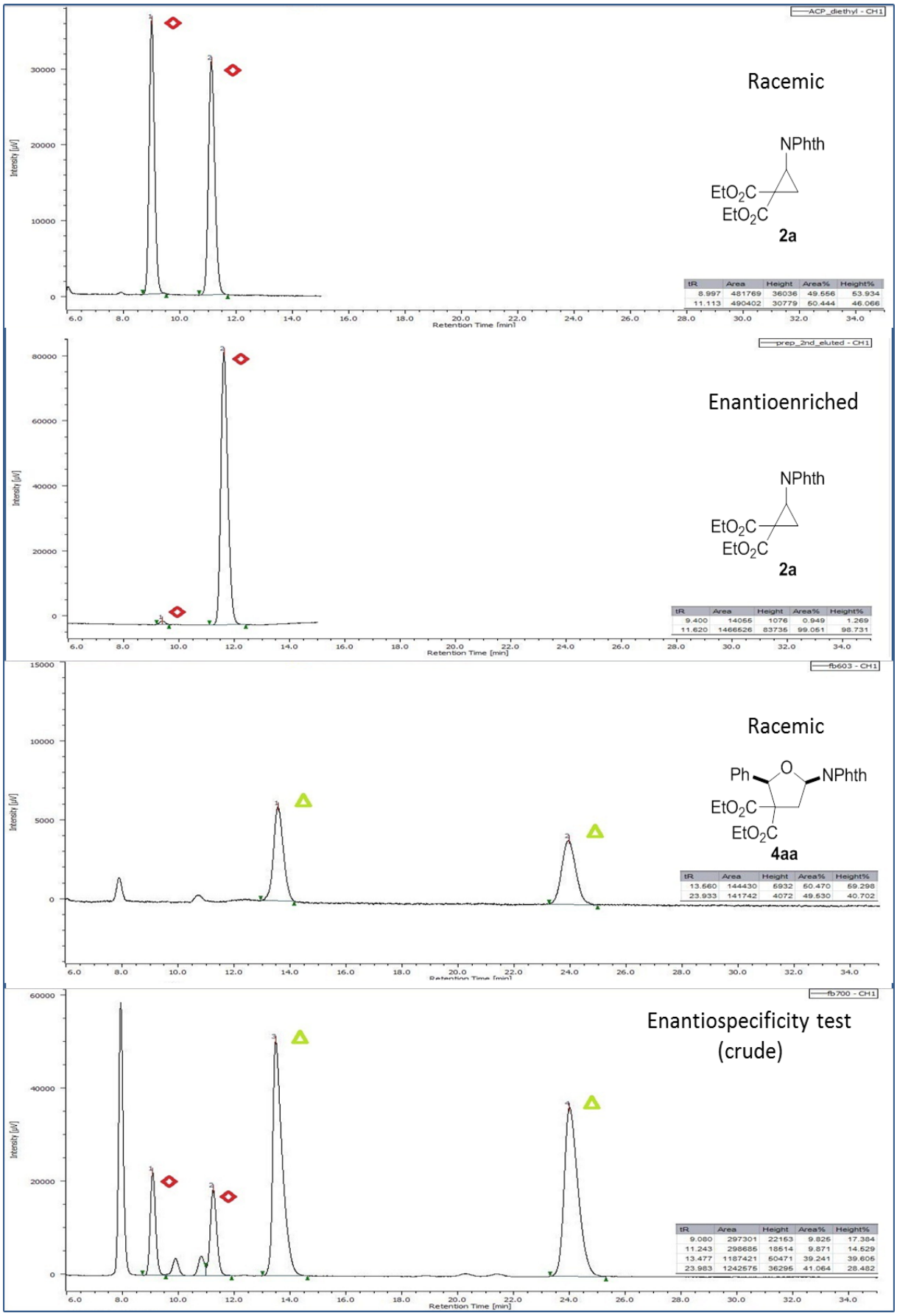
IR 2957 (w), 2866 (w), 1783 (w), 1724 (s), 1723 (s), 1467 (w), 1459 (w), 1436 (w), 1374 (m), 1339 (w), 1266 (m), 1265 (m), 1237 (w), 1236 (w), 1200 (w), 1184 (w), 1183 (w), 1135 (w), 1082 (w), 1081 (w), 1056 (w), 1055 (w), 1029 (w), 1007 (w), 970 (w), 960 (w), 913 (w), 871 (w), 721 (m), 673 (w), 659 (w), 651 (w), 635 (w);

HRMS (ESI) calcd for $C_{20}H_{24}NO_7^+$ $[M+H]^+$ 390.1553; found 390.1563.

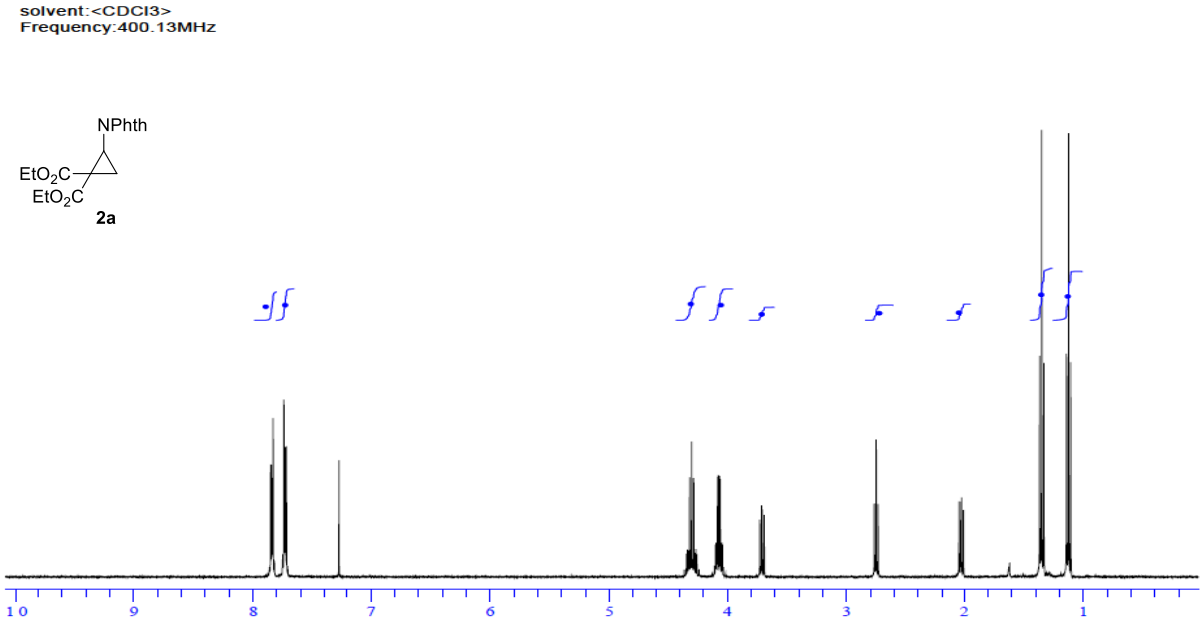
3 Enantiospecificity test

Following the standard procedure for the iron-catalysed [3+2] annulation (S5), using 28 mg (0.080 mmol, 1 eq) of enantioenriched aminocyclopropane **2a** (er = 99:1), 4 mg of $FeCl_3$-Al_2O_3 (4 μmol, 5 mol %) and 4 μL of benzaldehyde (**3a**) (0.04 mmol, 0.5 eq), 18 mg (0.040 mmol, 49 % yield, 99% in relation to aldehyde **3a**, racemic) of **4aa** were isolated, together with 4 mg (0.01 mmol, 14 % yield, racemic) of unreacted **2a** (reaction time = 30 min; if the reaction time was extended to 2 h, only **4aa** was isolated from the crude reaction mixture).

4 HPLC traces



5 Spectra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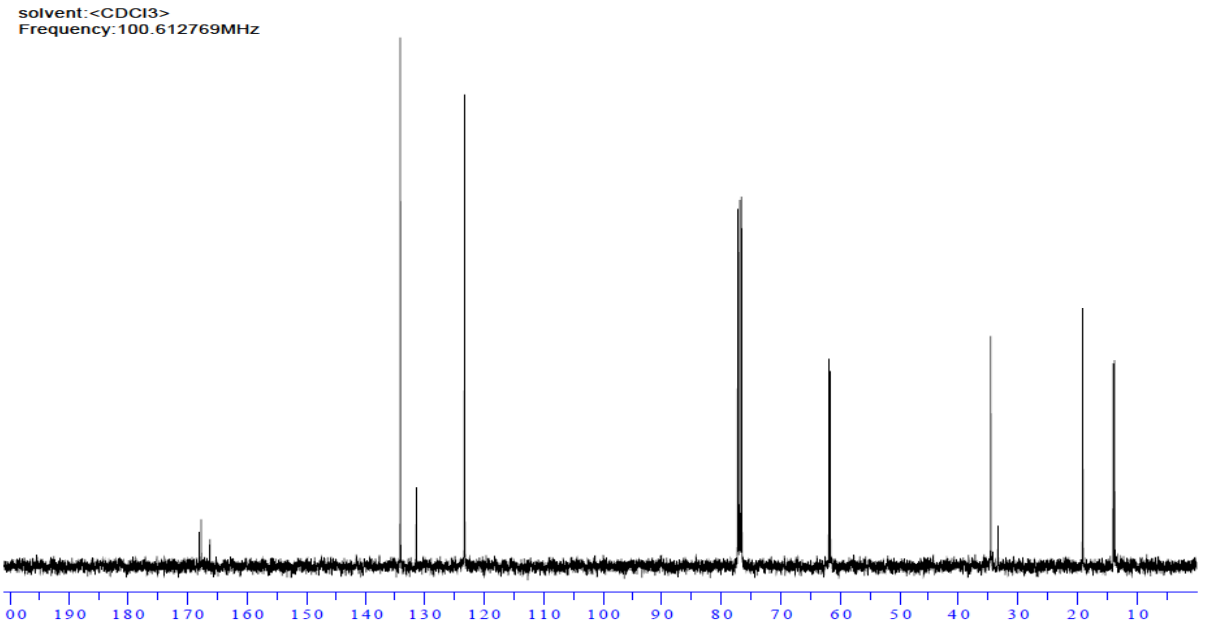
3
2
1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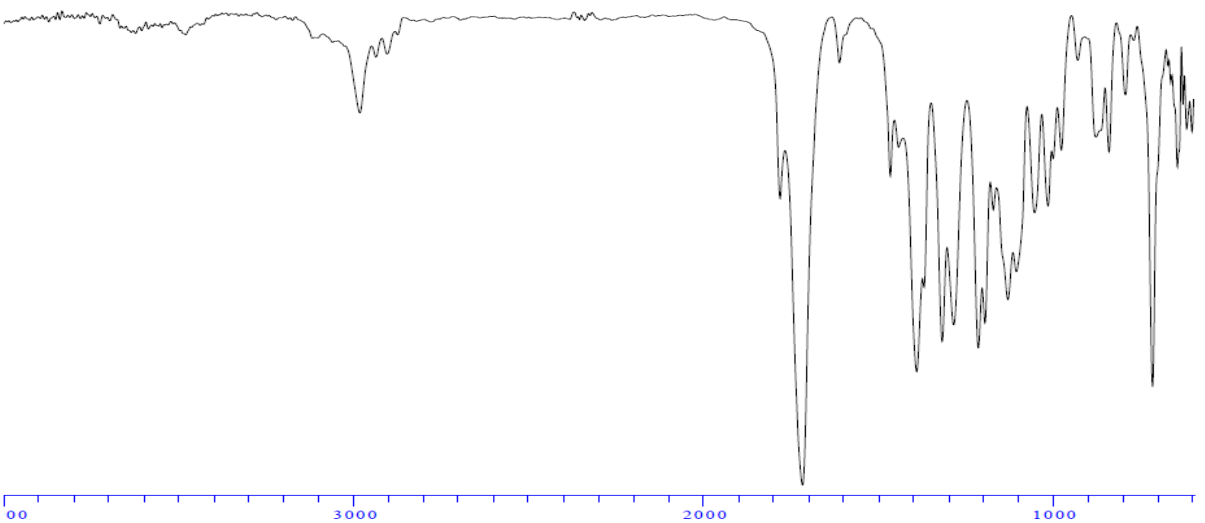
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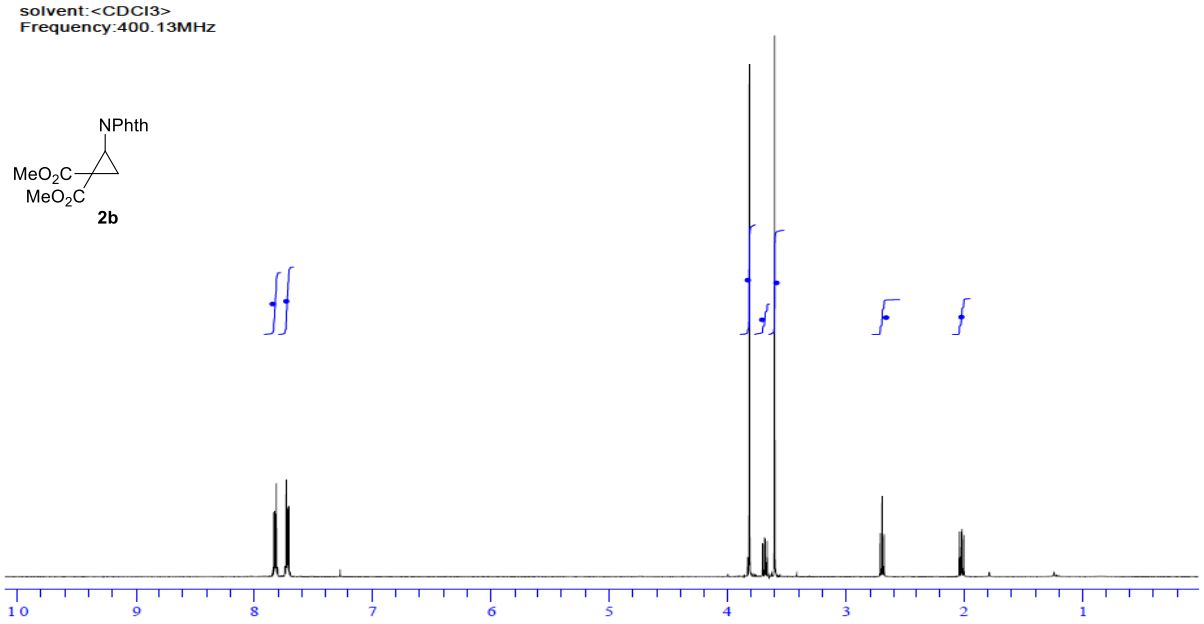
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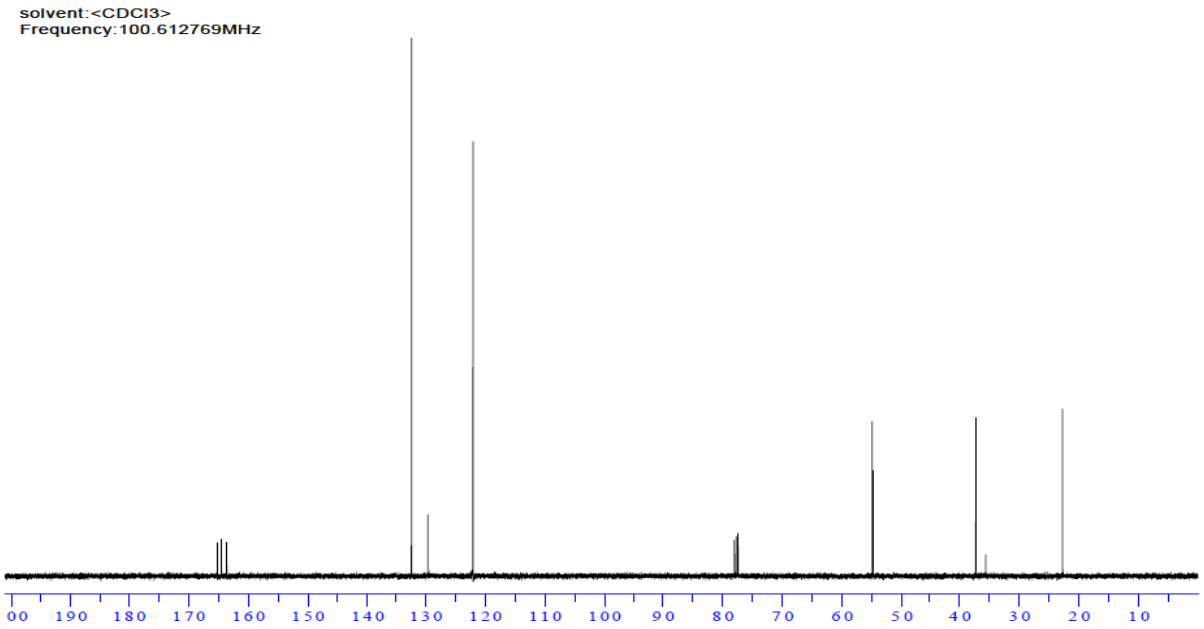
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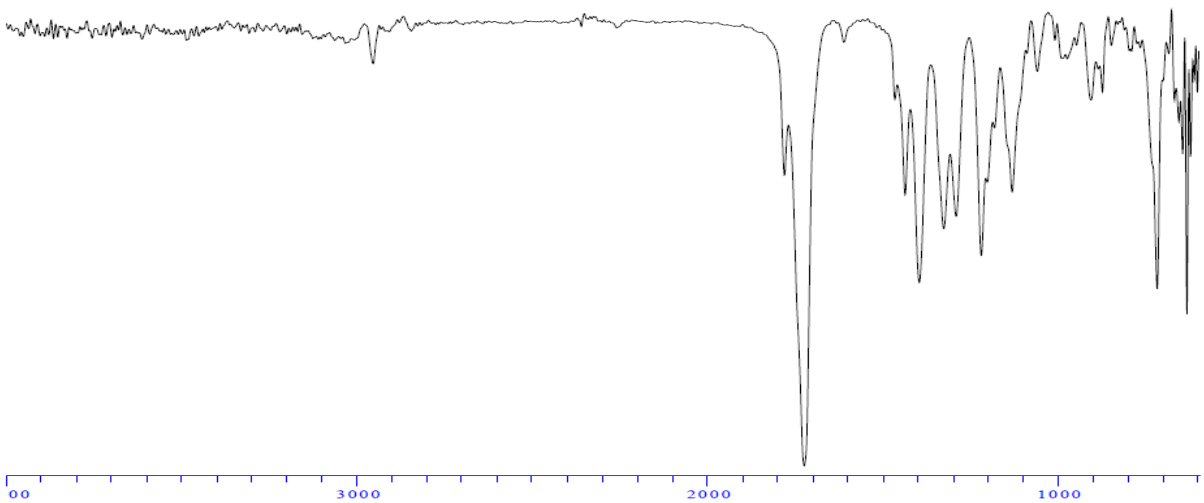
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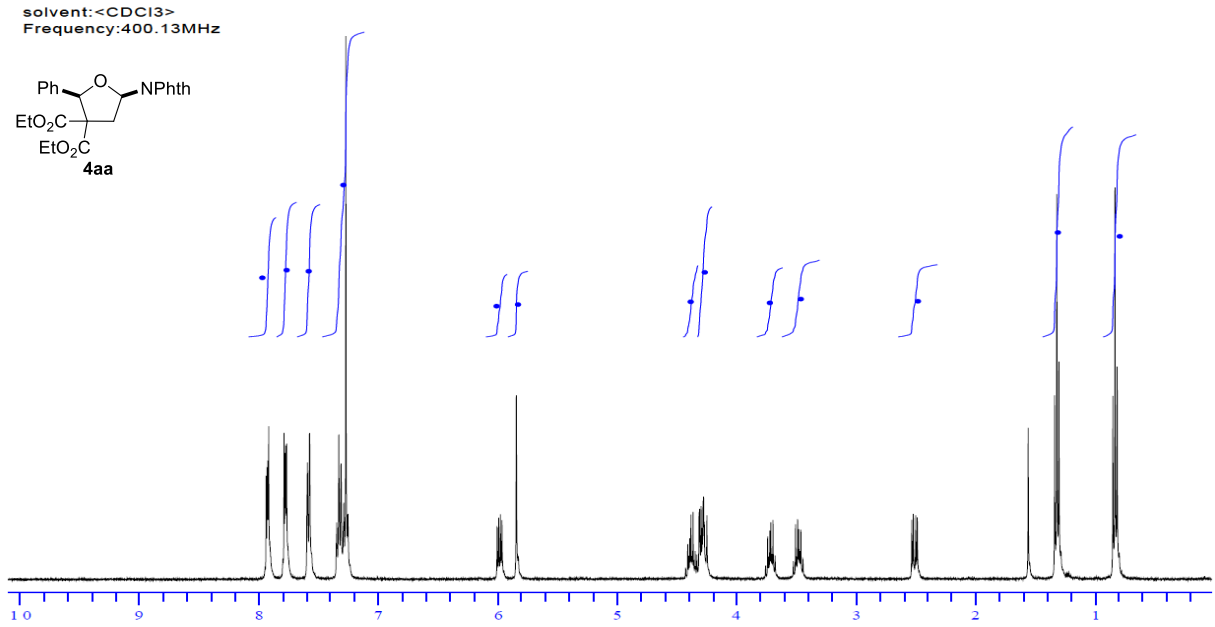
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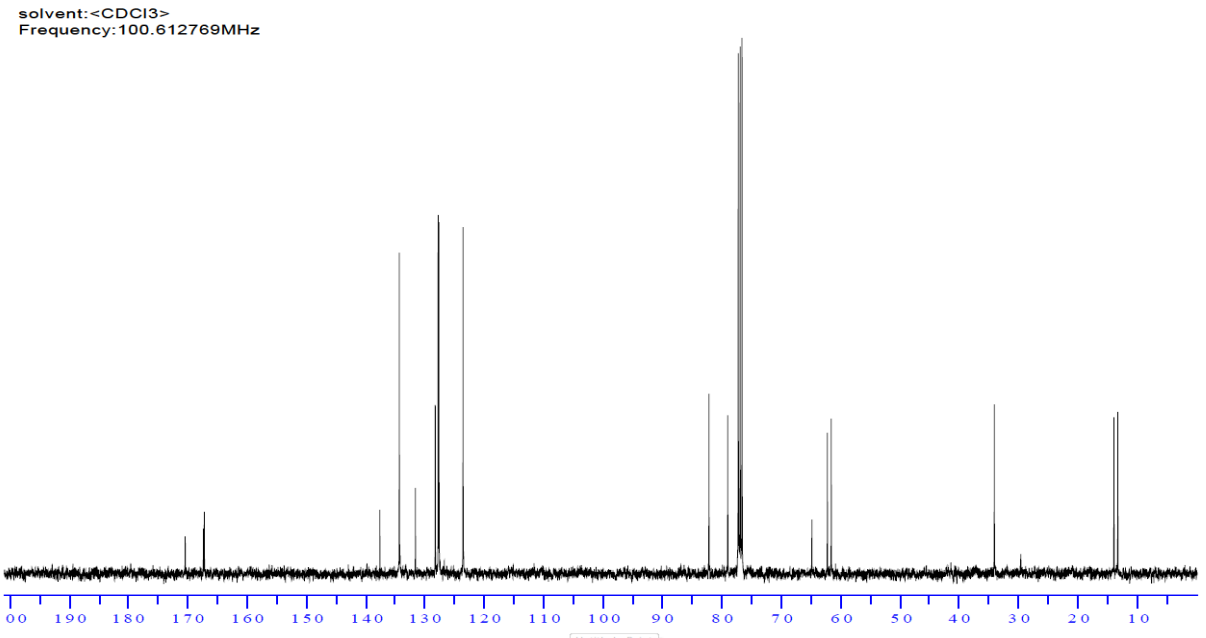
3
2
1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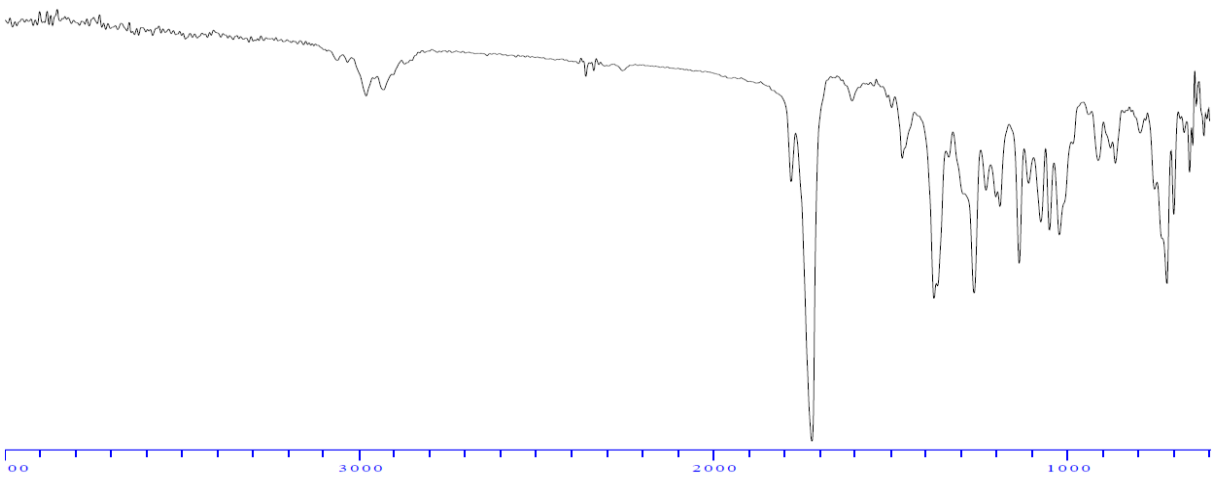
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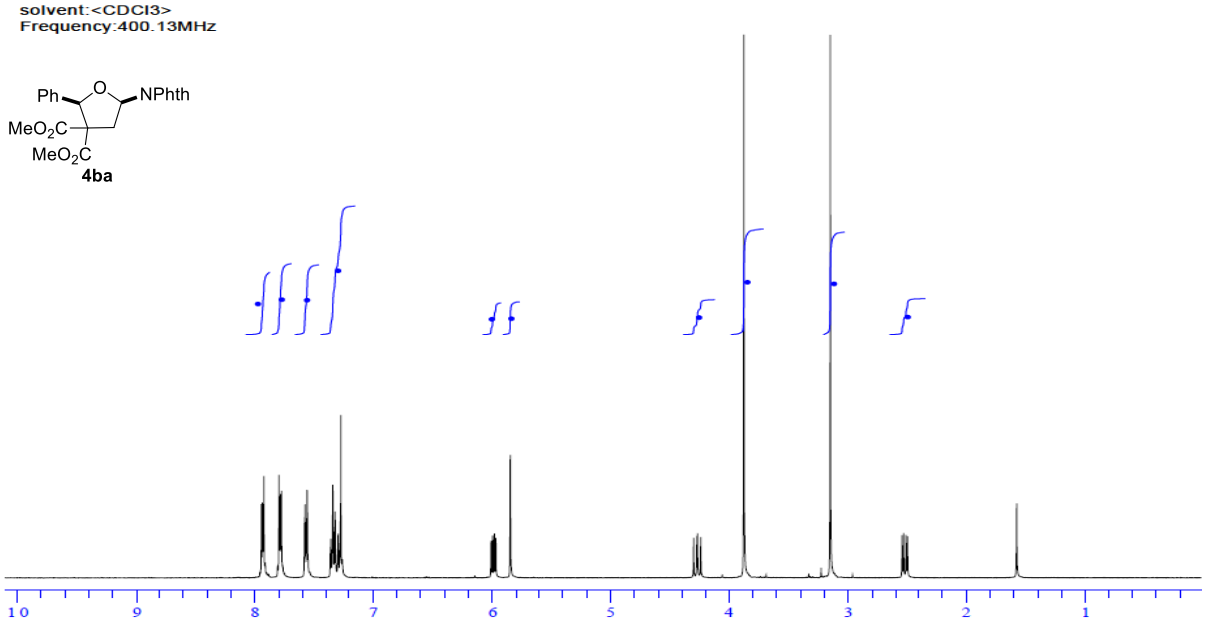
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MeO2C
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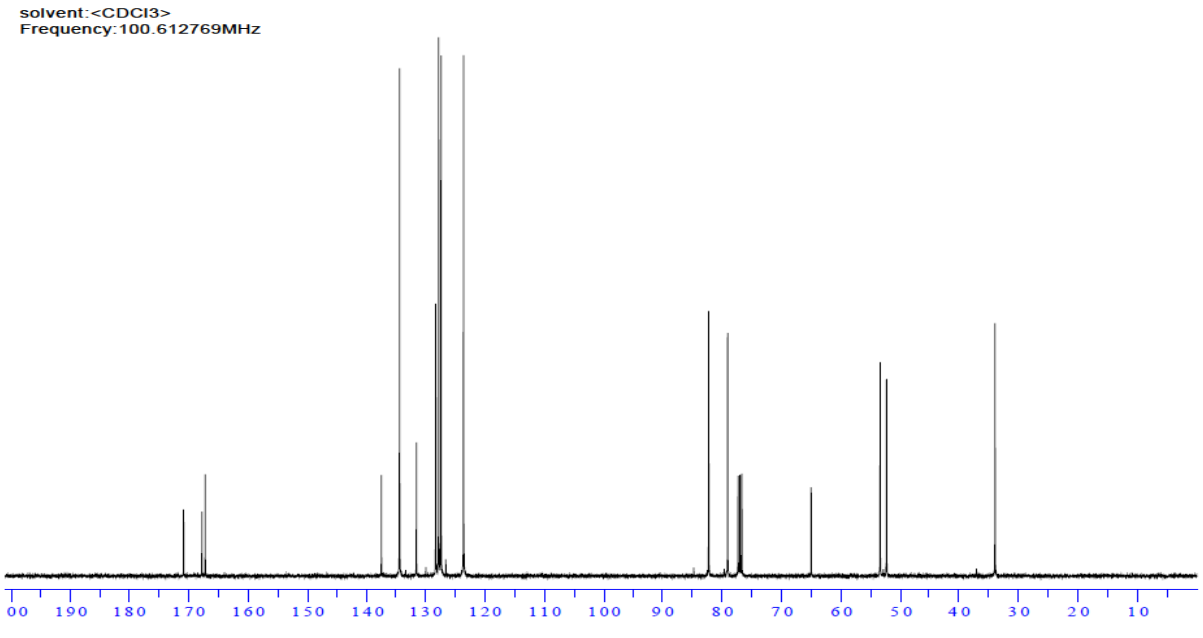
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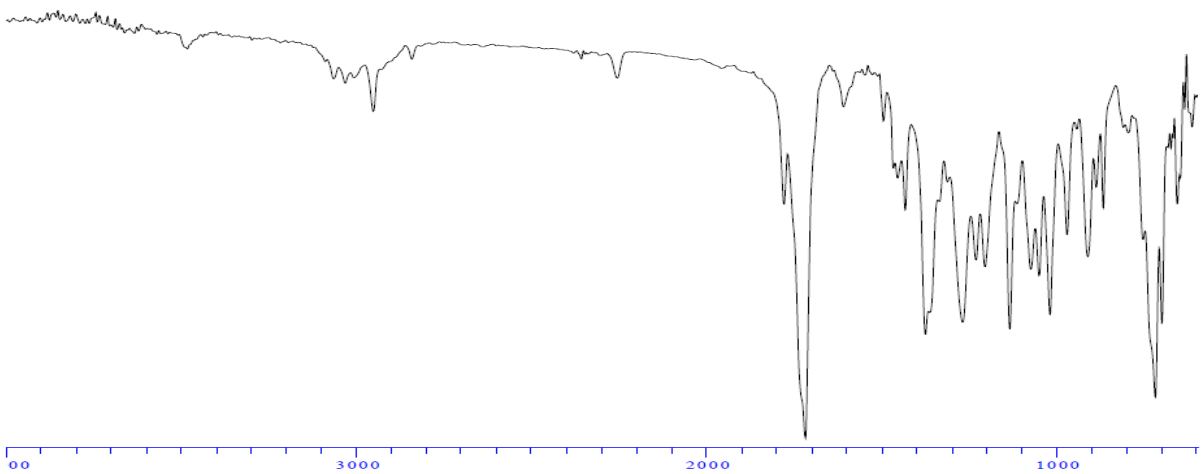
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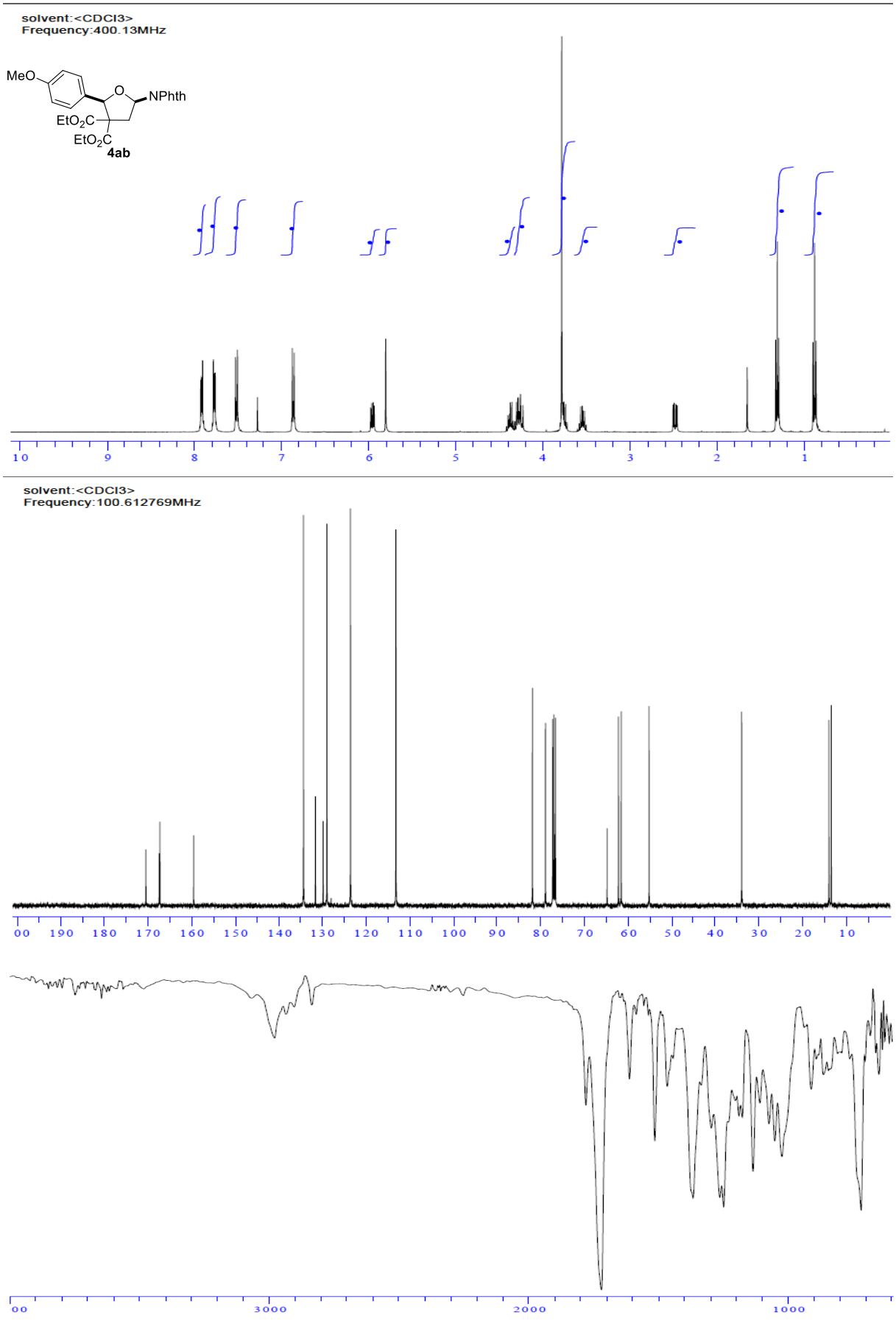
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EtO2C
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10
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6
5
4
3
2
1
solvent:<CDCl3>
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00
190
180
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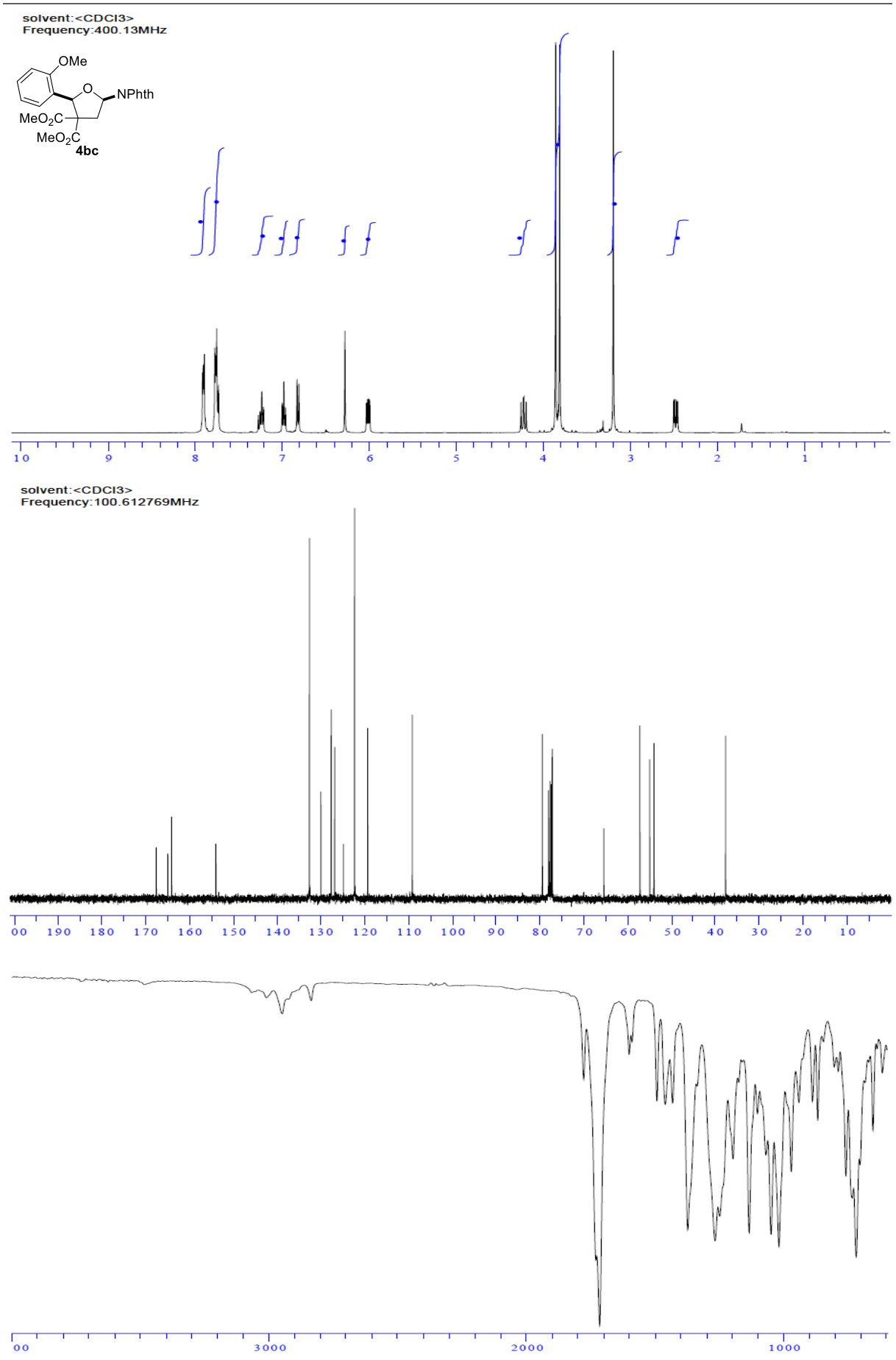
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MeO2C
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2
1
solvent:<CDCl3>
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00
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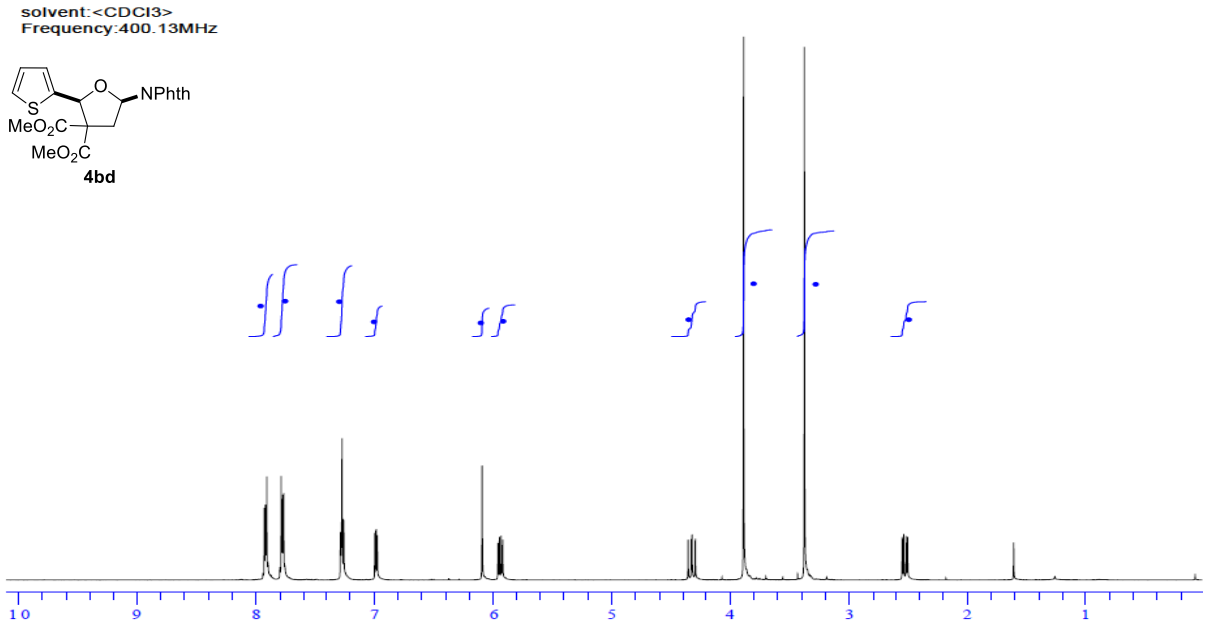
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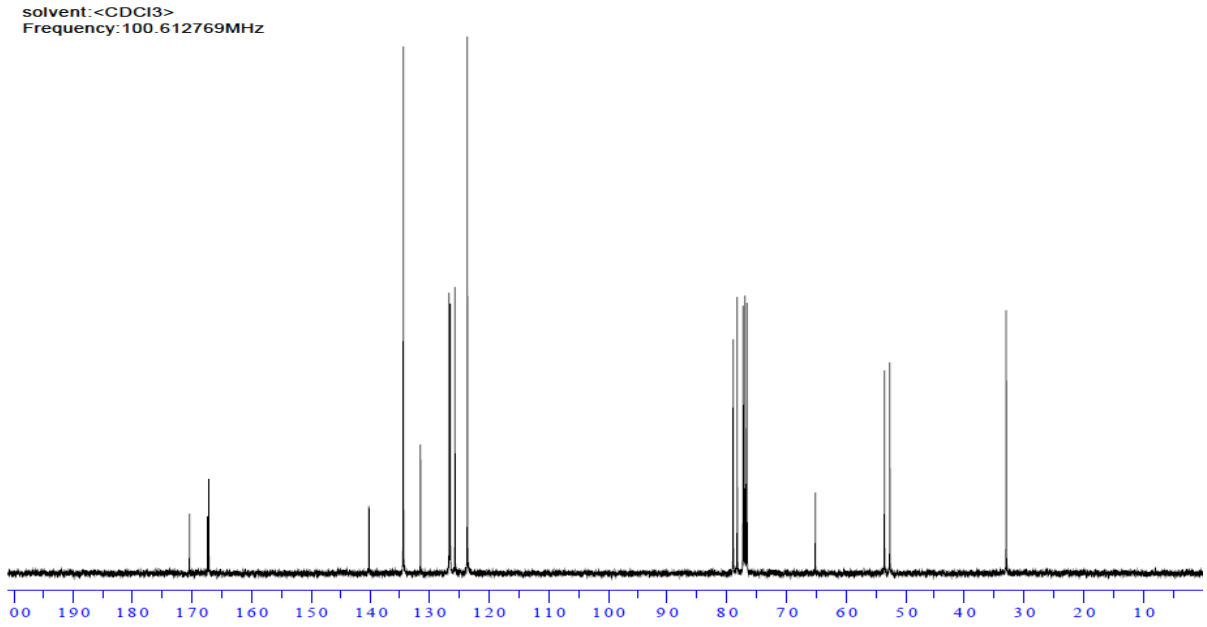
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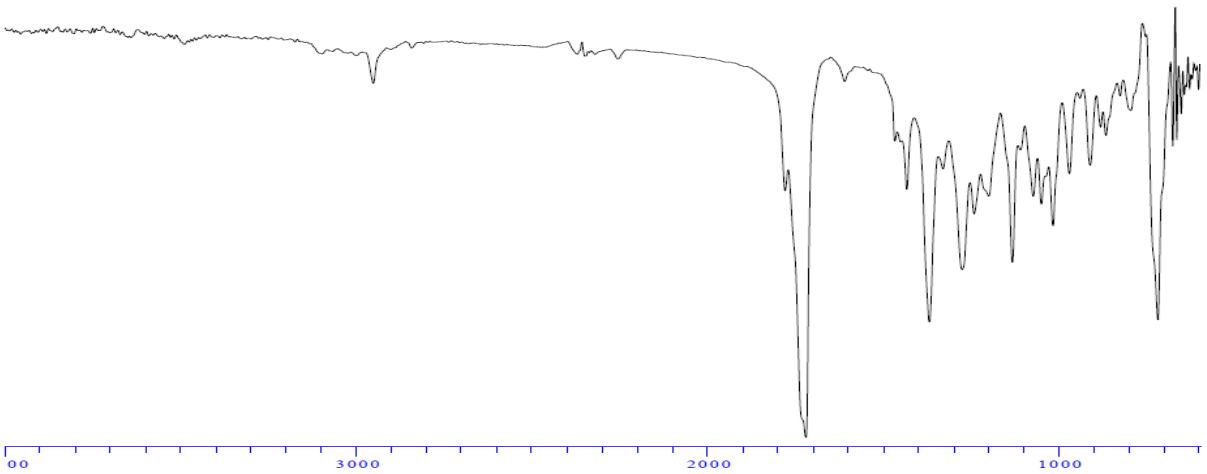
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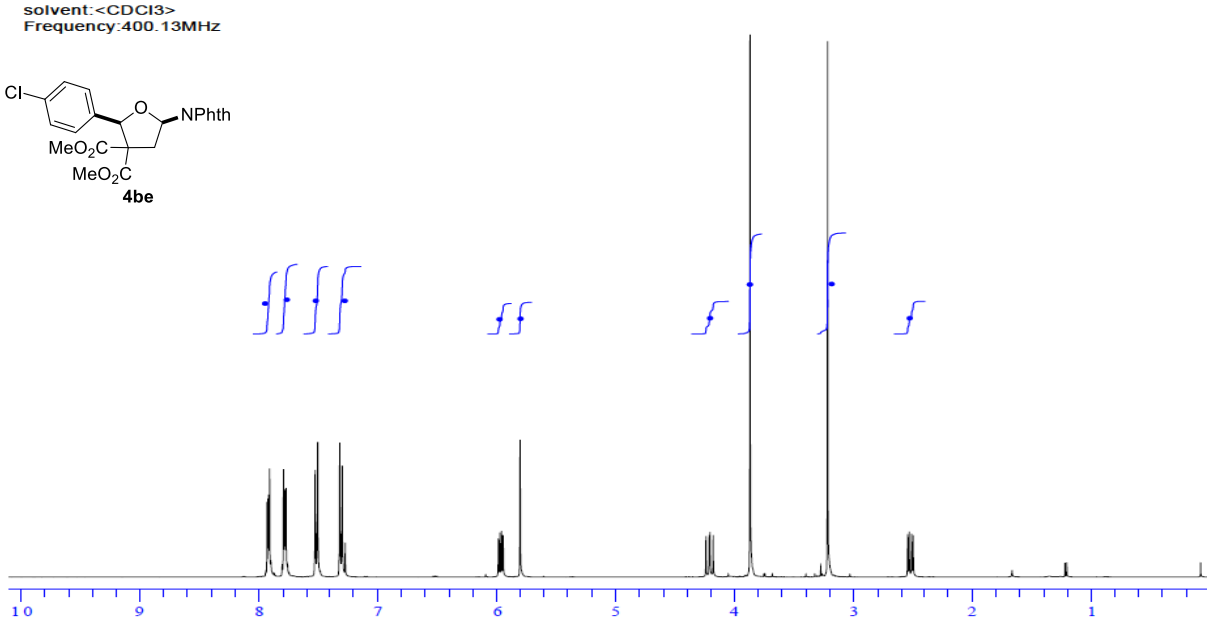
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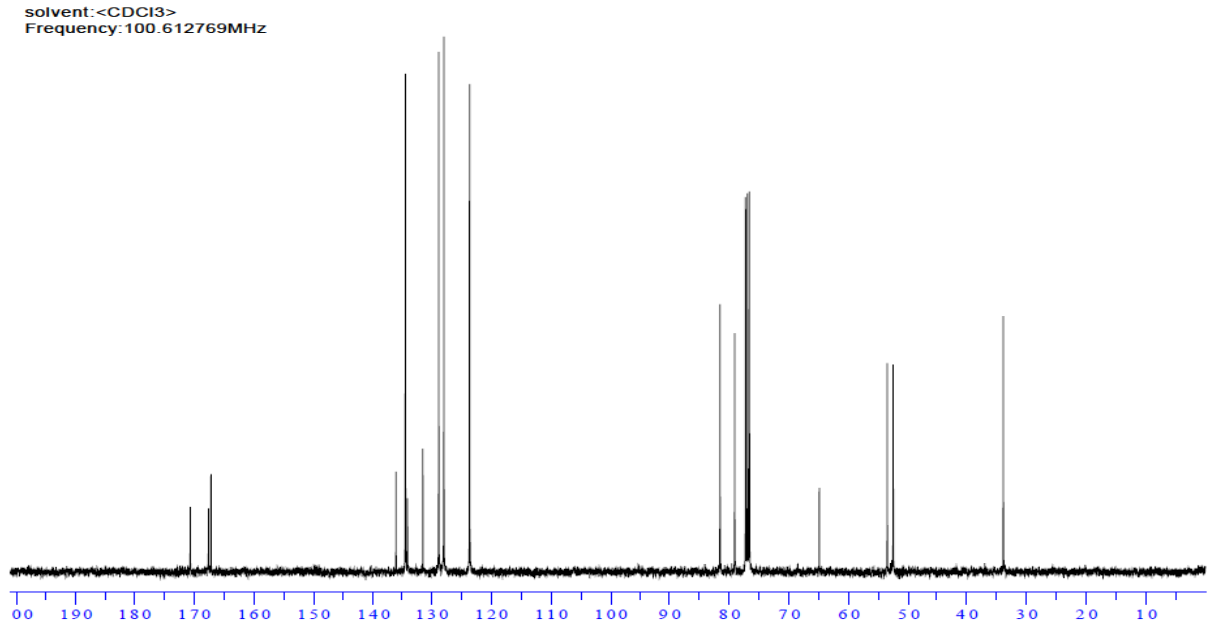
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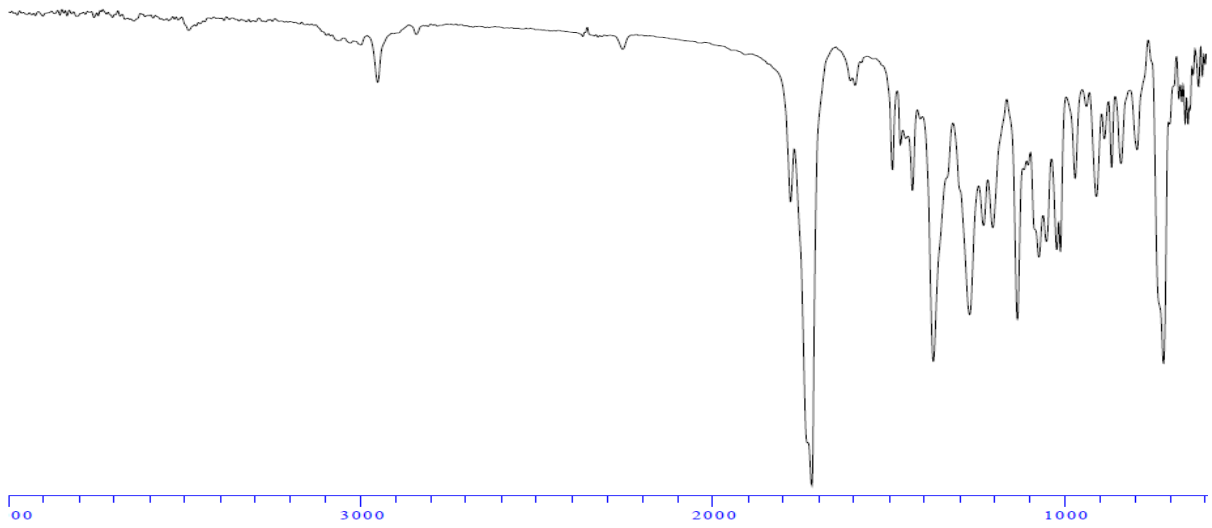
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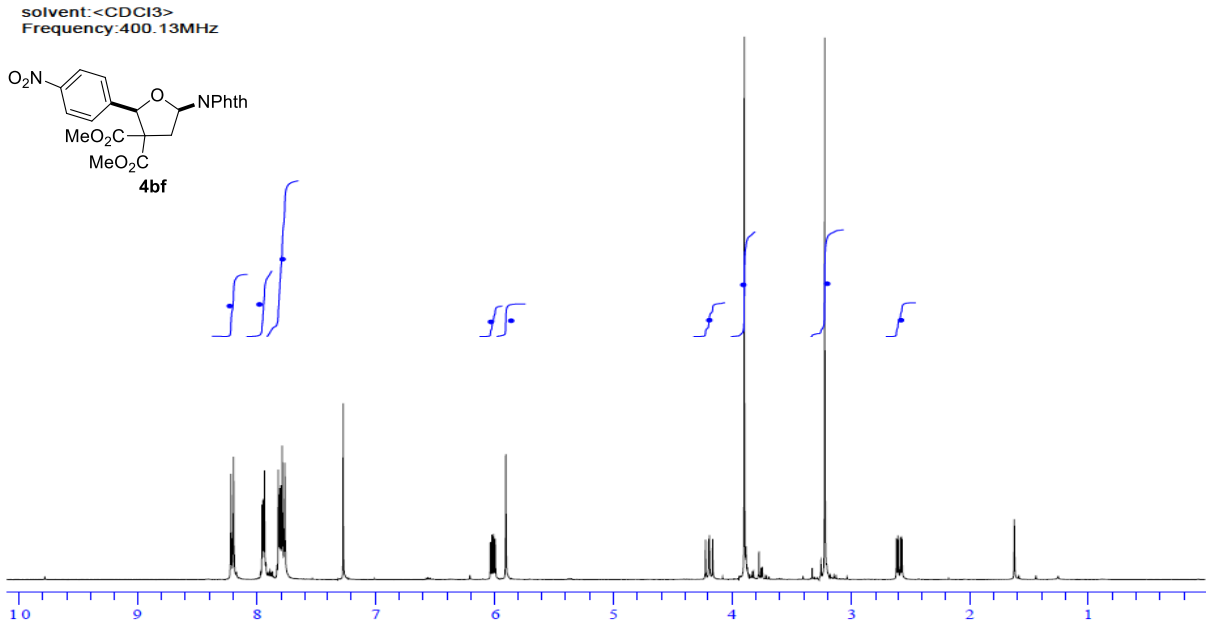
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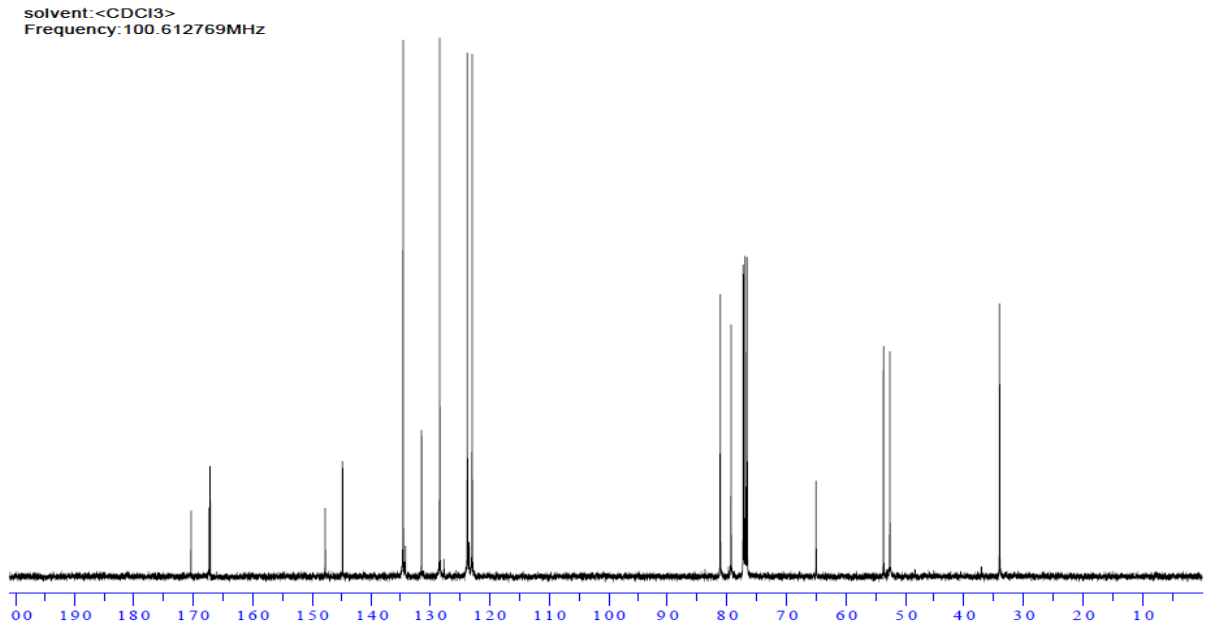
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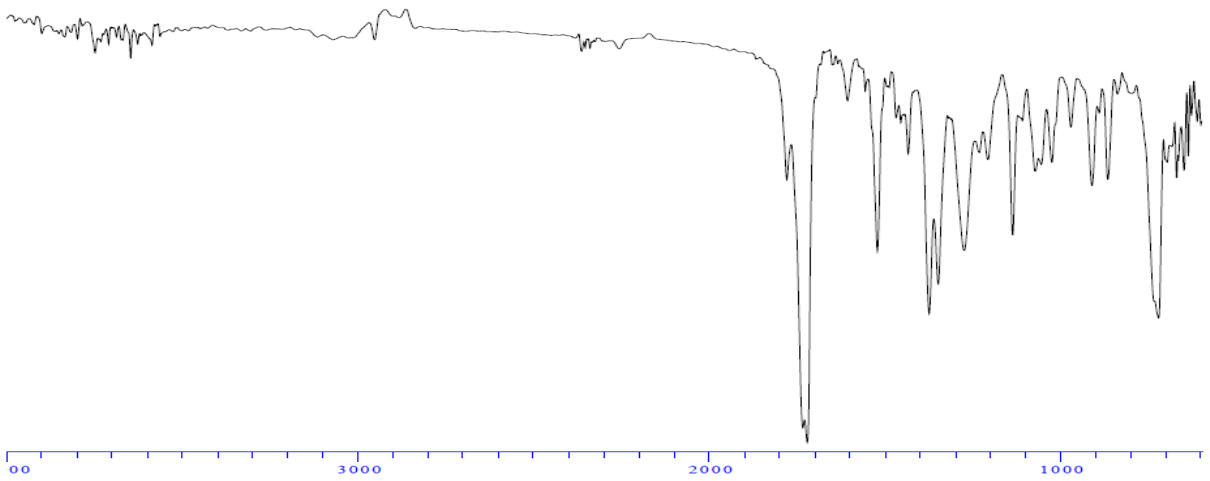
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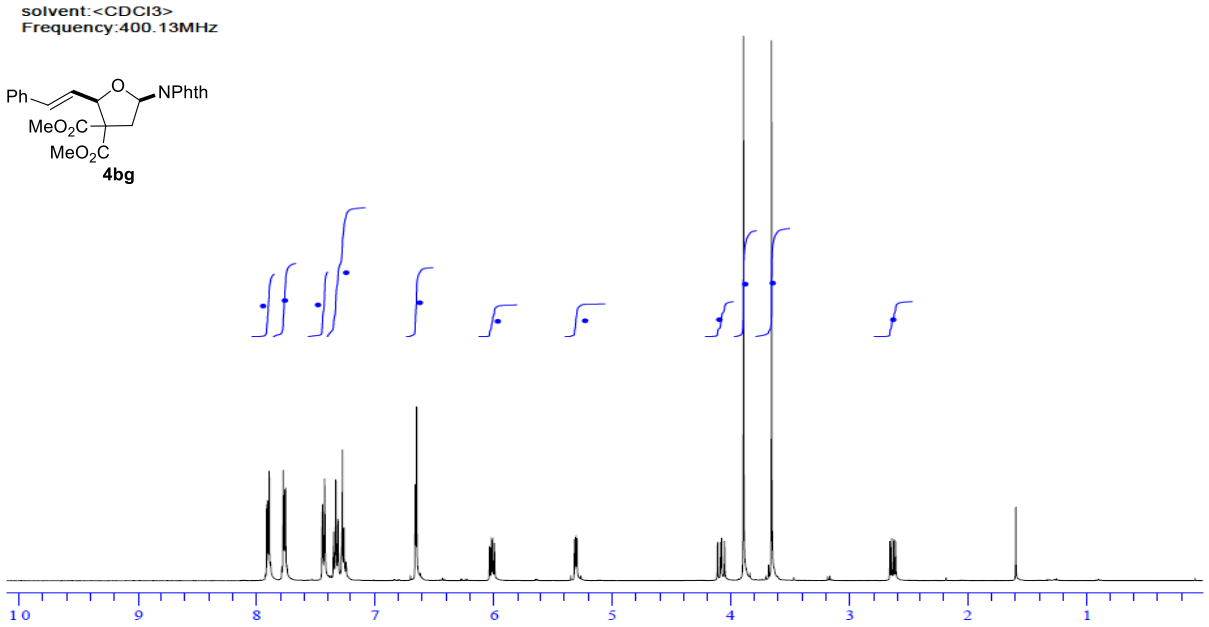
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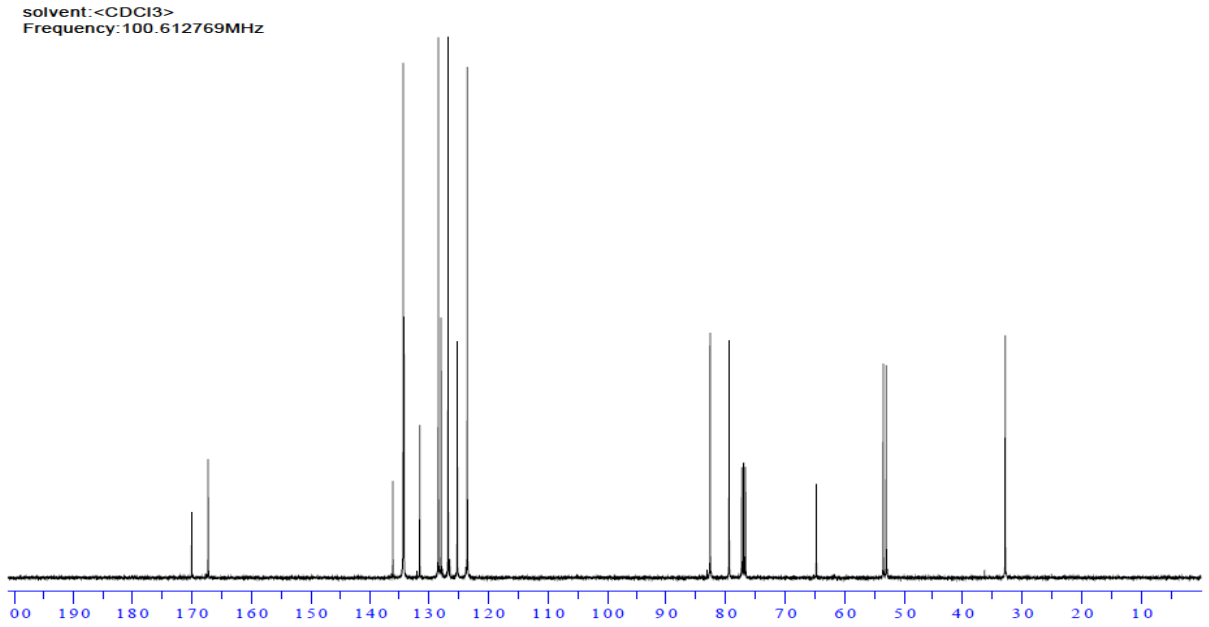
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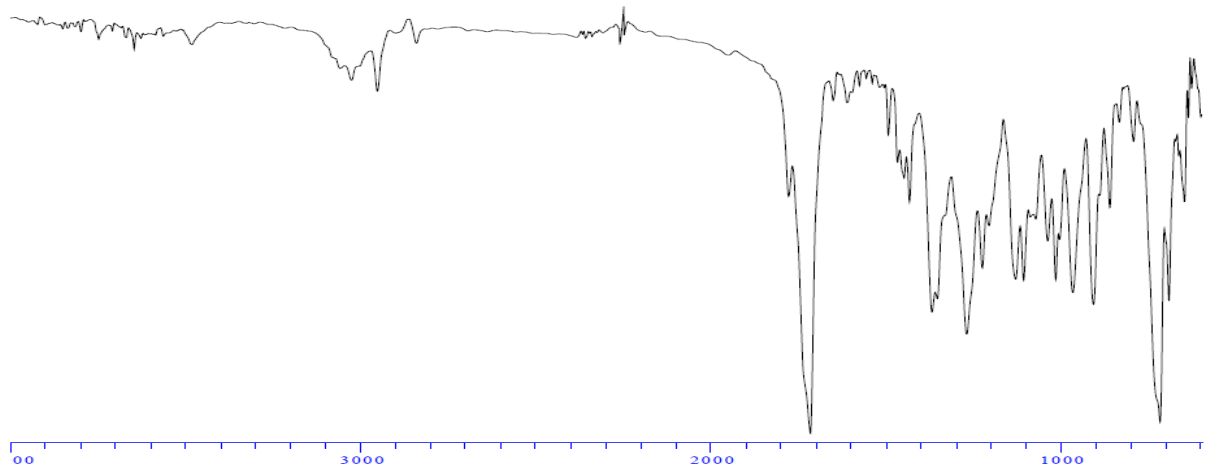
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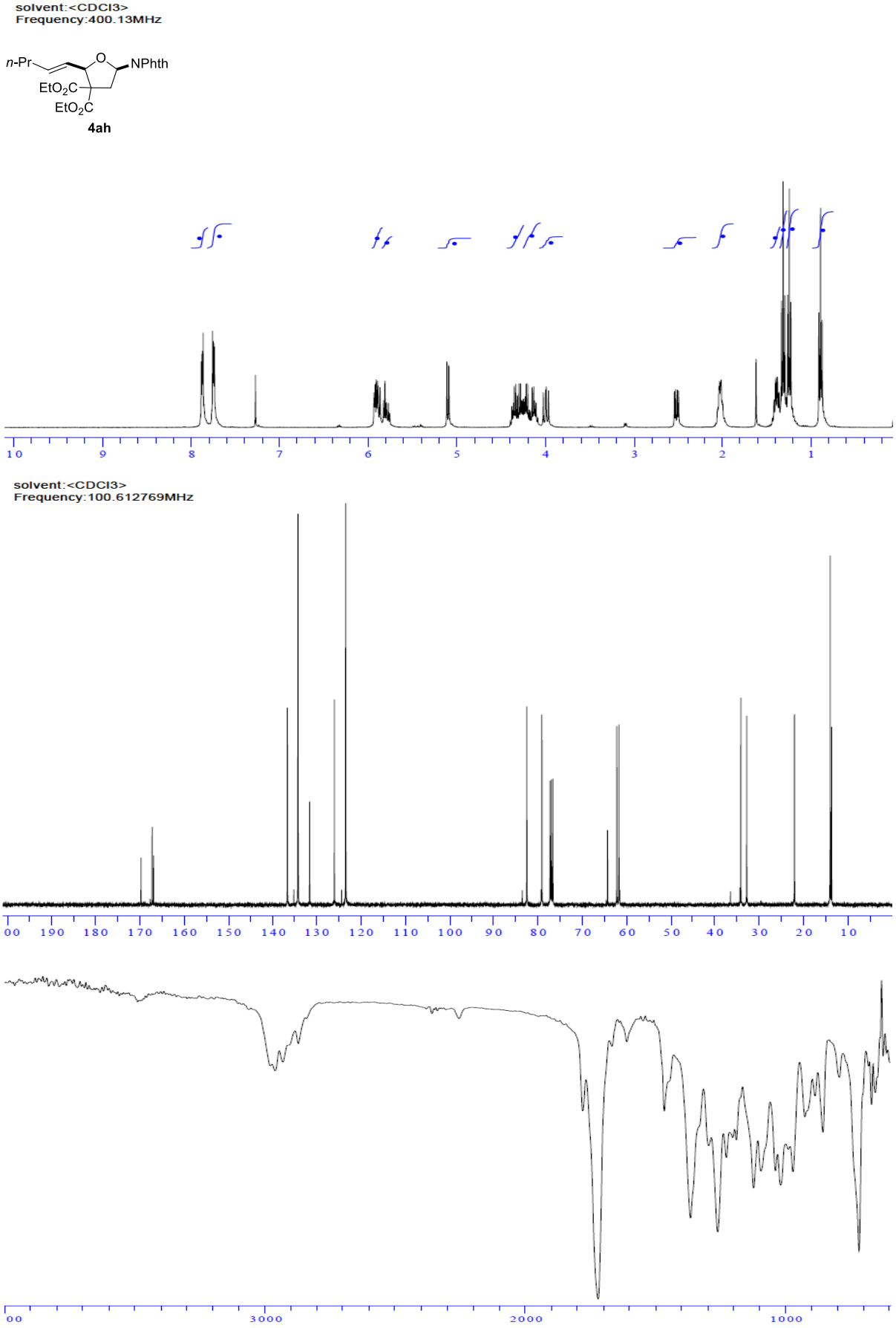
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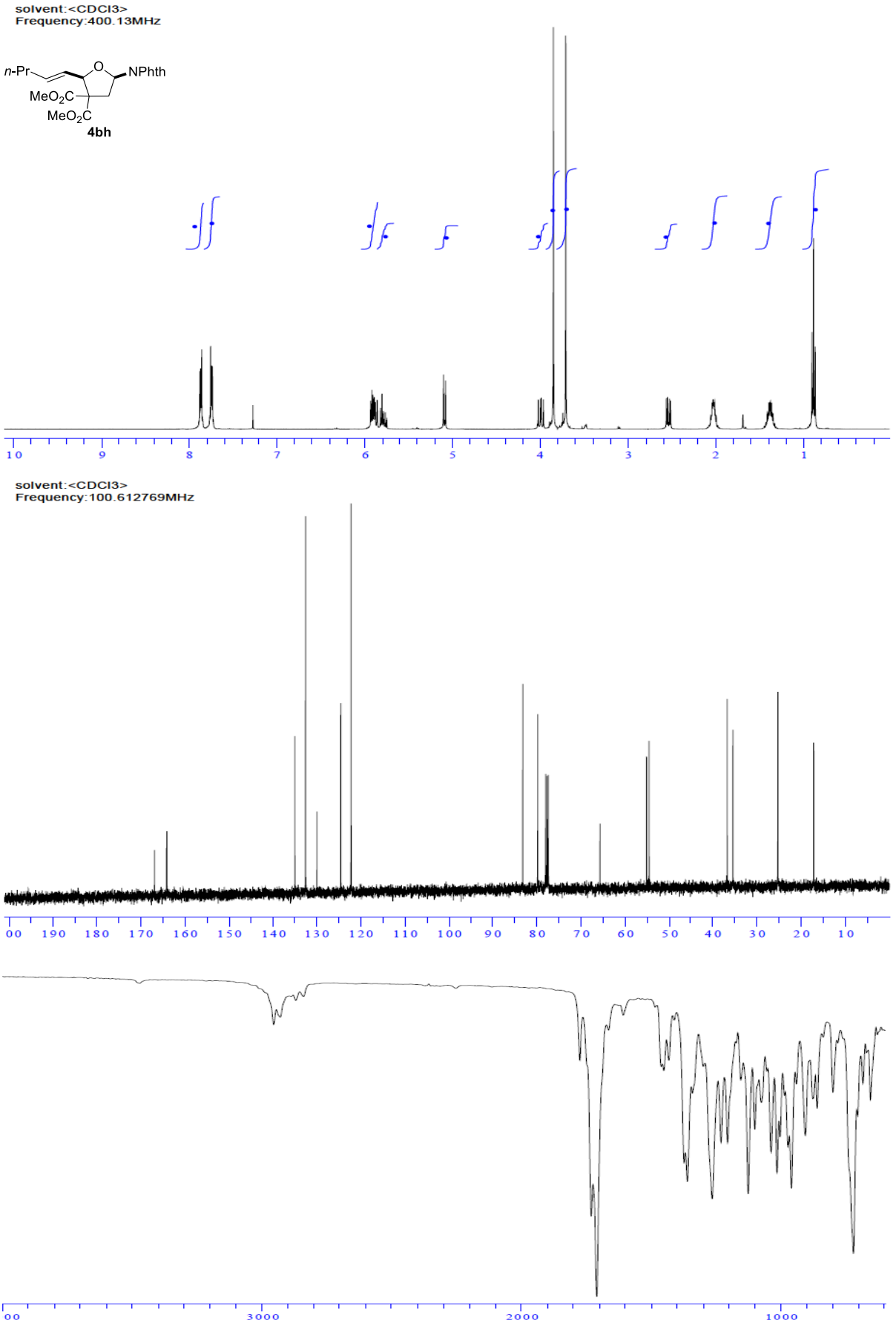
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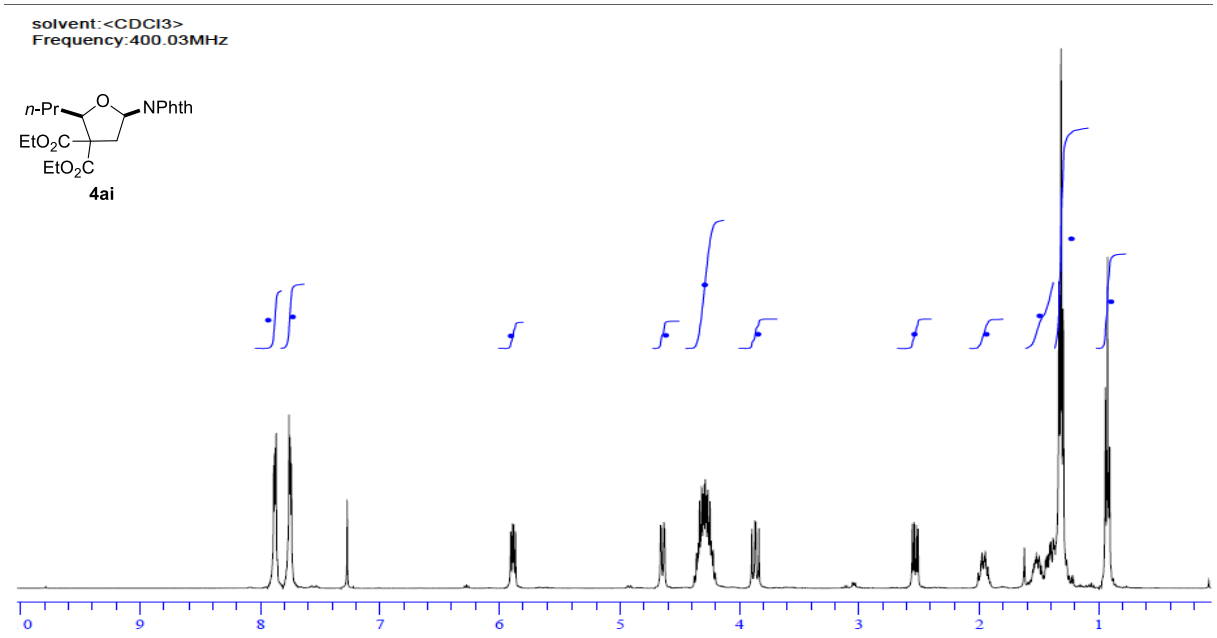
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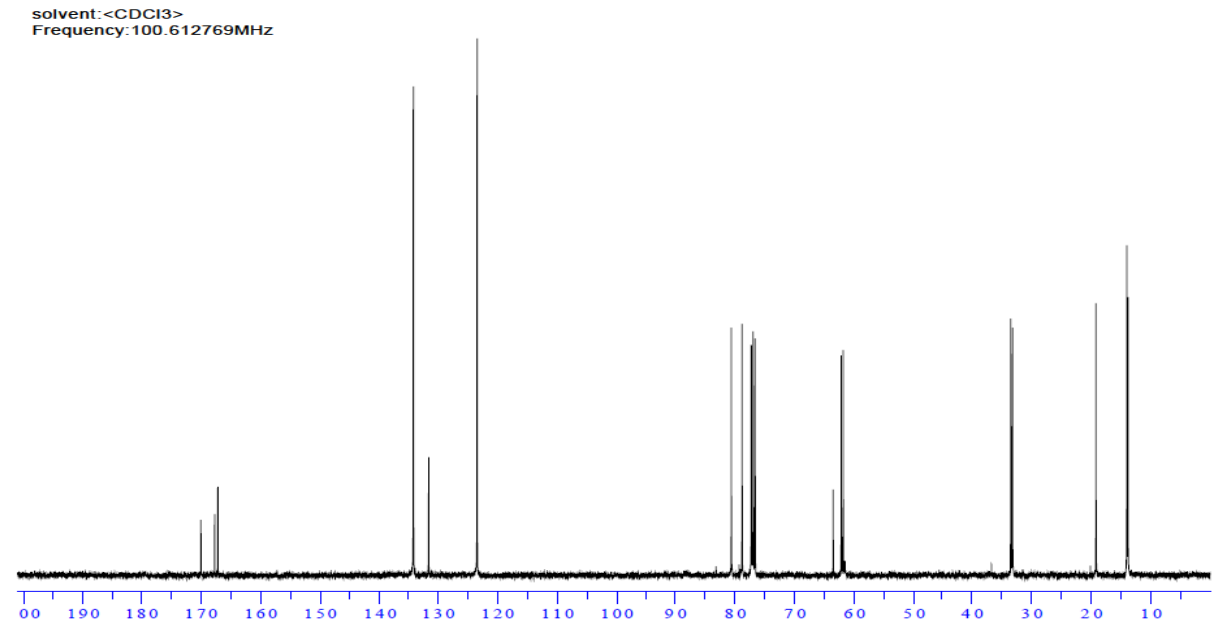
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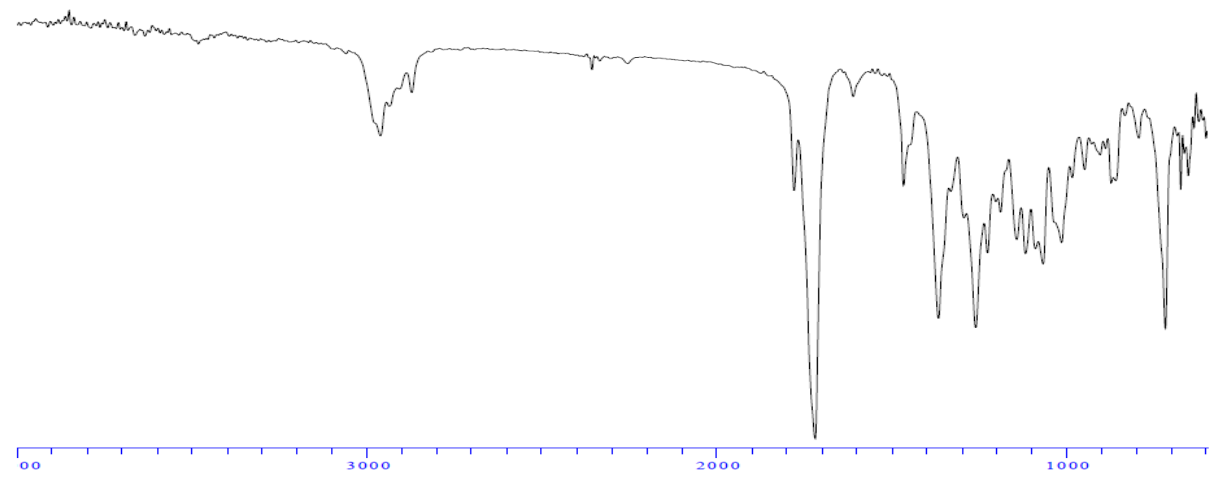
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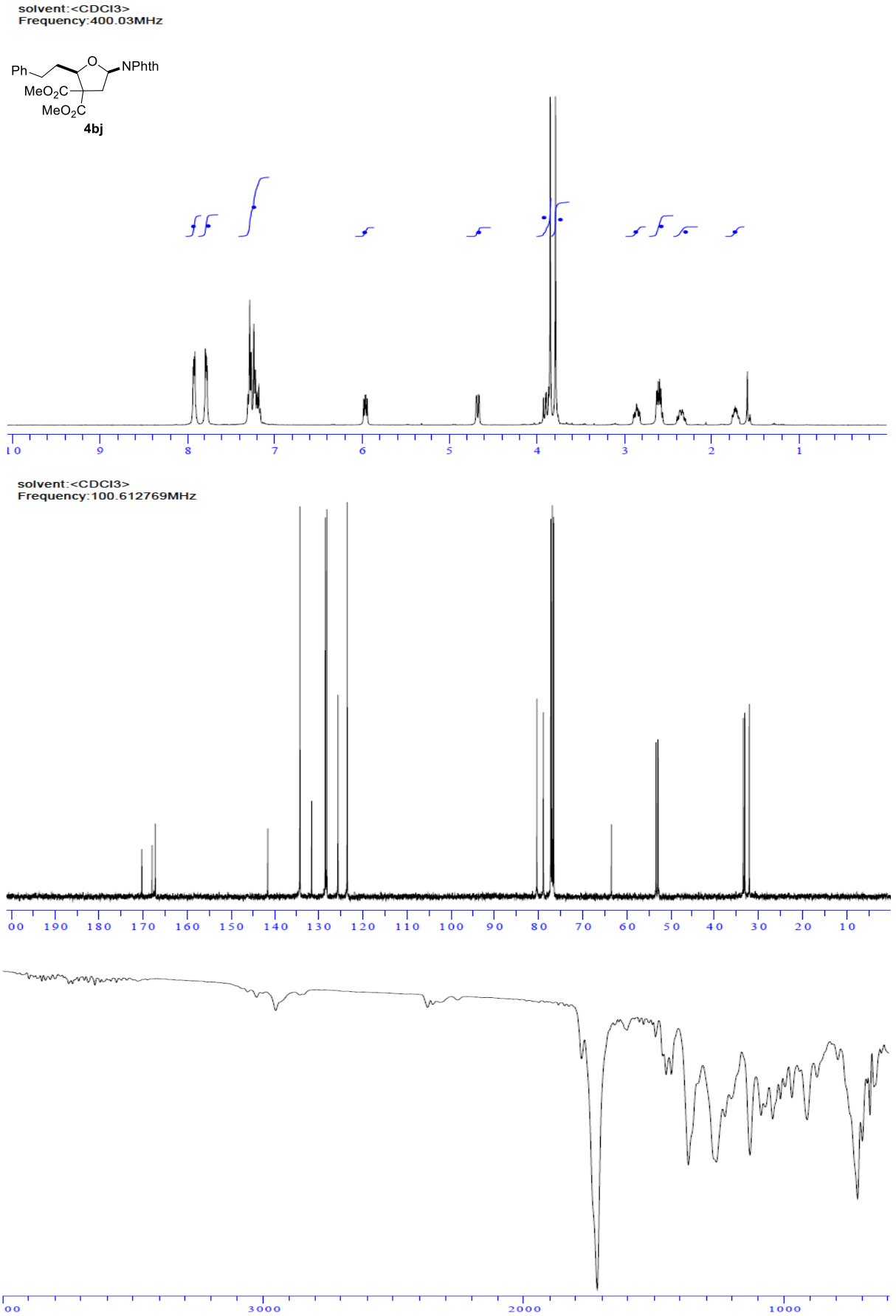
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3
2
1
solvent:<CDCl3>
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190
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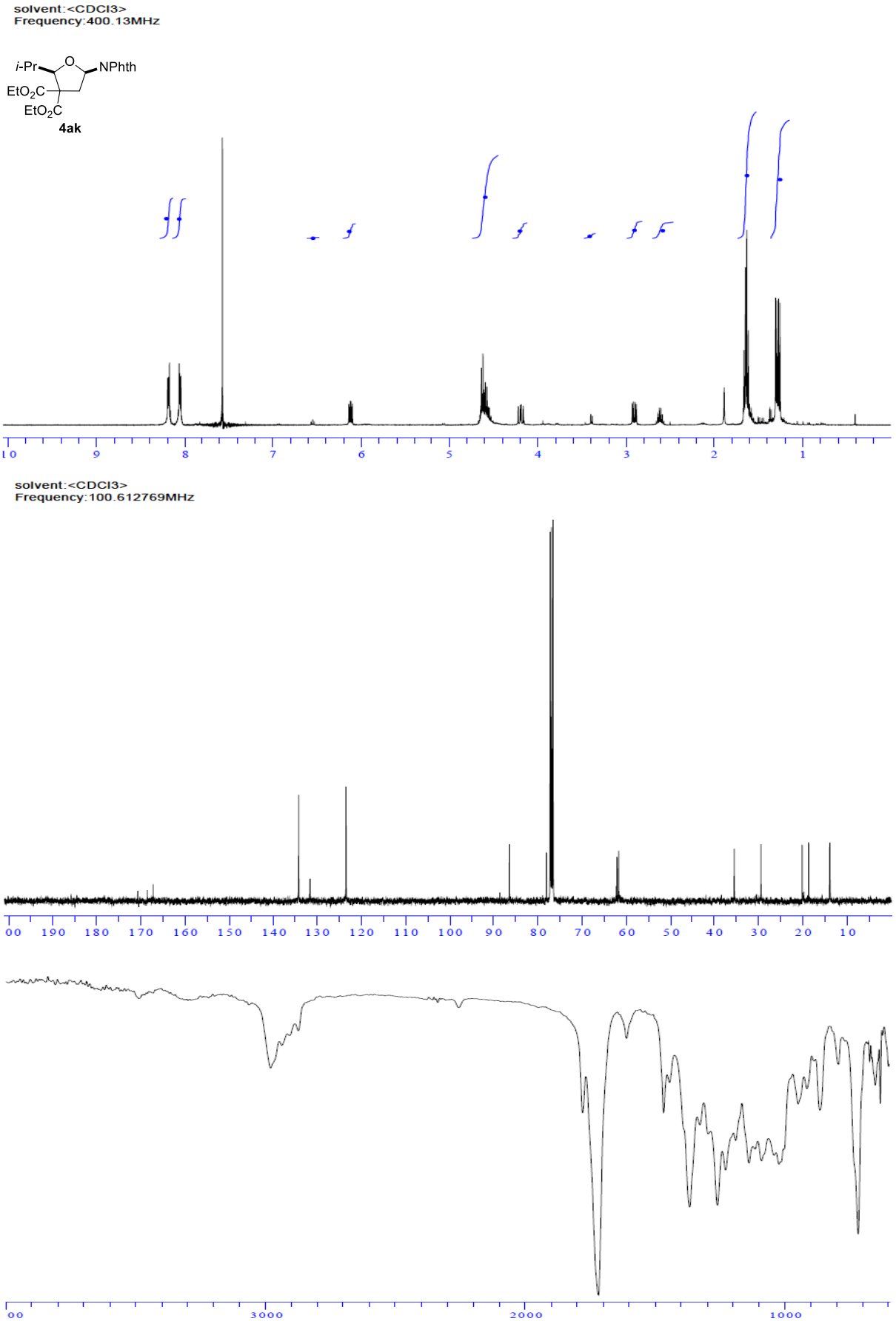
2000
1000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EtO2C
4ak
10
9
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1
solvent:<CDCl3>
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190
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10
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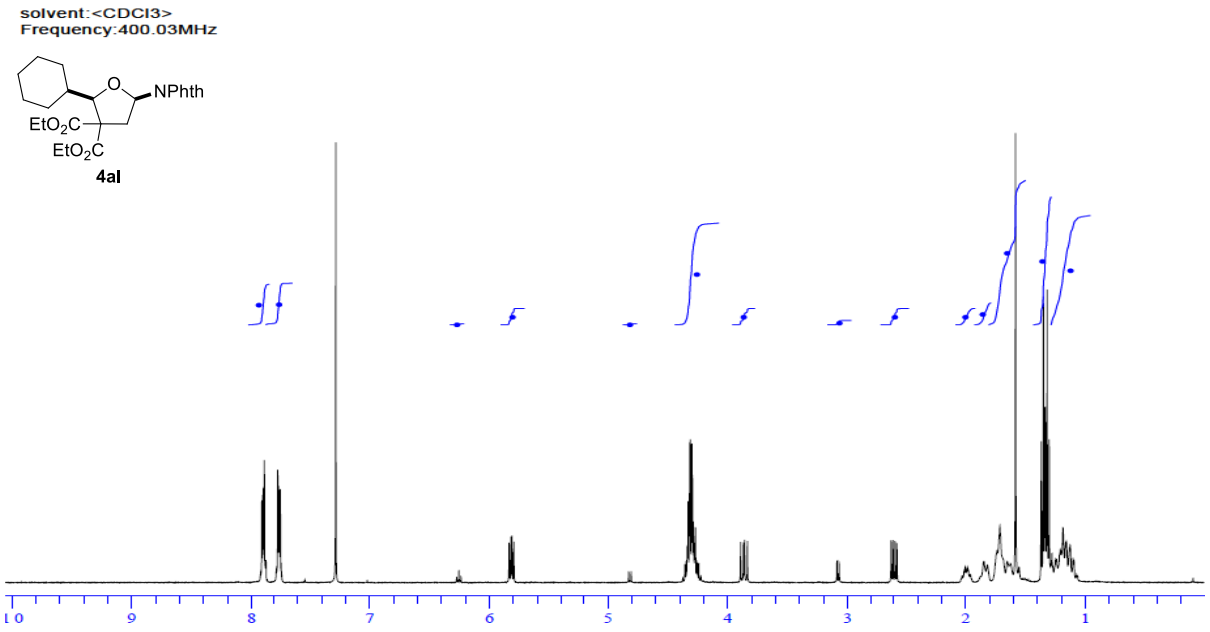
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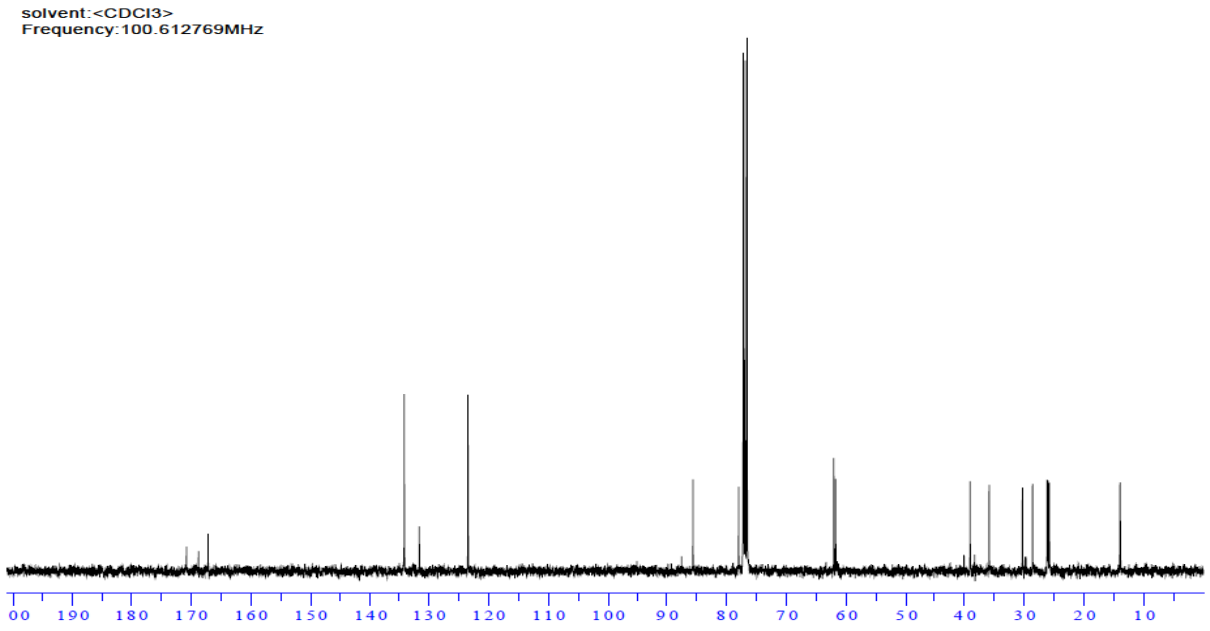
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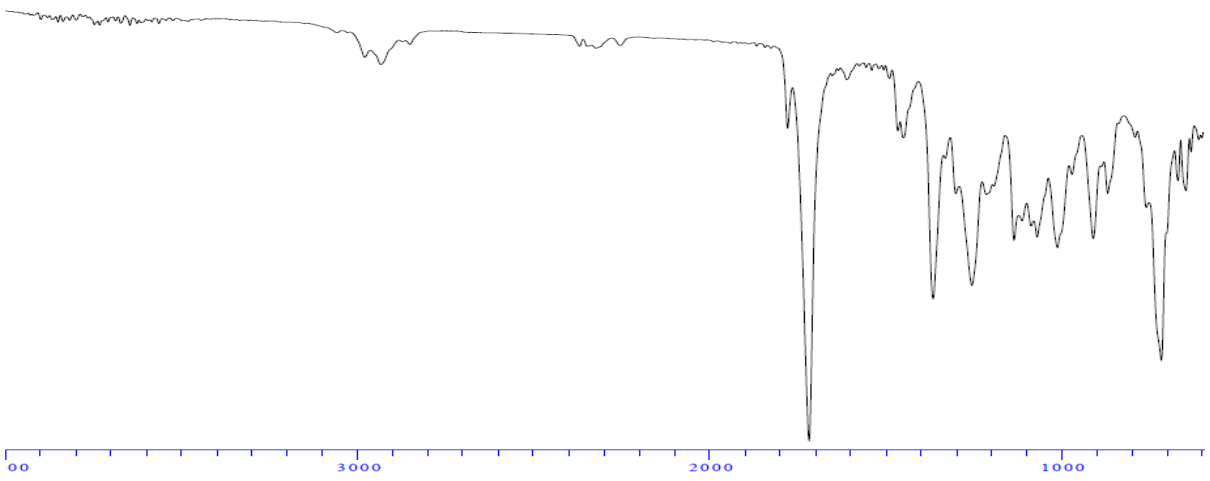
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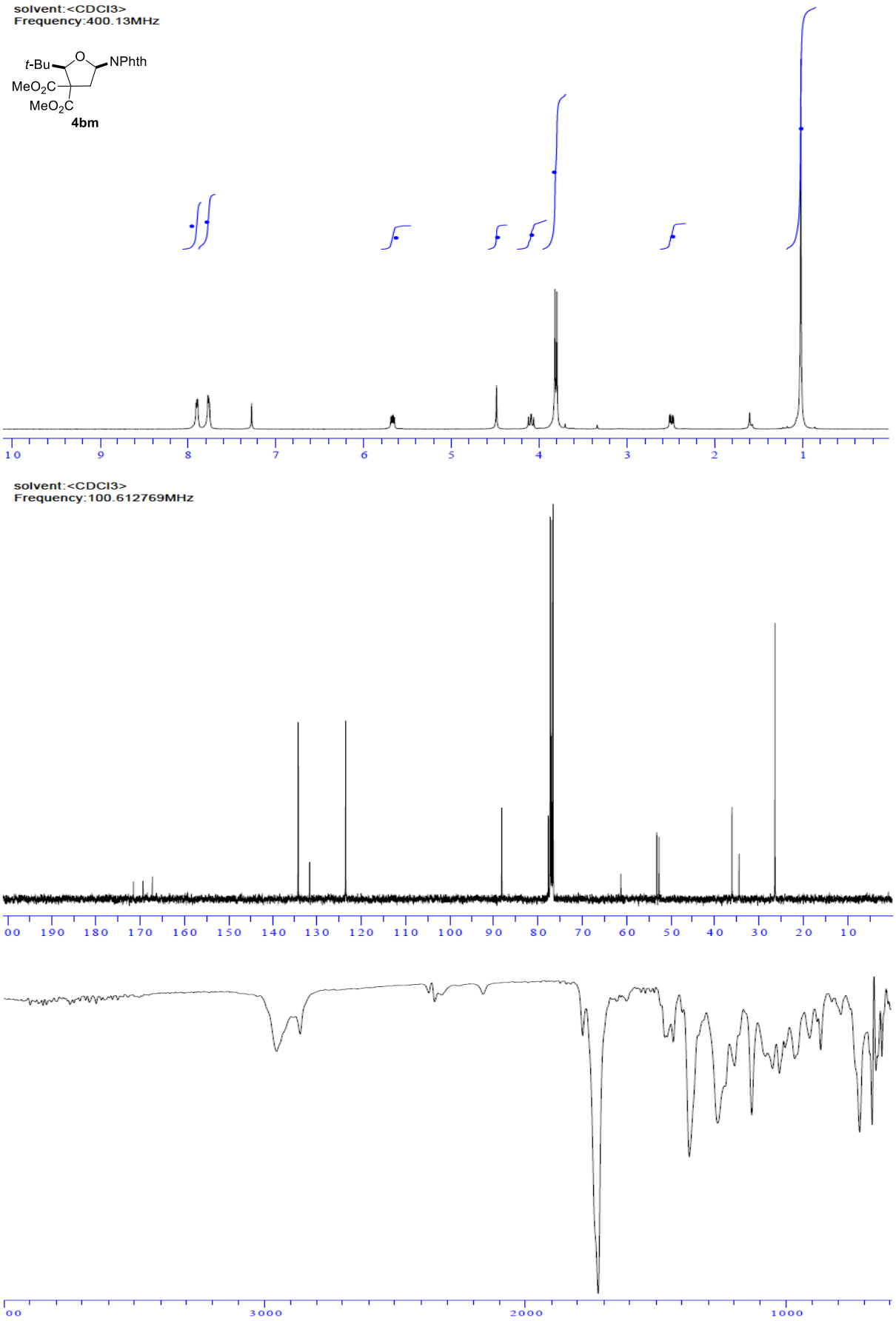
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6 Crystallographic data

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number : CCDC 855246.

Table 1. Crystal data and structure refinement for 4ab.

Identification code	4ab	
Empirical formula	$C_{25}H_{25.30}NO_{8.15}$	
Formula weight	470.25	
Temperature	140(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P*-1	
Unit cell dimensions	a = 8.3373(8) Å	α= 109.268(6)°.
	b = 10.8545(6) Å	β= 90.264(7)°.
	c = 14.1321(5) Å	γ = 106.447(5)°.
Volume	1151.07(13) $Å^3$	
Z	2	
Density (calculated)	1.357 Mg/m^3	
Absorption coefficient	0.102 mm^{-1}	
F(000)	495	
Crystal size	0.45 x 0.38 x 0.25 mm^3	
Theta range for data collection	3.07 to 27.49°.	
Index ranges	-10<=h<=10, -13<=k<=14, -18<=l<=18	
Reflections collected	17348	
Independent reflections	5206 [R(int) = 0.0233]	
Completeness to theta = 27.49°	98.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.6857	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5206 / 1 / 323	
Goodness-of-fit on F^2	1.087	
Final R indices [I>2sigma(I)]	R1 = 0.0414, wR2 = 0.0847	
R indices (all data)	R1 = 0.0586, wR2 = 0.0939	
Largest diff. peak and hole	0.258 and -0.205 $e.Å^{-3}$	

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

	x	y	z	U(eq)
O(1)	2102(1)	2816(1)	4407(1)	31(1)
O(2)	6000(1)	1379(1)	5735(1)	33(1)
O(3)	4680(1)	1491(1)	3145(1)	25(1)
O(4)	671(1)	1590(1)	-690(1)	34(1)
O(5)	5401(1)	5388(1)	2933(1)	33(1)
O(6)	7004(1)	4553(1)	1752(1)	25(1)
O(7)	8967(1)	2767(1)	2746(1)	31(1)
O(8)	9309(1)	5018(1)	3517(1)	28(1)
N(1)	4316(2)	2128(1)	4862(1)	26(1)
C(1)	2694(2)	2297(1)	4905(1)	26(1)
C(2)	4659(2)	1546(1)	5573(1)	27(1)
C(3)	3070(2)	1228(1)	6047(1)	29(1)
C(4)	2662(2)	537(2)	6725(1)	36(1)
C(5)	1030(3)	327(2)	7003(1)	43(1)
C(6)	-123(2)	814(2)	6632(1)	43(1)
C(7)	298(2)	1515(2)	5952(1)	35(1)
C(8)	1914(2)	1695(1)	5665(1)	29(1)
C(9)	5468(2)	2384(1)	4140(1)	24(1)
C(10)	5440(2)	2057(1)	2405(1)	22(1)
C(11)	6513(2)	3584(1)	3029(1)	21(1)
C(12)	5915(2)	3814(1)	4081(1)	25(1)
C(13)	4101(2)	1887(1)	1603(1)	22(1)
C(14)	2511(2)	1996(1)	1826(1)	24(1)
C(15)	1320(2)	1881(1)	1078(1)	25(1)
C(16)	1727(2)	1672(1)	94(1)	25(1)
C(17)	3312(2)	1545(2)	-145(1)	29(1)
C(18)	4474(2)	1639(1)	603(1)	26(1)
C(19)	-963(2)	1721(2)	-477(1)	38(1)
C(20)	6219(2)	4623(1)	2585(1)	22(1)
C(21)	6810(2)	5475(2)	1233(1)	33(1)
C(22)	7472(2)	5031(2)	230(1)	39(1)
C(23)	8393(2)	3709(1)	3066(1)	22(1)
C(24)	11133(2)	5344(2)	3455(1)	34(1)

C(25)	11534(2)	5609(2)	2491(1)	39(1)
O(9)	3779(9)	-1460(7)	2115(6)	35(3)

Table 3. Bond lengths [Å] and angles [°] for 4ab.

O(1)-C(1)	1.2140(18)
O(2)-C(2)	1.2146(19)
O(3)-C(9)	1.4418(16)
O(3)-C(10)	1.4444(16)
O(4)-C(16)	1.3760(18)
O(4)-C(19)	1.4321(19)
O(5)-C(20)	1.2048(16)
O(6)-C(20)	1.3407(17)
O(6)-C(21)	1.4628(16)
O(7)-C(23)	1.2051(16)
O(8)-C(23)	1.3390(16)
O(8)-C(24)	1.4710(18)
N(1)-C(1)	1.4138(19)
N(1)-C(2)	1.4164(18)
N(1)-C(9)	1.4445(18)
C(1)-C(8)	1.494(2)
C(2)-C(3)	1.492(2)
C(3)-C(8)	1.389(2)
C(3)-C(4)	1.389(2)
C(4)-C(5)	1.395(3)
C(4)-H(4)	0.9500
C(5)-C(6)	1.395(3)
C(5)-H(5)	0.9500
C(6)-C(7)	1.400(2)
C(6)-H(6)	0.9500
C(7)-C(8)	1.387(2)
C(7)-H(7)	0.9500
C(9)-C(12)	1.5211(19)
C(9)-H(9)	1.0000
C(10)-C(13)	1.515(2)
C(10)-C(11)	1.5854(18)
C(10)-H(10)	1.0000
C(11)-C(20)	1.5310(19)
C(11)-C(23)	1.5335(19)
C(11)-C(12)	1.5351(19)
C(12)-H(12A)	0.9900

C(12)-H(12B)	0.9900
C(13)-C(14)	1.3923(19)
C(13)-C(18)	1.4023(19)
C(14)-C(15)	1.398(2)
C(14)-H(14)	0.9500
C(15)-C(16)	1.392(2)
C(15)-H(15)	0.9500
C(16)-C(17)	1.399(2)
C(17)-C(18)	1.390(2)
C(17)-H(17)	0.9500
C(18)-H(18)	0.9500
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(21)-C(22)	1.500(2)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(24)-C(25)	1.503(2)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800
O(9)-H(9A)	1.00(10)
O(9)-H(9B)	1.00(10)

C(9)-O(3)-C(10)	109.60(10)
C(16)-O(4)-C(19)	117.49(12)
C(20)-O(6)-C(21)	116.19(11)
C(23)-O(8)-C(24)	116.59(11)
C(1)-N(1)-C(2)	111.70(12)
C(1)-N(1)-C(9)	126.10(12)
C(2)-N(1)-C(9)	121.98(12)
O(1)-C(1)-N(1)	125.52(13)
O(1)-C(1)-C(8)	129.00(14)

N(1)-C(1)-C(8)	105.48(12)
O(2)-C(2)-N(1)	124.82(14)
O(2)-C(2)-C(3)	129.76(14)
N(1)-C(2)-C(3)	105.41(13)
C(8)-C(3)-C(4)	121.79(15)
C(8)-C(3)-C(2)	108.64(13)
C(4)-C(3)-C(2)	129.51(15)
C(3)-C(4)-C(5)	116.85(16)
C(3)-C(4)-H(4)	121.6
C(5)-C(4)-H(4)	121.6
C(6)-C(5)-C(4)	121.38(15)
C(6)-C(5)-H(5)	119.3
C(4)-C(5)-H(5)	119.3
C(5)-C(6)-C(7)	121.46(16)
C(5)-C(6)-H(6)	119.3
C(7)-C(6)-H(6)	119.3
C(8)-C(7)-C(6)	116.68(17)
C(8)-C(7)-H(7)	121.7
C(6)-C(7)-H(7)	121.7
C(7)-C(8)-C(3)	121.81(14)
C(7)-C(8)-C(1)	129.52(15)
C(3)-C(8)-C(1)	108.58(13)
O(3)-C(9)-N(1)	108.34(11)
O(3)-C(9)-C(12)	104.43(11)
N(1)-C(9)-C(12)	115.77(11)
O(3)-C(9)-H(9)	109.4
N(1)-C(9)-H(9)	109.4
C(12)-C(9)-H(9)	109.4
O(3)-C(10)-C(13)	110.20(11)
O(3)-C(10)-C(11)	105.33(10)
C(13)-C(10)-C(11)	115.95(11)
O(3)-C(10)-H(10)	108.4
C(13)-C(10)-H(10)	108.4
C(11)-C(10)-H(10)	108.4
C(20)-C(11)-C(23)	108.41(11)
C(20)-C(11)-C(12)	111.28(11)
C(23)-C(11)-C(12)	110.99(11)
C(20)-C(11)-C(10)	112.90(11)

C(23)-C(11)-C(10)	109.93(10)
C(12)-C(11)-C(10)	103.29(10)
C(9)-C(12)-C(11)	102.04(10)
C(9)-C(12)-H(12A)	111.4
C(11)-C(12)-H(12A)	111.4
C(9)-C(12)-H(12B)	111.4
C(11)-C(12)-H(12B)	111.4
H(12A)-C(12)-H(12B)	109.2
C(14)-C(13)-C(18)	118.35(13)
C(14)-C(13)-C(10)	122.29(12)
C(18)-C(13)-C(10)	119.35(12)
C(13)-C(14)-C(15)	121.03(13)
C(13)-C(14)-H(14)	119.5
C(15)-C(14)-H(14)	119.5
C(16)-C(15)-C(14)	119.89(13)
C(16)-C(15)-H(15)	120.1
C(14)-C(15)-H(15)	120.1
O(4)-C(16)-C(15)	124.55(13)
O(4)-C(16)-C(17)	115.67(13)
C(15)-C(16)-C(17)	119.78(13)
C(18)-C(17)-C(16)	119.71(13)
C(18)-C(17)-H(17)	120.1
C(16)-C(17)-H(17)	120.1
C(17)-C(18)-C(13)	121.21(13)
C(17)-C(18)-H(18)	119.4
C(13)-C(18)-H(18)	119.4
O(4)-C(19)-H(19A)	109.5
O(4)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
O(4)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
O(5)-C(20)-O(6)	125.02(13)
O(5)-C(20)-C(11)	125.00(13)
O(6)-C(20)-C(11)	109.98(11)
O(6)-C(21)-C(22)	107.01(12)
O(6)-C(21)-H(21A)	110.3
C(22)-C(21)-H(21A)	110.3

O(6)-C(21)-H(21B)	110.3
C(22)-C(21)-H(21B)	110.3
H(21A)-C(21)-H(21B)	108.6
C(21)-C(22)-H(22A)	109.5
C(21)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(21)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
O(7)-C(23)-O(8)	124.78(13)
O(7)-C(23)-C(11)	125.14(12)
O(8)-C(23)-C(11)	110.08(11)
O(8)-C(24)-C(25)	109.78(12)
O(8)-C(24)-H(24A)	109.7
C(25)-C(24)-H(24A)	109.7
O(8)-C(24)-H(24B)	109.7
C(25)-C(24)-H(24B)	109.7
H(24A)-C(24)-H(24B)	108.2
C(24)-C(25)-H(25A)	109.5
C(24)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
C(24)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5
H(9A)-O(9)-H(9B)	104(10)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 4ab. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	37(1)	29(1)	32(1)	14(1)	10(1)	12(1)
O(2)	40(1)	28(1)	31(1)	11(1)	-2(1)	7(1)
O(3)	35(1)	18(1)	21(1)	8(1)	4(1)	3(1)
O(4)	34(1)	38(1)	29(1)	12(1)	0(1)	10(1)
O(5)	35(1)	25(1)	41(1)	10(1)	8(1)	16(1)
O(6)	27(1)	23(1)	30(1)	15(1)	5(1)	9(1)
O(7)	29(1)	24(1)	42(1)	10(1)	6(1)	12(1)
O(8)	26(1)	22(1)	33(1)	5(1)	-1(1)	5(1)
N(1)	34(1)	22(1)	24(1)	10(1)	9(1)	9(1)
C(1)	35(1)	18(1)	24(1)	6(1)	7(1)	6(1)
C(2)	41(1)	15(1)	21(1)	4(1)	3(1)	5(1)
C(3)	44(1)	17(1)	21(1)	4(1)	7(1)	6(1)
C(4)	62(1)	23(1)	24(1)	9(1)	12(1)	11(1)
C(5)	74(1)	24(1)	30(1)	11(1)	23(1)	9(1)
C(6)	55(1)	25(1)	38(1)	5(1)	27(1)	4(1)
C(7)	44(1)	23(1)	34(1)	6(1)	16(1)	8(1)
C(8)	41(1)	17(1)	24(1)	5(1)	10(1)	5(1)
C(9)	30(1)	21(1)	20(1)	6(1)	7(1)	7(1)
C(10)	26(1)	16(1)	22(1)	6(1)	7(1)	6(1)
C(11)	24(1)	17(1)	21(1)	5(1)	4(1)	6(1)
C(12)	31(1)	19(1)	23(1)	5(1)	9(1)	6(1)
C(13)	26(1)	14(1)	23(1)	5(1)	5(1)	4(1)
C(14)	29(1)	20(1)	22(1)	7(1)	9(1)	6(1)
C(15)	25(1)	22(1)	28(1)	7(1)	8(1)	7(1)
C(16)	29(1)	19(1)	25(1)	7(1)	1(1)	4(1)
C(17)	32(1)	29(1)	21(1)	7(1)	8(1)	7(1)
C(18)	25(1)	23(1)	25(1)	5(1)	8(1)	5(1)
C(19)	33(1)	36(1)	45(1)	14(1)	-2(1)	12(1)
C(20)	20(1)	16(1)	27(1)	6(1)	1(1)	3(1)
C(21)	38(1)	29(1)	40(1)	22(1)	4(1)	12(1)
C(22)	48(1)	38(1)	41(1)	26(1)	8(1)	13(1)
C(23)	27(1)	22(1)	18(1)	9(1)	3(1)	7(1)
C(24)	23(1)	29(1)	47(1)	10(1)	-7(1)	5(1)

C(25)	28(1)	35(1)	52(1)	14(1)	9(1)	9(1)
O(9)	36(5)	30(4)	34(5)	12(3)	-9(3)	1(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 4ab.

	x	y	z	U(eq)
H(4)	3457	221	6986	43
H(5)	698	-158	7455	52
H(6)	-1218	668	6846	51
H(7)	-483	1851	5699	42
H(9)	6522	2180	4282	29
H(10)	6227	1543	2073	26
H(12A)	6820	4469	4614	30
H(12B)	4922	4152	4138	30
H(14)	2232	2151	2498	29
H(15)	235	1945	1239	30
H(17)	3593	1395	-816	34
H(18)	5541	1534	435	31
H(19A)	-1590	972	-256	57
H(19B)	-1571	1680	-1088	57
H(19C)	-846	2599	57	57
H(21A)	7452	6432	1632	39
H(21B)	5610	5417	1138	39
H(22A)	8664	5109	335	59
H(22B)	7346	5617	-147	59
H(22C)	6838	4078	-152	59
H(24A)	11519	4569	3477	41
H(24B)	11731	6163	4038	41
H(25A)	11006	4774	1915	58
H(25B)	12755	5879	2472	58
H(25C)	11101	6345	2457	58
H(9A)	4180(160)	-440(110)	2360(100)	52
H(9B)	3580(160)	-1700(130)	2740(90)	52

Table 6. Torsion angles [°] for 4ab.

C(2)-N(1)-C(1)-O(1)	177.13(13)
C(9)-N(1)-C(1)-O(1)	-8.1(2)
C(2)-N(1)-C(1)-C(8)	-3.54(15)
C(9)-N(1)-C(1)-C(8)	171.20(12)
C(1)-N(1)-C(2)-O(2)	-174.90(13)
C(9)-N(1)-C(2)-O(2)	10.1(2)
C(1)-N(1)-C(2)-C(3)	4.49(15)
C(9)-N(1)-C(2)-C(3)	-170.50(11)
O(2)-C(2)-C(3)-C(8)	175.66(14)
N(1)-C(2)-C(3)-C(8)	-3.69(15)
O(2)-C(2)-C(3)-C(4)	-7.1(3)
N(1)-C(2)-C(3)-C(4)	173.52(14)
C(8)-C(3)-C(4)-C(5)	0.2(2)
C(2)-C(3)-C(4)-C(5)	-176.72(14)
C(3)-C(4)-C(5)-C(6)	-1.2(2)
C(4)-C(5)-C(6)-C(7)	1.1(2)
C(5)-C(6)-C(7)-C(8)	0.2(2)
C(6)-C(7)-C(8)-C(3)	-1.3(2)
C(6)-C(7)-C(8)-C(1)	174.99(14)
C(4)-C(3)-C(8)-C(7)	1.1(2)
C(2)-C(3)-C(8)-C(7)	178.57(13)
C(4)-C(3)-C(8)-C(1)	-175.84(13)
C(2)-C(3)-C(8)-C(1)	1.63(15)
O(1)-C(1)-C(8)-C(7)	3.7(3)
N(1)-C(1)-C(8)-C(7)	-175.57(14)
O(1)-C(1)-C(8)-C(3)	-179.64(14)
N(1)-C(1)-C(8)-C(3)	1.06(15)
C(10)-O(3)-C(9)-N(1)	157.33(11)
C(10)-O(3)-C(9)-C(12)	33.40(14)
C(1)-N(1)-C(9)-O(3)	-60.84(16)
C(2)-N(1)-C(9)-O(3)	113.39(13)
C(1)-N(1)-C(9)-C(12)	56.00(18)
C(2)-N(1)-C(9)-C(12)	-129.77(14)
C(9)-O(3)-C(10)-C(13)	-138.73(11)
C(9)-O(3)-C(10)-C(11)	-12.99(13)
O(3)-C(10)-C(11)-C(20)	-132.36(11)

C(13)-C(10)-C(11)-C(20)	-10.25(16)
O(3)-C(10)-C(11)-C(23)	106.45(12)
C(13)-C(10)-C(11)-C(23)	-131.44(12)
O(3)-C(10)-C(11)-C(12)	-12.06(13)
C(13)-C(10)-C(11)-C(12)	110.05(13)
O(3)-C(9)-C(12)-C(11)	-39.49(13)
N(1)-C(9)-C(12)-C(11)	-158.49(12)
C(20)-C(11)-C(12)-C(9)	152.13(11)
C(23)-C(11)-C(12)-C(9)	-87.04(13)
C(10)-C(11)-C(12)-C(9)	30.72(13)
O(3)-C(10)-C(13)-C(14)	36.11(16)
C(11)-C(10)-C(13)-C(14)	-83.38(16)
O(3)-C(10)-C(13)-C(18)	-145.30(12)
C(11)-C(10)-C(13)-C(18)	95.22(14)
C(18)-C(13)-C(14)-C(15)	-0.85(19)
C(10)-C(13)-C(14)-C(15)	177.76(12)
C(13)-C(14)-C(15)-C(16)	-0.9(2)
C(19)-O(4)-C(16)-C(15)	-0.46(19)
C(19)-O(4)-C(16)-C(17)	-179.76(13)
C(14)-C(15)-C(16)-O(4)	-177.72(12)
C(14)-C(15)-C(16)-C(17)	1.5(2)
O(4)-C(16)-C(17)-C(18)	178.82(12)
C(15)-C(16)-C(17)-C(18)	-0.5(2)
C(16)-C(17)-C(18)-C(13)	-1.2(2)
C(14)-C(13)-C(18)-C(17)	1.9(2)
C(10)-C(13)-C(18)-C(17)	-176.74(12)
C(21)-O(6)-C(20)-O(5)	-0.9(2)
C(21)-O(6)-C(20)-C(11)	178.94(11)
C(23)-C(11)-C(20)-O(5)	-132.96(14)
C(12)-C(11)-C(20)-O(5)	-10.63(19)
C(10)-C(11)-C(20)-O(5)	104.99(15)
C(23)-C(11)-C(20)-O(6)	47.18(14)
C(12)-C(11)-C(20)-O(6)	169.51(11)
C(10)-C(11)-C(20)-O(6)	-74.87(14)
C(20)-O(6)-C(21)-C(22)	-168.66(12)
C(24)-O(8)-C(23)-O(7)	11.2(2)
C(24)-O(8)-C(23)-C(11)	-169.63(11)
C(20)-C(11)-C(23)-O(7)	-129.89(14)

C(12)-C(11)-C(23)-O(7)	107.60(15)
C(10)-C(11)-C(23)-O(7)	-6.05(19)
C(20)-C(11)-C(23)-O(8)	50.92(14)
C(12)-C(11)-C(23)-O(8)	-71.59(14)
C(10)-C(11)-C(23)-O(8)	174.76(11)
C(23)-O(8)-C(24)-C(25)	85.75(15)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for 4ab [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(9)-H(9A)...O(3)	1.00(10)	1.94(11)	2.914(7)	165(11)
O(9)-H(9B)...O(2)#1	1.00(10)	2.08(11)	3.013(8)	155(11)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y,-z+1