# Chapter 2

## *A Facile Access to 3,6-Disubstituted α-Pyrones via Carbene Catalyzed Formal [4+2] Annulation of α-Chloroaldehydes and γ-Keto Sulfones*

## Part A: Introduction to α-pyrone and preparation of starting reagents

### 2.1 Introduction

The pyrones belongs to a family of six-membered unsaturated cyclic compounds bearing an oxygen atom. This class of compounds exist in two forms like α-pyrone **1** and γ-pyrone **2**. It reveals that γ-pyrone **2** is the vinylogous form of α-pyrone **1** which contains a lactonic structure and many of the chemical properties of these nuclei are similar (Figure 2.1).[1]

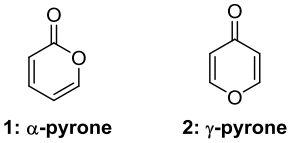



**Figure 2.1** Basic skeleton of pyrones

Importantly, α-pyrones are ubiquitous structural motifs and found in numerous natural products isolated from animals, bacteria, insects, marine organism and plants. They also exhibit interesting biological properties, such as antimicrobial**,** antifungal, enzyme inhibitive, and cytotoxic activities.[2] In this context, nectriapyrone A was isolated from an unidentified fungus acquired from a *Stylotella* sp. Sponge near Taveuni, Fiji by the Crews research group.[3] Moreover, the first metabolite isolated from *Gibberella fujikuroi* furnished gibepyrone A, which exhibit growth inhibitory against *Bacillus subtilis*.[4] Likely, griseulin reveal inhibitory activity against mosquito (*A. eagypti)* and

nematodes (*P. redivivus)* whereas wailupemycins A exhibited inhibitory properties against *E. coli* (Figure 2.2).[5]

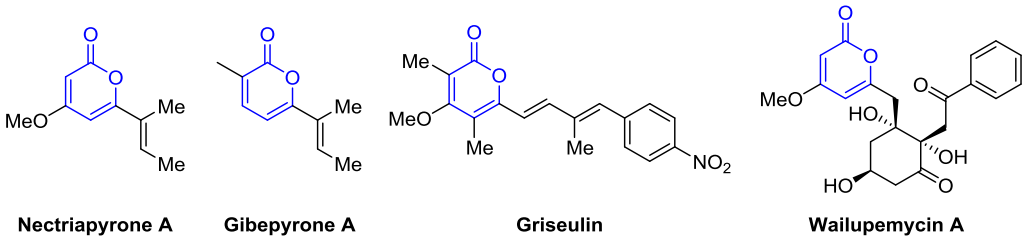



**Figure 2.2** Representative natural products containing α-pyrone motif

Alongside their biological importance, α-pyrone bear multiple reactive sites and can have great utility for the synthesis of sophisticated functional molecules. Importantly, a series of value-added heterocyclic and non-heterocyclic molecules can be accessed starting with simple α-pyrone motif because they show reactivity towards both electrophiles and nucleophiles.[6] In this context, the naturally occurring isocarbostryls such as narciclasine **3**, lycoricidine **4**, and pancratistatin **5** have been isolated from plants of the genus *Amaryllidaceae* and are known to show antiviral and antitumor activities. In addition, *trans*-dihydronarciclasine **6** exhibits two-to ten fold higher potency than pancratistatin against human cancer cell lines and has been isolated from the Chinese medicinal plant *Zephyranthes candida* (Figure 2.3).[7]

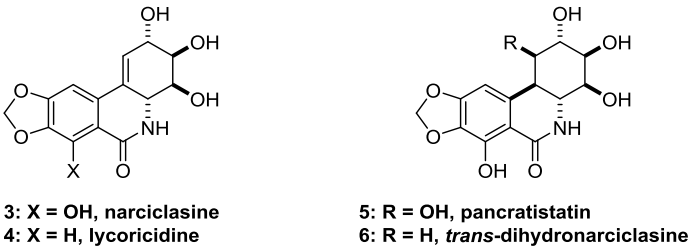


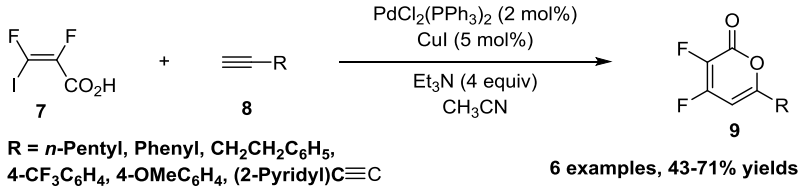

**Figure 2.3** Selected biologically active naturally occurring isocarbostryls

## 2.2 Review of literature

Based on significant importance of α-pyrone as a versatile building block for the construction of various key intermediates in synthetic organic chemistry as well as medicinal chemistry, a novel method affording α-pyrone motif is another synthetic target for an organic chemist. Several synthetic routes to access substituted α-pyrone have been documented in the literature.

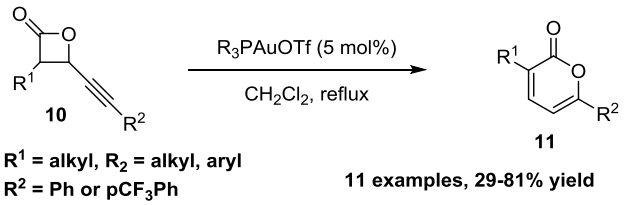
### 2.2.1 General methods for the synthesis of α-pyrone

In 2006, Burton and colleagues demonstrated an efficient protocol for the synthesis of difluorinated α-pyrone employing a Sonogashira alkynylation coupling reaction. This approach involves a reaction of (2E)-2,3-difluorinated-3-iodoacrylic acid **7** and a variety of terminal acetylenes **8** in the presence of $PdCl_2(PPh_3)_2$ in combination with CuI as a co-catalyst to deliver the desired difluorinated α-pyrone **9** in good yields (Scheme 2.1).[8]



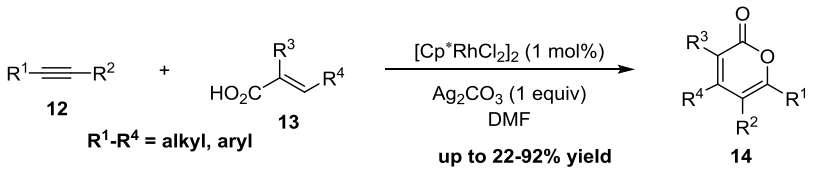

**Scheme 2.1** An approach to difluorinated α-pyrone involving Sonogashira alkynylation

In 2010, the Pale research group reported a two-step procedure to furnish substituted α-pyrones **11** in the presence of gold(1) catalyst through an unprecedented rearrangement of β-alkynylpropiolactones **10**. A wide range of α-pyrone **11** was obtained in two steps with good to high yields (Scheme 2.2).[9]



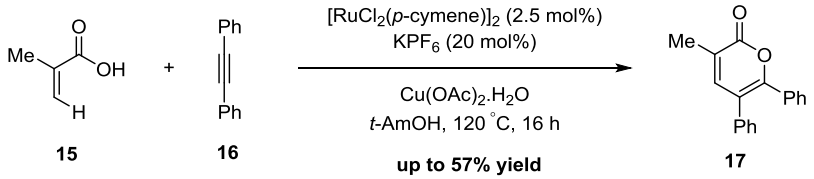

**Scheme 2.2** Gold-catalyzed rearrangement of β-alkynylpropiolactones to access α-pyrone

Moreover, Miura et al. developed a competent construction of α-pyrones **14** using rhodium-catalyzed oxidative coupling of acrylic acids **13** with alkynes **12** in 2009 (Scheme 2.3).[10] This catalytic protocol is also relevant to the coupling with alkenes and 1,3-diynes affording the desired α-pyrones **14** through vinylic C-H bond cleavage of acrylic acids.




**Scheme 2.3** Rhodium-catalyzed oxidative coupling of acrylic acids to access α-pyrone

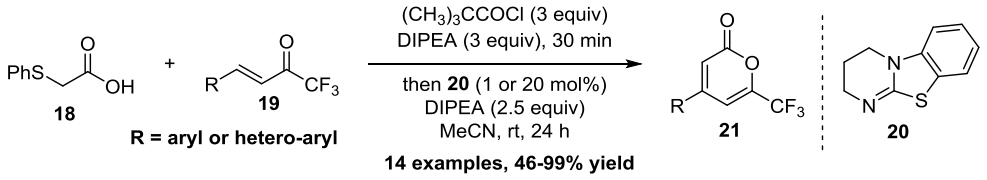
In 2012, Ackerman and colleagues developed a similar cyclization reaction using $[RuCl_2(p\text{-cymene})]_2$ instead of $[Cp^*RhCl_2]_2$. The cationic ruthenium(II) catalyst allowed the direct preparation of α-pyrone **17** in good to high yields through oxidative annulation of alkynes **16** by acrylic acid derivative **15** (Scheme 2.4).[11]




**Scheme 2.4** Ruthenium-catalyzed oxidative annulation of alkynes to access α-pyrone

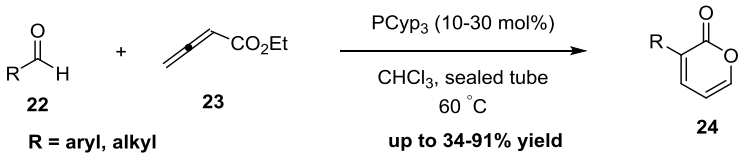
In 2014, Smith and co-workers reported a concise synthesis of di- and trisubstituted α-pyrone **21** from (thiophenyl)acetic acids **18** and α,β-unsaturated trifluoromethyl ketones

**19** through an isothiourea-mediated **20** one-pot Michael addition followed by lactonization and thiol elimination cascade sequence (Scheme 2.5).[12] This approach allows the formation of biologically active compounds in high yields.



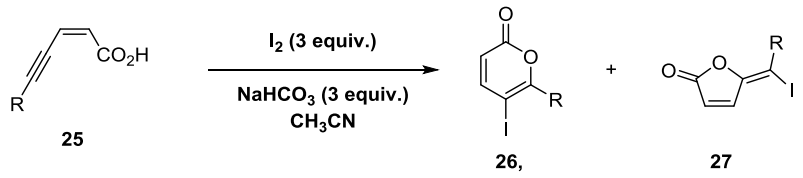

**Scheme 2.5** Isothiourea-catalyzed synthesis of α-pyrone

Moreover, the Kwon research group demonstrated a one-step Phosphine-catalyzed annulation between aldehydes **22** and ethyl allenoate **23** to furnished 6-substituted α-pyrone **24** in moderate to excellent yields (Scheme 2.6).[13] Notably, a variety of aliphatic as well as aromatic aldehydes were well tolerated and delivered the corresponding desired α-pyrone product.



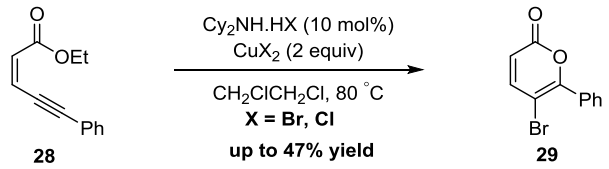

**Scheme 2.6** Phosphine-catalyzed synthesis of 6-substituted α-pyrone

In 2001, Rossi and co-workers demonstrated a Iodolactonization reaction to access α-pyrone even though a selectivity problem is apparent. In this context, the reaction of 5-substituted (Z)-2-en-4-ynoic acids **25** with Iodine and $NaHCO_3$ in $CH_3CN$ or with ICl in $CH_2Cl_2$ provides a mixture of 6-substituted 5-iodo-2(2*H*)-pyranones **26** and (E)-5-(1-iodoylidene)-2(5*H*)-furanones **27** in moderate to good yields, in which the pyranones **26** are the major products (Scheme 2.7).[14]



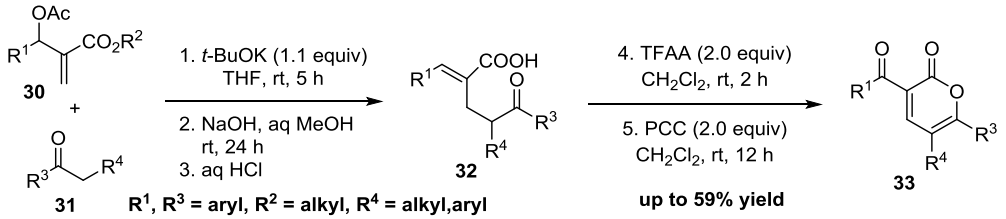

**Scheme 2.7** Iodolactonization strategy for the synthesis of α-pyrone

Furthermore, Li and co-workers developed a $Cy_2NH.HX$ catalytic system to overcome the selectivity problem remaining in the Iodolactonization strategy. The cyclization reaction of (Z)-ethyl 5-phenylpent-2-en-4-ynoate **28** in the presence of $Cy_2NH.HX$ and $CuBr_2$ furnished the desired 5-bromo-α-pyrone **29** in 47% yield (Scheme 2.8).[15] Notably, this approach further extends for various *o*-(alk-1-ynyl)benzoate to furnish the corresponding 4-haloisocoumarins products in good to high yields.



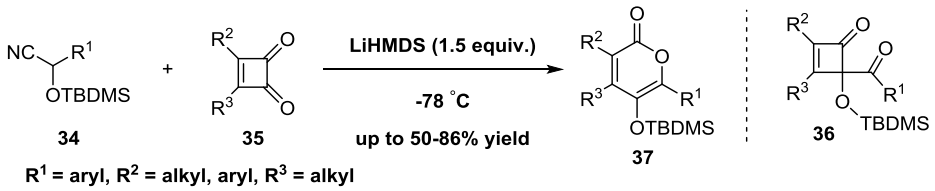

**Scheme 2.8** $Cy_2NH.HX$-catalyzed strategy for the synthesis of α-pyrone

In 2006, Kim and co-workers developed a efficient strategy for the synthesis of 3,5,6-trisubstituted α-pyrone **33** through the sequential introduction of ketone **31** at the primary position of Baylis-Hillman adduct **30** followed by lactonization and the oxidation with PCC (Scheme 2.9).[16]




**Scheme 2.9** Application of Baylis-Hillman reaction for the synthesis of α-pyrone

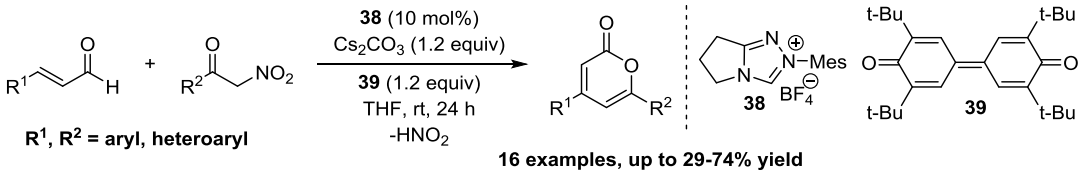
Moreover, Liebeskind and colleagues reported a new approach to deliver highly substituted α-pyrone. The reaction involves the addition of a lithiated *O*-silylated cyanohydrins **34** to a cyclobutenedione **35** followed by intramolecular 1,4-silyl migration and cyanide displacement generates 4-acylcyclobutenone **36**, which undergoes spontaneous ring expansion to furnish desired substituted α-pyrone **37** in good to high yields (Scheme 2.10).[17]




**Scheme 2.10** Application of Baylis-Hillman reaction for the synthesis of α-pyrone

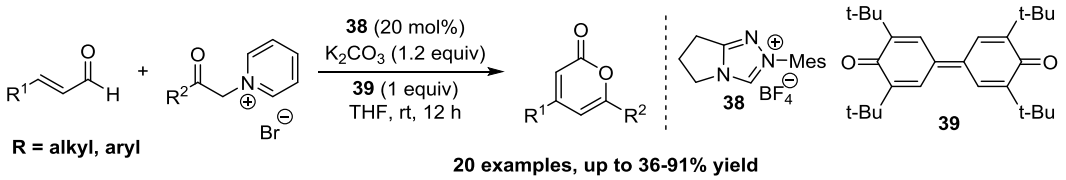
### 2.2.2 NHC-Catalyzed Synthesis of α-Pyrone

Apart from the above discussed methods, the synthesis of 4,6-disubstituted α-pyrone was also reported under the NHC-catalysis. In this context, the Studer research group reported a method for the synthesis of 4,6-disubstituted α-pyrone using aroyl-substituted nitromethanes and enals employing mesityl substituted triazolium precatalyst **38** and bisquinone **39** as an oxidant through Michael addition followed by elimination and lactonization sequence in 2016. Notably, the nitro group in the starting ketone stabilizes the enolate and acts as an ionic leaving group and thus leads to the formation of desired α-pyrone in moderate to good yields (Scheme 2.11).[18a]




**Scheme 2.11** Oxidative NHC-catalyzed synthesis of 4,6-disubstituted α-pyrone using enals and 2-nitroacetophenone

In 2019, the Chi research group demonstrated an NHC-mediated [3+3] cycloaddition transformation of enals with nitrogen ylides applying triazolium precatalyst **38** and bisquinone **39** as an oxidant for the synthesis of 4,6-disubstituted α-pyrone in good to high yields. The prepared 2'-pyridinium acetophenone bromide salts are employed as nitrogen ylide precursors in this approach (Scheme 2.12).[18b]




**Scheme 2.12** Oxidative NHC-catalyzed synthesis of 4,6-disubstituted α-pyrone

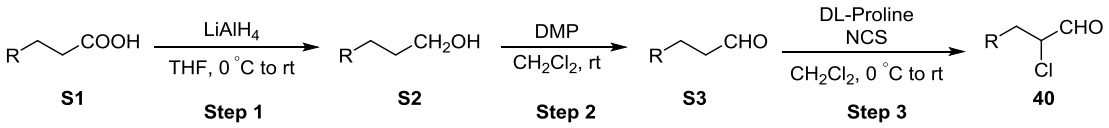
## 2.3 Statement of the Problem

As discussed in the introduction section, several methods have been reported in the literature for the synthesis of substituted α-pyrone. Although, to afford 3,6-disubstituted α-pyrone which are rare, both in nature and synthesis, there is a single gold catalyzed protocol was reported to the best of our knowledge (Scheme 2.2).[9] Therefore, the development of new organocatalytic and operationally simple approach is highly desirable. Notably, in the field of NHC-catalysis both previous approach produce 4,6-disubstituted α-pyrone under oxidative conditions. But, we envisioned the synthesis of 3,6-disubstituted α-pyrone under oxidant free NHC-catalysis. In this context, as per continuation of our ongoing research in territory of *N*-heterocyclic carbene catalysis, herein, we have matured a formal oxidant-free NHC-catalyzed [4+2] annulation between α-chloroaldehydes and γ-ketosulfones. Notably, the reaction proceeds through Michael addition-lactonization-elimination cascade sequence and affords a broad range of 3,6-disubstituted α-pyrone in good to excellent yields.

## 2.4 Preparation of Starting Materials and NHC-Precatalyst

### 2.4.1 Synthesis of α-Chloroaldehydes

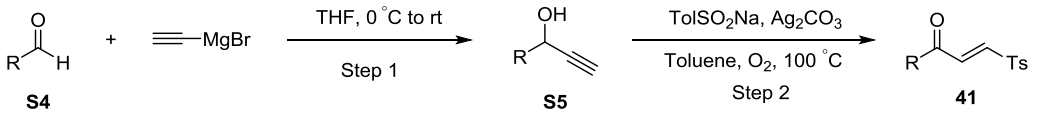
To probe the feasibility of the planed approach, starting substrates α-chloroaldehydes **40** were readily prepared according to the procedure reported previously in the literature.[19] A general route involves the reduction of saturated acid **S1** to corresponding alcohol **S2** using $LiAlH_4$, and subsequent oxidation in presence of Dess-Martin Periodane affords the corresponding aldehydes **S3**. This saturated aldehydes **S3** upon treatment with N-Chlorosuccinimide in presence of DL-Proline as a catalyst furnished the desired α-chloroaldehydes **40** in good yields (Scheme 2.13).




**Scheme 2.13** Synthesis of α-chloroaldehydes

### 2.4.2 Synthesis of γ-Ketosulfones

The starting substrate γ-ketosulfones **41** were readily synthesized following the procedure described previously in the literature.[20] A general approach involves the treatment of the commercially available aldehydes **S4** with ethynlmagnesium bromide for the formation of corresponding propargyl alcohol **S5**. The further reaction of this propargyl alcohol **S5** with sodium sulfinate in presence of silver carbonate as a catalyst provided the desired γ-ketosulfones **41** in good yields (Scheme 2.14).

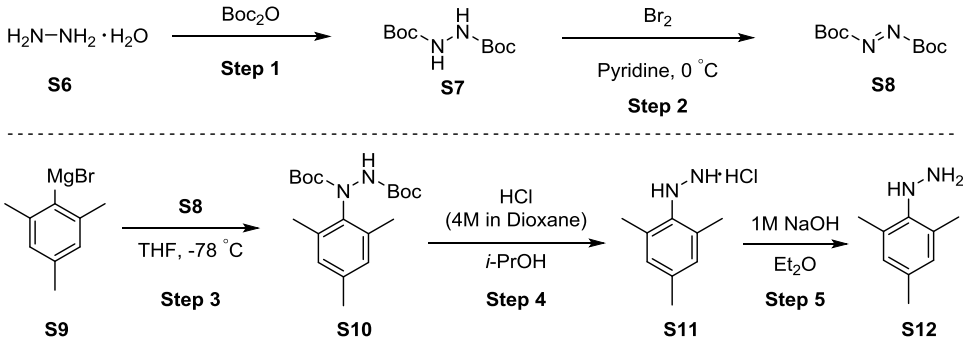



**Scheme 2.14** Synthesis of γ-ketosulfones

### 2.4.3 Synthesis of NHC-Precatalyst

As per our group's ongoing research in space of *N*-heterocyclic carbene catalysis a broad range of NHC-precatalyst have been synthesized by using the literature known protocols. Herein, we describe the synthesis of pyrrolidine based triazolium precatalyst **38** following the procedure reported earlier in the literature.[21]

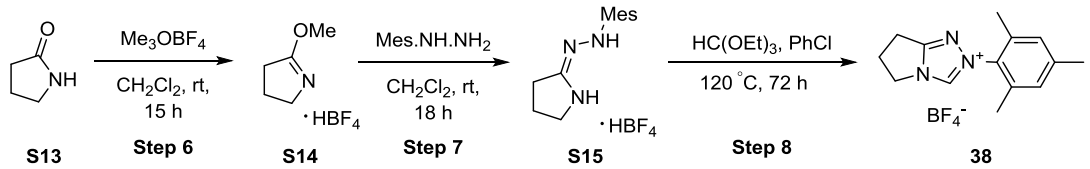
Firstly, this involve the preparation of mesitylhydrazine hydrochloride **S11**, starting from the reaction of hydrazine monohydrate **S6** with di-*tert*-butyl dicarbonate results in the formation of di-tert-butyl hydrazine-1,2-dicarboxylate **S7**, which upon treatment with bromine in presence of pyridine furnished di-*tert*-butyl azodicarboxylate **S8**, and its subsequent reaction with freshly prepared 2-mesitylmagnesium bromide **S9**, followed by Boc-deprotection provides the mesitylhydrazine hydrochloride **S11** which can be stored for a long period. Further reaction of this mesitylhydrazine hydrochloride **S11** with 1M aq. Sodium hydroxide provides free based mesitylhydrazine **S12** in good yields (Scheme 2.15).




**Scheme 2.15** Synthesis of mesitylhydrazine hydrochloride

After the preparation of mesitylhydrazine hydrochloride, we next move towards the preparation of pyrrolidine based NHC-precatalyst **38**. For this, the reaction of pyrrolidin-2-one **S13** with trimethyloxonium tetrafluoroborate provides 5-methoxy-3,4-

dihydro-2H-pyrrole **S14**, which upon further treatment with freshly prepared free based mesitylhydrazine **S12**, and subsequent cyclization using triethylorthoformate in chlorobenzene at 120 °C produces the desired NHC-precatalyst **38** in good yields (Scheme 2.16). Notably, this can be stored for a long period under an inert atmosphere.




**Scheme 2.16** Synthesis of pyrrolidine based NHC-precatalyst

## 2.5 Conclusion

In conclusion, we have synthesized the starting materials such as α-chloroaldehydes **40**, γ-ketosulfones **41** and pyrrolidine based NHC-precatalyst **38** for our designed strategy to access 3,6-disubstituted α-pyrone **42**. As the reaction proceeds through the generation of enolate intermediate in the presence of precatalyst **38** followed by Michael addition-lactonization-elimination cascade sequence. In this context, the detailed study on NHC-catalyzed generation of enolate intermediate and its application to access 3,6-disubstituted α-pyrone is presented in the following sections of part B of this chapter.

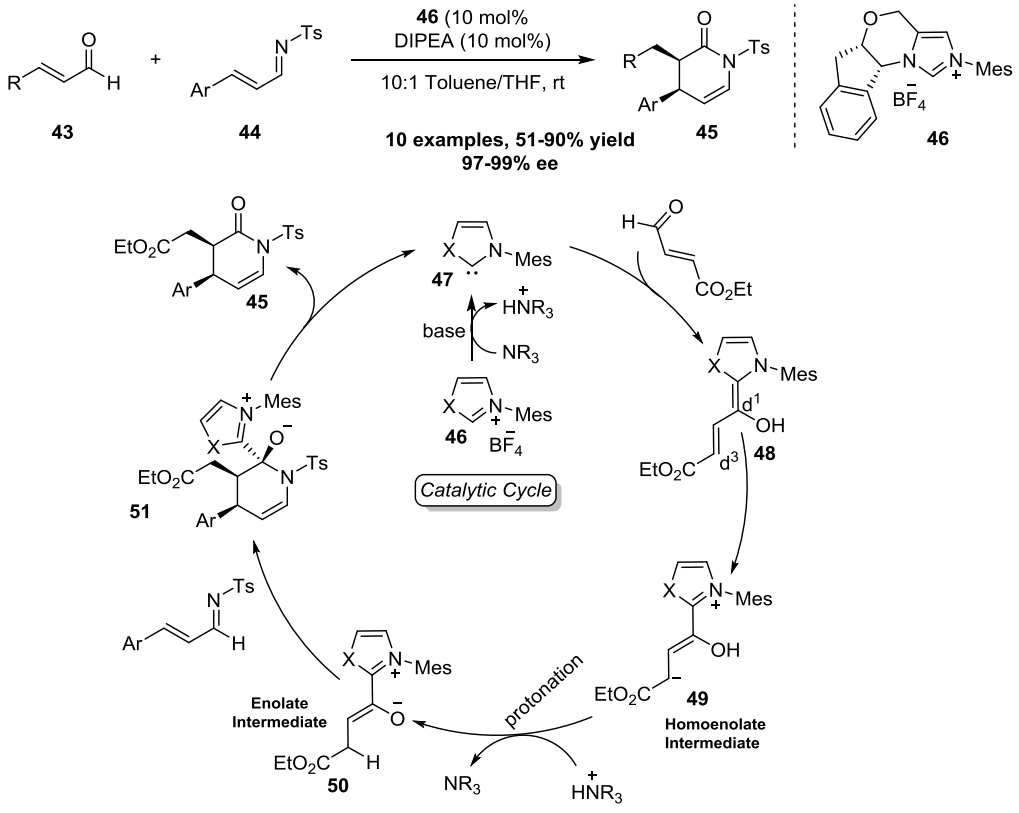
## Part B: Introduction to NHC-Bound Enolate Intermediate and its Application to access 3,6-Disubstituted α-Pyrone

### 2.6 NHC-Bound Enolate Intermediate-An Introduction

The design and development of *N*-heterocyclic carbene (NHC)-organocatalysis has attracted extensive interest in organic synthesis for the rapid construction of biologically and medicinally important molecules from simple starting materials. The NHCs mediated transformation proceeding through umpolung of aldehydes or their synthetic equivalents possess several modes of action such as nucleophilic Breslow intermediate, homoenolate, enolate, and electrophilic acyl azolium, each of which displays different kinds of reactivities.[22] The selective formation of each of these reactive intermediate can be achieved by proper choice of catalyst, substrate and reaction conditions. In this context, the generation of NHC-mediated enolate intermediate has been achieved from enals, α-functionalised aldehydes, ketenes, activated esters etc., which can trapped with electrophile to form a range of important heterocyclic scaffolds through formal cycloadditions.

In 2006, Bode and colleagues developed first approach to produce NHC-mediated nucleophilic enolate intermediate from enals **43**, which then undergo a subsequent hetero Diels-Alder with α,β-unsaturated imines **44** to access dihydropyridinone derivatives **45** in reasonable yields and enantioselectivity as a single *syn*-diastereoisomer (Scheme 2.17).[23] The transformation is postulated to advanced with initial coupling of carbene and enals **43** to generate homoenolate intermediate **49**. The secret to success of these reactions is to control of the unwanted homoenolate pathway and boost of the enolate mode of reactivity by the use of catalytic amount of mild

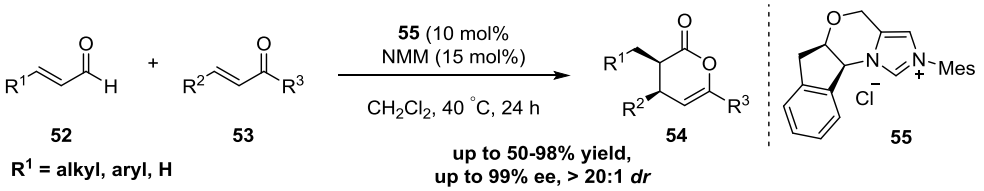
organic base. If the conjugate acid of the catalytic base formed through deprotonation of azolium salt is acidic enough to promote the protonation of homoenolate equivalent then the generation of enolate intermediate **50** take place. Therefore, the success of these reactions is decided by minimizing the competitive reaction pathways. A [4+2] cycloaddition between α,β-unsaturated imines **44** and the enolate equivalent **50** generates the alkoxide **51**, which further releases free carbene to deliver the desired dihydropyridinone derivatives **45** (Scheme 2.17, catalytic cycle).




**Scheme 2.17** NHC-catalyzed generation of enolate intermediate from enals

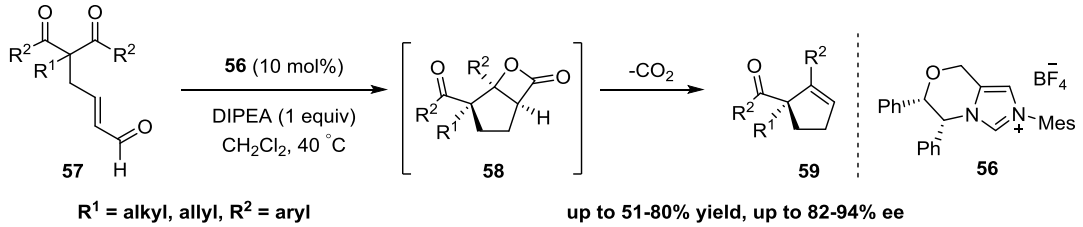
In 2010, Bode et al. developed the highly diastereo- and enantioselective [4+2] annulation of enal **52** and enones **53** using catalytic weak amine base such as *N*-methylmorpholine (NMM) with aminoindanol based triazolium precatalyst **55** to furnish dihydropyran-2-ones **54** (Scheme 2.18).[24] A wide range of alkyl or aryl enals

along with enones having electron deficient substituents were tolerated under the reaction condition and provide the desired product in good to excellent yields.




**Scheme 2.18** NHC-mediated asymmetric construction of dihydropyran-2-ones

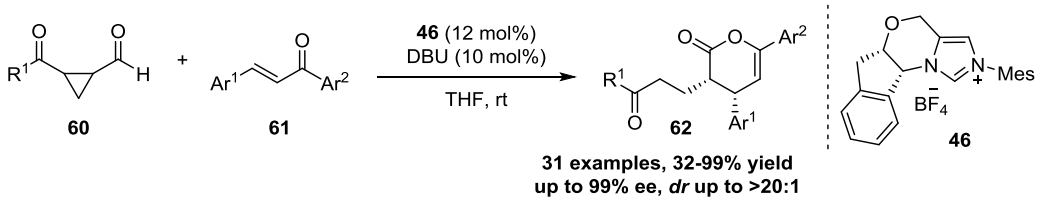
In 2007, Scheidt and colleagues trapped an azolium enolate intermediate from enal **57** followed by desymmetrising aldol addition with a decarboxylation of a β-lactone intermediate **58** to afford functionalised carbocycles **59** in satisfactory yields with excellent enantioselectivity (Scheme 2.19).[25]The scope of this approach was almost restricted to aryl ketones **57**. The use of alkyl ketones granted to afford lactone intermediate **58** in high enantioselectivity with close to diastereoisomeric purity.




**Scheme 2.19** NHC-catalyzed enantioselective synthesis of cyclopentenes

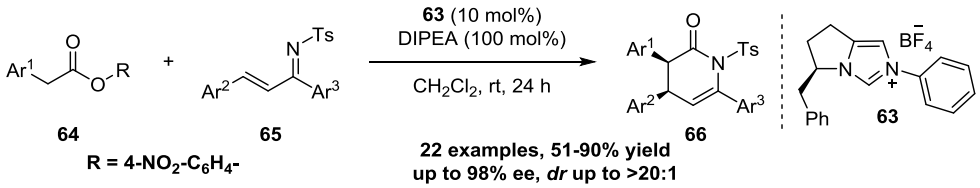
In 2011, Chi and colleagues reported the formal hetero Diels-Alder reaction between formyl cyclopropanes **60** and chalcones **61** for enantioselective synthesis of lactone products **62** in good yields with excellent diastero- and enantioselectivity (Scheme 2.20).[26] This was the first example to access azolium enolate intermediate from formylcyclopropane as starting material. A wide range of chalcones as well as various

aryl derivatives on the formylcyclopropane motif were endured beneath the transformation condition to afford desired product with no reduction in stereocontrol.



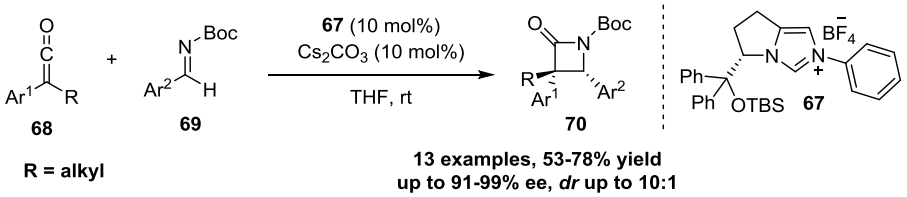

**Scheme 2.20** NHC-catalyzed generation of enolate intermediate from formylcyclopropanes

Furthermore, they have shown that activated carboxylic esters **64** can act as precursors to generate azolium enolates using NHC precursor **63**, which then undergo a formal asymmetric [4+2] annulation with α,β-unsaturated imines **65** to generate the desired dihydropyridinone products **66** in positive yields with valuable diastereo- and enantioselectivity (Scheme 2.21).[27] This approach is currently restricted to the use of arylacetic acid esters.




**Scheme 2.21** NHC-catalyzed generation of enolate intermediate from carboxylate esters

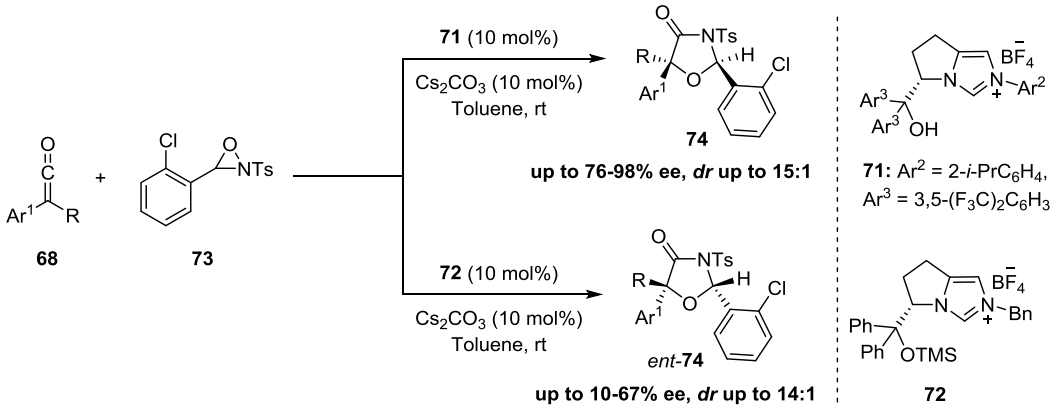
In 2008, Ye and co-workers accessed a ketene derived azolium enolate to develope a precise [2+2] cycloaddition transformation of alkylarylketenes **68** and *N-tert*-butoxycarbonyl imines **69** using (R)-pyroglutamic acid derived precatalyst **67** to furnish the analogous cis-β-lactams **70** in favorable yields with excellent diastereo- and enantioselectivity (Scheme 2.22).[28a] A wide range of ketenes and imines were tolerated under the reaction condition to give corresponding β-lactams.



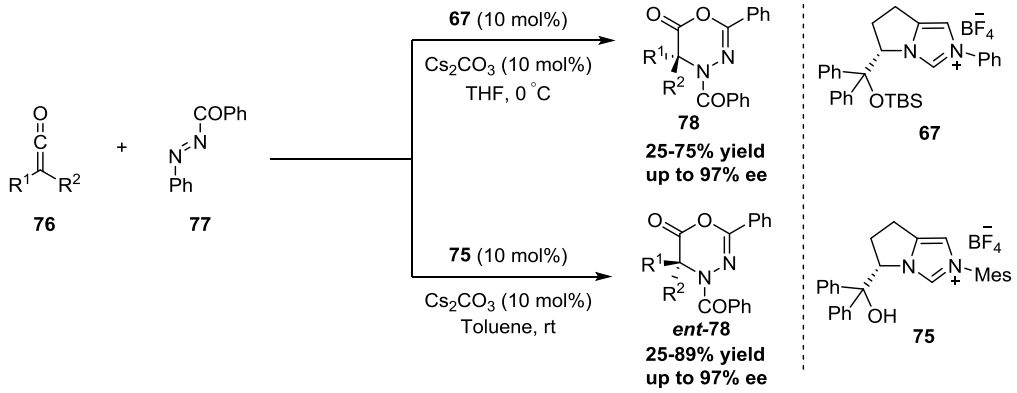

**Scheme 2.22** Generation of azolium enolate intermediate from ketenes

Further, the same group reported the formal [3+2] cycloaddition reaction between ketenes **68** and oxaziridines **73** employing precatalyst **71** for the synthesis of oxazolidin-4-ones **74** in acceptable yields with superb diastero- and enantioselectivity. Importantly, the use of precatalyst **72** furnished opposite stereochemical products, whereas both NHC precatalyst **71** and **72** have identical absolute configurations (Scheme 2.23).[28b] A variety of alkylarylketenes worked well for this transformation.

In 2009, the same research group developed the formal [4+2] cycloaddition reaction between ketenes **76** and *N*-benzoyldiazenes **77** using NHC precatalyst **67** or **75** to give 1,3,4-oxadiazin-6-one **78** in good yields and excellent enantioselectivity (Scheme 2.24).[28c] Importantly, the stereoselectivity of the product could be switched by adjusting the substituents in the NHC-catalyst.

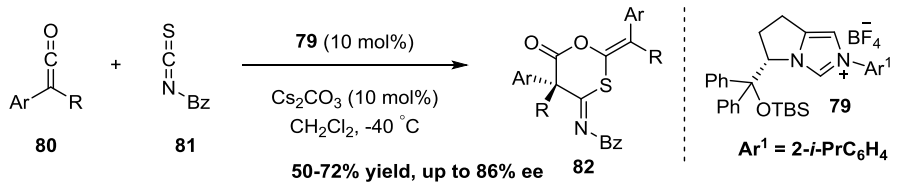



**Scheme 2.23** NHC-mediated [3+2] cycloaddition reaction




**Scheme 2.24** NHC-mediated [4+2] cycloaddition transformation

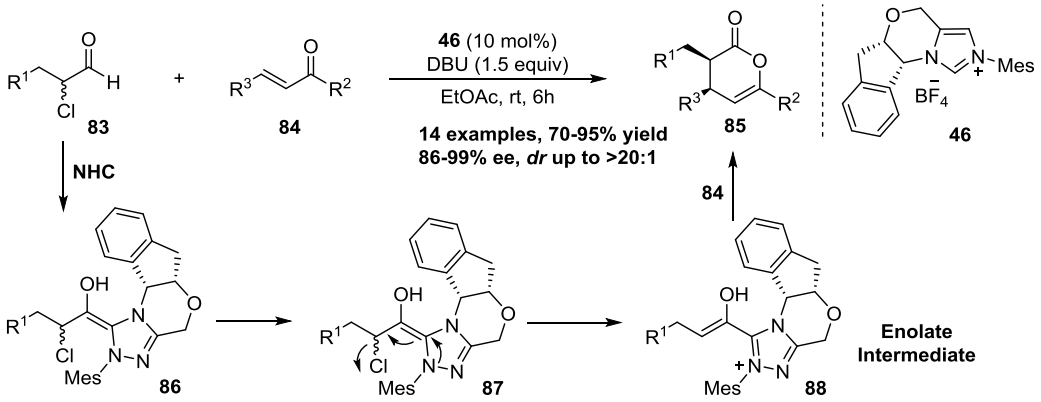
Moreover, Ye and co-workers demonstrated that a formal [2+2+2] pathway could be accessed under NHC-catalysis by employment of ketenes **80** with *N*-benzoylisothiocyanate **81** to afford heterocycles **82** at the reduced reaction temperature of -40 °C (Scheme 2.25).[29] This transformation shows the first asymmetric trimerization of dissimilar ketene equivalents, and provides the desired product in good yields and moderate enantioselectivity.




**Scheme 2.25** NHC-mediated [2+2+2] cycloaddition reaction

Furthermore, the high sensitivity and restricted synthetic diversity of the alkylarylketenes component resulted in the evolution of alternative approach that grant the *in situ* generation of azolium enolate intermediate. In this context, Bode and co-workers succeed to access azolium enolate intermediate **88** from racemic α-chloroaldehydes **83**, which further undergo [4+2] oxodiene Diels-Alder reaction with enones **84** to furnish enantiopure dihydropyranone product **85** (Scheme 2.26).[30] The low

catalyst loading of NHC precursor **46** were used to prepare desired products in excellent yield and high level of diastereo- and enantioselectivity.




**Scheme 2.26** NHC-catalyzed generation of enolate intermediate from α-chloroaldehydes

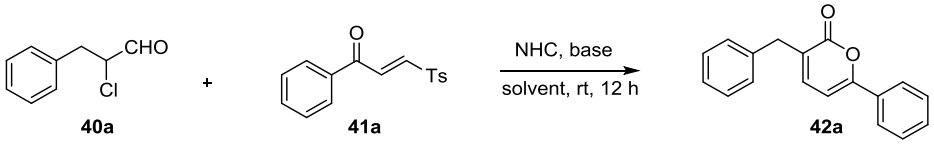
## 2.7 Results and Discussion

### 2.7.1 Optimization Studies

To find an optimal reaction condition, we started our investigation using α-chloroaldehydes **40a** and γ-ketosulfones **41a** as a model substrate (Table 2.1). Initially, the performance of different NHC-precatalyst were assessed using DBU as a base in THF solvent and it was found that imidazolium **89** and thiazolium **90** based catalyst gave inferior results (entry 1-2). However, pyrrolidine derived N-mesityl substituted triazolium precatalyst **38** provided the product **42a** in good yields (entry 4) as compare to N-pentafluorobenzene substituted precatalyst **91** (entry 3). So with NHC-precatalyst **38**, we further screened various bases and it was observed that other organic bases such as TMG and DABCO produced **42a** in reduced yields (entry 5 and 6). Interestingly, the replacement of organic base with inorganic base such as $K_2CO_3$ and $Cs_2CO_3$ provide the desired product **42a** with an improvement in the yield of 65% and 72% respectively (entry 7 and 8). This variation of bases conclude that $Cs_2CO_3$ to be preferred base (entry 8).

Therfore while keeping $Cs_2CO_3$ as a base, we further performed the reaction in different solvents like $CH_3CN$, toluene, $CH_2Cl_2$, chloroform and 1,2-dichloroethane (entry 9-13). It was observed that reaction provides good results in all tested solvents and among various best result with the yield of 94% were obtained while using dichloromethane solvent (entry 11). Notably, a reduction in the production 65% of **42a** was detected while reducing the loading of $Cs_2CO_3$ from 200 mol% to 100 mol% (entry 14). Importantly, the product **42a** was not formed in the absence of NHC-precatalyst **38**, demonstrating its key role in the process (entry 15).

**Table 2.1** Optimization of reaction conditions[a]




| Entry | NHC | Base | Solvent | Yield[b] (%) **42a** |
|---|---|---|---|---|
| 1 | **89** | DBU | THF | 0 |
| 2 | **90** | DBU | THF | 12 |
| 3 | **91** | DBU | THF | 23 |
| 4 | **38** | DBU | THF | 54 |
| 5 | **38** | TMG | THF | 51 |
| 6 | **38** | DABCO | THF | 38 |
| 7 | **38** | $K_2CO_3$ | THF | 65 |
| 8 | **38** | $Cs_2CO_3$ | THF | 72 |
| 9 | **38** | $Cs_2CO_3$ | $CH_3CN$ | 54 |
| 10 | **38** | $Cs_2CO_3$ | toluene | 76 |
| **11** | **38** | **$Cs_2CO_3$** | **$CH_2Cl_2$** | **94** |
| 12 | **38** | $Cs_2CO_3$ | $CHCl_3$ | 91 |
| 13 | **38** | $Cs_2CO_3$ | $(CH_2Cl)_2$ | 90 |
| 14[c] | **38** | $Cs_2CO_3$ | $CH_2Cl_2$ | 65 |
| 15 | - | $Cs_2CO_3$ | $CH_2Cl_2$ | 0 |


[a]Standard reaction condition, unless otherwise specified: **40a** (0.2 mmol), **41a** (0.1 mmol), NHC **38** (20 mol %), $Cs_2CO_3$ (200 mol %), $CH_2Cl_2$ (1.5 mL) at rt for 12 h. [b]Isolated yield of a **42a**.[c]100 mol % of $Cs_2CO_3$ used.

### 2.7.1.1 Characterization of Representative Product 3-benzyl-6-phenyl-2H-pyran-2-one (42a)

The compound **42a** was synthesized by reacting of 2-chloro-3-phenylpropanal **40a** and (E)-1-phenyl-3-tosylprop-2-en-1-one **41a** in presence of 20 mol% NHC-precatalyst **38** using 200 mol% $Cs_2CO_3$ in 1.5 mL of $CH_2Cl_2$ at room temperature for 12 h. The product **42a** was obtained as off white solid in 97% of yield with mp 118-120 $^oC$.

In the $^1H$ NMR of **42a** in $CDCl_3$ at 400 MHz, the appearance of the characteristic peak of protons $\mathbf{H_a}$, $\mathbf{H_b}$ and $\mathbf{H_c}$ at $\delta$ 3.84 (s, 2H), 6.57 (d, $J$ = 6.8 Hz, 1H) and 7.01 (d, $J$ = 6.8 Hz, 1H) in ppm respectively confirmed the formation of desired product **42a** (Figure 2.4). In DEPT-135 NMR spectrum ($CDCl_3$, 100 MHz) the appearance of total 9 signals out of which characteristic peak of $CH_2$ at δ 36.24 ppm confirmed the formation of product **42a** (Figure 2.5).

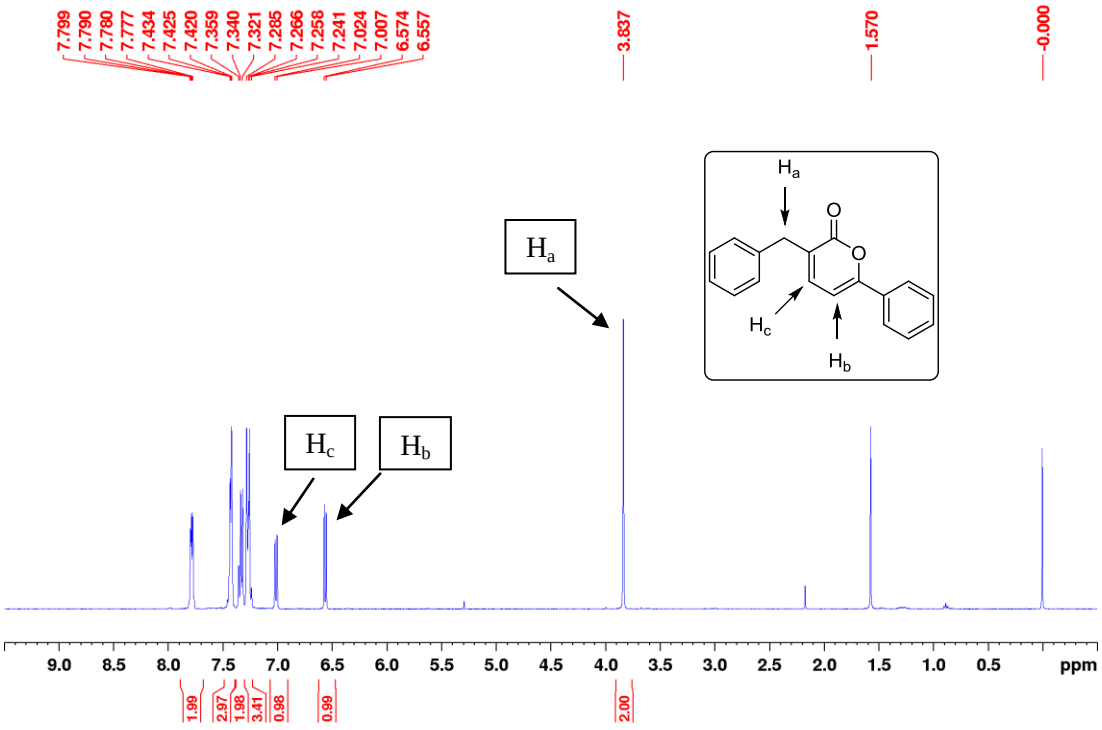



**Figure 2.4** $^1H$ NMR of 3-benzyl-6-phenyl-2H-pyran-2-one (**42a**) in $CDCl_3$ at 400 MHz.

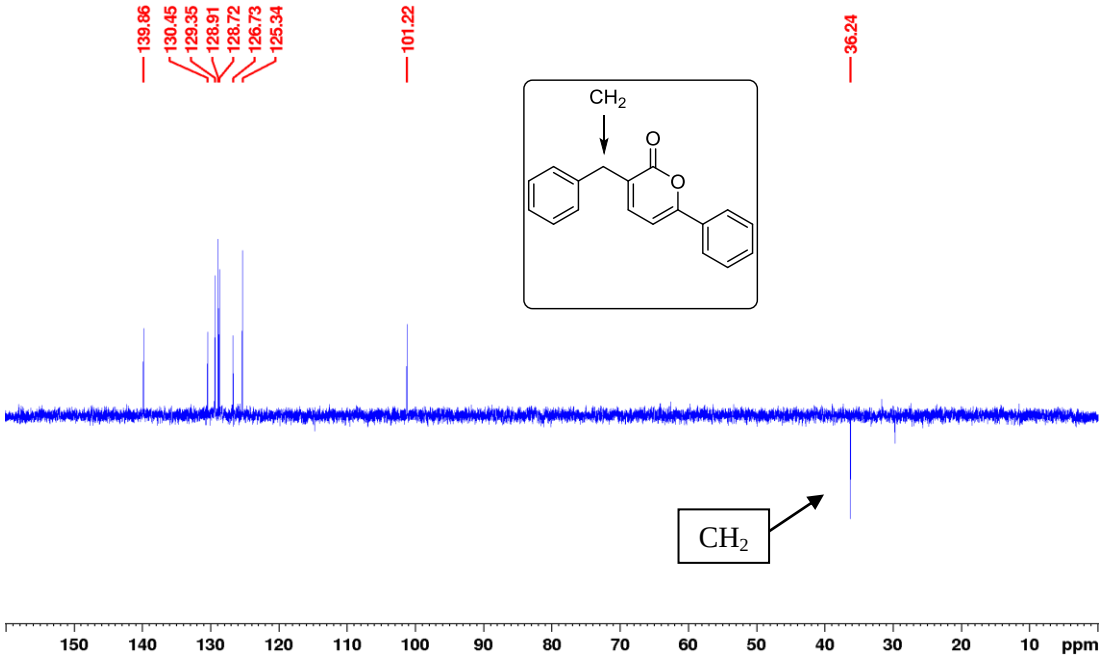



**Figure 2.5** DEPT-135 NMR of 3-benzyl-6-phenyl-2H-pyran-2-one (**42a**) in $CDCl_3$ at 100 MHz

Additionally, in the $^{13}C$ NMR spectrum ($CDCl_3$, 100 MHz), the appearance of four peaks of quaternary $\mathbf{C_q}$ carbon at $\delta$ 127.36, 131.44, 138.05, 158.71 ppm and one for cyclic ester $\mathbf{C_e}$ carbon at $\delta$ 162.78 ppm confirmed the product **42a** (Figure 2.6).

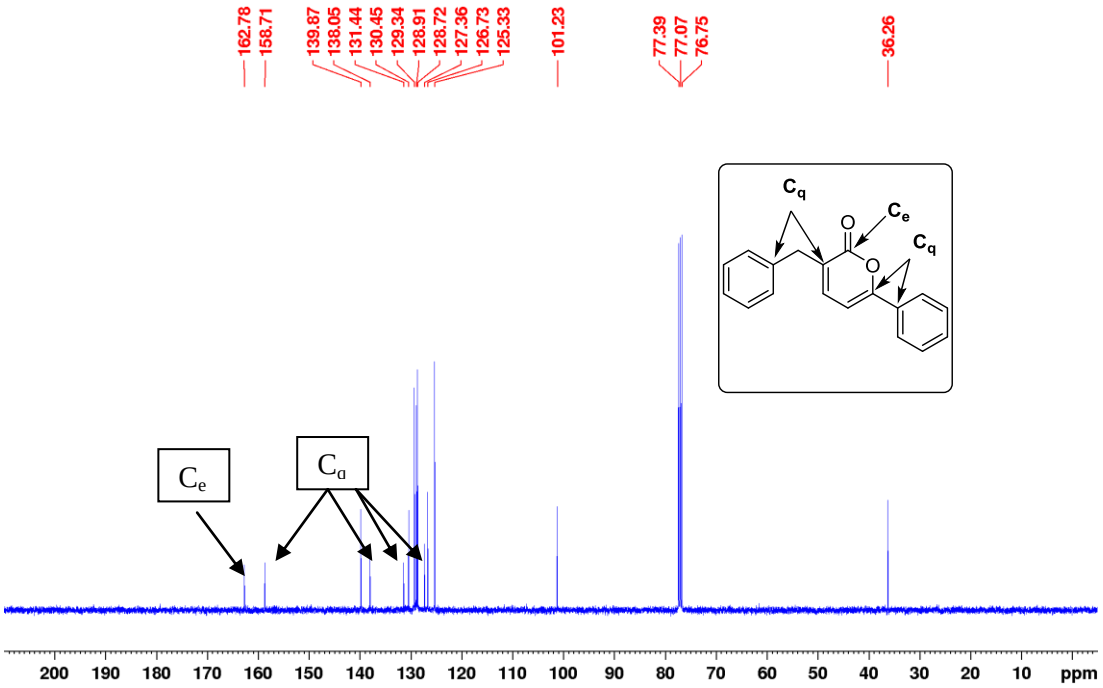


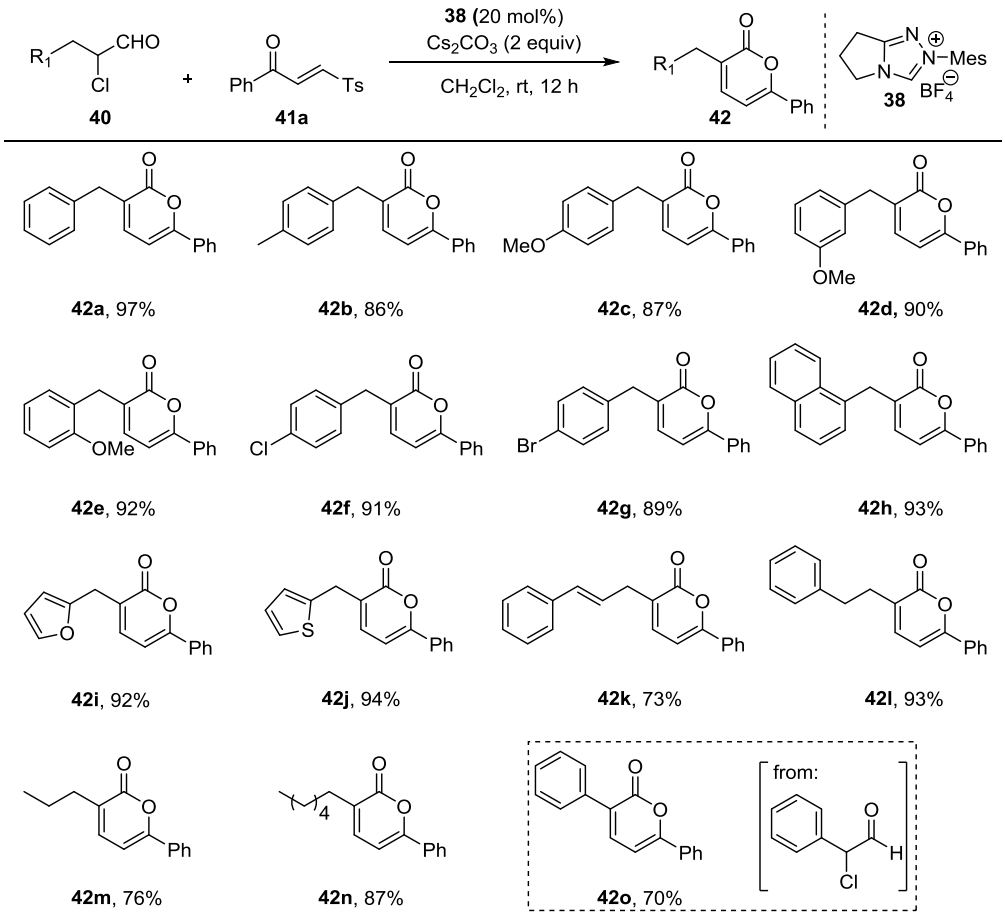

**Figure 2.6** $^{13}C\{1H\}$ NMR of 3-benzyl-6-phenyl-2H-pyran-2-one (**42a**) in $CDCl_3$ at 100 MHz

The appearance of these characteristic protons and carbons established the formation of 3-benzyl-6-phenyl-2H-pyran-2-one **42a**. Its HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{14}NaO_2^+$ 285.0886; found: 285.0884 confirmed its molecular formula to be $C_{18}H_{14}O_2$.

### 2.7.2 Scope of the Reaction for the Synthesis of 3,6-Disubstituted α-Pyrone

After getting the optimized condition (Table 2.1, entry 11) in hand, we then investigated the tolerance of this unique NHC-catalyzed Michael addition-lactonization-elimination cascade reaction with various α-chloro aldehyde **40** derivatives by employing 1-phenyl-3-tosylprop-2-en-1-one **41a** as a model Michael acceptor (Scheme 2.27).

**Scheme 2.27** Scope of α-Chloroaldehydes for the synthesis of 3,6-disubstituted α-pyrone[a,b]



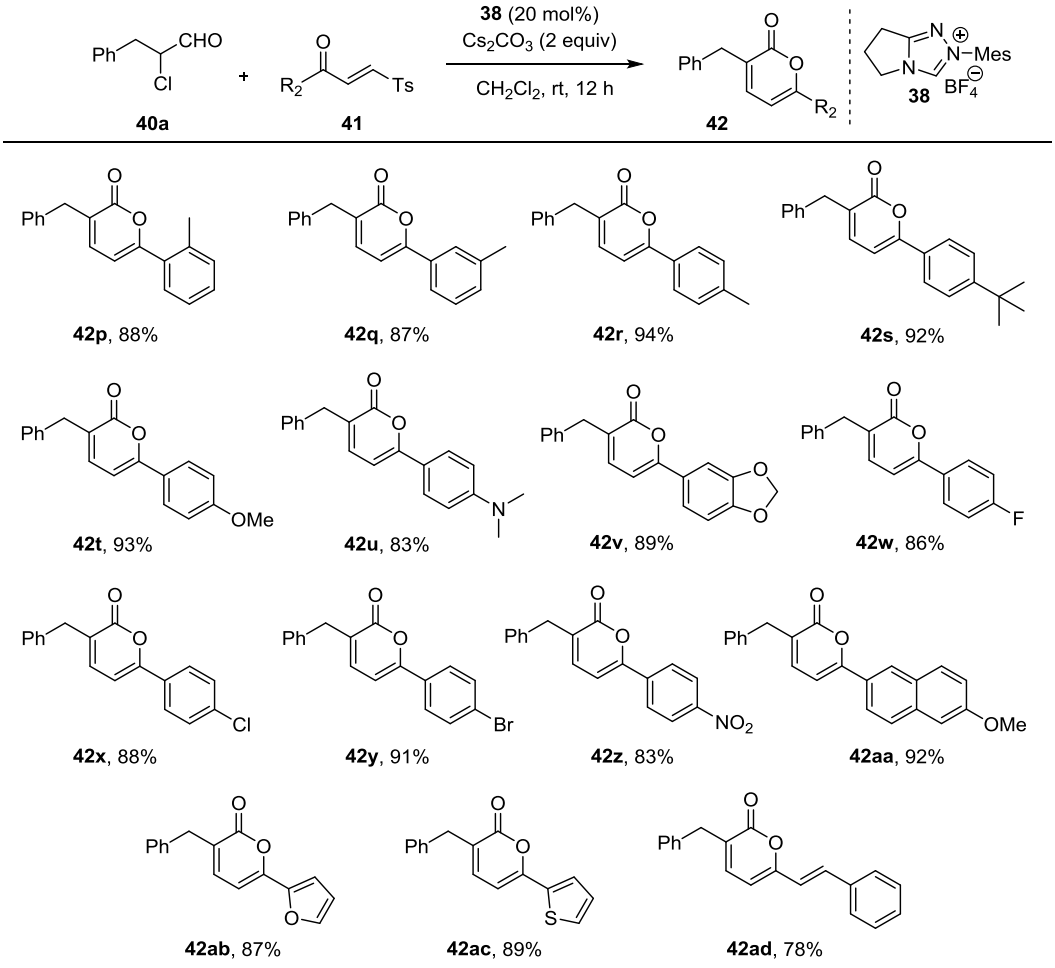

[a]General reaction condition: **40** (0.2 mmol), **41a** (0.1 mmol), NHC **38** (20 mol %), $Cs_2CO_3$ (200 mol %), $CH_2Cl_2$ (1.5 mL) at rt for 12 h. [b]Isolated yields of the product are given.

It was observed that electron-donating substituents at para-, meta- or ortho-position (4-$MeC_6H_4$, 4-$MeOC_6H_4$, 3-$MeOC_6H_4$ and 2-$MeOC_6H_4$) as well as electron-withdrawing substituents at para-position (4-$ClC_6H_4$ and 4-$BrC_6H_4$) of the β-aryl-α-chloroaldehyde underwent smooth reaction to furnish the corresponding α-pyrone (**42b-42g**) in good to excellent yields. Interestingly, the replacement of the β-phenyl substituent by a naphthyl or heteroaryl moiety were also well tolerated without affecting chemical yield (**42h-42j**). Notably, this transformation was not limited to this class of aldehydes. In this context, the presence of unsaturated elements were also compatible and thus providing **42k** in 73% yield. In addition, homobenzylic substituted aldehyde with a phenyl ring afforded the desired product **42l** with 93% yield. Pleasingly, aldehydes with linear alkyl substituent such as pentanal and octanal were also amenable, providing the corresponding product (**42m-42n**) in good yields under the optimized condition. Noteworthy, the replacement of the benzyl group by a phenyl group on α-chloroaldehyde **40a** did not affect the outcome of this reaction and corresponding product **42o** was successfully formed in 70% yield under the standard condition.

In view of these interesting results, we further explore the substrate scope by varying the substituents or substitution types on γ-ketosulfones **41** by using 2-chloro-3-phenylpropanal **40a** as a model substrate under the optimized reaction condition (Scheme 2.28). The various electron-donating substituents at ortho-, meta-, or para-position (2-Me, 3-Me, 4-Me, 4-$C(Me)_3$, 4-OMe and 4-$N(Me)_2$) underwent smooth reaction to furnish corresponding 3,6-disubstituted α-pyrone derivatives (**42p-42u**) in 68-80% yields. Notably, an α-pyrone (**42v**) possessing a piperonyl moiety at the $6^{th}$ position were synthesized using this approach. In addition, the introduction of an

electron-withdrawing substituents at para-position (4-F, 4-Cl, 4-Br and 4-$NO_2$) were also tolerated with the catalytic process, leading to the formation of corresponding α-pyrone (**42w-42z**) in 68-76% yields. Gratifyingly, the replacement of aryl units of **41** by the 6-methoxy 2-naphthyl, heteroaryl or cinnamyl units were also tolerated and thus providing the desired product (**42aa-42ad**) in 63-82% yields. More importantly, we next examined the scalability of the reaction with 1g of γ-ketosulfones **41a** and pleasingly, the desired product **42a** was isolated in 89% yield under the optimized reaction condition.

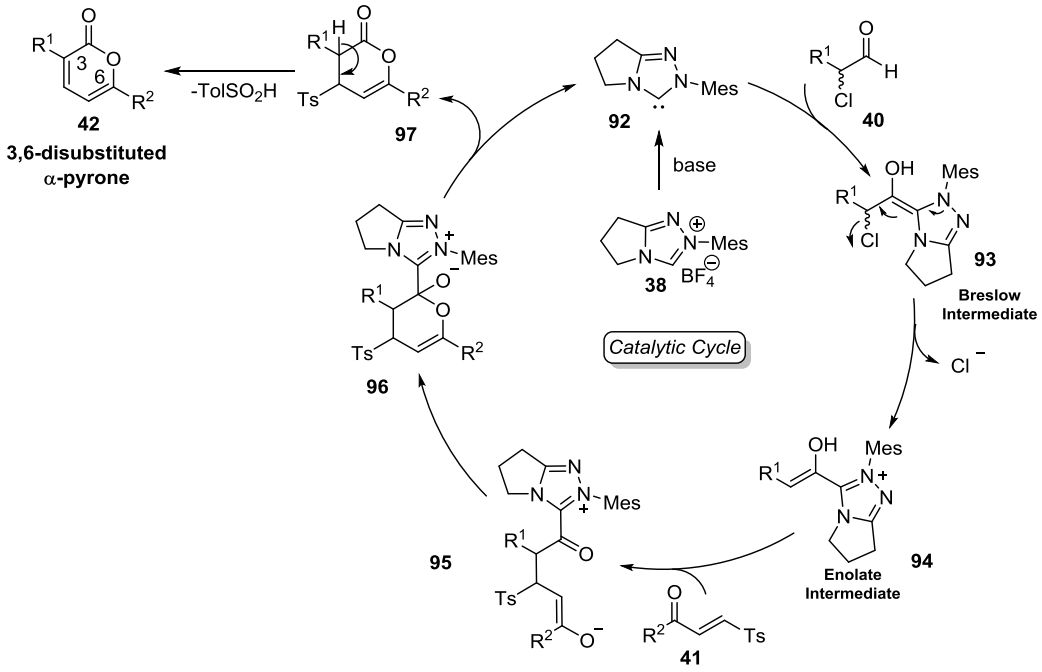
**Scheme 2.28** Scope of γ-ketosulfones for the synthesis of 3,6-disubstituted α-pyrone[a,b]




[a]General reaction condition: **40a** (0.2 mmol), **41** (0.1 mmol), NHC **38** (20 mol %), $Cs_2CO_3$ (200 mol %), $CH_2Cl_2$ (1.5 mL) at rt for 12 h. [b]Isolated yields of the product are given.

### 2.7.3 Proposed Reaction Mechanism

A mechanistic proposal of the transformation is illustrated in Scheme 2.29. Mechanistically, the reaction proceeds with the coupling of carbene **92** with α-chloroaldehyde **40** to generate Breslow intermediate **93**. After leaving of chloride ion an azolium enolate intermediate **94** formed,[30] which undergoes the 1,4-addition to the γ-ketosulfones **41** to produce alkoxide intermediate **95** and subsequent intramolecular cyclisation leads to the formation of sulfone containing dihydropyrone **97** with the release of carbene catalyst. This, dihydropyrone **97** with the release of tosylic acid produced the desired 3,6-disubstituted α-pyrone **42**.

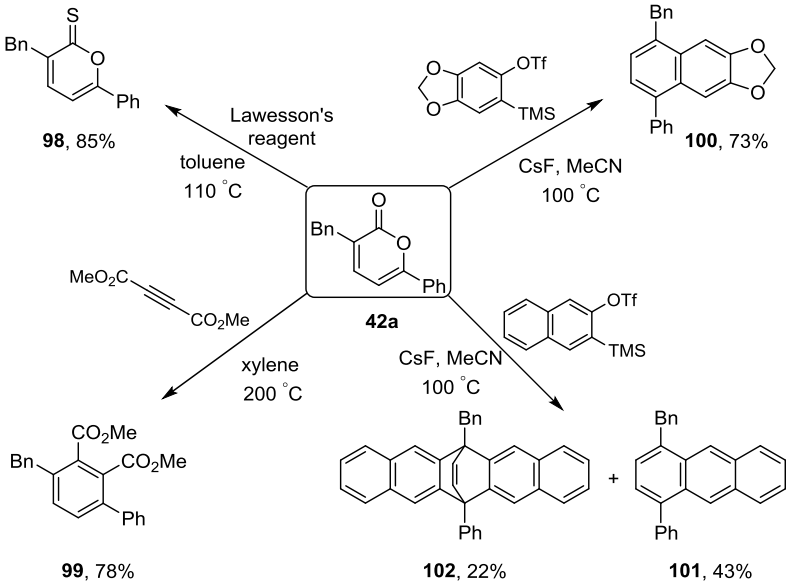



**Scheme 2.29** Plausible mechanism for the formation of 3,6-disubstituted α-pyrone

### 2.7.4 Synthetic Utility of 3,6-Disubstituted α-Pyrone

The synthetic utility of 3,6-disubstituted α-pyrone **42a** were further explored. We examined a series of derivatization to produce synthetically useful building blocks

(Scheme 2.30). In this context, the reaction of **42a** with Lawessons's reagent in dry toluene furnished 3-benzyl-6-phenyl-2H-pyran-2-thione **98** in 85% yield. Moreover, 3,6-disubstituted α-pyrone behaves as stable and reactive diene for Diels-Alder reaction which upon reaction with dienophiles produces cyclo-addition adduct. For instance, the Diels-Alder reaction of **42a** with dimethyl acetylene dicarboxylate produced a highly substituted benzene **99** in 78% yield. In addition, the reaction of **42a** with sesamol based benzyne in acetonitrile furnished a bicyclic adduct, which upon release of $CO_2$ by a retro-Diels-Alder reaction to give 5,8-disubstituted naphtho-1,3-dioxol **100** in 73% yield. Notably, the use of naphthynes instead of sesamol based benzyne delivered a mixture of 1,4-disubstituted anthracene **101** and 6,13-disubstituted ethenopentacene **102** in a relatively low yield.




**Scheme 2.30** Synthetic transformation of 3,6-disubstituted α-pyrone

## 2.8 Conclusion

In conclusion, we have described a NHC-catalyzed formal [4+2] annulation between α-chloro aldehydes and γ-keto sulfones to provide a variety of 3,6-disubstituted α-pyrone

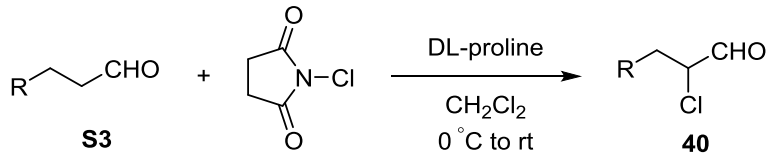
in good to excellent yields. The reaction proceeded through Michael addition followed by lactonization-elimination cascade sequence and provided the desired α-pyrone for a panel of α-chloro aldehydes using γ-ketosulfones as a key Michael acceptor. Notably, the present protocol is attractive due to its operationally simplicity and mild reaction conditions. In addition, we also performed the gram-scale synthesis for 3,6-disubstituted α-pyrone and synthetic utility of the product to access a series of value-added molecules.

## 2.9 Experimental Section

### 2.9.1 General Information and Method

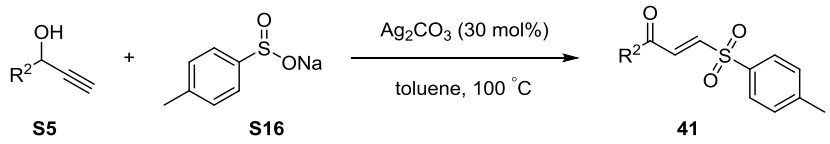
Aldehydes and other fine chemicals were obtained from commercial suppliers and used without purification. Solvents were dried and distilled following the standard procedures. TLC observation was carried out on precoated plates (Merck silica gel 60, $f_{254}$), and the spots were visualized with UV light or by charring the plates dipped in PMA/$KMnO_4$ solution. Flash chromatography was performed using silica gel (230-400 mesh) with distilled solvents. $^{1}H$ and $^{13}C\{^{1}H\}$ NMR for compounds were recorded at 400 MHz instruments and 100 MHz instrument, respectively, using $CDCl_3$ as the solvent unless stated otherwise. Chemical shifts were recorded in parts per million (ppm, δ). $^{1}H$ and $^{13}C\{H\}$ NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sext), septet (sep), doublet of doublet (dd), doublet of triplet (dt), triplet of doublets (td), multiplet (m) etc. High resolution mass spectral analysis (HRMS) was performed on Q-TOF Premier mass spectrometer.

### 2.9.2 General Procedure for the Synthesis of α-Chloro Aldehyde 40[19]




To a stirred solution of aldehyde derivative **S3** (10 mmol, 1 equiv.) in dichloromethane (40mL) at 0 °C was added under argon *DL*-Proline (2 mmol, 0.2 equiv.) and *N*-chlorosuccinimide (NCS, 10 mmol, 1 equiv.). The reaction mixture was stirred at 0 °C for 1 h, and then allowed to reach room temperature and stirred for additional 1.5 h. The reaction was monitored by $^1$H NMR. If the starting aldehyde is not totally consumed, extra NCS was added by small portions until full conversion. The reaction was quenched by addition of pentane (50 mL) and the precipitate was filtered off. The filtrate was concentrated under vacuum and the residue was purified by flash column chromatography on silica gel using hexane/ethyl acetate as eluent to afford the desired α-chloro-aldehyde derivative **40** as a colorless oil.

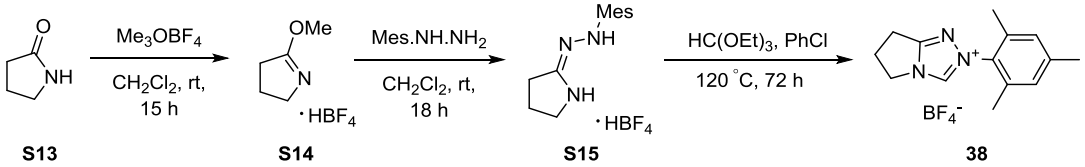
### 2.9.3 General Procedure for the Synthesis of γ-Keto Sulfones 41[20]




A screw-capped reaction vial was charged propargylic alcohol derivative **S5** (0.5 mmol, 1 equiv.) and sodium *p*-methylphenyl sulfinate **S16** (0.75 mmol, 1.5 equiv.) in toluene (2.0 mL) and stirred at room temperature. Subsequently, $Ag_2CO_3$ (0.15 mmol, 0.3 equiv.) was added and the reaction mixture was stirred at 100 °C until the propargylic alcohol **S5** was completely consumed as indicated by thin layer chromatography (TLC). The resulting mixture was concentrated and the residue was

taken up in ethyl acetate. The organic layer was dried over $NaSO_4$ and concentrated. Purification of the crude product by flash column chromatography on silica gel using hexane/ethyl acetate as eluent to afford the desired γ-Keto Sulfones derivative **41** as a colorless solid.

### 2.9.4 Procedure for the Synthesis of NHC-Precatalyst 38

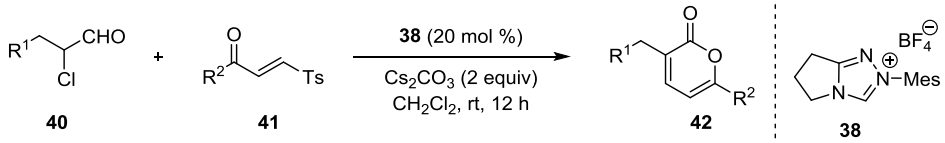



**S13** **S14** **S15** **38**

The triazolium salt **38** was prepared by following the general procedure of Rovis et al.[21b] To a solution of pyrrolidin 2-one (0.52 mL, 6.8 mmol) in anhydrous $CH_2Cl_2$ (25 mL) was added trimethyl oxonium tetrafluoroborate (1.03 g, 6.96 mmol) under argon atmosphere and the mixture was stirred for 18 hrs at room temperature. Then, mesitylhydrazine (1.06 g, 6.96 mmol) was added under inert atmosphere and the resulting orange solution stirred for a further 18 hrs at room temperature. The mixture was then concentrated in vacuo and upon addition of EtOAc (25 mL) the solid hydrazone was formed which was collected by filtration and washed with EtOAc (3 x 10 mL) and then dried under vacuum for several hours provided the hydrazone as an off-white solid (1.06 g) in 51% yield. To this hydrazone chlorobenzene (7 mL) and triethyl ortho-formate (2.89 mL, 17.4 mmol) was added and the mixture was stirred in sealed tube at 120 °C for 72 hours. Then, the mixture was concentrated in vacuo and EtOAc (15 mL) was added and the formed solid was collected by filtration followed by washing with EtOAc (3 x 10 mL). Then the solid was dried under vacuum for several hours to give 2-mesityl-6,7 dihydro-5H-pyrrolo[2,1 *c*] [1,2,4] triazol-2-ium tetrafluoroborate **38** as a an off-white solid (860 mg) in 79% yield.

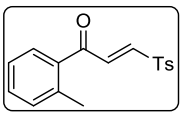
### 2.9.5 General Procedure for the Synthesis of 3,6-Disubstituted α-Pyrone 42

In an oven-dried Schlenk tube equipped with a magnetic stirrer was added under argon the NHC-pre-catalyst **38** (0.02 mmol, 20 mol %) and γ-Keto Sulfone **41** (0.1 mmol). The tube was sealed with a septum, evacuated and refilled with argon (3 cycles). Dichloromethane (1.5 mL), α-chloro aldehyde **40** (0.2 mmol, 2 equiv.), and $Cs_2CO_3$ (0.2 mmol, 2 equiv.) were then added and the reaction mixture was stirred at room temperature for 12 hours. After completion of the reaction, the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography using hexane/ethyl acetate as eluent to afford the desired product **42**.




### 2.9.6 Characterization Data

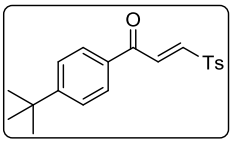
***(E)-1-(o-tolyl)-3-tosylprop-2-en-1-one (41p)***




The title compound was prepared following the general procedure **2.9.3** described above using **S5p** (0.5 mmol, 73 mg, 1.0 equiv.) and **S16** (0.75 mmol, 134 mg, 1.5 equiv.). The product was isolated in 56% yield (84 mg), pale yellow solid, mp 113-115 °C, eluent:(hexane/EtOAc, 90/10); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.47 (d, $J$ = 4.0 Hz, 6H), 7.18 (d, $J$ = 16.0 Hz, 1H), 7.27-7.35 (m, 2H), 7.38 (d, $J$ = 8.0 Hz, 2H), 7.45 (t, $J$ = 8.0 Hz, 1H), 7.56-7.65 (m, 2H), 7.82 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.0, 21.6, 125.9, 128.3, 129.6, 130.2, 132.1, 132.6, 135.6, 135.9, 139.2,

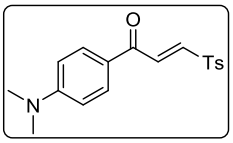
142.0, 145.5, 191.2; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{17}H_{16}NaO_3S^+$ 323.0712; found: 323.0714.

***(E)-1-(4-(tert-butyl) phenyl)-3-tosylprop-2-en-1-one (41s)***




The title compound was prepared following the general procedure **2.9.3** described above using **S5s** (0.5 mmol, 94 mg, 1.0 equiv.) and **S16** (0.75 mmol, 134 mg, 1.5 equiv.). The product was isolated in 53% yield (91 mg), light brown solid, mp 113-115 °C, eluent: (hexane/ EtOAc, 90/10); **$^1$H NMR (400 MHz, CDCl$_3$)**: $\delta$ 1.34 (s, 9H), 2.45 (s, 3H), 7.33 (d, $J$ = 12.0 Hz, 1H), 7.37 (d, $J$ = 8.0 Hz, 2H), 7.52 (d, $J$ = 8.0 Hz, 2H), 7.82 (d, $J$ = 8.0 Hz, 2H), 7.86-7.95 (m, 3H); **$^{13}$C{$^1$H} NMR (100 MHz, CDCl$_3$)**: $\delta$ 21.7, 30.9, 35.3, 126.0, 128.3, 128.9, 130.2, 132.8, 133.5, 135.7, 141.9, 145.5, 158.5, 187.2; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{20}H_{22}NaO_3S^+$ 365.1182; found: 365.1185.

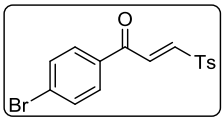
***(E)-1-(4-(dimethylamino) phenyl)-3-tosylprop-2-en-1-one (41u)***




The title compound was prepared following the general procedure **2.9.3** described above using **S5u** (0.5 mmol, 88 mg, 1.0 equiv.) and **S16** (0.75 mmol, 134 mg, 1.5 equiv.). The product was isolated in 61% yield (101 mg), red brown solid, mp 172-174 °C, eluent: (hexane/ EtOAc, 85/15); **$^1$H NMR (400 MHz, CDCl$_3$)**: $\delta$ 2.44 (s, 3H), 3.10 (s, 6H), 6.67 (d, $J$ = 8.0 Hz, 2H), 7.29 (d, $J$ = 16.0 Hz, 1H), 7.36 (d, $J$ = 8.0 Hz, 2H),

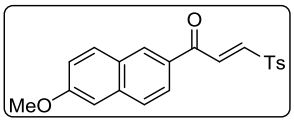
7.82 (d, *J* = 8.0 Hz, 2H), 7.88-7.97 (m, 3H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.7, 40.0, 110.9, 124.1, 128.2, 130.1, 131.5, 133.6, 136.1, 140.2, 145.2, 154.2, 184.3; **HRMS (ESI-TOF) m/z**: $[M + H]^+$ calcd for $C_{18}H_{20}NO_3S^+$ 330.1158; found: 330.1158.

***(E)-1-(4-bromophenyl)-3-tosylprop-2-en-1-one (41y)***




The title compound was prepared following the general procedure **2.9.3** described above using **S5y** (0.5 mmol, 106 mg, 1.0 equiv.) and **S16** (0.75 mmol, 134 mg, 1.5 equiv.). The product was isolated in 59% yield (108 mg), red brown solid, mp 147-149 °C, eluent: (hexane/ EtOAc, 85/15); **$^{1}H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.46 (s, 3H), 7.35 (d, *J* = 16.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.80-7.88 (m, 5H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.7, 128.4, 129.9, 130.3, 131.9, 132.4, 134.8, 135.5, 142.8, 145.7, 186.8; **HRMS (ESI-TOF) m/z**: $[M + H]^+$ calcd for $C_{16}H_{14}BrO_3S^+$ 364.9842; found: 364.9836.

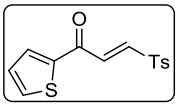
***(E)-1-(6-methoxynaphthalen-2-yl)-3-tosylprop-2-en-1-one (41aa)***




The title compound was prepared following the general procedure **2.9.3** described above using **S5aa** (0.5 mmol, 106 mg, 1.0 equiv.) and **S16** (0.75 mmol, 134 mg, 1.5 equiv.). The product was isolated in 65% yield (119 mg), yellow solid, mp 164-166 °C, eluent: (hexane/EtOAc, 80/20); **$^{1}H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.46 (s, 3H), 3.96 (s, 3H), 7.17 (s, 1H), 7.22-7.27 (m, 1H), 7.35-7.44 (m, 3H), 7.80 (d, *J* = 12.0 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 8.08 (d, *J* = 16.0

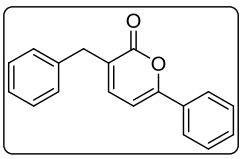
Hz, 1H), 8.44 (s, 1H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.7, 55.5, 105.9, 120.2, 124.6, 127.6, 127.8, 128.3, 130.2, 131.3, 131.5, 131.5, 132.8, 135.8, 138.0, 141.7, 145.5, 160.5, 186.9; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{21}H_{18}NaO_4S^+$ 389.0818; found: 389.0814.

***(E)-1-(thiophen-2-yl)-3-tosylprop-2-en-1-one (41ac)***




The title compound was prepared following the general procedure **2.9.3** described above using **S5ac** (0.5 mmol, 69 mg, 1.0 equiv.) and **S16** (0.75 mmol, 134 mg, 1.5 equiv.). The product was isolated in 53% yield (77 mg), yellow solid, mp 143-145 °C, eluent: (hexane/EtOAc, 80/20); **$^{1}H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.45 (s, 3H), 7.21 (t, $J$ = 4.0 Hz, 1H), 7.32-7.41 (m, 3H), 7.75 (d, $J$ = 16.0 Hz, 1H), 7.78-7.85 (m, 3H), 7.88 (d, $J$ = 4.0 Hz, 1H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.7, 128.3, 128.8, 130.2, 132.2, 134.1, 135.5, 136.7, 141.8, 143.7, 145.6, 179.3; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{14}H_{12}NaO_3S_2^+$ 315.0120; found: 315.0121.

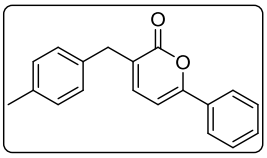
***3-benzyl-6-phenyl-2H-pyran-2-one (42a)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 97% yield (25.4 mg), white solid, mp 118-120 °C, eluent: (hexane/EtOAc, 95/5); **$^{1}H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.84 (s, 2H), 6.57 (d, $J$ = 6.8 Hz, 1H), 7.01 (d, $J$ = 6.8 Hz, 1H), 7.23-7.30 (m, 3H), 7.31-7.37 (m, 2H), 7.40-7.47

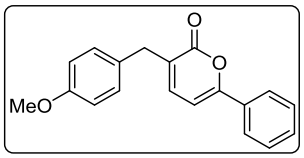
(m, 3H), 7.76-7.82 (m, 2H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.2, 101.2, 125.3, 126.7, 127.3, 128.7, 128.8, 129.3, 130.4, 131.4, 138.0, 139.8, 158.6, 162.7; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{14}NaO_2^+$ 285.0886; found: 285.0884.

***3-(4-methylbenzyl)-6-phenyl-2H-pyran-2-one (42b)***



The title compound was prepared following the general procedure **2.9.5** described above using **40b** (0.2 mmol, 36.5 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 86% yield (23.8 mg), white solid, mp 145-147 °C, eluent: (hexane/EtOAc, 95/5); **$^{1}H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.34 (s, 3H), 3.80 (s, 2H), 6.56 (d, $J$ = 8.0 Hz, 1H), 7.01 (d, $J$ = 8.0 Hz, 1H), 7.11-7.20 (m, 4H), 7.38-7.47 (m, 3H), 7.74-7.83 (m, 2H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.0, 35.8, 101.2, 125.3, 127.6, 128.9, 129.2, 129.4, 130.4, 131.4, 134.9, 136.2, 139.7, 158.6, 162.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_2^+$ 299.1043; found: 299.1042.

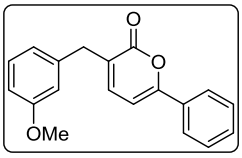
***3-(4-methoxybenzyl)-6-phenyl-2H-pyran-2-one (42c)***




The title compound was prepared following the general procedure **2.9.5** described above using **40c** (0.2 mmol, 39.7 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 87% yield (25.4 mg), white solid, mp 100-102 °C, eluent: (hexane/EtOAc, 90/10); **$^{1}H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.78 (s, 2H), 3.80 (s, 3H), 6.56 (d, $J$ = 8.0 Hz, 1H), 6.88 (d, $J$ = 8.0 Hz, 2H), 7.00 (d, $J$ = 8.0 Hz, 1H), 7.19 (d,

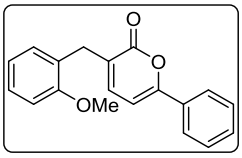
*J* = 8.0 Hz, 2H), 7.39-7.46 (m, 3H), 7.75-7.81 (m, 2H); **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 35.4, 55.3, 101.2, 114.1, 125.3, 127.8, 128.9, 130.0, 130.3, 130.4, 131.4, 139.6, 158.4, 158.6, 162.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_3^+$ 315.0992; found: 315.0984.

***3-(3-methoxybenzyl)-6-phenyl-2H-pyran-2-one (42d)***




The title compound was prepared following the general procedure **2.9.5** described above using **40d** (0.2 mmol, 39.7 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 90% yield (26.3 mg), pale yellow solid, mp 80-82 °C, eluent: (hexane/EtOAc, 90/10); **$^1H$ NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.81 (s, 5H), 6.57 (d, *J* = 8.0 Hz, 1H), 6.78-6.84 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 7.22-7.29 (m, 2H), 7.40-7.47 (m, 3H), 7.76-7.82 (m, 2H); **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.2, 55.2, 101.2, 112.1, 115.0, 121.7, 125.3, 127.2, 128.9, 129.7, 130.4, 131.4, 139.6, 139.9, 158.7, 159.9, 162.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_3^+$ 315.0992; found: 315.0985.

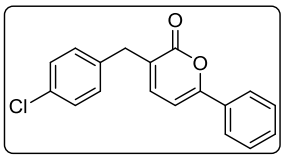
***3-(2-methoxybenzyl)-6-phenyl-2H-pyran-2-one (42e)***




The title compound was prepared following the general procedure **2.9.5** described above using **40e** (0.2 mmol, 39.7 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 92% yield (26.9 mg), pale yellow solid, mp 112-

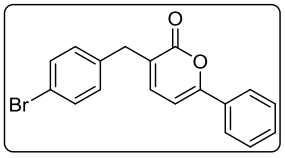
114 °C, eluent: (hexane/EtOAc, 90/10); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.81 (s, 3H), 3.83 (s, 2H), 6.54 (d, $J$ = 8.0 Hz, 1H), 6.87-6.99 (m, 3H), 7.22-7.29 (m, 2H), 7.38-7.46 (m, 3H), 7.74-7.81 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 30.6, 55.3, 101.3, 110.5, 120.7, 125.2, 126.2, 126.7, 128.2, 128.8, 130.2, 131.2, 131.6, 139.3, 157.6, 158.2, 162.9; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_3^+$ 315.0992; found: 315.0985.

***3-(4-chlorobenzyl)-6-phenyl-2H-pyran-2-one (42f)***




The title compound was prepared following the general procedure **2.9.5** described above using **40f** (0.2 mmol, 40.6 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 91% yield (27.0 mg), yellow solid, mp 103-105 °C, eluent: (hexane/EtOAc, 92/8); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.80 (s, 2H), 6.58 (d, $J$ = 8.0 Hz, 1H), 7.05 (d, $J$ = 8.0 Hz, 1H), 7.21 (d, $J$ = 8.0 Hz, 2H), 7.30 (d, $J$ = 8.0 Hz, 2H), 7.40-7.47 (m, 3H), 7.75-7.82 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 35.7, 101.1, 125.3, 126.7, 128.8, 128.9, 130.5, 130.6, 131.3, 132.5, 136.5, 140.0, 159.0, 162.6; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{13}ClNaO_2^+$ 319.0496; found: 319.0498.

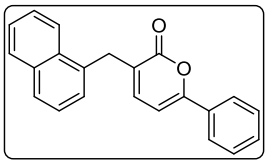
***3-(4-bromobenzyl)-6-phenyl-2H-pyran-2-one (42g)***




The title compound was prepared following the general procedure **2.9.5** described above using **40g** (0.2 mmol, 49.5 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0

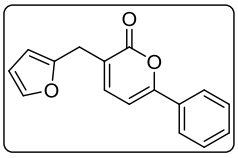
equiv.). The product was isolated in 89% yield (30.4 mg), yellow solid, mp 108-110 °C, eluent: (hexane/EtOAc, 90/10); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.78 (s, 2H), 6.58 (d, $J$ = 8.0 Hz, 1H), 7.05 (d, $J$ = 8.0 Hz, 1H), 7.16 (d, $J$ = 8.0 Hz, 2H), 7.39-7.47 (m, 5H), 7.74-7.82 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 35.7, 101.1, 120.6, 125.3, 126.6, 128.9, 130.5, 130.9, 131.3, 131.7, 137.0, 140.0, 159.0, 162.5; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{13}BrNaO_2^+$ 362.9991; found: 362.9986.

***3-(naphthalen-2-ylmethyl)-6-phenyl-2H-pyran-2-one (42h)***



The title compound was prepared following the general procedure **2.9.5** described above using **40h** (0.2 mmol, 43.7 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 93% yield (29.1 mg), yellow solid, mp 80-82 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 4.30 (s, 2H), 6.44 (d, $J$ = 8.0 Hz, 1H), 6.70 (d, $J$ = 8.0 Hz, 1H), 7.39-7.44 (m, 4H), 7.45-7.52 (m, 3H), 7.74-7.80 (m, 2H), 7.82 (d, $J$ = 8.0 Hz, 1H), 7.85-7.92 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 33.1, 101.2, 124.1, 125.3, 125.6, 125.8, 126.4, 126.6, 127.8, 128.1, 128.8, 128.8, 130.4, 131.3, 131.9, 133.8, 133.9, 139.9, 158.4, 162.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{22}H_{16}NaO_2^+$ 335.1043; found: 335.1044.

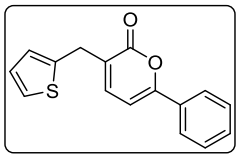
***3-(furan-2-ylmethyl)-6-phenyl-2H-pyran-2-one (42i)***



The title compound was prepared following the general procedure **2.9.5** described above using **40i** (0.2 mmol, 31.7 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The

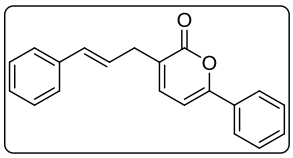
product was isolated in 92% yield (23.2 mg), reddish brown semi solid, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.87 (s, 2H), 6.20 (d, $J$ = 2.8 Hz, 1H), 6.35 (br, 1H), 6.61 (d, $J$ = 8.0 Hz, 1H), 7.14 (d, $J$ = 8.0 Hz, 1H), 7.37 (d, $J$ = 0.8 Hz, 1H), 7.41-7.46 (m, 3H), 7.77-7.82 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 28.6, 101.2, 107.5, 110.5, 124.2, 125.3, 128.9, 130.5, 131.3, 140.1, 141.9, 151.3, 159.0, 162.4; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{16}H_{12}NaO_3^+$ 275.0679; found: 275.0675.

***6-phenyl-3-(thiophen-2-ylmethyl)-2H-pyran-2-one (42j)***




The title compound was prepared following the general procedure **2.9.5** described above using **40j** (0.2 mmol, 34.9 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 94% yield (25.2 mg), reddish brown solid, mp 100-102 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 4.04 (s, 2H), 6.60 (d, $J$ = 8.0 Hz, 1H), 6.93-7.00 (m, 2H), 7.17 (d, $J$ = 8.0 Hz, 1H), 7.20 (d, $J$ = 4.8 Hz, 1H), 7.39-7.46 (m, 3H), 7.76-7.82 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 30.1, 101.2, 124.5, 125.3, 126.4, 126.5, 127.1, 128.8, 130.5, 131.2, 139.9, 140.0, 158.9, 162.4; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{16}H_{12}NaO_2S^+$ 291.0450; found: 291.0449.

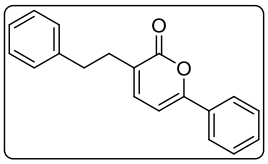
***3-cinnamyl-6-phenyl-2H-pyran-2-one (42k)***




The title compound was prepared following the general procedure **2.9.5** described above using **40k** (0.2 mmol, 38.9 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 73% yield (21.0 mg), yellow solid, mp 101-103 °C,

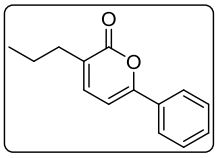
eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.42 (d, $J$ = 6.8 Hz, 2H), 6.34 (dt, $J$ = 16.0, 8.0 Hz, 1H), 6.55 (d, $J$ = 16.0 Hz, 1H), 6.63 (d, $J$ = 8.0 Hz, 1H), 7.19-7.35 (m, 4H), 7.39 (d, $J$ = 8.0 Hz, 2H), 7.41-7.48 (m, 3H), 7.77-7.85 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 33.5, 101.2, 125.3, 125.5, 126.1, 126.2, 127.4, 128.5, 128.9, 130.4, 131.4, 132.9, 137.0, 139.6, 158.8, 162.7; **HRMS (ESI-TOF) m/z**: [M + Na]$^+$ calcd for $C_{20}H_{16}NaO_2^+$ 311.1043; found: 311.1042.

***3-phenethyl-6-phenyl-2H-pyran-2-one (42l)***



The title compound was prepared following the general procedure **2.9.5** described above using **40l** (0.2 mmol, 36.5 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 93% yield (25.7 mg), white solid, mp 115-117 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.8 (t, $J$ = 8.0 Hz, 2H), 2.95 (t, $J$ = 8.0 Hz, 2H), 6.55 (d, $J$ = 8.0 Hz, 1H), 7.05 (d, $J$ = 8.0 Hz, 1H), 7.15-7.23 (m, 3H), 7.24-7.32 (m, 2H), 7.39-7.47 (m, 3H), 7.76-7.83 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 32.6, 34.0, 101.1, 125.2, 126.0, 126.6, 128.4, 128.5, 128.8, 130.3, 131.4, 139.8, 141.0, 158.6, 162.8; **HRMS (ESI-TOF) m/z**: [M + Na]$^+$ calcd for $C_{19}H_{16}NaO_2^+$ 299.1043; found: 299.1042.

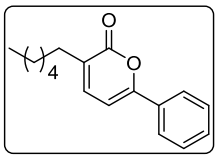
***6-phenyl-3-propyl-2H-pyran-2-one (42m)***



The title compound was prepared following the general procedure **2.9.5** described above using **40m** (0.2 mmol, 24.1 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0

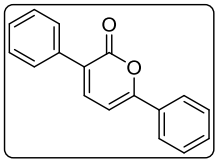
equiv.). The product was isolated in 76% yield (16.3 mg), colorless semi solid, eluent: (hexane/EtOAc, 97/3); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 0.99 (t, $J$ = 8.0 Hz, 3H), 1.65 (sext, $J$ = 8.0 Hz, 2H), 2.49 (t, $J$ = 8.0 Hz, 2.0H), 6.61 (d, $J$ = 8.0 Hz, 1H), 7.20 (d, $J$ = 8.0 Hz, 1H), 7.39-7.47 (m, 3H), 7.77-7.84 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 13.7, 21.2, 32.5, 101.2, 125.2, 127.8, 128.8, 130.3, 131.6, 139.1, 158.4, 163.0; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{14}H_{14}NaO_2^+$ 237.0886; found: 237.0883.

***3-hexyl-6-phenyl-2H-pyran-2-one (42n)***



The title compound was prepared following the general procedure **2.9.5** described above using **40n** (0.2 mmol, 32.5 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0 equiv.). The product was isolated in 87% yield (22.3 mg), colorless semi solid, eluent: (hexane/EtOAc, 97/3); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 0.82-0.94 (m, 3H), 1.20-1.44 (m, 6H), 1.57-1.65 (m, 2H), 2.50 (t, $J$ = 8.0 Hz, 2H), 6.61 (d, $J$ = 6.8 Hz, 1H), 7.19 (d, $J$ = 6.8 Hz, 1H), 7.40-7.47 (m, 3H), 7.77-7.84 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 14.0, 22.6, 27.9, 28.9, 30.5, 31.6, 101.2, 125.2, 128.1, 128.8, 130.2, 131.6, 138.9, 158.3, 163.0; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{17}H_{20}NaO_2^+$ 279.1356; found: 279.1354.

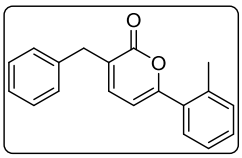
***3,6-diphenyl-2H-pyran-2-one (42o)***



The title compound was prepared following the general procedure **2.9.5** described above using **40o** (0.2 mmol, 30.9 mg, 2.0 equiv.) and **41a** (0.1 mmol, 28.6 mg, 1.0

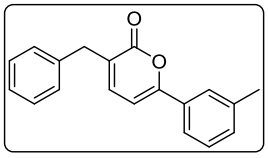
equiv.). The product was isolated in 70% yield (17.4 mg), light yellow solid, mp 153-155 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 6.80 (d, $J$ = 8.0 Hz, 1H), 7.34-7.50 (m, 6H), 7.58 (d, $J$ = 8.0 Hz, 1H), 7.73 (d, $J$ = 8.0 Hz, 2H), 7.84-7.92 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 101.7, 125.5, 125.7, 128.1, 128.4, 128.4, 128.9, 130.7, 131.2, 134.8, 140.3, 159.8, 161.4; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{17}H_{12}NaO_2^+$ 271.0730; found: 271.0727.

***3-benzyl-6-(o-tolyl)-2H-pyran-2-one (42p)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41p** (0.1 mmol, 30.1 mg, 1.0 equiv.). The product was isolated in 88% yield (24.3 mg), yellow solid, mp 107-109 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.45 (s, 3H), 3.83 (s, 2H), 6.23 (d, $J$ = 8.0 Hz, 1H), 6.99 (d, $J$ = 8.0 Hz, 1H), 7.20-7.25 (m, 2H), 7.27-7.38 (m, 6H), 7.43 (d, $J$ = 8.0 Hz, 1H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 20.8, 36.2, 105.2, 126.0, 126.7, 127.0, 128.7, 128.9, 129.4, 130.0, 131.2, 132.1, 136.5, 137.9, 139.6, 160.5, 163.0; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_2^+$ 299.1043; found: 299.1042.

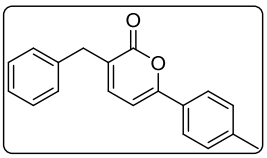
***3-benzyl-6-(m-tolyl)-2H-pyran-2-one (42q)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41q** (0.1 mmol, 30.1 mg, 1.0 equiv.). The

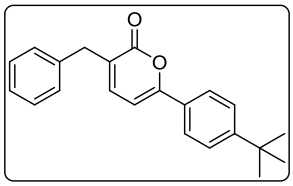
product was isolated in 87% yield (24.1 mg), yellow solid, mp 88-90 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.40 (s, 3H), 3.84 (s, 2H), 6.55 (d, $J$ = 8.0 Hz, 1H), 7.00 (d, $J$ = 8.0 Hz, 1H), 7.20-7.37 (m, 7H), 7.57 (d, $J$ = 8.0 Hz, 1H), 7.63 (s, 1H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.4, 36.2, 101.1, 122.4, 125.9, 126.7, 127.1, 128.7, 128.7, 129.3, 131.2, 131.3, 138.0, 138.7, 139.9, 158.9, 162.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_2^+$ 299.1043; found: 299.1042.

***3-benzyl-6-(p-tolyl)-2H-pyran-2-one (42r)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41r** (0.1 mmol, 30.1 mg, 1.0 equiv.). The product was isolated in 94% yield (26.0 mg), yellow solid, mp 102-104 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 2.39 (s, 3H), 3.83 (s, 2H), 6.52 (d, $J$ = 8.0 Hz, 1H), 6.71 (d, $J$ = 8.0 Hz, 1H), 7.20-7.29 (m, 5H), 7.30-7.36 (m, 2H), 7.68 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 21.4, 36.2, 100.6, 125.2, 126.6, 126.7, 128.6, 129.3, 129.6, 138.1, 140.0, 140.8, 158.9, 162.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_2^+$ 299.1043; found: 299.1042.

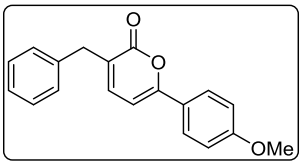
***3-benzyl-6-(4-(tert-butyl) phenyl)-2H-pyran-2-one (42s)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41s** (0.1 mmol, 34.3 mg, 1.0

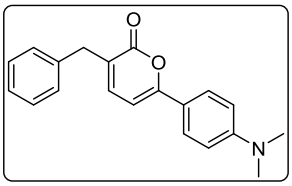
equiv.). The product was isolated in 92% yield (29.3 mg), light yellow solid, mp 129-131 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 1.33 (s, 9H), 3.82 (s, 2H), 6.53 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.21-7.29 (m, 3H), 7.30-7.37 (m, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 31.1, 34.8, 36.2, 100.7, 125.1, 125.8, 126.6, 126.7, 128.6, 128.6, 129.3, 138.1, 140.0, 153.9, 158.9, 162.9; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{22}H_{22}NaO_2^+$ 341.1512; found: 341.1513.

***3-benzyl-6-(4-methoxyphenyl)-2H-pyran-2-one (42t)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41t** (0.1 mmol, 31.6 mg, 1.0 equiv.). The product was isolated in 93% yield (27.2 mg), yellow solid, mp 86-88 °C, eluent: (hexane/EtOAc, 90/10); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.82 (s, 2H), 3.85 (s, 3H), 6.45 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.22-7.29 (m, 3H), 7.30-7.37 (m, 2H), 7.74 (d, *J* = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.1, 55.4, 99.8, 114.2, 124.0, 125.8, 126.6, 126.9, 128.6, 129.2, 138.2, 140.2, 158.9, 161.4, 162.9; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{16}NaO_3^+$ 315.0992; found: 315.0978.

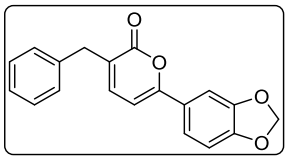
***3-benzyl-6-(4-(dimethylamino) phenyl)-2H-pyran-2-one (42u)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41u** (0.1 mmol, 33.0 mg, 1.0 equiv.). The

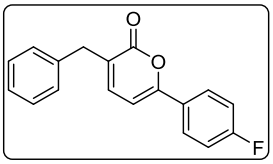
product was isolated in 83% yield (25.3 mg), yellow semi solid, eluent: (hexane/EtOAc, 85/15); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.02 (s, 6H), 3.80 (s, 2H), 6.38 (d, $J$ = 8.0 Hz, 1H), 6.68 (d, $J$ = 8.0 Hz, 2H), 6.97 (d, $J$ = 8.0 Hz, 1H), 7.20-7.35 (m, 5H), 7.67 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.1, 40.1, 98.3, 111.6, 118.7, 124.0, 126.5, 126.7, 128.6, 129.2, 138.6, 140.7, 151.6, 160.0, 163.3; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{20}H_{19}NNaO_2^+$ 328.1308; found: 328.1308.

***6-(benzo[d] [1,3] dioxol-5-yl)-3-benzyl-2H-pyran-2-one (42v)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41v** (0.1 mmol, 33.1 mg, 1.0 equiv.). The product was isolated in 89% yield (27.3 mg), yellow solid, mp 133-135 °C, eluent: (hexane/EtOAc, 85/15); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.81 (s, 2H), 6.01 (s, 2H), 6.41 (d, $J$ = 8.0 Hz, 1H), 6.84 (d, $J$ = 8.0 Hz, 1H), 6.98 (d, $J$ = 8.0 Hz, 1H), 7.22 (s, 1H), 7.23-7.29 (m, 3H), 7.30-7.36 (m, 3H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.1, 100.2, 101.6, 105.5, 108.6, 120.1, 125.6, 126.3, 126.6, 128.6, 129.2, 138.1, 140.0, 148.3, 149.6, 158.5, 162.7; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{19}H_{14}NaO_4^+$ 329.0784; found: 329.0784.

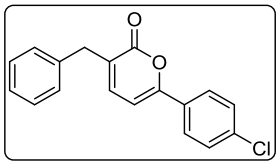
***3-benzyl-6-(4-fluorophenyl)-2H-pyran-2-one (42w)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41w** (0.1 mmol, 30.4 mg, 1.0

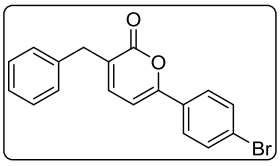
equiv.). The product was isolated in 86% yield (24.1 mg), yellow solid, mp 108-110 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.83 (s, 2H), 6.49 (d, $J$ = 8.0 Hz, 1H), 7.00 (d, $J$ = 8.0 Hz, 1H), 7.11 (t, $J$ = 8.0 Hz, 2H), 7.22-7.29 (m, 3H), 7.30-7.36 (m, 2H), 7.73-7.82 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.2, 100.9 (d, $J$ = 1.2 Hz), 116.0 (d, $J$ = 22.1 Hz), 126.7, 127.2, 127.4 (d, $J$ = 8.3 Hz), 127.7 (d, $J$ = 3.2 Hz), 128.7, 129.3, 137.9, 139.8, 157.8, 162.5, 164.0 (d, $J$ = 250 Hz); **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{13}FNaO_2^+$ 303.0792; found: 303.0793.

***3-benzyl-6-(4-chlorophenyl)-2H-pyran-2-one (42x)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41x** (0.1 mmol, 32.1 mg, 1.0 equiv.). The product was isolated in 88% yield (26.1 mg), light yellow solid, mp 106-108 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.83 (s, 2H), 6.55 (d, $J$ = 8.0 Hz, 1H), 7.01 (d, $J$ = 8.0 Hz, 1H), 7.27 (d, $J$ = 8.0 Hz, 3H), 7.31-7.38 (m, 2H), 7.41 (d, $J$ = 8.0 Hz, 2H), 7.72 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.2, 101.4, 126.5, 126.8, 127.8, 128.7, 129.2, 129.3, 129.9, 136.5, 137.8, 139.6, 157.5, 162.4; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{13}ClNaO_2^+$ 319.0496; found: 319.0498.

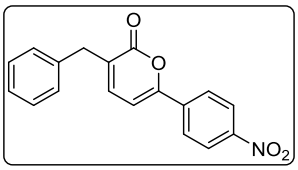
***3-benzyl-6-(4-bromophenyl)-2H-pyran-2-one (42y)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41y** (0.1 mmol, 36.5 mg, 1.0 equiv.). The

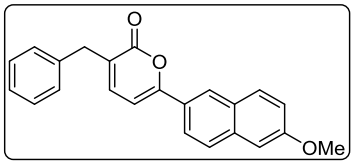
product was isolated in 91% yield (31.0 mg), yellow solid, mp 117-119 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.83 (s, 2H), 6.56 (d, $J$ = 8.0 Hz, 1H), 7.01 (d, $J$ = 8.0 Hz, 1H), 7.27 (d, $J$ = 8.0 Hz, 3H), 7.31-7.38 (m, 2H), 7.57 (d, $J$ = 8.0 Hz, 2H), 7.65 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.3, 101.4, 124.9, 126.7, 126.8, 127.9, 128.7, 129.3, 130.3, 132.2, 137.8, 139.6, 157.6, 162.4; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{13}BrNaO_2^+$ 362.9991; found: 362.9992.

***3-benzyl-6-(4-nitrophenyl)-2H-pyran-2-one (42z)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41z** (0.1 mmol, 33.1 mg, 1.0 equiv.). The product was isolated in 83% yield (25.5 mg), reddish brown solid, mp 124-126 °C, eluent: (hexane/EtOAc, 85/15); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.86 (s, 2H), 6.72 (d, $J$ = 6.8 Hz, 1H), 7.06 (d, $J$ = 8.0 Hz, 1H), 7.25-7.31 (m, 3H), 7.32-7.39 (m, 2H), 7.96 (d, $J$ = 8.0 Hz, 2H), 7.29 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.4, 103.7, 124.2, 125.9, 126.9, 128.8, 129.3, 129.9, 137.0, 137.4, 139.0, 148.5, 155.8, 161.8; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{18}H_{13}NNaO_4^+$ 330.0737; found: 330.0736.

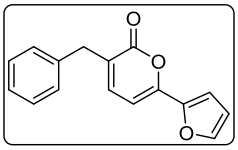
***3-benzyl-6-(6-methoxynaphthalen-2-yl)-2H-pyran-2-one (42aa)***




The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41aa** (0.1 mmol, 36.6 mg, 1.0

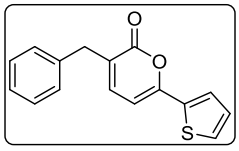
equiv.). The product was isolated in 92% yield (31.5 mg), yellow solid, mp 118-120 °C, eluent: (hexane/EtOAc, 85/15); **$^{1}$H NMR (400 MHz, CDCl$_3$)**: $\delta$ 3.84 (s, 2H), 3.91 (s, 3H), 6.60 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 7.10 (s, 1H), 7.16 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.22-7.30 (m, 3H), 7.30-7.37 (m, 2H), 7.67-7.75 (m, 2H), 7.77 (d, *J* = 8.0 Hz, 1H), 8.27 (s, 1H); **$^{13}$C{$^{1}$H} NMR (100 MHz, CDCl$_3$)**: $\delta$ 36.2, 55.3, 100.9, 105.7, 119.7, 122.4, 125.3, 126.2, 126.6, 127.4, 128.4, 128.6, 129.3, 130.4, 135.5, 138.1, 140.0, 158.9, 158.9, 162.9; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{23}H_{18}NaO_3^+$ 365.1148; found: 365.1149.

***3-benzyl-6-(furan-2-yl)-2H-pyran-2-one (42ab)***



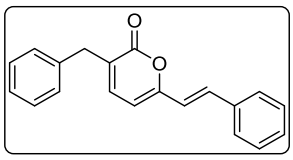
The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41ab** (0.1 mmol, 27.6 mg, 1.0 equiv.). The product was isolated in 87% yield (22.0 mg), reddish brown solid, mp 73-75 °C, eluent: (hexane/EtOAc, 95/5); **$^{1}$H NMR (400 MHz, CDCl$_3$)**: $\delta$ 3.81 (s, 2H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.49-6.53 (m, 1H), 6.95 (d, *J* = 3.2 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 7.23-7.29 (m, 3H), 7.30-7.36 (m, 2H), 7.47 (s, 1H); **$^{13}$C{$^{1}$H} NMR (100 MHz, CDCl$_3$)**: $\delta$ 36.3, 99.7, 111.0, 112.3, 126.7, 126.9, 128.7, 129.3, 137.9, 139.8, 144.4, 146.5, 150.8, 161.9; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{16}H_{12}NaO_3^+$ 275.0679; found: 275.0679.

***3-benzyl-6-(thiophen-2-yl)-2H-pyran-2-one (42ac)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41ac** (0.1 mmol, 29.3 mg, 1.0 equiv.). The product was isolated in 89% yield (23.9 mg), yellow solid, mp 103-105 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.80 (s, 2H), 6.38 (d, $J$ = 6.8 Hz, 1H), 6.95 (d, $J$ = 8.0 Hz, 1H), 7.07 (t, $J$ = 4.0 Hz, 1H), 7.21-7.28 (m, 3H), 7.29-7.35 (m, 2H), 7.39 (d, $J$ = 8.0 Hz, 1H), 7.53 (d, $J$ = 4.0 Hz, 1H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.3, 100.4, 126.7, 126.7, 128.2, 128.2, 128.7, 129.2, 135.1, 138.0, 139.8, 154.5, 162.0; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{16}H_{12}NaO_2S^+$ 291.0450; found: 291.0450.

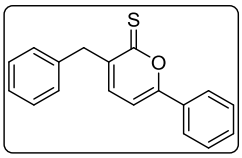
***(E)-3-benzyl-6-styryl-2H-pyran-2-one (42ad)***



The title compound was prepared following the general procedure **2.9.5** described above using **40a** (0.2 mmol, 33.7 mg, 2.0 equiv.) and **41ad** (0.1 mmol, 31.3 mg, 1.0 equiv.). The product was isolated in 78% yield (22.5 mg), yellow solid, mp 118-120 °C, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.82 (s, 2H), 6.07 (d, $J$ = 8.0 Hz, 1H), 6.59 (d, $J$ = 16.0 Hz, 1H), 6.92 (d, $J$ = 6.8 Hz, 1H), 7.22-7.29 (m, 3H), 7.30-7.40 (m, 5H), 7.45 (d, $J$ = 16.0 Hz, 1H), 7.49 (d, $J$ = 8.0 Hz, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 36.3, 105.2, 118.7, 126.7, 127.3, 127.7, 128.7, 128.9, 129.1,

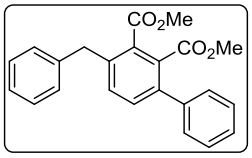
129.3, 134.2, 135.5, 138.0, 139.8, 157.4, 162.5; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{20}H_{16}NaO_2^+$ 311.1043; found: 311.1042.

***3-benzyl-6-phenyl-2H-pyran-2-thione (98)***




The title compound was prepared following the condition of Supuran et al.,[31] a solution of **42a** (0.1 mmol, 26.2 mg, 1.0 equiv.) and Lawesson's reagent (0.12 mmol, 48.5 mg, 1.2 equiv.) in dry toluene (2.0 mL) was refluxed until consumption of the starting material **42a** (TLC monitoring). Then the solvent was removed under vacuo and the obtained residue was purified by silica gel column chromatography to afford the title compound **98** in 85% yield (23.7 mg), yellow solid, mp 105-107 °C, eluent: (hexane/EtOAc, 97/3); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 4.10 (s, 2H), 6.83 (d, $J$ = 8.0 Hz, 1H), 6.89 (d, $J$ = 8.0 Hz, 1H), 7.22-7.30 (m, 3H), 7.31-7.38 (m, 2H), 7.43-7.49 (m, 3H), 7.84-7.89 (m, 2H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 39.9, 105.2, 125.6, 126.7, 128.7, 129.1, 129.5, 130.6, 131.2, 134.9, 137.9, 140.0, 163.9, 197.3; **HRMS (ESI-TOF) m/z**: $[M + H]^+$ calcd for $C_{18}H_{15}OS^+$ 279.0838; found: 279.0841.

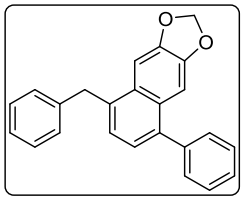
***Dimethyl 4-benzyl-[1,1'-biphenyl]-2,3-dicarboxylate (99)***




The title compound was prepared following the modified conditions of Ziegler et al.,[32] a solution of **42a** (0.1 mmol, 26.2 mg, 1.0 equiv.) and dimethylacetylene dicarboxylate (0.5 mmol, 62 µl, 5.0 equiv.) in xylene (0.2 mL) in a sealed tube was heated to 200 °C

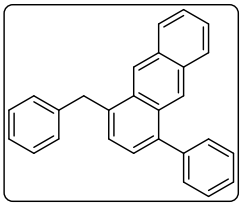
for 72 h. The reaction mixture was cooled to rt and the solvent was removed under vacuo to obtain the crude product which was purified by flash chromatography on silica gel to give **99** in 78% yield (28.1 mg), colorless liquid, eluent: (hexane/EtOAc, 95/5); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 3.57 (s, 3H), 3.77 (s, 3H), 4.17 (s, 2H), 7.18 (d, $J$ = 8.0 Hz, 2H), 7.21 (d, $J$ = 6.8 Hz, 1H), 7.27-7.32 (m, 5H), 7.34-7.42 (m, 4H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 38.9, 52.2, 52.5, 126.4, 127.6, 128.2, 128.3, 128.5, 129.1, 131.9, 132.1, 132.2, 132.2, 138.7, 139.2, 139.7, 139.9, 168.4, 169.0; **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ calcd for $C_{23}H_{20}NaO_4^+$ 383.1254; found: 383.1252.

***5-benzyl-8-phenylnaphtho[2,3-d][1,3]dioxole (100)***



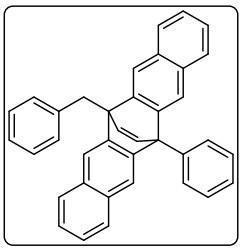
The title compound was prepared following the modified condition of Bronner et al.,[33] a solution of **42a** (0.1 mmol, 26.2 mg, 1.0 equiv.), 6-(trimethylsilyl) benzo[d][1,3] dioxol-5-yl trifluoromethane sulfonate (0.5 mmol, 172 mg, 5.0 equiv.) and CsF (0.5 mmol, 76.0 mg, 5.0 equiv.) in dry $CH_3CN$ (1.0 mL) was heated to 100 °C for 18 h. The reaction mixture was cooled to rt and the solvent was removed under vacuo to obtain the crude product which was purified by flash chromatography on silica gel to give **100** in 73% yield (24.7 mg), off-white solid, eluent: (hexane/EtOAc, 97/3); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 4.37 (s, 2H), 5.96 (s, 2H), 7.26 (s, 1H), 7.20-7.25 (m, 5H), 7.26-7.32 (m, 2H), 7.33 (s, 1H), 7.37-7.50 (m, 5H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 39.7, 101.0, 101.1, 103.1, 125.3, 125.8, 126.1, 127.1, 128.3, 128.5, 128.7, 129.2, 129.5, 130.0, 135.1, 138.6, 140.4, 141.3, 147.3, 147.5; **HRMS (ESI-TOF) m/z**: $[M + H]^+$ calcd for $C_{24}H_{19}O_2^+$ 339.1380; found: 339.1372.

***1-benzyl-4-phenylanthracene (101)***



The title compound was prepared following the modified condition of Bronner et al.,[33] a solution of **42a** (0.1 mmol, 26.2 mg, 1.0 equiv.), 3-(trimethylsilyl)naphthalen-2-yl trifluoromethane sulfonate (0.2 mmol, 70 mg, 2.0 equiv.) and CsF (0.2 mmol, 31.0 mg, 2.0 equiv.) in dry $CH_3CN$ (1.0 mL) was heated to 100 °C for 18 h. The reaction mixture was cooled to rt and the solvent was removed under vacuo to obtain the crude product which was purified by flash chromatography on silica gel to give **101** in 43% yield (14.8 mg), yellow semi solid, eluent: (hexane/$CH_2Cl_2$, 80/20); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$ 4.63 (s, 2H), 7.27-7.36 (m, 6H), 7.37-7.51 (m, 4H), 7.52-7.62 (m, 4H), 7.86 (d, $J$ = 8.0 Hz, 1H), 7.97 (d, $J$ = 8.0 Hz, 1H), 8.48 (s, 1H), 8.64 (s, 1H); **$^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$)**: $\delta$ 39.4, 123.2, 125.4, 125.6, 125.7, 125.9, 126.1, 126.2, 127.3, 128.3, 128.3, 128.5, 128.9, 130.2, 130.8, 130.9, 131.3, 131.3, 136.2, 139.4, 140.4, 141.1; **HRMS (ESI-TOF) m/z**: $[M + H]^+$ calcd for $C_{27}H_{21}^+$ 345.1638; found: 345.1632.

***6-benzyl-13-phenyl-6,13-dihydro-6,13-ethenopentacene (102)***



The title compound was also isolated from the above reaction in 22% yield (10.4 mg), colorless semi solid, eluent: (hexane/$CH_2Cl_2$, 80/20); **$^1$H NMR (400 MHz, $CDCl_3$)**: $\delta$

4.33 (s, 2H), 5.71 (s, 1H), 5.80 (s, 1H), 6.92-7.04 (m, 4H), 7.14 (d, $J$ = 8.0 Hz, 1H), 7.19 (d, $J$ = 8.0 Hz, 2H), 7.27-7.37 (m, 6H), 7.38 (s, 1H), 7.44-7.51 (m, 3H), 7.53-7.68 (m, 5H); **$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)**: $\delta$ 39.2, 50.3, 50.4, 121.4, 121.9, 123.6, 123.9, 125.4, 125.5, 125.5, 126.1, 126.5, 127.1, 127.1, 127.4, 128.4, 128.6, 128.9, 129.5, 131.7, 131.7, 133.7, 136.5, 140.6, 140.8, 141.7, 142.2, 142.5, 143.6, 144.4, 144.8; **HRMS (ESI-TOF) m/z**: $[M + H]^+$ calcd for $C_{37}H_{27}^+$ 471.2107; found: 471.2102.

## 2.10 References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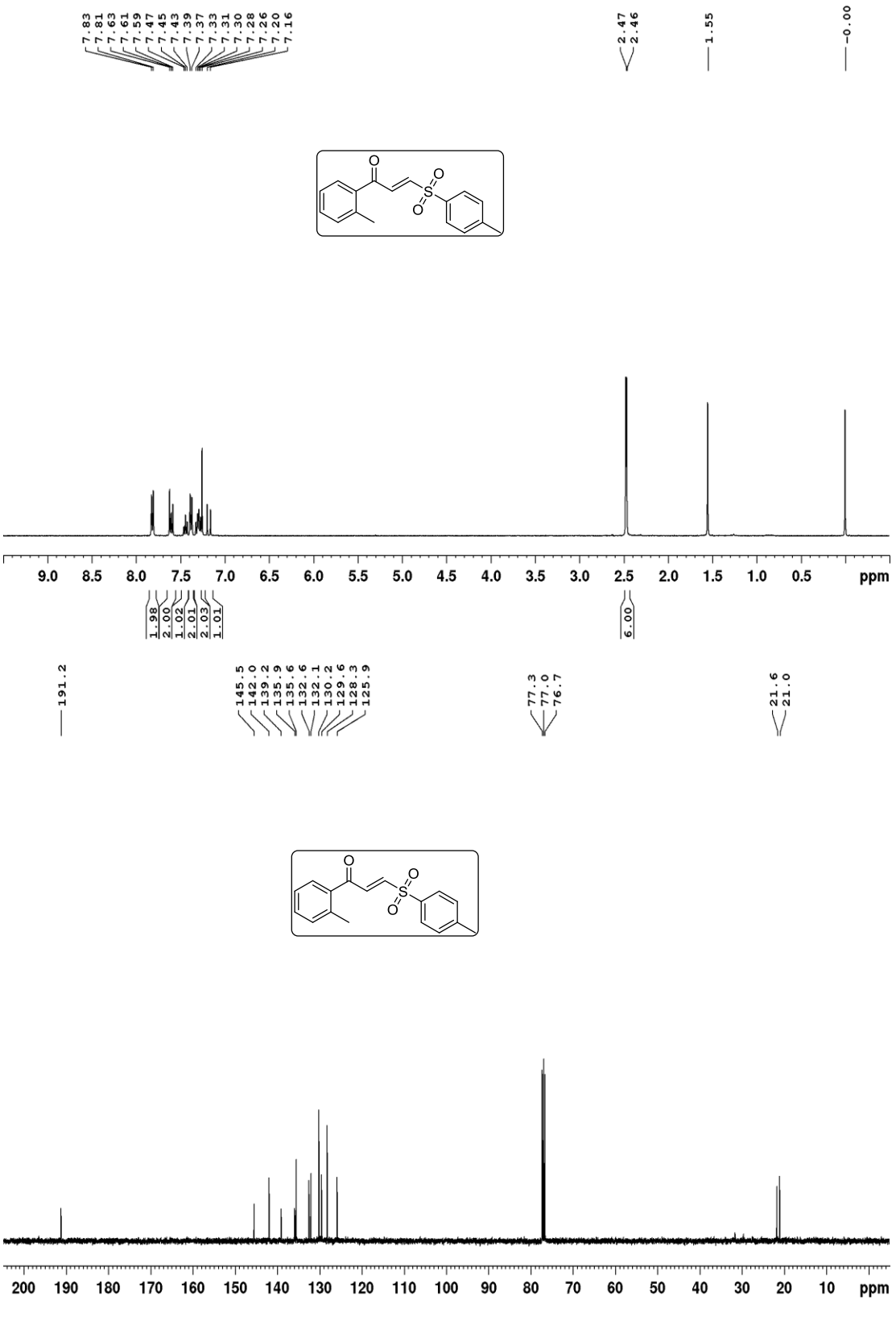
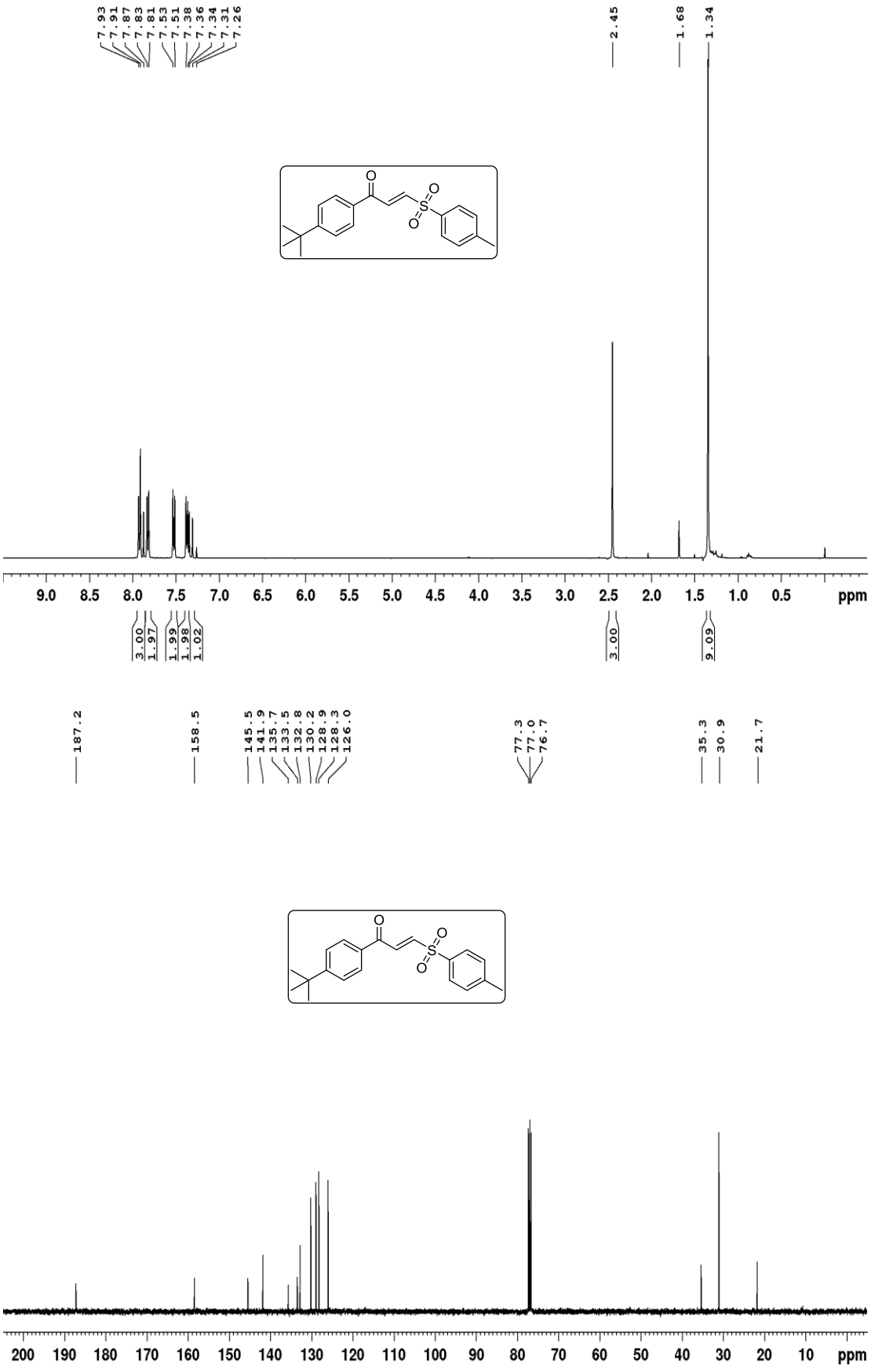
## 2.11 NMR Spectra of New Compounds [$^1$H NMR (400 MHz, $CDCl_3$) and $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$)]

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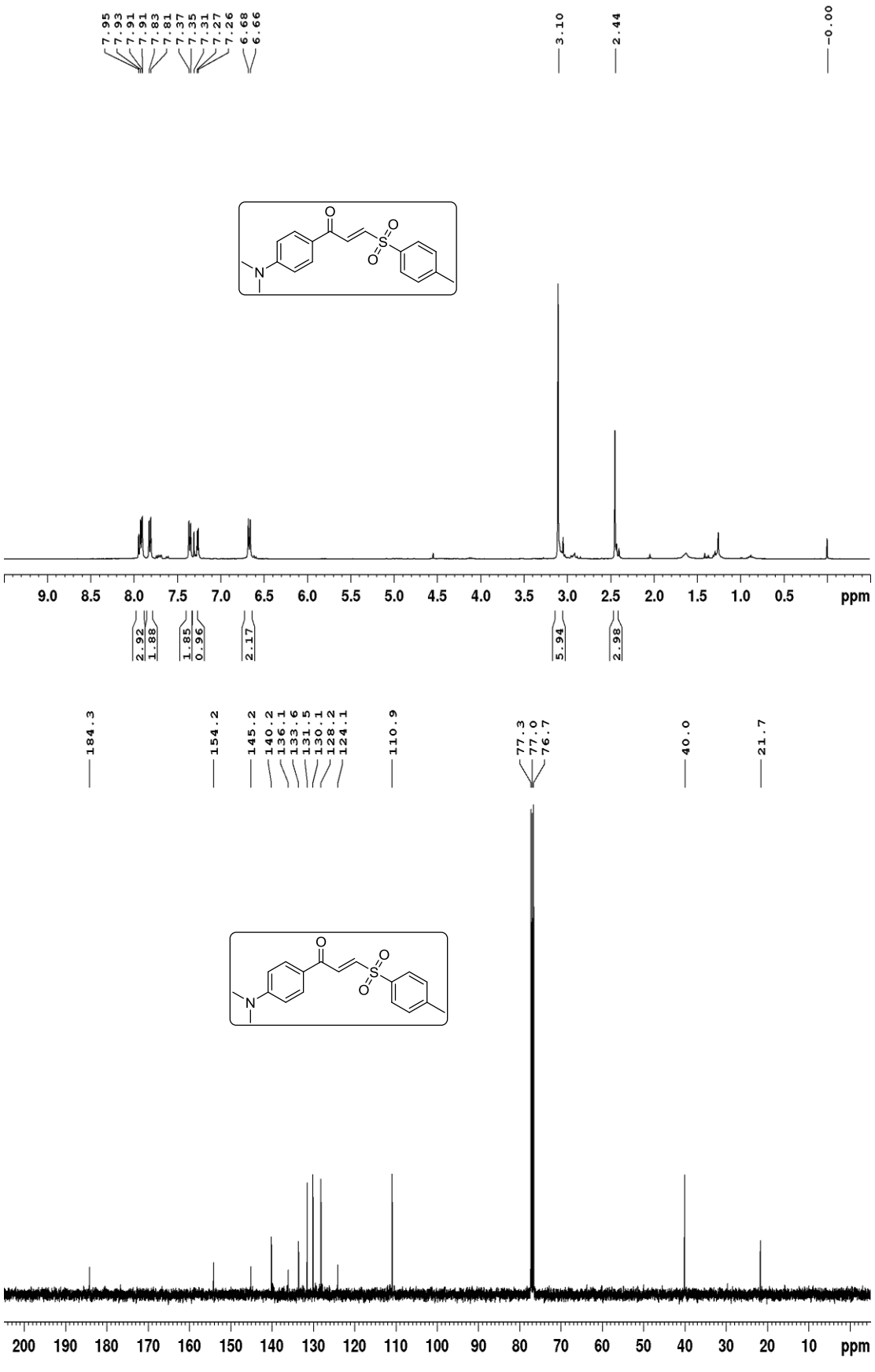
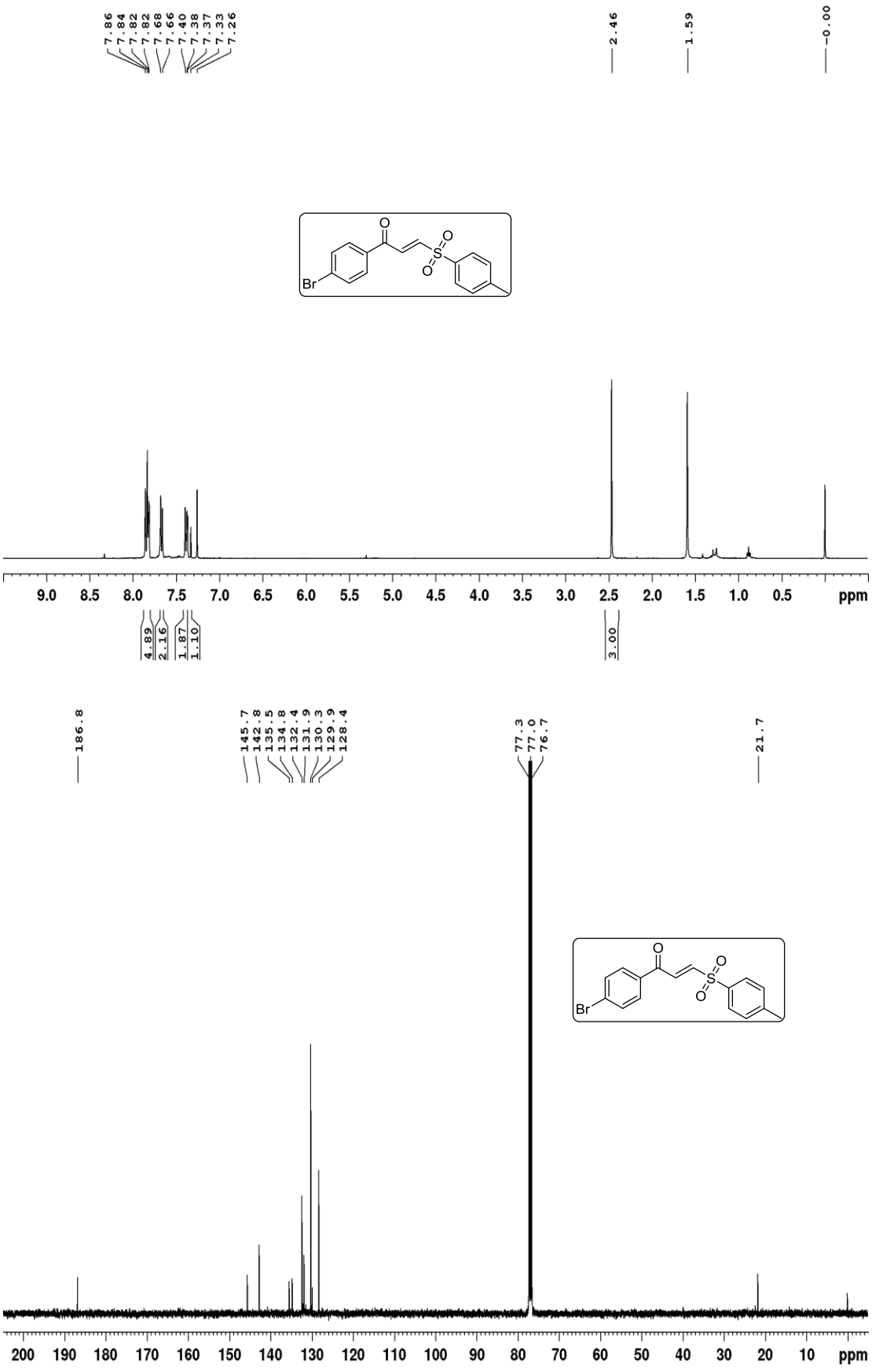
7.91
7.87
7.83
7.81
7.53
7.51
7.38
7.36
7.34
7.31
7.26
2.45
1.68
1.34
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
3.00
1.97
1.99
1.98
1.02
3.00
9.09
187.2
158.5
145.5
141.9
135.7
133.5
132.8
130.2
128.9
128.3
126.0
77.3
77.0
76.7
35.3
30.9
21.7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.95
7.93
7.91
7.91
7.83
7.81
7.37
7.35
7.31
7.27
7.26
6.68
6.66
3.10
2.44
0.00
O
O
S
O
N
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 ppm
2.92
1.88
1.85
0.96
2.17
5.94
2.98
184.3
154.2
145.2
140.2
136.1
133.6
131.5
130.1
128.2
124.1
110.9
77.3
77.0
76.7
40.0
21.7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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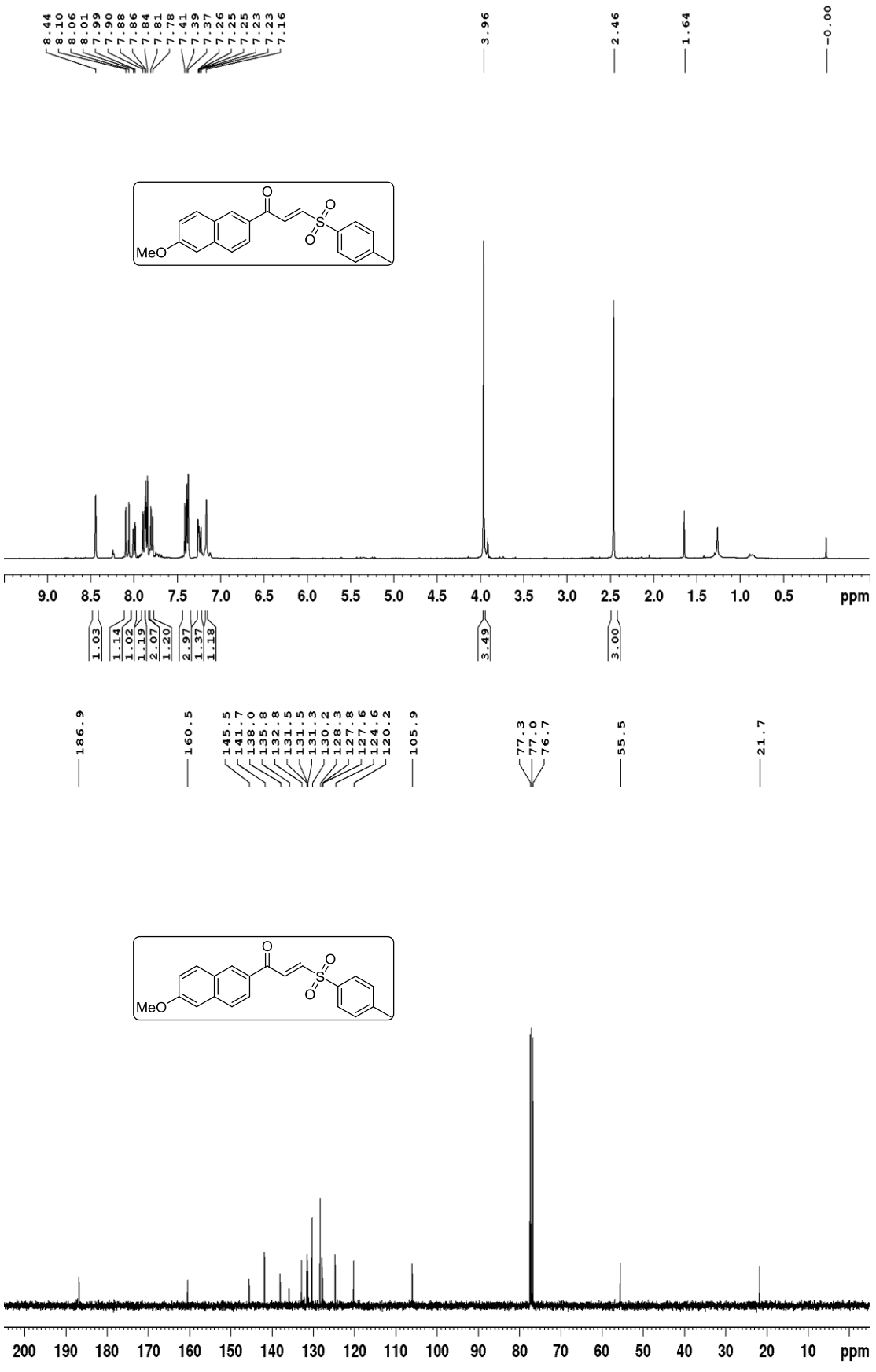
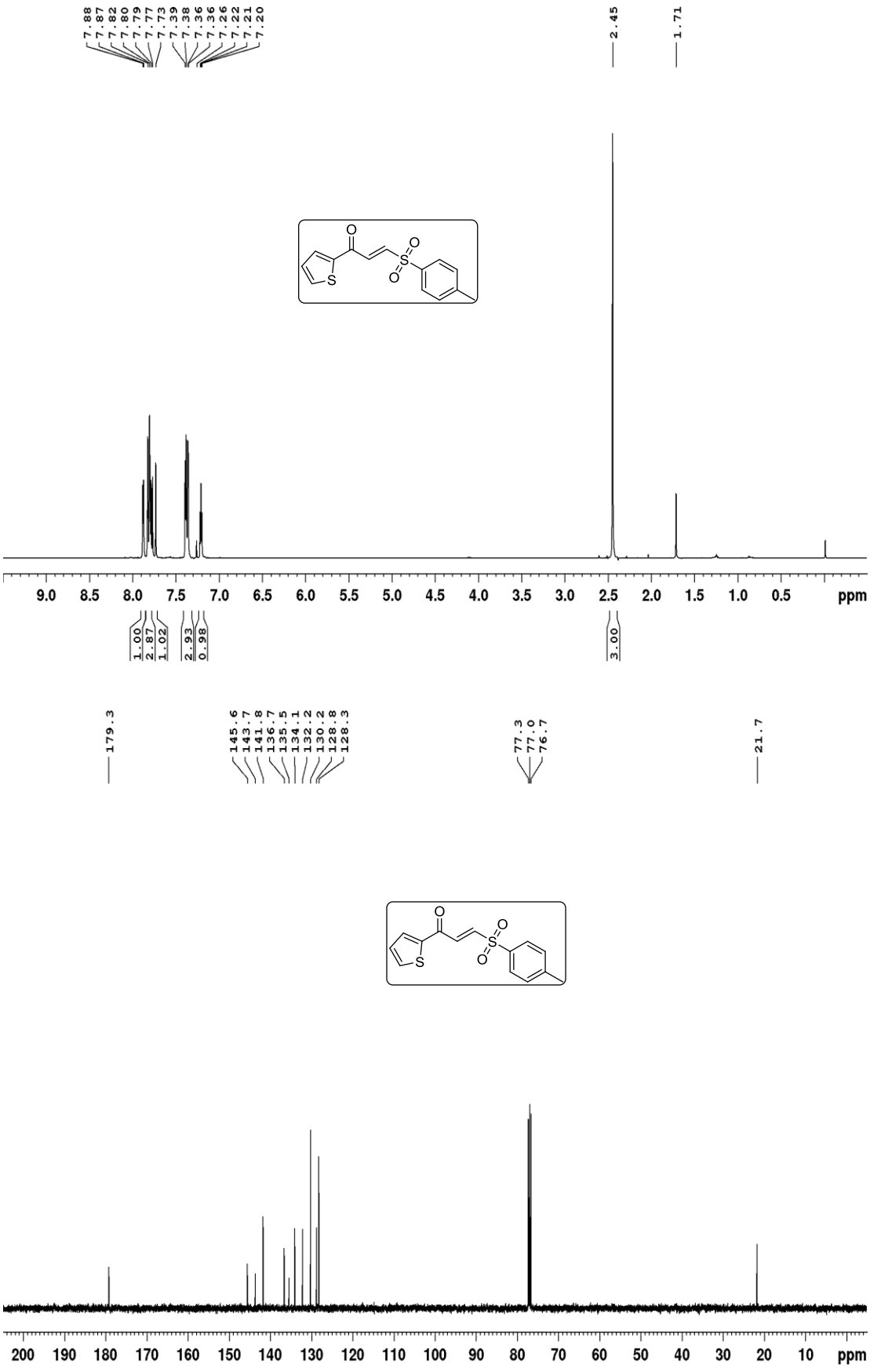
7.84
7.82
7.82
7.68
7.66
7.40
7.38
7.37
7.33
7.26
2.46
1.59
0.00
Br
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
4.89
2.16
1.87
1.10
3.00
186.8
145.7
142.8
135.5
134.8
132.4
131.9
130.3
129.9
128.4
77.3
77.0
76.7
21.7
Br
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.44
8.10
8.06
8.01
7.99
7.90
7.88
7.86
7.84
7.81
7.78
7.41
7.39
7.37
7.26
7.25
7.25
7.23
7.23
7.16
3.96
2.46
1.64
0.00
MeO
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 ppm
1.03
1.14
1.02
1.19
2.07
1.20
2.97
1.37
1.18
3.49
3.00
186.9
160.5
145.5
141.7
138.0
135.8
132.8
131.5
131.5
131.3
130.2
128.3
127.8
127.6
124.6
120.2
105.9
77.3
77.0
76.7
55.5
21.7
MeO
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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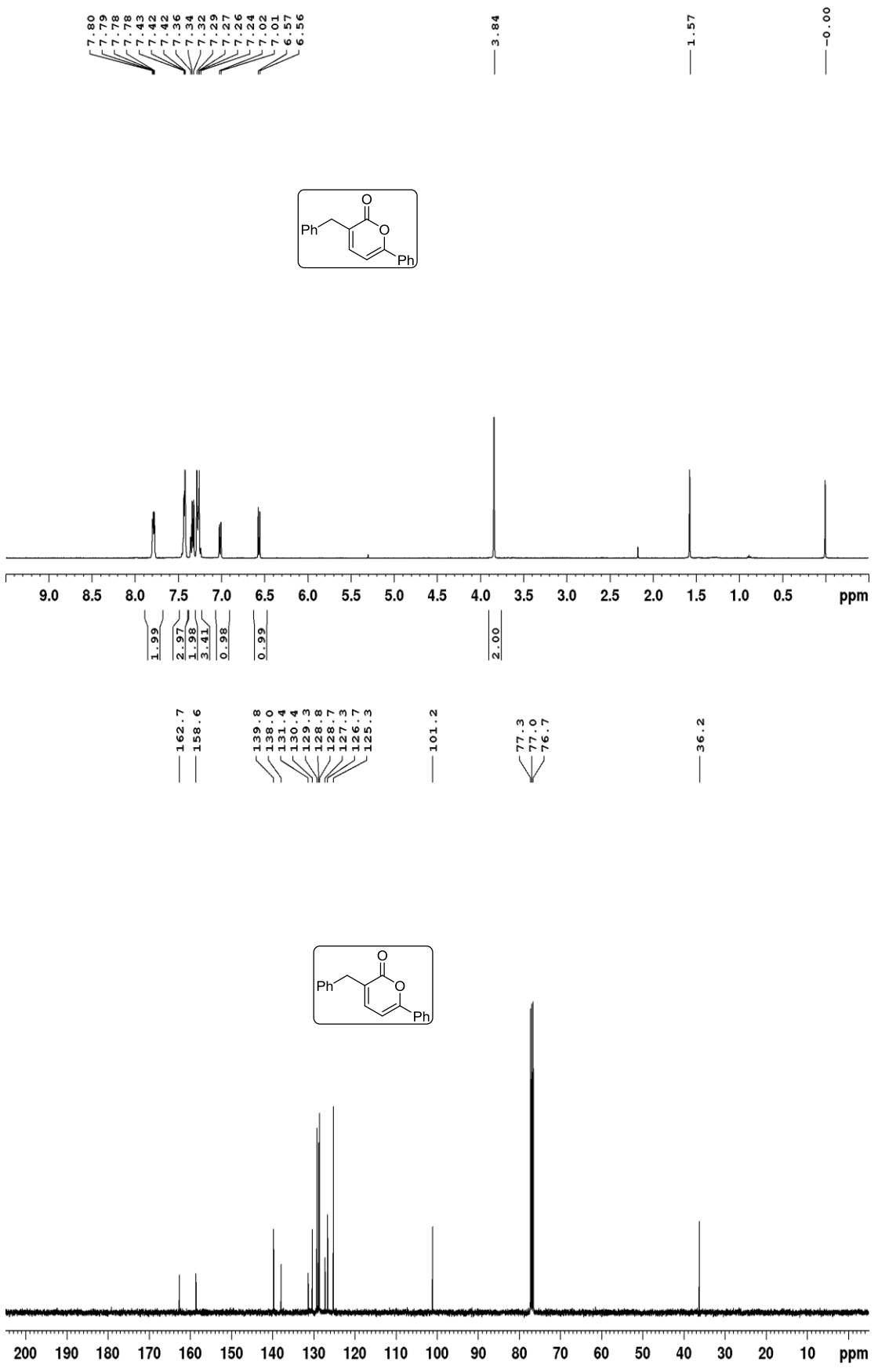
7.87
7.82
7.80
7.79
7.77
7.73
7.39
7.38
7.36
7.26
7.22
7.21
7.20
2.45
1.71
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
2.87
1.02
2.93
0.98
3.00
179.3
145.6
143.7
141.8
136.7
135.5
134.1
132.2
130.2
128.8
128.3
77.3
77.0
76.7
21.7
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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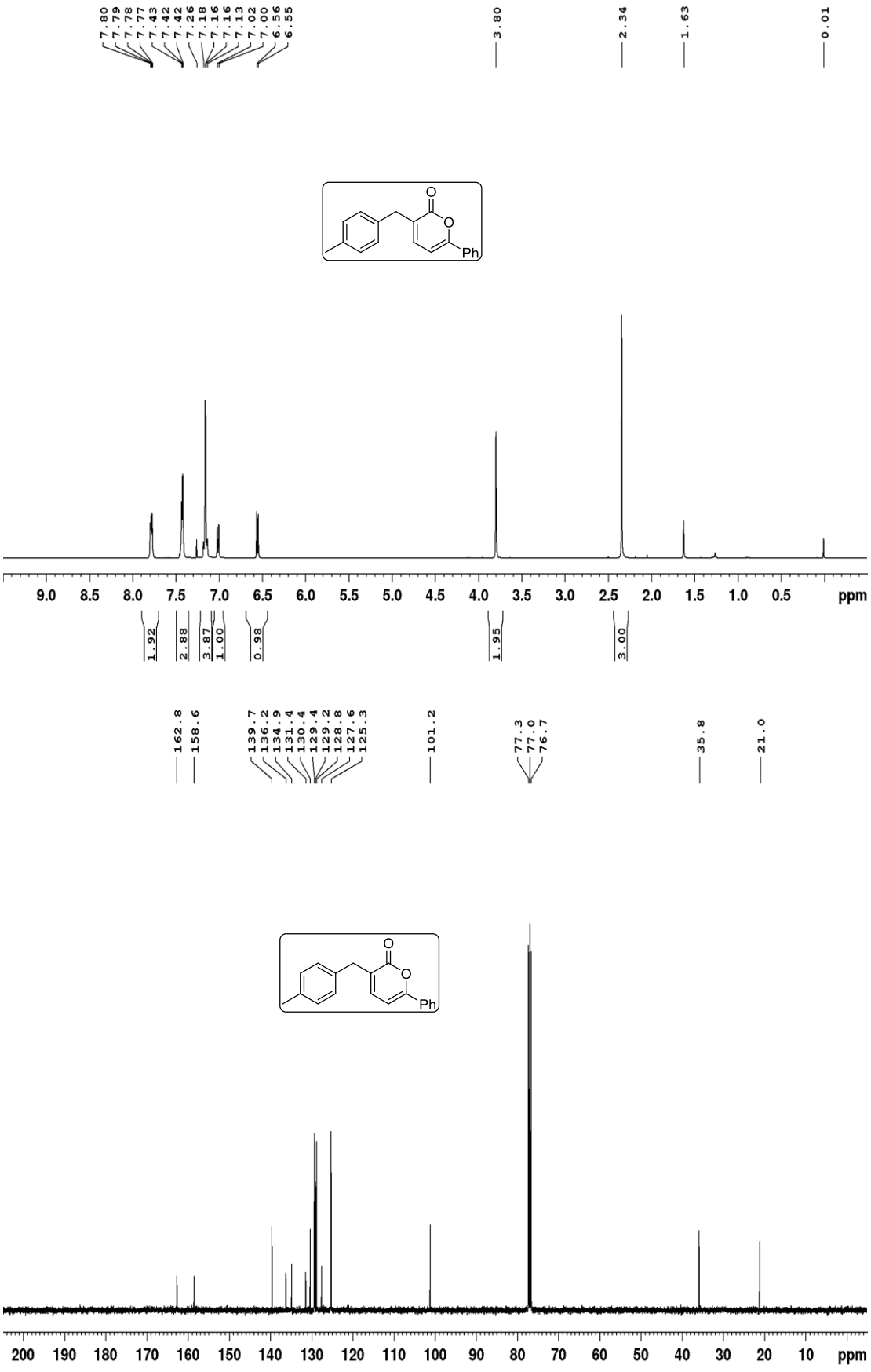
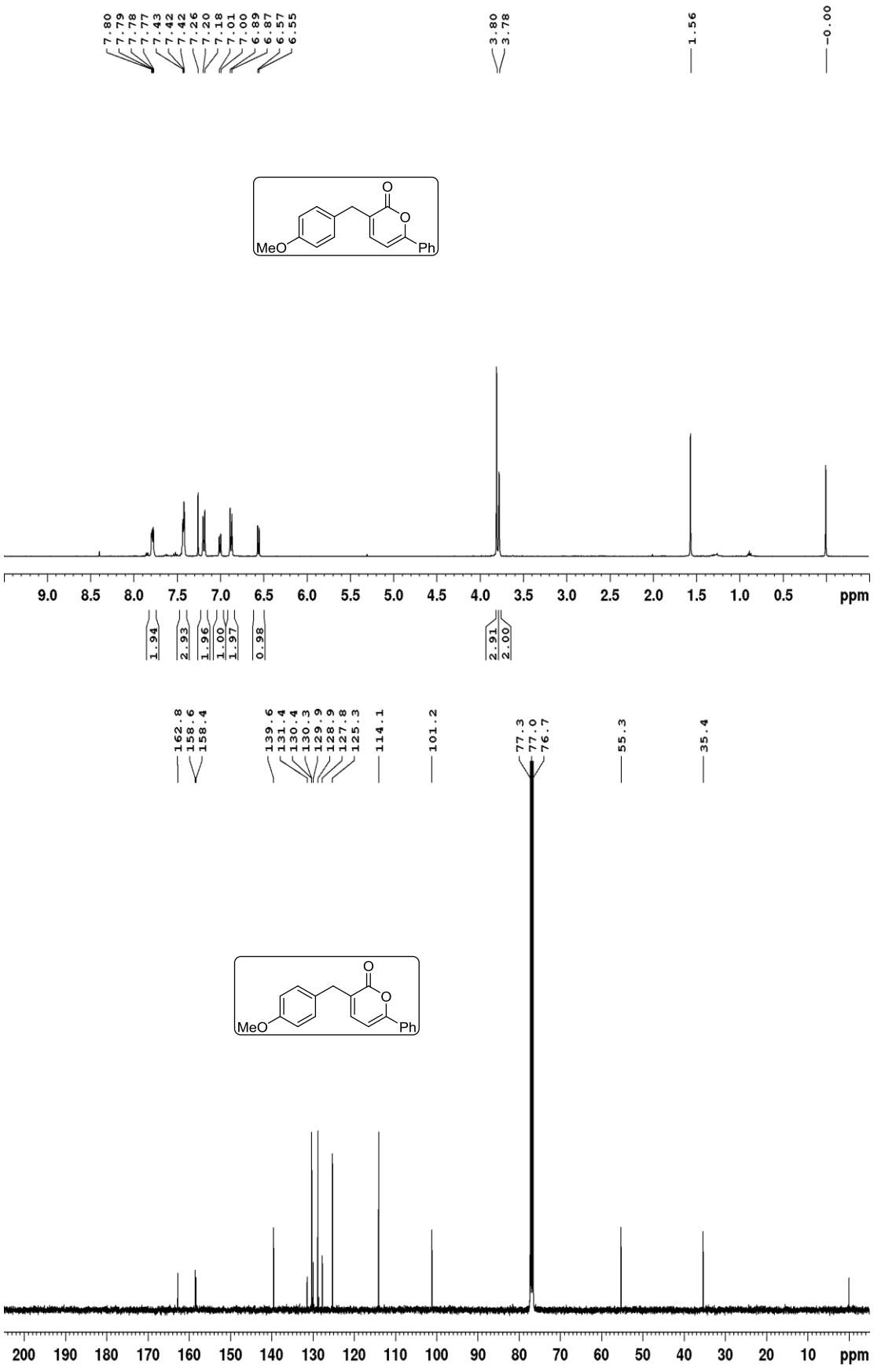
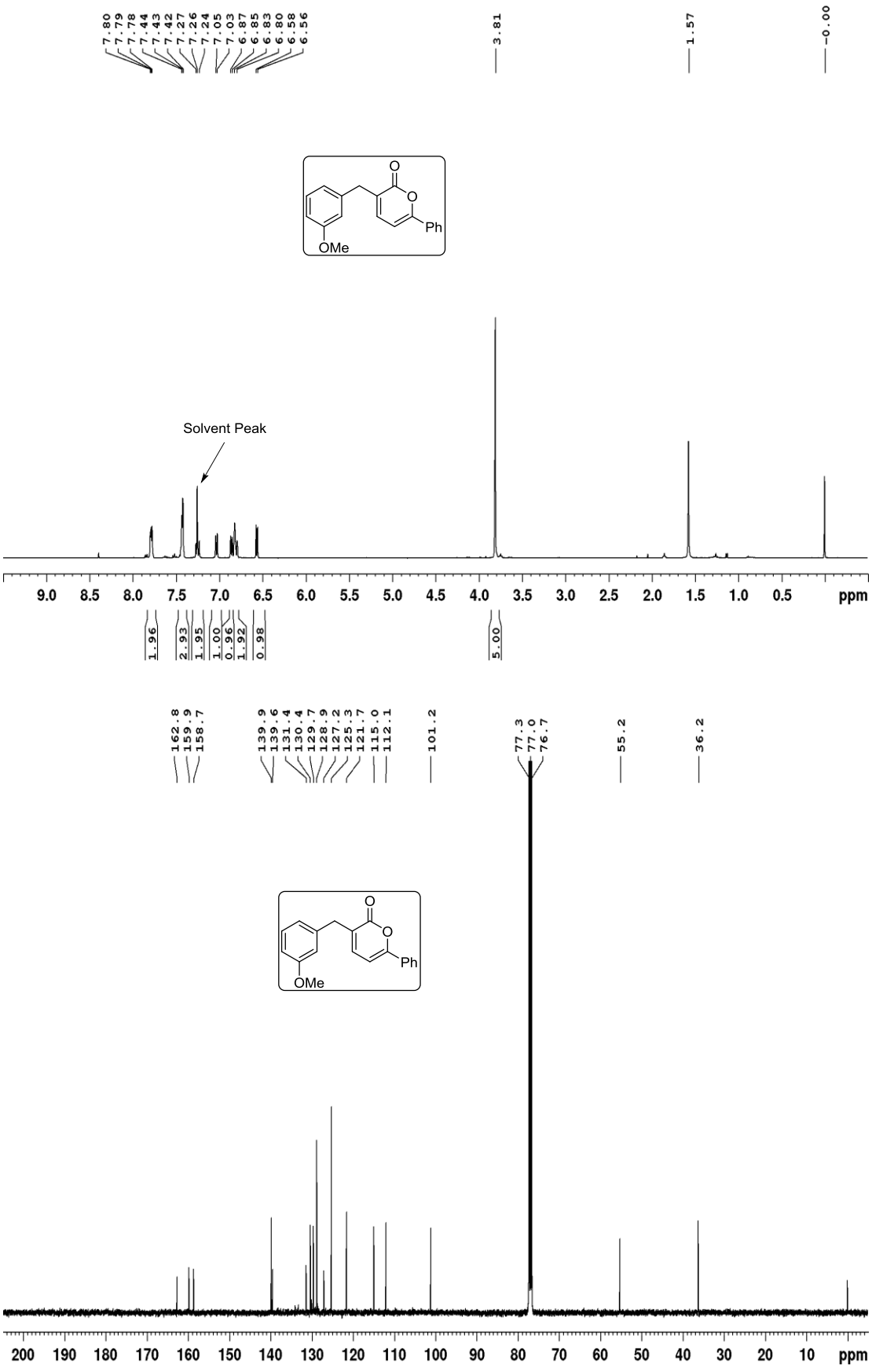
7.79
7.78
7.78
7.43
7.42
7.42
7.36
7.34
7.32
7.29
7.27
7.26
7.24
7.02
7.01
6.57
6.56
3.84
1.57
0.00
O
Ph
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.99
2.97
1.98
3.41
0.98
0.99
2.00
162.7
158.6
139.8
138.0
131.4
130.4
129.3
128.8
128.7
127.3
126.7
125.3
101.2
77.3
77.0
76.7
36.2
O
Ph
O
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.80
7.79
7.78
7.77
7.43
7.42
7.42
7.26
7.18
7.16
7.16
7.13
7.02
7.00
6.56
6.55
3.80
2.34
1.63
0.01
O
O
Ph
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 ppm
1.92
2.88
3.87
1.00
0.98
1.95
3.00
162.8
158.6
139.7
136.2
134.9
131.4
130.4
129.4
129.2
128.8
127.6
125.3
101.2
77.3
77.0
76.7
35.8
21.0
O
O
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.80
7.79
7.78
7.77
7.43
7.42
7.42
7.26
7.20
7.18
7.01
7.00
6.89
6.87
6.57
6.55
3.80
3.78
1.56
0.00
MeO
Ph
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 ppm
1.94
2.93
1.96
1.00
1.97
0.98
2.91
2.00
162.8
158.6
158.4
139.6
131.4
130.4
130.3
129.9
128.9
127.8
125.3
114.1
101.2
77.3
77.0
76.7
55.3
35.4
MeO
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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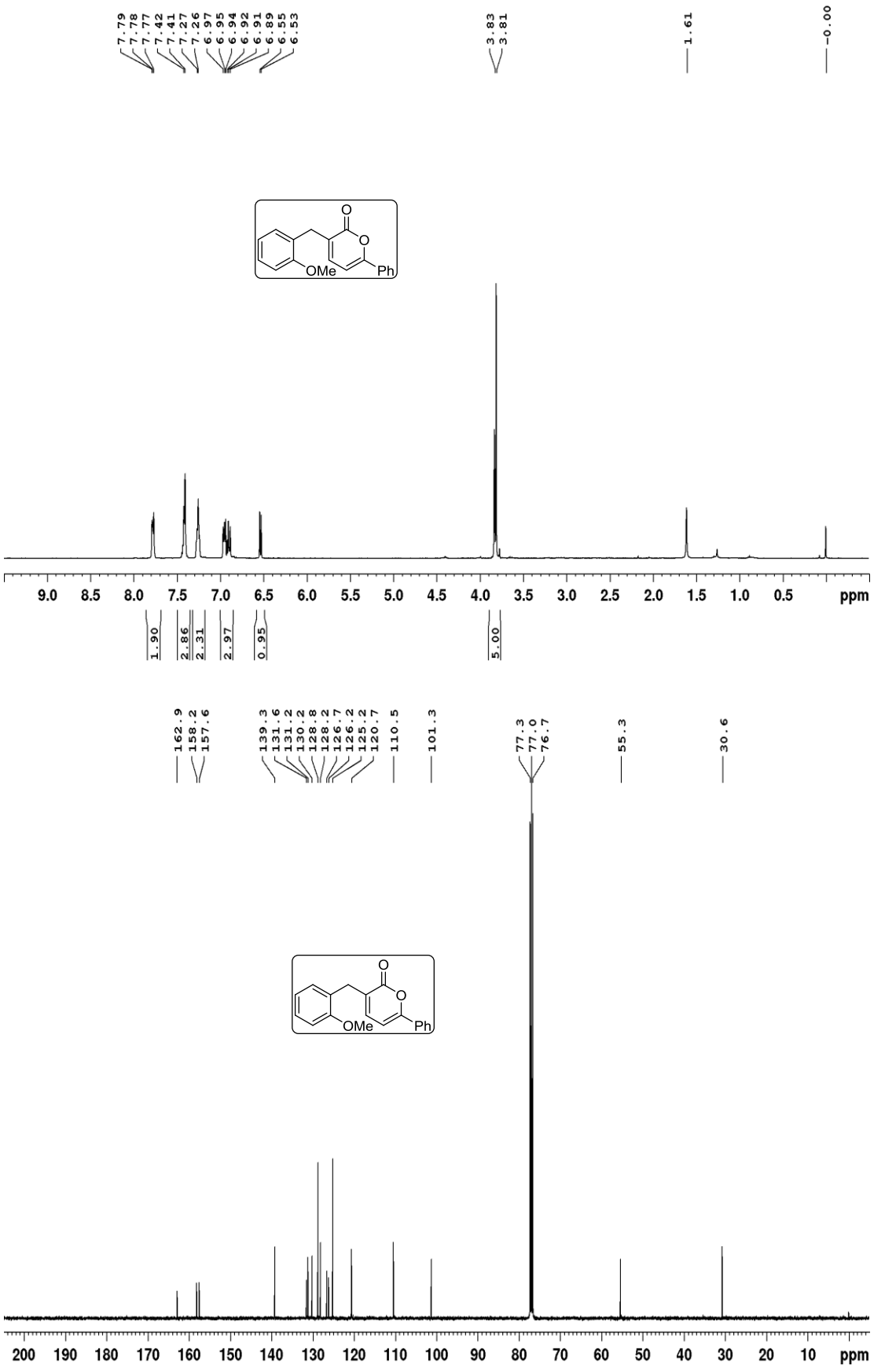
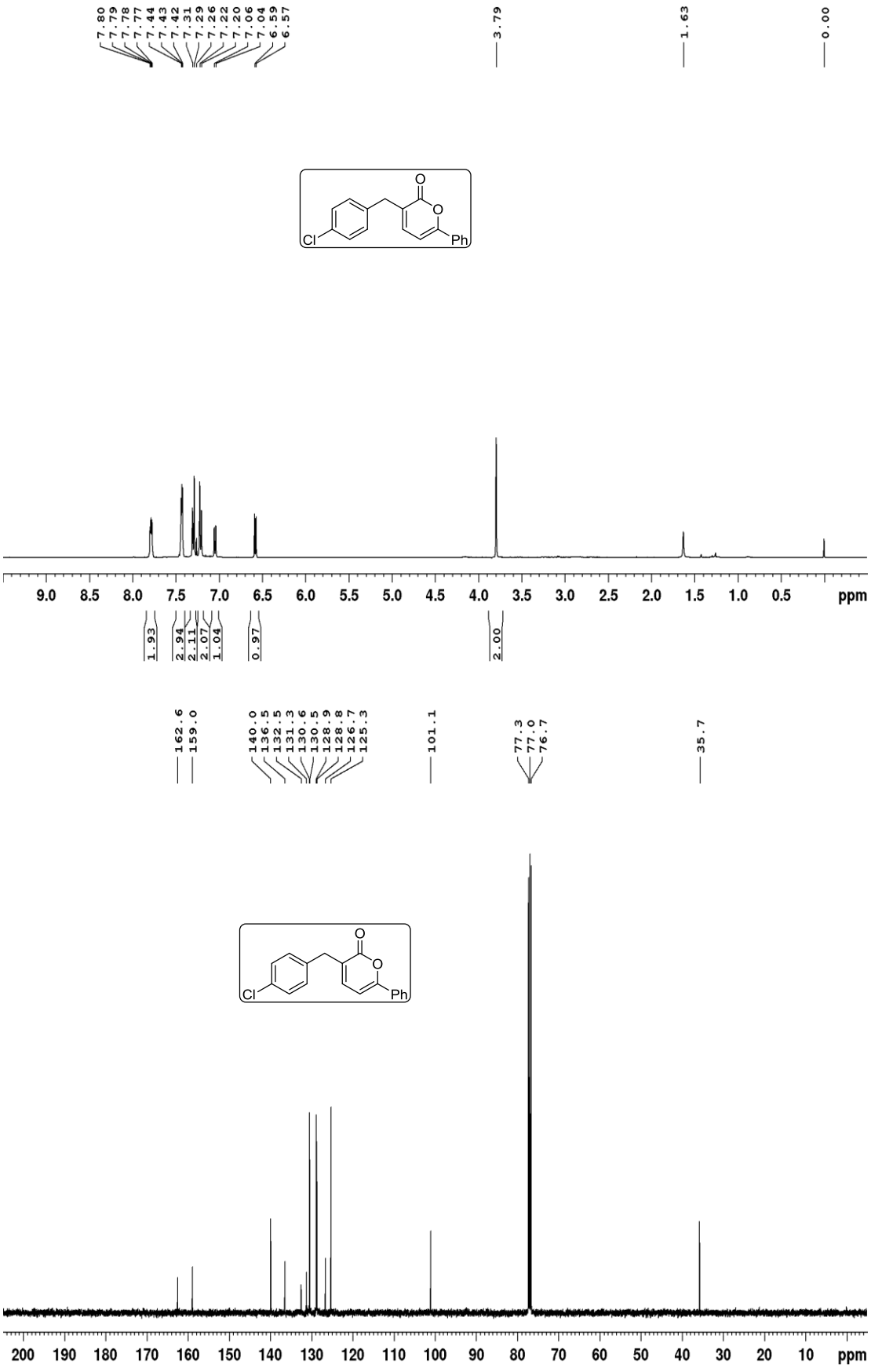
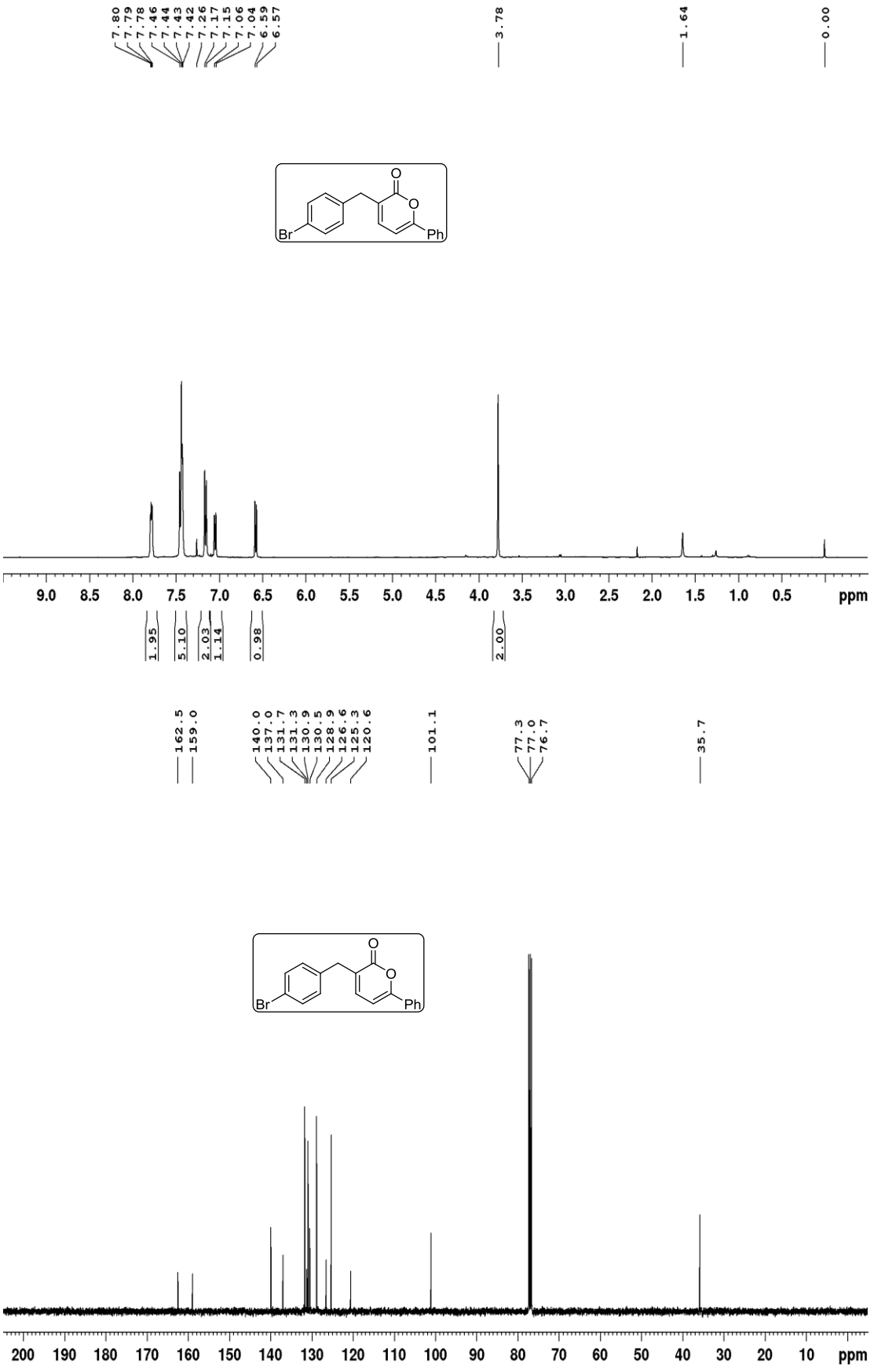
7.79
7.78
7.44
7.43
7.42
7.27
7.26
7.24
7.05
7.03
6.87
6.85
6.83
6.80
6.58
6.56
3.81
1.57
0.00
O
O
Ph
OMe
Solvent Peak
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.96
2.93
1.95
1.00
0.96
1.92
0.98
5.00
162.8
159.9
158.7
139.9
139.6
131.4
130.4
129.7
128.9
127.2
125.3
121.7
115.0
112.1
101.2
77.3
77.0
76.7
55.2
36.2
O
O
Ph
OMe
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.79
7.78
7.77
7.42
7.41
7.27
7.26
6.97
6.95
6.94
6.92
6.91
6.89
6.55
6.53
3.83
3.81
1.61
0.00
O
O
OMe
Ph
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 ppm
1.90
2.86
2.31
2.97
0.95
5.00
162.9
158.2
157.6
139.3
131.6
131.2
130.2
128.8
128.2
126.7
126.2
125.2
120.7
110.5
101.3
77.3
77.0
76.7
55.3
30.6
O
O
OMe
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.80
7.79
7.78
7.77
7.44
7.43
7.42
7.31
7.29
7.26
7.22
7.20
7.06
7.04
6.59
6.57
3.79
1.63
0.00
Cl
Ph
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 ppm
1.93
2.94
2.11
2.07
1.04
0.97
2.00
162.6
159.0
140.0
136.5
132.5
131.3
130.6
130.5
128.9
128.8
126.7
125.3
101.1
77.3
77.0
76.7
35.7
Cl
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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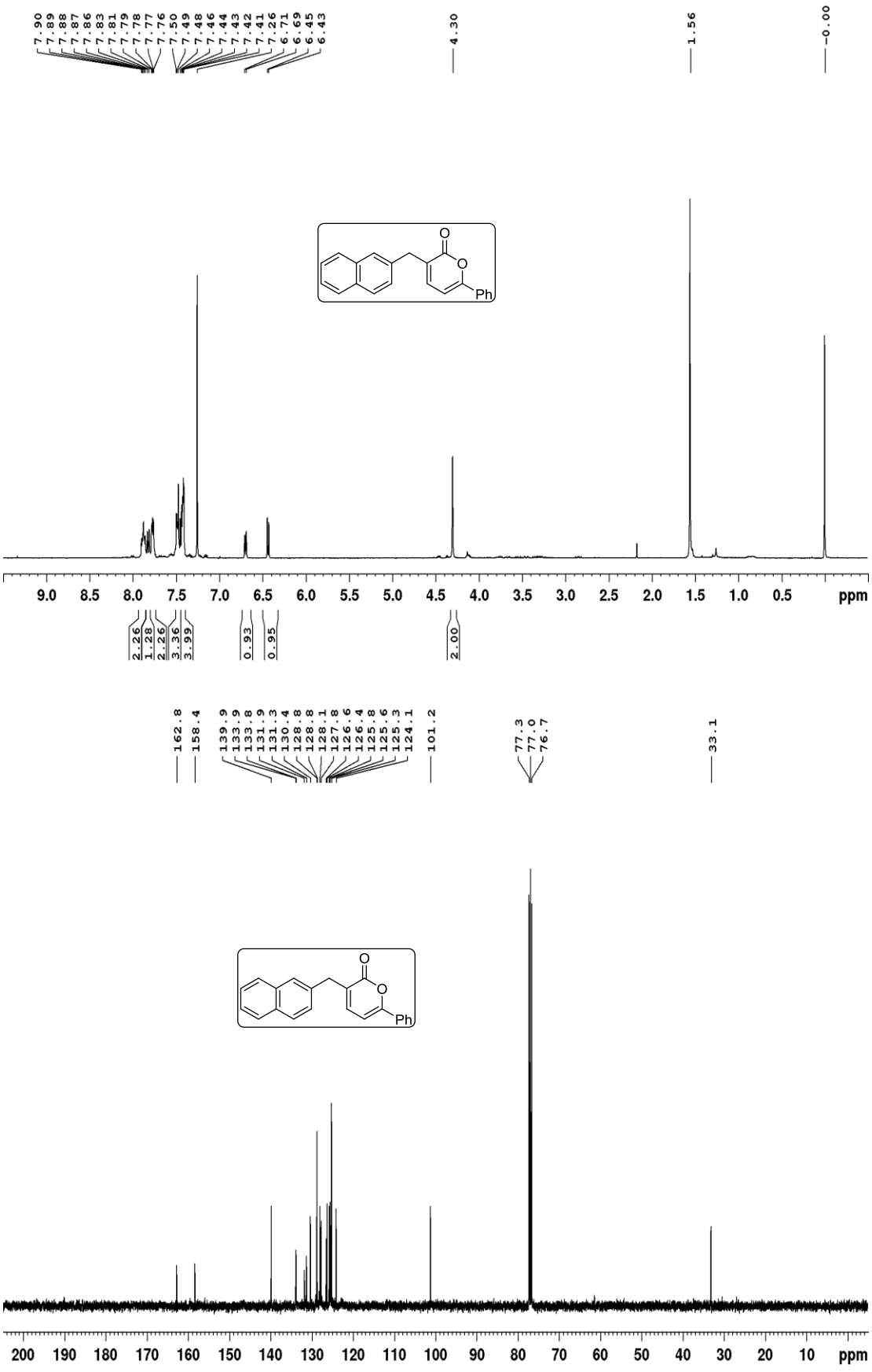
7.79
7.78
7.46
7.44
7.43
7.42
7.26
7.17
7.15
7.06
7.04
6.59
6.57
3.78
1.64
0.00
O
O
Br
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.95
5.10
2.03
1.14
0.98
2.00
162.5
159.0
140.0
137.0
131.7
131.3
130.9
130.5
128.9
126.6
125.3
120.6
101.1
77.3
77.0
76.7
35.7
O
O
Br
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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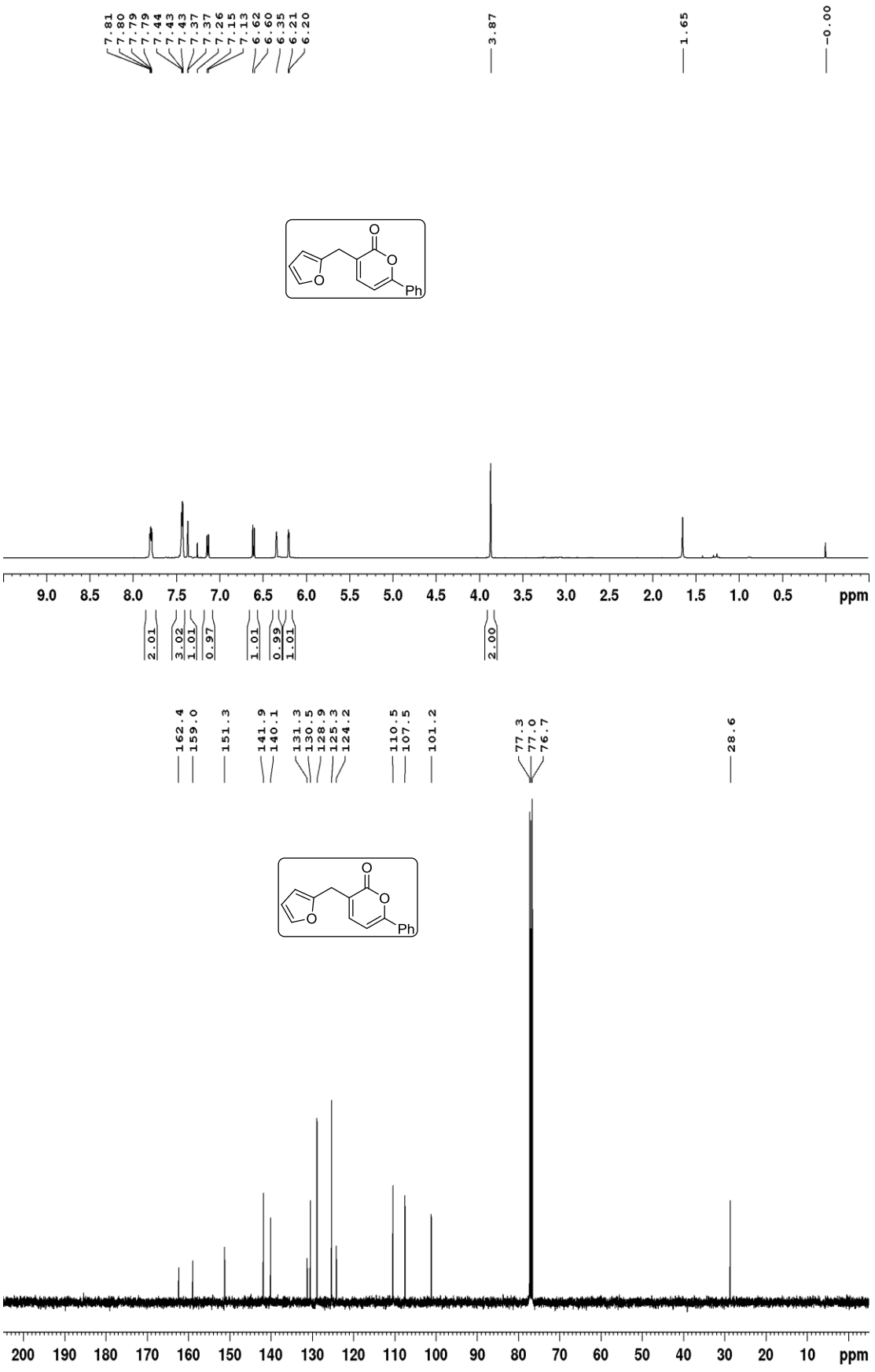
7.89
7.88
7.87
7.86
7.83
7.81
7.79
7.78
7.77
7.76
7.50
7.49
7.48
7.46
7.44
7.43
7.42
7.41
7.26
6.71
6.69
6.45
6.43
4.30
1.56
0.00
O
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.26
1.28
2.26
3.36
3.99
0.93
0.95
2.00
162.8
158.4
139.9
133.9
133.8
131.9
131.3
130.4
128.8
128.8
128.1
127.8
126.6
126.4
125.8
125.6
125.3
124.1
101.2
77.3
77.0
76.7
33.1
O
O
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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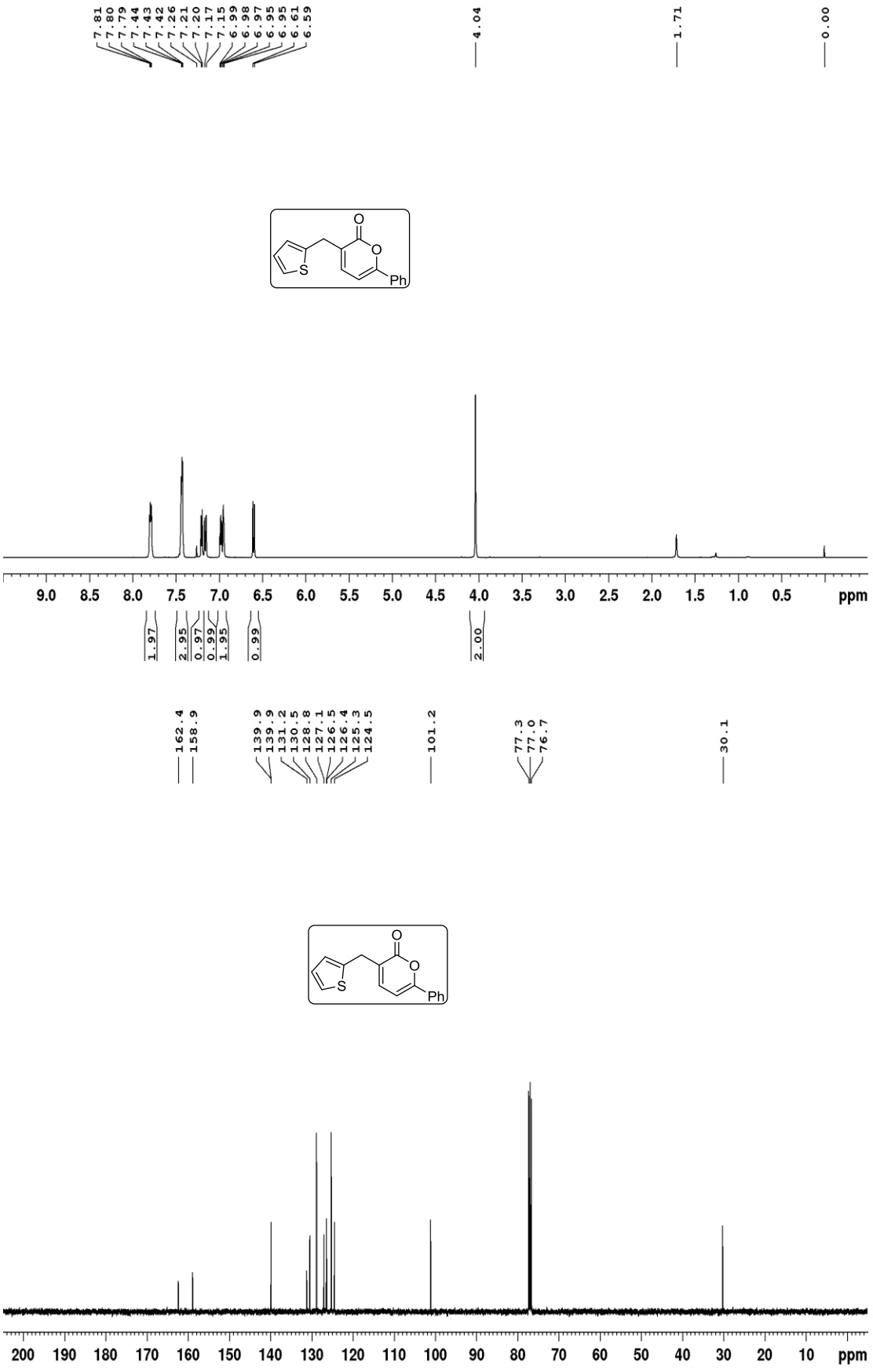
7.80
7.79
7.79
7.44
7.43
7.43
7.37
7.37
7.26
7.15
7.13
6.62
6.60
6.35
6.21
6.20
3.87
1.65
0.00
O
O
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.01
3.02
1.01
0.97
1.01
0.99
1.01
2.00
162.4
159.0
151.3
141.9
140.1
131.3
130.5
128.9
125.3
124.2
110.5
107.5
101.2
77.3
77.0
76.7
28.6
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.81
7.80
7.79
7.44
7.43
7.42
7.26
7.21
7.20
7.17
7.15
6.99
6.98
6.97
6.95
6.95
6.61
6.59
4.04
1.71
0.00
O
O
S
Ph
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 ppm
1.97
2.95
0.97
0.99
1.95
0.99
2.00
162.4
158.9
139.9
139.9
131.2
130.5
128.8
127.1
126.5
126.4
125.3
124.5
101.2
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O
S
Ph
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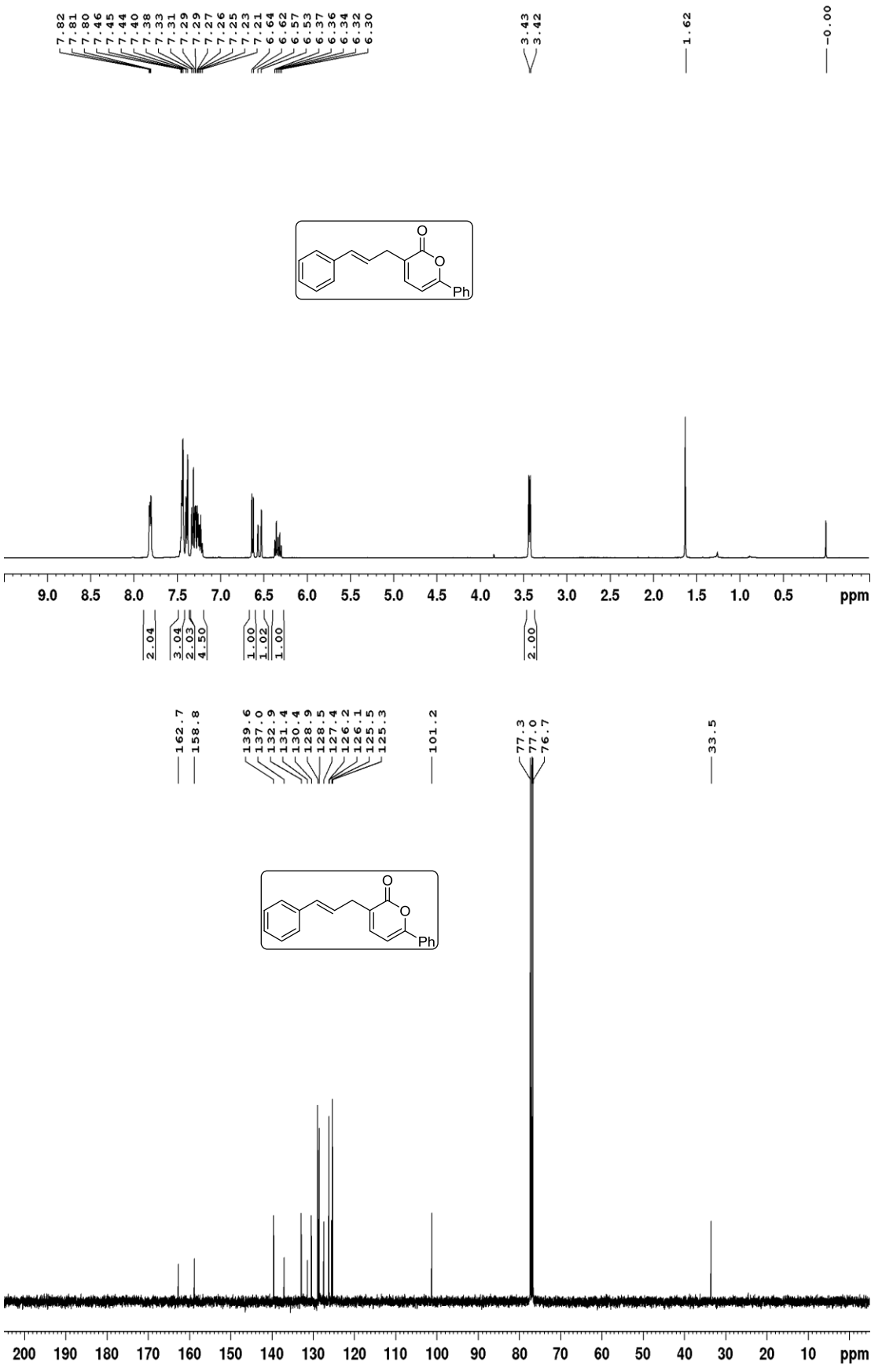
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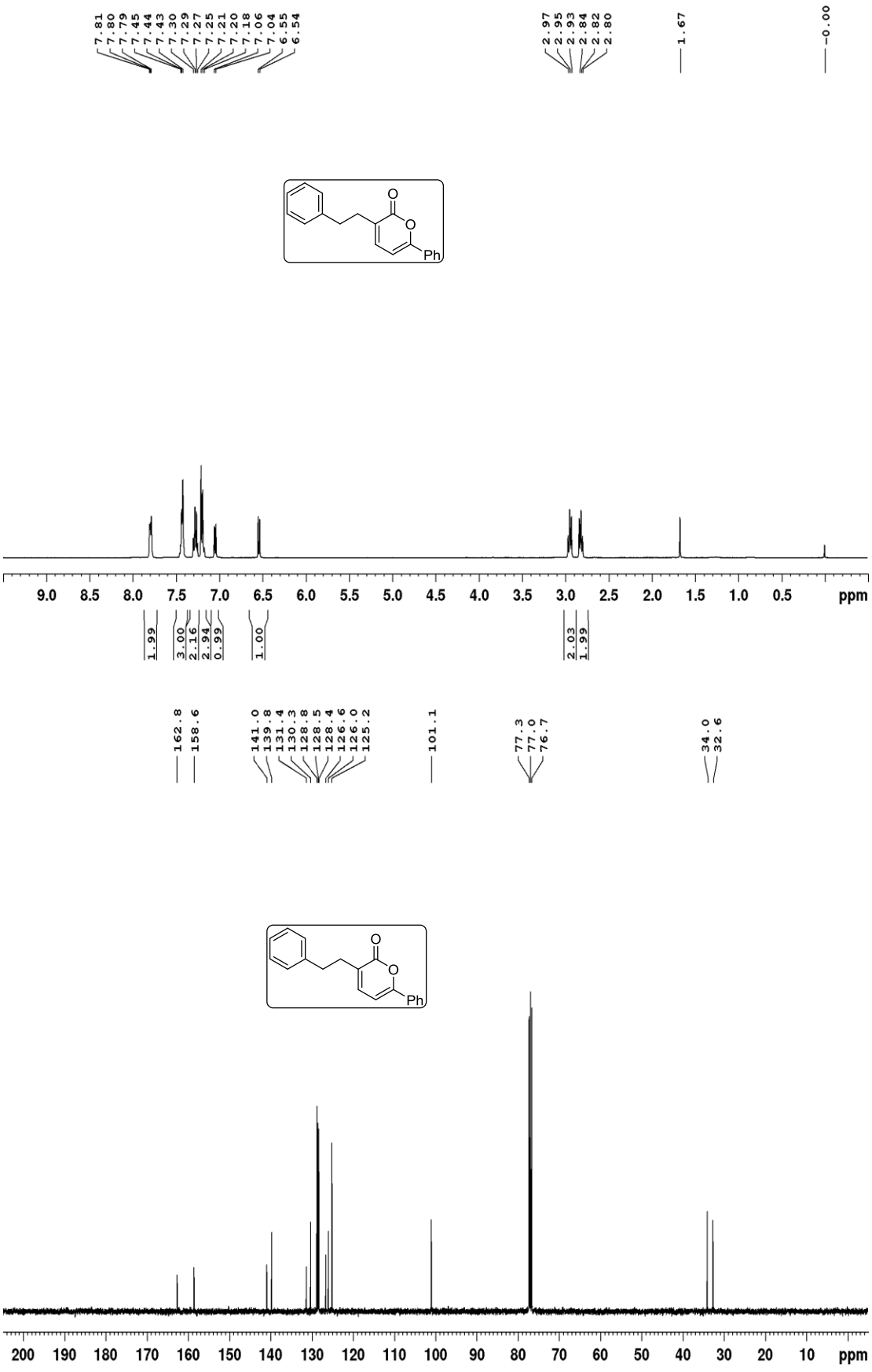
7.80
7.46
7.45
7.44
7.40
7.38
7.33
7.31
7.29
7.29
7.27
7.26
7.25
7.23
7.21
6.64
6.62
6.57
6.53
6.37
6.36
6.34
6.32
6.30
3.43
3.42
1.62
0.00
O
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.04
3.04
2.03
4.50
1.00
1.02
1.00
2.00
162.7
158.8
139.6
137.0
132.9
131.4
130.4
128.9
128.5
127.4
126.2
126.1
125.5
125.3
101.2
77.3
77.0
76.7
33.5
O
O
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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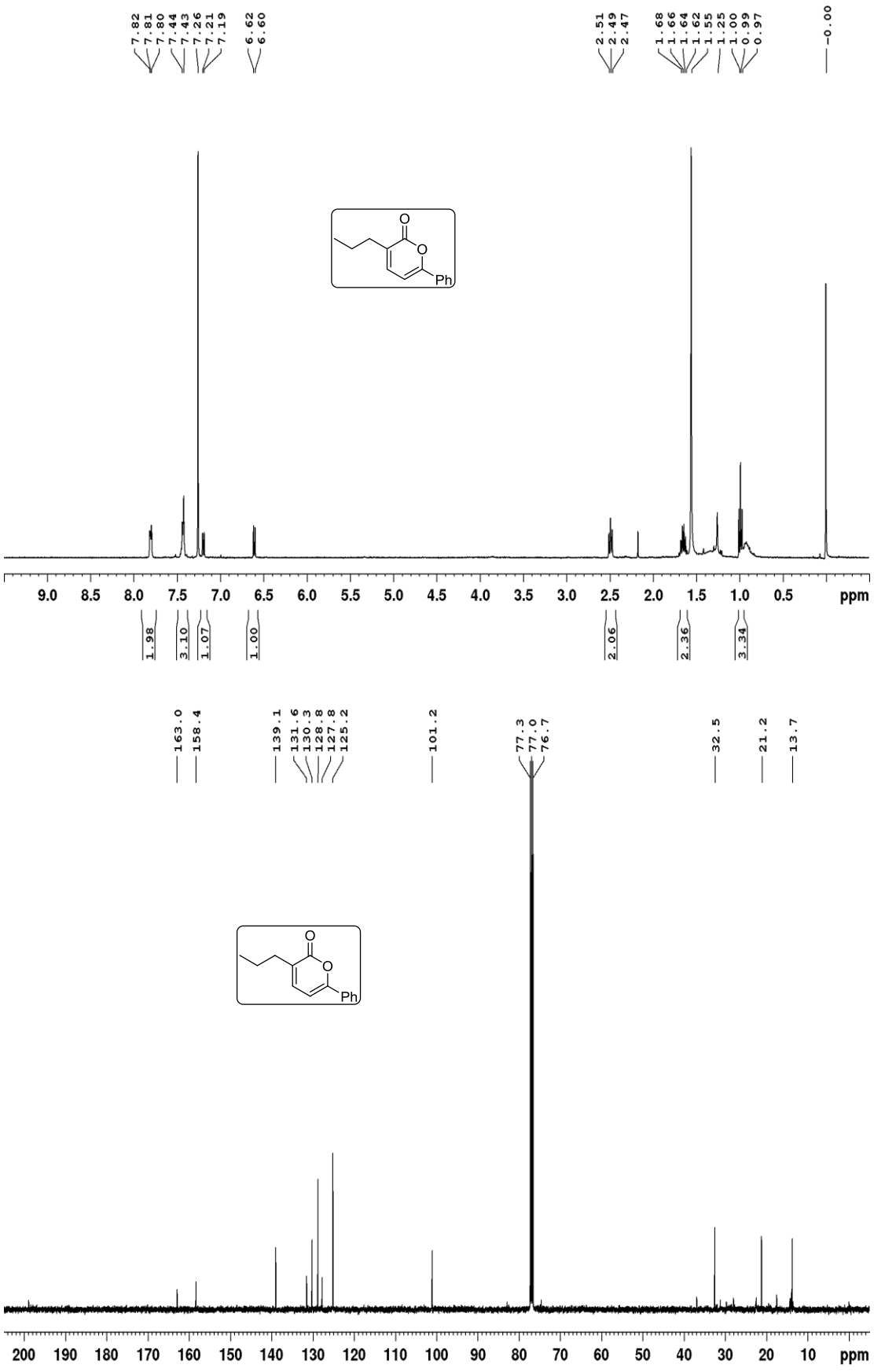
7.80
7.79
7.45
7.44
7.43
7.30
7.29
7.27
7.25
7.21
7.20
7.18
7.06
7.04
6.55
6.54
2.97
2.95
2.93
2.84
2.82
2.80
1.67
0.00
O
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.99
3.00
2.16
2.94
0.99
1.00
2.03
1.99
162.8
158.6
141.0
139.8
131.4
130.3
128.8
128.5
128.4
126.6
126.0
125.2
101.1
77.3
77.0
76.7
34.0
32.6
O
O
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.81
7.80
7.44
7.43
7.26
7.21
7.19
6.62
6.60
2.51
2.49
2.47
1.68
1.66
1.64
1.62
1.55
1.25
1.00
0.99
0.97
0.00
O
O
Ph
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 ppm
1.98
3.10
1.07
1.00
2.06
2.36
3.34
163.0
158.4
139.1
131.6
130.3
128.8
127.8
125.2
101.2
77.3
77.0
76.7
32.5
21.2
13.7
O
O
Ph
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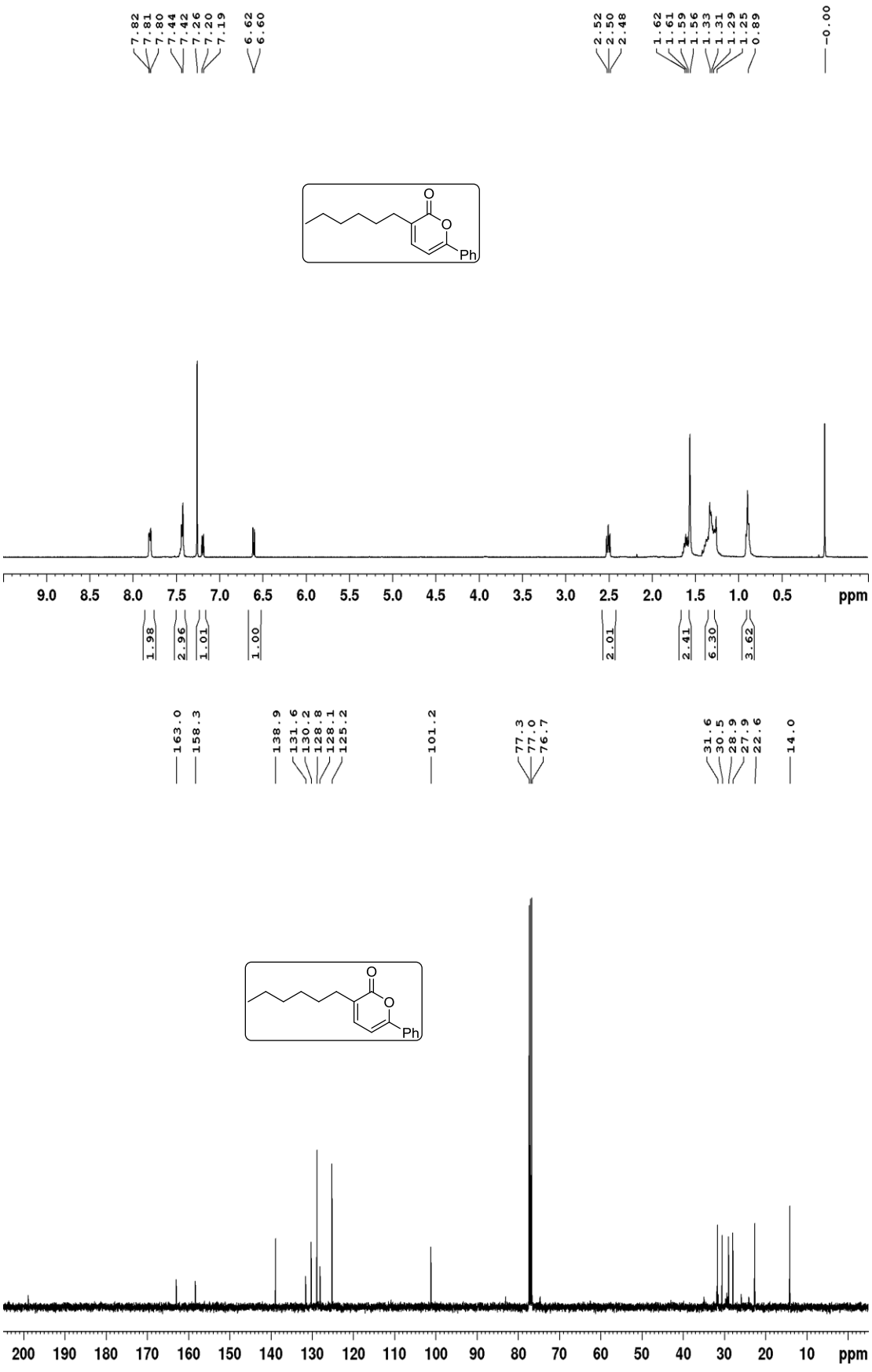
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7.81
7.80
7.44
7.42
7.26
7.20
7.19
6.62
6.60
2.52
2.50
2.48
1.62
1.61
1.59
1.56
1.33
1.31
1.29
1.25
0.89
0.00
O
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.98
2.96
1.01
1.00
2.01
2.41
6.30
3.62
163.0
158.3
138.9
131.6
130.2
128.8
128.1
125.2
101.2
77.3
77.0
76.7
31.6
30.5
28.9
27.9
22.6
14.0
O
O
Ph
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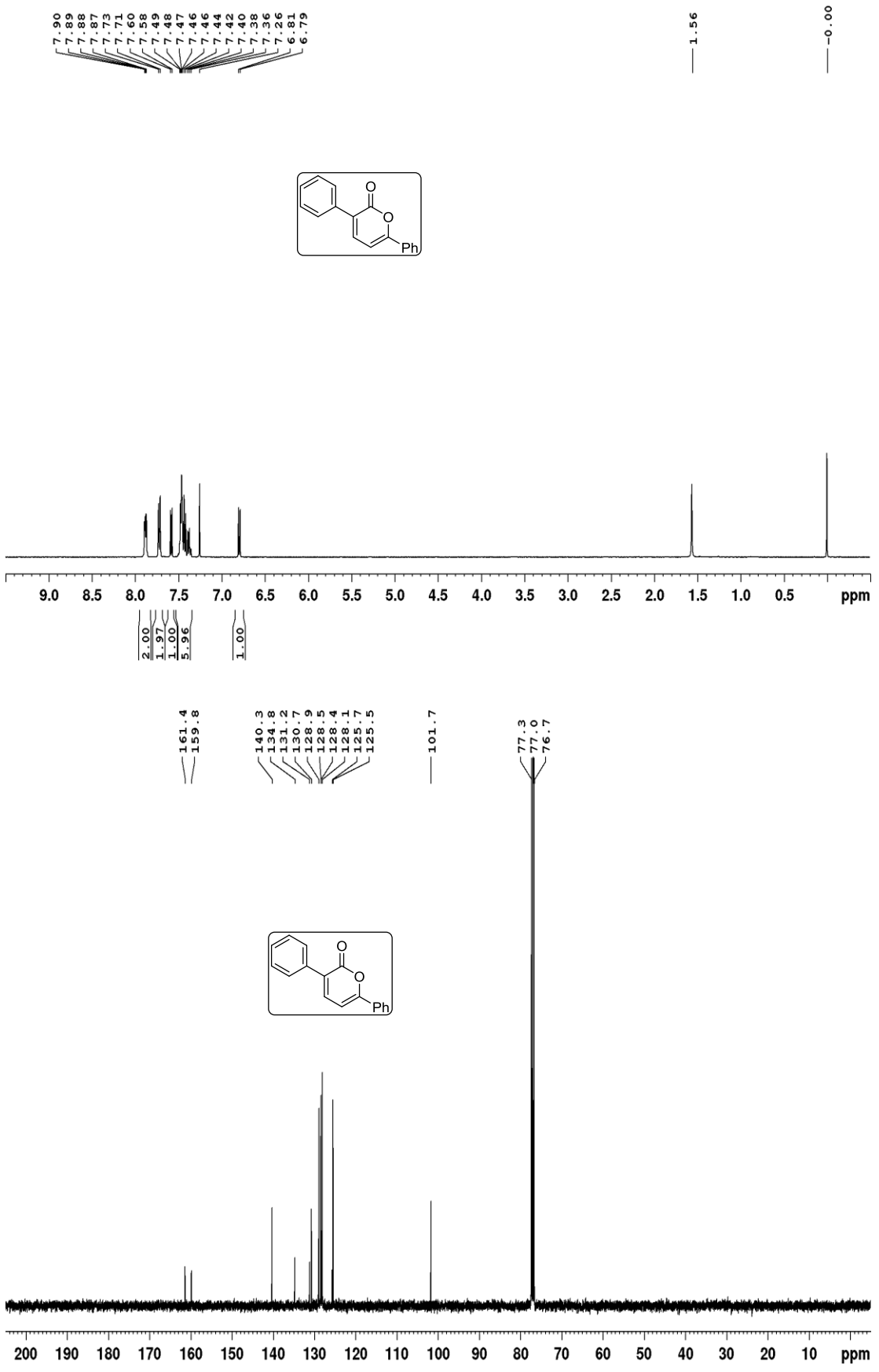
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7.89
7.88
7.87
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7.71
7.60
7.58
7.49
7.48
7.47
7.46
7.46
7.44
7.42
7.40
7.38
7.36
7.26
6.81
6.79
1.56
0.00
O
O
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00
1.97
1.00
5.96
1.00
161.4
159.8
140.3
134.8
131.2
130.7
128.9
128.5
128.4
128.1
125.7
125.5
101.7
77.3
77.0
76.7
O
O
Ph
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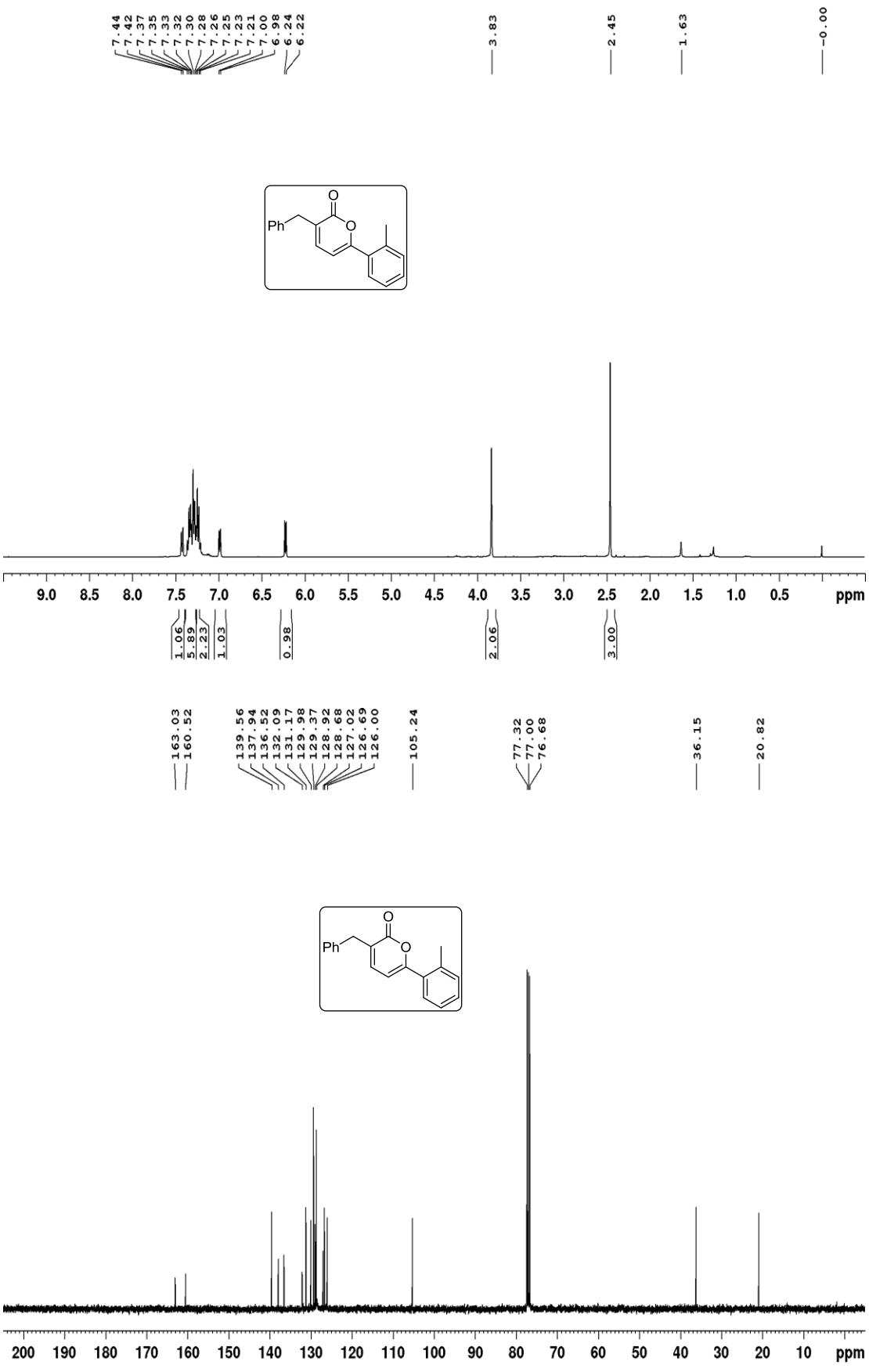
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7.42
7.37
7.35
7.33
7.32
7.30
7.28
7.26
7.25
7.23
7.21
7.00
6.98
6.24
6.22
3.83
2.45
1.63
0.00
O
Ph
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.06
5.89
2.23
1.03
0.98
2.06
3.00
163.03
160.52
139.56
137.94
136.52
132.09
131.17
129.98
129.37
128.92
128.68
127.02
126.69
126.00
105.24
77.32
77.00
76.68
36.15
20.82
O
Ph
O
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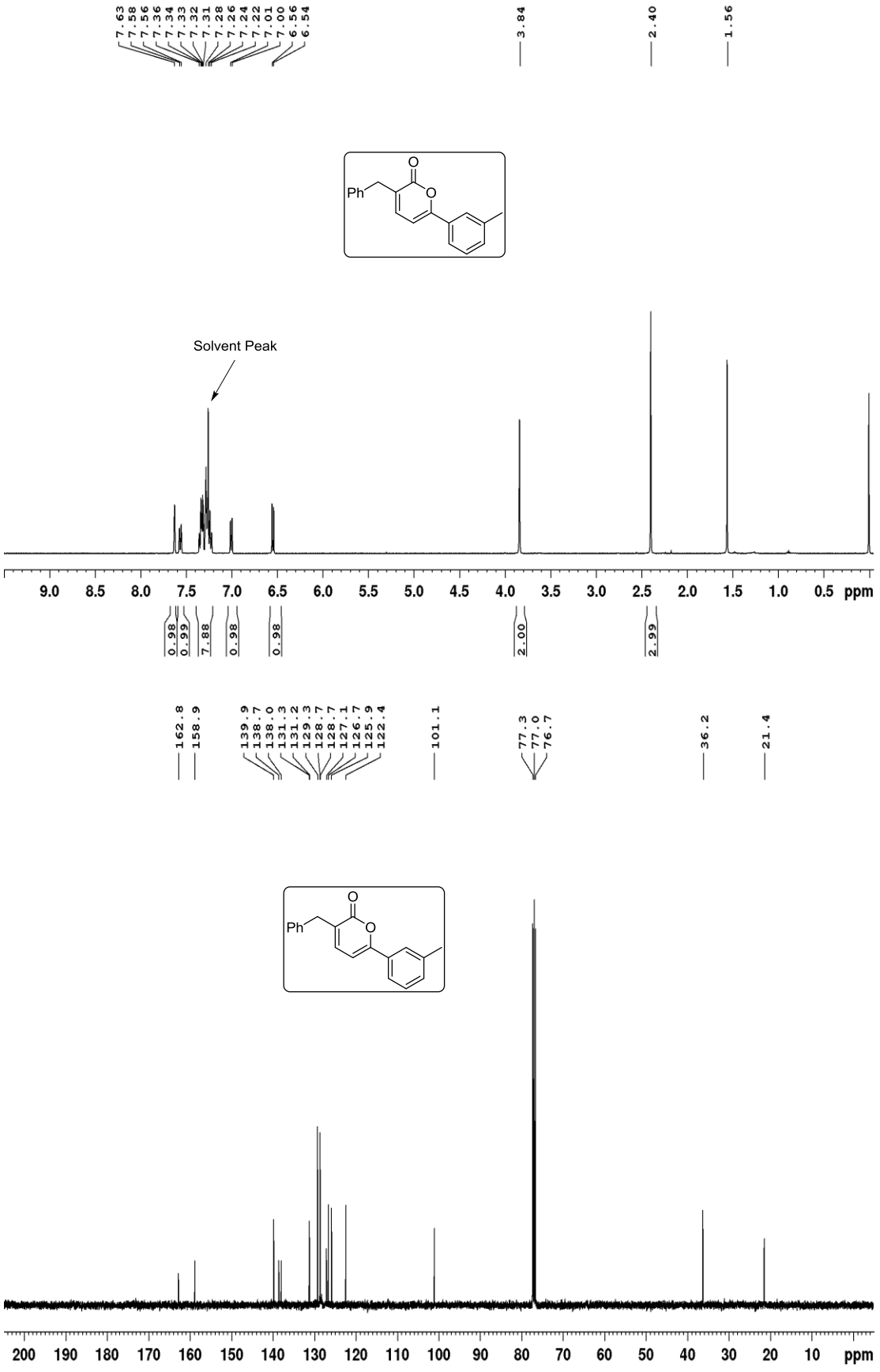
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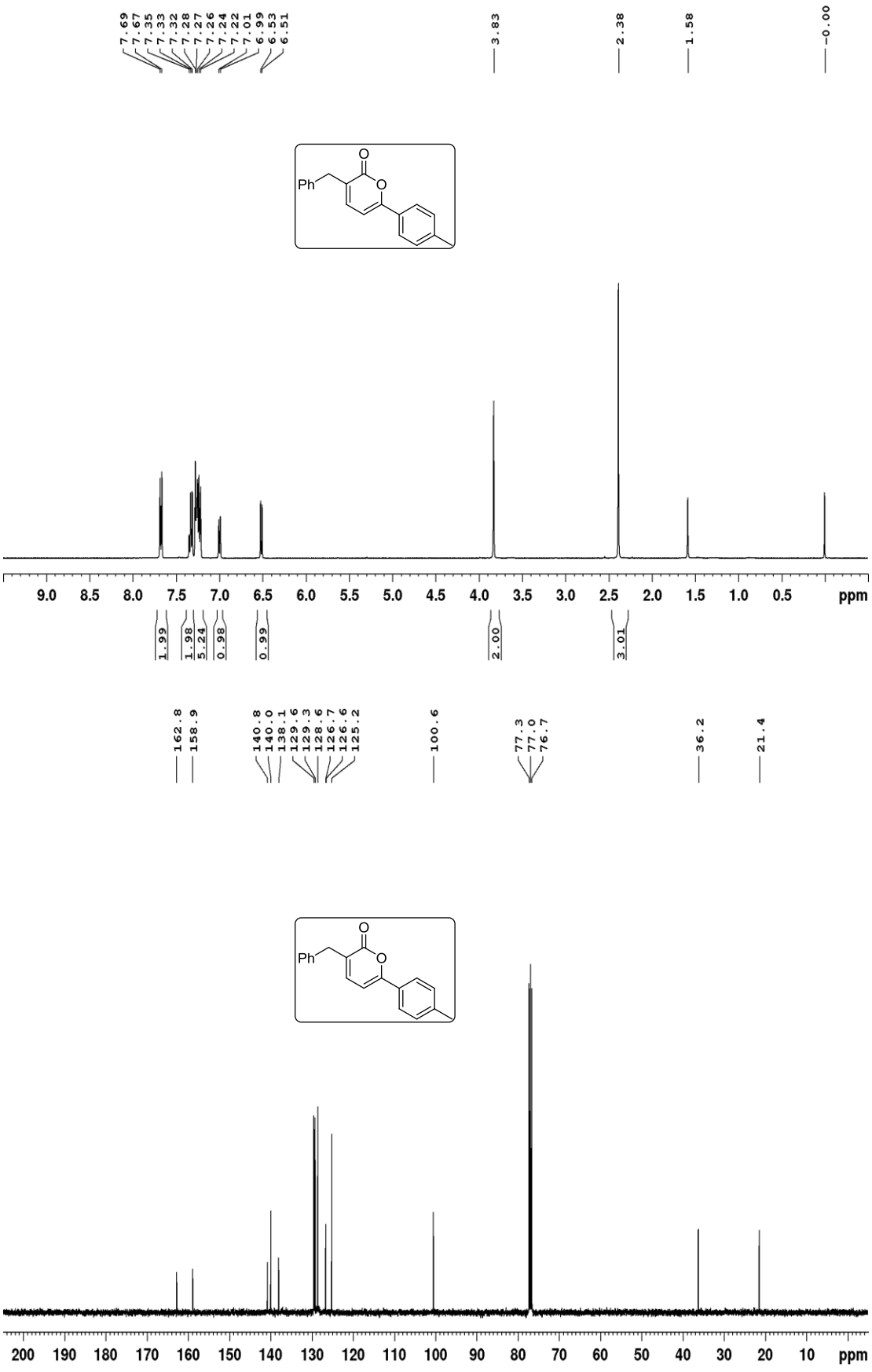
7.58
7.56
7.36
7.34
7.33
7.32
7.31
7.28
7.26
7.24
7.22
7.01
7.00
6.56
6.54
3.84
2.40
1.56
Ph
O
O
Solvent Peak
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.98
0.99
7.88
0.98
0.98
2.00
2.99
162.8
158.9
139.9
138.7
138.0
131.3
131.2
129.3
128.7
128.7
127.1
126.7
125.9
122.4
101.1
77.3
77.0
76.7
36.2
21.4
Ph
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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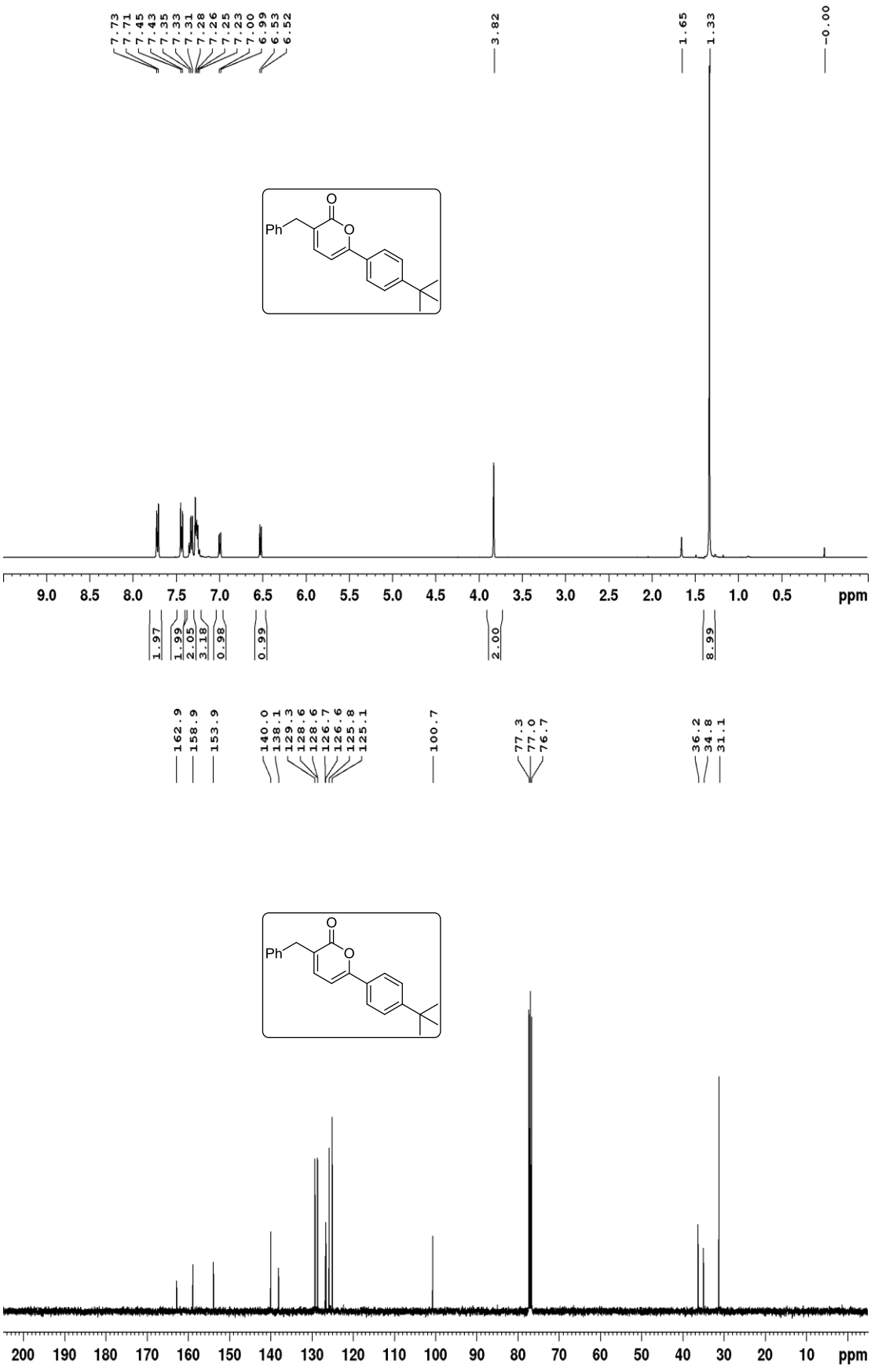
7.67
7.35
7.33
7.32
7.28
7.27
7.26
7.24
7.22
7.01
6.99
6.53
6.51
3.83
2.38
1.58
0.00
Ph
O
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.99
1.98
5.24
0.98
0.99
2.00
3.01
162.8
158.9
140.8
140.0
138.1
129.6
129.3
128.6
126.7
126.6
125.2
100.6
77.3
77.0
76.7
36.2
21.4
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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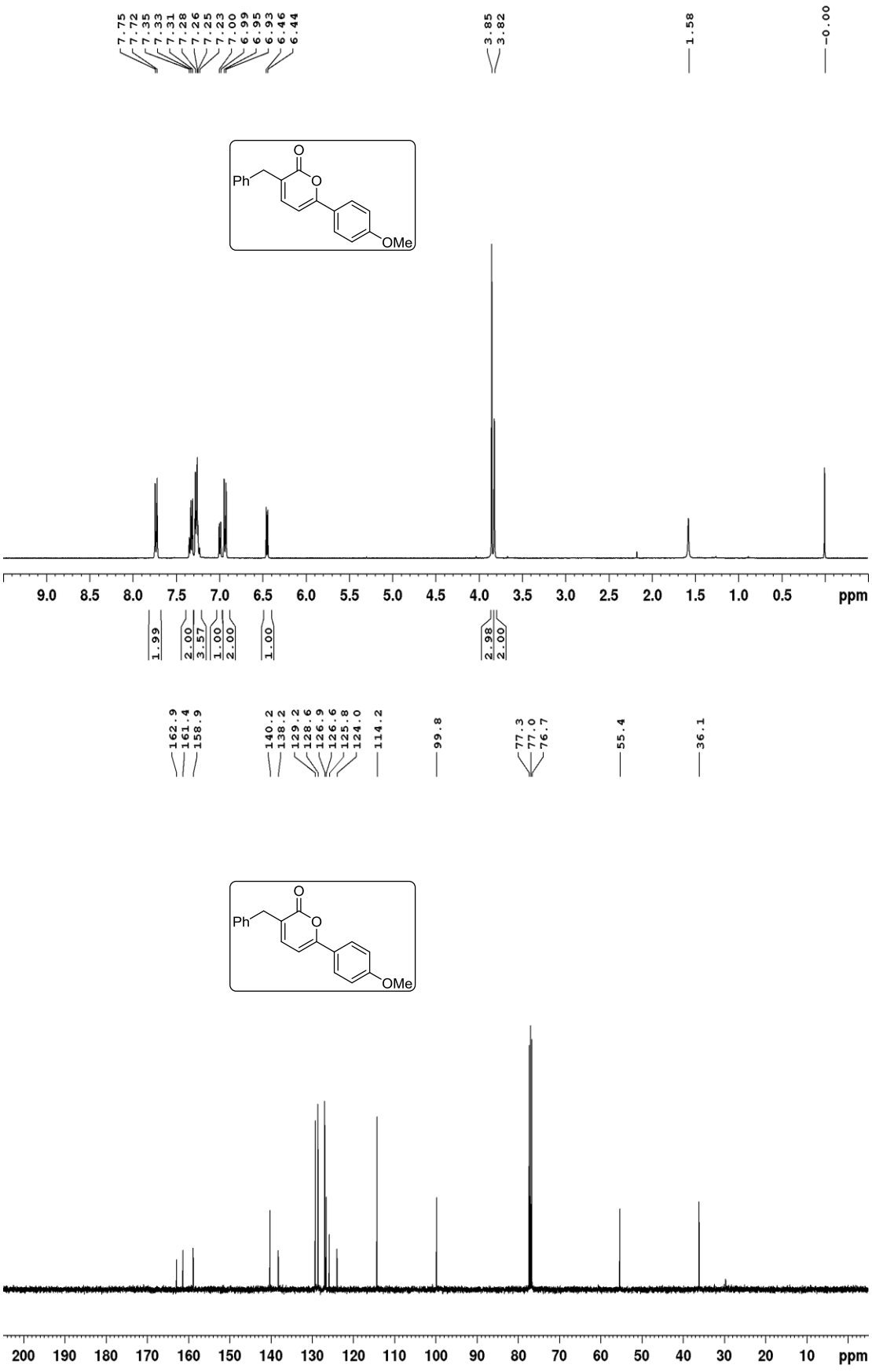
7.71
7.45
7.43
7.35
7.33
7.31
7.28
7.26
7.25
7.23
7.00
6.99
6.53
6.52
3.82
1.65
1.33
0.00
Ph
O
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.97
1.99
2.05
3.18
0.98
0.99
2.00
8.99
162.9
158.9
153.9
140.0
138.1
129.3
128.6
128.6
126.7
126.6
125.8
125.1
100.7
77.3
77.0
76.7
36.2
34.8
31.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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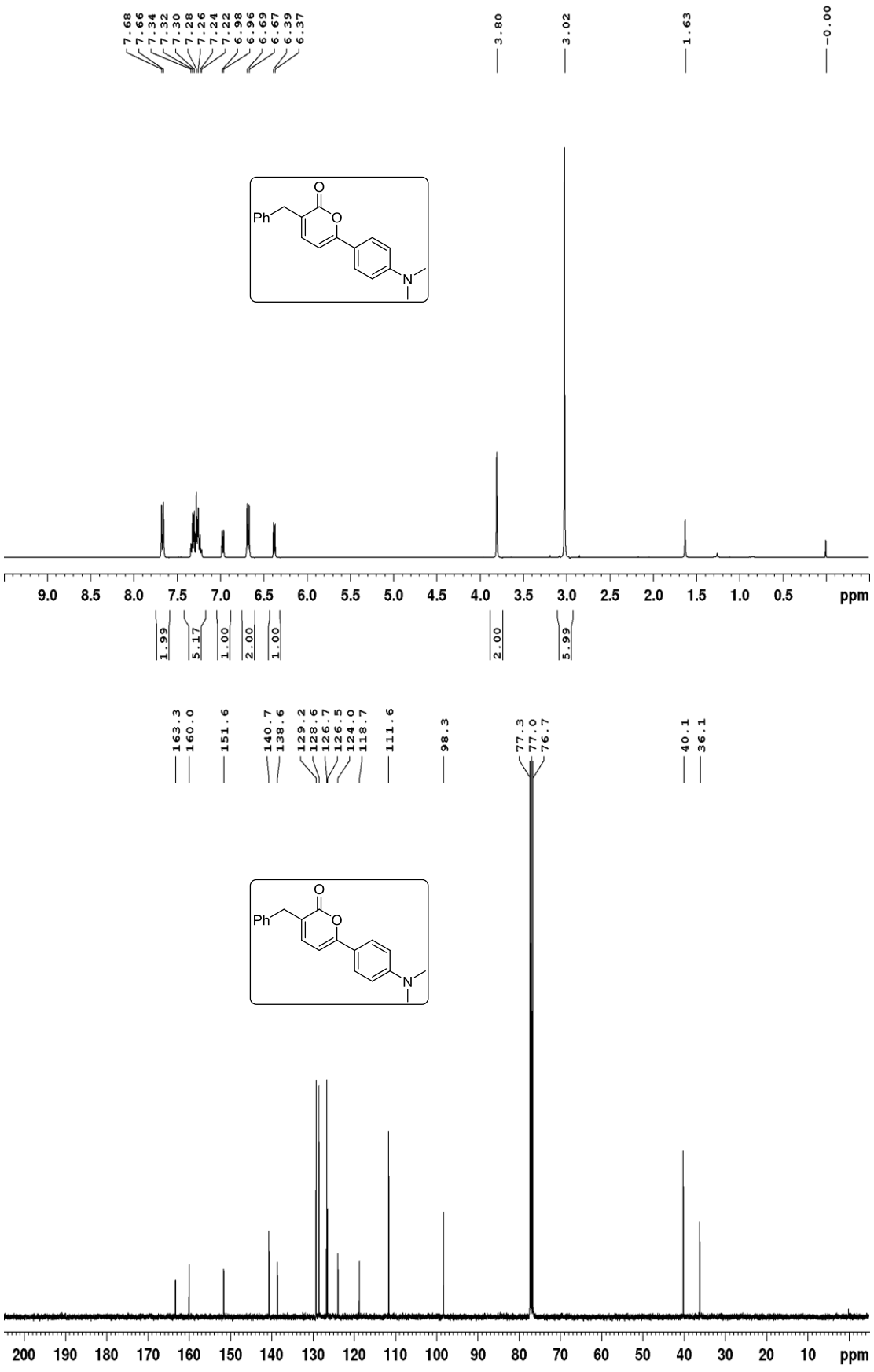
7.72
7.35
7.33
7.31
7.28
7.26
7.25
7.23
7.00
6.99
6.95
6.93
6.46
6.44
3.85
3.82
1.58
0.00
Ph
O
OMe
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.99
2.00
3.57
1.00
2.00
1.00
2.98
2.00
162.9
161.4
158.9
140.2
138.2
129.2
128.6
126.9
126.6
125.8
124.0
114.2
99.8
77.3
77.0
76.7
55.4
36.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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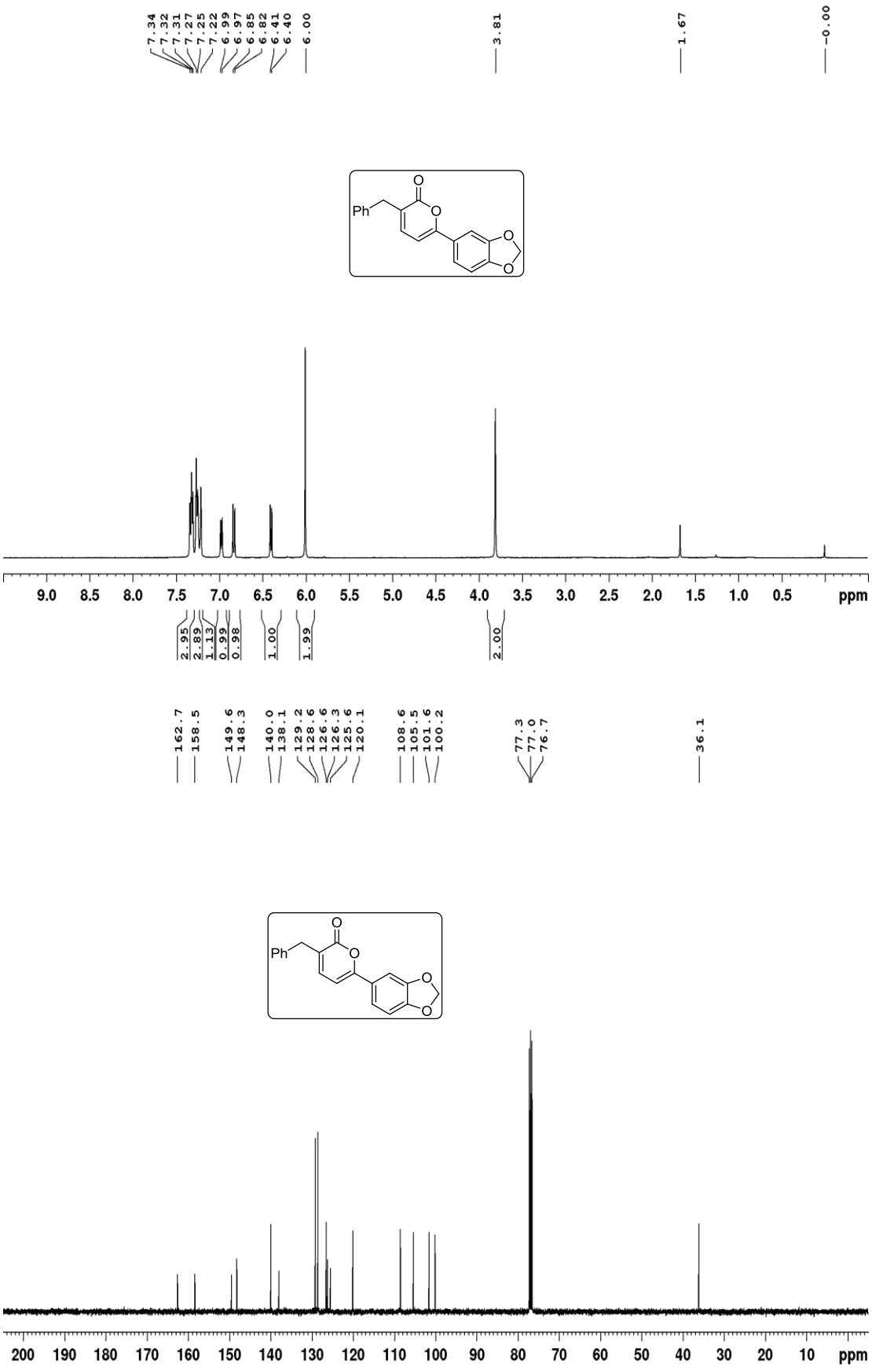
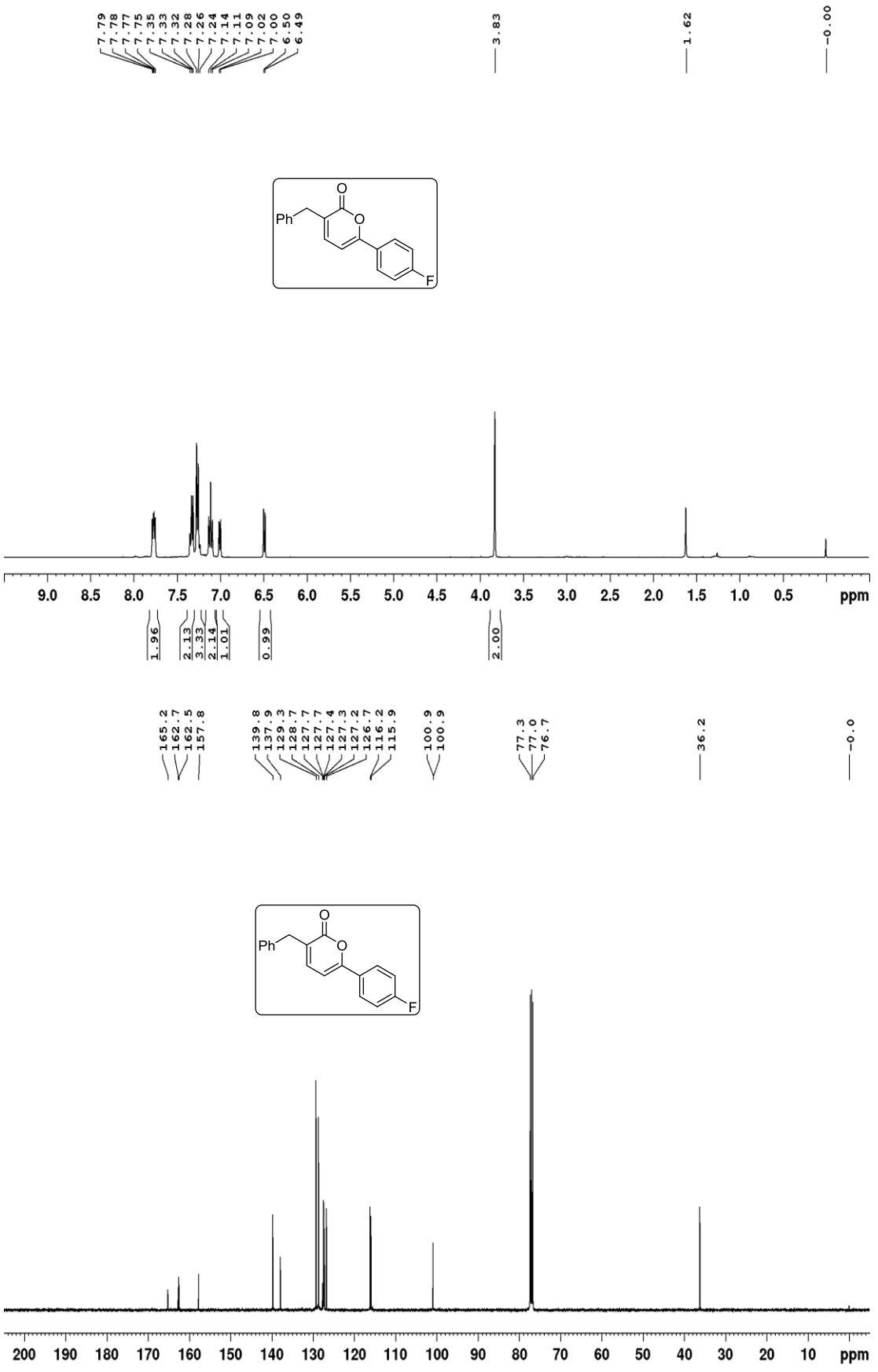
7.66
7.34
7.32
7.30
7.28
7.26
7.24
7.22
6.98
6.96
6.69
6.67
6.39
6.37
3.80
3.02
1.63
0.00
Ph
O
N
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.99
5.17
1.00
2.00
1.00
2.00
5.99
163.3
160.0
151.6
140.7
138.6
129.2
128.6
126.7
126.5
124.0
118.7
111.6
98.3
77.3
77.0
76.7
40.1
36.1
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.34
7.32
7.31
7.27
7.25
7.22
6.99
6.97
6.85
6.82
6.41
6.40
6.00
3.81
1.67
0.00
Ph
O
O
O
O
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 ppm
2.95
2.89
1.13
0.99
0.98
1.00
1.99
2.00
162.7
158.5
149.6
148.3
140.0
138.1
129.2
128.6
126.6
126.3
125.6
120.1
108.6
105.5
101.6
100.2
77.3
77.0
76.7
36.1
Ph
O
O
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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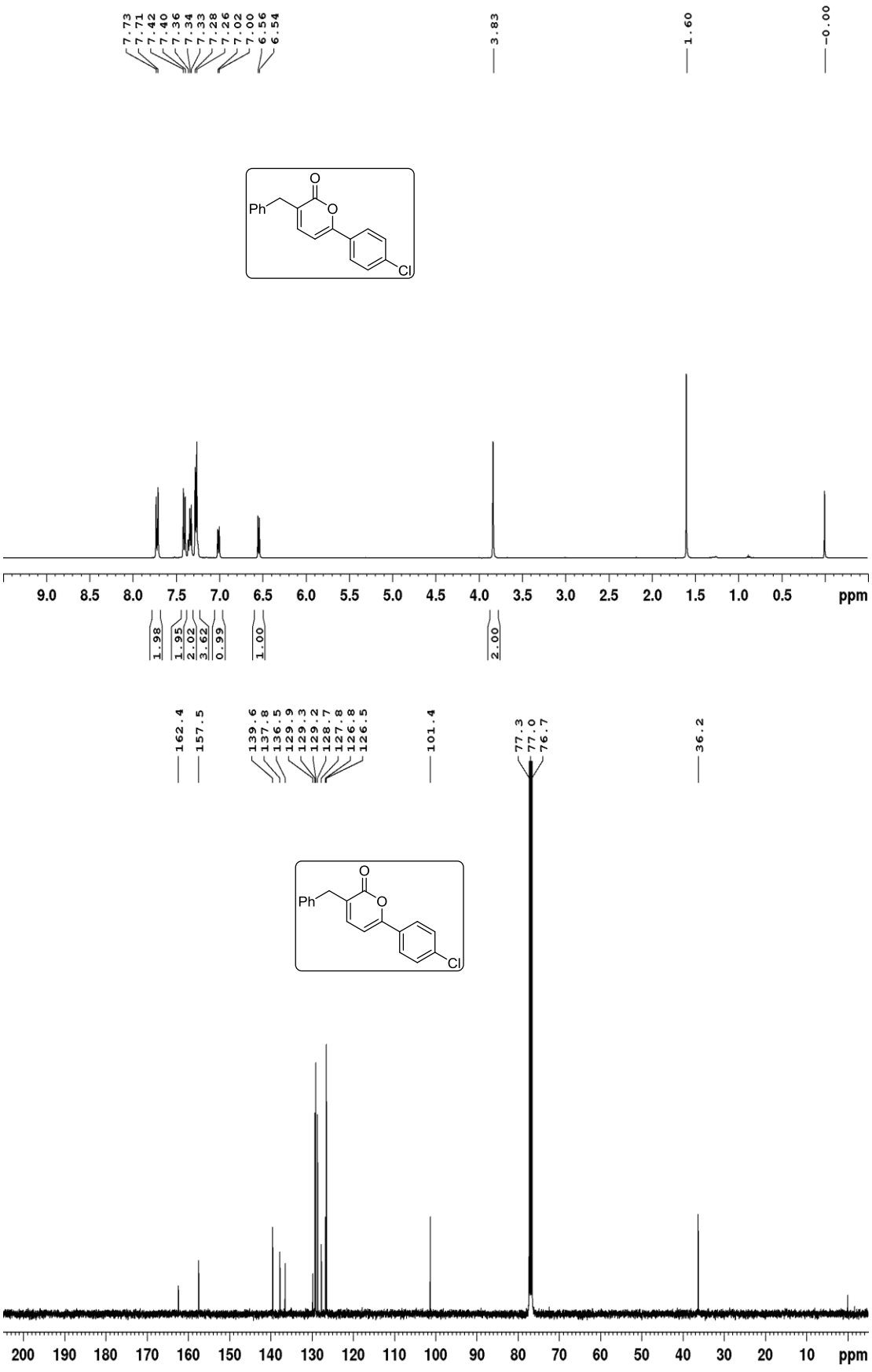
7.78
7.77
7.75
7.35
7.33
7.32
7.28
7.26
7.24
7.14
7.11
7.09
7.02
7.00
6.50
6.49
3.83
1.62
0.00
Ph
O
O
F
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.96
2.13
3.33
2.14
1.01
0.99
2.00
165.2
162.7
162.5
157.8
139.8
137.9
129.3
128.7
127.7
127.7
127.4
127.3
127.2
126.7
116.2
115.9
100.9
100.9
77.3
77.0
76.7
36.2
0.0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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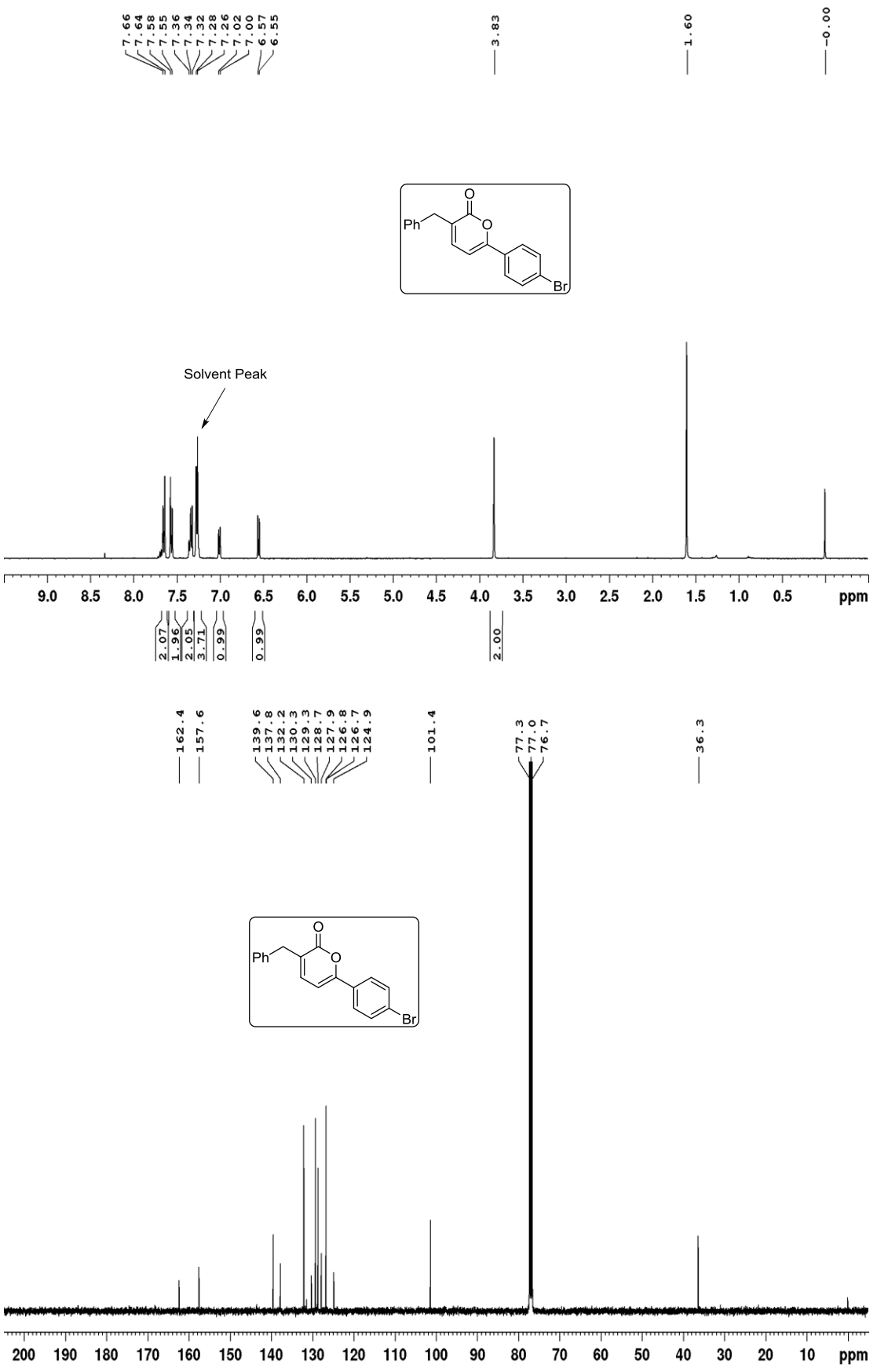
7.71
7.42
7.40
7.36
7.34
7.33
7.28
7.26
7.02
7.00
6.56
6.54
3.83
1.60
0.00
Ph
O
O
Cl
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.98
1.95
2.02
3.62
0.99
1.00
2.00
162.4
157.5
139.6
137.8
136.5
129.9
129.3
129.2
128.7
127.8
126.8
126.5
101.4
77.3
77.0
76.7
36.2
Ph
O
O
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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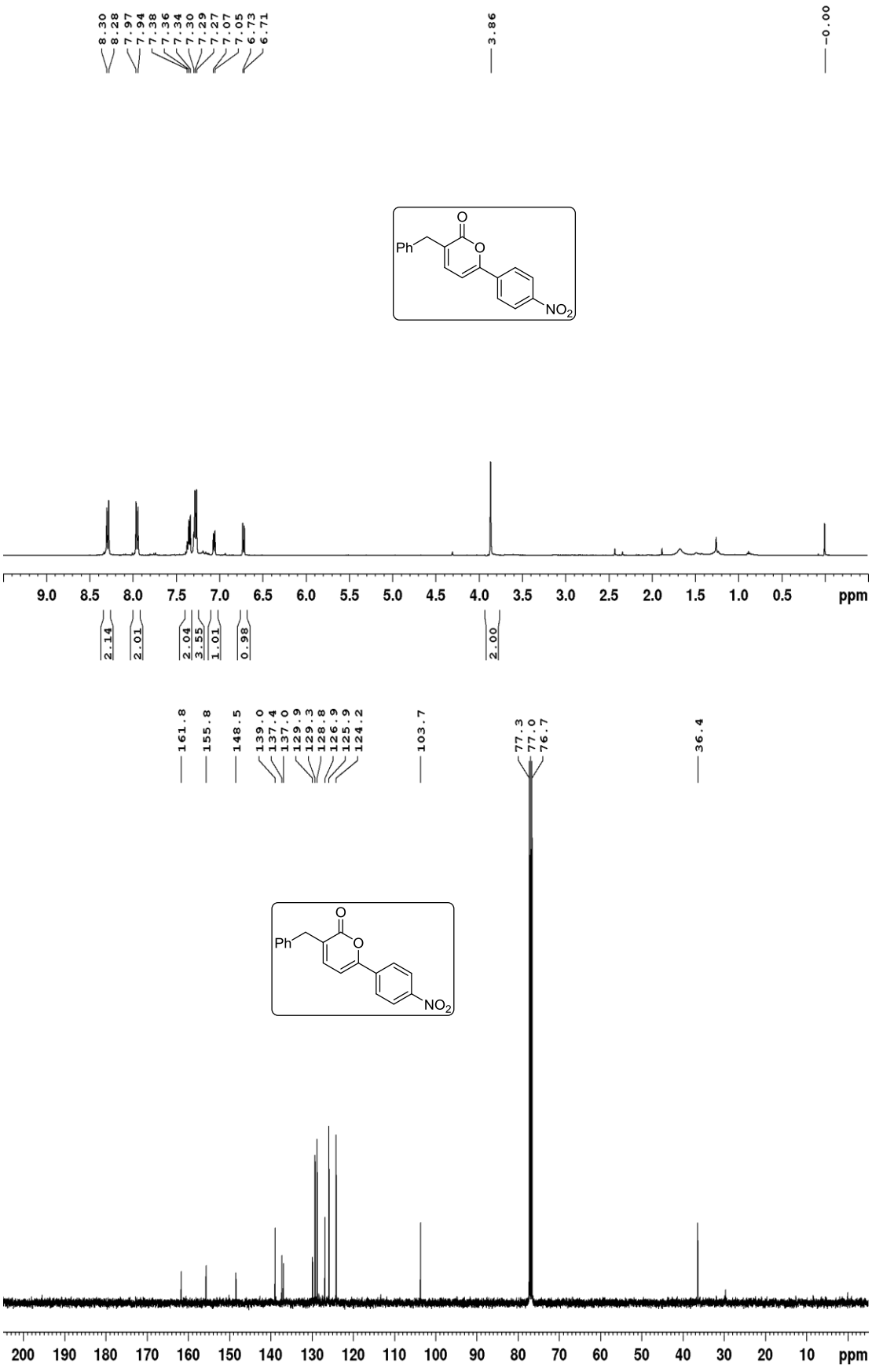
7.58
7.55
7.36
7.34
7.32
7.28
7.26
7.02
7.00
6.57
6.55
3.83
1.60
0.00
Ph
O
O
Br
Solvent Peak
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.07
1.96
2.05
3.71
0.99
0.99
2.00
162.4
157.6
139.6
137.8
132.2
130.3
129.3
128.7
127.9
126.8
126.7
124.9
101.4
77.3
77.0
76.7
36.3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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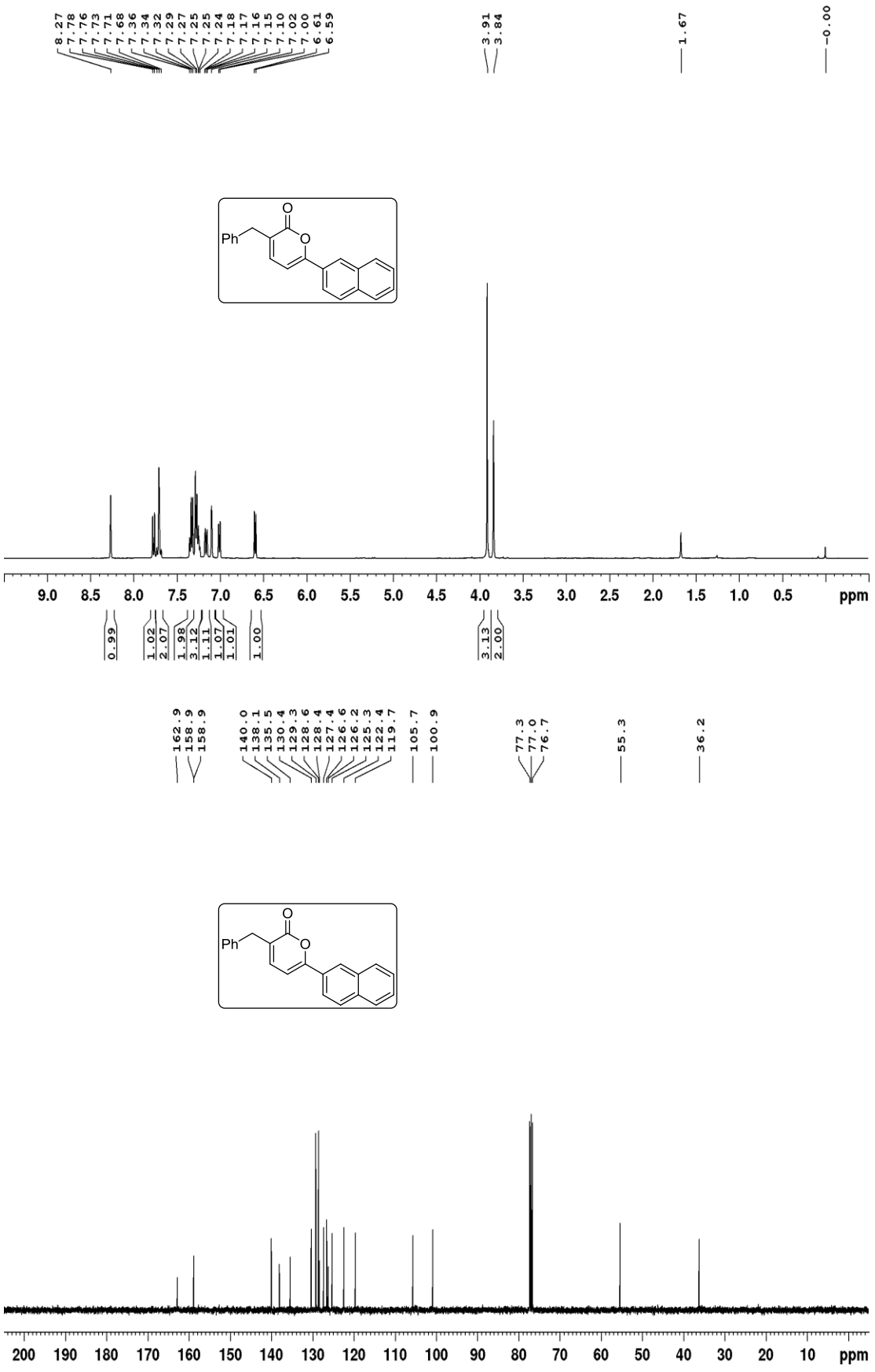
7.97
7.94
7.38
7.36
7.34
7.30
7.29
7.27
7.07
7.05
6.73
6.71
3.86
0.00
Ph
O
O
NO2
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.14
2.01
2.04
3.55
1.01
0.98
2.00
161.8
155.8
148.5
139.0
137.4
137.0
129.9
129.3
128.8
126.9
125.9
124.2
103.7
77.3
77.0
76.7
36.4
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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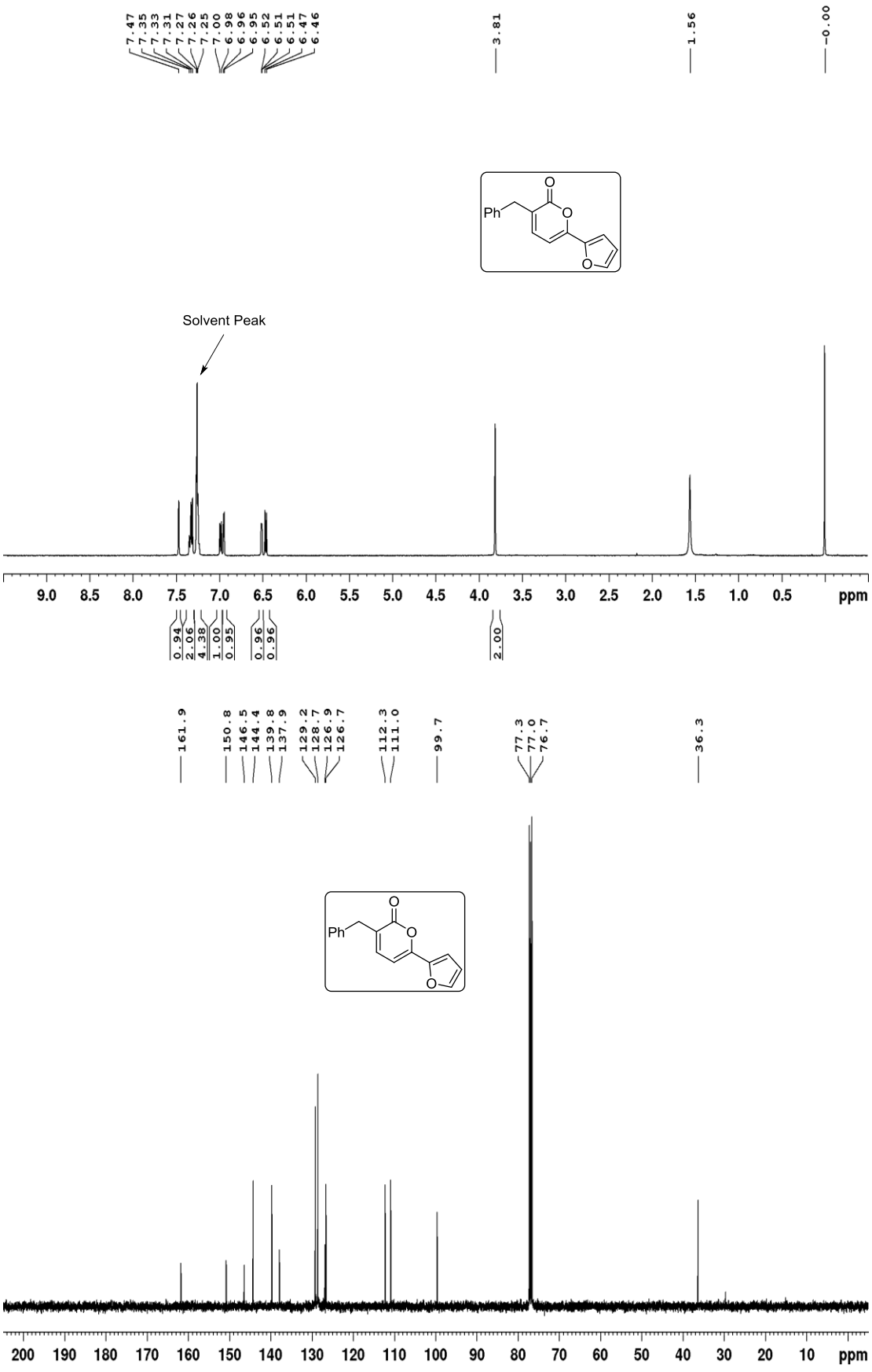
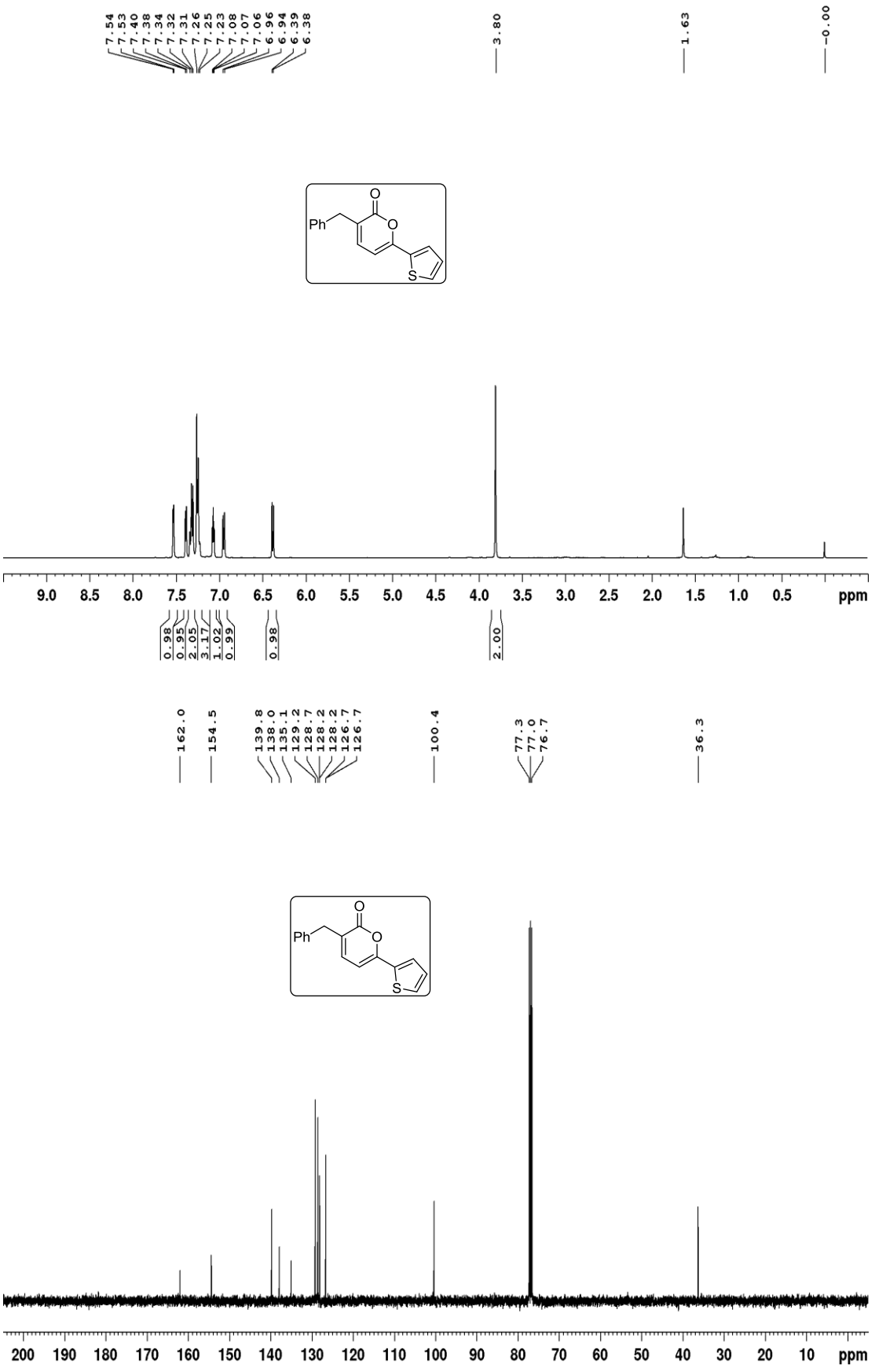
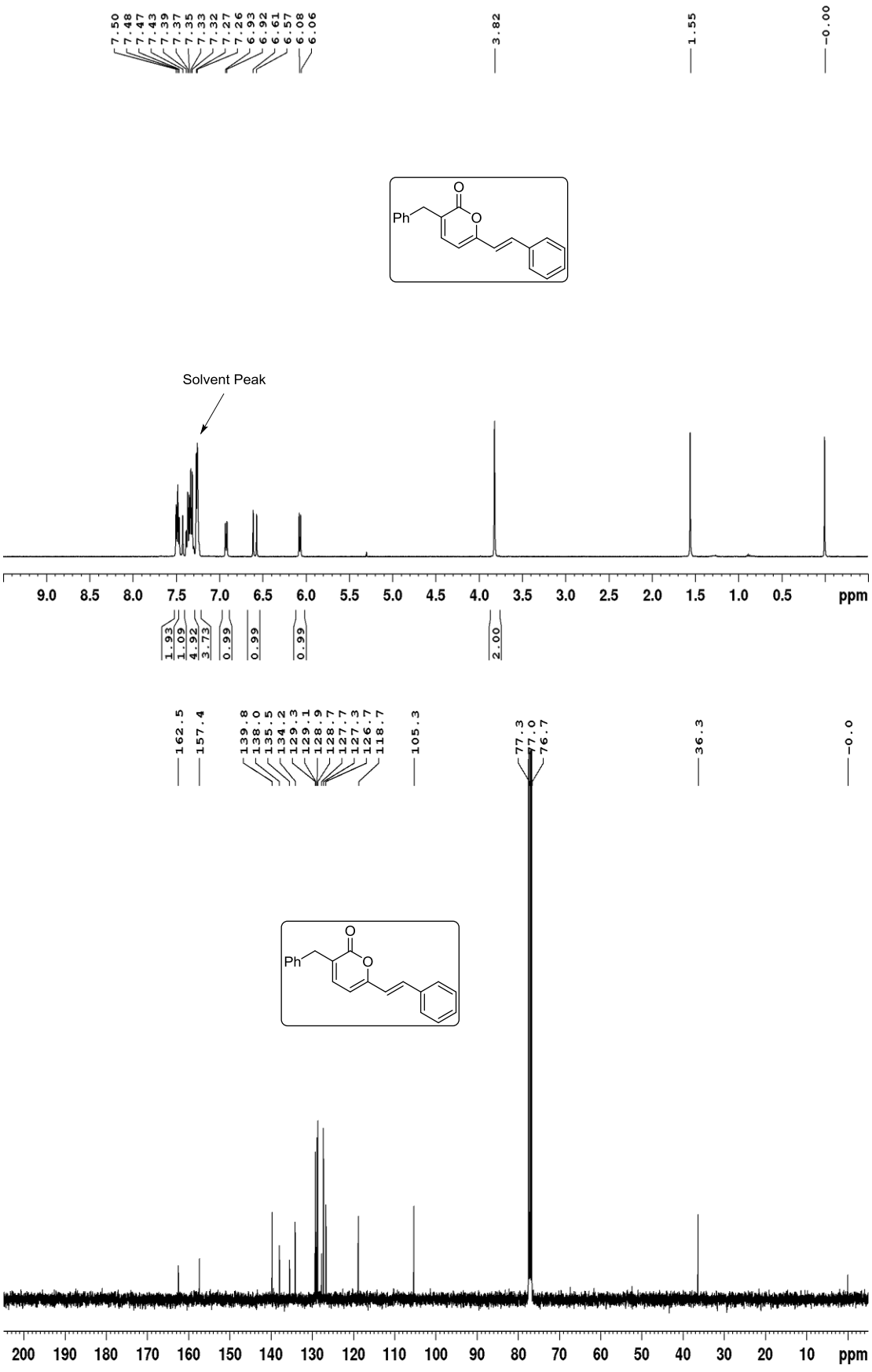
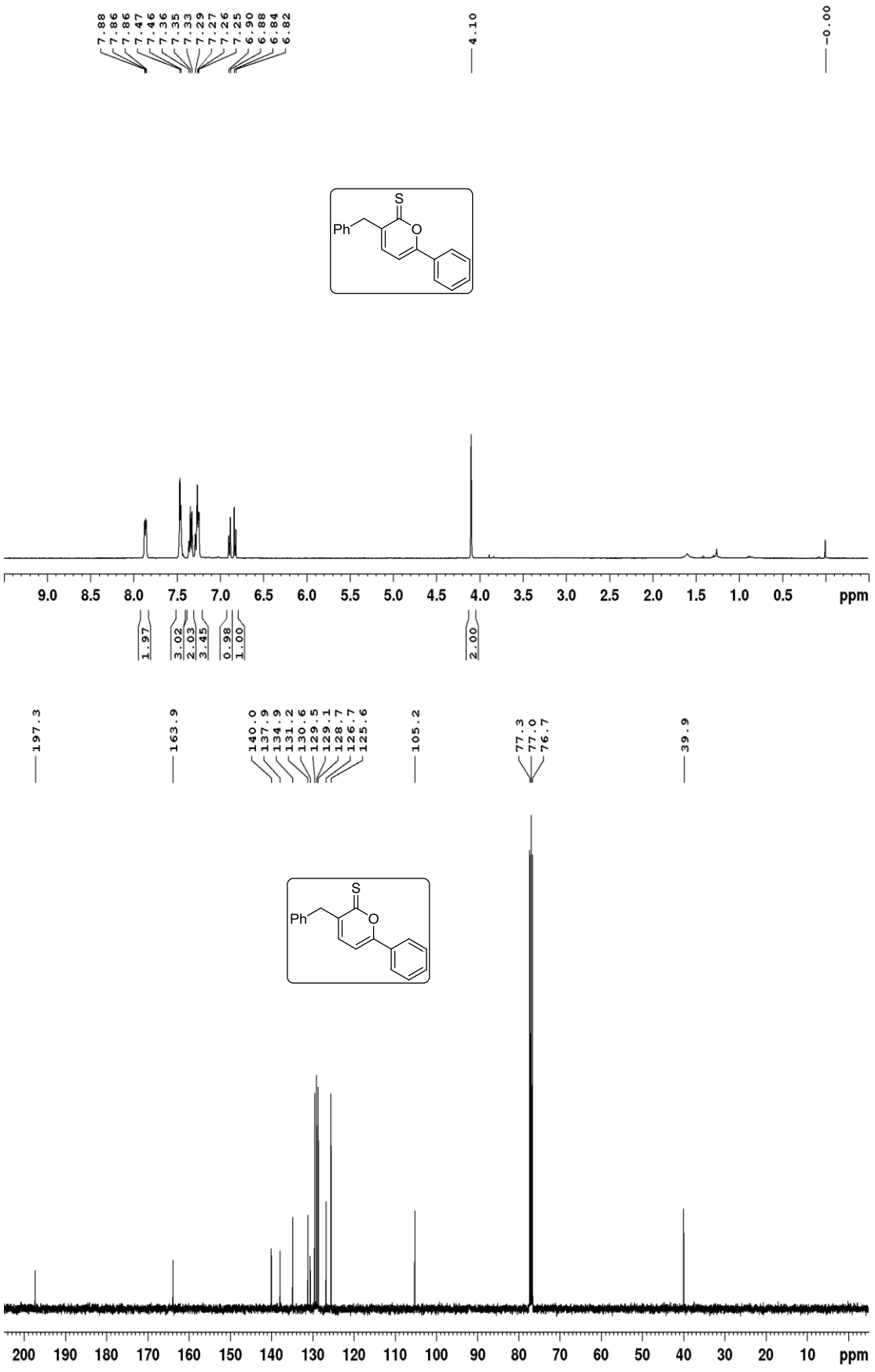
7.78
7.76
7.73
7.71
7.68
7.36
7.34
7.32
7.29
7.27
7.25
7.24
7.18
7.17
7.16
7.15
7.10
7.02
7.00
6.61
6.59
3.91
3.84
1.67
0.00
Ph
O
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.99
1.02
2.07
1.98
3.12
1.11
1.07
1.01
1.00
3.13
2.00
162.9
158.9
158.9
140.0
138.1
135.5
130.4
129.3
128.6
128.4
127.4
126.6
126.2
125.3
122.4
119.7
105.7
100.9
77.3
77.0
76.7
55.3
36.2
Ph
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.47
7.35
7.33
7.31
7.27
7.26
7.25
7.00
6.98
6.96
6.95
6.52
6.51
6.51
6.47
6.46
3.81
1.56
0.00
Ph
O
O
O
Solvent Peak
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 ppm
0.94
2.06
4.38
1.00
0.95
0.96
0.96
2.00
161.9
150.8
146.5
144.4
139.8
137.9
129.2
128.7
126.9
126.7
112.3
111.0
99.7
77.3
77.0
76.7
36.3
Ph
O
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.54
7.53
7.40
7.38
7.34
7.32
7.31
7.26
7.25
7.23
7.08
7.07
7.06
6.96
6.94
6.39
6.38
3.80
1.63
0.00
O
Ph
O
S
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 ppm
0.98
0.95
2.05
3.17
1.02
0.99
0.98
2.00
162.0
154.5
139.8
138.0
135.1
129.2
128.7
128.2
128.2
126.7
126.7
100.4
77.3
77.0
76.7
36.3
O
Ph
O
S
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.50
7.48
7.47
7.43
7.39
7.37
7.35
7.33
7.32
7.27
7.26
6.93
6.92
6.61
6.57
6.08
6.06
3.82
1.55
0.00
O
Ph
O
Solvent Peak
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 ppm
1.93
1.09
4.92
3.73
0.99
0.99
0.99
2.00
162.5
157.4
139.8
138.0
135.5
134.2
129.3
129.1
128.9
128.7
127.7
127.3
126.7
118.7
105.3
77.3
77.0
76.7
36.3
0.0
O
Ph
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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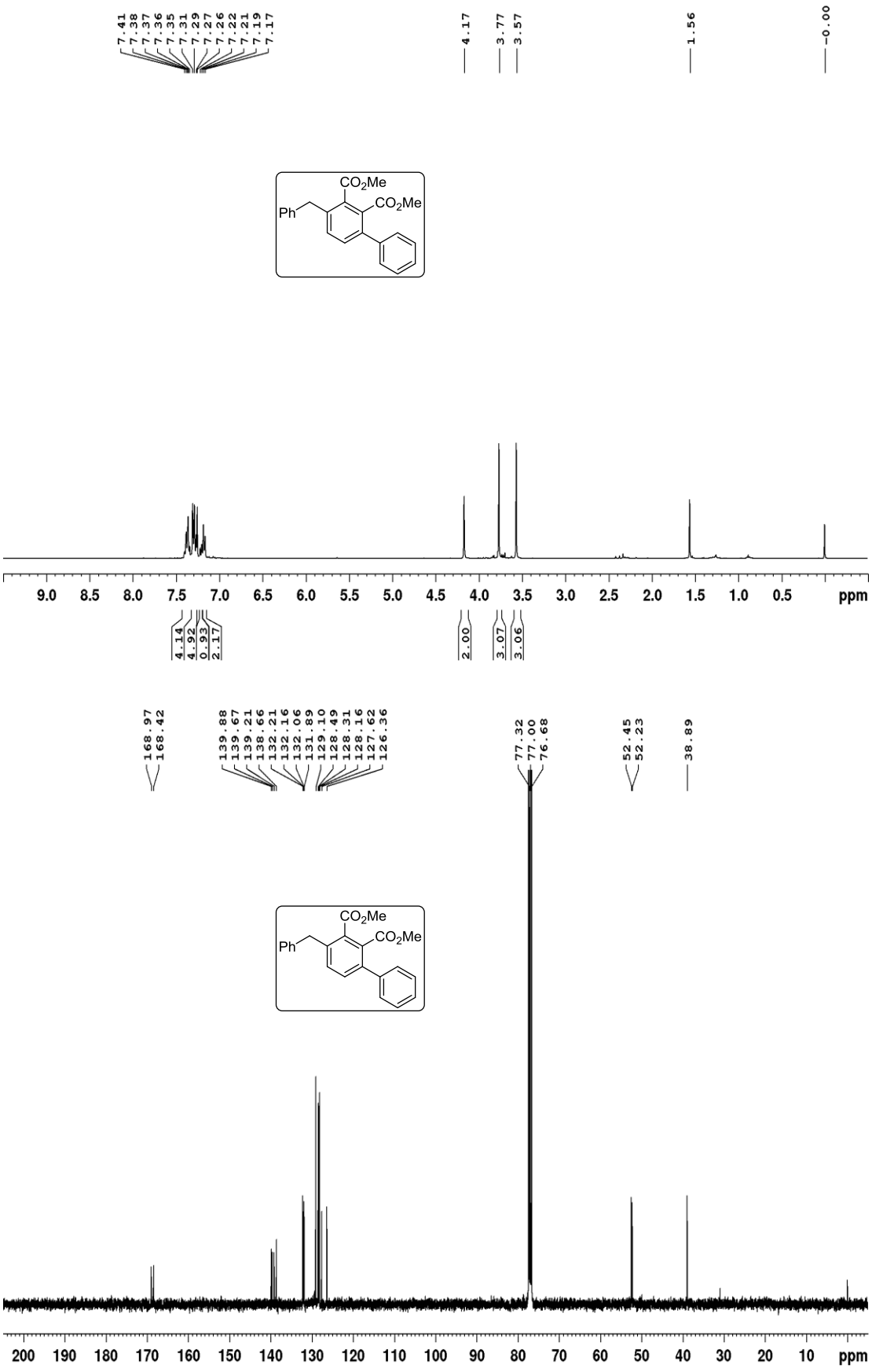
7.86
7.86
7.47
7.46
7.36
7.35
7.33
7.29
7.27
7.26
7.25
6.90
6.88
6.84
6.82
4.10
0.00
S
Ph
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.97
3.02
2.03
3.45
0.98
1.00
2.00
197.3
163.9
140.0
137.9
134.9
131.2
130.6
129.5
129.1
128.7
126.7
125.6
105.2
77.3
77.0
76.7
39.9
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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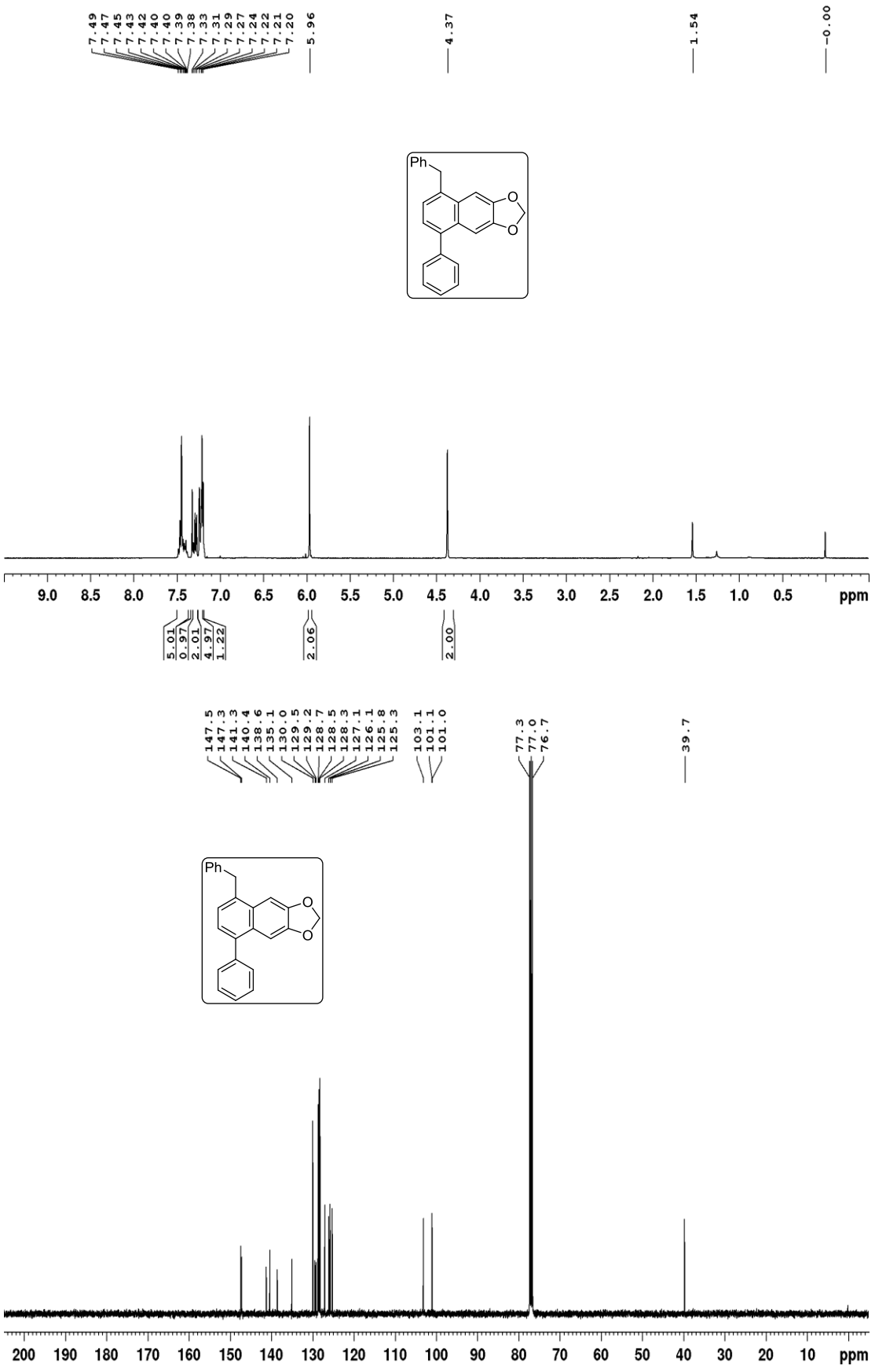
7.38
7.37
7.36
7.35
7.31
7.29
7.27
7.26
7.22
7.21
7.19
7.17
4.17
3.77
3.57
1.56
0.00
CO2Me
CO2Me
Ph
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
4.14
4.92
0.93
2.17
2.00
3.07
3.06
168.97
168.42
139.88
139.67
139.21
138.66
132.21
132.16
132.06
131.89
129.10
128.49
128.31
128.16
127.62
126.36
77.32
77.00
76.68
52.45
52.23
38.89
CO2Me
CO2Me
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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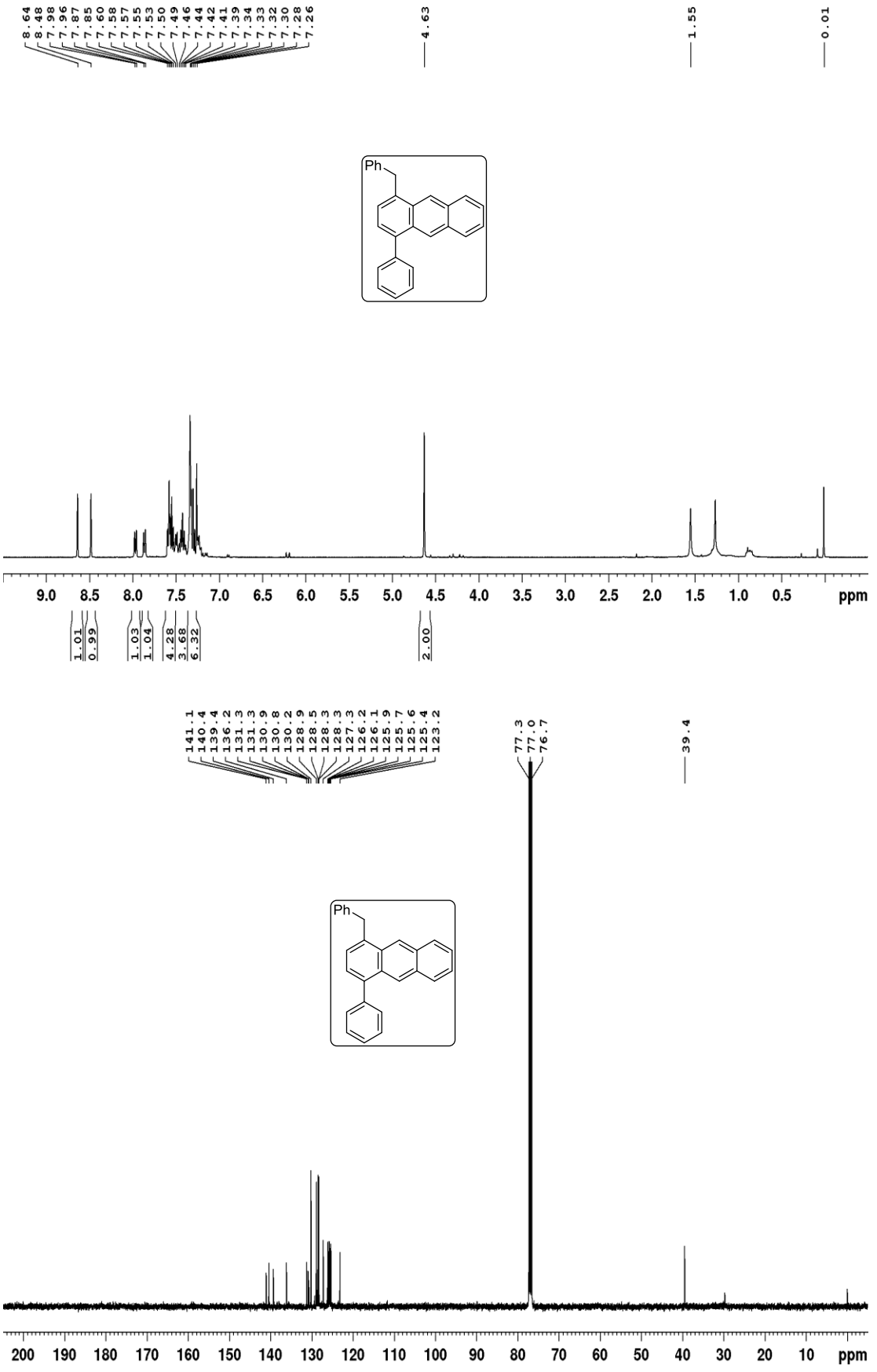
7.47
7.45
7.43
7.42
7.40
7.40
7.39
7.38
7.33
7.31
7.29
7.27
7.24
7.22
7.21
7.20
5.96
4.37
1.54
0.00
Ph
O
O
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
5.01
0.97
2.01
4.97
1.22
2.06
2.00
147.5
147.3
141.3
140.4
138.6
135.1
130.0
129.5
129.2
128.7
128.5
128.3
127.1
126.1
125.8
125.3
103.1
101.1
101.0
77.3
77.0
76.7
39.7
Ph
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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8.48
7.98
7.96
7.87
7.85
7.60
7.58
7.57
7.55
7.53
7.50
7.49
7.46
7.44
7.42
7.41
7.39
7.34
7.33
7.32
7.30
7.28
7.26
4.63
1.55
0.01
Ph
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 ppm
1.01
0.99
1.03
1.04
4.28
3.68
6.32
2.00
141.1
140.4
139.4
136.2
131.3
131.3
130.9
130.8
130.2
128.9
128.5
128.3
128.3
127.3
126.2
126.1
125.9
125.7
125.6
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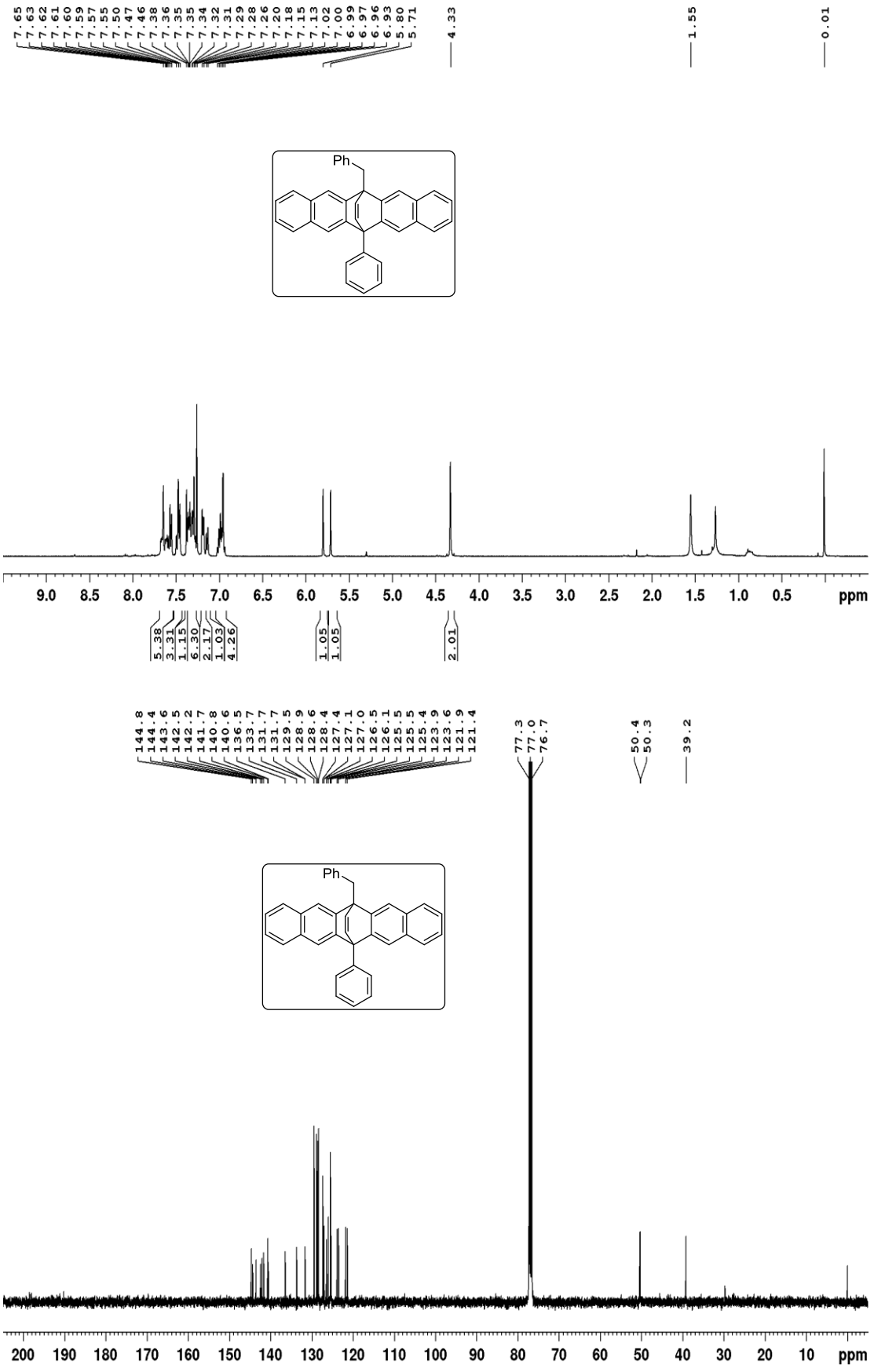
123.2
77.3
77.0
76.7
39.4
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.63
7.62
7.61
7.60
7.59
7.57
7.55
7.50
7.47
7.46
7.38
7.36
7.35
7.35
7.34
7.32
7.31
7.29
7.28
7.26
7.20
7.18
7.15
7.13
7.02
7.00
6.99
6.97
6.96
6.93
5.80
5.71
4.33
1.55
0.01
Ph
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 ppm
5.38
3.31
1.15
6.30
2.17
1.03
4.26
1.05
1.05
2.01
144.8
144.4
143.6
142.5
142.2
141.7
140.8
140.6
136.5
133.7
131.7
131.7
129.5
128.9
128.6
128.4
127.4
127.1
127.0
126.5
126.1
125.5
125.5
125.4
123.9
123.6
121.9
121.4
77.3
77.0
76.7
50.4
50.3
39.2
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm