2008

Thermal rearrangement of 4-aryl-4-hydroxy-2-cyclobuten-1-ones and application of the methodology in the formation of benzofuronaphthoquinones and benzocarbazolequinones

Kimberly Denise Fisher
West Virginia University

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Thermal Rearrangement of 4-Aryl-4-Hydroxy-2-Cyclobuten-1-ones and Application of the Methodology in the Formation of Benzofuronaphthoquinones and Benzocarbazolequinones

Kimberly Denise Fisher

Dissertation submitted to the
Eberly College of Arts and Sciences
at West Virginia University
in partial fulfillment of the requirements
for the degree of

Doctor of Philosophy
in
Chemistry

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2008

ABSTRACT

Thermal Rearrangement of 4-Aryl-4-Hydroxy-2-Cyclobuten-1-ones and Application of the Methodology in the Formation of Benzofuronaphthoquinones and Benzocarbazolequinones

Kimberly Denise Fisher

Cyclobutenediones have proven useful as starting materials for synthesis of highly functionalized biologically relevant molecules. The rearrangement of cyclobutenediones has a wide synthetic scope and can be utilized as a key step in the construction of quinones, benzo[o]isoxazoles, and 3-methylenoxoindoles having a variety of substitution patterns. Construction of these molecules involves thermolysis of 4-hydroxy-2,4-di-aryl-2-cyclobutenones derived from squaric acid ester. In each of the cases the mechanism proceeds through an initial ring opening of the cyclobutene to afford a ketene intermediate that subsequently undergoes a ring closure with various intermolecular nucleophiles. This methodology has been utilized in the construction of an ellipticine model system.

Acknowledgements

I would like to thank my research advisor, Dr. Björn C. G. Söderberg, for guidance and support through my graduate career at West Virginia University. There are many qualities you hold that I hope to possess in my future as a Professor. I would also like to thank the members of my graduate committee, Dr. Robert Griffith, Dr. John Penn, Dr. Jeffery Petersen, Dr. Alan Stolzenberg, and Dr. Kung Wang, for their time and assistance during my graduate studies.

I would like to thank Dr. Novrus Akhmedov for advanced NMR studies and Dr. Jeffrey Petersen for X-ray Crystallographic analysis included in this document.

I would also like to thank my colleagues and friends in the chemistry department whose presence in my life will go far beyond the limits of the time at WVU.

I would also like to thank: Albert “JR” Taylor, Allan Burns, Sherman Adams, Phillip Tucker, Don Feathers, Kevin Dixon, Ezenwa Dike, Mike Torries, Angie Johnson, Ginny Smith, Bob Smith, Brent Reschke, Dottie McCabe, Marianne MacDonald, Ken Enoch, Dr. Harry Finklea, Dr. Michelle Richards-Babb, Dr. George O’Doherty, Dr. Fred King, and Dr. Lisa Holland all of whom had a irreplaceable impact on my success at WVU.

I especially want to thank Mr. Sriganesh Balasubramanian for his constant help and understanding throughout the past months. I am indebted to you for the rest of my life. Thanks Sri!!

I would also like to thank my family for their constant love and support throughout this long road. Without you, there is no me. I love you.

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Commonly Used Acronyms

Ac	Acetyl ($\text{CH}_3\text{C}=\text{O}$)
Boc	<i>t</i> -Butyloxycarbonyl ($\text{C}(\text{O})\text{tC}_4\text{H}_9$)
Bz	Benzoyl
Bn	Benzyl
BRSM	(yield) based upon recovered starting material
CAN	Ceric Ammonium Nitrate
CSA	Camphorsulfonic Acid
DMAP	N,N-4-Dimethylaminopyridine
DMF	N,N-Dimethylformamide
DMSO	Dimethyl Sulfoxide
h	hour(s)
MOM	Methoxymethyl
n-BuLi	n-Butyllithium
Piv	Pivaloyl ($\text{O}(\text{tC}_4\text{H}_9)$)
Py	Pyridine
rt	room temperature
TBAF	Tetrabutylammonium fluoride
TBDMS	<i>t</i> -Butyldimethylsilyl
TBDPS	<i>t</i> -Butyldiphenylsilyl
TBS	<i>t</i> -Butyldimethylsilyl (also TBDMS)
t-BuLi	<i>t</i> -Butyllithium

TFAA	Trifluoroacetic anhydride
THF	Tetrahydrofuran
TMS	Trimethylsilyl
δ	Chemical shift (NMR) in ppm
^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
COSY	Correlation Spectroscopy (NMR)
DEPT	Distortionless Enhancement by Polarization Transfer (NMR)
EI	Electron Impact (MS)
^1H NMR	Hydrogen-1 Nuclear Magnetic Resonance
HETCOR	Heteronuclear Correlation (NMR)
IR	Infrared Spectroscopy
J	Coupling Constant (NMR)
MS	Mass spectrum
NMR	Nuclear Magnetic Resonance
NOE(SY)	Nuclear Overhauser Effect (Spectroscopy)
TLC	Thin Layer Chromatography
UV	Ultraviolet spectroscopy

Part 1

A. Background of Naphthoquinones

Naphthoquinone derivatives are found in a variety of natural products and pharmaceuticals, and belong to an even larger class of compounds known as quinones.¹ The core structure of the quinone family is characterized by a cyclohexadiene ring system with carbonyl functionalities on the 1 and 4 carbons of the ring (Scheme 1). Naphthoquinones are a subset of quinones that have a benzene ring fused to the quinone. In general, naphthoquinones are found in a variety of natural sources including fungi, bacteria, and plants.² Some notable examples of naphthoquinones are lapachol, hybocarpone, the brazanquinones, the vitamins K's, thysanone, and the rhinacanthin (Scheme 2).

Scheme 1 Quinones and Naphthoquinones

[1,4]Benzoquinone

[1,4]Naphthoquinone

Scheme 2 Notable Naphthoquinones

Quinones and naphthoquinones exhibit numerous biological activities.² Commercial and pharmaceutical uses of naphthoquinones includes antipsoriatics, bone metabolism, natural dyes, antipneumococcal, antimalarial, antibacterial, trypanocidal, antitumor, antithrombotic, inhibition of angiogenesis, antimicrobial, vascular biology and regulation of blood coagulation. Much of the biological activity that naphthoquinones exhibit has been attributed to its ability to participate in electron transfer reactions whereby the core quinone structure can accept one or two electrons thus becoming a radical anion or dianion based upon the number of electrons the molecule accepts. A 1,4-naphthoquinone becomes a 1,4-naphthohydroquinone in its reduced

form which is easily oxidized back to the corresponding naphthoquinone (Scheme 3). This ability to accept electrons gives naphthoquinones an extensive ability to participate in a variety of biologically important processes such as photophosphorylation and transport of electrons between various enzymes.²

Scheme 3 Naphthoquinone Redox Forms

B. Formation of Naphthoquinones

Syntheses of naphthoquinones have been carried out through a variety of processes (Scheme 4). Methods of synthesis³ include Stobbe Condensations (**A**), [4+2] cycloadditions (**B**), the addition of a phthalide anion to an α,β -unsaturated ketone or aldehyde using the Hauser-Kraus annulation reaction(**C**), the use of a Fischer aryl carbene complex with an alkyne via the Dötz reaction (**D**), cyclobutendione ring expansions (**E**), and oxidations (**F**). Detailed descriptions of the methods will be discussed in the following sections.

Scheme 4 Variety of Naphthoquinones Syntheses ³

I. The Dötz Reaction

Synthesis of naphthoquinones using the Dötz method implements a metal-alkoxycarbene complex and an alkyne. The synthesis of the metal-alkoxycarbene is achieved by a reaction of aryllithiums with group 6 metal carbonyls such as Cr(CO)₆, Mo(CO)₆, and W(CO)₆ followed by *o*-alkylation to form stable Fischer-type carbenes.⁴ Once the carbene is synthesized it can be

exposed to an alkyne to form the corresponding hydroquinone which can then be readily oxidized to the naphthoquinone (Scheme 5).

Scheme 5 Dötz Methodology

The utilization of the Dötz reaction is widespread because this protocol can accommodate a variety of aryl carbenes and alkynes tolerates a variety of functional groups within each of the starting materials. In addition to benzenes, aryl carbene variations have been derived from other arenes, such as naphthalenes, indoles, furans, pyrroles, and pyrazines and have included ortho, para and meta substitution within many of them.⁴ Alkyne variations have encompassed alkyl, alkylsilyl, boronates, esters, ethers, amides, ketones, aryl, and acetals, among others.⁴ The method has also been performed under various conditions including microwave, UV irradiation, heat, and silica gel promotion to form the hydroquinone. Some notable examples of the Dötz method for syntheses of naphthoquinones are found in the synthesis of shikonin⁵ and the natural product, 2-(1,1-dimethyl-2-propenyl)-3-hydroxy-1,4-naphthalenedione, isolated from *calceolaria andina* L.⁶ In both of the syntheses the reaction is used as a convergent point. Note that a nitro and a ketal group remain unaffected during the Dötz reaction (Scheme 6).

Scheme 6 Dötz Protocol in the Shikonin and *Calceolaria Andina* L Syntheses.

II. The Hauser-Kraus Annulation Reaction

Another method of preparation of naphthoquinones includes the use of the Hauser-Kraus annulation reaction. This method entails the addition of a phthalide anion that is added to an α,β -unsaturated ketone or aldehyde which acts as a Michael acceptor (Scheme 7). The anion created from the Michael addition then attacks the carbonyl of the phthalide forming a third ring. An alkoxide promoted ring opening then occurs with the elimination of the leaving group. Through tautomerization the hydroquinone is formed and aromaticity is gained. Finally, using various oxidation protocols, the naphthoquinone is obtained.

Scheme 7 Hauser-Kraus Annulation Reaction

This method accommodates a variety of functional groups on the phthalides including cyano,⁷ sulfide⁷ and sulfone⁸ (R_1) groups. An interesting use of this method can be seen in the asymmetric synthesis of both alkannin and shikonin⁹ (Scheme 8). This synthesis utilizes LDA as the base to form the cyanophthalide anion. Upon the Michael addition and elimination of cyanide, the hydroquinone core is established.

Scheme 8 Hauser-Kraus Annulation in the Assymetric Synthesis of Alkannin and Shikonin

III Cycloaddition Reaction

Another method of generating naphthoquinones is the use of a [4 + 2] cycloaddition reaction. The most common procedure is the cycloaddition employing quinones as the dienophile reacting with a substituted diene (Scheme 9).¹⁰ However, there are reported syntheses utilizing vinyl quinones as dienes.¹¹ Generally, the quinone dienophile is reacted with the diene to afford a bicyclic α,β -unsaturated diketone. The initial nonaromatic product can be subjected to various oxidation-elimination conditions to afford the corresponding naphthoquinones. Common oxidation-elimination reagents include air,¹² silica gel,¹³ chromium oxide,¹⁴ and manganese oxide.¹⁵

Scheme 9 [4+2] Cycloaddition Reaction Method

When unsymmetrical quinones and dienes are used the regiochemistry has been shown to be directed by electronic effects. However, prediction of the regiochemistry is not possible for all substrates because of its dependence on the diene, dienophile, Lewis acids and solvent.³ In particular the diene can be substituted with an alkoxy,¹⁶ silyoxy,¹⁷ or halogen group¹⁸ as well as vinyl aryl,¹⁹ vinyl furans²⁰ and vinyl pyroles.²¹ In addition to the use of quinones as dienophiles, alternate reaction conditions have included quinones being utilized as a diene¹¹ (Scheme 10) and as well as benzyne²² have been reported as dienophiles (Scheme 11).

Scheme 10 Quinone Diene Method

Scheme 11 Benzyne Dienophile Method

Application of the [4+2] cycloaddition can be seen in a variety of syntheses of biologically important molecules such as the synthesis of crisamicin A.²³ (Scheme 12) This method accommodates a pyran fused lactone quinone dienophile and an activated diene. The lactone was exposed to the diene promoting the cyclization, then the cyclized product was oxidized to provide the naphthoquinone. One key point to recognize is this synthesis was accomplished with a high regioselectivity (>20:1). The author attributes the success of the reaction to the stereoelectronic differentiation that is evident between the two quinone carbonyls as being dictated by the pyran fused lactones moieties.

Scheme 12 Synthesis of Crisamicin A.

IV Stobbe Condensation

This condensation method involves the reaction of succinic acids with benzaldehydes followed by Friedel Craft acylations providing the naphthalene core (Scheme 13). Upon saponification and oxidations, the quinones are obtained. A limitation of the method is that the

E isomer of the obtained from the condensation can only participate in the Friedel-Craft reactions and therefore the double bond geometry is a key to the success of the reaction.³

Scheme 13 Stobbe Condensation

One highlighted example recently reported using of the Stobbe condensation is in the synthesis of ventiloquinone F and isoventiloquinone F (Scheme 14).²⁴ The initial step of the synthesis is a Stobbe condensation between 2,4,5-trimethoxy benzaldehyde and dimethyl succinate under basic conditions to yield a hydronaphthoquinone which is oxidized later in the synthesis to afford the naphthoquinone core of both ventiloquinone F and iosventiloquinone F.

Scheme 14 Synthesis of Ventiloquinone and Isoventiloquinone

V Cyclobutenedione Rearrangements

Cyclobutenediones have been shown to be useful intermediates in quinone syntheses. This method requires the use of a cyclobutenedione which accepts a variety of nucleophiles to form 4-hydroxycyclobutenones (Scheme 15). When the 4-hydroxycyclobutenones are thermolyzed, they afford hydroquinones that can be readily oxidized to form quinones. This method includes numerous variations and is therefore a useful synthetic method for quinones and has been expanded for the synthesis of naphthoquinones.³

Scheme 15 General Thermal Rearrangements of 4 hydroxycyclobutenediones.

When benzocyclobutenediones are employed, three general variations have been shown to provide naphthoquinones (Scheme 16). First, when alkenes are added to benzocyclobutenedione followed by thermal rearrangement and oxidation, they can generate naphthoquinones having substituents on both the quinone and phenyl rings (Scheme 16, A).²⁵ Similarly, when alkyne nucleophiles are added to benzocyclobutenediones they can also form fully substituted naphthoquinones after thermolysis and oxidation (Scheme 16, B).²⁶ A final use of benzocyclobutenediones is the exposure of the cyclobutenedione to low valent metals to generate metallocycles (Scheme 16, C). When the metallocycles are reacted with alkynes, the reaction affords the naphthoquinones directionly and therefore the oxidation step necessary for many naphthoquinone syntheses is eliminated.

Scheme 16 Strategies for Forming Substituted Naphthoquinones from Cyclobutenediones

Cyclobutenediones, as opposed to benzocyclobutenediones, can be used to form naphthoquinones when aryl groups are added to them (Scheme 17).²⁵ Variations in this system can come from substituents on the aryl group or on the cyclobutendione.

Scheme 17 General Aryl Addition-Rearrangement

The mechanisms for all thermal rearrangement of 4-hydroxycyclobutenediones begin with a retro [2+2] electrocyclic cleavage to form ketene intermediates (Scheme 18). When alkenes and aryl groups are introduced, then retro [2+2] cycloaddition takes place, followed by an

electrocyclic ring closure. This intermediate then tautomerizes to form the hydroquinone.

During the final step the hydroquinone is oxidized, either by the addition of oxidative reagents or by simple exposure to air, to form naphthoquinones.

Scheme 18 Alkene Rearrangement Mechanism

In the case of alkynyl substituted cyclobutenones, the mechanism is slightly different. After a retro [2+2] cycloaddition, the reaction products can be explained through a zwitterion or radical intermediate (Scheme 19). In the zwitterion case a, the lone pair of electrons on oxygen promote a ring closure forming the zwitterion. Upon migration of the alkoxide group, the synthesis affords the naphthoquinone without oxidation.

Scheme 19 Alkyne Rearrangement Mechanism

An example of the use of a benzocyclobutenedione can be found in a report by Moore for the synthesis of deoxyfrenlicin (Scheme 20).²⁶ In the synthesis an alkyne nucleophile was added to 3-methoxybenzocyclobutene-1,2-dione and then was subjected to thermal rearrangement conditions. After the construction of a cyclic ether and a lactone they afford, deoxyfrenolicin was obtained.

Scheme 20 Deoxyfrenolicin Synthesis

The final example of the utility of benzocyclobutenedione in naphthoquinone synthesis involves the formation of a metallocycles. Benzocyclobutenedione is exposed to low valent metal complexes where the metal inserts between both carbonyls of benzocyclobutenediones²⁷ (Scheme 21). Alkynes can insert into the benzometallocycles and then the metal can reductively eliminate to form naphthoquinones without oxidation.

Scheme 21 Benzometallocycle Methodology

Use of the method can be found in Liebeskind's synthesis of nanomycin A (Scheme 22).²⁸ An alkyne nucleophile is added to 3-hydroxybenzocyclobutene-1,2-dione. The cobalt metallocycle is constructed and then employed for the synthesis of the naphthoquinone core.

Scheme 22 Nanaomycin A Synthesis

Part 2 Results and Discussion

Chapter 1 Ortho-Lithiation Directed Addition-Thermoylsis.

With the intention of exploring thermally induced benzannulations of aminoaryl substituted cyclobutenones, the addition of substituted anilines to substituted cyclobutenediones were initially examined (Scheme 23).

Scheme 23 Proposed Synthesis of Aminonaphthoquinones

Experimentation began with the focus on the dianion addition of carbamate aniline **4** to diisopropyl squarate. This protocol was used to allow the carbamate to direct the ortho-lithiation with the carbamates intention of creating the ortho-substituted Boc-aniline **5**. Therefore, aniline was protected using di-tert-butyl dicarbonate and potassium carbonate in THF:H₂O (Scheme 24).²⁹ With the protected aniline **4** now available, an ortho-lithiation protocol was used with 6 equivalents of t-BuLi at -78 °C for 4 h then adding diisopropyl squarate. It is unknown why the reaction needed 6 equivalents of base but it was found to be in agreement with a literature report³⁰ using excess t-BuLi to optimize ortho-lithiations of **4**. With 6 equivalents, the reaction proceeded to afford the addition product **5** in a 73% yield, however, N-(tert-butyloxycarbonyl)-aniline was usually recovered. It was also determined that the reaction was most effective when the reaction was quenched with 10% NH₄Cl in H₂O. This thermolysis precursor was now ready for cyclization and was heated in xylenes at 170 °C. The

reaction proceeded to completion in 3 h as monitored by TLC and was found to have created the naphthoquinone **6** in 81% yield.

Scheme 24 Carbamate Protected Aniline Addition-Thermolysis

Given the early success of the methodology, it was envisioned that various aniline derivatives could be prepared in an analogous manner. The first compounds that were studied were the methoxy substituted N-(tert-butyloxycarbonyl) anilines. The ortho, meta, and para anisidines were protected as described for compound **4**, a reaction that proceeded in high yields affording the corresponding protected derivatives **7**, **8**, and **9** in 98, 94 and 92% respectively (Scheme 25).²⁹

Scheme 25 Aminoanisidine Carbamate Protection

The focus then turned to the ortho-lithiation-additions to diisopropylsquarate. The protected aminoanisidines **7**, **8**, and **9**, were subjected to t-BuLi at cold temperatures and then diisopropyl squarate was added (Table 1). Subjecting the anisidine derivatives to the addition reactions was not as straightforward as in the initial study. It was discovered that the methoxy group competed with the carbamate as the ortho directing group. In each of the reactions, addition of squarate was observed adjacent to the carbamate, but it was also observed ortho to the methoxy group. In the case of the meta-anisidine derivative, a third product was also observed with the third product **14** being directed by both the carbamate and the methoxy group. In addition to the mixture of products, starting material was recovered in all cases.

Table 1 Boc-Aminoanisidine Additions

With a variety of hydroxycyclobutenones available, **10**, **11**, **12**, and **15** were subjected to standard thermoylsis conditions at temperatures between 170 °C and 180 °C in xylenes (Table

2), a manner analogous to the initial system (Scheme 24). This set of reactions also did not mimic the success of the original system. The yields were within the 21% to 30% range as compared to 81% obtained in the original system. It is unknown why the reactions did not mimic the original success.

Table 2 Boc-Aminoanisidine Thermolysis

starting materials	$\xrightarrow[\text{170 } ^\circ\text{C to 180 } ^\circ\text{C}]{\text{xylene}}$	products
<p>10</p>		<p>17 (27%, 33% BRSM)</p>
<p>11</p>		<p>18 (33%)</p>
<p>12</p>		<p>19 (21%, 26% BRSM)</p>
<p>15</p>		<p>20 (24%)</p>

Amino substituted pyridines were examined in an attempt to explore more electron rich molecules and potentially expand the library of compounds. Carbamate protection of 2-, 3-, and 4-amino pyridines was accomplished by a protocol reported by Lowary where the aminopyridines were exposed to di-tert-butyl dicarbonate in tert-butyl alcohol (Scheme 26).³¹ Each of the protections worked as expected to afford the corresponding amino-protected compounds **21**, **22**, and **23** in 98, 93, and 91% yields, respectively.

Scheme 26 Carbamate Aminopyridine Protection

It was envisioned that using a similar method to the original ortho-lithiation protocols, the protected amino pyridines could afford compounds analogous to the previously described substrates (Table 3). While this was the case, **24**, **25**, and **26** were synthesized but the compounds were very unstable. Purification was a challenge because of streaking on column chromatography and TLC, even with the exploration of alumina to eliminate acid-base interactions. In addition to complications during purification, the compounds were not stable upon storage.

Table 3 Boc-Amino Pyridine Additions

starting materials	1 3-4 eq <i>t</i> -BuLi, THF, -78 °C to -10 °C; 2 Diisopropyl squarate, THF	products
<p>21</p>		<p>24 (31%, 48% BRSM)</p>
<p>22</p>		<p>25 (26%, 30% BRSM)</p>
<p>23</p>		<p>26 (30%, 36% BRSM)</p>

With evidence of the intermediate alcohols **24-26** by ^1H NMR spectroscopy of the crude product and having isolated of small amounts of the compounds **24-26** it was known that some addition to diisopropylsquarate was occurring. With this knowledge and the poor stability of the products, it was decided that the hydroxycyclobutendones should be subjected to thermal rearrangement conditions as crude mixtures. The 4-amino-substituted anisidine **9** and 4-amino-substituted pyridine **23** were thermolyzed without purification of the intermediate addition products (Table 4). The para substituted derivatives were selected because regardless of the ortho-lithiation director, carbamate or methoxy, the reactions would afford the same

naphthoquinone products **20** and **27**. The sequence proved to be a possible method for synthesis of the desired compounds. However, because of the low yields, it seemed not to be the most efficient method for the synthesis of the amino substituted naphthoquinones.

Table 4 One Pot Thermolysis Sequence

starting material	1 3-4eq <i>t</i> -BuLi, THF, -78 °C to -10 °C 2 Diisopropyl squarate in THF 3 120 °C in Toluene	products
9		20 (20% two steps BRSM)
23		27 (31% two steps BRSM)

With questions of the carbamate protecting group's directing ability during the ortho-lithiation, it seemed necessary to explore other amine protecting groups. The amino pyridines were protected with a pivaloyl group by a reported method³² where amino pyridines in methylene chloride were exposed to pivaloyl chloride in the presence of triethylamine. The pivaloyl protected amino pyridines were reacted with *t*-BuLi followed by the addition of diisopropyl squarate (Table 5). The reactions yielded the desired compounds **31**, **32**, and **33** and they were subjected to thermolysis. Unfortunately the naphthoquinones were not observed aside from the trace amounts of naphthoquinone **34**.

Table 5 Pivaloyl-Protected Aminopyridine Additions

With an apparent need to return to a less functionalized system, aniline was then protected with a pivaloyl group. It was thought that using the parent aniline derivative would allowed a better understanding of the effectiveness of the ortho-lithiation and thermolysis conditions. After standard protections,³³ aryl amide **35** was subjected to the ortho-lithiation conditions then reacted with diisopropylsquarate to afford the hydroxycyclobutenone **36** in 45%, 67% BRSM (Scheme 27). Compound **36** underwent thermolysis in the presence of proton sponge.³⁴ Proton sponge has been reportedly used to eliminate acid catalyzed reactions.³⁴ The reaction

gave a 40% yield of the desired naphthoquinone **37** when performed at 120 °C. Notably, when the reaction was performed at 170 °C one of the isopropyl groups was lost during the reaction. Naphthoquinone alcohol **38** was elucidated via x-ray crystallography to determine which isopropyl group was removed and to ensure that the proposed structure was correct (Figure 1). At the time of this report, the reason for selectivity has not been determined.

Scheme 27 Pivaloyl Protect Aniline Addition Thermolysis

Figure 1 X-Ray Crystal Structure of 37

As an extension of the addition-thermal rearrangement methodology, functional groups other than protected amines were explored. The first idea came from a report where Knochel used phenylmagnesium chloride as a reagent for iodine magnesium exchanges (Scheme 28).³⁵ In addition to the ease of halogen exchange, that the paper reports the incorporation of a variety of functional groups attached to the nitrobenzenes by the addition of the appropriate electrophile.

Scheme 28 Nitrobenzene Halogen Exchange Protocol¹⁷

2-Iodo-nitrobenzene was subject to the Knochel protocol of iodine-magnesium exchange at $-40\text{ }^{\circ}\text{C}$ for 5 to 10 min, then diisopropyl squarate in THF was added via a cannula (Scheme 29). The method proved to be successful and the desired addition product **39** was obtained in 72% yield. Compound **39** was heated at $160\text{ }^{\circ}\text{C}$ in xylenes and the reaction went to completion in 1

h. Upon full characterization, the molecule was found to be the hydroxyquinonlinone **40** in 65% yield.

Scheme 29 NitroBenzene Addition-Thermolysis

The proposed mechanism for the synthesis of the hydroxyquinolinone **40**, begins with a retro [2+2] cycloaddition, similar to those in the previously reported mechanisms, to form the intermediate **42** (Scheme 30). From there, the nitro group attacks the newly formed ketene **42** to give the cyclized intermediate **43**. Ring opening produce resonance structure **44** and **45**. A second ring closure is accomplished via a nitroso attack an the carbocation to form the cyclized intermediate **46**. Decarboxylation followed by deprotonation-protonation would provide the isolated product **49**.

Scheme 30 Nitrobenzene Proposed Mechanism

To expand the scope of the halogen metal exchange protocols and to study thermolysis reactions of functional groups without nitrogens, 1,2-bromoiodobenzene was reacted with *n*-BuLi, then diisopropyl squarate was added to form **49** (Scheme 31).³⁶ It was then heated at 135 °C to afford **50**. Initial attempts of this reaction seemed to give mixtures of the quinone and hydroquinone derivative of **50**. Therefore the crude mixture following thermolysis was exposed to silver oxide to ensure the formation of the naphthoquinone **50**. This method proved to be successful giving naphthoquinone **50** in 70% yield. Additionally this sequence affords a

compound **50** that has highly versatile for a variety of metal-catalyzed coupling reactions to provide more complex naphthoquinones.

Scheme 31 BromoBenzene Addition-Thermolysis Method

Conclusion

Nucleophiles were successfully made through ortho-lithiation and lithium halogen exchange, were added to with diisopropyl squarate to afford a variety of 4-hydroxy-4-arylcyclobutenones. With respect to ortho-lithiations, the director, carbamate and methoxy, have been shown to compete for the addition site. A general route to a group of substituted-1,4-naphthoquinones has been developed with the best results coming from the Bromoaryl derivative. The quinones were prepared by thermolysis followed by oxidation of 4-hydroxy-4-aryl-substituted cyclobutenones to afford a variety of substituted naphthoquinones with varying success.

Chapter 2 Unsymmetrical Cyclobutendione Reactions.

It was reported in the literature by Moore³⁴ that rearrangements of hydroxycyclobutenones could be forced by employing TFAA in pyridine (Scheme 32) forming unsymmetrical cyclobutendiones like **53**. A paper by Liebeskind³⁷ reports that various nucleophiles can be added to unsymmetrical cyclobutendiones, like **53** and this can be accomplished with high regioselectivity (Scheme 33). The regioselectivity observed throughout the additions has been attributed to an electron deficiency of one the carbonyl carbons compared to the other. The electrons of methoxy group in **54** can be donated to one of the carbonyls and not to the other. Therefore one of the carbonyls becomes more electrophilic than the other. Lastly the Liebeskind report provides numerous examples of thermal rearrangement reactions that include aryl groups similar to **56**.

Scheme 32 Moore TFAA Rearrangement³⁴

Scheme 33 Liebeskind Aryl Addition-Thermolysis Protocol³⁷

As an extension of the previous studies, attention was focused on the use of unsymmetrical cyclobutendiones to obtaining aryl substituted naphthoquinones. Specifically, with combining

aspects of both the Moore's TFAA rearrangements³⁴ and Liebeskind regioselective addition-thermolysis protocols,³⁶ it should be possible to build molecules with a tetracyclic core structures (Scheme 34). A common intermediate **57** in the synthesis of the anti-cancer drug ellipticine contains a tetracyclic indoloquinone core.³⁸ It was envisioned that a model system of the core, with a phenyl ring instead of a pyridine ring, could be constructed through the aminoquinone intermediate **59** previously reported to readily cyclize to the indole **58**.³⁹ Therefore, if aryl substituted cyclobutenones such as **60** could be constructed utilizing the methods of Moore and Liebeskind (Scheme 32 and 33) and subjected to thermal rearrangement conditions then the core **58**, similar to that of ellipticine, could be synthesized in a limited number of steps.

Scheme 34 Ellipticine Model System

With the intermediate **60** as a target, the dianion addition reaction products **5** and **36** were revisited. Hydroxy cyclobutendones **5** and **36** were subjected to TFAA to form the desired

unsymmetrical cyclobutendiones **61** and **62** in 75 and 76% yields, respectively (Scheme 35).

Next they were reacted with PhLi to afford **63** and **64** in 89% and 82% yields. With the thermal rearrangement precursors available, temperatures and time of heating were varied to study their effect on the reactions. However, with both substrates **63** and **63** all reactions produced mixtures of unknown compounds that were very difficult to separate.

Scheme 35 Thermal Rearrangement of 63 and 64

The alcohol moiety was initially thought to be responsible for the unwanted reactions and therefore, the alcohol moieties of **63** and **64**, were protected as TMS ethers (Scheme 36). The N-pivaloyl substrate **64** was protected with TMSCl under basic conditions to afford **65** in 66% yield.⁴⁰ The carbamate **66** was synthesized by trapping, *in situ*, the alkoxide formed by the addition of PhLi to **61** by addition of TMSCl.⁴¹

Scheme 36 Synthesis of 65 and 66

The next step was to subject the silyl ethers to thermal rearrangements (Scheme 37). There was substantial evidence as seen by crude the ^1H NMR spectrum that both experiments had yielded a major product with small amounts of others in the mixture. While not the desired products, the structure of the major products **67** and **68** were elucidated by numerous NMR experiments. It should be noted that if thermolysis was attempted in temperatures lower than the $160\text{ }^\circ\text{C}$, the starting materials were recovered.

Scheme 37 Synthesis of 67 and 68

Mechanistic explanation of the result comes from an initial retro [2+2] cycloaddition forming the ketene intermediate **70** (Scheme 38). It is likely that addition of the nitrogen to the ketene promoted a cyclization forming intermediate **71**. Upon proton transfer and tautomerization the reaction could provide the oxindole **73**.

Scheme 38 Proposed Mechanism of 67 and 68

Upon full characterization of **67** and **68**, the reaction products from the thermal rearrangement of **64** were reinvestigated and determined to be derivative of the same oxindole core structure as seen in **67** and **68** (Scheme 39). For the structure **75**, key signals in the ^1H NMR spectrum at δ 4.1 (dd, $J = 7.7$ and 3.0 Hz), δ 3.8 (dd, $J = 18.3$ and 3.4 , 1H), and δ 3.5 (dd, $J = 18.3$ and 7.7 Hz, 1H) indicating the three diastereotopic geminal protons within the molecules were found. Similar signals were found for **74** and it was therefore elucidated based upon the finding in **75**.

Scheme 39 Reinvestigation of Thermal Rearrangement of **64** Products

In an attempt to alter the reaction pathway of the thermolysis, addition of an electron rich anisole to aryl substituted cyclobutenediones became a target. Therefore hydroxycyclobutenone **77** was synthesized from the addition of 4-anisylmagnesium bromide to **62** (Scheme 40). The reaction proceeded well in 74% yield. The substrate was then exposed to heat. After identifying the major product as **78**, compound **77** was found to undergo the reaction similarly to the previous examples. While the conditions did not promote the synthesis of naphthoquinones, the presence of an electron rich aromatic group did effect the synthesis of alkylidene oxindoles as observed from the 56% yield. In this sequence the nitrogen protecting group was also lost during the thermolysis reaction of **77** to **78**.

Scheme 40 Synthesis of 78

With the realization that carbamate and amide protected amines actively participate in alternate side reactions with the ketene intermediates, introduction of the amine group later in the synthesis seemed vital to the progress of the project. Estevez³⁹ published a report where the nitrophenylnaphthoquinone **79** was reduced with sodium borohydride to form aminonaphthoquinone intermediate **59** that readily cyclized to form the indolonaphthoquinones **58** (Scheme 41).

Scheme 41 Revised Methodology to 58

With a nitro substituted target core in mind, the synthesis of **79** began with iodonitrobenzene. Formation of the intermediate alcohol **59** was accomplished easily with the formation of the nitroarylmagnesium chloride reported by Knochel.³⁵ Similar to the report, 2-

iodonitrobenzene was subjected to PhMgCl at -40 °C . Then diisopropyl squarate was added to afford **80** in 72% yield (Scheme 42). The next step was attempted with and without further purification of the intermediate hydroxycyclobutenone **80** before treating it with TFAA. The rearrangement readily provided the desired cyclobutendione **81** in 95% yield or 68% (2 steps from iodonitrobenzene) for the unpurified sequence.

Scheme 42 Synthesis of **81**

With the desired nitrosubstituted cyclobutendione in hand, a reaction protocol for the addition of phenyl nucleophiles as well as thermolysis was explored. Phenylmagnesium chloride proved to be a good source for an aromatic nucleophile whereby it was added to the nitroaryl cyclobutendione **81** to give the desired hydroxycyclobutenone **82** (Scheme 43) as seen by crude ¹H NMR spectrum. However, all attempts to purify the compound resulted in unwanted reactions on silica gel. Therefore crude **82** was thermolysized without purification. It was determined that the reaction did not proceed as expected. It should be noted that the reaction was also attempted in the presence of proton sponge and the results were unchanged. Instead of performing the desired cyclization to the naphthoquinone, the reaction yielded a mixture of compounds that could not be characterized.

Scheme 43 Thermal Rearrangement of **82**

In an attempt to remove the possibility of unwanted reactions of the alcohol in hydroxycyclobutenone **82**, the aryl addition sequence was repeated, but the alcohol was trapped as the acetyl ester **84** using acetic anhydride (Scheme 44). The crude acetyl ester **84** was subjected to thermolysis and the reaction gave one product. Correlation NMR experiments of **85** were performed and the structure was elucidated to be the benzisoxazole **85**.

Scheme 44 Thermal Rearrangement of **84**

A mechanistic explanation of the reaction is proposed as proceeding via an initial retro [2+2] cycloaddition to form the ketene intermediate **86** (Scheme 45). Nucleophilic addition of one of the nitro oxygens to the ketene would induce a ring closure to form the intermediate **87**. After a ring opening of **87**, resonance forms **88** and **89** can form. Then a second ring closure by nucleophilic attack of the nitroso group forms intermediate **90**. Finally, decarboxylation forms the benzisoxazole **85**.

Scheme 45 Proposed Mechanism to 50

With some questions unanswered about the thermal rearrangements, it seemed interesting to perform the sequence with hydroxyl- and methoxy-substituted derivatives. 2-Bromophenol and 2-bromoanisole were subjected to lithium-halogen exchange⁴² followed by addition to diisopropyl squarate (Scheme 46). In the case of the hydroxy derivative, the expected product **91** was not observed. Instead, **92** was observed as the major product. A mechanistic reason for this product is currently unknown but it was assumed that the additional isopropoxy group might have been added from an additional molecule of diisopropylsquarate. In addition to the side product formed during the addition to squarate the compounds were very difficult to visualize on TLC, even with the aid of a variety of stains. In the 2-bromoanisole sequence the

reaction proceeded as expected to afford **94** in 79% yield. It is noteworthy that only a small amount of the isopropyl addition was observed product **95**.

Scheme 46 Methoxy and Hydroxy Derivatives

Because of the issues associated with the phenol sequence, formation of the desired **93** was performed as a one pot sequence starting from 2-bromophenol (Scheme 47). 2-Bromophenol was transmetallated and added to squarate followed by TFAA rearrangement to afford **93** in 48% yield over the three steps. With the anisole derivative **94** available, it reacted with TFAA to form **96** in 79% yield.

Scheme 47 Synthesis of **93** and **96**

After obtaining **93** and **96**, they were exposed to PhLi (Scheme 48). Each of the reactions proceeded well, obtaining the desired compounds **97** and **99** in 66% and 64% respectively. Then they were subjected to thermal rearrangements at 150 °C in xylenes. The phenol derivative **97** produced an unknown mixture of compounds, but the anisole derivative **99** afforded the desired naphthoquinone **100** with a high yield of 78%. It is again suspected that the hydroxy group on **99** participated in unwanted reactions and therefore thermal rearrangement of **99** is not a reliable method of synthesis of hydroxyaryl naphthoquinones. Thermal rearrangement of the methoxy derivative **99** proceeded very successfully in 78% yield. It is to be noted that if the free hydroxyl compound became a target molecule compound **100** could be easily converted to **98** if the through demethylation condtions with BBr₃.

Scheme 48 Synthesis of 100

Conclusion

From this set of experiments it can be concluded that with the functional groups on the aryl substituents of these unsymmetrical cyclobutendiones participate actively in the reaction forming various products most of which are not naphthoquinones. With that in mind, formation of naphthoquinones by this method can only be executed with non-nucleophilic substituted aryl groups. Conversely this method is effective at the synthesis of oxindoles and benzisoxazoles and further development of the method for their synthesis is an area for experimentation.

Chapter 3. Alternate Sequence the Benzocarbazolequinone Core.

After learning how susceptible the ketene intermediate during thermal rearrangements is susceptible to nucleophilic attack, a plan to introduce the nitrogen into the system after the thermolysis step was necessary. The focus shifted to a final cyclization of the tetracyclic ring system through an N-arylation coupling methods (Scheme 49). With numerous protocols for the aminations of arylhalides with amines utilizing both palladium and copper catalysts available, it was envisioned that the amine and aryl halide of **101** could be coupled to form the indolonaphthoquinone **58**. It was also proposed that the amine could be derived late in the synthesis from the amination of an ether intermediate similar to **102**.

Scheme 49 Alternate Route to 58

The execution of the method began with a reported metal-halogen exchange protocol³⁶ using 1,2-dibromo benzene and n-BuLi at -110 °C (Scheme 50). The paper reports that with a constant temperature of -110 °C, the reaction forms the lithium bromide exchange intermediate **103**. However, heating the reaction to -90 °C gives decomposition products derived from benzyne formation.

Scheme 50 Lithium Halogen Exchange of 1,2-Dibromobenzene

With the intention of using the reported method to add an aryl halide to squarate, iodobromobenzene was reacted with n-BuLi in the cosolvent system of THF-Et₂O at -110 °C (Scheme 51, Method A). After stirring for 30 min, diisopropylsquarate in THF was added and stirred for 5 h to give **49** in 88% yield. An alternate method was employed for the synthesis of the halogen metal exchange using diisopropyl magnesium. In this method, diisopropyl magnesium was prepared *in situ* by dissolving isopropyl magnesium chloride in dioxane.⁴³ From there the iodobromobenzene was subjected to the freshly prepared diisopropyl magnesium at reduced temperatures of -40 °C, then exposed to diisopropyl squarate to provide **49** in 47% (Scheme 51, Method B). From the comparison of the two reports it is easy to note that while method A gave a better yield, however, it is very sensitive in comparison to method B. When there was slight increase in temperatures, method A provided little to no **49**. Therefore method B is a viable method when -110 °C cannot be ensured since it is more robust. From there **49** was treated with the TFAA to afford the bromoarylcyclobutendione **104** in 99% yields.

Scheme 51 Synthesis of **104**

Phenylmagnesium chloride was added to **104** to afford **105** in 82% yield (Scheme 52).

Hydroxycyclobutenone **105** was then heated in toluene at 125 °C for 30 min. To much delight, the reaction afforded the desired naphthoquinone **106** in 98% yield.

Scheme 52 Synthesis of **106**

With two steps of the proposed methodology left to complete the synthesis of the indolonaphoquinone core, attention was turned to the amination of **106**. In 2005 it was reported⁴⁴ that nucleophilic displacement of 2-methoxylapachol **107** with 30% ammonium hydroxide solution yielded the amino derivative **108** in 45% yield (Scheme 53).

Scheme 53 Amination of 2-Methoxylapachol.

From this work it was envisioned that the isopropyl group of **106** could be replaced with an amine group in a similar manner. Therefore, the naphthoquinone **106** was exposed to 30% ammonium hydroxide in MeOH to afford the desired amino derivative **109** in 61% yield (Scheme 54). The compound's solubility proved to be a challenge but best results came from the reactions with a minimum amount of methanol.

Scheme 54 Synthesis of **109**

With only the final ring closure left in the synthesis of the indolonaphthoquinone core, protocols for N-arylation were explored. Many aromatic coupling have been reported and a variety of protocols are available. The work of Buchwald was initially chosen which reports in the literature of Pd/BINAP catalyzed aminations of aryl halides (Scheme 55).⁴⁵ The report cites various substrates reacting at reaction times between 16-20 h to afford a variety of aminated products with a variety of substituents in high yield. Because of the flexibility and the extensive versatility of the method it was chosen as a first attempt. However in two trials at temperature

of 90 °C and 120 °C, the reaction returned starting material as was seen in the crude ^1H NMR spectrum and thus the method was abandoned (Table 6).

Scheme 55 Standard Buchwald Amination Conditions

The next method selected was from a paper that reported a highly efficient palladacycle precatalyst that is air, moisture, and thermally stable (Scheme 56).⁴⁶ The report also establishes the use of the catalyst with a variety of aryl chlorides and amines to afford the coupled products. However, this method was unsuccessful on the precursor **109** because when it was exposed to the report reaction conditions, it also resulted in recovery of only starting material (Table 6).

Scheme 56 Expansion of Buchwald's Methodology

With the previous two failures, palladium catalyzed reactions were abandoned. With copper also a possible catalyst, a report was selected where aryl halides and amines were exposed to CuI, K_2CO_3 , and pipercolinic acid, in DMF (Scheme 57).⁴⁷ When compound **109** was

reacted under these copper catalyzed conditions, the reaction afforded the naphthoquinone **110** in a 59% yield (Table 6).

Scheme 57 Copper Catalyzed N-Arylation

Table 6 Trials for the Synthesis of **110**

Conditions	Yield
2 mol % <i>rac</i> -BINAP, 2 mol % Pd ₂ (dba) ₃ , NaOtBu, toluene, 90 °C	starting material
4 mol % <i>rac</i> -BINAP, 3 mol % Pd ₂ (dba) ₃ , NaOtBu, toluene, 120 °C	starting material
 NaOtBu, toluene 100 °C 2 mol %	trace amount
 CuI, K ₂ CO ₃ , DMF	59 %

With a successful protocol for the formation of the indolonaphthoquinone core, expansion of the method to include other functionalities became increasingly interesting. The next nucleophile added to the bromoaryl cyclobutendione **104** was 4-anisylmagnesium bromide (Scheme 58). The addition proceeded well giving **111** in 81% yield. The formed hydroxycyclobutenone was exposed to the thermal rearrangement conditions and the reaction proceeded to completion within 2 h. The naphthoquinone **112** was then subjected to nucleophilic displacement conditions to afford the amine **113** in 58% yield. It should be noted that the solubility issues from the model system continued to be problematic, but the use of a limited amount of methanol and longer reaction times seemed to be most effective. With the indole ring closure as the sole remaining step, amine **113** was subject to the same copper-catalyzed N-arylation as previously reported to produce the desired methoxy derivative **114** in 50% yield.

Scheme 58 Synthesis of **114**

With success in two systems, increased sterics during the thermal rearrangement became another area to vary in the system. Therefore 2-methoxyphenylmagnesium bromide was added to the bromoaryl cyclobutendione **104** (Scheme 59). The reaction sequence proceeded in a similar manner as that of the previously reported substrate **105** with the exception of the thermal rearrangement reaction which provided the desired **116** in 63% yield. Perhaps the added sterics impacted the outcome of the cyclization. Overall the sequence of reactions again afforded the desired **118** in limited number of steps.

Scheme 59 Synthesis of 118

For a final example of the use of the method that has been developed, the cyclization to a furan ring instead of the reported indole ring was explored. It was reported in the literature⁴⁸ that **119** can be coupled under Ullmann coupling conditions to afford the benzo[b]naphtha[2,3-d] furan-6,11-dione **120** (Scheme 60).

Scheme 60 Reported Furan Coupling Reaction

Also reported in the literature is the demethylation of **121** in the presence of BBr_3 at cold temperatures (Scheme 61).⁴⁹ The reaction proceeded to form the naphthazarin **122** in quantitative yield.

Scheme 61 Demethylation Conditions

Compound **106** was synthesized as previously reported, then demethylation conditions were applied to **106** where it was reacted with BBr_3 to applied to **106** it afforded the alcohol **119** in a quantitative yield. From this experiment it is concluded that the established methodology can be applied as a new method of synthesis of benzo[b]naphtha[2,3-d] furan-6,11-diones in addition to the method to form benzocarbazolequinones. Another impressive point about the synthesis of **119**, is that the method presented accomplishes the synthesis in 5 steps in contrast to the reported synthesis in 7 steps.

Scheme 62 Synthesis of 119

Conclusion

A new methodology for the synthesis of benzocarbazolequinones and benzofurannaphthoquinones has been developed. The synthesis is accomplished in six steps, some of which can proceed without purification of the crude intermediates. Variations of functional groups on the naphthoquinone rings should be explored for further versatility. It is also noteworthy that the method is projected to be adapted to form carbazolquinones when alkyne nucleophiles are implemented instead of aryl nucleophiles.

Part 3

Experimental Section

1. General Procedures

All NMR spectra were determined in CDCl_3 at 270 MHz (^1H NMR) and 67.5 MHz (^{13}C NMR) or at 600 MHz (^1H NMR) and 150 MHz (^{13}C NMR), respectively. The chemical shifts are expressed in δ values relative to $(\text{Me})_4\text{Si}$ (0.00 ppm, ^1H and ^{13}C) or CDCl_3 (77.0 ppm, ^{13}C) internal standards. ^1H - ^1H coupling constants are reported as measured from spectra; thus a slight difference between $J_{a,b}$ and $J_{b,a}$ is usually obtained. Results of Attached Proton Test- ^{13}C NMR experiments are shown in parenthesis where, relative to the CDCl_3 , (-) denotes CH_3 or CH and (+) denotes CH_2 or C . Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl prior to use. Ether, toluene, and triethyl amine were passed through a steel column filled with activated alumina (8 X 14 mesh, Sorbent Technology) using argon pressure. Hexanes, xylenes, toluene and ethyl acetate were distilled from calcium hydride. Chemicals prepared according to literature procedures have been footnoted first time used; all other reagents were obtained from commercial sources and used as received. All reactions were performed under nitrogen atmosphere with oven dried (120°C) glassware unless stated otherwise. Solvents were removed from reaction mixtures and products on rotary evaporator at water aspirator pressure unless stated otherwise. Cooling bath temperatures were controlled with the aid of a Polyscience cryocooler. Column Chromatography was performing using silica gel with a particle size of 40-63 μm . All Infrared Spectra were obtained neat on a Perkin Elmer Spectrum One FT-IR Spectrometer. Melting points were determined on a MelTemp apparatus and are uncorrected.

High Resolution Mass Spectra were obtained using a ThermoElectron Corporation LTQFT Ultra. Electrospray Ionization (ESI) was used as the ionization method and ions were detected in an ion cyclotron resonance (ICR) cell. All HRMS were completed by Brent Reschke from the Dr. Aaron Timperman Laboratories, C. Eugene Bennett Department of Chemistry.

tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)phenylcarbamate (5) At -78 °C under N₂ atmosphere, t-BuLi (1.1 mL, 1.76 mmol, 1.6 M in pentane) was added to the mixture of tert-Butyl phenylcarbamate (55 mg, 0.28 mmol) in THF (1.0 mL) then warmed to -20 °C. After stirring for 4 h, squarate (90 mg, 0.43 mmol) in THF (2 mL) was added via cannula. After stirring for 30 min, the reaction was quenched at -20 °C with 10% NH₄Cl in H₂O and extracted with ether. The combined organic portions were dried over MgSO₄, filtered then solvents were removed under reduced pressure. The residue was purified via chromatography (hexane:EtOAc, 9:1) to afford **5** (81 mg, 0.21 mmol, 73%) as a colorless oil. ¹H NMR (270 MHz) δ 8.66 (br s, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 7.7 and 1.5 Hz, 1H), 7.29 (t, *J* = 6.9, 1H), 6.98 (t, *J* = 7.7 Hz, 1H), 5.00 (sept, *J* = 6.2 Hz, 1H), 4.92 (sept, *J* = 6.2 Hz, 1H), 1.54 (s, 9H), 1.47 (d, *J* = 6.2 Hz, 6H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.24 (d, *J* = 6.2 Hz, 3H); ¹³C NMR (67.5 MHz) δ 184.1 (+), 165.7 (+), 153.6 (+), 137.3 (+), 132.0 (+), 129.5 (-), 127.6 (+), 126.5 (-), 122.9 (-), 122.1 (-), 86.7 (+), 80.0 (+), 77.8 (-), 74.0 (+), 28.4 (-), 22.8 (-), 22.7 (-), 22.6 (-), 22.2 (-); IR (neat) 3477, 3338, 2972, 1781, 1728, 1588, 1343, 1163 cm⁻¹.

tert-Butyl 1,4-dihydro-2,3-diisopropoxy-1,4-dioxonaphthalen-5-ylcarbamate (6) Compound 5

(52 mg, 0.13 mmol) dissolved in xylenes (2 mL) was transferred to a pressure tube and then the reaction vessel was sealed and submerged into a sand bath at 170 °C. After heating for 3 h, solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc 95:5) to afford **6** (42 mg, 0.11 mmol, 81%). ¹H NMR (270 MHz) δ 11.21 (br s, 1H), 8.76 (dd, *J* = 8.4 and 1.2 Hz, 1 H), 7.73 (dd, *J* = 7.7 and 1.2 Hz, 1H), 7.60 (t, *J* = 8.2 Hz, 1H), 4.95 (sept, *J* = 6.2 Hz, 2H), 1.54 (s, 9H), 1.36 (d, *J* = 6.2 Hz, 6H), 1.35 (d, *J* = 6.2 Hz, 6H); ¹³C NMR (67.5 MHz) δ 185.9 (+), 182.3 (+), 153.0 (+), 148.1 (+), 147.0 (+), 142.0 (+), 134.7 (-), 131.8 (+), 124.4 (-), 120.6 (-), 114.4 (+), 81.1 (+), 76.2 (-), 76.1 (-), 28.2 (-), 22.7 (-), 22.6 (-); IR (neat): 2979, 1733, 1585, 1516, 1150, 1090, 755 cm⁻¹.

tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-6-methoxyphenylcarbamate

(10) and tert-Butyl 3-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-2-

methoxyphenylcarbamate(11) t-BuLi (1.8 mL, 3.02 mmol, 1.8 M in) was added to 2-Boc

aminoanisole **7** (227 mg, 1.02 mmol) in THF (5 mL) at -40 °C. The reaction was warmed to -10 °C and was stirred for 3 h. Squarate (370 mg, 1.83 mmol) in THF (5 mL) was added via cannula at -20 °C. After stirring at -20 °C for 2 h, the reaction was quenched with 10% NH₄Cl in H₂O,

extracted with ether. The combined organic portions were dried over MgSO_4 , filtered, and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:EtOAc, 95:5, 9:1, 85:15, 8:2) to afford the hydroxycyclobutenones **10** (129 mg, 0.31 mmol, 30%, 40% BRSM), **11** (64 mg, 0.15 mmol), and starting material **7** (57 mg, 0.25 mmol) (**10**) ^1H NMR (600 MHz) δ 7.24 (br s, 1H), 7.22 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.90 (dd, J = 8.4 and 1.2 Hz, 1H), 4.99 (sept, J = 6.0 Hz, 1H), 4.91 (sept, J = 6.0 Hz, 1H), 3.84 (s, 3H), 1.50 (s, 9H), 1.46 (d, J = 6.0 Hz, 3H), 1.45 (d, J = 6.0 Hz, 3H), 1.31 (d, J = 6.0 Hz, 3H), 1.22 (d, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz) δ 184.3 (C), 165.5 (C), 155.6 (C), 136.3 (C), 131.9 (C), 127.5 (CH), 124.4 (C), 118.8 (CH), 112.1 (CH), 86.4 (C), 80.1 (C), 77.3 (CH), 73.6 (CH), 55.9 (CH_3), 28.2 (CH_3), 22.7 (CH_3), 22.6 (CH_3), 22.5 (CH_3), 22.2 (CH_3). (**11**) ^1H NMR (600 MHz) δ 8.03 (br s, 1H), 7.10 (t, J = 7.8 Hz, 1H), 6.88 (dd, J = 7.8 and 1.2 Hz, 2H), 5.39 (s, 1H), 4.93 (sept, J = 6.0 Hz, 1H), 4.92 (sept, J = 6.0 Hz, 1H), 4.04 (s, 3H), 1.53 (s, 9H), 1.45 (d, J = 6.0 Hz, 3H), 1.40 (d, J = 6.0 Hz, 3H), 1.35 (d, J = 6.0 Hz, 3H) 1.29 (d, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz) δ 183.7, 163.5, 152.6, 146.7, 133.4, 132.6, 129.7, 125.0, 121.1, 119.9, 89.0, 80.9, 77.3, 73.7, 63.4, 28.3, 22.7, 22.7, 22.5, 22.3.

tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-5-methoxyphenylcarbamate (12**), tert-Butyl 4-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-3-methoxyphenylcarbamate (**13**) and tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-3-methoxyphenylcarbamate (**14**)** tBuLi (2.0 mL, 3.2 mmol, 1.6 M in THF) was added to a

solution of Bocaminoanisidine **8** (226 mg, 1.01 mmol) in THF (5 mL) at -45 °C. The reaction was allowed to warm to -10 °C for 3 h. Squarate (362 mg, 1.82 mmol) in THF (5 mL) was added via cannula at -20 °C. After stirring for 12 h, the reaction was quenched with 10% NH₄Cl in H₂O and extracted with ether. The combined organic portions were dried over MgSO₄, filtered, and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1, 85:15, 8:2) to afford **12** (54 mg, 0.13 mmol, 13%, 17% BRSM), **14** (53 mg, 0.13 mmol, 13%, 17% BRSM), **13** (31 mg, 0.074 mmol, 7%, 10% BRSM impure), and starting material **8** (54 mg, 0.24 mmol). (**12**) ¹H NMR (270 MHz) δ 8.70 (s, 1H), 7.69 (d, *J* = 2.7 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 6.51 (dd, *J* = 8.4 and 2.5 Hz, 1H), 4.99 (sept, *J* = 6.2 Hz, 1H), 4.91 (sept, *J* = 6.2 Hz, 1H), 3.80 (s, 3H), 1.53 (s, 9H), 1.48 (d, *J* = 5.4 Hz, 3H), 1.46 (d, *J* = 6.2 Hz, 3H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.24 (d, *J* = 6.2 Hz, 3H). (**14**) ¹H NMR (270 MHz) δ 8.57 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.23 (t, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 4.90 (sept, *J* = 6.2 Hz, 2H), 3.75 (s, 3H), 1.51 (s, 9H), 1.42 (d, *J* = 6.2 Hz, 3H), 1.38 (d, *J* = 6.6 Hz, 3H), 1.31 (d, *J* = 6.0 Hz, 3H), 1.26 (d, *J* = 6.2 Hz, 3H).

tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-4-methoxyphenylcarbamate (15) and tert-Butyl 3-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-4-

methoxyphenylcarbamate (16) t-BuLi (2.2 mL, 3.52 mmol, 1.6M in THF) was added to a solution of **9** (229 mg, 1.02 mmol) in THF (6 mL) at -50 °C. The reaction warmed to -10 °C and was stirred for 4 h. Squarate (364 mg, 1.84 mmol) in THF (5 mL) was added via cannula at -20

°C. After stirring for 2 h, the reaction was quenched with 10% NH₄Cl in H₂O and extracted with ether. The combine organic portions were dried over MgSO₄, filtered and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 97:3, 95:5, 9:1) to afford **15** (134 mg, 0.32 mmol, 32%, 36% BRSM) and **16** (20 mg, 0.047 mmol, 5%, 6% BRSM). (**15**) ¹H NMR (270 MHz) δ 8.42 (br s, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 6.98 (d, *J* = 2.9 Hz, 1H), 6.81 (dd, *J* = 8.9 and 3.0 Hz, 1H), 5.00 (sept, *J* = 6.2 Hz, 1H), 4.90 (sept, *J* = 6.2 Hz, 1H), 3.76 (s, 3H), 1.50 (s, 9H), 1.46 (d, *J* = 6.2 Hz, 6H), 1.31 (d, *J* = 6.2 Hz, 6H), 1.24 (d, *J* = 6.2, 3H). (**16**) ¹H NMR (270 MHz), 7.24 (d, *J* = 8.9 Hz, 1H), 6.88 (d, *J* = 8.9 Hz, 1H), 6.41 (s, 1H), 4.93 (sept, *J* = 6.2 Hz, 1H), 4.92 (sept, *J* = 6.2 Hz, 1H), 4.88 (s, 1H), 3.88 (s, 3H), 1.50 (s, 9H), 1.45 (d, *J* = 6.0 Hz, 3H), 1.41 (d, *J* = 6.0 Hz, 3H), 1.33 (d, *J* = 6.0 Hz, 3H), 1.28 (d, *J* = 6.0 Hz, 3H).

tert-Butyl 1,4-dihydro-2,3-diisopropoxy-5-methoxy-1,4-dioxonaphthalen-6-ylcarbamate (18**)**

11 (65 mg, 0.15 mmol) was dissolved in toluene (3 mL) and transferred to a pressure tube. The reaction vessel was sealed and submerged into a 140 °C oil bath for 20 h. Then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 9:1, 85:15, 8:2) to afford **18** (21 mg, 0.05 mmol, 33%). ¹H NMR (270 MHz) δ 8.46 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.49 (s, 1H), 4.93 (sept, *J* = 6.0 Hz, 1H), 4.87 (sept, *J* = 6.2 Hz, 1H), 3.92 (s, 3H), 1.55 (s, 9H), 1.36 (d, *J* = 6.2 Hz, 6H), 1.34 (d, *J* = 6.2 Hz, 6H).

tert-Butyl 1,4-dihydro-2,3-diisopropoxy-6-methoxy-1,4-dioxonaphthalen-8-ylcarbamate (19)

Compound **12** (56 mg, 0.13 mmol) was dissolved in toluene (3 mL) and transferred to a pressure tube. The vessel was sealed then submerged in a 120 °C oil bath. After stirring 12 h, the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 95:5) to afford **19** (15 mg, 0.036 mmol, 27%, 33% BRSM). ¹H NMR (270 MHz) δ 11.4 (s, 1H), 8.30 (d, *J* = 2.7 MHz, 1H), 7.28 (d, *J* = 2.7 Hz, 1H), 4.99 (sept, *J* = 6.2 Hz, 1H), 4.86 (sept, *J* = 6.2 Hz, 1H), 1.53 (s, 9H), 1.35 (d, *J* = 5.9, 6H), 1.33 (d, *J* = 5.7 Hz, 6H).

tert-Butyl 1,4-dihydro-2,3-diisopropoxy-5-methoxy-1,4-dioxonaphthalen-8-ylcarbamate (20)

Compound **15** (25 mg, 0.059 mmol) was dissolved in toluene (2 mL) and transferred to a pressure tube. The vessel was sealed and submerged in a 170 °C oil bath and was stirred for 12 h. Then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford the naphthoquinone **20** (6 mg, 0.014 mmol, 24%). ¹H NMR (600 MHz) δ 11.3 (br s, 1H), 8.76 (d, *J* = 9.6 Hz, 1H), 7.29 (d, *J* = 9.6 Hz, 1H), 4.94 (sept, *J* = 6.0 Hz, 1H), 4.87 (sept, *J* = 6.0 Hz, 1H), 3.97 (s, 3H), 1.53 (s, 9H), 1.34 (d, *J* = 6.2 Hz, 12H). ¹³C NMR (150 MHz) δ 186.1 (C), 181.4 (C), 154.9 (C), 153.4 (C), 148.0 (C), 146.0 (C), 136.2

(C), 126.9 (CH), 120.9 (CH), 118.4 (C), 115.8 (C), 80.9 (C), 76.0 (CH), 75.8 (CH), 56.8 (CH), 28.3 (CH₃), 27.7 (C), 22.8 (CH₃), 22.6 (CH₃); IR (neat): 2977, 1766, 1625, 1505, 1154, 1099, 765 cm⁻¹. HRMS calcd for C₂₂H₃₀NO₇ (M+H⁺): 420.2017, Found:420.2022.

tert-Butyl 5,8-dihydro-6,7-diisopropoxy-5,8-dioxoquinolin-4-ylcarbamate (27) t-BuLi (2.1 mL, 3.36 mmol, 1.6 M in THF) was added to tert-butyl pyridin-4-ylcarbamate **23** (201 mg, 1.03 mmol) in THF (5 mL) at -50 °C. After stirring for 2 h, diisopropyl squarate (370 mg, 1.87 mmol) in THF (6 mL) was added via cannula. After stirring for 7 h, the reaction was quenched with 10 % NH₄Cl in H₂O, extracted with ether, dried over MgSO₄, filtered and then solvents were removed under reduced pressure. The residue was dissolved in toluene and transferred to a pressure tube. The vessel was sealed and then submerged in a 120 °C oil bath. After stirring for 30 min, the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes;EtOAc, in order of elution: 9:1, 85:15, 8:2, 7:3) to afford **23** (129 mg, 0.33 mmol, 32%). ¹H NMR (600 MHz) δ 8.88 (s, 1H), 8.42 (s, 1H), 8.30 (d, *J* = 6.0 Hz, 1H), 8.13 (d, *J* = 6.0 Hz, 1H), 5.00 (sept, *J* = 6.0 Hz, 1H), 4.92 (sept, *J* = 6.0 Hz, 1H), 1.53 (s, 9H), 1.46 (d, *J* = 6.0 Hz, 6H), 1.32 (d, *J* = 6.0 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 1H); ¹³C NMR (150 MHz) δ 183.2, 165.2, 152.5, 150.4, 147.2, 145.4, 132.1, 121.9, 113.5, 85.2, 81.2, 78.2, 74.2, 28.3, 22.8, 22.7, 22.6, 22.3.

N-(2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)phenyl)pivalamide (36) At 0 °C under N₂ atmosphere, nBuLi (9.5 mL, 15.2 mmol, 1.6 M in hexanes) was added to a solution of N-phenylpivalamide **35** (890 mg, 5.02 mmol) in ether (10 mL) and THF (7.5 mL). After stirring for 2 h, the mixture was cooled to -78 °C and squarate (1.97 g, 9.94 mmol) in THF (3 mL) was added via cannula. After stirring for 4 h at rt, the was quenched with H₂O and extracted with ether. The combined organic portions were dried over MgSO₄, filtered, and then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexane:EtOAc, 100:0, 95:5, 9:1, 85:15, 8:2) to afford **36** (885 mg, 2.36 mmol 45%, 67% BRSM). ¹H NMR (600 MHz) δ 9.55 (br s, 1H), 9.05 (d, *J* = 9.0 Hz, 1H), 7.38 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.31 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.04 (dt, *J* = 7.2 and 1.2, 1H), 5.03 (sept, *J* = 6.0 Hz, 1H), 4.91 (sept, *J* = 6.0 Hz, 1H), 3.22 (s, 1H), 1.49 (d, *J* = 6.0 Hz, 3H), 1.47 (d, *J* = 6.0 Hz, 3H), 1.34 (s, 9H), 1.32 (d, *J* = 6.0 Hz, 3H), 1.24 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (150 MHz) δ 184.3 (C), 177.8 (C), 165.9 (C), 137.1 (C), 132.0 (C), 129.4 (CH), 128.6 (C), 126.3 (CH), 124.5 (CH), 87.1 (C), 77.9 (CH), 74.0 (CH), 39.7 (C), 27.4 (CH₃), 22.8 (CH₃), 22.7 (CH₃), 22.6 (CH₃), 22.3 (CH₃).

N-(1,4-dihydro-2,3-diisopropoxy-1,4-dioxonaphthalen-5-yl)pivalamide (37) Compound **36** (100 mg, 0.27 mmol) and Proton Sponge (57 mg, 0.27 mmol) were dissolved in xylenes (40 mL) and transferred to a 350 mL pressure tube then the reaction vessel was sealed and submerged in a 120 °C sand bath. After heating for 2 h, solvents were removed under reduced pressure. The residue was purified via column chromatography (hexanes:EtOAc in the order of elution, 98:2,

95:5, 9:1) to afford **37** (56 mg, 0.27 mmol, 64%). ^1H NMR (270 MHz) δ 12.2 (br s, 1H), 9.16 (dd, J = 8.7 and 1.2 Hz, 1H), 7.82 (dd, J = 7.4 and 1.2 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 5.04 (sept, J = 6.0 Hz, 1H), 1.40 (d, J = 6.0 Hz, 6H), 1.34 (s, 9H).

N-(1,4-dihydro-2-hydroxy-3-isopropoxy-1,4-dioxonaphthalen-5-yl)pivalamide (38) Compound **36** (100 mg, 0.27 mmol) and Proton Sponge (101 mg, 0.47 mmol) were dissolved in xylenes (20 mL) and transferred to a pressure tube then the reaction vessel sealed and submerged in a 170 °C oil bath. After heating for 2 days, the solvents were removed under reduced pressure. The residue was purified via column chromatography (hexanes:EtOAc in the order of elution, 98:2, 95:5, 9:1) to afford **38** (40 mg, 0.11 mmol, 40%). ^1H NMR (270 MHz) δ 12.2 (br s, 1H), 9.10 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 7.4 Hz, 1H), 7.65 (t, J = 7.9 Hz, 1H), 4.98 (sept, J = 6.2 Hz, 1H), 4.90 (sept, J = 6.2 Hz, 1H), 1.39 (s, 9H), 1.35 (d, J = 6.2 Hz, 12H), ^{13}C NMR (67.5 MHz) δ 185.9 (+), 181.9 (+), 179.1 (+), 142.5 (+), 142.1 (+), 138.9 (+), 134.6 (-), 129.7 (+), 127.4 (-), 121.6 (-), 114.9 (+), 75.8 (-), 40.6 (+), 27.6 (-), 22.7 (-); IR (neat) 3263, 2973, 1657, 1631, 1284, 1184, 757 cm^{-1} .

4-hydroxy-2,3-diisopropoxy-4-(2-nitrophenyl)cyclobut-2-enone (39) At -40 °C,

Phenylmagnesium chloride (7.2 mL, 14.76 mmol, 2.0 M in THF) was added to a solution of 2-iodonitrobenzene (3.25g, 13.05 mmol) in THF (30 mL) under N_2 atmosphere. After stirring for

10 min, squarate (3.36g, 16.95 mmol) in THF (20 mL) was added via cannula. After stirring for 13 h, the reaction was quenched with 10% NH₄Cl in H₂O, extracted with ether. The combined organic portions were dried over MgSO₄, filtered, and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1, 85:15, 8:2) to afford the alcohol **39** (3.03 g, 9.43 mmol, 72%). ¹H NMR (600 MHz) δ 7.96 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.79 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.60 (dt, *J* = 7.8 and 1.2 Hz, 1H), 7.47 (dt, *J* = 7.8 and 1.2 Hz, 1H), 4.95 (sept, *J* = 6.0 Hz, 1H), 4.92 (sept, *J* = 6.0 Hz, 1H), 4.71 (br s, 1H), 1.44 (d, *J* = 6.0 Hz, 3H), 1.38 (d, *J* = 6.0 Hz, 3H), 1.32 (d, *J* = 6.0 Hz, 3H), 1.24 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (150 MHz) δ 181.1 (C), 164.2 (C), 149.3 (C), 133.5 (CH), 132.3 (C), 132.2 (C), 129.3 (CH), 128.6 (CH), 125.0 (CH), 84.6 (C), 77.8 (CH), 74.1 (CH), 22.7 (CH₃), 22.7 (CH₃), 22.3 (CH₃), 22.3 (CH₃); HRMS Calcd For C₆H₁₉NO₆Na (M+Na⁺): 344.1110 Found: 344.1105.

2,3-diisopropyl-1-hydroxy-4(1H)-quinolinone (40) Hydroxycyclobutenedone **39** in xylenes was placed in a pressure tube then the reaction vessel sealed and submerged in a 160 °C oil bath. After stirring for 1 h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 85:15) to afford **40** (59 mg, 0.21 mmol). ¹H NMR (600 MHz) δ 8.00 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.54 (dt, *J* = 8.4 and 1.2 Hz), 7.35 (dt, *J* = 8.4 and 1.2 Hz, 1H), 6.53 (br s, 1H), 5.63 (sept, *J* = 6.0 Hz, 1H), 4.65 (sept, *J* = 6.0 Hz, 1H), 1.45 (d, *J* = 6.0 Hz, 6H), 1.37 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (150 MHz) δ 156.1 (C), 151.0 (C),

142.9 (C), 128.4 (CH), 126.7 (CH), 125.5 (C), 123.1 (CH), 121.6 (CH), 118.1 (C), 68.4 (CH₃), 22.5 (CH₃), 22.1 (CH₃); HRMS Calcd for C₁₅H₁₉NO₄ (M+H⁺): 278.1387 Found: 278.1388.

4-(2-bromophenyl)-4-hydroxy-2,3-diisopropoxycyclobut-2-enone (49) At -110 °C, *n*BuLi (2.2 mL, 3.96 mmol, 1.8 M in hexanes) was added to a solution of 1-iodo-2-bromobenzene (1.068 g, 3.76 mmol) in a THF (60 mL) and ether (60 mL). After 30 mins, diisopropyl squarate (810 mg, 4.08 mmol) dissolved in THF (10 mL) was added via cannula. After stirring overnight, the reaction was quenched with 10% NH₄Cl in H₂O and extracted with EtOAc. The combined organic portions were dried over MgSO₄, filtered, then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford **49** (1.18 g, 3.32 mmol, 88%) as a colorless oil. ¹H NMR (600 MHz) δ 7.63 (dd, *J* = 7.8 and 1.8 Hz, 1H), 7.58 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.30 (dt, *J* = 7.8 and 1.2 Hz, 1H), 7.16 (dt, *J* = 7.8 and 1.8 Hz, 1H), 4.95 (sept, *J* = 6.0 Hz, 2H), 3.69 (br s, 1H), 1.44 (d, *J* = 6.6 Hz, 3H), 1.42 (d, *J* = 6.0 Hz, 3H), 1.34 (d, *J* = 6.0 Hz, 1H), 1.29 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (150 MHz) δ 182.3 (C), 164.2 (C), 136.9 (C), 134.4 (CH), 133.8 (C), 129.7 (CH), 129.2 (CH), 127.5 (CH), 120.7 (C), 88.1 (C), 77.5 (CH), 73.9 (CH), 22.9 (CH₃), 22.8 (CH₃), 22.6 (CH₃), 22.3 (CH₃); IR (neat) 3379, 2981, 1771, 1599, 1316, 1091, 942, 750 cm⁻¹ HRMS Calcd for C₁₆H₂₀BrO₄ (M+H⁺): 355.0539 Found: 355.0540

5-bromo-2,3-diisopropoxynaphthalene-1,4-dione (50) Compound **49** (70 mg, 0.20 mmol) was dissolved in xylenes (5 mL) and transferred to a pressure tube. The vessel was sealed and then submerged in a 135 °C oil bath. After stirring for 5 h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 95:5) to afford **50** (48 mg, 0.14 mmol, 70%) as a light orange oil. ¹H NMR (600 MHz) δ 8.11 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.92 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.47 (t, *J* = 7.8 and 1.2 Hz, 1H), 4.96 (sept, *J* = 6.0 Hz, 1H), 4.92, sept, *J* = 6.0 Hz, 1H), 1.37 (d, *J* = 6.0 Hz, 6H), 1.35 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (150 MHz) δ 181.4 (C), 180.9 (C), 148.8 (C), 146.5 (C), 140.6 (CH), 134.1 (C), 133.2 (CH), 128.4 (C), 126.4 (CH), 121.7 (C), 76.5 (CH), 76.5 (CH), 22.8 (CH₃), 22.7 (CH₃); IR (neat) 2979, 1664, 1607, 1194, 11096, 1000, 747 cm⁻¹; HRMS Calcd for C₁₆H₁₈BrO₄ (M+H⁺): 353.0383 Found:353.03837.

tert-Butyl 2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenylcarbamate (61) At 0 °C, TFAA (1.6 mL, 11.5 mmol) was added to a solution of **5** (3.585 g, 9.16 mmol) and pyridine (1.0 mL, 12.9 mmol) in ether (135 mL). After stirring for 45 min, the reaction was quenched with H₂O and extracted with EtOAc. The mixture was dried over MgSO₄, filtered, and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford **61** (2.32g, 6.45 mmol, 76%) in a yellow solid. ¹H NMR (600 MHz) δ 9.50 (br s, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 5.65 (sept, *J* = 6.0, 1H), 1.55 (d, *J* = 6.6 Hz, 6H), 1.51 (s, 9H); ¹³C NMR (150 MHz) δ 193.7 (C), 193.3 (C), 188.8 (C), 173.5 (C), 152.9 (C), 139.6 (C), 133.9 (CH), 128.8 (CH), 122.5 (CH),

120.8 (CH), 117.6 (C), 81.3 (CH), 80.5 (C), 28.2 (CH₃), 22.8 (CH₃); IR (neat) 2981, 1770, 1716, 1562, 1388, 1130, 762 cm⁻¹, HRMS calcd for C₁₈H₂₂NO₅ (M+H⁺) 332.1493, Found 332.1493.

N-(2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenyl)pivalamide (62) TFAA (0.5 mL, 3.5 mmol) was added to a solution of **36** (700 mg, 1.87 mmol) and pyridine (1 mL, 12.4 mmol) in ether (70 mL). After stirring for 1 h, the reaction was quenched with NH₄Cl in H₂O and extracted with ether. The combined organic portions were dried over MgSO₄, filtered, and then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford **62** (446 mg, 1.42 mmol, 76%) as a light yellow solid. ¹H NMR (600 MHz) δ 9.93 (s, 1H), 8.35 (d, *J* = 8.4 Hz, 1H), 7.77 (dd, *J* = 7.8 and 1.8 Hz, 1H), 7.50 (dt, *J* = 8.4 and 1.2 Hz, 1H), 7.16 (t, *J* = 7.2 Hz, 1H), 5.70 (sept, *J* = 6.0 Hz, 1H), 1.59 (d, *J* = 6.6 Hz, 6H), 1.35 (s, 9H); ¹³C NMR (150 MHz) δ 194.5 (+), 194.3 (+), 189.0 (+), 178.3 (+), 174.2 (+), 139.3 (+), 133.6 (-), 128.8 (-), 124.3 (-), 123.8 (-), 118.7 (+), 81.6 (-), 40.2 (+), 27.2 (-), 23.0 (-); IR (neat) 2955, 1779, 1550, 1387, 1159, 767 cm⁻¹; HRMS Calcd for C₁₈H₂₂NO₄ (M+H⁺): 316.1543 Found 316.1543.

tert-Butyl 2-(3-hydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenylcarbamate (63) At -78 °C under N₂ atmosphere, PhLi (1.0 mL, 1.5 mmol, 1.5 M in diButylether) was added to a

solution of **61** (302 mg, 0.91 mmol) in THF (10 mL). After stirring for 2 h at -50 °C, the reaction was quenched with 10% NH₄Cl in H₂O. It was extracted with EtOAc, dried over MgSO₄, then filtered. The solvents were removed under reduced pressure and the residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 98:2, 95:5, 9:1) to afford **63** (330 mg, 0.81 mmol, 89%). ¹H NMR (270 MHz) δ 9.43 (br s, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.41-7.24(m, 4H), 6.99 (dt, *J* = 7.4 and 1.2 Hz, 1H), 4.87 (sept, *J* = 6.2 Hz, 1H), 1.50 (s, 9H), 1.45 (d, *J* = 6.2 Hz, 3H), 1.10 (d, *J* = 6.2 Hz, 3H); ¹³C NMR (67.5 MHz) δ 187.9 (+), 179.7 (+), 153.6 (+), 136.8 (+), 136.2 (+), 129.4 (-), 128.7 (-), 128.7 (-), 128.4 (-), 125.5 (-), 125.2 (+), 122.4 (-), 120.3 (-), 118.2 (+), 91.1 (+), 80.4 (-), 80.0 (+), 28.4 (-), 22.9 (-), 22.5 (-), IR (neat) 3385, 2981, 1731, 1580, 1300, 1157, and 750 cm⁻¹, HRMS Calcd for C₂₄H₂₈NO₅ (M+H⁺): 410.1962, Found 410.1964.

N-(2-(3-hydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenyl)pivalamide (64**)** At -78

°C under N₂ atmosphere, PhLi (0.7 mL, 1.13 mmol, 1.6 M in diButylether) was added to a solution of **62** (324 mg, 1.03 mmol) in THF (17 mL). After stirring for 3 days, the reaction was quenched with 10% NH₄Cl in H₂O. It was extracted with ether, dried over MgSO₄, then filtered. The solvents were removed under reduced pressure and the residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 98:2, 95:5, 9:1, 85:15) to afford **64** (330 mg, 0.84 mmol, 82%). ¹H NMR (270 MHz) δ 9.61 (s, 1H), 8.06 (d, *J* = 7.7 Hz, 1H), 7.57 (dd, *J*

= 7.7 and 1.7 Hz, 1H), 7.51 (dd, J = 7.7 and 1.2, 1H), 7.41-7.32 (m, 4H), 7.25 (dt, J = 8.4 and 1.5 Hz, 1H), 7.06 (dt, J = 7.7 and 1.2 Hz, 1H), 4.90 (sept, J = 6.0 Hz, 1H), 4.81 (br s, 1H), 1.47 (d, J = 6.2 Hz, 3H), 1.23 (s, 9H), 1.05 (d, J = 6.2 Hz, 3H); ^{13}C NMR (67.5 MHz) δ 188.5 (+), 181.0 (+), 178.1 (+), 136.2 (+), 129.0 (-), 128.7 (-), 128.6 (-), 128.5 (-), 125.4 (-), 125.3 (+), 124.1 (-), 123.9 (-), 119.0 (+), 91.8 (+), 80.3 (-), 39.9 (+), 27.3 (-), 22.8 (-), 22.4 (-); IR (neat) 3284, 2982, 1732, 1660, 1575, 1387, 1083, 907, 750 cm^{-1} .

N-(2-(3-Trimethylsilylhydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenyl)pivalamide

(65) TMSCl (0.16 mL, 1.25 mmol) was added to a mixture of **64** (350 mg, 0.89 mmol) and DMAP (195 mg, 1.29 mmol) in DMF (1.5 mL) under N_2 atmosphere. After stirring for 12 h at rt, the reaction was quenched with H_2O and extracted with ether. The organic portions were dried over MgSO_4 and the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 98:2, 95:5, 9:1) to afford **65** (269, 0.58 mmol, 65%). ^1H NMR (270 MHz) δ 9.77 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.63 (dd, J = 7.9 and 1.5 Hz, 1H), 7.51-7.29 (m, 6H), 7.12 (t, J = 7.7 Hz, 1H), 4.88 (sept, J = 5.9 Hz, 1H), 1.45 (d, J = 6.2 Hz, 3H), 1.29 (s, 9H), 0.97 (d, J = 6.2 Hz, 3H).

tert-Butyl 2-(3-Trimethylsilylhydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-

enyl)phenylcarbamate (66) At -78 °C under N₂ atmosphere, PhLi (2.20 mL, 3.74 mmol, 1.7 M in diButylether) was added to a solution of **61** (1.027 g, 3.10 mmol) in THF(16 mL). After stirring for 50 min, TMSCl (0.65 mL, 5.14 mmol) was added via syringe and allowed to stir at 0 °C for 1.5 h. The reaction was quenched with 10% NH₄Cl in H₂O then extracted with EtOAc, dried over MgSO₄, and filtered. The solvents were removed under reduced pressure and the residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 98:2, 95:5, 9:1) to afford **66** (607 mg, 1.26 mmol, 41%). ¹H NMR (270 MHz) δ 9.26 (br s, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.68 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.50-7.48 (m, 1H), 7.39-7.29 (m, 4H), 7.06 (dt, *J* = 7.2 and 1.2 Hz, 1H), 4.88 (sept, 6.0 Hz, 1H), 1.51 (s, 9H), 1.44 (d, *J* = 6.0 Hz, 3H), 0.99 (*J* = 6.0 Hz, 3H), 0.28 (s, 9H). ¹³C NMR (150 MHz) δ 187.5 (C), 180.2 (C), 153.2 (C), 137.5 (C), 137.0 (C), 129.3 (CH), 128.6 (CH), 128.6 (CH), 128.2 (CH), 125.6 (C), 125.5 (CH), 122.7 (CH), 121.6 (CH), 119.1 (C), 93.4 (C), 79.7 (C), 79.4 (CH), 28.3 (CH₃), 22.7 (CH₃), 22.4(CH₃), 1.12 (CH₃), IR (neat) 2979, 1726, 1251, 1148, 1086, 839 and 747 cm⁻¹, HRMS Calcd for C₂₇H₃₆NO₅ (M+H⁺): 482.2357, Found 482.2357.

3-(2-trimethylsilylhydroxy-1-isopropoxy-2-phenylethylidene)-1-(pivaloyl)indolin-2-one (67)

65 (230 mg, 0.49 mmol) was dissolved in xylenes (12 mL) and then transferred to a pressure tube. The reaction vessel was sealed then submerged in a 150 °C oil bath for 4 h. Then solvents were removed under reduced pressure. The residue was purified by column

chromatography (hexane:EtOAc, 98:2, 95:5, 9:1) to afford the oxindole **67** (100 mg, 0.21 mmol, 43%). ^1H NMR (270 MHz) δ 7.85 (dd, J = 7.7 and 1.8 Hz, 1H), 7.57 (s, 1H), 7.37-7.15 (m, 5H), 7.12 (dt, J = 7.9 and 1.5 Hz, 1H), 7.02 (dt, J = 7.7 and 1.2 Hz, 1H), 5.33 (sept, J = 6.0 Hz, 1H), 1.38 (s, 9H), 1.28 (d, J = 6.0 Hz, 3H), 0.66 (d, J = 6.2 Hz, 3H), 0.15 (s, (H)); ^{13}C NMR (67.5 MHz) δ 183.8, 170.8, 167.7, 139.8, 137.1, 128.5, 127.1, 126.7, 124.7, 124.3, 123.4, 112.5, 105.9, 75.1, 67.7, 43.6, 31.6, 27.1, 23.1, 22.5, -0.13.

tert-Butyl 3-(2-Trimethylsilylhydroxy-1-isopropoxy-2-phenylethylidene)-2-oxoindoline-1-carboxylate (68) Compound **66** (310 mg, 0.64 mmol) was dissolved in xylenes (30 mL) and transferred to a pressure tube. The reaction vessel was sealed then submerged in a 160 °C oil bath and was stirred for 12 h. Then the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford the oxindole **68** (242 mg, 0.50 mmol, 78%). ^1H NMR (270 MHz) δ 7.97 (dd, J = 7.4 and 1.0 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.70 (s, 1H), 7.43-7.21 (m, 5H), 7.13 (dt, J = 7.7 and 1.0 Hz, 1H), 5.32 (sept, J = 6.0 Hz, 1H), 1.67 (s, 9H), 1.37 (d, J = 6.0 Hz, 3H), 0.74 (d, J = 6.0 Hz, 3H), 0.24 (s, 9H); ^{13}C NMR (150 MHz) δ 171 (C), 167.1 (C), 149.5 (C), 140.0 (C), 136.0 (C), 128.4 (CH), 127.0 (CH), 126.7 (CH), 124.9 (CH), 123.7 (C), 123.6 (CH), 113.8 (CH), 106.0 (C), 83.8 (C), 75.2 (CH), 67.9 (CH), 28.2 (CH₃), 23.1 (CH₃), 22.6 (CH₃), -0.15 (CH₃); IR (neat) 2976, 1728, 1610, 1087, 746 cm⁻¹.

3-(2-phenyl-ethan-2-one)-1-(pivaloyl)indolin-2-one (74) and 3-(2-phenyl-ethan-2-one)-indolin-2-one (75) and 3-(1-isopropoxy-2-oxo-2-phenylethylidene)-1-(pivaloyl)indolin-2-one (76)

Hydroxycyclobutenone **64** (1.02 g, 2.59 mmol) was dissolved in xylenes (20 mL) and transferred to a pressure tube. The pressure tube was sealed then submerged in 175 °C oil bath and was stirred for 5 h. Then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1, 85:15, 8:2) to afford **75** (90 mg, 0.27 mmol, 10%), **74** (70 mg, 0.28 mmol, 11%) and **76** (94 mg, 0.24 mmol, 9%). (**74**) ^1H NMR (270 MHz) δ 7.97 (d, J = 7.2 Hz, 1H), 7.61-7.43 (m, 5H), 7.25 (t, J = 8.7 Hz, 1H), 7.20 (d, J = 7.4 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 4.19 (dd, J = 7.7 and 3.0 Hz, 1H), 3.85 (dd, J = 18.3 and 3.4 Hz, 1H), 3.55 (dd, J = 18.3 and 7.7 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (67.5 MHz) δ 196.1 (+), 182.4 (+), 176.9 (+), 141.4 (+), 136.0 (+), 133.5 (-), 128.9 (+), 128.6 (-), 128.1 (-), 124.1 (-), 123.7 (-), 114.2 (-), 109.9 (-), 43.3 (+), 41.8 (-), 39.9 (+), 26.8 (-); (**75**) ^1H NMR (270 MHz) δ 8.85 (s, 9H), 7.99 (d, J = 7.4 Hz, 2H), 7.59 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 7.20 (t, J = 8.2 Hz, 2H), 6.98 (d, J = 7.7 Hz, 1H), 6.92 (d, J = 7.7 Hz, 1H), 4.11 (dd, J = 8.6 and 3.2 Hz, 1H), 3.84 (dd, J = 18.3 and 3.2 Hz, 1H), 3.47 (dd, J = 18.3 and 8.6 Hz, 1H) ^{13}C NMR (67.5 MHz) δ 196.8 (+), 180.3 (+), 141.5 (+), 136.2 (+), 133.5 (-), 129.6 (+), 128.7 (-), 128.1 (-), 128.0 (-), 124.5 (-), 122.4 (-), 109.8 (-), 41.6 (-), 39.7 (+); HRMS Calcd for $\text{C}_{16}\text{H}_{14}\text{NO}_2$ ($\text{M}+\text{H}^+$): 252.1019 Found: 252.1018 (**76**)

^1H NMR (270 MHz) δ 8.05 (dd, J = 8.2 and 1.2 Hz, 2H), 7.88 (dd, J = 7.2 and 1.2 Hz, 1H), 7.68-7.49 (m, 4H), 7.26 (dt, J = 7.4 and 1.5 Hz, 1H), 7.17 (dt, J = 7.7 and .2 Hz, 1H), 4.51 (sept J = 6.2 Hz, 1H), 1.38-1.36 (m, 6H), 1.28 (s, 9H); ^{13}C NMR (67.5 mHz) δ 191.0 (+), 182.3 (+), 166.3 (+), 160.9 (+), 139.1 (+), 135.0 (+), 134.5 (-), 129.0 (-), 127.7 (-), 123.8 (-), 123.1 (-), 122.7 (+), 113.8 (-), 109.0 (-), 107 (+), 75.6 (-), 43.1 (+), 26.7 (-), 23.2 (-).

N-(2-(3-hydroxy-2-isopropoxy-3-(4-methoxyphenyl)-4-oxocyclobut-1-enyl)phenyl)pivalamide

(77) 4-anisylmagnesium bromide (3.0 mL, 1.2 mmol, 0.4 M in THF) was added to **62** (304 mg, 0.97 mmol) in THF (35 mL) under N_2 atmosphere at -78°C . After stirring for 2 days, it was quenched with 10% NH_4Cl in H_2O , washed with brine, and dried over MgSO_4 . The mixture was filtered then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 9:1, 85:15) to afford **77** (303 mg, 0.72 mmol, 74%) as a colorless oil. ^1H NMR (600 MHz) δ 9.61 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.61 (dd, J = 7.8 and 1.2 Hz, 1H), 7.44 (d, J = 9.0, 2H), 7.30 (, dt, J = 7.2 and 1.2 Hz, 1H), 7.10 (dt, J = 7.2 and 1.2 Hz, 1H), 6.92 (d, J = 9.0 Hz, 2H), 4.89 (sept, J = 6.0 Hz, 1H), 3.82 (s, 3H), 1.48 (d, J = 6.0 Hz, 3H), 1.27 (s, 9H), 1.10 (d, J = 6.0 Hz, 3H); ^{13}C NMR (150 MHz) δ 188.5 (C), 180.9 (C), 178.0 (C), 159.9 (C), 136.5 (C), 129.1 (CH), 128.6 (CH), 127.9 (CH), 126.7 (CH), 125.5 (C), 124.2 (CH), 123.9 (CH), 119.6 (C), 114.3 (CH), 91.7 (C), 80.2 (CH), 55.3 (CH_3), 39.9 (C), 27.3 (CH_3), 22.9 (CH_3), 22.5 (CH_3); IR (neat) 3286, 2965, 1736, 1577, 1386, 1250, 1099, 753 cm^{-1} , HRMS calcd for $\text{C}_{25}\text{H}_{30}\text{NO}_5$ ($\text{M}+\text{H}^+$): 424.2118, Found 424.2124.

3-(1-isopropoxy-2-(4-methoxyphenyl)-2-oxoethylidene)indolin-2-one (**78**)

Hydroxycyclobutenone **77** (105 mg, 0.25 mmol) was dissolved in xylenes (5 mL) and transferred to a pressure tube. The reaction vessel was sealed then submerged in a 120 °C oil bath. After 5 h the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford **78** (46 mg, 0.14 mmol, 56%) as a orange oil. ^1H NMR (600 MHz) δ 8.47 (br s, 1H), 8.02 (d, J = 9.0, 2H), 7.76 (d, J = 7.8 Hz, 1H), 7.13 (dt, J = 7.8 and 1.2 Hz, 1H), 7.01 (dt, J = 7.2 and 1.2 Hz, 1H), 6.94 (d, J = 9.0 Hz, 2H), 6.67 (d, J = 7.2 Hz, 1H), 4.51 (sept, J = 6.0 Hz, 1H), 3.85 (s, 3H), 1.41 (br d, J = 6.0 Hz, 3H), 1.31 (br d, J = 5.4 Hz, Hz, 3H); ^{13}C NMR (150 MHz) δ 189.6 (C), 169.2(C), 164.6 (C), 160.5 (C), 139.4 (C), 131.5 (CH), 128.7 (C), 127.4 (CH), 123.4 (CH), 122.5 (C), 121.6 (CH), 114.3 (CH), 109.4 (CH), 108.5(C), 75.3 (CH), 55.5 (CH₃), 23.3 (CH₃); IR (neat) 2980, 1694, 1594, 1464, 1257, 1097, 811, 732 cm⁻¹. HRMS Cald for C₂₀H₂₀NO₄ (M+H⁺): 338.1387. Found: 338.1390.

3-isopropoxy-4-(2-nitrophenyl)cyclobut-3-ene-1,2-dione (81) TFAA was added to a solution of **39** and pyridine in ether under N₂ atmosphere at 0 °C. After stirring for 1 h, the reaction was

quenched with H₂O and extracted with EtOAc. The combined organic portions were dried over MgSO₄, filtered and the solvents were removed under reduced atmosphere. The residue was purified by column chromatography (hexanes:EtOAc, 7:3) to afford the cyclobutenedione **81** (2.275 g, 8.71 mmol, 95%) ¹H NMR (270 MHz) δ 8.04 (d, *J* = 7.7 Hz, 1H), 7.98 (d, *J* = 7.4 Hz, 1H), 7.76 (t, *J* = 7.4 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 5.59 (sept, *J* = 6.2 Hz, 1H), 1.51 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (67.5 MHz) δ 194.7, 192.3, 190.3, 170.9, 147.0, 133.3, 131.9, 129.2, 125.0, 121.2, 81.3, 22.8.

4-hydroxy-3-isopropoxy-2-(2-nitrophenyl)-4-phenylcyclobut-2-enone (81) Phenylmagnesium chloride (0.7 mL, 1.44 mmol, 2.05 M in THF) was added to **81** (305 mg, 1.17 mmol) in THF (6 mL) under N₂ atmosphere at -78 °C. After stirring for 5 h, the reaction was quenched with 10% NH₄Cl in H₂O and extracted with EtOAc. The combined organic portions were dried over MgSO₄, filtered, and then the solvents were removed under reduced pressure to afford **82** (391 mg, 1.15 mmol, 98%) without further purification because of its sensitivity to chromatographic methods. ¹H NMR (270 MHz) δ 7.93 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.67-7.58 (m, 3H), 7.49-7.35 (m, 4H), 4.80 (sept, *J* = 6.2 Hz, 1H), 3.84 (br s, 1H), 1.40 (d, *J* = 6.2 Hz, 3H), 1.09 (d, *J* = 6.2 Hz, 3H).

2-(benzo[c]isoxazol-3-yl)-2-isopropoxy-1-phenylvinyl acetate (85). To **81** (700 mg, 2.68 mmol) in THF (20 mL) was added PhMgCl (1.8 mL, 3.6 mmol, 2.0 M in THF) at -78 °C. After stirring for 1 h, the reaction was warmed to -50 °C and was stirred for 2h. Then Ac₂O (0.6 mL, 6.38 mmol) was added via syringe. The reaction mixture warmed to rt then 10% NH₄Cl in H₂O was added and was extracted with EtOAc. The combined organic portions were dried over MgSO₄ then filtered and then the solvents were removed under reduced pressure. The residue was then dissolved in xylenes (20 mL) and transferred to a pressure tube. The reaction vessel was sealed then submerged in a 160 °C oil bath. After stirring for 2 h, then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1) to afford **85** (450 mg, 0.13 mmol 50%) ¹H NMR (600 MHz) δ 7.50 (d, *J* = 9.0 Hz, 1H), 7.23-7.15 (m, 8H), 6.82 (dd, *J* = 8.4 and 6.0 Hz, 1H), 3.94 (sept, *J* = 6.0 Hz, 1H), 2.29 (s, 3H), 1.25 (d, *J* = 6.6 Hz, 6H); ¹³C NMR (150 MHz) δ 168.5 (C), 160.1 (C), 157.3 (C), 141.2 (C), 133.1 (C), 133.1 (C), 130.7 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 124.7 (CH), 120.0 (CH), 117.4 (C), 115.1 (CH, 74.0 (CH). HRMS Calcd for C₂₀H₂₀NO₄ (M+H⁺): 338.1387. Found: 338.1389.

3-(2-hydroxyphenyl)-4-isopropoxycyclobut-3-ene-1,2-dione (93) At -10 °C, 2-bromophenol (0.5 mL, 4.2 mmol) was added to a solution of *n*BuLi (4.0 mL, 5.4 mmol, 2.7M in hexanes) in ether (95 mL) under N₂ atmosphere. After stirring for 3.5 h, the mixture was cooled to -78 °C then diisopropyl squarate (916 mg, 4.6 mmol) in THF (5 mL) was added via cannula. After stirring for 12 h, the mixture was quenched with 10% NH₄Cl and extracted with EtOAc. The combined organic portions were washed with brine and the solvents were removed under reduced pressure. TFAA (0.75 mL, 5.3 mmol) was added to a residue and pyridine (0.46 mL) in Et₂O (55 mL) at -10 °C. After stirring for 3 h, the reaction was quenched with the addition of H₂O, extracted with ether, washed with brine and dried over MgSO₄. The mixture was filtered and the solvents were removed under reduced pressure. The residue was purified via column chromatography (hexanes:EtOAc, 9:1) to afford **93** (479 mg, 2.06 mmol, 48%) as a colorless oil.

¹H NMR (600 MHz) δ 9.91 (s, 1H), 7.67 (dd, *J* = 7.8 and 1.8 Hz, 1H), 7.41 (dt, *J* = 7.8 and 1.8 Hz, 1H), 7.00 (dd, *J* = 8.4 and 0.6 Hz, 1H), 6.94 (dt, *J* = 7.2 and 0.6 Hz, 1H), 5.68 (sept, *J* = 6.0 Hz, 1H), 1.59 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (150 MHz) δ 196.7 (C), 193.7 (C), 186.0 (C), 173.0 (C), 159.0 (C), 135.7 (CH), 128.8 (CH), 120.2 (CH), 119.0 (CH), 114.7 (C), 81.5 (CH), 23.0 (CH₃), 23.0 (CH₃); IR (neat) 3163, 2917, 1776, 1724, 1554, 1391, 1089, 768 cm⁻¹; HRMS Calcd for C₁₃H₁₃O₄ (M+H⁺): 233.0808 Found: 233.0809.

4-hydroxy-2,3-diisopropoxy-4-(2-methoxyphenyl)cyclobut-2-enone (94) At -80 °C, *n*BuLi (1.85 mL, 5.00 mmol, 2.7 M in) was added to 2-bromoanisole (0.50 mL, 4.21 mmol) in ether (90 mL). After 1.5 h, squarate (970 mg, 4.89 mmol) in THF (5 mL) was added via cannula. After stirring for 12 h, the reaction was quenched with 10% NH₄Cl in H₂O and extracted with EtOAc. The combined organic portions were dried over MgSO₄, filtered, and solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 9:1, 85:15) to afford **94** (1.02 g, 3.32 mmol, 79%) as a yellow oil. ¹H NMR (270 MHz) δ 7.31-7.28 (m, 2H), 6.99-6.93 (m, 2H), 4.97 (s, 1H), 4.92 (sept, *J* = 6.2 Hz, 2H), 3.93 (s, 3H), 1.45 (d, *J* = 6.2 Hz, 6H), 1.40 (d, *J* = 6.2 Hz, 6H), 1.32 (d, *J* = 6.2 Hz, 6H), 1.27 (d, *J* = 6.2 Hz, 6H); ¹³C NMR (67.5 MHz) δ 184.1 (+), 164.1 (+), 157.6 (+), 132.8 (+), 129.6 (-), 127.4 (-), 125.8 (+), 121.3 (-), 112.1 (-), 88.3 (+), 73.4 (-), 56.4 (-), 27.8 (-); IR (neat) 3307, 1747, 1589, 1488, 1386, 1253, 1083, 760 cm⁻¹.

3-isopropoxy-4-(2-methoxyphenyl)cyclobut-3-ene-1,2-dione (96) At -10 °C, 2-bromoanisole (0.5 mL, 4.2 mmol) was added to a solution of *n*BuLi (2.0 mL, 5.4 mmol, 2.7M in hexanes) in ether (80 mL) under N₂ atmosphere. After stirring for 2 h, the reaction was cooled to -78 °C then diisopropyl squarate (888 mg, 4.42 mmol) in THF (5 mL) was added via cannula. After stirring for 2 days, the mixture was quenched with 10% NH₄Cl and extracted with EtOAc. The combined organic portions were washed with brine, dried over MgSO₄, filtered, and then solvents were removed under reduced pressure. TFAA (0.73 mL, 5.2 mmol) was added the reaction residue

and pyridine (0.44 mL) in Et₂O (55 mL) at -10 °C. After stirring for 3 h, the reaction was quenched with H₂O and extracted with ether. The combined organic portions were washed with brine, dried over MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1) to afford **96** (815 mg, 3.30 mmol, 79%) as a yellow solid: mp=79-81 °C; ¹H NMR (600 MHz) δ 8.04 (dd, *J* = 7.8 and 1.6 Hz, 1H), 7.48 (dt, *J* = 7.8 and 1.8 Hz, 1H), 7.05 (dt, *J* = 7.8 and 1.2 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 5.64 (sept, *J* = 6.0 Hz, 1H), 3.90 (s, 3H), 1.51 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (150 MHz) δ 193.5 (C), 193.4 (C), 192.5 (C), 173.4 (C), 157.3 (C), 134.0 (CH), 129.4 (CH), 120.7 (CH), 117.6 (C), 111.4 (CH), 78.9 (CH), 55.4 (CH₃), 23.0 (CH₃), 23.0 (CH₃); IR (neat) 2976, 1776, 1736, 1571, 1389, 1098, 1027 cm⁻¹. HRMS Calcd for C₁₄H₁₅O₄ (M+H⁺): 247.0965 Found: 247.0964.

4-hydroxy-2-(2-hydroxyphenyl)-3-isopropoxy-4-phenylcyclobut-2-enone (97) To a solution of cyclobutendione **93** (150 mg, 0.65 mmol) in THF (25 mL) under N₂ atmosphere, was added PhLi (0.90 mL, 1.35 mmol, 1.5 M in diButylether) at -78 °C. After stirring for 24 h, the reaction was quenched with 10% NH₄Cl in H₂O, extracted with ether and washed with brine. The combined organic portions were dried over MgSO₄, filtered and solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford the desired alcohol **96** (131 mg, 0.42 mmol, 66%). ¹H NMR (600 MHz) δ 9.47 (br s, 1H), 7.57 (dd, *J* = 7.8 and 1.8 Hz, 1H), 7.52-7.50 (m, 2H), 7.39-7.36 (m, 2H), 7.34-7.31 (m, 1H), 7.19 (dt, *J* = 7.8

and 1.8 Hz, 1H), 6.89 (dd, $J = 8.4$ and 1.2 , 1H), 6.85 (dt, $J = 7.8$ and 1.2 Hz, 1H), 4.88 (sept, $J = 6.0$ Hz, 1H), 1.47 (d, $J = 6.0$ Hz, 3H), 1.08 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (150 MHz) δ 189.9 (C), 180.0 (C), 155.3 (C), 135.9 (C), 130.7 (CH), 128.8 (CH), 128.8 (CH), 128.6 (CH), 128.3 (CH), 125.6 (CH), 125.6 (CH), 125.4 (C), 119.7 (CH), 117.7 (CH), 114.8 (C), 91.6 (C), 80.6 (CH), 22.9 (CH₃), 22.4 (CH₃); IR (neat): 3359, 1725, 1622, 1575, 1388, 1081, 735 cm⁻¹. HRMS Calcd for C₁₉H₁₉O₄ (M+H⁺): 311.1283 Found: 311.1278.

4-hydroxy-3-isopropoxy-2-(2-methoxyphenyl)-4-phenylcyclobut-2-enone (99) To a solution of cyclobutendione **96** (201 mg, 0.82 mmol) in THF (35 mL) under N₂ atmosphere was added PhLi (0.78 mL, 1.17 mmol, 1.5 M in diButylether) at -57 °C. After stirring for 5 h, the reaction was quenched with 10% NH₄Cl in H₂O and extracted with EtOAc. The combined organic portions were washed with brine, dried over MgSO₄, filtered and then concentrated under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1) to afford the desired alcohol **99** (169 mg, 0.52 mmol, 64%) as a yellow oil. ^1H NMR (600 MHz) δ 7.61-7.59 (m, 3H), 7.37 (d, $J = 7.2$ Hz, 1H), 7.36 (d, $J = 7.8$ Hz, 1H), 7.31-7.26 (m, 2H), 6.93 (dt, $J = 7.8$ and 0.9 Hz, 1H), 6.90 (d, $J = 8.4$ Hz, 1H), 4.80 (sept, $J = 6.0$ Hz, 1H), 4.73 (br s, 1H), 3.85 (s, 3H), 1.37 (d, $J = 6.0$ Hz, 3H), 1.07 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (150 MHz) δ 188.0 (C), 179.7 (C), 156.9 (C), 137.2 (C), 129.8 (CH), 129.6 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 125.7 (CH), 123.4 (C), 120.5 (CH), 117.8 (C), 111.2 (CH), 92.9 (C), 78.4 (CH), 55.5 (CH₃),

22.7 (CH₃), 22.3 (CH₃); IR (neat) 3308, 2981, 1742, 1616, 1488, 1082, 694 cm⁻¹. HRMS Calcd for C₂₀H₂₁O₄ (M+H⁺): 325.1440 Found: 325.1434.

2-isopropoxy-3-(2-methoxyphenyl)naphthalene-1,4-dione (100) Starting alcohol **99** (78 mg, 0.24 mmol) dissolved in xylenes (5 mL) was placed in a pressure tube and then the reaction vessel was submerged in a 150 °C oil bath. The mixture was stirred for 24 h then the solvent was removed under reduced pressure. The resulting mixture was purified by column chromatography (hexanes:EtOAc, 9:1) to afford the naphthoquinone **100** (60 mg, 0.19 mmol, 78%). ¹H NMR (600 MHz) δ 8.13-8.10 (m, 2H), 7.72 (q, *J* = 1.8 Hz, 2H), 7.40-7.37 (m, 1H), 7.17 (dd, *J* = 7.2 and 1.8 Hz, 1H), 7.02 (dt, *J* = 7.2 and 0.9 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 4.69 (sept, *J* = 6.0 Hz, 1H), 3.76 (s, 3H), 1.18 (d, *J* = 6.0 Hz, 3H), 1.06 (d, *J* = 6.0 Hz, 3H) ¹³C NMR (150 MHz) δ 184.1 (C), 182.4 (C), 157.1 (C), 156.6 (C), 133.8 (CH), 133.1 (CH), 132.6 (C), 132.3 (C), 131.6 (C), 131.1 (CH), 130.0 (CH), 126.5 (CH), 126.2 (CH), 121.1 (C), 120.3 (CH), 110.9 (CH), 76.3 (CH), 55.6 (CH₃), 22.8 (CH₃), 22.5 (CH₃); IR (neat) 2932, 1667, 1594, 1491, 1245, 998 cm⁻¹; HRMS Calcd for C₂₀H₁₉O₄ (M+H⁺): 323.1278. Found 323.1278.

3-(2-bromophenyl)-4-isopropoxycyclobut-3-ene-1,2-dione (104) At 0 °C, TFAA (0.6 mL, 4.33 mmol) was added to a solution of **49** (1.25 g, 3.52 mmol), and pyridine (0.35 mL, 4.33 mmol) in

ether (53 mL). After stirring for 1h, the mixture was quenched with H₂O and extracted with EtOAc. The combined organic portions were dried over MgSO₄, filtered and solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 9:1, 85:15) to afford **104** (1.04 g, 3.54 mmol, 99%) as a yellow oil. ¹H NMR (600 MHz) δ 7.70 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.66 (dd, *J* = 7.8 and 1.8 Hz, 1H), 7.43 (dt, *J* = 7.2 and 1.2 Hz, 1H), 7.33 (dt, *J* = 7.8 and 1.8 Hz, 1H), 5.64 (sept, *J* = 6.0 Hz, 1H), 1.56 (d, *J* = 6.0 Hz, 6H) ¹³C NMR (150 MHz) 194.6 (C), 194.0 (C), 191.4 (C), 176.0 (C), 134.0 (CH), 132.6 (CH), 130.0 (CH), 129.2 (C), 127.6 (CH), 122.0 (C), 80.6 (CH), 23.1 (CH₃), 23.1 (CH₃). IR (neat): 2986, 1784, 1756, 1599, 1578, 1388 cm⁻¹. HRMS Calcd for C₁₃H₁₂BrO₃ (M+H⁺): 294.9964 Found: 294.9965.

2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-phenylcyclobut-2-enone (105) At -65 °C PhMgCl (0.6 mL, 0.96 mmol, 1.6 M in THF) was added to a solution of cyclobutendione **104** (270 mg, 0.92 mmol) in THF (20 mL) under N₂ atmosphere. After stirring overnight, the reaction was warmed to -45 °C and was stirred for an additional 2 h. The reaction was quenched with 10% NH₄Cl and extracted with EtOAc. The combined organic portions were washed with brine and dried over MgSO₄, then filtered and solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 8:2, 7:3) to afford the alcohol **105** (280 mg, 0.75 mmol, 82%). ¹H NMR (270 MHz) δ 7.69-7.60 (m, 3H), 7.50-7.16 (m, 6H), 4.81 (sept, *J* = 6.2 Hz, 1H), 4.42 (br s, 1H), 1.38 (d, *J* = 6.2 Hz, 3H), 1.11

(d, $J = 6.2$ Hz, 3H); IR (neat) 3353, 2982, 1755, 1654, 1319 cm^{-1} ; HRMS Calcd for $\text{C}_{19}\text{H}_{18}\text{BrO}_3$ ($\text{M}+\text{H}^+$): 373.0434 Found: 373.0435.

2-(2-bromophenyl)-3-isopropoxynaphthalene-1,4-dione (106) Starting alcohol **105** (200 mg, 0.54 mmol) dissolved in toluene (10 mL) was placed in a pressure tube, then the reaction vessel was sealed then submerged in a 125 °C oil bath. The mixture was stirred for 30 min then the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 7:3) to afford **106** (194 mg, 0.52 mmol, 98%) as a yellow-orange solid. ^1H NMR (600 MHz) δ 8.11 (d, $J = 8.4$ Hz, 2H), 7.75-7.70 (m, 2H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.38 (t, $J = 7.2$ Hz, 1H), 7.27-7.23 (m, 2H), 4.90 (sept, $J = 6.0$ Hz, 1H), 1.20 (d, $J = 6.0$ Hz, 3H), 1.12 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (150 MHz) δ 183.3 (C), 182.1 (C), 156.4 (C), 134.0 (CH), 133.7 (C), 133.3 (C), 133.3 (CH), 132.1 (CH), 131.8 (C), 131.4 (C), 131.4 (CH), 129.7 (CH), 126.8 (CH), 126.5 (CH), 126.2 (CH), 123.7 (C), 76.8 (CH), 22.9 (CH_3), 22.8 (CH_3). IR (neat) 2980, 1670, 1595, 1330, 1201, 997, 721; HRMS Calcd for $\text{C}_{19}\text{H}_{16}\text{BrO}_3$ ($\text{M}+\text{H}^+$): 371.0277 Found: 371.0277.

2-amino-3-(2-bromophenyl)naphthalene-1,4-dione (109) To a round bottom flask containing naphthoquinone **106** (194 mg, 0.52 mmol) was added 30% NH₄OH (30 mL) followed by MeOH (8 mL). The mixture was stirred for 3 days and was quenched with 10% NH₄Cl and extracted with EtOAc. The combined organic portions were washed with brine, dried over MgSO₄, filtered and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 8:2, 7:3) to afford the amine **109** (104 mg, 0.32 mmol, 62%) as a red-orange solid. ¹H NMR (600 MHz) δ 8.16 (dd, *J* = 7.8 and 1.2 Hz, 1H), 8.12 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.75 (dt, *J* = 7.8 and 1.2 Hz, 1H), 7.73 (dd, *J* = 8.4 and 1.2 Hz, 1H), 7.67 (dt, *J* = 7.8 and 1.2 Hz, 1H), 7.43 (dt, *J* = 7.8 and 1.2 Hz, 1H), 7.30-7.27 (m, 2H), 5.03 (br s, 2H); ¹³C NMR (150 MHz) δ 181.5 (+), 180.9 (+), 145.1 (+), 134.8, (-), 133.6 (+), 133.4 (-), 133.2 (+), 132.3 (-), 132.0 (-), 130.5 (+), 130.1 (-), 128.0 (-), 126.7 (-), 126.0 (-), 124.7(+), 116.9 (+); IR (neat) 3476, 3337, 1683, 1605, 1567, 1351, 757 cm⁻¹; HRMS Calcd for C₁₆H₁₁BrNO₃ (M+H⁺): 327.9968 Found: 327.9968.

5H-benzo[b]carbazole-6,11-dione (110) To a pressure tube was added **109** (150 mg, 0.46 mmol), CuI (14 mg, 0.074 mmol), K₂CO₃ (130 mg, 0.94 mmol), and pipecolinic acid (12 mg, 0.093 mmol) in DMF (1 mL). The reaction vessel was sealed then submerged in a 100 °C oil bath. After stirring for 12 h, the mixture was diluted with EtOAc and filtered through celite. The solvents were removed under reduced pressure and the residue was purified by column chromatography (hexanes:EtOAc, 8:2) to afford **110** (65 mg, 0.27 mmol, 59%) as an orange

solid. ^1H NMR in DMSO (600 MHz) δ 8.17 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 8.05 (d, J = 7.8 Hz, 1H), 7.81 (t, J = 7.2 Hz, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.57, (d, J = 7.8 Hz, 1H), 7.39 (dt, J = 7.2 and 1.2 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H); ^{13}C NMR (67.5 MHz) δ 180.3 (+), 177.5 (+), 138.2 (+), 137.1 (+), 134.2 (-), 134.0 (+), 133.1 (-), 132.6 (+), 126.9 (-), 126.0 (-), 125.9 (-), 124.0 (-), 122.3 (-), 117.4 (+), 113.8 (-); IR (neat) 3261, 1645, 1520, 1397, 1212, 753 cm^{-1} , HRMS calcd for $\text{C}_{16}\text{H}_{10}\text{NO}_2(\text{M}+\text{H}^+)$: 248.0706 Found: 248.0706.

2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-(4-methoxyphenyl)cyclobut-2-enone (111) At -75 °C 4-anisylmagnesium bromide (1.6 mL, 0.80 mmol, 5 M in THF) was added to **104** (215 mg, 0.73 mmol) dissolved in THF (18 mL). After stirring for 48 h, the reaction was quenched with 10% NH_4Cl in H_2O and extracted with EtOAc. The combined organic portions were washed with brine, dried over MgSO_4 , filtered and then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1, 85:15, 8:2) to afford **111** (179 mg, 0.44 mmol, 61%) as a colorless oil: ^1H NMR (270 MHz) δ 7.63-7.55 (m, 2H), 7.47 (dd, J = 7.4 and 1.2 Hz, 1H), 7.32 (dt, J = 7.4 and 1.2 Hz, 1H), 7.20 (dt, J = 7.9 and 1.7 Hz, 1H), 6.96-6.93 (m, 2H), 4.80 (sept, J = 6.2 Hz, 1H), 3.83 (s, 3H), 1.39 (d, J = 6.2, 3H), 1.14 (d, J = 6.2 Hz, 3H); ^{13}C NMR (67.5 MHz) 188.2 (+), 180.9 (+), 159.5 (+), 132.9 (-), 131.0 (-), 129.8 (+), 129.5 (-), 128.6 (+), 127.1 (-), 125.3 (+), 122.4 (+), 114.0 (-), 92.6 (+), 79.2 (-), 55.2 (-), 22.7 (-), 22.4 (-).

3-(2-bromophenyl)-2-isopropoxy-6-methoxynaphthalene-1,4-dione (**112**)

Hydroxycyclobutenone **111** (44 mg, 0.11 mmol) dissolved in xylenes (5 mL) was placed in a pressure tube and then the reaction vessel was sealed then submerged in a 136 °C oil bath. After stirring for 3h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes :EtOAc, 9:1) to afford the naphthoquinone **112** (43 mg, 0.11 mmol, 100%) as an orange oil: ^1H NMR (600 MHz) δ 8.07 (d, J = 9.0 Hz, 1H), 7.66 (dd, J = 8.4 and 1.2 Hz, 1 H), 7.57 (d, J = 2.4 Hz), 7.38 (dt, J = 7.2 and 1.2 Hz, 1H), 7.26 (dt, J = 7.8 and 1.8 Hz, 1H), 7.22 (dd, J = 7.2 and 1.2 Hz, 1H), 7.20 (dd, J = 9.0 and 1.8 Hz, 1H), 4.92 (sept, J = 6.0 Hz, 1H), 3.95 (s, 3H), 1.20 (d, J = 6.0 Hz, 3H), 1.11 (d, J = 6.2 Hz, 3H), ^{13}C NMR (150 MHz) δ 183.5 (C), 181.2 (C), 164.5 (C), 156.9 (C), 134.2 (C), 133.6 (C), 133.4 (C), 132.4 (CH), 131.5 (CH), 129.7 (CH), 128.9 (CH), 126.9 (CH), 125.1 (C), 123.9 (C), 120.0 (CH), 110.0 (CH), 76.9 (CH), 56.0 (CH), 23.0 (CH₃), 23.0 (CH₃), IR (neat) 2930, 1667, 1594, 1318, 1239, 1006, 751 cm⁻¹, HRMS Calcd for C₂₀H₁₈BrO₄ (M+H⁺):401.0383, Found:401.0385.

2-amino-3-(2-bromophenyl)-6-methoxynaphthalene-1,4-dione (113**)** To a round bottom flask containing isopropyl naphthoquinone **112** (1.10g, 2.75 mmol), was added 30% NH₄OH (30 mL)

followed by MeOH (30mL). The mixture was stirred for 2 days and was quenched with 10% NH₄Cl and extracted with EtOAc. The combined organic portions were washed with brine then dried over MgSO₄, filtered and the solvents were removed under reduced pressure. The compound was purified by column chromatography (Hexanes:EtOAc in the order of elution, 85:15, 8;2) to afford the amine **113** (575 mg, 1.6 mmol, 58%). ¹H NMR (600 MHz) δ 8.06 (d, *J* = 8.4, 1H), 7.72 (dd, *J* = 8.4 and 1.2, 1H), 7.62 (d, *J* = 3.0, 1H), 7.42 (dt, *J* = 7.8 and 1.2, 1H), 7.29-7.26 (m, 2H), 7.11 (dd, *J* = 8.4 and 3.0, 1H), 3.95 (s, 3H) ¹³C NMR (150 MHz) δ 180.6 (C), 180.2 (C), 165.1 (C), 145.5 (C), 135.8 (C), 133.8 (C), 133.3 (CH), 132.0 (CH), 130.0 (CH), 128.8 (CH), 128.0 (CH), 124.8 (C), 123.9 (C), 118.7 (CH), 116.4 (C), 110.5 (CH), 55.9 (CH₃); IR (neat) 3315, 1675, 1556, 1340, 1262, 750 cm⁻¹; HRMS Calcd for C₁₇H₁₃BrNO₃ (M+H⁺): 358.0078 Found: 358.0073.

9-methoxy-5H-benzo[b]carbazole-6,11-dione (114) **113** (49 mg, .14 mmol), CuI (2.7 mg, .014 mmol), pipecolic acid (3.6 mg, 0.028 mmol), and K₂CO₃ (39 mg, 0.282 mmol) in DMF (0.2 mL) were added to a pressure tube then the reaction vessel was sealed then submerged in a 110 °C oil bath. After stirring for 24 h, the mixture filtered with through celite, washing with EtOAc The solvent was the removed under reduced pressure and the residue was purified by column chromatography (hexanes:EtOAc, 8:2) to afford the desired carbazolequinone **114** (22 mg, 0.08 mmol, 58%). ¹H NMR (600 MHz, DMSO) δ 13.01 (br s, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 3.0 Hz, 1H), 7.43 (dt, *J* = 8.4 and 1.2 Hz, 1H), 7.36

(dt, $J = 7.8$ and 0.6 Hz, 1H), 7.29 (dd, $J = 8.4$ and 3.0 , 1H), 3.95 (s, 3H) ^{13}C NMR (150 MHz, DMSO) δ 180.6, 177.4, 164.7, 138.7, 138.3, 137.2, 129.4, 127.4, 126.5, 124.7, 124.6, 122.9, 118.7, 117.9, 114.5, 111.8, 56.6; IR (neat): 3217, 2922, 1656, 1585, 1394, 1257, 1017, 756 cm^{-1} , HRMS Calcd for $\text{C}_{17}\text{H}_{12}\text{NO}_3$ ($\text{M}+\text{H}^+$): 278.0812 Found: 278.0812

2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-(2-methoxyphenyl)cyclobut-2-enone (115) At $-78\text{ }^{\circ}\text{C}$. 2-anisylmagnesium bromide (1.6 mL, 1.12 mmol, 0.7 M in THF) was added to **104** (301 mg, 1.02 mmol) dissolved in THF (35 mL) under N_2 atmosphere. After stirring for 1h, the reaction was quenched with 10% NH_4Cl in H_2O and extracted with EtOAc. The combined organic portions were washed with brine, dried over MgSO_4 , filtered and then the solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 9:1, 85:15) to afford the alcohol **115** (397 mg, 0.98 mmol, 97%) as a colorless oil: ^1H NMR (600 MHz) δ 7.56 (dd, $J = 8.4$ and 0.9 Hz, 1H); 7.53 (dd, $J = 7.8$ and 1.2 Hz, 1H), 7.47 (dd, $J = 7.8$ and 1.8 Hz, 1H), 7.3-7.26 (m, 2H) 7.14 (dt, $J = 7.8$ and 1.8 Hz, 1H), 6.99 (dt, $J = 7.8$ and 0.9 Hz, 1H), 6.94 (d, $J = 7.8$, 1H), 5.44 (s, 1H), 4.83 (sept, $J = 6.0$ Hz, 1H), 3.86 (s, 3H), 1.38 (d, $J = 6.0$ Hz, 3H), 1.22 (d, $J = 6.0$ Hz, 3H) ^{13}C NMR (150 MHz) 180.9 (C), 179.2 (C), 157.1 (C), 132.7 (CH), 130.7 (CH), 129.7 (CH), 129.6 (CH), 129.5 (C), 127.6 (CH), 126.9 (CH), 124.5 (C), 124.3 (C), 122.3 (C), 121.1 (CH), 111.7 (CH), 93.168 (C), 78.6 (CH), 55.9 (CH_3), 22.4 (CH_3), 22.0 (CH_3); δ IR (neat) 3339, 2982, 1743, 1615, 1578, 1384, 1058 cm^{-1} .

2-(2-bromophenyl)-3-isopropoxy-5-methoxynaphthalene-1,4-dione (116) The arylalcohol **115** (390 mg, 0.97 mmol) was dissolved in xylenes (10 mL) and transferred to a pressure tube. Then the reaction vessel was sealed then submerged in a 150 °C oil bath. After stirring for 5h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc, 9:1) to afford **116** (245 mg, 0.61 mmol, 63%) as an orange oil: ¹H NMR (600 MHz) δ 7.77 (dd, 7.8 and 0.9 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.64 (dt, *J* = 8.4 and 0.9 Hz, 1H), 7.36 (dt, *J* = 7.2 and 1.2 Hz, 1H), 7.29-7.22 (m, 3H), 4.88 (sept, *J* = 6.0 Hz, 1H), 4.01 (s, 3H), 1.21 (d, *J* = 6.0 Hz, 3H), 1.11 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (150 MHz) δ 183.3 (C), 180.7 (C), 159.5 (C), 157.5 (C), 135.1 (CH), 134.2 (C), 133.2 (C), 132.2 (CH), 131.6 (C), 131.4 (CH), 129.5 (CH), 126.8 (CH), 123.7 (C), 119.4 (C), 119.1 (CH), 117.2 (CH), 76.7 (CH), 56.4 (CH₃), 22.9 (CH₃), 22.8 (CH₃); IR (neat) 2979, 1665, 1583, 1282, 1187, 999 cm⁻¹; HRMS Calcd for C₂₀H₁₈BrNO₄ (M+H⁺): 401.0383 Found: 401.0388.

3-amino-2-(2-bromophenyl)-5-methoxynaphthalene-1,4-dione (117) To a round bottom flask containing **116** (123 mg, 0.31 mmol) was added 30% NH₄OH (20 mL) followed by MeOH (2 mL).

The mixture was stirred for 3 days and was quenched with 10% NH₄Cl and extracted with EtOAc. The combined organic portions were washed with brine, dried over MgSO₄, filtered and then solvents were removed under reduced pressure. The residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 9:1, 85:15) to afford the amine **117** (52 mg, 0.15 mmol, 48%) as a red-orange solid. ¹H NMR (600 MHz) δ 7.84 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.71 (dd, *J* = 7.8 and 1.2 Hz, 1H) 7.69 (dd, *J* = 7.8 and 0.6, 1H), 7.42 (dt, *J* = and 1.2 Hz, 1H), 7.29-7.26 (m, 2H) 7.23 (dd, *J* = 8.4 and 1.2 Hz, 1H) 4.04 (s, 3H); ¹³C NMR (150 MHz) δ 180.4 (C), 179.8 (C), 160.0 (C), 146.1 (C), 136.0 (CH), 135.6 (C), 133.8 (C), 133.3 (CH), 132.1 (CH), 130.0 (CH), 128.0 (CH), 124.8 (C), 119.6 (CH) 118.3 (C), 116.1 (CH), 115.3 (C), 56.3 (CH₃); IR (neat) 3447, 3340, 1610, 1574, 1471, 749 cm⁻¹; HRMS Calcd for C₁₇H₁₃BrNO₃ (M+H⁺): 358.0073 Found: 358.0073.

7-methoxy-5H-benzo[b]carbazole-6,11-dione (118) To a pressure tube was added **117** (15 mg, 0.042 mmol), CuI (1 mg, 0.0053 mmol), K₂CO₃ (12 mg, 0.087 mmol), and pipercolinic acid (1 mg, 0.0078 mmol) in DMF (1 mL). The reaction vessel was sealed then submerged in a 110 °C oil bath. After stirring for 12 h, the mixture was diluted with EtOAc and filtered through celite. The solvents were removed under reduced pressure and the residue was purified by column chromatography (hexanes:EtOAc in the order of elution, 95:5, 9:1, 85:15, 8:2) to afford **118** (5 mg, 0.0018 mmol, 43%) as an orange solid. ¹H NMR in DMSO (600 MHz) δ 12.8 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 1H), 7.79 (t, *J* = 8.4 Hz, 1H), 7.78 (dd, *J* = 7.8 and 1.2 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H),

7.53 (dd, $J = 7.8$ and 1.2 Hz, 1H), 7.42 (dt, $J = 7.2$ and 1.2 Hz, 1H), 7.34 (dt, $J = 7.2$ and 1.2 Hz, 1H) 3.97 (s, 3H); ^{13}C NMR (150 MHz) δ 180.4 (C), 177.5 (C), 160 (C), 139.4 (C), 138.4 (C), 137.2 (C), 136.2 (CH), 127.1 (CH), 124.4 (CH), 124.3 (C), 122.9 (CH), 120.2 (C), 119.5 (CH), 119.2 (CH), 116.2 (CH), 114.4 (CH), 57.1 (C); IR (neat) 3242, 1646, 1584, 1235, 1019, 741 cm^{-1} , HRMS calcd for $\text{C}_{17}\text{H}_{12}\text{NO}_3$ ($\text{M}+\text{H}^+$): 278.0812 Found: 278.0812.

2-(2-bromophenyl)-3-hydroxynaphthalene-1,4-dione (119) To a solution of **106** (43 mg, 0.12 mmol) in methylene chloride (4 mL) was added BBr_3 (0.11 mL, 0.11 mmol). After stirring for 2 h, the reaction was quenched with H_2O , and extracted with methylene chloride. The combined organic portions were dried over MgSO_4 , filtered and then the solvent was removed under reduced pressure. (**119**) ^1H NMR (600 MHz) δ 8.20 (dd, $J = 7.8$ and 0.6 Hz, 1H), 8.18 (dd, $J = 7.8$ and 1.2 Hz, 1H), 7.83 (dt, $J = 7.8$ and 1.2 Hz, 1H), 7.76 (dt, $J = 7.8$ and 1.2 Hz, 1H), 7.69 (dd, $J = 7.8$ and 1.2 Hz, 1H), 7.41 (dt, $J = 7.8$ and 1.2 Hz, 1H), 7.29 (dt, $J = 7.8$ and 1.8 Hz, 1H), 7.27 (dd, $J = 7.2$ and 1.2 Hz, 1H); ^{13}C NMR δ 182.7 (C), 181.6 (C), 152.7 (C), 135.4 (CH), 133.2 (CH), 132.8 (C), 132.8 (CH), 131.9 (C), 131.5 (CH), 130.2 (CH), 129.4 (C), 127.3 (CH), 127.2 (CH), 126.4 (CH), 123.9 (C), 122.7 (C); IR(neat) 3229, 1674, 1640, 1595, 1364, 1004, 726 cm^{-1} ; HRMS Calcd for $\text{C}_{16}\text{H}_{10}\text{BrO}_3$ ($\text{M}+\text{H}^+$): 328.9808 Found: 328.9809.

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Appendix

^{13}C NMR tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)phenylcarbamate (5)

¹H NMR tert-Butyl 1,4-dihydro-2,3-diisopropoxy-1,4-dioxonaphthalen-5-ylcarbamate (6)

¹³C NMR tert-Butyl 1,4-dihydro-2,3-diisopropoxy-1,4-dioxonaphthalen-5-ylcarbamate (6)

¹H NMR tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-6-methoxyphenylcarbamate (10)

¹³C NMR tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-6-methoxyphenylcarbamate (10)

¹H NMR tert-Butyl 3-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-2-methoxyphenylcarbamate(11)

¹³C NMR tert-Butyl 3-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-2-methoxyphenylcarbamate(11)

¹H NMR tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-5-methoxyphenylcarbamate (12)

¹H NMR tert-Butyl 2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-3-methoxyphenylcarbamate (14)

¹H NMR tert-Butyl 3-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)-4-methoxyphenylcarbamate (16)

¹H NMR tert-Butyl 1,4-dihydro-2,3-diisopropoxy-5-methoxy-1,4-dioxonaphthalen-6-ylcarbamate (18)

¹H NMR tert-Butyl 1,4-dihydro-2,3-diisopropoxy-6-methoxy-1,4-dioxonaphthalen-8-ylcarbamate (19)

¹H NMR tert-Butyl 1,4-dihydro-2,3-diisopropoxy-5-methoxy-1,4-dioxonaphthalen-8-ylcarbamate (20)

¹³C NMR tert-Butyl 1,4-dihydro-2,3-diisopropoxy-5-methoxy-1,4-dioxonaphthalen-8-ylcarbamate (20)

^1H NMR tert-Butyl 5,8-dihydro-6,7-diisopropoxy-5,8-dioxoquinolin-4-ylcarbamate (27)

^{13}C NMR tert-Butyl 5,8-dihydro-6,7-diisopropoxy-5,8-dioxoquinolin-4-ylcarbamate (27)

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11/2004

¹H NMR N-(2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)phenyl)pivalamide (36)

¹³C NMR N-(2-(1-hydroxy-2,3-diisopropoxy-4-oxocyclobut-2-enyl)phenyl)pivalamide (36)

¹H NMR N-(1,4-dihydro-2,3-diisopropoxy-1,4-dioxonaphthalen-5-yl)pivalamide (37)

¹H NMR N-(1,4-dihydro-2-hydroxy-3-isopropoxy-1,4-dioxonaphthalen-5-yl)pivalamide (38)

¹³C NMR N-(1,4-dihydro-2-hydroxy-3-isopropoxy-1,4-dioxonaphthalen-5-yl)pivalamide (38)

¹H NMR 4-hydroxy-2,3-diisopropoxy-4-(2-nitrophenyl)cyclobut-2-enone (39)

^{13}C NMR 4-hydroxy-2,3-diisopropoxy-4-(2-nitrophenyl)cyclobut-2-enone (39)

¹H NMR ,3-diisopropyl-1-hydroxy-4(1H)-quinolinone (40)

^{13}C NMR ,3-diisopropyl-1-hydroxy-4(1H)-quinolinone (40)

¹H NMR 4-(2-bromophenyl)-4-hydroxy-2,3-diisopropoxycyclobut-2-enone (49)

^{13}C NMR 4-(2-bromophenyl)-4-hydroxy-2,3-diisopropoxycyclobut-2-enone (49)

KDF-375-I-1-h1
 Archive directory: /export/home/vnmr1/vnmrsys/data
 Sample directory:
 File: PROTON
 Pulse sequence: s2pu1

¹H NMR 5-bromo-2,3-diisopropoxynaphthalene-1,4-dione (50)

¹³C NMR 5-bromo-2,3-diisopropoxynaphthalene-1,4-dione (50)

¹H NMR tert-Butyl 2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenylcarbamate (61)

¹³C NMR tert-Butyl 2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenylcarbamate (61)

STANDARD PROTON PARAMETERS

Archive directory: /export/home/vnmr1/vnmrsys/data
 Sample directory: /
 File: 00000000

HETCOR tert-Butyl 2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenylcarbamate (61)

^1H NMR N-(2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenyl)pivalamide (62)

KDF-111-I-2-C13

Pulse Sequence: s2pul

¹³C NMR N-(2-(2-isopropoxy-3,4-dioxocyclobut-1-enyl)phenyl)pivalamide (62)

¹H NMR tert-Butyl 2-(3-hydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenylcarbamate (63)

^{13}C NMR tert-Butyl 2-(3-hydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenylcarbamate (63)

¹H NMR N-(2-(3-hydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenyl)pivalamide (64)

¹³C NMR N-(2-(3-hydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenyl)pivalamide (64)

¹H NMR N-(2-(3-Trimethylsilylhydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenyl)pivalamide (65)

¹H NMR tert-Butyl 2-(3-Trimethylsilylhydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenylcarbamate (66)

¹³C NMR tert-Butyl 2-(3-Trimethylsilylhydroxy-2-isopropoxy-4-oxo-3-phenylcyclobut-1-enyl)phenylcarbamate (66)

¹H NMR 3-(2-trimethylsilylhydroxy-1-isopropoxy-2-phenylethylidene)-1-(pivaloyl)indolin-2-one (67)

¹H NMR tert-Butyl 3-(2-Trimethylsilylhydroxy-1-isopropoxy-2-phenylethylidene)-2-oxoindoline-1-carboxylate (68)

¹³C NMR tert-Butyl 3-(2-Trimethylsilylhydroxy-1-isopropoxy-2-phenylethylidene)-2-oxoindoline-1-carboxylate (68)

STANDARD CARBON PARAMETERS

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:
File: PROTON

Pulse Sequence: hetcor

Solvent: CDCl3
Temp. 28.0 C / 301.1 K
User: 1-14-87
INOVA-600 "Inova600"

Relax. delay 1.000 sec
Acq. time 0.150 sec
Width 27275.8 Hz
F2 Width 5126.6 Hz
F2 repetitions

13C repetitions
OBSERVE C13, 150.7863875 MHz
DECOUPLE H1, 599.6894076 MHz

Power 40 dB
on during acquisition
off during delay
WALTZ-16 modulated

DATA PROCESSING
Gauss window 0.100 sec
Gauss order 2
F1 DATA PROCESSING
Gauss window 0.044 sec
center at 0.014 sec
FT size 4096 x 1024
Total time 2 hr, 46 min, 57 sec

HETCOR tert-Butyl 3-(2-Trimethylsilylhydroxy-1-isopropoxy-2-phenylethylidene)-2-oxoindoline-1-carboxylate (68)

¹H NMR 3-(2-phenyl-ethan-2-one)-1-(pivaloyl)indolin-2-one (74)

¹³C NMR 3-(2-phenyl-ethan-2-one)-1-(pivaloyl)indolin-2-one (74)

¹H NMR 3-(2-phenyl-ethan-2-one)-indolin-2-one (75)

¹³C NMR 3-(2-phenyl-ethan-2-one)-indolin-2-one (75)

¹H NMR 3-(1-isopropoxy-2-oxo-2-phenylethylidene)-1-(pivaloyl)indolin-2-one (76)

¹³C NMR 3-(1-isopropoxy-2-oxo-2-phenylethylidene)-1-(pivaloyl)indolin-2-one (76)

¹H NMR N-(2-(3-hydroxy-2-isopropoxy-3-(4-methoxyphenyl)-4-oxocyclobut-1-enyl)phenyl)pivalamide (77)

¹³C NMR N-(2-(3-hydroxy-2-isopropoxy-3-(4-methoxyphenyl)-4-oxocyclobut-1-enyl)phenyl)pivalamide (77)

¹³C NMR 3-(1-isopropoxy-2-(4-methoxyphenyl)-2-oxoethylidene)indolin-2-one (78)

¹H NMR 3-isopropoxy-4-(2-nitrophenyl)cyclobut-3-ene-1,2-dione (81)

¹³C NMR 3-isopropoxy-4-(2-nitrophenyl)cyclobut-3-ene-1,2-dione (81)

¹H NMR 4-hydroxy-3-isopropoxy-2-(2-nitrophenyl)-4-phenylcyclobut-2-enone (82)

¹H NMR 2-(benzo[c]isoxazol-3-yl)-2-isopropoxy-1-phenylvinyl acetate (85)

¹³C NMR 2-(benzo[c]isoxazol-3-yl)-2-isopropoxy-1-phenylvinyl acetate (85)

¹H NMR 3-(2-hydroxyphenyl)-4-isopropoxycyclobut-3-ene-1,2-dione (93)

¹³C NMR 3-(2-hydroxyphenyl)-4-isopropoxycyclobut-3-ene-1,2-dione (93)

¹H NMR 4-hydroxy-2,3-diisopropoxy-4-(2-methoxyphenyl)cyclobut-2-enone (94)

¹³C NMR 4-hydroxy-2,3-diisopropoxy-4-(2-methoxyphenyl)cyclobut-2-enone (94)

¹H NMR 3-isopropoxy-4-(2-methoxyphenyl)cyclobut-3-ene-1,2-dione (96)

¹³C NMR 3-isopropoxy-4-(2-methoxyphenyl)cyclobut-3-ene-1,2-dione (96)

KDF-357-I-1
 Archive directory: /export/home/vnmr1/vnmrsys/data
 Sample directory:
 Pulse Sequence: s2pu1

¹H NMR 4-hydroxy-2-(2-hydroxyphenyl)-3-isopropoxy-4-phenylcyclobut-2-enone (97)

¹³C NMR 4-hydroxy-2-(2-hydroxyphenyl)-3-isopropoxy-4-phenylcyclobut-2-enone (97)

¹³C NMR 4-hydroxy-3-isopropoxy-2-(2-methoxyphenyl)-4-phenylcyclobut-2-enone (99)

¹H NMR 2-isopropoxy-3-(2-methoxyphenyl)naphthalene-1,4-dione (100)

¹³C NMR 2-isopropoxy-3-(2-methoxyphenyl)naphthalene-1,4-dione (100)

¹³C NMR 3-(2-bromophenyl)-4-isopropoxycyclobut-3-ene-1,2-dione (104)

¹H NMR 2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-phenylcyclobut-2-enone (105)

KDF-289-2-III-1
 Archive directory: /export/home/vnari/vnmrSYS/data
 Sample directory:
 File: PROTON
 Pulse Sequence: s2pul

¹H NMR 2-(2-bromophenyl)-3-isopropoxynaphthalene-1,4-dione (106)

¹³C NMR 2-(2-bromophenyl)-3-isopropoxynaphthalene-1,4-dione (106)

KDF-290-I-3
Archive directory: /export/home/vnmr1/vnmrsys
Sample directory:
File: PROTON
Pulse Sequence: s2pu1

¹H NMR 2-amino-3-(2-bromophenyl)naphthalene-1,4-dione (109)

¹³C NMR 2-amino-3-(2-bromophenyl)naphthalene-1,4-dione (109)

¹H NMR 5H-benzo[b]carbazole-6,11-dione (110)

¹³C NMR 5H-benzo[b]carbazole-6,11-dione (110)

¹H NMR 2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-(4-methoxyphenyl)cyclobut-2-enone (111)

^{13}C NMR 2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-(4-methoxyphenyl)cyclobut-2-enone (111)

¹H NMR 3-(2-bromophenyl)-2-isopropoxy-6-methoxynaphthalene-1,4-dione (112)

¹³C NMR 3-(2-bromophenyl)-2-isopropoxy-6-methoxynaphthalene-1,4-dione (112)

¹H NMR 2-amino-3-(2-bromophenyl)-6-methoxynaphthalene-1,4-dione (113)

KDF-bromoaminomethoxynaphthoquinone

¹³C NMR 2-amino-3-(2-bromophenyl)-6-methoxynaphthalene-1,4-dione (113)

¹³C NMR 9-methoxy-5H-benzo[b]carbazole-6,11-dione (114)

¹H NMR 2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-(2-methoxyphenyl)cyclobut-2-enone (115)

¹³C NMR 2-(2-bromophenyl)-4-hydroxy-3-isopropoxy-4-(2-methoxyphenyl)cyclobut-2-enone (115)

¹H NMR 2-(2-bromophenyl)-3-isopropoxy-5-methoxynaphthalene-1,4-dione (116)

¹³C NMR 2-(2-bromophenyl)-3-isopropoxy-5-methoxynaphthalene-1,4-dione (116)

¹H NMR 3-amino-2-(2-bromophenyl)-5-methoxynaphthalene-1,4-dione (117)

¹³C NMR 3-amino-2-(2-bromophenyl)-5-methoxynaphthalene-1,4-dione (117)

¹H NMR 7-methoxy-5H-benzo[b]carbazole-6,11-dione (118)

KDF-289-2-III-3-h1
Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pu1

¹H NMR 2-(2-bromophenyl)-3-hydroxynaphthalene-1,4-dione (119)

¹³C NMR 2-(2-bromophenyl)-3-hydroxynaphthalene-1,4-dione (119)

KDF-289-2-III-3-c13
Pulse Sequence: s2pul