EXPLORATIONS OF CASCADING MICHAEL ADDITIONS

by

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DISSERTATION ABSTRACT

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Intramolecular cascading Michael additions have the ability to transform simple, symmetric substrates into densely functionalized compounds containing new ring structures and chiral centers. The Rauhut-Currier (RC) reaction, also known as the vinylogous Morita-Baylis-Hillman reaction, utilizes this type of reactivity by cyclizing tethered, activated alkenes using phosphine or thiolate catalysis. This dissertation describes the expansion of the scope of the RC reaction, the introduction and importance of co-catalysts to cascading Michael additions, the development of the first amine-catalyzed RC reaction, and the transformation of cyclization products into fused, polycyclic aromatic compounds.

Chapter I reviews the development and applications of the Rauhut-Currier reaction. Chapter II describes the regioselective synthesis of di-substituted indenes and introduces phenol as a rate- and selectivity-enhancing co-catalyst. Although tertiary amine nucleophiles were found to be inferior to phosphines as cyclization catalysts, chapter III discusses the ability of unhindered primary and secondary amines to undergo a diastereoselective, cascading aza-Michael-Michael addition to yield a wide variety of amino-indanes in the presence of an acid catalyst. Recognizing the importance of protic

environments and small nucleophiles, the development of the first amine-catalyzed intramolecular RC is introduced in chapter IV.

Chapter V describes the conversion of methyl ketone-substituted indenes to fluorene derivatives via an intramolecular aldol reaction. Chapter VI describes the serendipitous discovery and synthesis of indenopyrylium salts. Chapter VII details the novel production of indenopyridines from di-substituted indenes.

Lastly, chapter VIII provides a summary and suggests future directions for this research.

This dissertation includes previously published and unpublished co-authored material.

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CHAPTER I

THE HISTORY AND DEVELOPMENT OF THE RAUHUT-CURRIER REACTION

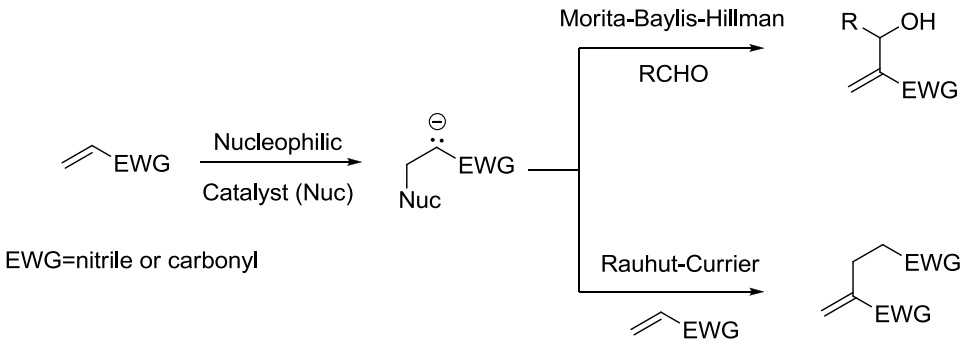
1.1. Introduction

Carbon-carbon bond forming reactions are among the most important transformations in organic synthetic chemistry. A vast amount of research has been devoted to the development of atom economical, stereoselective and chemoselective C-C forming reactions.[1,2] Among the myriad methods established for the formation of carbon-carbon bonds, the use of nucleophilic organocatalysis is receiving increased attention.[3-10] In particular, there has been a growing interest in the use of enones as latent enolates.[11-12] Both the Morita-Baylis-Hillman (MBH) and the Rauhut-Currier[i] (RC) reaction incorporate the use of catalytic conjugate additions to generate enolates that are then coupled to an electrophilic partner. While the MBH involves the coupling of an activated alkene (typically α,β-unsaturated nitriles, ketones or esters) and an aldehyde,[13-14] the RC is comprised of the homo- or hetero-coupling of two activated alkenes (Scheme 1).[15]

Not only have the intramolecular, enantioselective, and aza-MBH reactions been described in great detail, the highly functionalized MBH products have found use in a variety of subsequent transformations.[16-30] On the other hand, due in part to the low reactivity of the substrates and the difficulty in controlling selectivity in the mixed coupling reactions, the RC has received much less attention. However, in the last decade

[i] Also known as the "vinylogous" Morita-Baylis-Hillman reaction.

the RC reaction has experienced a rebirth as groups begin to report the high reactivity, specificity and enantioselectivity of the intramolecular Rauhut-Currier reaction (iRC).[16]



Scheme 1. The MBH and RC reactions couple activated alkene to different electrophiles.

1.2. Survey of the Intermolecular Rauhut-Currier Reaction

Rauhut and Currier disclosed the dimerization of electron deficient alkenes in a patent issued in 1963.[15] Catalyzed by trialkyl or triaryl phosphines, the transformation is believed to proceed through a reversible phospha-Michael addition to enone **I**, generating enolate **II**. Conjugate addition to a second activated alkene, **I**, produces intermediate **III**. A proton transfer yields **IV**, which then eliminates the nucleophilic catalyst to produce **V** (Figure 1).

The alkene homocoupling reported by Rauhut and Currier was later confirmed in experiments by Baiter and Anderson.[31] Acrylonitrile was successfully dimerized in the presence of tributylphosphine, while triphenylphosphine was found to be an inferior catalyst, giving low yields of **1** and **2** (Scheme 2).

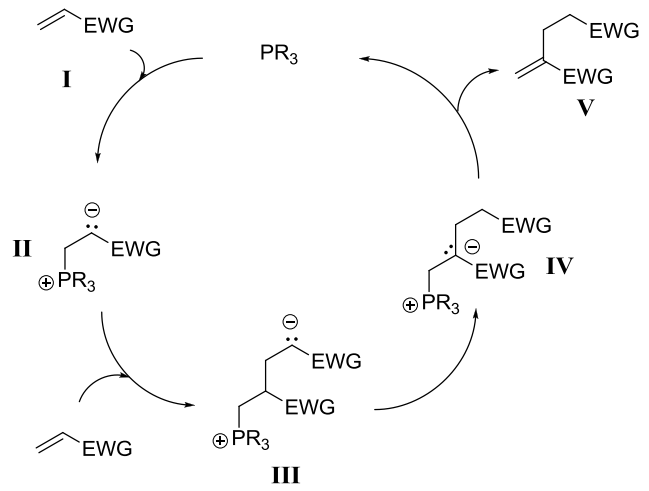
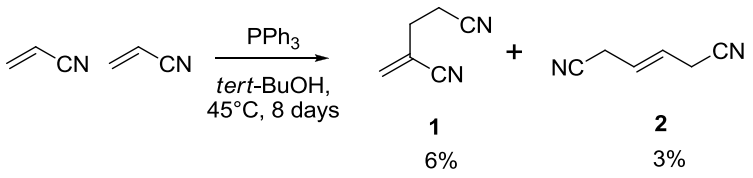
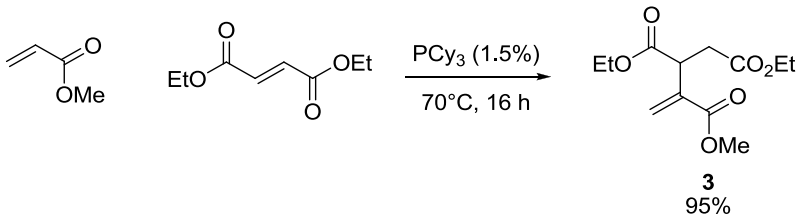


Figure 1. The proposed mechanism for the RC reaction.



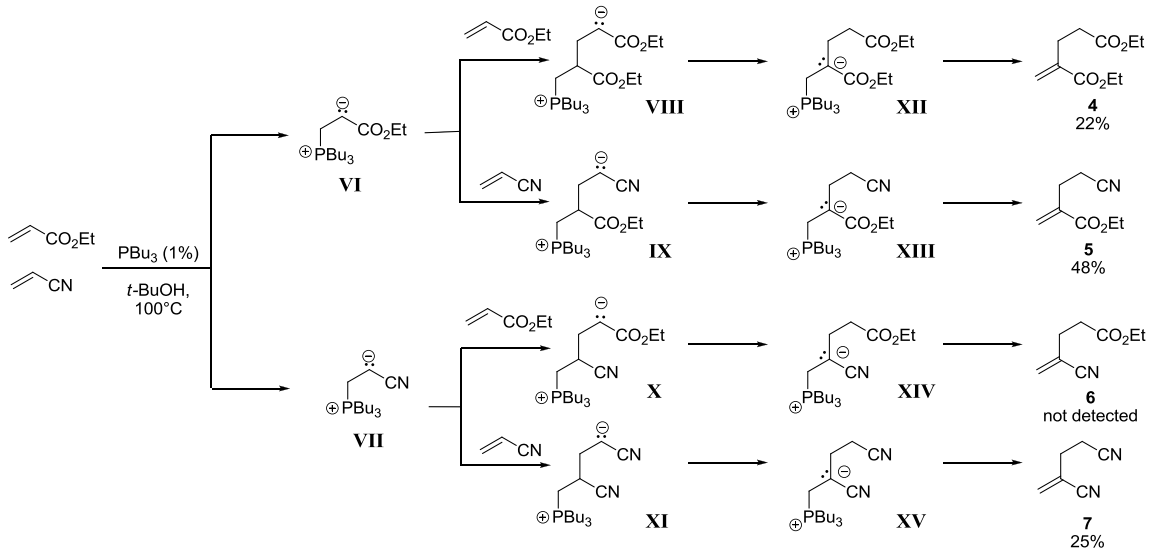
Scheme 2. Baizer and Anderson found triphenylphosphine to possess greatly reduced reactivity.

In 1969, Morita and Kobayashi presented the first cross-coupled RC reaction.[32] The use of tricyclohexylphosphine allowed for the coupling of fumaric and maleic esters with methyl acrylate and acrylonitrile in a selective manner. For example, while four coupling products are possible for the reaction between diethyl fumarate and methyl acrylate, only **3** was detected (Scheme 3).



Scheme 3. The first example of a mixed RC reaction.

One year later, McClure performed a revealing cross-coupling experiment.[33] Treatment of a 1:1 mixture of ethyl acrylate and acrylonitrile with PBu_3 generated only three of the four potential coupling products (Scheme 4). The formation of **4** and **7** suggests that both ethyl acrylate and acrylonitrile can undergo the phospha-Michael to form intermediates **VI** and **VII**. McClure and co-workers suggest that the absence of **6** is due to the unfavorable proton transfer step to generate intermediate **XIV**. In each other case, it is presumed that the proton transfer step is energetically favorable, preparing the substrate for the elimination of the phosphine catalyst. This study suggests that it is not the initial conjugate addition that determines the product formation, but the generation of the final zwitterionic intermediate.

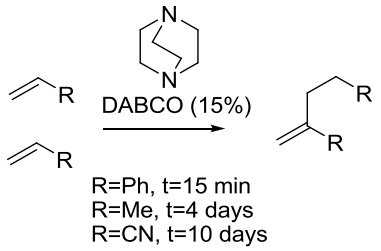


Scheme 4. McClure found that the mixed RC reaction between ethyl acrylate and acrylonitrile did not produce **6**.

It was not until 16 years later that the amine catalyzed RC was first reported. Amri and Villieras discovered that in the presence of DABCO,[ii] methyl vinyl ketone slowly dimerized.[34] Similarly, Basavaiah coupled a variety of α,β-unsaturated ketones

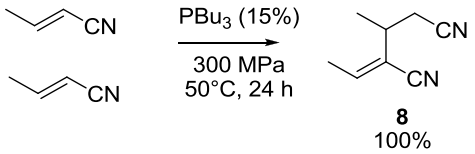
[ii] DABCO= 1,4-diazabicyclo[2.2.2]octane

and acrylonitrile using DABCO, giving moderate yields (40-60%). The reaction times ranged from minutes to hours depending on the alkene (Scheme 5).[35] Over the next 5 years, the scope of the iRC expanded to include vinyl sulfones as coupling partners and DBU as a nucleophilic catalyst.[iii],[36-38]



Scheme 5. DABCO catalyzed dimerization of various electron-poor alkenes.

Attempts to couple highly substituted alkenes using the RC reaction have proven to be difficult. The dimerization of hindered alkenes like cyclohexenone or crotonitrile proceeded sluggishly when DBU or DABCO were used. However, treatment of crotonitrile with tributylphosphine at elevated pressures produced **8** in quantitative yields (Scheme 6).[39]

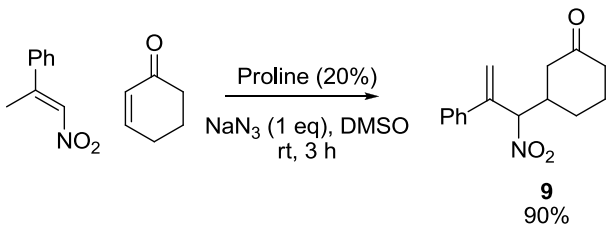


Scheme 6. The coupling of hindered alkenes requires elevated temperatures.

In 2007, Shi et al. reported the first successful intermolecular RC reaction between nitro and carbonyl activated olefins. Testing a variety of nucleophilic catalysts such as DABCO, imidazole, PPh_3, $P(OMe)_3$ and DMAP, they found that proline was the

[iii] DBU=1,8-diazabicyclo[5.4.0]undec-7-ene.

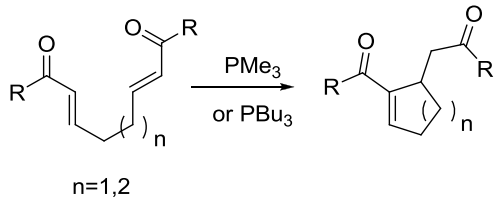
most effective catalyst for the coupling of a nitro alkene to an unsaturated ketone. While proline proved an efficient catalyst on its own, the addition of sodium azide increased the yield of **9** from 80% to 90% (Scheme 7).[40]



Scheme 7. Proline and sodium azide are used in a mixed RC to generate **9**.

1.3. The Intramolecular Rauhut-Currier Reaction

In 2002, Krische and Roush independently reported the first intramolecular variants, using simple aliphatically-linked reactants.[41,42] The treatment of ethylene- or propylene-tethered activated alkenes with a nucleophilic catalyst generated a variety of substituted five and six membered rings (Scheme 8). While amine catalysts such as DABCO, DBU, diethylamine and DMAP were shown to be ineffective, trimethyl and tributyl phosphine proved to efficiently cyclize the substrates.



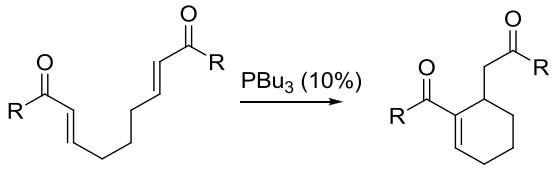
Scheme 8. The intramolecular Rauhut-Currier reaction.

Both groups observed faster reaction rates in more polar solvents (alcohols or acetonitrile versus CH_2Cl_2), while Krische noted that the use of DMSO led to a

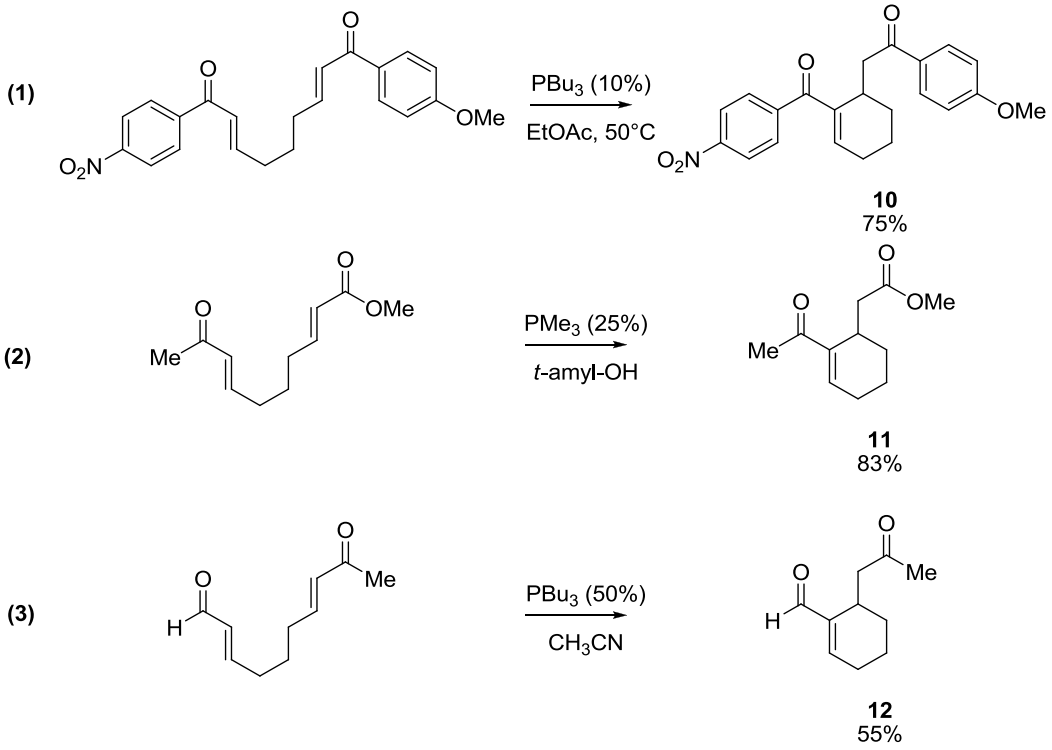
significant amount of oligomerization. Also, the formation of cyclopentene products proceeded more quickly and in higher yields than the formation of cyclohexenes.

While the reaction conditions were not universally applicable, Krische and co-workers report the cyclization of a variety of symmetrical alkyl and aryl ketones (Table 1). Asymmetric substrates were also cyclized and found to exhibit good to excellent chemoselectivity (Scheme 9). Additionally, steric effects were evaluated by each group, revealing that the phosphine added to the less hindered alkene (Scheme 10). Finally, good diastereoselectivity was found for the cyclization of substrates with pre-existing chiral centers. Roush achieved a diastereomer ratio of 10:1 when cyclizing bis(enal) **15** (Scheme 11, equation 1). Similarly, Krische found that the chiral substrate **17** cyclized to give a 95:5 ratio of diastereomers (Scheme 11, equation 2).

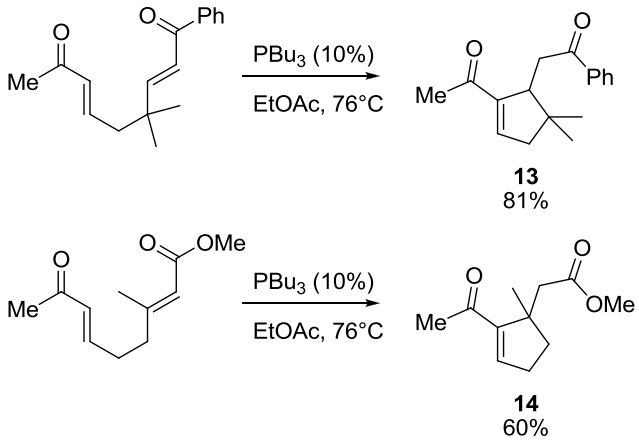
Table 1. Different substrates require unique reaction conditions.



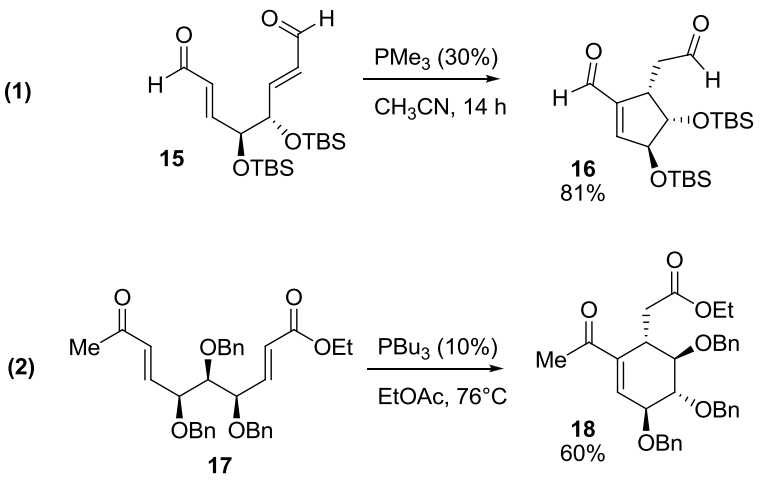
R=	Solvent	Temp (ºC)	Yield (%)
Me	*t*-BuOH	84	61
Ph	Acetone	25	82
4-OMe-C_6H_4	Acetone	50	78
4-CF_3-C_6H_4	EtOAc	50	79



Scheme 9. Asymmetric substrates were shown to display excellent chemoselectivity by Krische (equation 1) and Roush (equations 2 and 3).

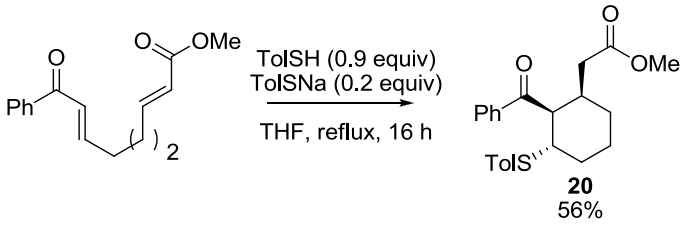


Scheme 10. The reaction conditions are very sensitive to the steric environment around the alkene.



Scheme 11. Roush (equation 1) and Krische (equation 2) report that chiral iRC substrates induce excellent diastereoselectivity.

That same year, Murphy and co-workers found that while phosphines catalyze the cyclization of Krische/Roush-type substrates, aryl thiolates do not.[43,44] While the thiolates cyclize the bis(enone), they are not eliminated, generating tri-substituted cyclohexanes which support the proposed mechanism for the iRC (Scheme **12**).

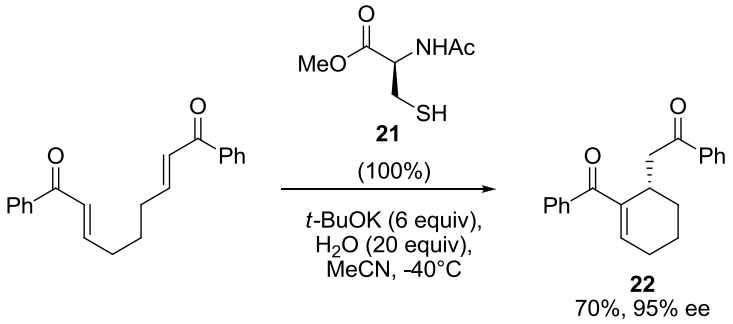


Scheme 12. Thiolates undergo a sulfa-Michael/Michael cascade, generating compounds that resemble proposed intermediates for the iRC mechanism.

1.4. The Enantioselective Rauhut-Currier Reaction

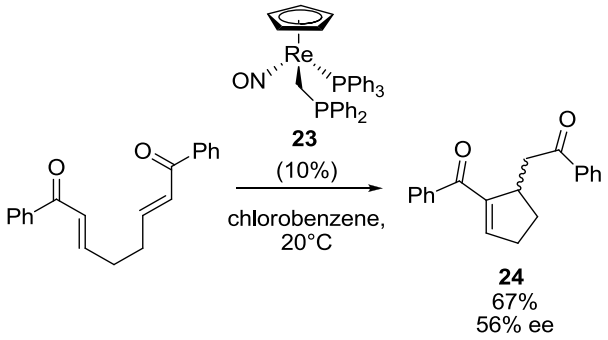
During the 40 years following the inception of the RC reaction, the majority of studies focused on expanding the substrate scope of the reaction. To this end, many new reagents and reaction conditions were introduced. However it was not until 2007 that the first enantioselective iRC reaction was reported by Miller and co-workers.[45,46] Utilizing

an N- and O-protected cysteine catalyst, **21**, they found that up to 95% ee could be achieved. However, it was found that 100% catalyst loading and 6 equivalents of potassium *tert*-butoxide were necessary to affect the desired transformation. Like Murphy and co-workers discovered, Miller found that the thiol group on the cysteine is not amenable to the final elimination step. As a result, excess base is needed to eliminate **21**, generating the desired product, **22** (Scheme 13).



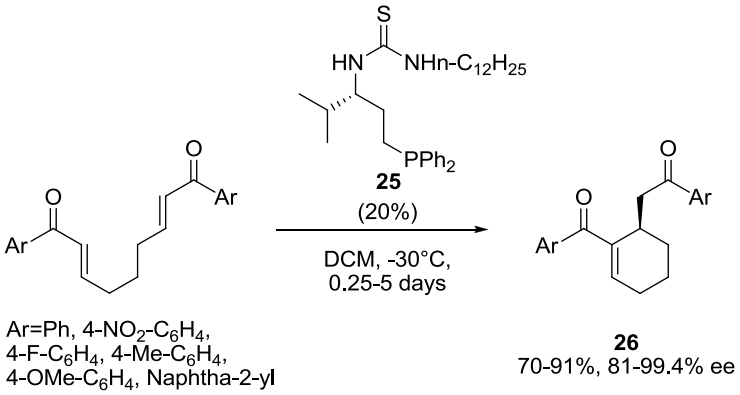
Scheme 13. The use of protected cysteine catalyst **21** induces excellent enantioselectivity.

Two months later, Seidel and Gladysz reported the first true use of a chiral catalyst to induce an enantioselective iRC reaction.[47] Treatment of either **23** or the thioester analogue with enantiopure (η^5-C_5H_5)Re(NO)(PPh_3)(CH_2PPh_2), **24**, produced modest enantioselectivities and good yields (Scheme 14).



Scheme 14. The chiral phosphine-containing rhenium complex catalyzed the enantioselective iRC reaction.

Recently, Wu and co-workers introduced a highly enantioselective iRC reaction of bis(enones) catalyzed by a bifunctional phosphinothiourea derived from valine, **25**.[48] It is noteworthy that Wu's protocol produces the opposite enantiomer from that produced under Miller's conditions. Treatment of aryl ketones with **25** at low temperatures produces high yields and excellent enantioselectivities (Scheme 15).

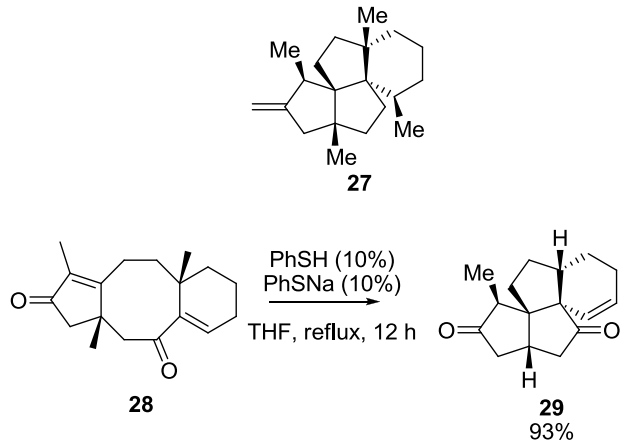


Scheme 15. The organophosphine-catalyzed enantioselective iRC.

1.5. Applications to Natural Product Synthesis

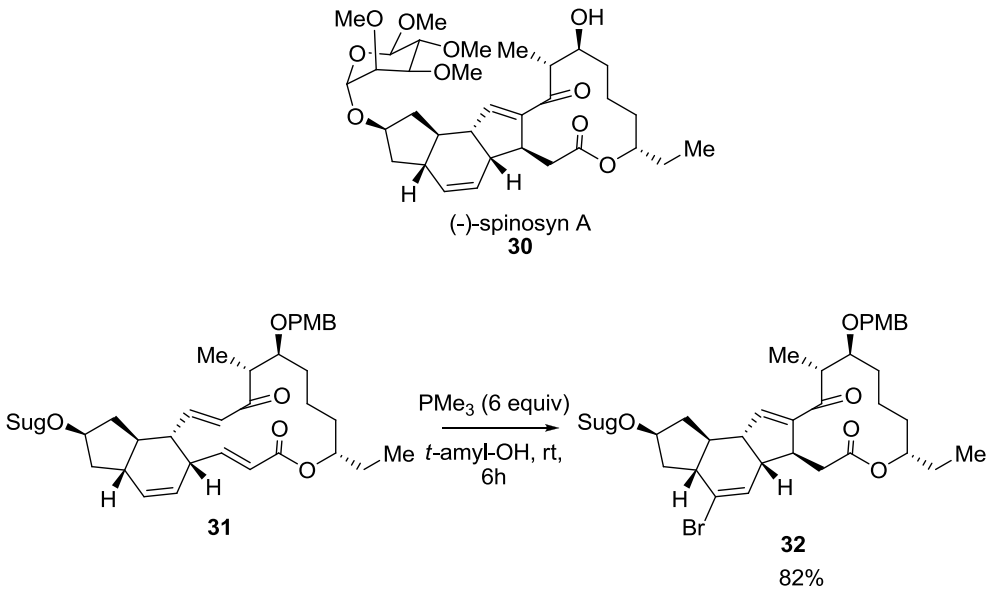
The developments of the last decade have allowed the intramolecular Rauhut-Currier reaction to become an excellent method to generate new stereogenic centers and densely functionalized rings. As a result, the iRC has been demonstrated to be a vital tool in the total synthesis of a number of natural products.

In 1999, Moore and Egruden presented a novel, transannular iRC used during the synthesis of waihoensene, a diterpene extracted from the New Zealand rimu tree (Scheme 15, compound **27**).[49] By treating tricycle **28** with catalytic amounts of thiophenol, the transannular conjugate addition generated **29** in excellent yields (Scheme 16). By utilizing the iRC reaction, Moore and Egruden were able to generate an additional ring and 3 new chiral centers, two of which are quaternary carbons.



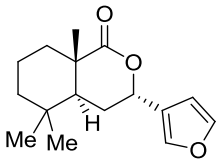
Scheme 16. The first transannular iRC reaction.

A similar transannular, intramolecular Rauhut-Currier was performed by Roush and co-workers.[50,51] In studies leading to the successful synthesis of (-)spinosyn A (**30**), compound **31** was cyclized to generate a new cyclopentene ring and the desired *S* stereocenter (Scheme 17). Subsequent transformations produced the target insecticide, **30**.

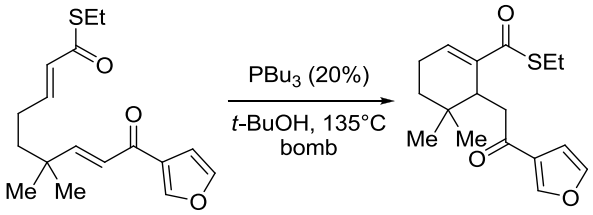


Scheme 17. The total synthesis of **30** utilizes a transannular iRC reaction.

Additionally, Krische and co-workers reported that thioenoates participate in highly chemoselective catalytic crossed Michael cycloisomerization with tethered aryl ketone and enoate partners to afford cyclopentene products, enabling the total synthesis of the potent molluscicide (±)-ricciocarpin A, **33** (Scheme 18).[52]



(±)-ricciocarpin A
33



Scheme 18. Towards the synthesis of **33**.

1.6. Conclusion

While the Morita-Baylis-Hillman and the Rauhut-Currier reactions are approximately the same age, the poor selectivity and slow reaction rates of the intermolecular RC hindered its development. However, since the intramolecular RC was reported, the reach and utility of the reaction have improved dramatically. Recent developments introducing the enantioselective iRC will further increase the scope of the reaction, providing chemists with a new method of stereoselective carbon-carbon bond formation. Future research is likely to uncover new catalytic protocols, expand the substrate scope and selectivity and reveal new, exciting transformations for the products

generated by the inter- and intramolecular Rauhut-Currier reaction. In fact, the research presented in the following chapters addresses all three of these areas.

This dissertation includes previously published and unpublished co-authored material. The crystal structures presented in Chapters II, III, IV, and VI were solved by Lev N. Zakharov. Chapter III contains experimental work performed by Francis M. Hacker. Chapters IV, VI, and VII contain experimental work performed by John W. Bassett.

CHAPTER II

THE DEVELOPMENT OF A REGIOSELECTIVE SYNTHESIS OF INDENES VIA PHOSPHINE CATALYSIS

Crystal structure determination was performed by Lev N. Zakharov. The writing of this chapter and all other work was performed by the author. Professor Kenneth M. Doxsee provided editorial assistance and scientific guidance for all material (published and un-published) covered in this chapter.

2.1. Introduction

Phosphine-mediated transformations are receiving increasing attention as powerful tools for the construction of carbon-carbon bonds.[1-5] The trialkylphosphine-catalyzed dimerization of electron deficient alkenes[6,7] – the so-called Rauhut-Currier reaction – predates the better-known Morita-Baylis-Hillman reaction,[8-14] but gained visibility when Krische and Roush independently reported the first intramolecular variants, using simple aliphatically-linked reactants (Figure 1, left) and yielding a variety of cyclopentanes and cyclohexanes.[15-20] Since then, a number of publications have introduced various catalysts that effect the intramolecular Rauhut-Currier (iRC) reaction, including thiolates and chiral phosphines.[21-26] However, to date the majority of advances of the iRC focus on the cyclization of ethylene or propylene linked enones. We anticipated that linking the two electron-poor alkenes with an aromatic ring (Figure 1,

right) would result in increased reactivity due to the structurally enforced proximity of the reacting alkenes and introduce a virtually unexplored method of indene preparation.[iv, 21,22] Generally synthesized either by metal-catalyzed (Pd, Ni, or Co) annulations or strong acid-mediated electrophilic cyclization reactions,[27-31] indenes are widespread in both synthetic and naturally-occurring biologically active compounds and of considerable utility as ancillary ligands in organometallic chemistry.[28-31]

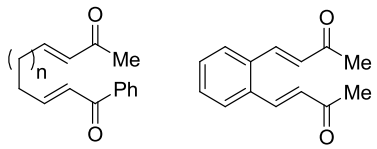


Figure 1. Left, Krische and Roush-type cyclization substrates with ethylene linker. Right, phenylene linked indene precursor, **1a**.

In addition to the synthesis of indenes, we envisioned using our tethered enones to investigate the use of amine nucleophiles to affect the iRC. To date, the only organocatalysts shown to induce the iRC contain either a nucleophilic phosphorous or sulfur atom.[6,7,15-26] Because amine nucleophiles tend to be less prone to oxidation, provide access to the chiral pool, and are often easy to handle solids (e.g., DABCO, DMAP, quinuclidine), the introduction of amine catalysts to the synthetic chemist's toolkit would prove to be a significant advancement.

While attempts to cyclize aliphatically linked bis(enones) using amine catalysts have been unsuccessful[15,24], we suspected that our phenylene linked substrates may be more amenable to amine catalysis due to their potentially increased reactivity. Compared to ethylene or propylene linked enones, our substrates possess more electrophilic β

[iv] To our knowledge, there is only one instance of indene formation using an iRC reaction. See references 21 and 22.

carbons and the appended arms have fewer degrees of freedom, thus increasing the likelihood of proper orientation for the intramolecular conjugate addition.

Be that as it may, our initial attempts to use amine catalysis to cyclize a variety of tethered enones proved unfruitful (Figure 2). As a result we embarked on a series of experiments to determine if our substrates are resistant to cyclization or if nucleophilic amines are simply unfit as catalysts for intramolecular Rauhut-Currier reactions.

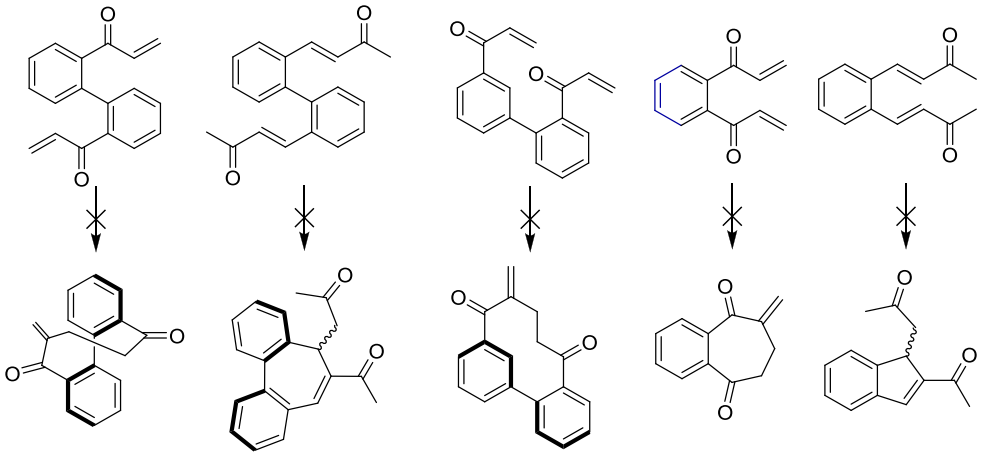


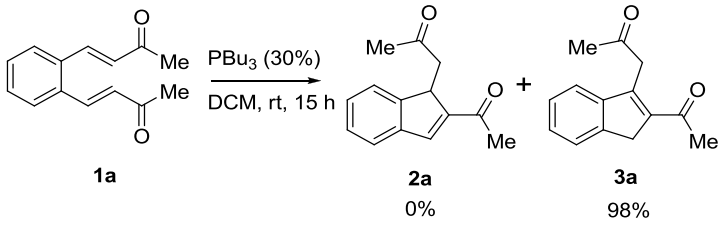
Figure 2. Various bis(enone) substrates that failed to cyclize upon exposure to amines.

In this chapter, we confirm that phenylene linked bis(enones) are, in fact, much more reactive that their aliphatically linked counterparts. In the course of these experiments we also introduce the use of co-catalysts to aid in the specificity and rate of di-substituted indene synthesis, expanding the utility of the phosphine-catalyzed iRC reaction.

2.2. Results and Discussion

Our initial cyclization attempts were performed with **1a** as the substrate. Amine catalysts such as DMAP, quinuclidine, DABCO, DBU and triethylamine proved to be

unreactive in a variety of solvents (DCM, THF, dioxane, toluene, and acetone). To ascertain whether the lack of reactivity was due to the choice of nucleophile or the substrate, we exposed **1a** to tributylphosphine, a known catalyst for the iRC (Scheme 1).[v] We were pleased to discover that **1a** cyclized, but were surprised to detect not the predicted product, **2a**, but solely the more stable indene isomer, **3a** (Figure 3). Based on previous work by Murphy and co-workers, we were expecting a mixture of primarily 1-(2-oxopropyl)-2-acetyl-1*H*-indene, **2a**, with some small amount of the 2-acetyl-3-(2-oxopropyl)-1*H*-indene, **3a**.[21,22] Intrigued by the presence of multiple isomeric indenes, we set out to more carefully explore and describe the iRC reaction.



Scheme 1. Initial indene product ratio from the cyclization of **1a**.

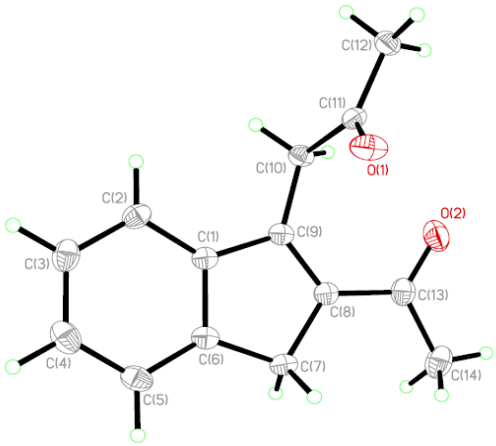
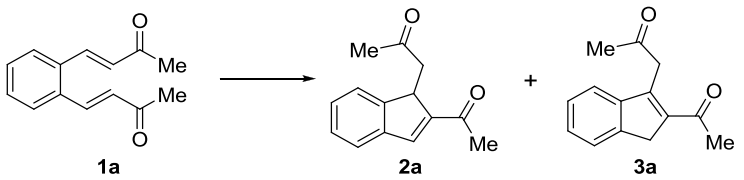


Figure 3. ORTEP representation of compound **3a**.

[v] See references 15-20.

Closer examination revealed that the reaction conditions provided quantitative conversion of starting material in less than thirty minutes. Ethylene- and propylene-linked analogues of **1a** required reaction times three to four times longer, indicating the increased reactivity of phenylene-linked substrates.[15] The reduction of reaction time from 15 hours to 30 minutes allowed for the presence of the 1,2-disubstitued indene, **2a**¸ to be detected, albeit in small amounts (Table 1, entries 1-3). Replacement of PBu_3 with PMe_3 and moving from dichloromethane to toluene did not affect the yield or selectivity (Table 1, entry 3 versus 4), while decreasing the catalyst loading to 15% (Table 1, entry 5) or lowering the reaction temperature (-78 ,-20, 0 ^{o}C) increased the time required for complete consumption of the starting material and led to inferior product ratios. Aprotic solvents proved to be equally suitable reaction media (chloroform, dioxane, toluene, ethyl acetate). However, protic solvents (2,2,2-trifluoroethanol, t-butanol, and 1:4 H_2O/THF mixture) considerably slowed the reaction and produced inferior product ratios.

Table 1. Optimization of cyclization conditions for **1a**.[a]



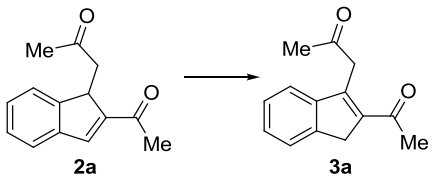
Entry	Catalyst	Co-Catalyst	Time (h)	Yield	Ratio[b]
1	PBu_3 (30%)	-	15	98	nd : >98
2	PBu_3 (30%)	-	4	94	8:92
3	PBu_3 (30%)	-	0.5	94	12:88
4	PMe_3 (30%)	-	0.5	96	14:86
5	PMe_3 (15%)	-	3	97	18:92
6	PMe_3 (20%)	NEt_3 (50%)	1	98	nd: > 98
7	NEt_3 (50%)	-	168	0	-
8	PPh_3 (50%)	-	168	0	-
9	PMe_2Ph (30%)	-	16	48	54:46
10	PMe_2Ph (30%)	Phenol (150%)	16	97	94:6
11	Phenol (150%)	-	168	0	-
12	PMe_3 (20%)	Benzoic Acid (50%)	0.5	55	89:11
13	PMe_3 (20%)	Ethanol (50%)	0.5	47	92:8
14	PMe_3 (20%)	Phenol (50%)	0.5	97	77:23
15	PMe_3 (20%)	Phenol (100%)	0.5	98	80:23
16	PMe_3 (20%)	Phenol (150%)	0.5	96	86:14

[a]All reactions were carried out in toluene at room temperature under a nitrogen atmosphere with the exception of entries 1-3, which were carried out in dichloromethane. [b]Ratio of **2a** to **3a** (by ^{1}H NMR).

We hypothesized that both the acidity of the indene and the basicity of the trialkylphosphine were the underlying causes of the isomerization of **2a** to the more stable 2,3-disubstitued indene, **3a**. As a result, we isolated **2a** by chromatography and subjected it to a variety of acidic and basic conditions (Table 2).[vi] We found that **2a** does not isomerize to **3a** in neutral solution and that it is not particularly sensitive to acidic conditions. On the other hand, **2b** does isomerize at an observable rate in the presence of trimethylphosphine and quickly in the presence of triethylamine.

[vi] Indenes **2a-i** are presumably more acidic than indene (pKa ca. 20) due to their electron deficient nature.

Table 2. The effect of neutral, acidic and basic conditions on the isomerization of **2a**.



Entry	Reagent[a]	Time (h)	Yield of **3b** (%)
1	-	168	Not detected
2	CH_3CO_2H	48	5
3	PMe_3	24	32
4	NEt_3	1	>98

[a]Indene **2a** and 20 mol % of reagent were stirred in toluene at room temperature.

To reinforce this observation, **1a** was cyclized with PMe_3 (20 mol %) in the presence of triethyl amine (50 mol %) to almost exclusively yield **3a** (Table 1, entry 6). Treatment with triethyl amine alone does not induce cyclization (Table 1 entry 7).

Turning to less basic catalysts in order to avoid isomerization (Table 3), we found triphenylphosphine to be ineffective (Table 1, entry 8). Dimethylphenylphosphine effected a slow and partial conversion of bis(enone) **1a** (Table 1, entry 9); the inferior control over isomerization in this reaction is presumably due to the prolonged exposure of initially-formed **2b** to the phosphine catalyst. Noting that phenol has been reported to act as an accelerant for the mechanistically-related Morita-Baylis-Hillman reaction,[36-38] we found that the addition of phenol as a co-catalyst not only speeds up the dimethylphenylphosphine catalyzed reaction, but dramatically improved the isomeric selectivity of the reaction (Table 1, entry 10). In the absence of a phosphine catalyst, phenol does not mediate the cyclization reaction (Table 1, entry 11).

Table 3. The acidity and nucleophilicity of select phosphine catalysts.[39]

Phosphine	pKa	k_{nuc}
PMe_3	8.65	2.24×10^{-3}
PBu_3	8.43	1.62×10^{-3}
PMe_2Ph	6.41	7.60×10^{-4}
PPh_3	2.73	3.78×10^{-5}

While we have not investigated the role of phenol beyond confirmation that it does not itself serve as a catalyst for the cyclization reaction, we suspect that its hydrogen bond donating ability may help to stabilize one of the various enolate intermediates generated during the course of the reaction, most likely enolate **II** (Figure 4). It is believed that the mechanism for the intramolecular Rauhut-Currier involves the reversible conjugate addition of a nucleophilic catalyst to an electron poor alkene, generating enolate **I**. The subsequent enolate undergoes a conjugate addition to the tethered enone moiety to generate intermediate **II**. A proton transfer produces the more stable zwitterion **III** which then undergoes an $E1_{CB}$ type elimination, releasing the catalyst. In the case of indene formation, a base catalyzed isomerization likely occurs via the deprotonation of the 1,2-disubstitued indene, followed by the protonation of the resulting indenide **IV,** yielding the more stable 2,3-disubstitued indene (Figure 4).

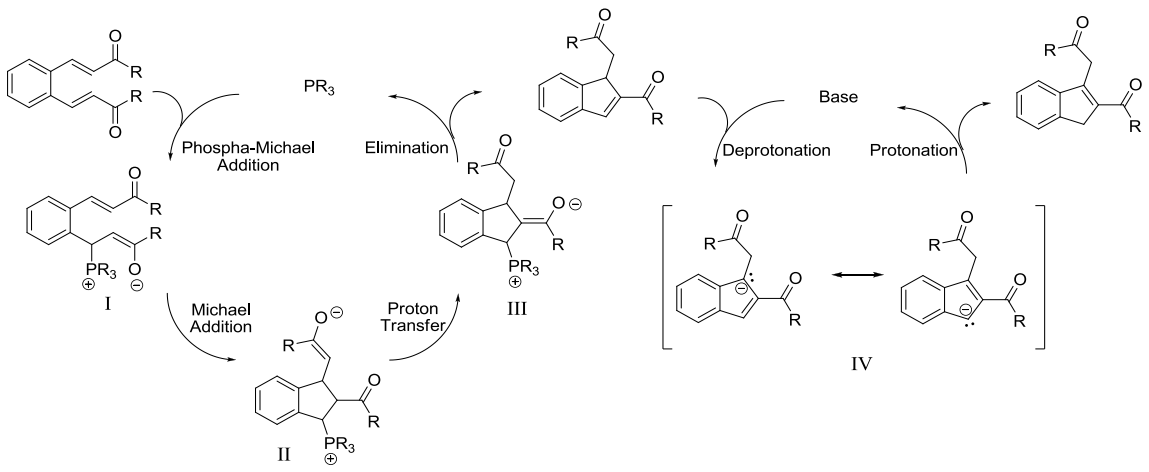
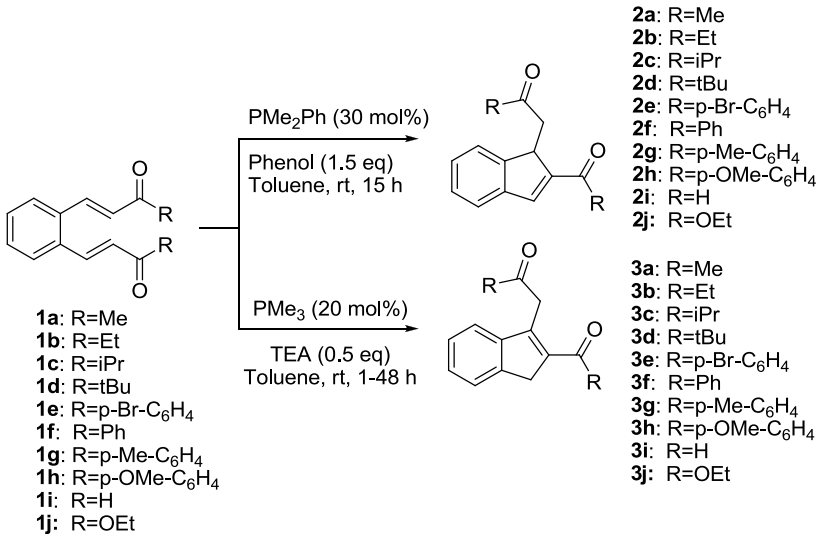


Figure 4. Proposed mechanism of the phosphine-catalyzed intramolecular Rauhut-Currier and the isomerization of the resulting 1,2-disubstituted indene.

Curious if any hydrogen bond donor would behave in a similar fashion, we subjected **1a** to trimethyl phosphine and 0.5 molar equivalents of benzoic acid, ethanol, or phenol. Both benzoic acid and ethanol reduced the isomerization of **2a** to **3a** but unfortunately hindered the conversion of starting material (Table 1, entries 12 and 13). On the other hand, adding an excess of phenol greatly suppressed the isomerization whilst maintaining excellent yields (Table 1, entries 14-16), though the effects are not as pronounced as seen in the dimethylphenylphosphine catalyzed reaction.

Taking advantage of the reversed effects that triethyl amine and phenol have on the indene selectivity, we were able to develop two operable sets of optimized reaction procedures (Scheme 2).



Scheme 2. Two optimized sets of reaction conditions allow for the selection of a specific indene regioisomer.

Substrates **1a-1j** were cyclized under a variety of conditions (Table 4). In each case it was found that treatment of the bis(enone) with 30 mol% of PMe_2Ph and 1.5 equivalent of phenol in toluene (Table 4, entries 3, 7, 11, 16, 19, 23, and 26) improved the selectivity for unisomerized indene **2** when compared to a simple treatment with 20 mol% PMe_3 (Table 4, entries 1, 5, 9, 14, 17, 21, and 24). On the other hand, treatment with 20 mol% of PMe_3 and 50 mol% of triethylamine provided almost exclusively the isomerized indene, **3** (Table 4, entries 2, 6, 10, 15, 18, 22, and 25).

The cyclization of bis(enal) **1i** led to incomplete conversion of starting material (Table 4, entries 27-29). The detection of trimethylphosphine oxide led us to believe that Wittig-type side reactions are consuming the catalyst and leading to side product formation. Increasing the catalyst loading of PMe_2Ph to 200 mol % and using two equivalents of phenol allowed for complete consumption of **1i** however did not produce indenes **2i** or **3i** (Table 4, entry 30). The single isolable compound in the reaction mixture was analyzed by ^{1}H and ^{13}C NMR, DEPT, HMQC and NOESY spectroscopy. It was

determined that the product was an indenyl fluorene derivative, **4.** Compound **4** is likely formed via the condensation of two equivalents of **3i** that then suffer an intramolecular aldol, generating a new aromatic ring (Figure 5). However, the yield of **4** remained moderate due to large amounts of insoluble side products that adhered to the reaction flask.

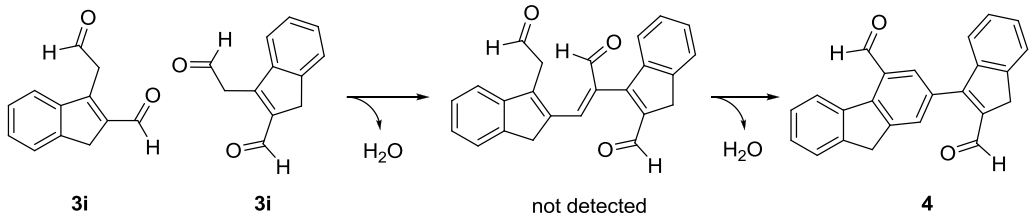
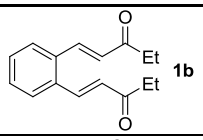
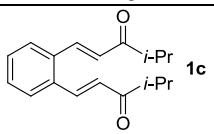
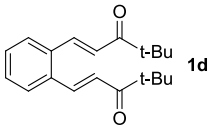
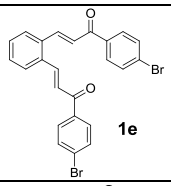
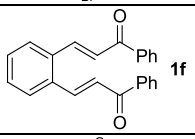
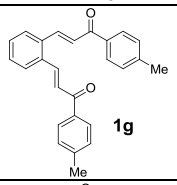
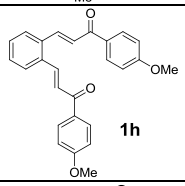
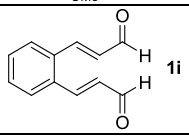
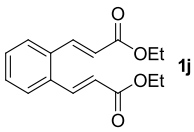


Figure 5. Indenyl fluorene **4** is produced through a series of aldol reactions.

The bis(enoate) **1j** proved to be unreactive to the abovementioned reaction conditions (Table 4, entries 31-33). Under more forcing conditions, the cyclization of both **1d** and **1j** produced exclusively the isomerized 1,2-indene in excellent yields (Table 4, entries 13 and 35).

Highlighting its role as a rate- and selectivity-enhancing co-catalyst, addition of phenol to the cyclization of **1b**, **1c**, **1d** and **1f** with the more active trimethylphosphine (Table 4, entries 4, 8, 12, and 20) also led to enhanced rate and selectivity for the unisomerized product (**2**). Unfortunately, the addition of phenol had no effect on the cyclization of bis(enoate) **1j** (Table 4, entry 34). In the absence of phenol, increased bulk of the alkyl ketones or increased electron density of the aryl ketones corresponded to lower yields and diminished the isomeric selectivity. Interestingly, the steric and electronic effects of the starting materials were all but eliminated in the presence of phenol.

Table 4. Substrate scope of cyclization reactions.

Entry	Substrate	Procedure[a]	Time (h)	Yield (%)[b]	Ratio[c]
1	 **1b**	A	15	82	22 : 78
2		B	16	93	7 : 93
3		C	15	97	72 : 28
4		D	1	95	85 : 15
5	 **1c**	A	17	78	33 : 67
6		B	18	87	<2 : >98
7		C	15	95	92 : 8
8		D	2	80	41 : 59
9	 **1d**	A	48	41	59 : 41
10		B	48	38	<2 : >98
11		C	48	88	94 : 6
12		D	48	96	65 : 35
13		E	48	95	0 : 100
14	 **1e**	A	0.3	92	78 : 22
15		B	0.3	90	<2 : >98
16		C	15	94	95 : 5
17	 **1f**	A	0.5	92	87 : 13
18		B	0.5	96	<2 : >98
19		C	16	95	97 : 3
20		D	1	94	95 : 5
21	 **1g**	A	1	97	85 : 15
22		B	1.5	96	5 : 95
23		C	16	95	95 : 5
24	 **1h**	A	7	89	43 : 57
25		B	8	86	8 : 92
26		C	16	95	80 : 20
27	 **1i**	A	1	34[e]	-
28		B	1	15[e]	-
29		C	16	42[e]	-
30		-[f]	15	61[e]	-
31	 **1j**	A	48	0[d]	-
32		B	48	0[d]	-
33		C	48	0[d]	-
34		D	48	0[d]	-
35		E	48	95	0 : 100

[a]Procedure A: PMe_3 (20%); B: PMe_3 (20%), NEt_3 (50%); C: PMe_2Ph (30%), phenol (1.5 equiv.); D: PMe_3 (20%), phenol (1.5 eq); E: heated at reflux in *t*-butanol with PBu_3 (50%). [b]Yield of isolated product(s). [c]Ratio of **2**:**3**. Unless otherwise stated, all reactions were carried out under N_2 in toluene at room temperature. [d]No conversion of starting material. [f]Conditions: PMe_2Ph (200%), phenol (200%). [e]Neither indene was detected, only **4**.

2.3. Conclusion

In summary, we have developed new protocols for the organocatalytic synthesis of substituted indenes. Tethered bis(enones) can be selectively cyclized, giving good to excellent yields of either desired indene isomer. By introducing the use of dimethylphenylphosphine instead of the trialkyl phosphines commonly used as catalysts for the iRC reaction, base-catalyzed side reactions are greatly reduced. This research also represents the first example of co-catalysis in the Rauhut-Currier reaction. While other protic co-catalysts reduce side reactions, we found that only phenol enhances both the rate and the product selectivity of the reaction.

Furthermore, it is important that phenylene-linked bis(enones) proved to be more susceptible to cyclization than their aliphatic counterparts. This observation allows us to dismiss the hypothesis that the abovementioned substrates are resistant to intramolecular cyclizations. We can therefore deduce that either amines are unreactive towards these substrates or the reaction environment disfavors the aza-iRC. Chapter III addresses the question as to whether amines are able to undergo an aza-Michael-intramolecular-Michael cascade.

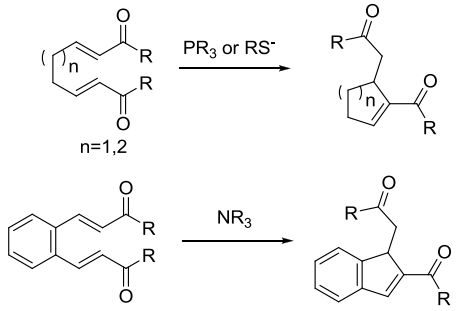
CHAPTER III

AZA-MICHAEL-MICHAEL ADDITIONS TO TETHERED ENONES: THE SYNTHESIS OF AMINOINDANES USING A RECOVERABLE ACID CATALYST

Crystal structure determination was performed by Lev N. Zakharov. A portion of the optimization experiments and amine screening were performed by Francis M. Hacker. The writing of this chapter and all other work was performed by the author. Professor Kenneth M. Doxsee provided editorial assistance and scientific guidance for all material (published and un-published) covered in this chapter.

3.1. Introduction

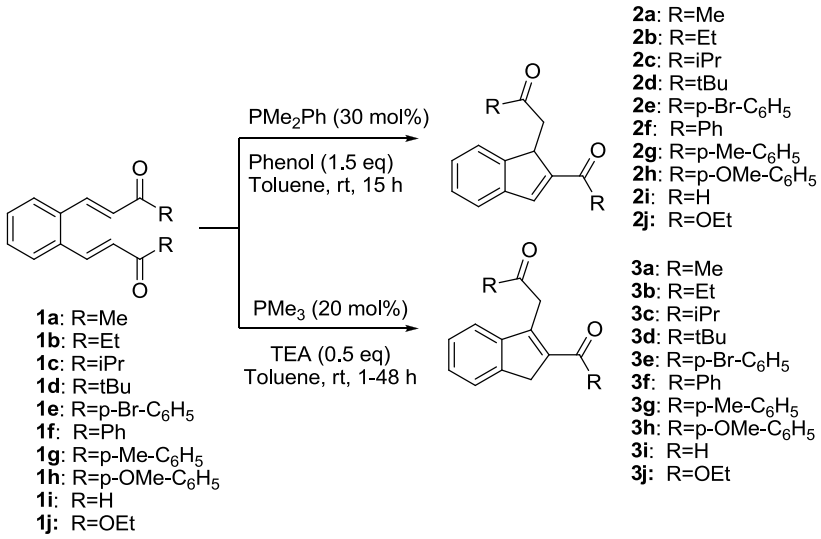
Comprised of cascading Michael additions, the intramolecular Rauhut-Currier (iRC) reaction is a powerful tool for generating densely functionalized five and six membered rings.[1] While the vast majority of investigations regarding the iRC focus on cyclizing ethylene or propylene linked bis(enones) with thiolates or phosphines (Equation 1),[1-13] our group is interested in exploring the use of amine catalysts and phenylene tethered bis(enones) (Equation 2).



(1)

(2)

Unfortunately, amine catalysts such as DMAP, quinuclidine, DABCO, DBU and triethylamine proved to be ineffective cyclization catalysts in a variety of solvents (DCM, THF, dioxane, toluene, and acetone).[vii,viii] Undaunted by these results, we planned a series of investigations to determine whether phenylene tethered enones are not amenable to cyclization or if amines are unable to add in a Michael fashion to induce cyclization. Our plan was to test the first hypothesis by subjecting compounds **1a-i** to well established phosphine catalysts. In chapter II we established that **1a-i** are in fact more susceptible to the phosphine catalyzed iRC than their aliphatically linked counterparts (Scheme 1).

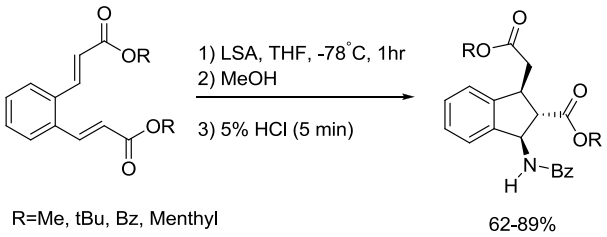


Scheme 1. When subjected to phosphine catalysis, tethered, activated alkenes **1a-j** cyclize to yield indenes.

[vii] DMAP = N,N-dimethyl-4-amino-pyridine, DABCO = 1,4-Diazabicyclo[2.2.2]octane, DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene, DCM = dichloromethane, THF = tetrahydrofuran

[viii] See Chapter II

After confirming that phenylene linked enones, enals, and enoates can undergo cyclization, we returned our attention to the addition of amines to these compounds. Although the aza-Michael addition of primary and secondary amines to α,β-unsaturated systems is well established,[14-24] there are few examples of amines inducing cyclization in tethered systems.[25] Related work by Voigt and co-workers showed that N-protected lithium amide salts can add into a number of phenylene linked bis(enoates) in a diastereoselective fashion at cryogenic temperatures (Scheme 2).[26] Our goal was to achieve the same sort of reactivity using neutral amines in an effort to mimic the behavior of a tertiary amine catalyzing an aza-iRC reaction.



Scheme 2. The addition of that lithium benzyl(trimethylsilyl)amide (LSA) to various bis(enoates) presented by Voigt, et al.

The aza-Michael reaction is an important method for the synthesis of β-amino carbonyl compounds, a class of compounds that are both pharmacologically and synthetically important. As precursors to both natural and unnatural β-amino acids, alcohols, and lactams, these functional groups of great interest in pharmaceuticals and fine chemical production.[27-38]

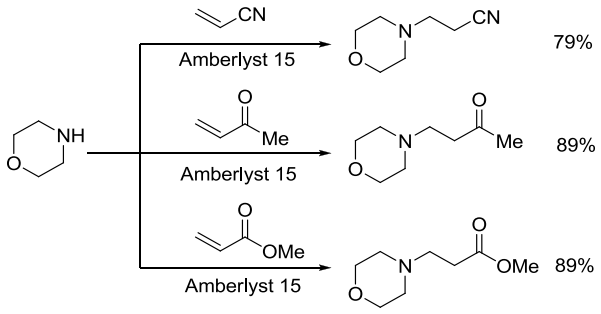
This chapter presents the development of an efficient, highly diastereoselective synthesis of β-aminoketone-containing aminoindanes using a reusable acid catalyst at atmospheric conditions. Primary and secondary amines effect an aza-Michael-

intramolecular-Michael cascade upon addition to a variety of tethered bis(enones) and the sulfonic acid resin, Dowex 50WX4.

3.2. Results and Discussion

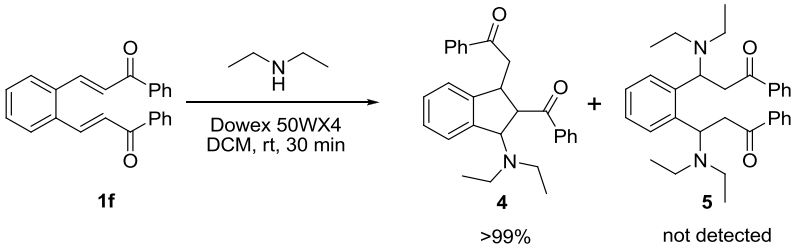
Our initial cyclization attempts focused on bis(enone) **1f** as the substrate. A simple treatment of **1f** with diethyl amine in a variety of solvents (DCM, THF or acetone) for three days showed no conversion of starting material. The addition of copper (II) chloride,[39] bismuth (III) nitrate,[40] zirconium (IV) chloride,[41] or thiourea[42] as co-catalysts had no effect.

Finding no success with Lewis acid catalysis and hydrogen bond donors, we turned to Brønsted-Lowry acid catalysis. Das and Chowdhury reported that primary and secondary amines quickly and cleanly added to various α,β-unsaturated nitriles, esters and ketones in the presence of Amberlyst-15, a sulfonic acid resin, with no solvent (Scheme 3).[43]



Scheme 3. Examples of sulfonic acid resin catalysis for aza-Michael additions performed by Das and Chowdhury.

Treatment of **1f** with diethyl amine and the sulfonic acid resin Dowex 50WX4 in a minimal amount[ix] of DCM led to the quantitative formation of amino-indane **4** (Scheme 5). We were pleased by two important observations. First, the absence of β-amino carbonyl compound **5** in the reaction mixture indicates that **1f** is more prone to cyclization than an additional aza-Michael addition. Second, the reaction conditions generate a racemic mixture of exclusively the *trans,trans* isomer of **4**. The relative stereochemistry of **4** was confirmed by 1D-NOESY[x] experiments (Figure 1).



Scheme 4. The initial cyclization of phenyl ketone **1f** with diethyl amine in the presence of Dowex 50WX4 solely yielded amino indane **4**.

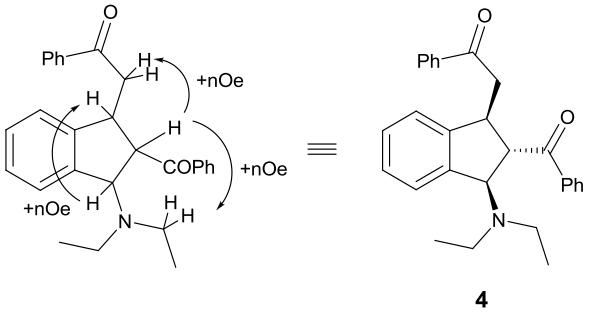


Figure 1. NOE spectroscopy confirmed the *trans,trans* stereochemistry of **4.**

Subsequent optimization revealed that the rate and yield of the reaction was critically dependent on the ratio of diethylamine to Dowex 50WX4. While the reaction

[ix] 0.05 grams **1f** was dissolved in 0.3 mL DCM.

[x] NOESY = Nuclear Overhauser Effect Spectroscopy

does not proceed in the absence of the acidic resin, the use of excess resin is equally detrimental (Table 1, entry 1). Dowex50WX4 provides approximately 4.8 mmol of sulfonic acid per gram of resin.[44] To prevent the complete protonation of diethylamine we found that there must be one molar equivalent more diethylamine than Dowex (Table 1, entries 1 and 2 versus 3-5). Two equivalents of excess, free amine quickly produced **5** in excellent yield (Table 1, entry 3). However, an abundance of Dowex proved to be more important than a glut of diethylamine as long as an excess of diethylamine was maintained (Table 1, entries 4 and 5). Not only does the use of Dowex beads facilitate work-up, but the recovered beads can be reused (without reactivation) ten times with virtually no decrease in activity (Figure 2). Substituting DCM with other aprotic solvents (ethyl acetate, acetone, THF) or decreasing the concentration to 0.25 M led to significantly increased reaction times.

Table 1. The optimization of reagent ratios for the formation of **4.**[a]

Entry	Diethylamine (Equivalents)	Dowex 50WX4 (Equivalents)	Time (h)	Yield of **4** (%)[b]
1	1	1	240	not detected
2	1.5	1	120	48.5
3	3	1	2	94
4	4.5	1.5	1	>98
5	3	2	1	>98

[a]A solution of 0.15 mmol of **1f** in 0.3 mL DCM was stirred in atmospheric conditions for the allotted time.
[b]Determined by ^{1}H NMR.

Figure 2. Dowex 50WX4 was reused ten times to catalyze the reaction between diethylamine and **1f**, displaying no loss in efficiency

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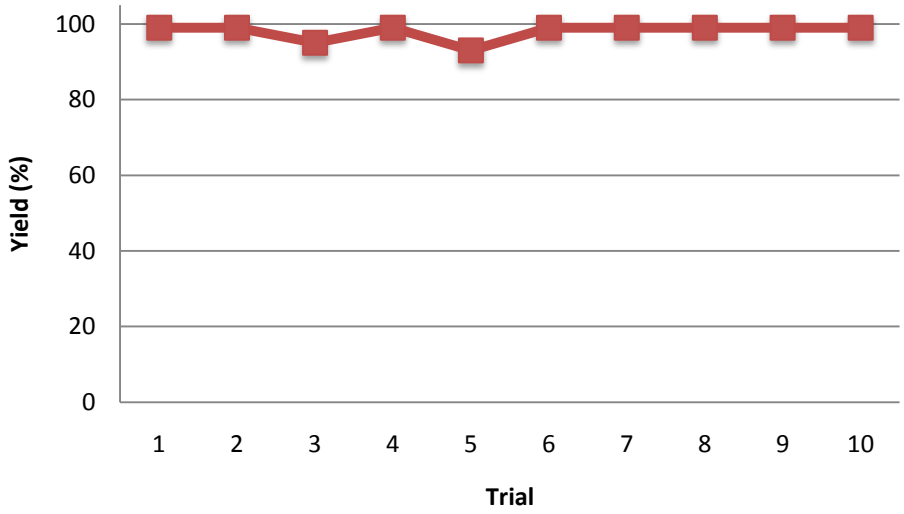
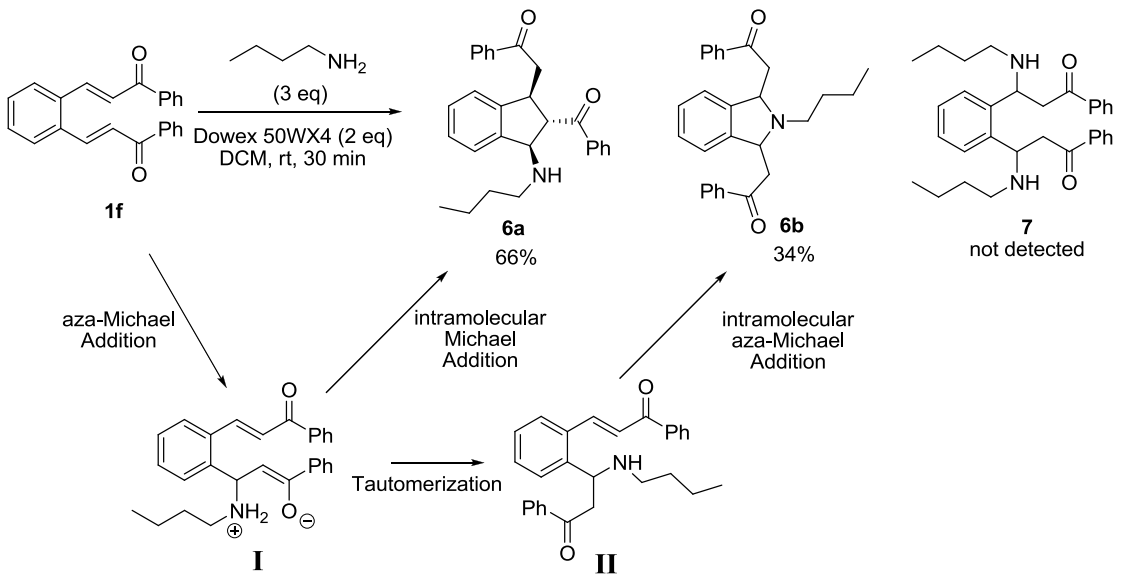


We discovered early on that primary amines behave differently when exposed to these reaction conditions. Upon treatment with *n*-butylamine and Dowex50WX4, **1f** formed both the expected aminoindane **6a** and the isoindoline **6b** (Scheme 5). As with the addition of diethylamine, there was no evidence for a diamino product, **7**. Both **6a** and **6b** presumably arise from an initial aza-Michael addition, forming (unobserved) intermediate **I**, which can either close to **6a** via an intramolecular Michael addition or tautomerize to **II**, followed by an intramolecular aza-Michael addition, affording **6b**. In an effort to decrease the amount of isoindoline **6b**, solvent choice and concentration were reevaluated. Dilution of the reagents lengthened reaction times and increased the proportion of **6b** (Table 2, entries 1-3). Solvent choice appeared to have little to no effect on the yield or product ratio, but did increase the reaction time required for consumption of starting material (Table 3, entries 4-7). High concentration in DCM remains the best system in terms of yield, product ratio and reaction time.



Scheme 5. Upon exposure to *n*-butylamine, **1f** yields **6a** and **6b** in a 3:2 ratio.

Table 2. The addition of *n*-butylamine to **1f** under a variety of reaction conditions.[a]

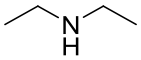
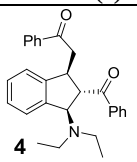
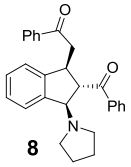
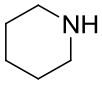
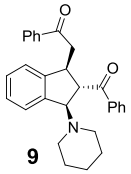
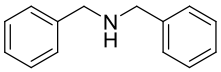
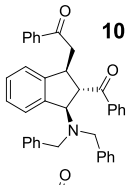
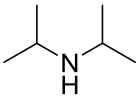
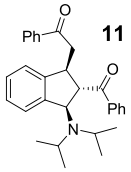
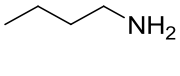
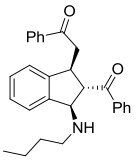
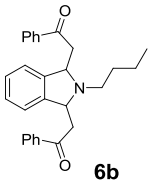
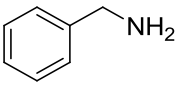
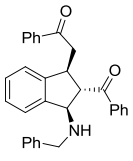
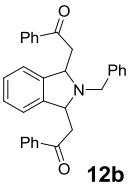
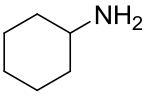
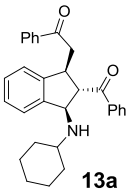
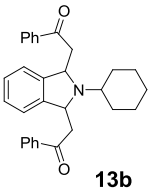
Entry	Solvent	Concentration (M)	Time (h)	Yield (%)	Product Ratio[b]
1	DCM	0.5	1	98	66 : 34
2	DCM	0.25	24	89	30 : 70
3	DCM	0.025	120	70[c]	25 : 75
4	Toluene	0.5	24	90	62 : 38
5	THF	0.5	24	95	65 : 35
6	Ethanol	0.5	24	92	67 : 33
7	Ethyl Acetate	0.5	24	93	71 : 29

[a]All reactions were carried out with 3 equiv. of amine and 2 equiv. of Dowex50WX4 at atmospheric conditions. [b]Ratio of **6a** to **6b** determined by ^{1}H NMR. [c]Unreacted starting material was recovered from the reaction mixture.

With an optimized set of reaction conditions established, the addition of other primary and secondary amines was examined. Small, secondary amines quickly added to **1f** with excellent yields (Table 3, entries 1-3). The bulkier dibenzylamine exhibited a reduced rate of reaction whilst maintaining excellent yields; however the very bulky diisopropylamine displayed severely retarded reactivity (Table 3, entries 4 and 5). Primary amines produced aminoindane products with moderate to good yields and larger amines seemed to suppress formation of the isoindoline products (Table 3, entries 6-8).

Aniline displayed no reactivity, suggesting that aromatic amines are not adequately nucleophilic to undergo the cascading conjugate addition under these conditions. Also, attempts at using DABCO to induce an aza-iRC showed no conversion of starting material over a two week period. Prolonged exposure (>4 days) of aminoindane products to Dowex led to the formation of the corresponding 2,3-disubstituted indene (**3f**).

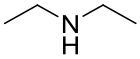
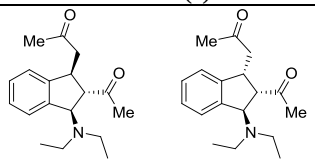
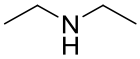
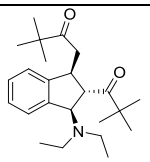
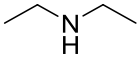
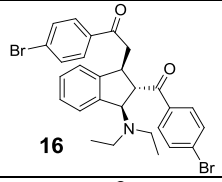
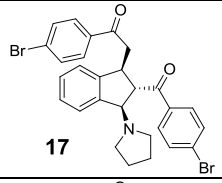
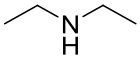
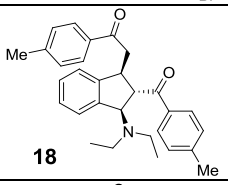
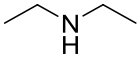
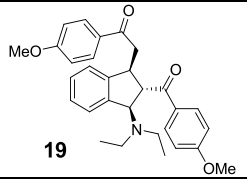
Table 3. Phenyl ketone **1f** was subjected to a variety of amines.[a]

Entry	Amine	Time (h)	Yield (%)[b]	Product Ratio[c]	Product(s)
1		0.5	>98	-	 **4**
2		1	91	-	 **8**
3		1	85	-	 **9**
4		36	72	-	 **10**
5		336	<5[d]	-	 **11**
6		1	97	66 : 34	 **6a**  **6b**
7		36	96	90 : 10	 **12a**  **12b**
8		36	93	81 : 19	 **13a**  **13b**

[a]All reactions were performed with a 0.6 M solution of **1f** in DCM with 3 mole equivalents of the specified amine and 2 mole equivalents of Dowex 50WX4. [b]Isolated yield. [c]Ratio of aminoindane (**a)** to isoindoline (**b)**. [d]Aminoindane **11** was detected by ^{1}H NMR, but not isolated.

Exploration of the substrate scope involved exposing a variety of enone, enal, and enoate containing compounds to the developed protocol. In most cases it was found that treatment with 3 equivalents of either diethylamine or pyrrolidine and 2 equivalents of Dowex 50WX4 quickly and cleanly generated the desired aminoindane in good to excellent yields as solely the *trans,trans* stereoisomer (Table 4, 3-6). As an exception, methylketone **1a** reacted over three days to produce a mixture of the *trans, trans* (**14a)** and *trans,cis* (**14b**) isomers in a 77 to 23 ratio (Table 4, entry 1). We speculate that the relatively small methyl group is less effective at dictating the *trans,trans* stereochemistry sterically enforced by larger aryl group during the course of the reaction. Alkyl ketone(s) appear to be less reactive that even the most electron rich aryl ketone (Table 4, entry 1 versus 6). The tert-butyl ketone proved to be too sterically hindered to react at an appreciable rate (Table 4, entry 2). Attempts to cyclize the bis(enal) **1i** led to a mixture of unidentified side products. Bis(enoate) **1j** proved to be unreactive to the protocol. We were pleased that the reaction of pyrrolidine and bromophenyl ketone **1e** produced a crystalline product (Table 4, entry 4). The slow evaporation of a water/acetone solution containing **17** produced x-ray quality crystals, confirming the *trans,trans* assignment of the aminoindanes (Figure 3).

Table 4. Substrate scope of reaction between amines and bis(enones).[a]

Entry	Substrate	Amine	Time (h)	Yield (%)[b]	Product(s)
1	**1a**		72	79[c]	 **14a** **14b**
2	**1d**		168	<5[d]	 **15**
3	**1e**		1	97	 **16**
4	**1e**		1	99	 **17**
5	**1g**		3	88	 **18**
6	**1h**		4	85	 **19**

[a]All reactions were performed in a 0.6 M solution of DCM in atmospheric conditions with 3 mole equivalents of the specified amine and 2 mole equivalents of Dowex 50WX4. [b]Isolated yield. [c]Ratio of **14a**:**14b** was 77:23. [d]Product was observed by 1H NMR, but not isolated.

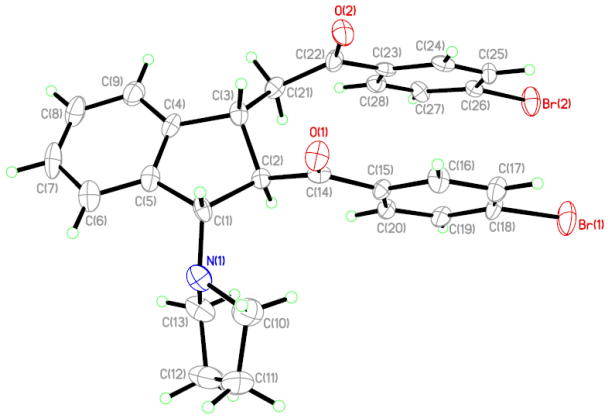
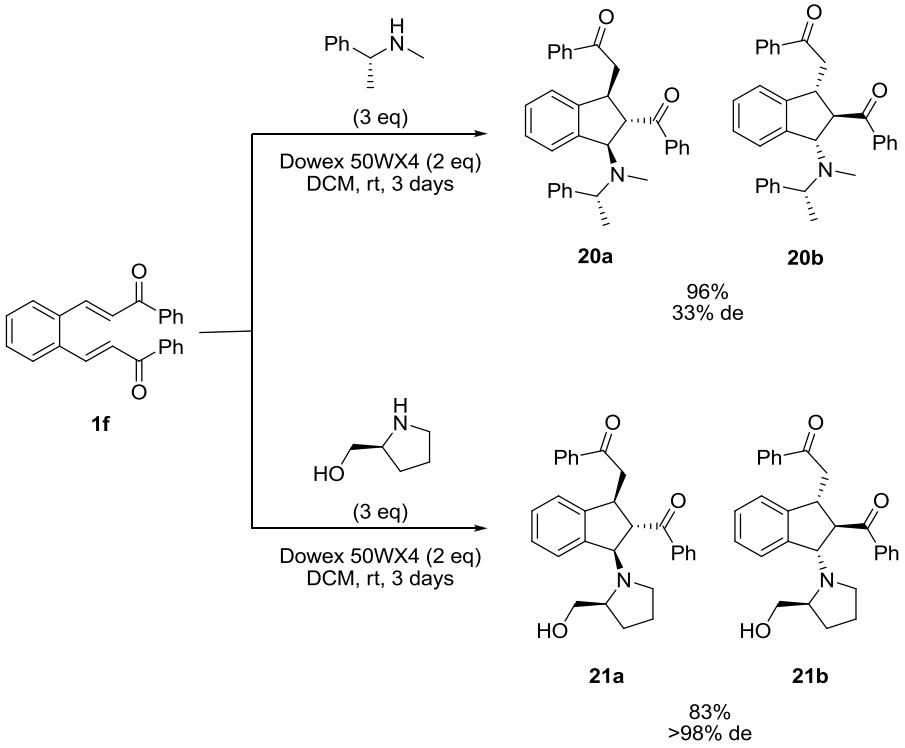


Figure 3. ORTEP representation of compound **17**.

The excellent *trans,trans* selectivity that achiral amines exhibit with aryl ketones demanded that we expose **1f** to a chiral amine to determine the degree of enantioselectivity that can be induced. The addition of (*S*)-(−)-*N*,α-dimethylbenzylamine to **1f** produced an inseparable mixture of stereoisomers in a disappointing 2:1 ratio (Scheme 6). The enantiomeric excess of **20a** and **20b** was determined by ^{1}H NMR spectroscopy, however we are unable to determine which isomer is in excess. On the other hand, the addition of (*S*)-(+)-2-(hydroxymethyl)pyrrolidine produced a single isomer, **21b**, though the yield was lower. The identity of 21b was determined by NOE spectroscopy and DFT calculations, performed on the M06-2X/6-31G** level of theory, suggest that **21b** is 8.18 kcal/mol lower in energy than **21a**. We hypothesize that either the rigid ring structure in (*S*)-(+)-2-(hydroxymethyl)pyrrolidine is better able to transfer chiral information during the course of the reaction or that the hydroxy group is able to hydrogen bond with the carbonyl of **1f** helping to guide the amine to the *re*-face of the enone.



Scheme 6. The additions of chiral amines to **1f** vary in diastereoselectivity.

The critical role of excess acid and amine indicate the importance of carbonyl activation by a proton or more likely a hydrogen bond with a mono- or dialkylammonium ion. By keeping the reactants very concentrated, the proximity of ammonium ions is assured, facilitating the activation of carbonyls and assisting in the transfer of protons. While no mechanistic studies have been performed, we propose that a likely mechanism for the formation of aminoindanes involves the reversible conjugate addition of an amine to the activated α,β-unsaturated carbonyl system **III**, producing enol **IV** (Figure 4). The newly generated enol **IV** (which is in equilibrium with its tautomer), quickly proceeds via an intramolecular Michael addition to yield **V**. The final proton transfer step produces the aminoindane **VI**.

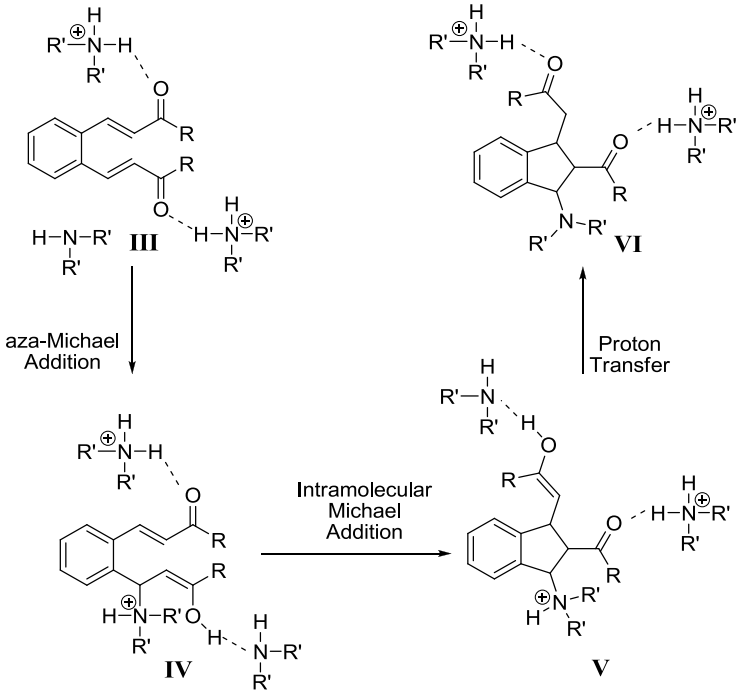


Figure 4. A proposed mechanism for the formation of aminoindanes by way of cascading conjugate additions.

3.3. Conclusion

In summary, we have developed a new, mild method for synthesis of trisubstituted indanes via cascading conjugate additions. Dowex 50WX4, a sulfonic acid resin, proved to be an extremely effective, easy to handle, and reusable catalyst. Various primary and secondary amines readily react with tethered aryl ketones, producing excellent yields of *trans*,*trans* aminoindanes. Lastly, we have shown that the use of chiral amines can induce moderate to excellent diastereoselectivities.

The research presented in this chapter confirms that amines can add to phenylene-linked bis(enones) to form new five-membered rings. This discovery describes the exact type of reactivity that a tertiary amine catalyst must possess in order to catalyze the aza-

iRC reaction. Chapter IV synthesizes the observations made in chapters II and III to develop a protocol for the first intramolecular aza-Rauhut-Currier reaction.

CHAPTER IV

DEVELOPMENT OF THE AMINE-CATALYZED INTRAMOLECULAR RAUHUT-CURRIER REACTION

Crystal structure determination was performed by Lev N. Zakharov. John W. Bassett contributed greatly to the exploratory work presented in this chapter. The initial development of the reaction, writing of this chapter and all other work was performed by the author. Professor Kenneth M. Doxsee provided editorial assistance and scientific guidance for all material (published and un-published) covered in this chapter.

4.1. Introduction

Our group is interested in the development of ring forming reactions catalyzed by small organic molecules. In chapter II we described our work on the phosphine-catalyzed intramolecular Rauhut Currier (iRC) reaction.[1,2] These experiments revealed that the addition of phenol, a weakly acidic hydrogen bond donor, increased the rate of iRC reactions and reduced the amount of base-catalyzed side products. While we developed a very efficient, selective protocol for the phosphine induced cyclization of tethered enones, we found tertiary amines to be completely ineffective catalysts. Other groups have also noted the inability of common nucleophilic amine catalysts such as DMAP,

DABCO, DBU, quinuclidine, and triethylamine to induce cyclization in a variety of bis(enone) substrates.[xi,3,4]

In chapter III we describe the addition of a variety of primary and secondary amines to phenyl ketone **1a** via an aza-Michael/intramolecular-Michael cascade, mimicking the reactivity required for an amine catalyzed iRC (Figure 1). Like the phospha-Michael-Michael additions described in chapter II, these aza-Michael-Michael additions are accelerated by a protic additive, in this case Dowex 50WX4. Because the rate of addition is very sensitive to the size of the substituents on the amine, we hypothesized that tertiary amines were simply too large to undergo the requisite conjugate addition.

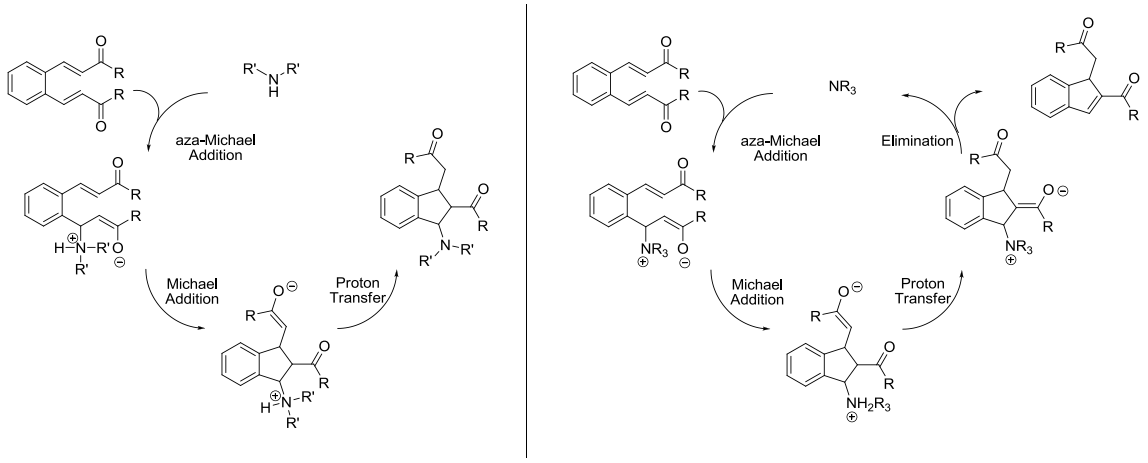


Figure 1. Left, the formation of aminoindanes via an aza-Michael-Michael cascade. Right, the proposed mechanism of the amine catalyzed iRC proceeding through an aza-Michael-Michael cascade followed by elimination of the catalyst.

These observations proved to be essential for the development of an amine catalyzed iRC. To date, the only organocatalysts shown to induce the iRC contain either a nucleophilic phosphorous or sulfur atom.[1,2,5-16] Because amine nucleophiles tend to be

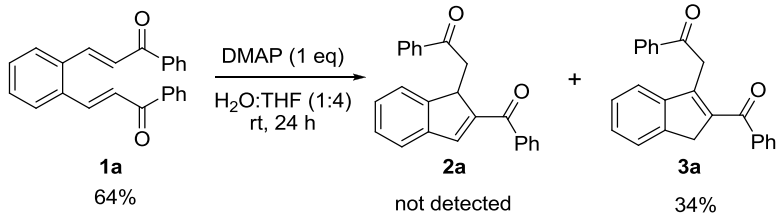
[xi] DMAP = N,N-dimethyl-4-aminopyridine, DABCO = 1,4-Diazabicyclo[2.2.2]octane, DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene

less prone to oxidation, provide access to the chiral pool, and are often easy to handle solids (e.g., DABCO, DMAP, quinuclidine), the introduction of amine catalysts to the synthetic chemist's toolkit would prove to be a significant addition.

Chapter IV describes the development of the first amine catalyzed iRC reaction.

4.2. Results and Discussion

Our initial cyclization attempts were performed with **1a** as the substrate. To confirm that the previous lack of reactivity of tertiary amines was due to the aprotic reaction environment, we exposed **1a** to DMAP, a planar, nucleophilic amine catalyst, in a solution of tetrahydrofuran and water (Scheme 1). We were pleased to discover that DMAP was able to cyclize **1a** to generate the more stable indene isomer, **3a**, albeit slowly (Scheme 1 and Figure 2). Because we already established that 1,2-disubstituted indenes isomerize in the presence of amines, the absence of indene **2a** was expected. Encouraged by the cyclization of **1a**, we set out to more carefully explore and describe the amine-catalyzed iRC reaction.



Scheme 1. Indene **3a** was generated from the cyclization of a 0.06 M solutions of **1a** in aqueous THF.

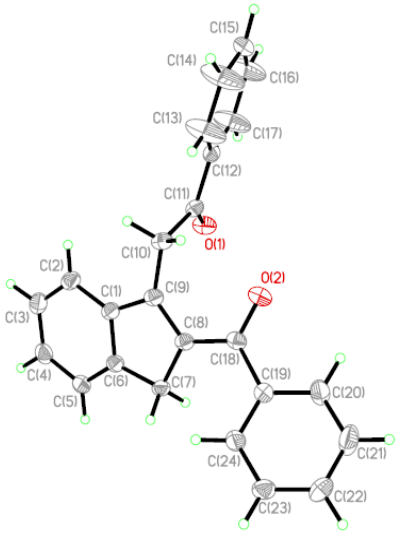
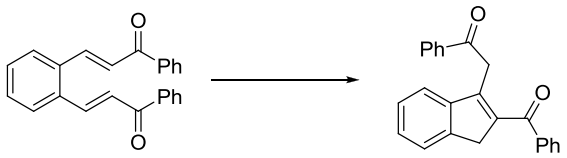


Figure 2. X-ray crystal structure of **3a**. [xii]

We first varied the amount of water in the THF solutions. We found that water was essential for the reaction to proceed (Table 1, entries 1-3 versus 5), however solutions with high proportions of water failed to dissolve the starting materials (Table 1, entry 2). Interestingly, the addition of ethanol did not have the same effect as water (Table 1, entry 4). It became clear that a hydrogen bond donor was essential for the DMAP catalyzed cyclization of **1a**. Given the success of phenol as an additive in our previous research, we were unsurprised when addition of phenol led to an increase in reaction rate when compared to water (Table 1, entries 6 and 7). No longer constrained by water-miscible solvents, the cyclization of **1a** was performed in a variety of solvents (Table 1, entries 6-14). Good yields were obtained in *tert*-amyl alcohol, though only in the presence of phenol (Table 1, entry 13 versus 14).

[xii] Crystals were grown by allowing a solution of DCM/Hexanes to slowly evaporate through a septum.

Table 1. Solvent effects on the cyclization of **1a** to **3a** by DMAP.[a]



1a **3a**

Entry	Solvent	Co-Catalyst	Time (h)	Yield (%)[b]
1	H_2O/THF (1:4)	none	72	31
2	H_2O/THF (1:1)	none	72	24
3	H_2O/THF (1:9)	none	72	20
4	EtOH/THF (1:4)	none	72	NR
5	THF	none	72	NR
6	THF	Phenol (0.5eq)	24	9
7	THF	Phenol (1.5eq)	24	28
8	Ethyl Acetate	Phenol (1.5eq)	24	57
9	Toluene	Phenol (1.5eq)	72	24
10	Dichloromethane	Phenol (1.5eq)	72	33
11	Acetonitrile	Phenol (1.5eq)	24	32
12	Dimethylsulfoxide	Phenol (1.5eq)	24	8
13	*tert*-Amyl Alcohol	Phenol (1.5eq)	24	82
14	*tert*-Amyl Alcohol	none	24	NR
15	3,3,3-Trifluoroethanol	Phenol (1.5eq)	24	95
16	3,3,3-Trifluoroethanol	none	24	97

[a]All reactions were run at 0.03 M with 1 equivalent of DMAP at room temperature. [b]Determined by 1H NMR.

As with the phosphine catalyzed iRC described in chapter II, we found that the addition of phenol greatly speeds up the rate of cyclization. We suspect that its hydrogen bond donating ability may help to stabilize one or all of the various enolate intermediates (**I**, **II**, or **III**) generated during the course of the reaction (Figure 3). The proposed mechanism for the intramolecular Rauhut-Currier first involves the conjugate addition of the nucleophile to an enone to generate enolate **I**. The enolate subsequently undergoes an intramolecular conjugate addition to the tethered enone moiety, producing intermediate **II**. A proton transfer produces the more stable zwitterion **III** which then eliminates the nucleophile, regenerating the catalyst. In the case of indene formation, a base catalyzed isomerization results from the deprotonation of the newly generated 1,2-disubstitued

indene, followed by the protonation of the resulting indenide **IV**, to produce the more stable 2,3-disubstitued indene (Figure 3).

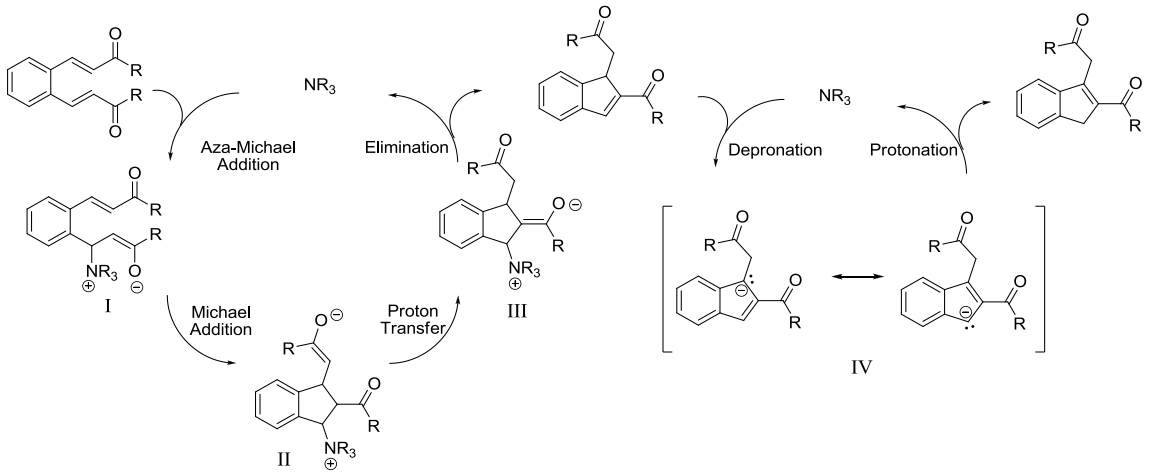


Figure 3. Proposed mechanism of the DMAP catalyzed intramolecular Rauhut-Currier and the isomerization of the resulting 1,2-disubstituted indene.

We hypothesized that either the superior hydrogen bond donating ability or the acidity of phenol was the reason for its remarkable performance as an additive (Table 2, entry 1,2 versus 3). To test this theory, we subjected **1a** to DMAP in 3,3,3-trifluoroethanol (TFE), a solvent with similar hydrogen bonding ability to phenol (Table 2, entries 3 and 4). We were extremely pleased to find that the use of TFE allowed for the complete conversion of **1a** both with and without phenol as an additive (Table 1, entries 15 and 16). The disparity in reactivity between *tert*-amyl alcohol and TFE as reaction media highlights the role that hydrogen bond donating ability or acidity have on the rate of the reaction (Table 1, entry 14 versus 16 and Table 2, entry 1 versus 4). Interestingly, we found that the cyclization of **1a** proceeded at the same rate in a 1:4 mixture of H_2O/THF and a 1:4 mixture of D_2O/THF. The lack of a detectable kinetic isotope effect suggests that protic additives do not act as acids during the rate determining

step. As a result we currently believe that the observed rate enhancement is due to charge stabilizing ability of these additives.

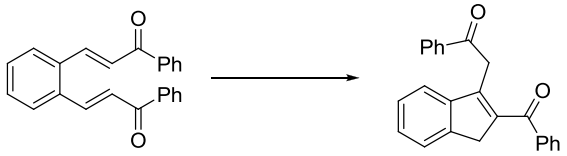
Table 2. The acidity (pKa) and hydrogen bond donor ability (α) of water, phenol, and 3,3,3-trifluoroethanol.[17]

Entry	Compound	pKa[a]	α[b]
1	tertiary alcohols[c]	18.5-19.5	0.319
2	water	15.7	0.353
3	phenol	9.95	0.597
4	3,3,3-trifluoroethanol	12.39	0.567

[a]Lower pKa values indicate greater acidity. [b]Higher α values indicate greater hydrogen bond donating ability. [c]Simple tertiary alcohols include *tert*-butanol and *tert*-amyl alcohol.

Closer examination of the reaction conditions revealed DMAP to be the only nucleophilic amine catalyst that we tested capable of cyclizing **1a** (Table 3, entries 1-7). Decreased catalyst loading corresponded to reduced reaction rates (Table 3, entries 7-10). Conversely, heating and/or concentrating the reactions increased the rate, although higher concentrations led to solubility issues (Table 3, entries 11-15). We found the synthesis of **3a** using a 50 mol % catalyst loading for DMAP at 40º C to be the most efficient use of time and materials (Table 3, entry 12).

Table 3. Catalyst screening and optimization of reaction conditions in 3,3,3-trifluoroethanol.[a]



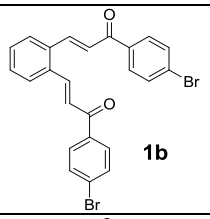
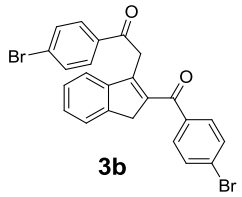
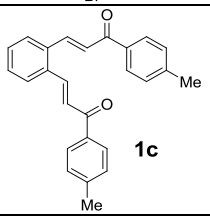
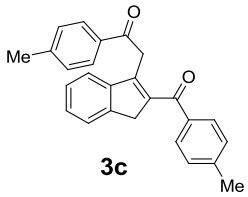
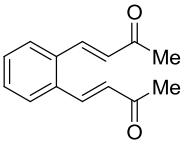
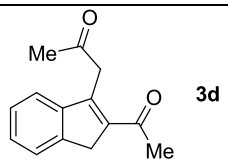
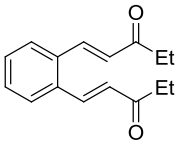
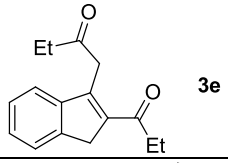
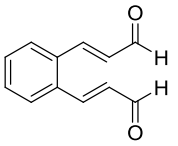
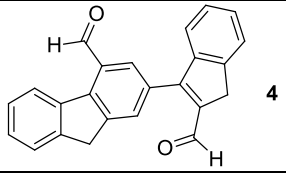
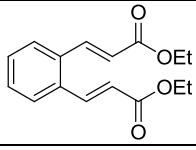
1a **3a**

Entry	Concentration (M)	Catalyst (mol%)	Temp (°C)	Conversion (%)[b]
1	0.030M	Pyridoxine (100)	22	0
2	0.030M	Triethylamine (100)	22	0
3	0.030M	DABCO (100)	22	0
4	0.030M	Quinuclidine (100)	22	0
5	0.030M	Pyridine (100)	22	0
6	0.030M	1-methylimidazole	22	0
7	0.030M	DMAP (100)	22	90
8	0.030M	DMAP (50)	22	68
9	0.030M	DMAP (25)	22	15
10	0.030M	DMAP (10)	22	8
11	0.060M	DMAP (10)	22	40
12	0.030M	DMAP (50)	40	92
13	0.030M	DMAP (25)	40	61
14	0.060M	DMAP (25)	40	88
15	0.060M	DMAP (10)	40	74

[a]Reactions were stirred at room temperature or in an oil bath for 24 hours. [b]Determined by 1H NMR.

With a set of optimized reaction conditions in hand, we explored the substrate scope by treating substrates **1b-g** to DMAP (50 mol %) in 3,3,3-trifluoroethanol (Table 4). The cyclization was very sensitive to the electronic environment of the aryl ketones (Table 4, entries 1 and 2) and the size of the substituents on the akyl ketones (Table 4, entries 3 and 4). Bis(enoate) **1g** proven to be unreactive in these conditions and bis(enal) **1f** was consumed in 24 hours to yield compound **4**, mirroring the reactivity it displayed in chapter II.

Table 4. Substrate scope of the amine catalyzed intramolecular Rauhut-Currier reaction.

Entry	Substrate	Time (days)	Temp (ºC)	Yield (%)	Product
1	 **1b**	1	40	96	 **3b**
2	 **1c**	7	80	93	 **3c**
3	 **1d**	4	80	81	 **3d**
4	 **1e**	8	80	75	 **3e**
5	 **1f**	1	22	78	 **4**
6	 **1g**	8	80	0	-

4.3. Conclusion

The research described here represents the first example of an amine catalyzed iRC reaction. When performed in 3,3,3-trifluoroethanol, the DMAP catalyzed reaction proceeds without the aid of co-catalysis. By using an amine catalyst, air- and water-free conditions are not necessary, a significant advantage over the phosphine catalyzed

variant. Both aryl and alkyl ketones are cyclized under these conditions, generating the more stable 2,3-disubstitued indene isomer exclusively. This research also indicates that strong hydrogen bond donors enhance the rate of the iRC not by donating protons, but through the stabilization of the zwitterionic intermediates.

CHAPTER V

TRANSFORMATIONS OF DISUBSTITUTED INDENES:

THE FORMATION OF 1-HYDROXYFLUORENES

Crystal structure determination was performed by Lev N. Zakharov. The writing of this chapter and all other work was performed by the author. Professor Kenneth M. Doxsee provided editorial assistance and scientific guidance for all material (published and un-published) covered in this chapter.

5.1. Introduction

The aldol condensation is the reaction between two carbonyl compounds in which one carbonyl acts as the electrophile while the other, in the enol or enolate form, acts as the nucleophile.[1-5] A powerful carbon-carbon bond forming reaction, the intramolecular aldol has been used to synthesize a variety of biologically important molecules including fused β-lactams,[6] (+)-wortmannin,[7] rotenoids,[8] and furocoumarins (Figure 1).[9] New five- and six- membered rings are typically generated by subjecting tethered diketones (most often 1,5-diketones) to either acidic or basic conditions.[1-5]

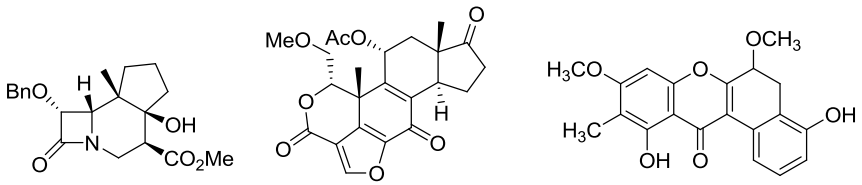
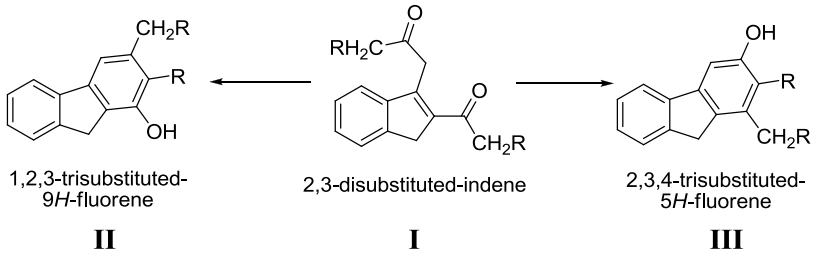


Figure 1. The intramolecular aldol reaction is an important step in the total synthesis of a variety of natural products.

During the course of our studies of the intramolecular Rauhut-Currier reaction (iRC), we generated a library of indenes that contained 1,5-ketones (Scheme 1, **I**).[xiii] These iRC products have the potential to be transformed into a variety of fused polycyclic aromatic compounds. By performing an intramolecular aldol condensation, we anticipated the formation of substituted fluorenes, a class of compounds that show significant potential in electronic materials (Scheme 1, **II** and **III**).[10-22]



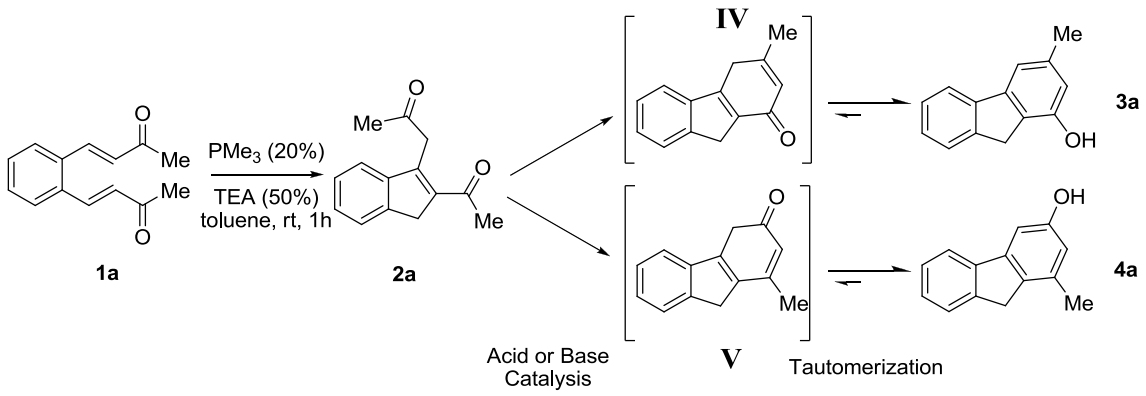
Scheme 1. Both fluorenes **II** and **III** could arise from the intramolecular aldol reaction of **I** .

This chapter presents the synthesis of a variety of fluorene derivatives via a regioselective, one-pot transformation of phenylene-tethered bis(enones).

5.2. Results and Discussion

During the course of our research on the iRC, we found that catalytic amounts of trimethyl- or tributylphosphine in the presence of triethylamine cyclize bis(enone) **1a** to form indene **2a** (Scheme 2). Possessing enolizable carbonyl groups in a 1,5-relationship, we anticipated that **2a** would easily undergo an intramolecular aldol reaction upon exposure to acidic or alkaline solutions, generating hydroxymethyl fluorene **3a** or **4a** (Scheme 2).[23,24]

[xiii] See chapters II and IV.



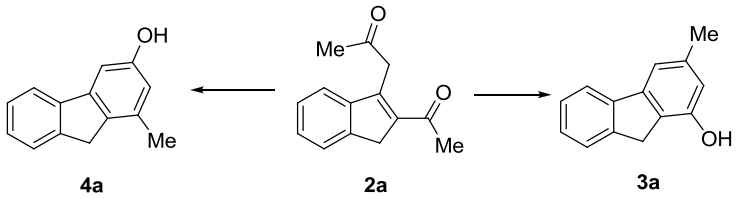
Scheme 2. The intramolecular aldol condensation of **2a** could proceed through either intermediate **IV** or **V** to generate the corresponding fluorene.

We predicted that enolization of the α,β-unsaturated ketone would generate **3a** via tautomerization of cyclohexenone **IV**. Alternatively, enolization of the β,γ-unsaturated ketone would produce intermediate cyclohexene **V,** which would aromatize to yield **4a**. A priori, we could not predict if **3a** or **4a** would be the major product.

Our initial attempts at inducing an intramolecular aldol reaction used **2a** as the substrate. Treatment of **2a**, a white solid, with catalytic or stoichiometric amounts of potassium *tert*-butoxide in THF generated a dark-green solution within five minutes (Table 1, entries 1 and 2). However the color disappeared instantly when the reaction was quenched with 10% HCl 30 minutes later, showing no conversion of starting material. We postulate that the observed color change is due to the deprotonation of the relatively acidic α-hydrogen on the exocyclic methylene group (Figure 2). Moving from basic to acidic conditions, we allowed a 0.035 M solution of **2a** and 10 equivalents of HCl in ethanol to stir overnight.[25] These conditions provided the complete consumption of starting material but generated an unidentifiable product that was insoluble in organic

solvents (THF, acetone, toluene, chloroform, DCM). Chapter VI discusses this reaction and product in more detail.

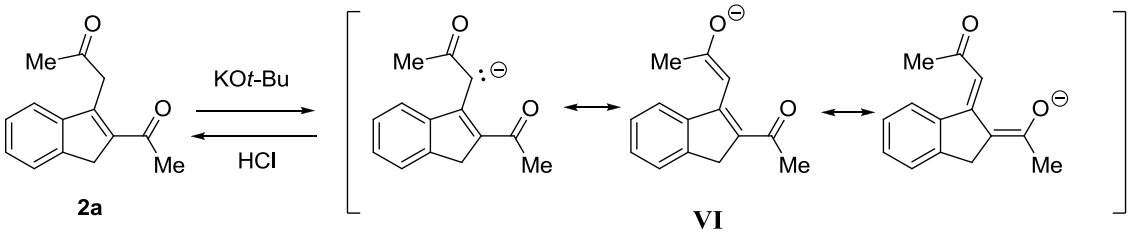
Table 1. Optimization of conditions for the conversion of **2a** to either fluorene **3a** or **4a**.



4a **2a** **3a**

Entry	Reagent	Temp (°C)	Time (h)	Yield of **3a** (%)	Yield of **4a** (%)
1	KO*t*-Bu (25%)	0	0.5	0	0
2	KO*t*-Bu (100%)	0	0.5	0	0
3[a]	HCl (1000%)	22	15	0	0
4	PBu_3 (100%)	50	15	93	nd[b]

[a]Provided complete consumption of starting material. [b]Not detected by ^{1}H NMR.



2a **VI**

Figure 2. Deprotonation of **2a** likely generates the stable enolate **VI** instead of **3a** or **4a**.

Undeterred by these results, we turned to less conventional methods for the induction of aldol condensations. A literature search revealed that Thalji and Roush reported a phosphine catalyzed intramolecular aldol reaction of unsaturated 1,5-diketones.[26] Using the literature procedure, we treated **2a** with 1 equivalent of tributylphosphine in 3,3,3-trifluoroethanol to generate solely **3a** in 93% yield (Table 1, entry 4). The regiochemistry of **3a** was determined by NOE experiments showing the

proximity of the methyl group to the only two aromatic singlets, while irradiation of the hydroxy group revealed its location near the fluorene methylene group (Figure 3).

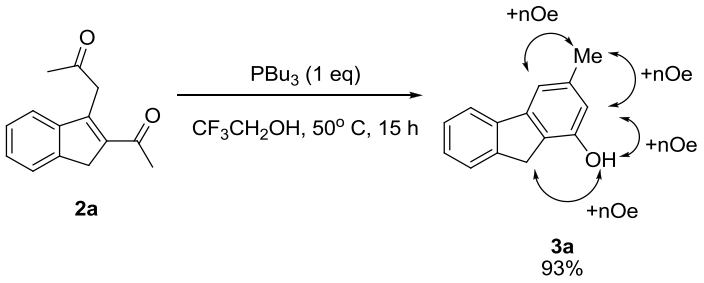
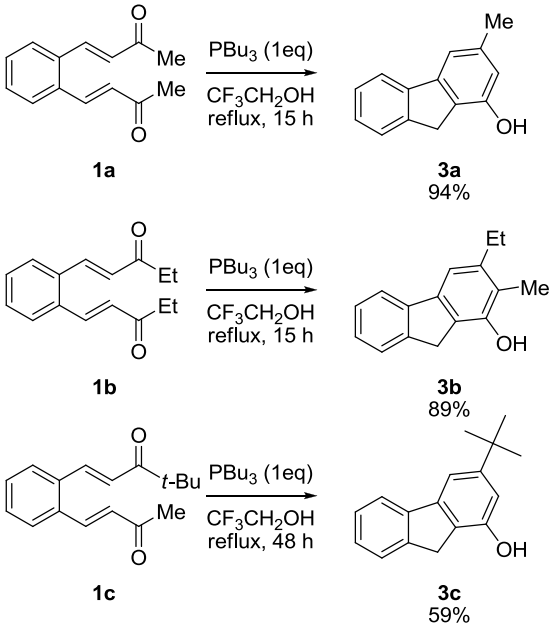


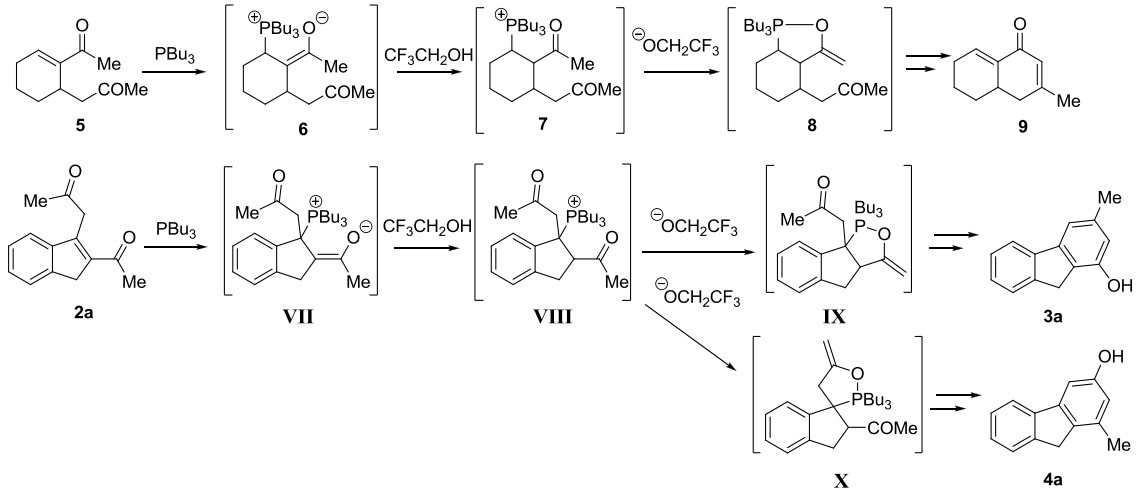
Figure 3. Treatment of **2a** produces solely fluorene **3a**.

Given that **2a** is produced by a phosphine catalyzed reaction, it followed that a one-pot conversion of **1a** to **3a** should be attempted. By refluxing a solution of **1a** and tributylphosphine in 3,3,3-trifluoroethanol overnight, we completely converted the starting material to **3a**. This general procedure was equally successful for the conversion of **1b,** however 40% of **1c** remained after 48 hours at reflux (Scheme 3).



Scheme 3. The regiospecific one-pot synthesis of fluorenes **3a**, **3b**, and **3c**.

The reason for the high degree of regioselectivity is not clear. The experiments performed by our group and Roush's both indicate that the unsaturated ketone is enolized and attacks the saturated carbonyl (Scheme 2, intermediate **IV**). Roush explains this regioselectivity by positing that tributylphosphine undergoes a phospha-Michael addition to **5**, generating the zwitterion **6**. Protonation of **6** by a solvent molecule forms **7**, which in turn undergoes an acid/base reaction with the newly formed alkoxide. It is proposed that the appended phosphonium ion stabilizes an enolate formed at the proximal, not the distal, methyl ketone. The stabilization of intermediate **8** is the rationale for the observed regioselectivity. However, because the phosphonium ion is roughly equidistant to each methyl ketone in intermediate **VIII**, this line of reasoning does not follow for our compounds. A potential explanation is that intermediate **X** is less favorable because the spiro structure is less stable and because it places the enolate orthogonal to the electrophilic carbonyl. On the other hand, the formation of **IX** leads to neither of these problems.



Scheme 4. Top, the proposed intermediates proposed by Roush. Bottom, the proposed intermediates for the transformation of **2a** to either **3a** or **4a**.

5.3. Conclusion

We have prepared a set of di- and tri-substituted fluorenes via an intramolecular aldol condensation. While exposure to acidic and basic conditions did not induce the aldol reaction, we found that treatment tributylphosphine in 3,3,3-trifluorethanol generated the desired fluorenes in a highly regiospecific manner. We also found that fluorenes could be cleanly synthesized from the precursor bis(enones) in a one-pot, tandem iRC/aldol reaction.

CHAPTER VI

TRANSFORMATIONS OF DISUBSTITUTED INDENES: THE FORMATION OF 9*H*-INDENO[2,1-*c*]PYRYLIUM SALTS

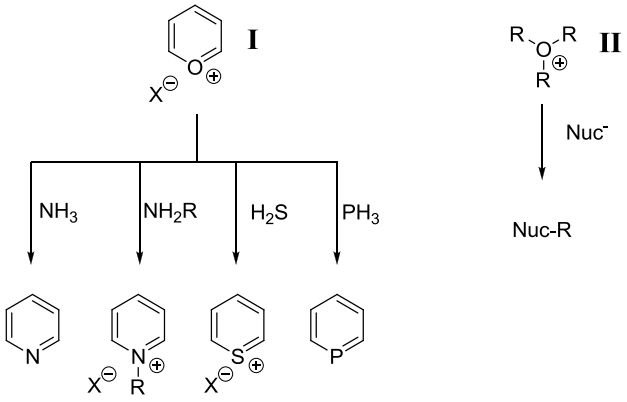
Crystal structure determination was performed by Lev N. Zakharov. Some of the compounds in this chapter were synthesized by John W. Bassett. The writing of this chapter and all other work was performed by the author. Professor Kenneth M. Doxsee provided editorial assistance and scientific guidance for all material (published and un-published) covered in this chapter.

6.1. Introduction

Pyrylium cations are the heterocyclic oxonium derivative of benzene (Scheme 1, **I**). Due to its aromatic stability, the pyrylium cation is significantly more stable than its trialkyoxonium analogue (Scheme 1, **II**).[1,2] While unable to undergo electrophilic aromatic substitution, pyrylium ions readily accept nucleophiles at the 2, 4 or 6 position. When attacked by a nucleophile, pyrylium salts undergo what is called an ANRORC reaction (Attack by Nucleophile, Ring Opening, Ring Closure). This type of reactivity allows pyrylium salts to be transformed into a wide variety of heterocyclic, aromatic compounds (Scheme 1).[3,4]

Many brightly-colored pyrylium compounds can be found in nature. For example, anthocyanidins are a class of plant pigments that are responsible for many of the red, purple, and blue colors found in flowers, fruits and leaves. (Figure 1).[6-8]

Unnatural pyrylium salts have many interesting properties and uses including their multi-photon absorption which allows them to be used in optical data storage, lasing, photodynamic therapy and as photosensitizers for photo-induced electron transfer.[9-14] Pyrylium salts are also used in synthetic chemistry as a method of converting primary amines into pyridinium salts, increasing the amine's leaving group ability.[15-16]



Scheme 1. Pyrylium salts, **I**, undergo ANRORC reactions upon exposure to nucleophiles whereas trialkyloxonium ions, **II**, act as alkylating agents.

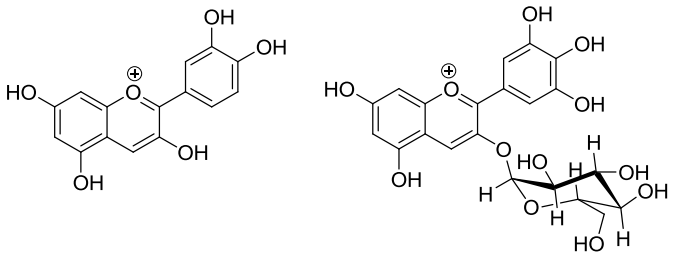
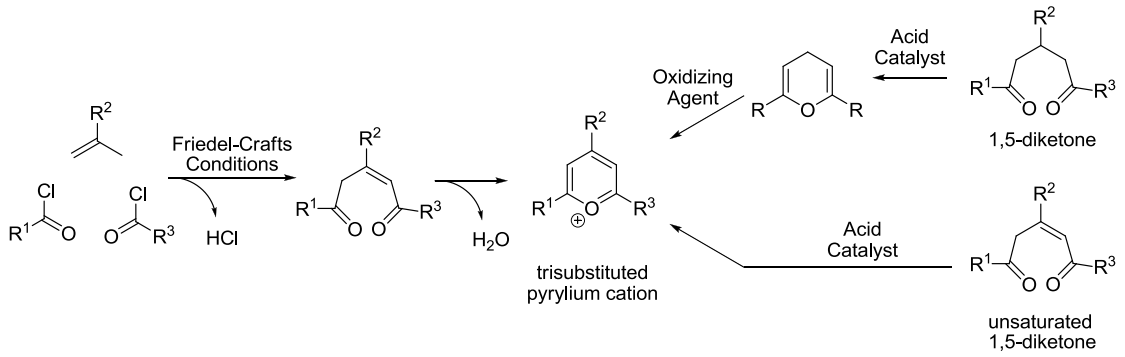


Figure 1. Examples of pyrylium containing anthocyanidins commonly found in nature.

Pyrylium salts are typically synthesized by either the acylation of alkenes or the dehydration of 1,5 diketones (Scheme 2).[17-20] While these methods are able to produce a wide variety of pyrylium, chromenylium, and flavylium cations, we found only the [2,1-*b*] isomer of the indenopyrylium cation reported in the literature (Figure 2).[21-39]



Scheme 2. Pyrylium salts can be prepared by the dehydration of 1,5-diketones or the oxidation of 4*H*-pyrans.

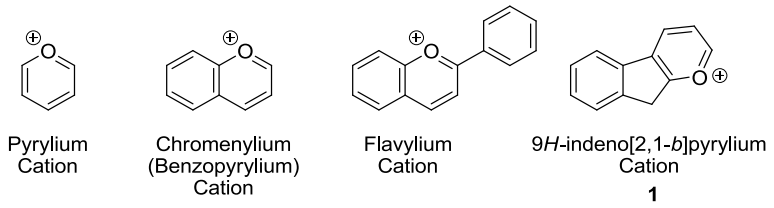
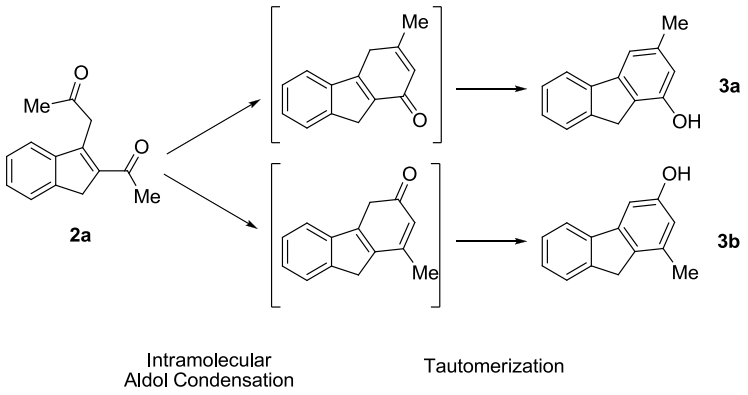


Figure 2. The structures of the parent pyrylium, chromenylium, and flavylium cations along with indenopyrylium **1**.

Chapter VI presents the serendipitous discovery of a route to a novel indenopyrylium isomer. By subjecting 2,3-disubstituted indenes to hydrochloric acid, the previously unknown 1,3-disubstituted-9*H*-indeno[2,1-*c*]pyrylium chlorides are generated in excellent yield under ambient laboratory conditions.

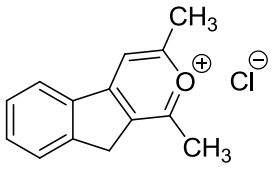
6.2. Results and Discussion

As described in chapter V, our group realized the potential to transform the indenes generated from the intramolecular Rauhut-Currier (iRC) reaction into fused polycyclic aromatic systems. Initially we anticipated that methyl ketone, **2a**, would undergo an intramolecular aldol reaction upon exposure to acidic or alkaline solutions, generating hydroxymethyl fluorene **3a** or **3b** (Scheme 3).[40,41]



Scheme 3. Literature preparations for intramolecular aldol condensations failed to produce **3a** or **3b**.

While treatment with a variety of bases (sodium hydroxide, sodium methoxide, potassium *tert*-butoxide) showed no conversion, exposure of **2a** to acidic conditions completely consumed the starting material and generated a single, unexpected product. The pale orange solid product was poorly soluble in common organic solvents (THF, toluene, chloroform, DCM, diethyl ether) but extremely soluble in water, methanol and ethanol. These observations coupled with close inspection of the ^{1}H and ^{13}C NMR spectra allowed us to identify the product as 1,3-dimethyl-9*H*-indeno[2,1-*c*]pyryrlium chloride, **4a (**Figure 3). X-ray diffraction analysis of orange crystals grown by the vapor diffusion of ethyl ether into an ethanol solution of **4a** confirmed the proposed structure (Figure 4).



4a

1,3-dimethyl-9*H*-indeno[2,1-*c*]pyrylium chloride

Figure 3. Treatment of **2a** with HCl affords **4a**.

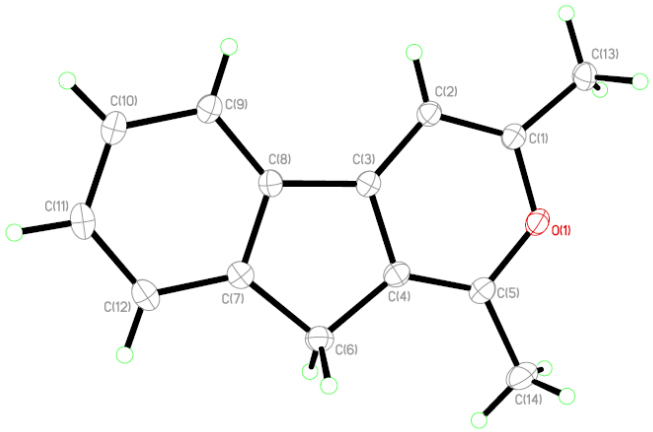
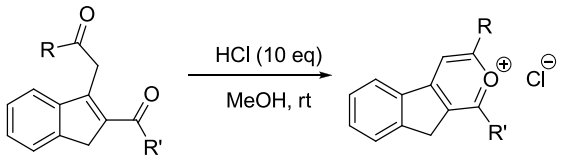
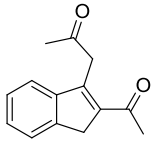
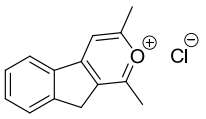
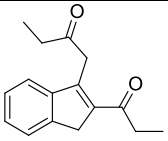
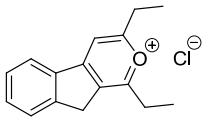
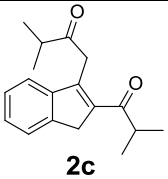
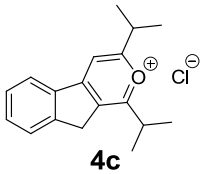
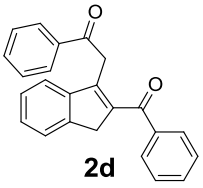
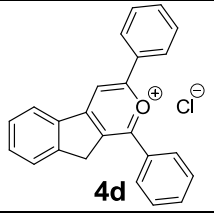
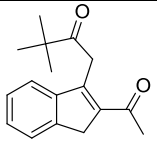
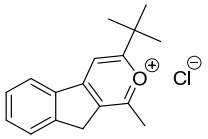


Figure 4. The molecular structure of **4a** as determined by single crystal x-ray diffraction analysis. The chloride ion and water have been omitted for clarity.

To test the reproducibility of the transformation, we introduced indenes **2a**-**2e** to a solution of methanol and hydrochloric acid at room temperature (Table 1). In each case the pyrylium salt was produced in excellent yield (Table 1, entries 1-5). The steric bulk of the alkyl substituents seemed to have little effect on the reaction rate, however conversion of the phenyl ketone, **2d**, occurred at a much slower rate (Table 1, entries 1-3,5 versus 4). Interestingly, we found the 1,2-disubstitued indene isomers to be unreactive when subjected to these reaction conditions. The regiochemistry of **4e** was confirmed by NOE experiments (Figure 5).

Table 1. The formation of a variety of 1,3-disubstituted-9*H*-indeno[2,1-*c*]pyrylium chloride salts.



Entry	Substrate[a]	Time (h)	Yield[b] (%)	Product
1	 **2a**	24	>98	 **4a**
2	 **2b**	24	95	 **4b**
3	 **2c**	13	97	 **4c**
4	 **2d**	47	81	 **4d**
5	 **2e**	45	92	 **4e**

[a]For synthesis of substrates, see chapter II. [b]Isolated yields.

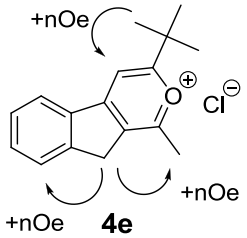


Figure 5. Nuclear Overhauser Effect spectroscopy confirmed the regiochemistry of **4e**.

The likely mechanism for the formation of **4a** via the dehydration of the unsaturated 1,5-diketone **2a** is presented below (Figure 6).[42-44] Acid-catalyzed enolization of the non-conjugated ketone is followed by intramolecular addition of the enol to the adjacent carbonyl group. Finally, the resulting hemiacetal undergoes acid-catalyzed dehydration.

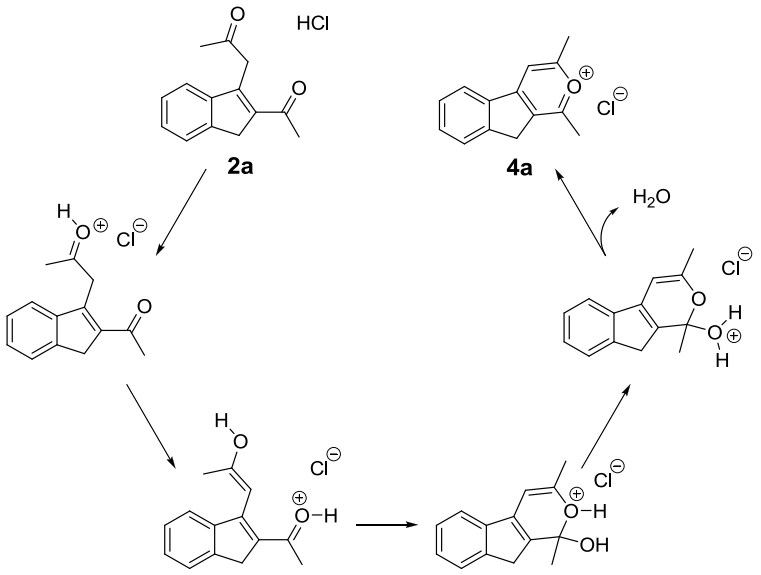


Figure 6. The proposed mechanism for the formation of **4a**.

6.3. Conclusion

We have synthesized a set of novel 1,3-disubstituted-9*H*-indeno[2,1-*c*]pyrylium chlorides. Produced from the iRC reaction, 2,3-disubstituted indenes cleanly and smoothly generate the desired pyrylium salt in excellent yield upon exposure to hydrochloric acid. This methodology provides a straightforward and general approach to a new class of fused, heterocyclic aromatic compounds.

CHAPTER VII

TRANSFORMATIONS OF DISUBSTITUTED INDENES: THE FORMATION OF 9*H*-INDENO[2,1-*c*]PYRIDINES

John W. Bassett contributed to the work presented in this chapter. The writing of this chapter and all other work was performed by the author. Professor Kenneth M. Doxsee provided editorial assistance and scientific guidance for all material (published and un-published) covered in this chapter.

7.1. Introduction

Pyridines are an important class of heterocycles found in many natural products, pharmaceuticals, and synthetic materials (Figure 1).[1-5] As a result, pyridine synthesis enjoys a rich history of myriad synthetic methods.[6-9] Recently, aza-Diels-Alder reactions,[10] 6π-electrocyclic reactions,[11] and ring closing metathesis reactions have been shown as efficient methods for the synthesis of a wide variety of substituted pyridines.[12,13] Historically pyridine synthesis relied on the condensation of an amine with either a mixture of carbonyl compounds or 1,5-diketones (Scheme 1).[14,15]

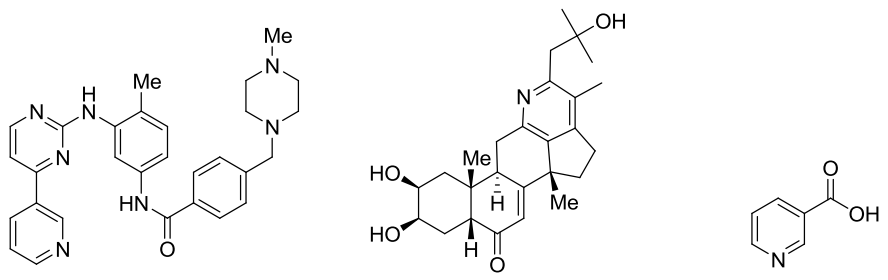
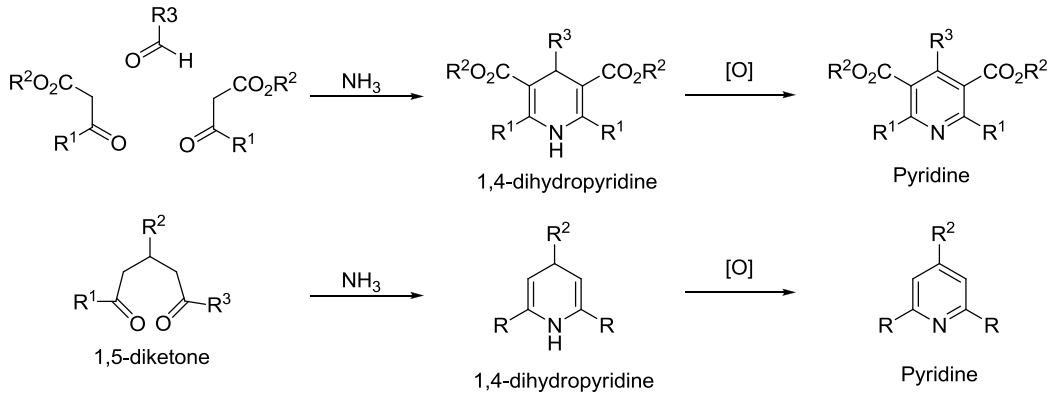


Figure 1. The anti-cancer drug, Imatinib, the natural product, Diplocidine, and nicotinic acid all contain pyridine rings.



Scheme 1. Examples of ammonia addition to carbonyls yielding 1,4-dihydropyridines which are subsequently oxidized to produce the desired pyridine.

During the course of our work on the intramolecular Rauhut-Currier (iRC) reaction, we generated a wide variety of 1,2- and 2,3-disubstituted indenes (Figure 2).[xiv] As discussed in chapters V and VI, our group realized the potential to transform the 2,3-disubstituted indene isomer into fused polycyclic aromatic systems. Possessing 1,5-diketones, we recognized the potential for these indenes to be transformed into 9*H*-indeno[2,1-*c*]pyridines.

[xiv] See chapters II and IV.

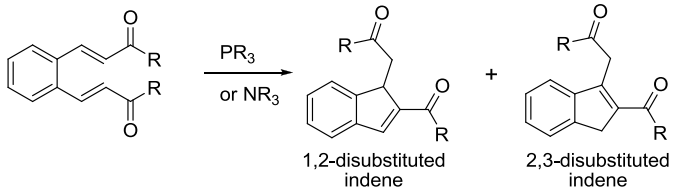


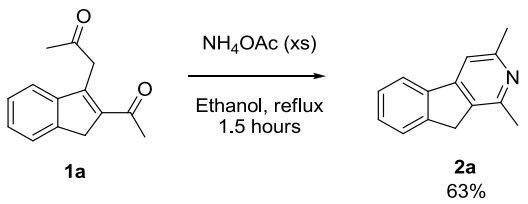
Figure 2. The cyclization of phenylene-linked bis(enones) generates isomeric indenes.

Indenopyridines and their derivatives possess many interesting properties including antiinflammatory,[16] calcium modulating,[17] cytotoxic,[18,19] and antispermatogenic activity.[20,21] They also display two-photon absorptions[22] and patents are being issued for organic light emitting diodes containing indenopyridine structures.[23-25]

This chapter details the condensation of 2,3-disubstituted indenes with ammonium acetate to generate 1,3-disubstituted-9*H*-indeno[2,1-*c*]pyridines.

7.2. Results and Discussion

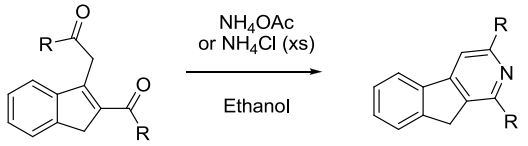
With the successful synthesis of an assortment of indenopyrylium salts (chapter VI), we turned our attention to the generation of nitrogen containing rings. Because the methyl ketone indene **1a** was an unsaturated 1,5-diketone, we envisioned that pyridine formation should proceed in a single step, without the need for a final oxidation step.[26] In fact, treatment of **1a** with excess ammonium acetate in refluxing ethanol rapidly produced 1,3-dimethyl-9*H*-indeno[2,1-*c*]pyridine in 63% yield.[27]

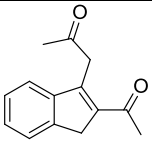
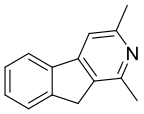
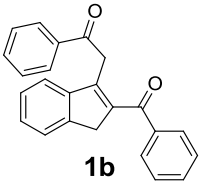
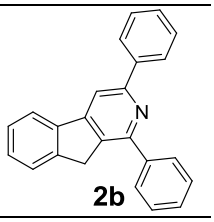
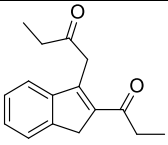
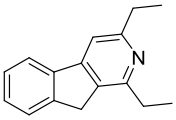
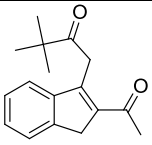
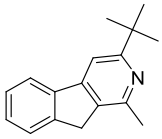


Scheme 2. Indene **1a** undergoes a dehydration reaction with ammonium acetate to produce **2a**.

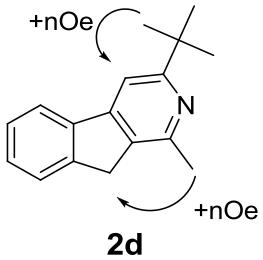
Subsequent optimization revealed that the nitrogen source and reaction temperature were crucial to the successful conversion of starting material (Table 1). Ammonium chloride was found to be an inferior nitrogen source for the formation of pyridines (Table 1, entries 1 versus 2). Also, elevated temperatures seemed to be detrimental to yield, likely due to the evaporation of ammonia during the course of the reaction (Table 1, entry 1 versus 3 and entry 4 versus 5). Indenes **1b**, **1c**, and the asymmetric t-butyl-methyl indene **1d** also reacted smoothly to yield the corresponding indenopyridines (Table 2, entries 5 and 6). The structure of **2d** was confirmed by nuclear Overhauser enhancement spectroscopy (Figure 2). As with the synthesis of indenopyrylium salts, we found the 1,2-disubstitued indene isomers to be unreactive when subjected to these reaction conditions.

Table 1. The formation of a variety of 1,3-disubstituted-9*H*-indeno[2,1-*c*]pyridines.



Entry	Substrate[a]	Reagent	Temp (°C)	Time (h)	Yield[b] (%)	Product
1	 **1a**	NH_4OAc	78	1.5	63	 **2a**
2		NH_4Cl	78	5	0	
3		NH_4OAc	22	1.5	92	
4	 **1b**	NH_4OAc	78	1.5	43	 **2b**
5		NH_4OAc	22	36	88	
6	 **1c**	NH_4OAc	22	4	96	 **2c**
7	 **1d**	NH_4OAc	22	45	91	 **2d**

[a]For synthesis of substrates, see chapter II. [b]Isolated yields.



2d

Figure 3. Nuclear Overhauser Effect spectroscopy confirmed the regiochemistry of **2d**.

7.3. Conclusion

We have presented a third and final transformation of 2,3-disubstituted indenes. This chapter described the facile, room temperature synthesis of four 9H-indeno[2,1-c]pyridine derivatives. Capitalizing on the unsaturation already present in the indenes, we were able to perform a condensation reaction in the presence of ammonium acetate to generate the pyridines in a single step.

CHAPTER VIII

SUMMARY AND FUTURE DIRECTIONS

8.1. Research Summary

Intramolecular cascading Michael additions have the ability to transform simple, symmetric substrates into densely functionalized compounds containing new ring structures and chiral centers. We have described an expansion of the scope of the Rauhut-Currier reaction, the introduction of co-catalysts to cascading Michael additions, the development of the first amine-catalyzed Rauhut-Currier reaction, and the transformation of cyclization products into fused, polycyclic aromatic compounds.

Chapter I summarized the development and applications of the intramolecular Rauhut-Currier (iRC) reaction. Chapter II reported the regioselective synthesis of di-substituted indenes and introduced phenol as a powerful rate- and selectivity-enhancing additive for the phosphine-catalyzed iRC reaction. A wide variety of di-substituted indenes were synthesized, exploring the effects that steric and electronic factors have on reaction performance. While tertiary amine nucleophiles were found to be unreactive under these conditions, chapter III explored the ability of primary and secondary amines to undergo a diastereoselective, cascading aza-Michael-Michael addition to yield a wide variety of amino-indanes in the presence of an acid catalyst, Dowex 50XW4. In chapters II and III we made two important discoveries crucial for the development of the amine catalyzed iRC. We found that cascading conjugate additions are very sensitive to the sterics of the incoming nucleophile and they are promoted by protic environments. Aided

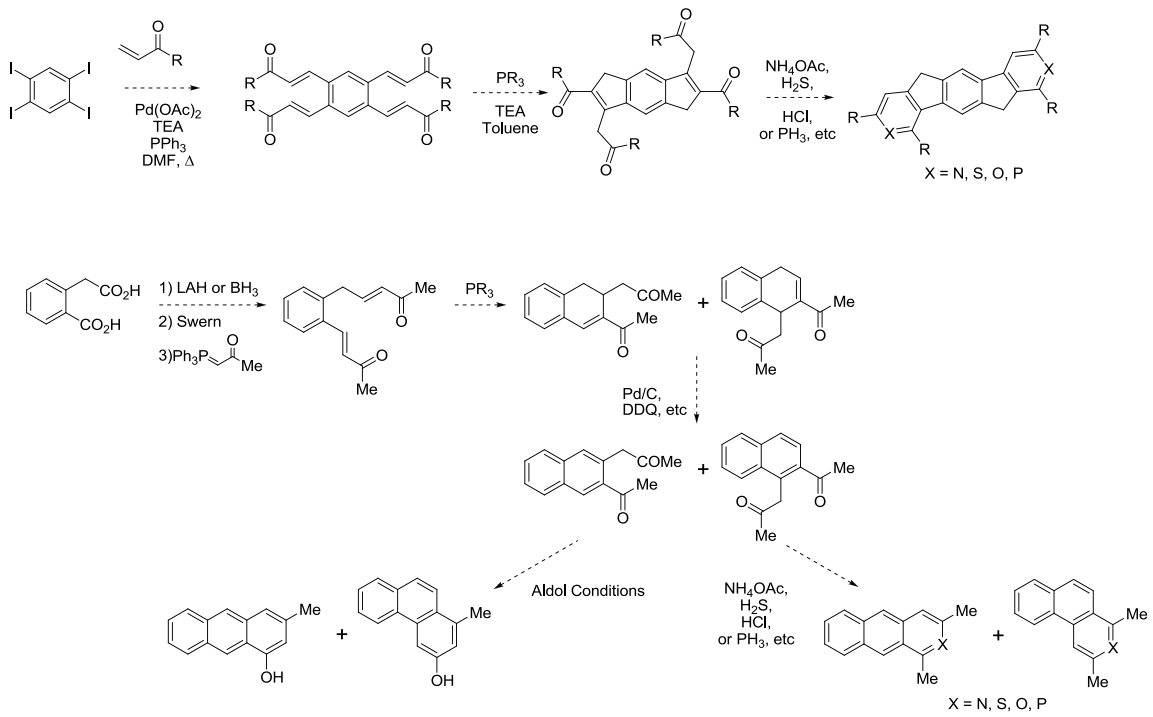
by these observations, we developed the first amine-catalyzed iRC reaction as described in chapter IV.

The indenes generated by the reactions in chapters II and IV possess unsaturated 1,5-diketones, a synthetic precursor to a variety of aromatic compounds. Chapter V described the conversion of these indenes into fluorene derivatives via an intramolecular aldol reaction. Chapter VI told the tale of our serendipitous discovery and synthesis of 9*H*-indeno[2,1-*c*]pyrylium salts. Lastly, chapter VII detailed the transformation of iRC generated indenes into indenopyridines.

8.2. Future Directions

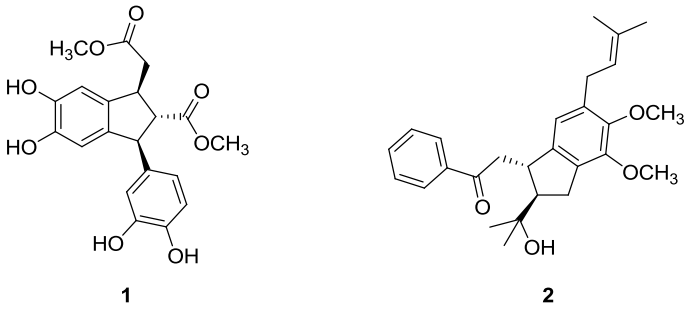
The research described in this dissertation has opened the doors to many avenues of research. We envision the introduction of new protocols for the synthesis of fused polycyclic aromatic compounds, the application of the iRC reaction to the total synthesis of natural products, and the exploration of chiral phosphine and amine catalysts on the enantioselectivity of cascading conjugate additions.

Not only can the 2,3-disubstituted indenes formed by the iRC reaction be used to synthesize the corresponding phosphinines and pyridinium and thiopyrylium salts, but we anticipate the development of new methods to generate a variety of aromatic compounds (Scheme 1).



Scheme 1. A sample of fused polycyclic aromatic compounds incorporating methods established in this dissertation.

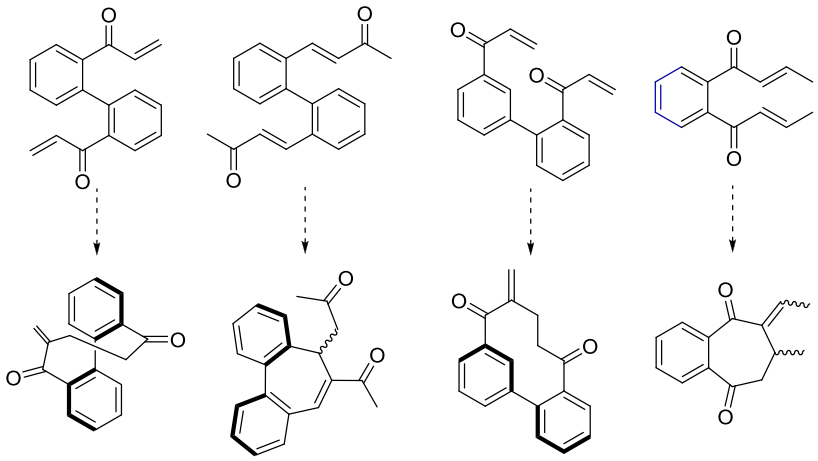
Also, the total synthesis of a variety of natural products using the iRC reaction described herein could be attempted. For example, both the sunflower antioxidant derivative (**1**) and antiarone J (**2**) contain the indane skeleton that can be generated using the protocols established by our research (Figure 1).[1,2]



1 **2**

Figure 1. Examples of natural products that could be synthesized using cascading conjugate additions.

Armed with lessons learned from our research, a revisitation of our original cyclization substrates is in order. While initially found to be unreactive, new insight in the reaction conditions required for cyclization should help to realize the potential of these substrates (Scheme 2).



Scheme 2. Early, abandoned cyclization substrates.

In addition to the pursuit of new synthetic targets, new reaction protocols should be explored. While the enantioselective cyclization of propylene-tethered bis(enones) has been recently introduced using chiral phosphinothioureas (**3**),[3] bifunctional chiral phosphinophenols (**4**)[4,5] or chiral DMAP derivatives (**5** and **6**)[6,7] have yet to be tested on any bis(enone) (Figure 2).

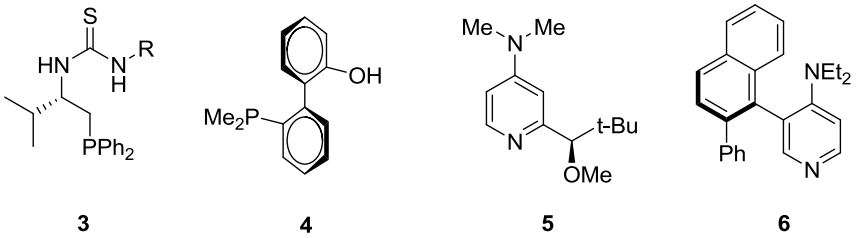


Figure 2. Examples of chiral, nucleophilic catalysts for use in the Rauhut-Currier reaction.

Hopefully, continued work on this project will further expand the scope and utility of the Rauhut-Currier reaction and other cascading conjugate additions.

APPENDIX A

SUPPORTING INFORMATION FOR CHAPTER II

A.1. Experimental Details

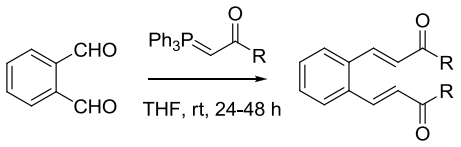
A.1.1. General Methods. Reactions were carried out under an Ar atmosphere using standard Schlenk techniques and, when necessary, glassware was flame-dried (under vacuum) before use. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using either a Varian Inova 300 (^{1}H: 299.93 MHz, ^{13}C: 75.42 MHz) or 500 (^{1}H: 500.11 MHz, ^{13}C: 125.75 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm relative to residual chloroform (^{1}H: 7.26 ppm, ^{13}C: 77.160 ppm). Coupling constants are given in Hertz (Hz). Melting points were recorded on a Melt-Temp II melting point apparatus in open-end capillary tubes. IR spectra were recorded using a Nicolet Magna FTIR 550 spectrometer. High resolution mass spectra were recorded on a Waters Micromass MALDI Q-ToF or JEOL MS Route Magnetic Sector mass spectrometer.

Diffraction intensities for **3a** was collected at 173(2) K on a Bruker Apex CCD diffractometer using MoKα radiation λ= 0.71073 Å. Space groups were determined based on systematic absences. Absorption corrections were applied by SADABS[G. M. Sheldrick, *Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, 1998.]. Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms in **3a** were found on residual density maps and refined with isotropic thermal parameters. All H atoms in **kd94** were refined in calculated positions in a rigid group model. All calculations were performed by

the Bruker SHELXTL (v. 6.10) package [SHELXTL-6.10 "Program for Structure Solution, Refinement and Presentation" BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA].

A.1.2. Starting Materials. Dimethylphenylphosphine was purchased from Strem. With the exception of pinacolonyltriphenylphosphonium bromide, all ylide precursors and phthalaldehyde were purchased from TCI. Remaining reagents and all solvents were purchased from Aldrich. Anhydrous toluene was dried over $MgSO_4$ immediately before use. Unless otherwise stated, all reagents were used as received.

A.1.3. Synthesis of Substrates



1a: R=Me
1b: R=Et
1c: R=iPr
1d: R=tBu
1e: R=p-Br-C_6H_4
1f: R=Ph
1g: R=p-Me-C_6H_4
1h: R=p-OMe-C_6H_4
1i: R=H
1j: R=OEt

General procedure A for formation of substrates. The triphenylphosphonium salt (22 mmol) was suspended in 60 mL of dichloromethane. A solution of 1.80 g of NaOH (45 mmol) in 50 of mL water was added to the stirred suspension. When the biphasic mixture became completely clear, or after 20 minutes, the layers were separated, and the organic layer was washed thrice with water and once with brine. The organic layer was dried over $MgSO_4$ and the solvent was removed *in vacuo.* The crude ylide was redissolved in dry THF (50 mL) and phthalaldehyde (10 mmol) was added. After

18 hours of stirring, the solvent was removed on a rotary evaporator. The resulting residue was purified by column chromatography.

General procedure B for formation of substrates. A solution of α-bromoketone (30 mmol) in 10 mL of toluene was slowly added to a flask containing triphenylphosphine (31 mmol) in 50 mL of toluene. After 6 hr, a white suspension had formed, and a solution of NaOH (33 mmol) in 50 mL of H_2O was added. Once the biphasic mixture became clear (30 min), the layers were separated, and the organic layer was washed thrice with water and once with brine. The organic fraction was dried over $MgSO_4$ and the solvent was removed *in vacuo* in a tared flask allowing for the determination of the mass of crude ylide. The crude ylide was redissolved in dry THF (50 mL) and 1.34g of phthalaldehyde (10 mmol) was added. After 18 hours of stirring, the solvent was removed on a rotary evaporator. The resulting residue was purified by column chromatography.

(3E,3'E)-4,4'-(1,2-phenylene)dibut-3-en-2-one (**1a**). (Triphenylphosphoranylidene)acetone (10.0 g, 31.41 mmol) and phthalaldehyde (1.685 g, 12.56 mmol) were allowed to react in dry THF (50 mL) according to procedure A. The resulting residue was purified by passage through a 6 cm diameter plug of 65 grams of silica, eluting with 50% EtOAc in hexanes (Rf = 0.31), affording **1a** (2.21 g, 82%) as a white solid, mp 88-90 °C. IR (NaCl, neat): 3038, 1678, 1653, 1622, 1596, 1475, 1366, 1256, 1218, 1203, 962, 763, 560 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, *J* = 16.0 Hz, 2H, C**H**=CHC=O), 7.58 (dd, *J* = 5.8, 3.5 Hz, 2H, Ar**H**), 7.41 (dd, *J* = 5.8, 3.4 Hz, 2H, Ar**H**), 6.61 (d, *J* = 16.0

Hz, 2H, CH=C**H**C=O), 2.39 (s, 6H, C**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.84, 139.78, 134.59, 130.45, 130.37, 127.87, 28.15; HRMS (MALDI): Exact mass calcd for $C_{14}H_{14}NaO_2$ $[M+Na]^+$: 237.0891, found: 237.0886.

(3E,3'E)-4,4'-(1,2-phenylene)dipent-3-en-2-one (**1b**). (Triphenylphosphoranylidene)-2-butanone (1.4 g, 3.63 mmol) and phthalaldehyde (0.162 g, 1.21 mmol) were allowed to react in dry THF (7 mL) according to procedure B. The resulting residue was purified by passage through a 6 cm diameter plug of 20 grams of silica, eluting with 50% EtOAc in hexanes (Rf = 0.51), affording **1b** (0.202 g, 69%) as a white solid, mp 47-48 °C. IR (NaCl, neat): 2976, 2937, 1693, 1668, 1612, 1457, 1355, 118, 1120, 1036, 974, 753 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 16.0 Hz, 2H), 7.63 – 7.55 (m, 2H), 7.44 – 7.38 (m, 2H), 6.65 (d, *J* = 15.9 Hz, 2H), 2.72 (q, *J* = 7.3 Hz, 4H), 1.19 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.52, 138.92, 134.92, 130.23, 129.57, 127.88, 34.60, 8.25; HRMS (CI): Exact mass calcd for $C_{16}H_{19}O_2$ $[M+H]^+$: 243.1385, found: 243.1390.

(1E,1'E)-1,1'-(1,2-phenylene)bis(4-methylpent-1-en-3-one) (**1c**). Bromine (0.63 mL, 11.61 mmol) was added all at once to a stirred solution of 3-methyl-2-butanone (1.0 g, 11.61 mmol) in 7.5 mL methanol at 0 °C. The solution was stirred until red color faded away, approximately 1 hour. Then 3 mL of water were added and the solution was allowed to stir at room temperature overnight. The reaction mixture was partitioned using 10 mL of water and 10 mL of ethyl ether. The aqueous layer was extracted three additional times and the combined organic layers were washed with a 10% Na_2CO_3

solution and water twice. The organic fraction was then dried over $MgSO_4$ and the solvent was removed by rotary evaporation. The colorless oil (1.892 g, 98.7% yield) was used in procedure B to generate (triphenylphosphoranylidene)3-methyl-2-butanone. (Triphenylphosphoranylidene)3-methyl-2-butanone (1.44g, 4.15 mmol) and phthalaldehyde (0.134g, 1.0 mmol) were allowed to react in dry THF (7 mL) according to procedure B. The resulting residue was purified by passage through a 6 cm diameter plug of 20 grams of silica, eluting with 50% EtOAc in hexanes (Rf = 0.55), affording **1c** (0.238 g, 88%) as a white, mp 34-36 °C. IR (NaCl, neat): 2969, 2931, 2872, 1688, 1664, 1609, 1466, 1382, 1203, 1147, 1054, 977, 760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 7.94 (d, *J* = 12.2 Hz, 2H), 7.63 – 7.57 (m, 2H), 7.47 – 7.37 (m, 2H), 6.72 (d, *J* = 11.7 Hz, 2H), 3.01 – 2.87 (sept, 2H), 1.18 (d, *J* = 7.2 Hz, 12H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 203.38, 139.31, 135.13, 130.12, 128.17, 128.00, 39.63, 18.54; HRMS (CI): Exact mass calcd for $C_{18}H_{23}O_2$ $[M+H]^+$: 271.1698, found: 271.1696.

(1E,1'E)-1,1'-(1,2-phenylene)bis(4,4-dimethylpent-1-en-3-one) (**1d**). (Triphenylphosphoranylidene)pinacolone (8.29 g, 23.0 mmol) was allowed to react with phthalaldehyde (1.276 g, 9.53 mmol) in dry THF (65 mL). After 2 hr of stirring, the solvent was removed on a rotary evaporator and the resulting residue was purified by flash chromatography on 100 grams of silica, eluting with 33% Et_2O in hexanes (Rf = 0.33), affording **1d** (0.750 g, 58.7%) as a white solid, mp 111-112 °C (recrystallized from hexanes). IR (NaCl, neat): 2973, 1680, 1609, 1473, 1326, 1075, 1005, 756 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, *J* = 15.5 Hz, 2H), 7.58 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.39 (dd, *J* = 5.8, 3.4 Hz, 2H), 6.98

(d, *J* = 15.5 Hz, 2H), 1.23 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.83, 140.28, 135.58, 129.81, 128.34, 124.93, 43.39, 26.39; HRMS (MALDI): Exact mass calcd for $C_{20}H_{26}NaO_2$ $[M+Na]^+$: 321.1830, found: 321.1836.

(2E,2'E)-3,3'-(1,2-phenylene)bis[1-(4-bromophenyl)prop-2-en-1-one] (1e). (Triphenylphosphoranylidene)p-bromoacetophenone (7.85 g, 17.1 mmol) and phthalaldehyde (0.576 g, 4.29 mmol) were allowed to react in dry THF (20 mL) according to procedure B. The resulting residue was purified by passage through a 6 cm diameter plug of 30 grams of silica, eluting with 50% Et_2O in hexanes (Rf = 0.41), affording **1e** (1.64 g, 77%) as a white solid, mp 136-140 °C. IR (NaCl, neat): 3061, 1683, 1663, 1585, 1397, 1214, 1070, 1008, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (d, *J* = 15.5 Hz, 2H), 7.95 – 7.88 (m, 4H), 7.72 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.69 – 7.62 (m, 4H), 7.49 (dd, *J* = 5.9, 3.3 Hz, 2H), 7.39 (d, *J* = 15.5 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 188.95, 142.29, 136.72, 135.42, 132.20, 130.48, 130.26, 128.44, 128.40, 125.62; HRMS (CI): Exact mass calcd for $C_{24}H_{16}Br_2O_2$ $[M+H]^+$ 494.9595, found: 494.9552.

(2E,2'E)-3,3'-(1,2-phenylene)bis(1-phenylprop-2-en-1-one) (**1f**). To a solution of phthalaldehyde (1.128 g, 8.4 mmol) in dry 1,4-dioxane (30 mL) was added (triphenylphosphoranylidene)acetophenone (8.01 g, 21.1 mmol) in 10 mL of dichloromethane. After 18 hours of stirring, the solvent was removed on a rotary evaporator. The resulting residue was purified by passage through a 6 cm diameter plug of 60 grams of silica, eluting with 33% EtOAc in hexanes (Rf =

0.65), affording **1f** (1.536 g, 54%) as a white solid, mp 122-124 °C (recrystallized from EtOAc/hexanes). IR (NaCl, neat): 3061, 3027, 1666, 1609, 1476, 1447, 1331, 1219, 1016 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (2H, d, *J* = 15.6 Hz, C**H**=CHC=O), 8.04 (4H, dd, *J* = 7.2, 1.5 Hz, Ar**H**), 7.72 (2H, AA'BB', *J* = 5.7, 3.5 Hz, Ar**H**), 7.60 (2H, tt, 7.2, 1.5 Hz, Ar**H**), 7.52 (4H, dd, Ar**H**), 7.48 (2H, AA'BB', *J* = 5.7, 3.5 Hz, Ar**H**), 7.44 (2H, d, *J* = 15.6 Hz, CH=C**H**C=O); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.20, 141.84, 137.99, 135.50, 133.13, 130.29, 128.84, 128.74, 128.31, 126.16; HRMS (MALDI): Exact mass calcd for $C_{24}H_{18}NaO_2$ $[M+Na]^+$: 361.1204, found: 361.1188; Anal. Calcd for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36, found: C, 84.90; H, 5.40.

(2E,2'E)-3,3'-(1,2-phenylene)bis(1-p-tolylprop-2-en-1-one) (**1g**). (Triphenylphosphoranylidene)-p-methylacetophenone (1.0 g, 4.69 mmol) and phthalaldehyde (0.146 g, 0.465 mmol) were allowed to react in dry THF (5 mL) according to procedure B. The resulting residue was purified by passage through a 6 cm diameter plug of 30 grams of silica, eluting with 50% Et_2O in hexanes (Rf = 0.31), affording **1e** (0.301 g, 66%) as a white solid, mp 130-132 °C. IR (NaCl, neat): 3030, 2920, 1717, 1677, 1659, 1606, 1329, 1180, 1015, 758 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (d, *J* = 15.6 Hz, 2H), 7.95 (d, *J* = 8.2 Hz, 4H), 7.71 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.460 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.421 (d, *J* = 15.8 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 4H), 2.43 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 189.75, 143.98, 141.50, 135.62, 135.49, 130.14, 129.55, 128.91, 128.32, 126.30, 21.86; HRMS (CI): Exact mass calcd for $C_{26}H_{23}O_2$ $[M+H]^+$: 367.1698, found: 367.1716.

(2E,2'E)-3,3'-(1,2-phenylene)bis(1-(4-methoxyphenyl)prop-2-en-1-one) (**1h**). (Triphenylphosphoranylidene)-p-methoxyacetophenone (1.72 g, 4.37 mmol) and phthalaldehyde (0.145 g, 0.460 mmol) were allowed to react in dry THF (10 mL) according to procedure B. The resulting residue was purified by passage through a 6 cm diameter plug of 20 grams of silica, eluting with 50% ethyl ether in hexanes (Rf = 0.49), affording **1e** (0.301 g, 66%) as a white solid, mp 137-138 °C. IR (NaCl, neat): 2934.61, 2839, 1659, 1599, 1573, 1306, 1262, 1221, 1170, 1022 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (d, *J* = 15.5 Hz, 2H), 8.09 – 8.02 (m, 4H), 7.71 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.46 (dd, *J* = 5.8, 3.3 Hz, 4H), 7.41 (d, *J* = 15.3 Hz, 2H), 6.97 (m, 4H), 3.89 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 188.52, 163.70, 141.21, 135.70, 131.11, 131.01, 130.03, 128.38, 126.21, 114.08, 55.66; HRMS (CI): Exact mass calcd for $C_{26}H_{23}O_4$ $[M+H]^+$: 399.1596, found: 399.1612.

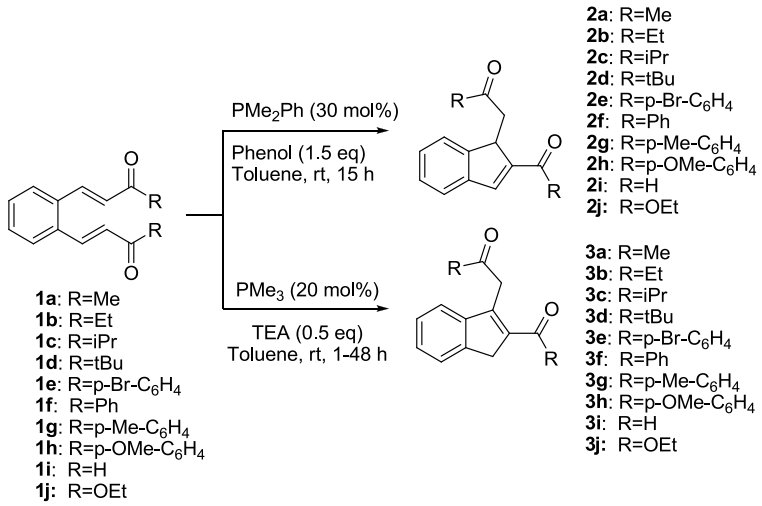
(2E,2'E)-3,3'-(1,2-phenylene)bis(prop-2-en-1-al) (**1i**). Potassium *t*-butoxide (2.63g, 23.44 mmol) was slowly added to a flask containing (1,3-dioxolan-2-yl)-methyltriphenylphosphonium bromide (10.002 g, 23.3 mmol) in 100 mL of toluene cooled in an ice bath. After 30 min, the solution turned deep yellow and a solution of phthalaldehyde (1.358 g, 10.13 mmol) in 20 mL of THF was slowly added. The reaction mixture was stirred for 7 hours at ambient temperature. The mixture was partitioned with 30 mL of dichloromethane and 30 mL of water. The aqueous layer was extracted twice with dichloromethane, and the combined organic layers were washed with water (2x), then brine. The organic fraction was dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was redissolved in 10 mL of acetone and 5 mL of 10% HCl was

added. The reaction mixture was stirred overnight to ensure complete deprotection. The reaction was partitioned with 10 mL of ethyl acetate and 10 mL of water. The organic layer was washed with 5% $NaHCO_3$, water (2x), then brine. The organic fraction was dried over $MgSO_4$ and the solvent was removed *in vacuo*. The resulting residue was purified by flash chromatography on 50 grams of silica, eluting with 50% Et_2O in hexanes (Rf = 0.32), affording **1i** (0.414 g, 22%) as a white solid, mp 106-109 °C. IR (NaCl, neat): 2824, 1670, 1653, 1635, 1620, 1593, 1128, 975, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 9.80 (d, *J* = 7.5 Hz, 2H), 7.88 (d, *J* = 15.8 Hz, 2H), 7.67 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.51 (dd, *J* = 5.9, 3.3 Hz, 2H), 6.69 (dd, *J* = 15.8, 7.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.21, 148.29, 133.91, 132.19, 131.29, 128.21; HRMS (CI): Exact mass calcd for $C_{12}H_{10}O_2$ $[M+H]^+$: 186.0681, found: 186.0687.

(2E,2'E)-3,3'-(1,2-phenylene)di(2-propenoic acid ethyl ester) (**1j**). To a solution of phthalaldehyde (0.490 g, 3.65 mmol) in dry 1,4-dioxane (18 mL) was added ethyl (triphenylphosphoranylidene)acetate (3.338 g, 9.98 mmol). After 15 hours of stirring, the solvent was removed on a rotary evaporator. The resulting residue was purified by passage through a 6 cm diameter plug of silica (30 g), eluting with 30% EtOAc in hexanes (Rf = 0.44), affording **1d** (0.920 g, 91%) as a white solid, mp 72-74 °C. IR (NaCl, neat): 2986, 1711 (C=O), 1635, 1626, 1480, 1310, 1184, 985, 770 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.03 (d, *J* = 15.8 Hz, 2H), 7.57 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.39 (dd, *J* = 5.8, 3.4 Hz, 2H), 6.35 (d, *J* = 15.8 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.55, 141.38, 134.44, 130.13, 127.75, 122.06, 60.85, 14.46;

HRMS (MALDI): Exact mass calcd for $C_{16}H_{18}NaO_4$ $[M+Na]^+$: 297.1103, found: 297.1097.

Intramolecular Rauhut-Currier Cyclizations



Cyclization Procedure A: To a stirred 0.015 M solution of **1a-j** (0.47 mmol) in toluene, 0.47 mL of a 0.2 M solution of PMe_3 (0.094 mmol, 20 mol %) in toluene was added. The solution was allowed to stir for 30 minutes under nitrogen. The reaction was then quenched by pouring over an ice-cold mixture of 20 mL of Et_2O and 20 mL of 10% HCl. The aqueous fraction was extracted twice more with ether and the combined organic layers were then washed with 30 mL portions of 10% HCl, water (twice), and finally a saturated NaCl solution. The organic fraction was dried over sodium sulfate and the solvent removed *in vacuo*. The residue was then purified via column chromatography or crystallization.

Cyclization Procedure B: To a stirred 0.015 M solution of **1a-j** (0.47 mmol) and triethylamine (24 mg, 0.24 mmol, 50 mol %) in toluene, 0.47 mL of a 0.2 M solution of PMe_3 (0.094 mmol, 20 mol %) in toluene was added. The

solution was allowed to stir for 30 minutes under nitrogen, then worked up as in procedure A.

Cyclization Procedure C: To a stirred 0.015 M solution of **1a-j** (0.47 mmol) and phenol (66.3 mg, 0.71 mmol, 1.5 equiv.) in toluene, 0.71 mL of a 0.2 M solution of PMe_2Ph (0.141 mmol, 30 mol %) in toluene was added. The solution was allowed to stir overnight (16 h) under nitrogen, then worked up as in procedure A.

Cyclization Procedure D: To a stirred 0.015 M solution of **1a-d, f, j** (0.47 mmol) and phenol (66.3 mg, 0.71 mmol, 1.5 equiv.) in toluene, 0.47 mL of a 0.2 M solution of PMe_3 (0.094 mmol, 20 mol %) in toluene was added. The solution was allowed to stir for 30 minutes under nitrogen, then worked up as in procedure A.

Cyclization Procedure E: To a stirred 0.015 M solution of **1d** and **1j** (0.47 mmol) and phenol (66.3 mg, 0.71 mmol, 1.5 equiv.) in *tert*-butanol, 0.24 mL of a 1.0 M solution of PBu_3 (0.24 mmol, 50 mol %) in toluene was added. The solution was heated at reflux for 48 hours under nitrogen and monitored by thin-layer chromatography. After allowing the solution to cool to room temperature, the reaction mixture was worked up as in procedure A.

1-(2-acetyl-1H-inden-1-yl)propan-2-one (**2a**). Method C was used to afford **2a** in 91 % yield (0.091g, yellow oil) after flash chromatography on silica using 1:2 EtOAc/hexanes as eluent. Rf = 0.52 (50% EtOAc/Hexanes); IR (NaCl, neat): 3070, 2963, 1716, 1657, 1605, 1558, 1472, 1363, 1199, 757 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 1.6 Hz, 1H, C**H**=C(Ac)CH), 7.56 – 7.51 (m, 1H, Ar-**H**), 7.47 (dd, *J* = 6.7, 1.9 Hz, 1H, Ar-**H**), 7.37 – 7.30 (m, 2H, Ar-**H**), 4.27 (ddd, *J* = 8.9, 3.1, 1.6, 1H, C=C(Ac)C**H**CHaHb), 3.41 (dd, *J* = 17.5, 3.1 Hz, 1H, CHC**Ha**HbCO), 2.50 (dd, *J* = 17.5, 9 Hz, 1H, CHCHa**Hb**CO), 2.49 (s, 3H, C**H3**), 2.16 (s, 3H, C**H3**); ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.93, 195.43, 149.82, 148.14, 141.85, 141.29, 128.67, 127.46, 124.42, 124.03, 44.57, 44.09, 30.37, 26.93; HRMS (MALDI): Exact mass calcd for $C_{14}H_{14}NaO_2$ $[M+Na]^+$: 237.0891, found: 237.0886.

1-(2-propionyl-1H-inden-1-yl)butan-2-one (**2b**). Method D was used to afford **2b** in 80 % yield (0.034 g, yellow oil) after flash chromatography on silica using 1:2 Et_2O /hexanes as eluent. Rf = 0.51 (55% Et_2O/Hexanes); IR (NaCl, neat): 3067, 2974, 2937, 1713, 1658, 1607, 1560, 1459, 1405, 1373, 117, 1148, 1114, 759 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55 (d, *J* = 1.6 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.26 – 7.22 (m, 2H), 4.22 (d, *J* = 8.5 Hz, 1H), 3.30 (dd, *J* = 17.3, 3.5 Hz, 1H), 2.83 – 2.79 (m, 1H), 2.45 (q, *J* = 7.37 Hz, 2H), 2.29 (q, *J* = 7.30 Hz, 2H), 1.10 (t, *J* = 7.31 Hz, 3H), 0.99 (t, *J* = 7.35 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 209.86, 198.77, 149.96, 140.63, 128.67, 127.59, 127.15, 124.52, 124.13, 121.80, 44.56, 43.50, 36.52, 35.30, 8.83, 8.04; HRMS (CI): Exact mass calcd for $C_{16}H_{19}O_2$ $[M+H]^+$: 243.1385, found: 243.1382.

1-(2-isobutyryl-1H-inden-1-yl)-3-methylbutan-2-one (**2c**). Method C was used to afford **2c** in 87 % yield (0.032 g, yellow oil) after flash chromatography on silica using 1:2 Et_2O /hexanes as eluent. Rf = 0.63 (33% Et_2O/Hexanes); IR (NaCl, neat): 2969, 2931, 1712, 1661, 1589, 1561, 1463, 1381, 1357, 1193, 1147, 1037, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53 (d, *J* = 1.4 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.37 – 7.30 (m, 2H), 4.32 (m, 1H), 3.5 – 3.35 (m, 2H), 2.65 – 2.5 (m, 2H), 1.98 (d, *J* = 6.98 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H); HRMS (CI): Exact mass calcd for $C_{18}H_{23}O_2$ $[M+H]^+$: 271.1698, found: 271.1706.

3,3-dimethyl-1-(2-pivaloyl-1H-inden-1-yl)butan-2-one (**2d**). Method C was used to afford **2d** in 62 % yield (0.087 g, colorless oil) after flash chromatography on silica using 1:9 EtOAc/hexanes as eluent. Rf = 0.36 (10% EtOAc/Hexanes); IR (NaCl, neat): 2967, 1706, 1685, 1646, 1617, 1554, 1476, 1366, 1138 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.61 (2, *J* = 1.8 Hz, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.38 – 7.27 (m, 3H), 4.38 (ddd, *J* = 1.8, 2.9, 9.4 Hz, 1H), 3.28 (dd, *J* = 17.9, 2.9 Hz, 1H), 2.60 (dd, *J* = 17.9, 9.4 Hz, 1H), 1.37 (s, 9H), 1.12 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 214.18, 204.17, 149.07, 145.89, 142.01, 138.79, 128.11, 127.33, 124.08, 123.86, 46.29, 44.49, 44.15, 38.58, 28.51, 26.64; HRMS (MALDI): Exact mass calcd for $C_{20}H_{26}NaO_2$ $[M+Na]^+$: 321.1830, found: 321.1832.

2-(2-(4-bromobenzoyl)-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (**2e**). Method C was used to afford **2e** in 88 % yield (0.044 g, colorless oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.63 (50% Et_2O /Hexanes); IR (NaCl, neat): 3066, 2961, 2916, 1686, 1628, 1585, 1553, 1396, 1347, 1221, 1070, 1010, 908, 818, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 7.81 – 7.75 (m, 2H), 7.64 – 7.60 (m, 2H), 7.57 (d, *J* = 8.5 Hz, 2H), 7.53 – 7.49 (m, 2H), 7.44 – 7.39 (m, 3H), 7.27 (dd, *J* = 4.6, 1.8 Hz, 1H), 4.54 (d, *J* = 8.6 Hz, 1H), 3.90 (dd, *J* = 17.0, 3.4 Hz, 1H), 3.10 (dd, *J* = 17.0, 9.1 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 194.77, 193.66, 146.50, 144.06, 143.42, 140.30, 138.71, 135.22, 131.99, 131.74, 129.98, 129.92, 129.67, 129.44, 128.12, 127.05, 124.16, 121.73, 44.97, 40.76; HRMS (CI): Exact mass calcd for $C_{24}H_{16}Br_2O_2$ $[M+H]^+$ 494.9595, found: 494.9610.

2-(2-benzoyl-1H-inden-1-yl)-1-phenylethanone (**2f**). Method C was used to afford **2f** in 98% yield (0.178 g, yellow oil) after flash chromatography on silica using 1:2 Et_2O/hexanes as eluent. Rf = 0.58 (50% Et_2O/Hexanes); IR (NaCl, neat): 3066, 2919, 1700, 1684, 1652, 1628, 1597, 1554, 1457, 1345, 1248, 1119, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.02 (dt, *J* = 6.9, 1.3, 2H), 7.84 (dt, *J* = 6.9, 1.3, 2H), 7.60 – 7.42 (m, 8H), 7.38 – 7.28 (m, 2H), 4.69 (dt, *J* = 9.5, 2.4, 1H), 4.05 (dd, *J* = 17.1, 3.2 Hz, 1H), 3.18 (dd, *J* = 17.1, 9.5 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$): δ 198.60, 193.13, 149.65, 147.62, 144.37, 141.78, 139.38, 137.06, 133.25, 132.12, 129.13, 128.76, 128.52, 128.38, 127.66, 124.71, 124.33, 45.53, 39.68; HRMS (MALDI): Exact mass calcd for $C_{24}H_{18}NaO_2$ $[M+Na]^+$: 361.1204, found: 361.1205.

2-(2-(4-methylbenzoyl)-1H-inden-1-yl)-1-p-tolylethanone (**2g**). Method C was used to afford **2g** in 90 % yield (0.042 g, yellow oil) after flash chromatography on silica using 1:2 Et_2O /hexanes as eluent. Rf = 0.42 (50% Et_2O/Hexanes); IR (NaCl, neat): 2918, 1715, 1678, 1629, 1605, 1550, 1346, 1179 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 6.6 Hz, 2H), 7.48 (s, 1H), 7.35 – 7.27 (m, 3H), 7.24 (d, *J* = 8.1 Hz, 2H), 4.67 (d, *J* = 9.3 Hz, 1H), 4.00 (dd, *J* = 16.9, 3.2 Hz, 1H), 3.11 (dd, *J* = 16.9, 9.6 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.30, 192.69, 149.47, 147.58, 143.85, 143.48, 141.69, 136.59, 134.57, 129.28, 129.19, 129.03, 128.41, 128.37, 127.42, 124.59, 124.02, 45.55, 39.40, 21.64; HRMS (CI): Exact mass calcd for $C_{26}H_{23}O_2$ $[M+H]^+$: 367.1698, found: 367.1710

2-(2-(4-methoxybenzoyl)-1H-inden-1-yl)-1-(4-methoxyphenyl)ethanone (**2h**). Method C was used to afford **2h** in 76 % yield (0.021 g, colorless oil) after flash chromatography on silica using 1:2 EtOAc/hexanes as eluent. Rf = 0.42 (50% EtOAc/Hexanes); IR (NaCl, neat): 3069, 3006, 2934, 2938, 1675, 1625, 1600, 1573, 1509, 1343, 1254, 1169, 1028, 833, 771, 732 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 8.02 – 7.98 (m, 2H), 7.89 – 7.84 (m, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 1.8 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.01 – 6.95 (m, 2H), 6.91 (dd, *J* = 6.8, 5.0 Hz, 2H), 4.66 (d, *J* = 9.2 Hz, 1H), 3.95 (dd, *J* = 16.6, 3.3 Hz, 1H), 3.90 (s, 3H), 3.85 (s, 3H), 3.08 (dd, *J* = 16.6, 9.6 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 197.12, 191.81, 163.62, 163.08, 149.44, 148.13, 142.71, 141.90, 132.05, 131.49, 130.70, 130.18, 128.39, 127.54, 124.71, 124.02, 113.89, 113.77, 55.65, 55.60, 46.00, 39.21; HRMS (CI): Exact mass calcd for $C_{26}H_{23}O_4$ $[M+H]^+$: 399.1596, found: 399.1607.

1-(2-acetyl-1H-inden-3-yl)propan-2-one (**3a**). Method B was used to afford **3a** as clear, colorless crystals, mp 115-117°C, in 93 % yield (0.093g) after crystallization from dichloromethane/hexanes. Rf = 0.38 (50% EtOAc/Hexanes); IR (NaCl, neat): 2912, 1714, 1663, 1568, 1360, 1249, 1156, 749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 – 7.44 (m, 2H Ar-**H**), 7.44 – 7.33 (m, 2H, Ar-**H**), 4.22 (s, 2H, C$\mathbf{H_2}$C=C), 3.80 (s, 2H, C=CC$\mathbf{H_2}$C=O), 2.44 (s, 3H, C$\mathbf{H_3}$), 2.29 (s, 3H, C$\mathbf{H_3}$); ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.74, 196.91, 147.32, 144.48, 143.22, 138.50, 128.74, 127.40, 124.50, 122.16, 77.51, 77.26, 77.01, 42.37, 39.79, 30.31, 30.09; HRMS (MALDI): Exact mass calcd for $C_{14}H_{14}NaO_2$ $[M+Na]^+$: 237.0891, found: 237.0882.

1-(2-propionyl-1H-inden-3-yl)butan-2-one (**3b**). Method B was used to afford **3a** as an off-white solid, mp 113-116 °C, in 86 % yield (0.066 g). Rf = 0.47 (50% Et_2O/Hexanes); IR (NaCl, neat): 2975, 2936, 1710, 1662, 1585, 1565, 1457, 1411, 1364, 1228, 1172, 1107, 1024, 769 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 – 7.43 (m, 2H), 7.42 – 7.32 (m, 2H), 4.22 (s, 2H), 3.79 (s, 2H), 2.78 (q, *J* = 7.2 Hz, 2H), 2.64 (q, *J* = 7.3 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.35, 199.66, 147.05, 144.55, 142.96, 138.17, 128.44, 127.23, 124.31, 122.04, 41.28, 39.10, 36.05, 35.23, 7.90, 7.85; HRMS (CI): Exact mass calcd for $C_{16}H_{19}O_2$ $[M+H]^+$: 243.1385, found: 243.1392.

1-(2-isobutyryl-1H-inden-3-yl)-3-methylbutan-2-one (**3c**). Method B was used to afford **3c** as a yellow oil, in 86% yield (0.034 g). Rf = 0.48 (33% Et_2O/Hexanes); IR (NaCl, neat): 2969, 2931, 1712, 1661, 1561, 1463, 1381, 1231, 1193, 1147, 1037, 760

cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 (d, *J* = 6.5 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.41 – 7.34 (m, 2H), 4.31 (d, *J* = 13.9 Hz, 2H), 3.80 (d, *J* = 18.9 Hz, 2H), 3.11 (dt, *J* = 13.7, 6.8 Hz, 1H), 2.88 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.19 (t, *J* = 6.8 Hz, 6H), 1.16 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 210.46, 203.62, 148.11, 144.73, 143.00, 137.95, 128.31, 127.16, 124.24, 121.92, 41.00, 39.43, 39.25, 38.79, 18.93, 18.55; HRMS (CI): Exact mass calcd for $C_{18}H_{23}O_2$ $[M+H]^+$: 271.1698, found: 271.1695.

3,3-dimethyl-1-(2-pivaloyl-1H-inden-3-yl)butan-2-one (**3d**). Method E was used to afford **3d** as a white solid, mp 112-116 °C, in 95 % yield (0.133 g) after flash chromatography on silica using 1:9 EtOAc/hexanes as eluent. Rf = 0.42 (10% EtOAc/Hexanes); IR (NaCl, neat): 2967, 1708, 1652, 1553, 1476, 1363, 1148, 1092, 997, 757 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 – 7.43 (m, 1H), 7.35 – 7.27 (m, 3H), 4.15 (t, *J* = 1.2 Hz, 2H), 3.89 (s, 2H), 1.29 (s, 9H), 1.28 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 211.38, 206.94, 146.34, 144.12, 142.67, 140.28, 127.41, 126.87, 123.88, 120.83, 44.78, 44.56, 40.89, 35.17, 27.06, 26.98.; HRMS (MALDI): Exact mass calcd for $C_{20}H_{26}NaO_2$ $[M+Na]^+$: 321.1830, found: 321.1846.

2-(2-(4-bromobenzoyl)-1H-inden-3-yl)-1-(4-bromophenyl)ethanone (**3e**). Method B was used to afford **3e** as colorless oil, in 90 % yield (0.055 g). Rf = 0.52 (50% Et_2O/Hexanes); IR (NaCl, neat): 3066, 2972, 2932, 1686, 1585, 1567, 1483, 1458, 1396, 1359, 1261, 1210, 1175, 1070, 1009, 985, 910, 831, 760 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.74 (t, *J* = 8.6 Hz, 2H), 7.53 (t, *J* = 6.7 Hz, 4H), 7.48 – 7.42 (m, 4H), 7.32 (dd, *J* = 12.2, 4.6 Hz, 2H), 4.38 (s, 2H), 3.81 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 194.77,

193.66, 146.50, 144.06, 143.42, 140.30, 138.71, 135.22, 131.99, 131.74, 129.98, 129.67, 128.12, 127.05, 127.01, 124.16, 124.04, 121.73, 44.97, 37.28; HRMS (CI): Exact mass calcd for $C_{24}H_{17}Br_2O_2$ $[M+H]^+$ 494.9595, found: 494.9599.

2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (**3f**). Method B was used to afford **3f** as a colorless solid, mp 142-144 °C, in 92 % yield (0.146 g) after crystallization from dichloromethane/hexanes. Rf = 0.52 (50% Et_2O/Hexanes); IR (NaCl, neat): 3059, 2915, 1668, 1635, 1597, 1578, 1447, 1359, 1324, 1264, 1212, 723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.97 – 7.88 (dd, *J* = 6.9, 1.4 Hz, 2H), 7.75 (dd, *J* = 6.9, 1.5 Hz, 2H), 7.61 – 7.50 (m, 2H), 7.49 – 7.32 (m, 8H), 4.46 (s, 2H), 3.92 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.98, 195.14, 146.22, 144.55, 143.64, 141.18, 140.21, 136.69, 133.45, 132.21, 128.75, 128.65, 128.59, 128.33, 127.95, 127.07, 124.25, 121.94, 40.95, 37.66; HRMS (MALDI): Exact mass calcd for $C_{24}H_{18}NaO_2$ $[M+Na]^+$: 361.1204, found: 361.1219.

2-(2-(4-methylbenzoyl)-1H-inden-3-yl)-1-p-tolylethanone (**3g**). Method B was used to afford **3g** as white powder, mp 104-114°C, in 91 % yield (0.017g). Rf = 0.49 (50% Et_2O/Hexanes); IR (NaCl, neat): 2919, 1716, 1679, 1630, 1605, 1571, 1460, 1358, 1263, 1178, 911, 758 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.50 (s, 1H), 7.41 – 7.31 (m, 3H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 4.39 (s, 2H), 3.91 (s, 2H), 2.40 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.73, 195.05, 145.40, 144.67, 144.23, 143.54, 143.08, 141.57, 137.41, 134.30, 129.38, 129.30, 128.98, 128.49, 127.68, 127.01, 124.18, 121.94, 40.99, 37.59,

21.81, 21.71; HRMS (CI): Exact mass calcd for $C_{26}H_{23}O_2$ $[M+H]^+$: 367.1698, found: 367.1688.

2-(2-(4-methoxybenzoyl)-1H-inden-3-yl)-1-(4-methoxyphenyl)ethanone (**3h**). Method B was used to afford **3h** as tan powder, mp 115-118°C, in 79 % yield (0.033g). Rf = 0.49 (50% EtOAc/Hexanes); IR (NaCl, neat): 3006, 2934, 2838, 1676, 1599, 1573, 1509, 1418, 1360, 1255, 1168, 1027, 985, 840, 761, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.88 (dd, *J* = 14.3, 8.7 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 2H), 7.55 – 7.47 (m, 1H), 7.39 (dd, *J* = 5.9, 2.5 Hz, 1H), 7.36 – 7.30 (m, 2H), 6.90 (t, *J* = 5.9 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.34 (s, 2H), 3.91 (s, 2H), 3.86 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 194.68, 194.12, 163.78, 163.27, 144.71, 144.23, 143.40, 141.89, 132.50, 131.49, 131.42, 130.69, 129.84, 127.42, 126.98, 124.13, 121.87, 113.89, 55.64, 55.55, 41.08, 37.44; HRMS (CI): Exact mass calcd for $C_{26}H_{23}O_4$ $[M+H]^+$: 399.1596, found: 399.1607.

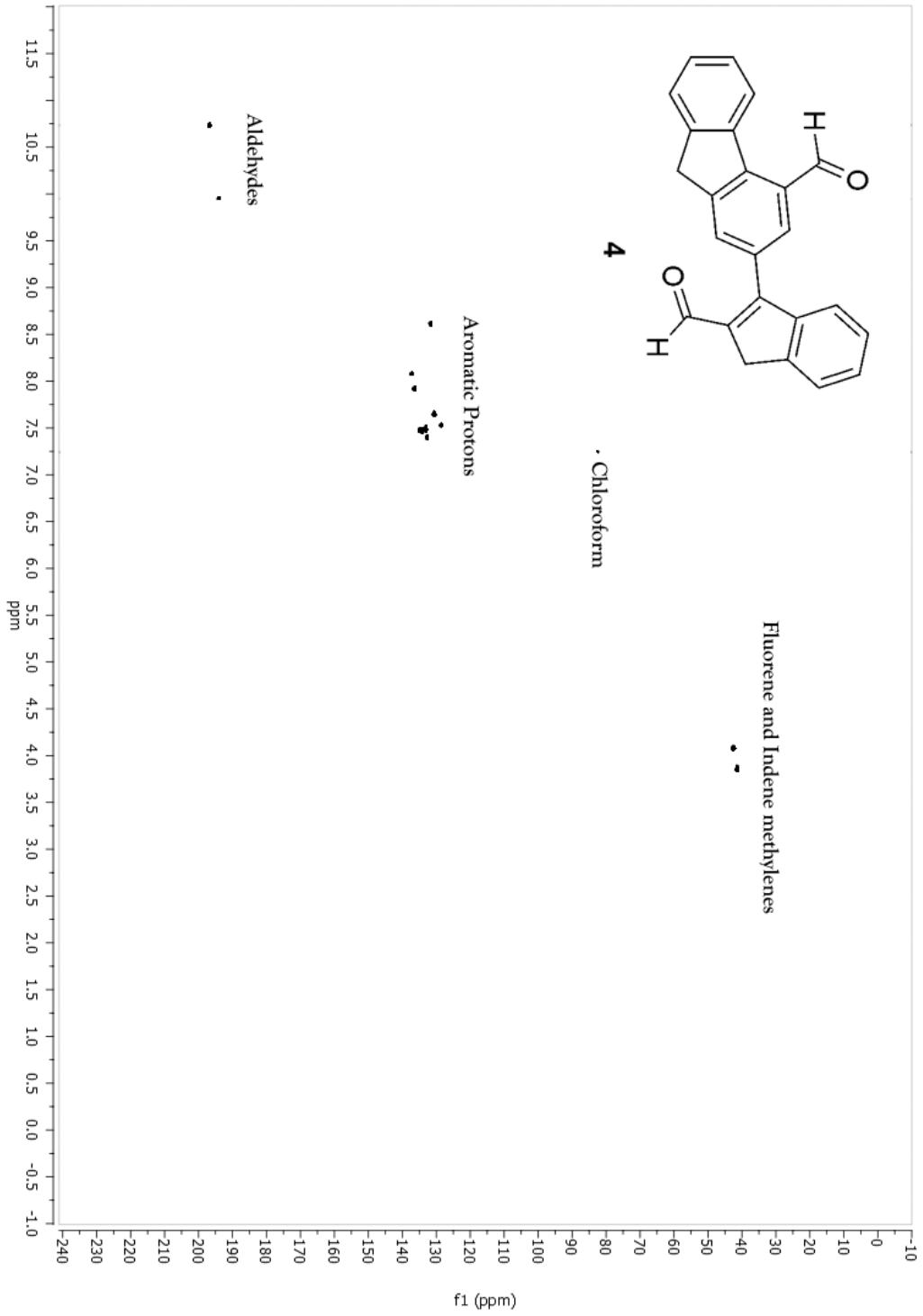
Ethyl 3-(2-ethoxy-2-oxoethyl)-1H-indene-2-carboxylate (**3j**). Method E was used to afford **3j** in 98 % yield (0.126 g, yellow oil) after flash chromatography on silica using 30% dichloromethane/hexanes as eluent. Rf = 0.59 (50% Et_2O/Hexanes); IR (NaCl, neat): 2980, 1734, 1700, 1612, 1317, 1255, 1198, 1108, 1078, 1029, 759 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.53 – 7.45 (m, 2H), 7.36 (dd, *J* = 5.6, 3.2 Hz, 2H), 4.30 (q, *J* = 7.1 Hz, 2H), 4.17 (q, *J* = 7.1, 2H), 4.16 (s, 2H), 3.74 (s, 2H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 170.19, 165.41, 146.77, 144.18, 143.53, 132.85, 127.94, 126.84, 124.27, 121.34, 61.12, 60.42, 39.06, 32.50, 14.48, 14.32; HRMS

(MALDI) Exact mass calcd for $C_{16}H_{18}NaO_4$ $[M+Na]^+$: 297.1103, found: 297.1089.

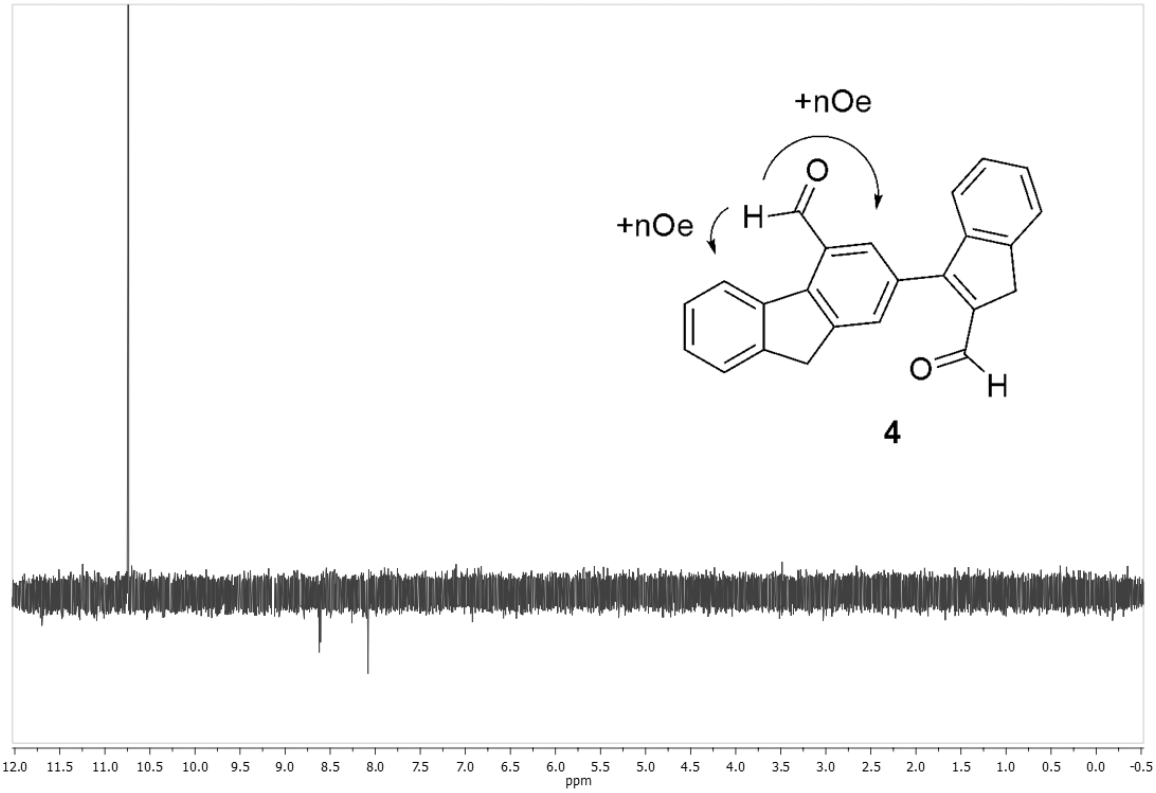
2-(2-formyl-1H-inden-3-yl)-9H-fluorene-4-carbaldehyde (4). To a stirred 0.015 M solution of **1j** (0.05, 0.269 mmol) and phenol (51 mg, 0.537 mmol, 2 equiv.) in 3 mL of toluene, 2.7 mL of a 0.2 M solution of PMe_2Ph (0.54 mmol, 200 mol %) in toluene was added. The solution was allowed to stir overnight (16 h) under argon, then worked up as in procedure A. Compound **4** was isolated in 61 % yield (0.028 g, pink solid, mp = 236-240 °C) after flash chromatography on silica using 30% ethyl ether/hexanes as eluent. Rf = 0.60 (1:1 Et_2O/Hexanes); IR (NaCl, neat): 2850, 1890, 1682, 1649, 1607, 1565, 1460, 1391, 1353, 1149, 1022, 778, 734 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 10.75 (s, 1H), 9.97 (s, 1H), 8.62 (d, *J* = 7.2 Hz, 1H), 8.09 (s, 1H), 7.94 (s, 1H), 7.66 (t, *J* = 7.6 Hz, 2H), 7.56 – 7.45 (m, 4H), 7.41 (t, *J* = 7.5 Hz, 1H), 4.10 (s, 2H), 3.88 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 191.20, 188.61, 157.55, 145.95, 144.63, 144.39, 143.40, 141.16, 139.66, 132.51, 131.69, 130.90, 130.31, 129.41, 128.76, 127.55, 127.25, 126.09, 125.13, 125.04, 123.09, 37.22, 36.18; HRMS (CI) Exact mass calcd for $C_{24}H_{17}O_2$ $[M+H]^+$: 337.1229, found: 337.1239.

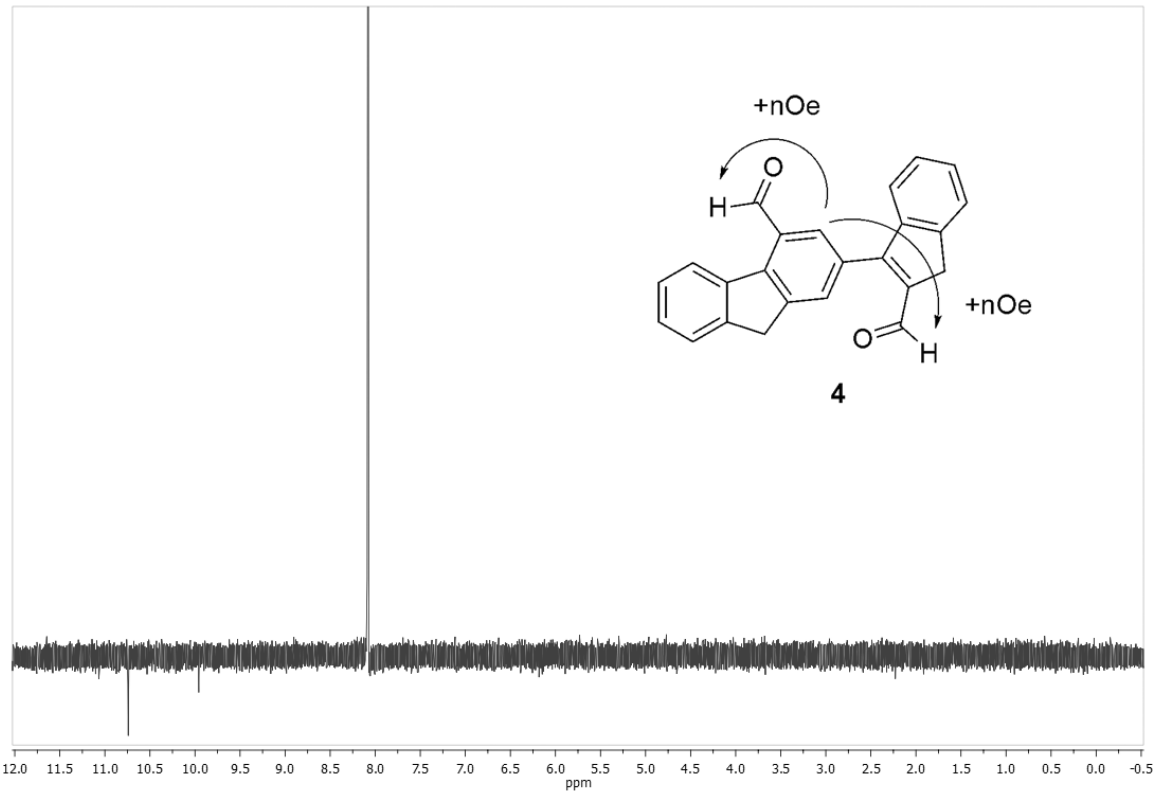
A.2. Additional Spectra for the Identification of 2-(2-formyl-1H-inden-3-yl)-9H-fluorene-4-carbaldehyde (4)

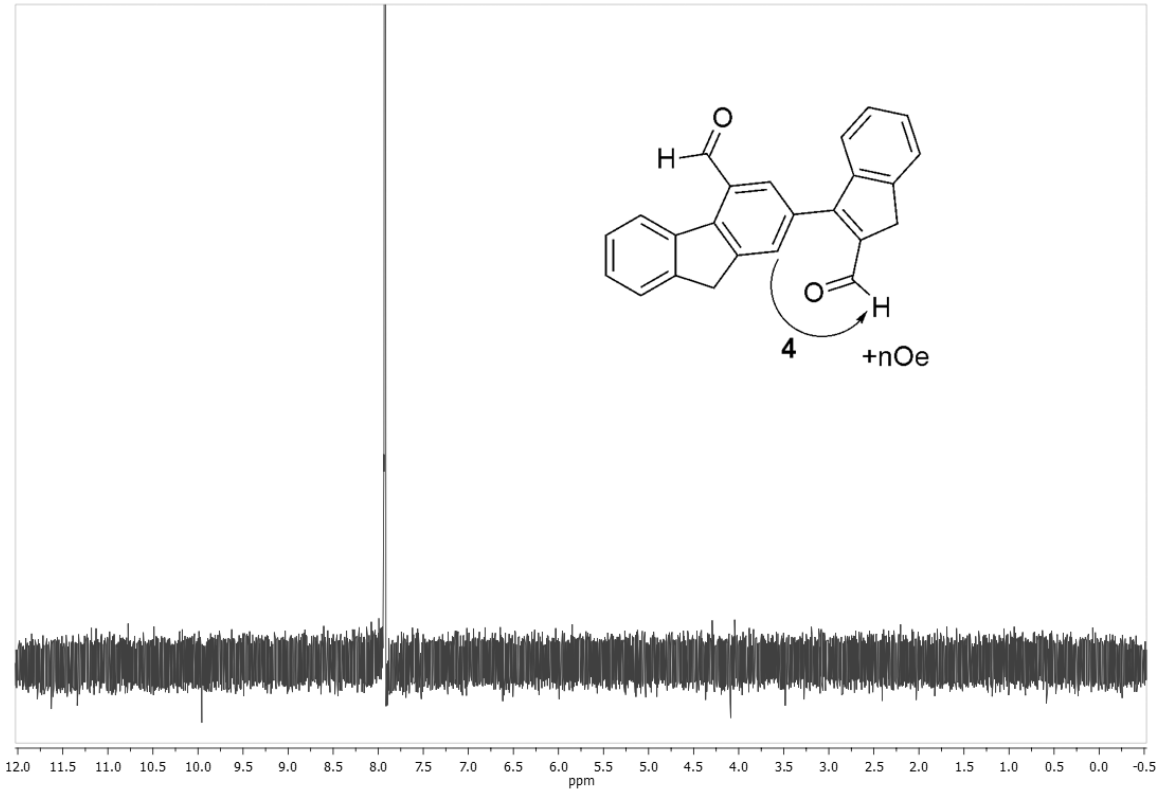
HMQC Spectrum – ^{1}H versus ^{13}C



NOE Experiments






O
H
O
H
4
+nOe
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

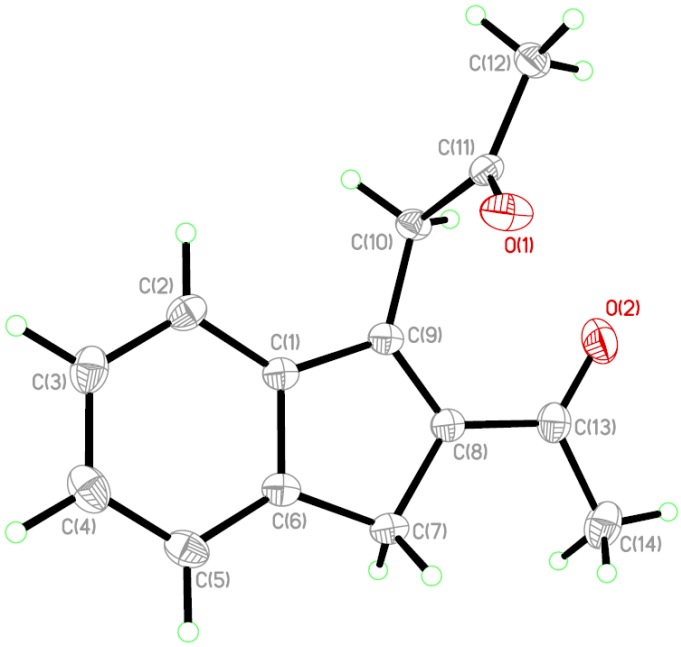
A.3. Crystal Structures

A.3.1. Table 1. Crystal data and structure refinement for 1-(2-acetyl-1H-inden-3-yl)propan-2-one (3a).

Empirical formula	C14 H14 O2	
Formula weight	214.25	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 8.1837(14) Å	a= 90°
	b = 16.426(3) Å	b= 90.754(3)°
	c = 16.655(3) Å	g = 90°
Volume	2238.6(7) $Å^3$	
Z	8	
Density (calculated)	1.271 Mg/m^3	
Absorption coefficient	0.084 mm^{-1}	
F(000)	912	
Crystal size	0.41 x 0.26 x 0.16 mm^3	
Theta range for data collection	1.74 to 27.00°.	
Index ranges	-10<=h<=10, -20<=k<=20, -21<=l<=21	
Reflections collected	25260	
Independent reflections	4892 [R(int) = 0.0392]	
Completeness to theta = 27.00°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9867 and 0.9664	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4892 / 0 / 401
Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R1 = 0.0430, wR2 = 0.0973
R indices (all data)	R1 = 0.0587, wR2 = 0.1088
Largest diff. peak and hole	0.229 and -0.169 e.$Å^{-3}$

A.3.2. Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 1-(2-acetyl-1H-inden-3-yl)propan-2-one (3a). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.



	x	y	z	U(eq)
O(1)	739(1)	4221(1)	1821(1)	44(1)
O(2)	1545(2)	3029(1)	119(1)	55(1)
C(1)	3475(2)	5411(1)	709(1)	27(1)
C(2)	4276(2)	5844(1)	1314(1)	34(1)
C(3)	4514(2)	6672(1)	1206(1)	42(1)
C(4)	3957(2)	7060(1)	514(1)	45(1)
C(5)	3157(2)	6632(1)	-87(1)	38(1)
C(6)	2926(2)	5801(1)	6(1)	29(1)
C(7)	2115(2)	5189(1)	-532(1)	31(1)
C(8)	2232(2)	4412(1)	-48(1)	29(1)
C(9)	3031(2)	4552(1)	657(1)	27(1)

C(10)	3390(2)	3954(1)	1312(1)	31(1)
C(11)	1948(2)	3797(1)	1848(1)	29(1)
C(12)	2125(2)	3109(1)	2432(1)	36(1)
C(13)	1542(2)	3632(1)	-315(1)	37(1)
C(14)	788(3)	3602(1)	-1143(1)	50(1)
O(1')	4456(1)	8818(1)	1679(1)	44(1)
O(2')	3196(2)	10632(1)	2079(1)	54(1)
C(1')	1741(2)	9333(1)	-82(1)	27(1)
C(2')	972(2)	8629(1)	-360(1)	36(1)
C(3')	821(2)	8517(1)	-1184(1)	47(1)
C(4')	1435(2)	9082(1)	-1717(1)	50(1)
C(5')	2215(2)	9779(1)	-1443(1)	40(1)
C(6')	2355(2)	9906(1)	-625(1)	29(1)
C(7')	3113(2)	10595(1)	-165(1)	29(1)
C(8')	2876(2)	10343(1)	696(1)	27(1)
C(9')	2084(2)	9621(1)	733(1)	26(1)
C(10')	1634(2)	9152(1)	1464(1)	33(1)
C(11')	3058(2)	8732(1)	1884(1)	28(1)
C(12')	2613(2)	8191(1)	2566(1)	40(1)
C(13')	3451(2)	10831(1)	1383(1)	35(1)
C(14')	4373(2)	11594(1)	1195(1)	47(1)

A.3.3. Table 3. Bond lengths [Å] and angles [°] for 1-(2-acetyl-1H-inden-3-yl)propan-2-one (3a).

O(1)-C(11)	1.2106(16)
O(2)-C(13)	1.2263(19)
C(1)-C(2)	1.391(2)
C(1)-C(6)	1.4027(19)
C(1)-C(9)	1.461(2)
C(2)-C(3)	1.386(2)
C(2)-H(2)	0.963(16)
C(3)-C(4)	1.389(2)
C(3)-H(3)	0.992(18)
C(4)-C(5)	1.382(2)
C(4)-H(4)	0.984(19)
C(5)-C(6)	1.387(2)
C(5)-H(5)	0.967(17)
C(6)-C(7)	1.496(2)
C(7)-C(8)	1.511(2)
C(7)-H(7A)	0.974(17)
C(7)-H(7B)	1.028(16)
C(8)-C(9)	1.355(2)
C(8)-C(13)	1.467(2)
C(9)-C(10)	1.4942(19)
C(10)-C(11)	1.5115(19)

C(10)-H(10A)	0.974(17)
C(10)-H(10B)	0.976(17)
C(11)-C(12)	1.496(2)
C(12)-H(12A)	0.97(2)
C(12)-H(12B)	0.97(2)
C(12)-H(12C)	0.945(19)
C(13)-C(14)	1.505(2)
C(14)-H(14A)	0.95(2)
C(14)-H(14B)	0.95(2)
C(14)-H(14C)	0.99(2)
O(1')-C(11')	1.2057(17)
O(2')-C(13')	1.2244(19)
C(1')-C(2')	1.392(2)
C(1')-C(6')	1.403(2)
C(1')-C(9')	1.4618(19)
C(2')-C(3')	1.388(2)
C(2')-H(2')	0.953(16)
C(3')-C(4')	1.384(3)
C(3')-H(3')	0.960(19)
C(4')-C(5')	1.385(3)
C(4')-H(4')	0.98(2)
C(5')-C(6')	1.382(2)
C(5')-H(5')	1.009(18)

C(6')-C(7')	1.497(2)
C(7')-C(8')	1.5072(19)
C(7')-H(7C)	0.999(16)
C(7')-H(7D)	0.993(15)
C(8')-C(9')	1.352(2)
C(8')-C(13')	1.470(2)
C(9')-C(10')	1.4913(19)
C(10')-C(11')	1.518(2)
C(10')-H(10C)	0.961(18)
C(10')-H(10D)	0.997(18)
C(11')-C(12')	1.492(2)
C(12')-H(12D)	0.95(2)
C(12')-H(12E)	0.98(2)
C(12')-H(12F)	0.98(2)
C(13')-C(14')	1.498(2)
C(14')-H(14D)	0.97(2)
C(14')-H(14E)	1.00(2)
C(14')-H(14F)	0.98(2)

C(2)-C(1)-C(6)	120.94(14)
C(2)-C(1)-C(9)	130.67(13)
C(6)-C(1)-C(9)	108.38(12)
C(3)-C(2)-C(1)	118.23(15)

C(3)-C(2)-H(2)	120.7(10)
C(1)-C(2)-H(2)	121.1(10)
C(2)-C(3)-C(4)	120.91(16)
C(2)-C(3)-H(3)	118.9(10)
C(4)-C(3)-H(3)	120.2(10)
C(5)-C(4)-C(3)	120.97(16)
C(5)-C(4)-H(4)	119.2(11)
C(3)-C(4)-H(4)	119.8(11)
C(4)-C(5)-C(6)	118.92(15)
C(4)-C(5)-H(5)	121.2(10)
C(6)-C(5)-H(5)	119.8(10)
C(5)-C(6)-C(1)	120.02(14)
C(5)-C(6)-C(7)	130.88(14)
C(1)-C(6)-C(7)	109.09(12)
C(6)-C(7)-C(8)	102.92(12)
C(6)-C(7)-H(7A)	113.0(10)
C(8)-C(7)-H(7A)	110.8(10)
C(6)-C(7)-H(7B)	111.2(9)
C(8)-C(7)-H(7B)	110.5(9)
H(7A)-C(7)-H(7B)	108.4(13)
C(9)-C(8)-C(13)	126.12(14)
C(9)-C(8)-C(7)	110.25(13)
C(13)-C(8)-C(7)	123.63(13)

C(8)-C(9)-C(1)	109.35(12)
C(8)-C(9)-C(10)	127.57(14)
C(1)-C(9)-C(10)	123.05(13)
C(9)-C(10)-C(11)	113.39(12)
C(9)-C(10)-H(10A)	112.2(10)
C(11)-C(10)-H(10A)	104.1(9)
C(9)-C(10)-H(10B)	111.6(9)
C(11)-C(10)-H(10B)	107.2(9)
H(10A)-C(10)-H(10B)	107.9(13)
O(1)-C(11)-C(12)	122.14(13)
O(1)-C(11)-C(10)	121.50(13)
C(12)-C(11)-C(10)	116.32(12)
C(11)-C(12)-H(12A)	111.3(12)
C(11)-C(12)-H(12B)	111.7(12)
H(12A)-C(12)-H(12B)	106.8(16)
C(11)-C(12)-H(12C)	110.6(11)
H(12A)-C(12)-H(12C)	108.4(16)
H(12B)-C(12)-H(12C)	107.8(16)
O(2)-C(13)-C(8)	121.92(15)
O(2)-C(13)-C(14)	120.76(16)
C(8)-C(13)-C(14)	117.31(15)
C(13)-C(14)-H(14A)	109.3(14)
C(13)-C(14)-H(14B)	109.1(14)

H(14A)-C(14)-H(14B)	114.2(19)
C(13)-C(14)-H(14C)	111.1(12)
H(14A)-C(14)-H(14C)	103.0(18)
H(14B)-C(14)-H(14C)	110.0(17)
C(2')-C(1')-C(6')	120.48(14)
C(2')-C(1')-C(9')	131.15(14)
C(6')-C(1')-C(9')	108.37(12)
C(3')-C(2')-C(1')	118.19(16)
C(3')-C(2')-H(2')	120.9(10)
C(1')-C(2')-H(2')	120.9(10)
C(4')-C(3')-C(2')	121.13(17)
C(4')-C(3')-H(3')	121.7(11)
C(2')-C(3')-H(3')	117.2(11)
C(3')-C(4')-C(5')	120.87(16)
C(3')-C(4')-H(4')	120.2(11)
C(5')-C(4')-H(4')	118.9(11)
C(6')-C(5')-C(4')	118.71(16)
C(6')-C(5')-H(5')	120.5(10)
C(4')-C(5')-H(5')	120.8(10)
C(5')-C(6')-C(1')	120.61(14)
C(5')-C(6')-C(7')	130.31(14)
C(1')-C(6')-C(7')	109.08(12)
C(6')-C(7')-C(8')	102.81(11)

C(6')-C(7')-H(7C)	109.8(9)
C(8')-C(7')-H(7C)	112.0(9)
C(6')-C(7')-H(7D)	111.5(9)
C(8')-C(7')-H(7D)	113.5(8)
H(7C)-C(7')-H(7D)	107.3(12)
C(9')-C(8')-C(13')	126.22(13)
C(9')-C(8')-C(7')	110.60(12)
C(13')-C(8')-C(7')	123.18(13)
C(8')-C(9')-C(1')	109.14(12)
C(8')-C(9')-C(10')	127.86(13)
C(1')-C(9')-C(10')	122.98(13)
C(9')-C(10')-C(11')	114.48(12)
C(9')-C(10')-H(10C)	112.6(11)
C(11')-C(10')-H(10C)	104.1(11)
C(9')-C(10')-H(10D)	110.8(10)
C(11')-C(10')-H(10D)	104.6(10)
H(10C)-C(10')-H(10D)	109.8(15)
O(1')-C(11')-C(12')	121.84(13)
O(1')-C(11')-C(10')	122.81(13)
C(12')-C(11')-C(10')	115.35(13)
C(11')-C(12')-H(12D)	111.9(12)
C(11')-C(12')-H(12E)	111.1(11)
H(12D)-C(12')-H(12E)	112.6(16)

C(11')-C(12')-H(12F)	108.3(12)
H(12D)-C(12')-H(12F)	104.9(16)
H(12E)-C(12')-H(12F)	107.7(16)
O(2')-C(13')-C(8')	122.30(15)
O(2')-C(13')-C(14')	120.94(15)
C(8')-C(13')-C(14')	116.76(14)
C(13')-C(14')-H(14D)	110.7(12)
C(13')-C(14')-H(14E)	108.6(11)
H(14D)-C(14')-H(14E)	112.4(16)
C(13')-C(14')-H(14F)	109.8(11)
H(14D)-C(14')-H(14F)	109.3(16)
H(14E)-C(14')-H(14F)	105.8(16)

A.3.4. Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 1-(2-acetyl-1H-inden-3-yl)propan-2-one (3a). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	33(1)	62(1)	38(1)	14(1)	7(1)	15(1)
O(2)	54(1)	42(1)	68(1)	7(1)	-1(1)	-13(1)
C(1)	23(1)	33(1)	25(1)	1(1)	5(1)	4(1)
C(2)	31(1)	44(1)	28(1)	-3(1)	1(1)	3(1)
C(3)	42(1)	43(1)	41(1)	-13(1)	6(1)	-5(1)
C(4)	57(1)	33(1)	46(1)	-4(1)	15(1)	0(1)
C(5)	46(1)	35(1)	34(1)	4(1)	8(1)	7(1)
C(6)	28(1)	34(1)	26(1)	1(1)	6(1)	6(1)
C(7)	29(1)	39(1)	26(1)	3(1)	1(1)	6(1)
C(8)	24(1)	34(1)	29(1)	1(1)	4(1)	3(1)
C(9)	21(1)	34(1)	27(1)	3(1)	6(1)	4(1)
C(10)	26(1)	35(1)	31(1)	6(1)	1(1)	4(1)
C(11)	26(1)	35(1)	24(1)	-1(1)	-2(1)	0(1)
C(12)	32(1)	39(1)	36(1)	8(1)	2(1)	-2(1)
C(13)	29(1)	40(1)	42(1)	-4(1)	5(1)	-2(1)
C(14)	48(1)	57(1)	47(1)	-18(1)	0(1)	-7(1)
O(1')	26(1)	57(1)	50(1)	21(1)	3(1)	3(1)
O(2')	53(1)	80(1)	29(1)	-10(1)	-4(1)	-6(1)
C(1')	22(1)	28(1)	30(1)	1(1)	-2(1)	5(1)

C(2')	26(1)	32(1)	50(1)	-3(1)	-3(1)	3(1)
C(3')	37(1)	48(1)	58(1)	-24(1)	-13(1)	6(1)
C(4')	51(1)	65(1)	35(1)	-15(1)	-12(1)	18(1)
C(5')	46(1)	49(1)	26(1)	1(1)	-2(1)	14(1)
C(6')	28(1)	30(1)	28(1)	2(1)	-1(1)	8(1)
C(7')	31(1)	27(1)	30(1)	6(1)	3(1)	2(1)
C(8')	25(1)	29(1)	27(1)	1(1)	0(1)	4(1)
C(9')	21(1)	31(1)	27(1)	4(1)	1(1)	4(1)
C(10')	26(1)	42(1)	31(1)	11(1)	1(1)	0(1)
C(11')	29(1)	29(1)	27(1)	2(1)	1(1)	1(1)
C(12')	36(1)	47(1)	37(1)	16(1)	4(1)	6(1)
C(13')	27(1)	43(1)	37(1)	-9(1)	-3(1)	6(1)
C(14')	43(1)	35(1)	63(1)	-15(1)	-8(1)	1(1)

A.3.5. Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 1-(2-acetyl-1H-inden-3-yl)propan-2-one (3a).

	x	y	z	U(eq)
H(2)	4679(19)	5575(10)	1791(10)	38(4)
H(2')	511(19)	8249(10)	5(10)	37(4)
H(3)	5120(20)	6982(11)	1624(11)	52(5)
H(3')	280(20)	8030(11)	-1365(11)	54(5)
H(4)	4120(20)	7650(12)	451(10)	55(5)
H(4')	1320(20)	8993(11)	-2298(12)	63(6)
H(5)	2730(20)	6904(10)	-560(10)	48(5)
H(5')	2670(20)	10190(11)	-1833(11)	54(5)
H(7A)	980(20)	5322(10)	-655(9)	42(4)
H(7B)	2729(19)	5129(9)	-1063(10)	38(4)
H(7C)	2529(19)	11112(10)	-296(9)	37(4)
H(7D)	4278(19)	10671(9)	-308(9)	32(4)
H(10A)	4240(20)	4146(10)	1679(10)	41(4)
H(10B)	3732(19)	3429(11)	1098(9)	39(4)
H(10C)	1170(20)	9491(11)	1873(11)	53(5)
H(10D)	860(20)	8703(11)	1325(10)	51(5)
H(12A)	2120(20)	2590(12)	2161(12)	64(6)
H(12B)	1240(30)	3096(12)	2808(12)	69(6)

H(12C)	3110(20)	3158(11)	2730(11)	54(5)
H(12D)	1800(30)	8430(12)	2895(12)	64(6)
H(12E)	3590(20)	8023(11)	2874(11)	61(6)
H(12F)	2100(30)	7698(13)	2347(12)	70(6)
H(14A)	-10(30)	4022(15)	-1196(14)	84(8)
H(14B)	380(30)	3070(15)	-1240(13)	84(7)
H(14C)	1600(30)	3747(12)	-1557(13)	70(6)
H(14D)	4750(20)	11858(12)	1683(13)	67(6)
H(14E)	3650(20)	11956(13)	857(12)	66(6)
H(14F)	5320(20)	11463(11)	861(11)	59(6)

A.3.6. Table 6. Torsion angles [°] for 1-(2-acetyl-1H-inden-3-yl)propan-2-one (3a).

C(6)-C(1)-C(2)-C(3)	0.2(2)
C(9)-C(1)-C(2)-C(3)	-178.94(14)
C(1)-C(2)-C(3)-C(4)	0.5(2)
C(2)-C(3)-C(4)-C(5)	-0.3(2)
C(3)-C(4)-C(5)-C(6)	-0.5(2)
C(4)-C(5)-C(6)-C(1)	1.2(2)
C(4)-C(5)-C(6)-C(7)	179.80(15)
C(2)-C(1)-C(6)-C(5)	-1.0(2)
C(9)-C(1)-C(6)-C(5)	178.30(13)
C(2)-C(1)-C(6)-C(7)	-179.91(13)
C(9)-C(1)-C(6)-C(7)	-0.62(15)
C(5)-C(6)-C(7)-C(8)	-177.58(15)
C(1)-C(6)-C(7)-C(8)	1.18(15)
C(6)-C(7)-C(8)-C(9)	-1.39(15)
C(6)-C(7)-C(8)-C(13)	177.71(13)
C(13)-C(8)-C(9)-C(1)	-177.99(13)
C(7)-C(8)-C(9)-C(1)	1.08(15)
C(13)-C(8)-C(9)-C(10)	0.0(2)
C(7)-C(8)-C(9)-C(10)	179.12(13)
C(2)-C(1)-C(9)-C(8)	178.91(14)

C(6)-C(1)-C(9)-C(8)	-0.29(15)
C(2)-C(1)-C(9)-C(10)	0.8(2)
C(6)-C(1)-C(9)-C(10)	-178.44(12)
C(8)-C(9)-C(10)-C(11)	-79.61(19)
C(1)-C(9)-C(10)-C(11)	98.18(15)
C(9)-C(10)-C(11)-O(1)	-11.8(2)
C(9)-C(10)-C(11)-C(12)	170.35(13)
C(9)-C(8)-C(13)-O(2)	4.8(2)
C(7)-C(8)-C(13)-O(2)	-174.12(14)
C(9)-C(8)-C(13)-C(14)	-176.44(15)
C(7)-C(8)-C(13)-C(14)	4.6(2)
C(6')-C(1')-C(2')-C(3')	-0.5(2)
C(9')-C(1')-C(2')-C(3')	-179.93(14)
C(1')-C(2')-C(3')-C(4')	0.9(2)
C(2')-C(3')-C(4')-C(5')	-0.3(3)
C(3')-C(4')-C(5')-C(6')	-0.7(2)
C(4')-C(5')-C(6')-C(1')	1.0(2)
C(4')-C(5')-C(6')-C(7')	-179.57(15)
C(2')-C(1')-C(6')-C(5')	-0.4(2)
C(9')-C(1')-C(6')-C(5')	179.13(13)
C(2')-C(1')-C(6')-C(7')	-179.94(12)
C(9')-C(1')-C(6')-C(7')	-0.42(15)
C(5')-C(6')-C(7')-C(8')	-178.89(15)

C(1')-C(6')-C(7')-C(8')	0.59(15)
C(6')-C(7')-C(8')-C(9')	-0.58(15)
C(6')-C(7')-C(8')-C(13')	179.21(12)
C(13')-C(8')-C(9')-C(1')	-179.43(12)
C(7')-C(8')-C(9')-C(1')	0.36(15)
C(13')-C(8')-C(9')-C(10')	-0.9(2)
C(7')-C(8')-C(9')-C(10')	178.91(13)
C(2')-C(1')-C(9')-C(8')	179.49(14)
C(6')-C(1')-C(9')-C(8')	0.04(15)
C(2')-C(1')-C(9')-C(10')	0.8(2)
C(6')-C(1')-C(9')-C(10')	-178.60(12)
C(8')-C(9')-C(10')-C(11')	-73.8(2)
C(1')-C(9')-C(10')-C(11')	104.56(16)
C(9')-C(10')-C(11')-O(1')	5.3(2)
C(9')-C(10')-C(11')-C(12')	-174.02(14)
C(9')-C(8')-C(13')-O(2')	-3.0(2)
C(7')-C(8')-C(13')-O(2')	177.28(14)
C(9')-C(8')-C(13')-C(14')	177.15(14)
C(7')-C(8')-C(13')-C(14')	-2.6(2)

APPENDIX B

SUPPORTING INFORMATION FOR CHAPTER III

B.1. Experimental Details

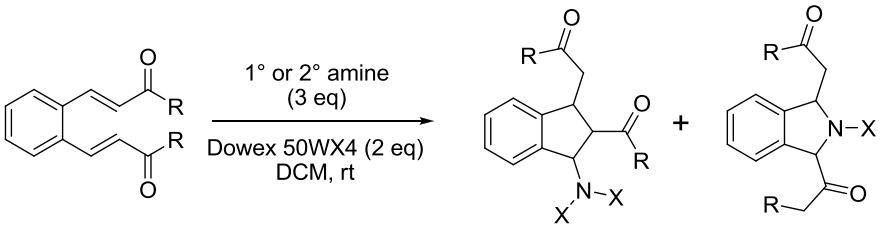
B.1.1. General Methods. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using either a Varian Inova 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) or 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz) or Agilent VNMRS 600 (^{1}H: 600 MHz, ^{13}C: 151 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm relative to the residual chloroform (^{1}H: 7.26 ppm, ^{13}C: 77.160 ppm) reference. Coupling constants are given in Hertz (Hz). Melting points were recorded on a Melt-Temp II melting point apparatus in open-end capillary tubes. IR spectra were recorded using a Nicolet Magna FTIR 550 spectrometer. High resolution mass spectra were recorded on a Waters Micromass MALDI Q-ToF or JEOL MS Route Magnetic Sector mass spectrometer.

Diffraction intensities for **17** was collected at 173(2) K on a Bruker Apex CCD diffractometer using MoKα radiation λ= 0.71073 Å. Space groups were determined based on systematic absences and intensity statistics. Absorption corrections were applied by SADABS[G. M. Sheldrick, *Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, 1998.]. Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms 1**7** were found on residual density maps and refined with isotropic thermal parameters. All H atoms in **17** were refined in calculated positions in a rigid group model. Highly disordered solvent acetone molecule in the crystal structures of **17** was treated by SQUEEZE [Van der Sluis,

P. & Spek, A. L. (1990) *Acta Cryst., Sect. A,* **A46**, 194-201.]. Correction of the X-ray data by SQUEEZE is 142 electron/cell; the required value is 120 electron/cell for four molecules in the full unit cells. All calculations were performed by the Bruker SHELXTL (v. 6.10) package [SHELXTL-6.10 "Program for Structure Solution, Refinement and Presentation" BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA].

B.1.2. Starting Materials. All reagents and solvents were purchased from Aldrich or TCI. Unless otherwise stated, all reagents were used as received. The preparation of bis(enones) **1a** and **1d-e** is described in chapter II.

B.1.3. General Procedure for the Aza-Michael-Michael Reaction.



1a: R=Me
1d: R=*t*-Bu
1e: R=p-Br-C_6H_4
1f: R=Ph
1g: R=p-Me-C_6H_4
1h: R=p-OMe-C_6H_4

4, 6a, 8 9, 10, 12a, 13a, 14a, 14b, 15, 17, 18, 19, 20a, 20b, 21b

6b, 12b, 13b

To a stirred 0.15 M solution of **1a** or **1d-h** (0.15 mmol) in 0.3 mL of dichloromethane, 0.062 g of Dowex 50WX4 (0.3 mmol, 2 equiv) and the desired amine (0.45 mmol, 3 equiv) was added. The solution was stirred at ambient temperatures for 30 minutes to 14 days. When thin layer chromatography showed complete conversion of starting material, the solution was pipetted away from the Dowex beads. The sulfonic acid resin was then rinsed twice with 2 mL fractions of dichloromethane. The combined dichloromethane fractions were

placed under vacuum and, if necessary, the crude residue was purified by flash chromatography, to yield the aminoindane or isoindoline.

***Trans-trans*-2-(2-benzoyl-3-(diethylamino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (4**). The general procedure was used to afford **4** in quantitative yield (0.053 g, yellow oil). Rf = 0.5 (50% Et_2O /Hexanes). IR (NaCl, neat): 3063, 3027, 2969, 2930, 2872, 2812, 1678, 1596, 1580, 1478, 1448, 1382, 1353, 1286, 1252, 1226, 1206, 1180, 1000, 9000, 774, 749, 701, 670, 531 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.85 – 7.77 (m, 2H), 7.58 – 7.49 (m, 2H), 7.47 – 7.36 (m, 4H), 7.36 – 7.30 (m, 1H), 7.28 – 7.23 (m, 2H), 7.17 – 7.10 (m, 1H), 5.01 (d, *J* = 7.1 Hz, 1H), 4.24 – 4.14 (m, 1H), 4.16 – 4.07 (m, 1H), 3.56 (dd, *J* = 17.3, 5.0 Hz, 1H), 3.29 (dd, *J* = 17.3, 7.5 Hz, 1H), 2.59 (tt, *J* = 14.5, 7.3 Hz, 2H), 2.29 (dq, *J* = 13.8, 6.9 Hz, 2H), 0.98 (t, *J* = 7.1 Hz, 6H; ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.35, 198.53, 143.66, 143.16, 137.83, 137.00, 133.27, 132.98, 128.77, 128.71, 128.66, 128.15, 128.03, 127.40, 124.93, 123.36, 72.02, 54.76, 45.19, 44.22, 43.83, 14.63; HRMS (CI): Exact mass calcd for $C_{28}H_{30}NO_2$ $[M+H]^+$: 412.2277, found: 412.2282.

***Trans-trans*-2-(2-benzoyl-3-(butylamino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (6a**). The general procedure was used to afford **6a** in 64% yield (0.034 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes and 1% TEA as eluent. Rf = 0.25 (50% Et_2O /Hexanes). IR (NaCl, neat): 3059, 2958, 2931, 2871, 1681, 1620, 1597, 1490, 1447, 1361, 1323, 1265, 1177, 1157, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 8.07 – 8.02 (m, 2H), 7.86 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.58 – 7.51 (m, 2H), 7.43 (dt, *J* = 17.3, 7.9 Hz, 4H), 7.36 – 7.32 (m, 1H), 7.29 – 7.24 (m, 3H), 7.23 – 7.16 (m,

1H), 4.59 (d, *J* = 6.1 Hz, 1H), 4.21 (dd, *J* = 13.1, 7.0 Hz, 1H), 4.01 (t, *J* = 6.5 Hz, 1H), 3.57 (dd, *J* = 17.2, 5.5 Hz, 1H), 3.35 (dd, *J* = 17.2, 7.9 Hz, 1H), 2.66 (dt, *J* = 11.3, 6.9 Hz, 1H), 2.53 (dt, *J* = 11.2, 7.1 Hz, 1H), 1.56 – 1.34 (m, 3H), 1.34 – 1.20 (m, 2H), 0.82 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 201.93, 198.61, 144.23, 143.58, 137.68, 137.02, 133.29, 133.09, 128.76, 128.73, 128.71, 128.30, 128.20, 127.53, 124.38, 123.84, 68.30, 61.30, 47.10, 44.44, 43.17, 32.70, 20.49, 14.05;HRMS (CI): Exact mass calcd for $C_{28}H_{30}NO_2$ $[M+H]^+$: 412.2277, found: 412.2289.

2,2'-(2-butylisoindoline-1,3-diyl)bis(1-phenylethanone) (6b). The general procedure was used to afford **6b** in 32% yield (0.016 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.63 (50% Et_2O /Hexanes). IR (NaCl, neat): 2958, 2931, 2872, 1712, 1682, 1597, 1580, 1448 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 8.3, 1.2 Hz, 4H), 7.59 – 7.54 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 4H), 7.22 – 7.17 (m, 2H), 7.17 – 7.13 (m, 2H), 4.83 (t, *J* = 5.9 Hz, 2H), 3.41 (dd, *J* = 16.6, 5.2 Hz, 2H), 3.33 (dd, *J* = 16.7, 6.8 Hz, 2H), 2.82 – 2.76 (m, 2H), 1.46 – 1.40 (m, 2H), 1.25 – 1.17 (m, 2H), 0.82 (t, *J* = 7.4 Hz, 3H; ^{13}C NMR (151 MHz, $CDCl_3$): δ 199.62, 143.04, 137.65, 133.20, 128.70, 128.43, 127.54, 122.78, 65.20, 54.60, 48.21, 29.47, 20.74, 14.12; HRMS (CI): Exact mass calcd for $C_{28}H_{30}NO_2$ $[M+H]^+$: 412.2277, found: 412.2257.

***Trans-trans*-2-((1S,2S,3R)-2-benzoyl-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (8**). The general procedure was used to afford **8** in 91% yield (0.055 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.20 (50% Et_2O /Hexanes). IR (NaCl, neat): 3063, 2964, 2798, 1680, 1596,

1447, 1352, 1253, 1222, 1001, 750, 689 cm-1; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (d, *J* = 7.5 Hz, 2H), 7.86 (d, *J* = 7.3 Hz, 2H), 7.59 – 7.48 (m, 2H), 7.47 – 7.37 (m, 4H), 7.33 (dd, *J* = 13.9, 10.1 Hz, 1H), 7.25 (d, *J* = 4.5 Hz, 2H), 7.19 (dd, *J* = 8.3, 4.7 Hz, 1H), 4.86 (d, *J* = 5.6 Hz, 1H), 4.21 (t, *J* = 6.0 Hz, 1H), 4.13 (dd, *J* = 12.6, 6.8 Hz, 1H), 3.55 (dd, *J* = 17.2, 5.2 Hz, 1H), 3.43 (dd, *J* = 17.4, 8.0 Hz, 1H), 2.66 (dd, *J* = 10.7, 5.1 Hz, 2H), 2.52 (dd, *J* = 8.5, 5.5 Hz, 2H), 1.78 – 1.66 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.44, 198.74, 144.24, 142.25, 137.33, 137.01, 133.31, 133.01, 128.86, 128.77, 128.73, 128.72, 128.52, 128.20, 128.05, 127.24, 125.63, 123.72, 71.10, 54.14, 49.57, 44.24, 43.91, 23.93; HRMS (CI): Exact mass calcd for $C_{28}H_{28}NO_2$ $[M+H]^+$: 410.2120, found: 410.2114.

***Trans-trans*-2-((1S,2S,3R)-2-benzoyl-3-(piperidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (9)**. The general procedure was used to afford **9** in 85% yield (0.053 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.23 (50% Et_2O /Hexanes. IR (NaCl, neat): 3060, 2933, 2850, 2800, 1680, 1596, 1447, 1352, 1228, 1198, 1112, 1000, 909, 749, 689 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.1 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 2H), 7.42 (dt, *J* = 15.4, 7.8 Hz, 4H), 7.35 (d, *J* = 5.3 Hz, 1H), 7.26 – 7.23 (m, 2H), 7.15 (d, *J* = 6.0 Hz, 1H), 4.79 (d, *J* = 7.0 Hz, 1H), 4.25 (t, *J* = 7.3 Hz, 1H), 4.13 (dd, *J* = 13.0, 7.3 Hz, 1H), 3.54 (dd, *J* = 17.3, 5.2 Hz, 1H), 3.30 (dd, *J* = 17.3, 7.9 Hz, 1H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.38 (d, *J* = 6.6 Hz, 2H), 1.56 (s, 2H), 1.48 (s, 2H), 1.41 – 1.33 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.94, 198.53, 143.86, 141.97, 137.60, 137.01, 133.28, 133.01, 128.86, 128.72, 128.70, 128.16, 128.14, 127.34, 125.31, 123.46, 76.22, 53.42, 50.74, 44.01, 43.86, 26.65, 24.83; HRMS (CI): Exact mass calcd for $C_{29}H_{30}NO_2$ $[M+H]^+$: 424.2277, found: 424.2286.

***Trans-trans*-2-(2-benzoyl-3-(dibenzylamino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (10)**. The general procedure was used to afford **10** in 72% yield (0.057 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.39 (50% Et_2O /Hexanes). IR (NaCl, neat): 3062, 3028, 2802, 1680, 1596, 1579, 1493, 1448, 1352, 1222, 1204, 1027, 909, 731, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.3 Hz, 2H), 7.91 – 7.84 (m, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.53 (dt, *J* = 21.2, 7.5 Hz, 4H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.38 – 7.13 (m, 14H), 4.87 (d, *J* = 6.6 Hz, 1H), 4.39 (t, *J* = 6.9 Hz, 1H), 4.12 (dd, *J* = 12.6, 7.8 Hz, 1H), 3.75 (d, *J* = 13.6 Hz, 2H), 3.61 (dd, *J* = 17.3, 4.8 Hz, 1H), 3.40 – 3.30 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.10, 198.58, 144.17, 142.57, 139.31, 137.60, 136.94, 133.38, 133.17, 128.99, 128.86, 128.78, 128.70, 128.42, 128.33, 128.22, 127.72, 127.11, 125.15, 123.50, 77.41, 77.16, 76.91, 70.76, 54.65, 53.49, 44.53, 44.06; HRMS (CI): Exact mass calcd for $C_{38}H_{34}NO_2$ $[M+H]^+$: 536.2590, found: 536.2601.

***Trans-trans*- 2-(2-benzoyl-3-(benzylamino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (12a)**. The general procedure was used to afford **12a** in 93% yield (0.056 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.16 (50% Et_2O /Hexanes). IR (NaCl, neat): 3062, 3027, 2926, 2850, 1680, 1596, 1579, 1448, 1359, 1221, 1025, 1001, 908, 750, 696, 670 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, *J* = 7.7 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 2H), 7.57 (dd, *J* = 17.5, 7.7 Hz, 2H), 7.50 – 7.41 (m, 4H), 7.39 (d, *J* = 4.2 Hz, 1H), 7.30 – 7.22 (m, 8H), 4.68 (d, *J* = 5.8 Hz, 1H), 4.25 (dd, *J* = 13.2, 6.6 Hz, 1H), 4.10 (t, *J* = 6.2 Hz, 1H), 3.85 (d, *J* = 13.0 Hz,

1H), 3.78 (d, *J* = 13.1 Hz, 1H), 3.61 (dd, *J* = 17.2, 5.3 Hz, 1H), 3.40 (dd, *J* = 17.2, 8.1 Hz, 1H), 1.72 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 201.81, 198.59, 144.40, 143.32, 140.37, 137.62, 137.00, 133.33, 133.17, 128.82, 128.77, 128.75, 128.50, 128.44, 128.22, 127.60, 127.16, 124.50, 123.95, 67.91, 61.21, 51.57, 44.49, 43.15; HRMS (CI): Exact mass calcd for $C_{31}H_{28}NO_2$ $[M+H]^+$: 446.2120, found: 446.2130.

2,2'-(2-benzylisoindoline-1,3-diyl)bis(1-phenylethanone) (12b). The general procedure was used to afford **12b** in 9% yield (0.006 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.16 (50% Et_2O /Hexanes). IR (NaCl, neat): 3060, 2917, 1680, 1596, 1448, 1352, 1285, 1207, 745, 689 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.7 Hz, 4H), 7.54 (t, *J* = 7.4 Hz, 2H), 7.39 (dt, *J* = 23.2, 11.9 Hz, 5H), 7.26 (s, 2H), 7.20 (t, *J* = 6.6 Hz, 4H), 7.12 (dd, *J* = 13.2, 7.7 Hz, 3H), 4.90 (t, *J* = 5.9 Hz, 2H), 4.02 (s, 2H), 3.30 (dd, *J* = 16.6, 5.0 Hz, 2H), 3.22 (dd, *J* = 16.6, 6.9 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.39, 199.38, 142.67, 139.41, 137.45, 133.16, 129.42, 128.67, 128.48, 128.38, 128.37, 127.62, 127.58, 127.26, 122.79, 65.93, 59.57, 47.75; HRMS (CI): Exact mass calcd for $C_{31}H_{28}NO_2$ $[M+H]^+$: 446.2120, found: 446.2119.

***Trans-trans*-2-(2-benzoyl-3-(cyclohexylamino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (13a**). The general procedure was used to afford **13a** in 75% yield (0.049 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.33 (50% Et_2O /Hexanes). IR (NaCl, neat): 3063, 2925, 2851, 1684, 1635, 1596, 1448, 1357, 1253, 1219, 1001, 908, 750, 690 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.06 – 8.03 (m, 2H), 7.89 – 7.85 (m, 2H), 7.54 (dd, *J* = 13.4, 7.3 Hz, 2H), 7.47 – 7.38 (m,

4H), 7.36 – 7.32 (m, 1H), 7.26 – 7.22 (m, 2H), 7.20 – 7.16 (m, 1H), 4.65 (d, *J* = 6.2 Hz, 1H), 4.19 (dd, *J* = 13.4, 6.8 Hz, 1H), 3.93 (t, *J* = 6.6 Hz, 1H), 3.56 (dd, *J* = 17.2, 5.6 Hz, 1H), 3.34 (dd, *J* = 17.2, 7.7 Hz, 1H), 2.45 (m, 1H), 1.83 (s, 1H), 1.69 – 1.53 (m, 4H), 1.47 (t, *J* = 20.6 Hz, 3H), 1.25 (s, 1H), 1.12 – 0.93 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.27, 198.62, 144.83, 144.10, 137.86, 137.03, 133.29, 133.03, 128.84, 128.73, 128.62, 128.22, 127.62, 124.22, 123.80, 65.55, 63.47, 55.46, 44.59, 43.36, 34.42, 33.65, 26.18, 25.02, 24.88; HRMS (CI): Exact mass calcd for $C_{30}H_{32}NO_2$ $[M+H]^+$: 438.2433, found: 438.2435.

2,2'-(2-cyclohexylisoindoline-1,3-diyl)bis(1-phenylethanone) (13b). The general procedure was used to afford **13b** in 17% yield (0.11 g, yellow oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.36 (50% Et_2O /Hexanes). IR (NaCl, neat): 3060, 2929, 2853, 1680, 1653, 1597, 1448, 1357, 1265, 1211, 1179, 750, 690 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (dt, *J* = 8.5, 1.7 Hz, 4H), 7.60 – 7.50 (m, 2H), 7.49 – 7.39 (m, 4H), 7.20 – 7.13 (m, 4H), 5.00 (dd, *J* = 6.9, 5.4 Hz, 2H), 3.33 (qd, *J* = 16.5, 6.2 Hz, 4H), 2.64 (t, *J* = 11.2 Hz, 1H), 1.74 – 1.50 (m, 6H), 1.27 – 0.95 (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.83, 143.88, 137.80, 133.13, 128.65, 128.48, 127.42, 122.80, 62.44, 62.08, 50.05, 29.99, 26.27; HRMS (CI): Exact mass calcd for $C_{30}H_{32}NO_2$ $[M+H]^+$: 438.2433, found: 438.2430.

***Trans-trans*-1-(2-acetyl-3-(diethylamino)-2,3-dihydro-1H-inden-1-yl)propan-2-one (14a**). The general procedure was used to afford **14a** in 55% yield (0.034 g, yellow oil) after flash chromatography on silica using 15% acetone/hexanes as eluent. Rf = 0.55

(30% Acetone /Hexanes). IR (NaCl, neat): 2968, 2923, 1678, 1606, 1349, 1228, 1181, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 – 7.27 (m, 2H), 7.21 (dd, *J* = 9.2, 4.7 Hz, 2H), 7.13 – 7.05 (m, 1H), 4.68 (d, *J* = 7.8 Hz, 1H), 3.78 (dt, *J* = 13.3, 6.6 Hz, 1H), 3.12 – 2.96 (m, 2H), 2.73 – 2.55 (m, 3H), 2.46 (tt, *J* = 14.7, 7.4 Hz, 2H), 2.35 (s, 3H), 2.20 (s, 3H), 1.06 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 211.27, 207.45, 143.20, 142.49, 127.85, 127.14, 124.82, 123.26, 70.36, 61.64, 49.02, 45.00, 41.06, 30.20, 29.81, 14.86; HRMS (CI): Exact mass calcd for $C_{18}H_{26}NO_2$ $[M+H]^+$: 288.1964, found: 288.1949.

***Cis-trans*-1-(2-acetyl-3-(diethylamino)-2,3-dihydro-1H-inden-1-yl)propan-2-one (14b**). The general procedure was used to afford **14b** in 17% yield (0.007 g, yellow oil) after flash chromatography on silica using 15% Et_2O/hexanes as eluent. Rf = 0.67 (30% Acetone /Hexanes). IR (NaCl, neat): 2968, 2928, 2817, 1712, 1662, 1587, 1563, 1456, 1418 ,1358, 1250, 1159, 1068, 750 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.31 – 7.27 (m, 1H), 7.21 (p, *J* = 6.5 Hz, 2H), 7.09 – 7.06 (m, 1H), 4.93 (d, *J* = 8.7 Hz, 1H), 4.01 – 3.94 (m, 1H), 3.65 (t, *J* = 8.5 Hz, 1H), 2.98 (dd, *J* = 18.7, 10.2 Hz, 1H), 2.56 (dq, *J* = 14.5, 7.2 Hz, 2H), 2.44 (dd, *J* = 18.6, 3.9 Hz, 1H), 2.33 – 2.23 (m, 5H), 2.06 (s, 3H), 1.05 (q, *J* = 7.2 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 211.86, 208.11, 144.20, 143.25, 128.01, 127.38, 125.07, 123.83, 68.71, 54.57, 46.84, 45.03, 40.76, 32.32, 30.43, 14.73; HRMS (CI): Exact mass calcd for $C_{18}H_{26}NO_2$ $[M+H]^+$: 288.1964, found: 288.1968.

***Trans-trans*- 2-(2-(4-bromobenzoyl)-3-(diethylamino)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (16**). The general procedure was used to afford **16** in

97% yield (0.045 g, yellow oil) after flash chromatography on silica using 1:2 Et_2O/hexanes as eluent. Rf = 0.25 (33% Et_2O /Hexanes). IR (NaCl, neat): 3067, 2968, 2929, 2812, 1684, 1584, 1482, 1396, 1226, 1071, 1009, 907, 749, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 7.2 Hz, 4H), 7.35 – 7.29 (m, 1H), 7.29 – 7.26 (m, 2H), 7.17 (dd, *J* = 12.2, 6.3 Hz, 3H), 4.93 (d, *J* = 7.2 Hz, 1H), 4.17 – 4.07 (m, 1H), 4.04 (t, *J* = 7.5 Hz, 1H), 3.55 (dd, *J* = 17.2, 4.5 Hz, 1H), 3.20 (dd, *J* = 17.2, 8.7 Hz, 1H), 2.58 (dq, *J* = 14.2, 7.1 Hz, 2H), 2.29 (dq, *J* = 13.5, 6.9 Hz, 2H), 0.98 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.24, 197.58, 143.32, 142.78, 136.53, 135.54, 132.10, 131.93, 130.36, 129.66, 128.69, 128.21, 128.17, 127.57, 125.05, 123.32, 72.35, 55.38, 45.24, 43.99, 43.88, 14.66; HRMS (CI): Exact mass calcd for $C_{28}H_{28}Br_2NO_2$ $[M+H]^+$: 568.0487, found: 568.0469.

***Trans-trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17**). The general procedure was used to afford **4** in 99% yield (0.226 g, red oil). Rf = 0.27 (33% Et_2O /Hexanes). IR (NaCl, neat): 3066, 2962, 16884, 1653, 1584, 1566, 1483, 1396, 1359, 1259, 1207, 1070, 1009, 986, 908, 815, 750, 731 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.6 Hz, 2H), 7.59 – 7.54 (m, 4H), 7.34 (d, *J* = 6.7 Hz, 1H), 7.26 (s, 2H), 7.18 (d, *J* = 6.8 Hz, 1H), 4.79 (d, *J* = 5.6 Hz, 1H), 4.11 (dd, *J* = 9.1, 4.7 Hz, 1H), 4.07 (t, *J* = 5.9 Hz, 1H), 3.53 (dd, *J* = 17.3, 4.6 Hz, 1H), 3.35 (dd, *J* = 17.3, 9.0 Hz, 1H), 2.67 (d, *J* = 8.4 Hz, 2H), 2.56 – 2.49 (m, 2H), 1.77 – 1.67 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.44, 198.74, 144.24, 142.25, 137.33, 137.01, 133.31, 133.01, 128.76, 128.73, 128.20, 127.24,

125.63, 123.72, 71.10, 54.14, 49.57, 44.24, 43.91, 23.93; HRMS (CI): Exact mass calcd for $C_{28}H_{26}Br_2NO_2$ $[M+H]^+$: 566.0331, found: 566.0333.

***Trans-trans*-2-(3-(diethylamino)-2-(4-methylbenzoyl)-2,3-dihydro-1H-inden-1-yl)-1-p-tolylethanone (18)**. The general procedure was used to afford **18** in 88% yield (0.016 g, colorless oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.34 (50% Et_2O /Hexanes). IR (NaCl, neat): 3029, 2968, 1678, 1606, 1349, 1228, 1181 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 6.6 Hz, 1H), 7.26 – 7.16 (m, 6H), 7.12 (d, *J* = 6.6 Hz, 1H), 5.00 (d, *J* = 7.4 Hz, 1H), 4.18 (t, *J* = 7.9 Hz, 1H), 4.08 (dd, *J* = 13.6, 7.1 Hz, 1H), 3.48 (dd, *J* = 17.0, 5.5 Hz, 1H), 3.25 (dd, *J* = 17.0, 7.4 Hz, 1H), 2.58 (dq, *J* = 14.4, 7.2 Hz, 2H), 2.39 (s, 3H), 2.38 (s, 3H), 2.29 (dq, *J* = 13.7, 6.9 Hz, 2H), 1.00 (dt, *J* = 14.1, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 202.94, 198.18, 144.02, 143.79, 143.75, 143.30, 135.35, 134.62, 129.39, 129.35, 128.91, 128.31, 127.96, 127.31, 124.86, 123.36, 71.86, 54.45, 45.19, 44.42, 43.57, 21.78, 14.64; HRMS (CI): Exact mass calcd for $C_{30}H_{33}NO_2$ $[M+H]^+$: 440.2590, found: 440.2583.

***Trans-trans*-2-(3-(diethylamino)-2-(4-methoxybenzoyl)-2,3-dihydro-1H-inden-1-yl)-1-(4-methoxyphenyl)ethanone (19)**. The general procedure was used to afford **19** in 85% yield (0.045 g, coloress oil) after flash chromatography on silica using 1:1 Et_2O/hexanes as eluent. Rf = 0.12 (50% Et_2O /Hexanes). IR (NaCl, neat): 2967, 2933, 2838, 2813, 1671, 1600, 1574, 1510, 1420, 1353, 1265, 1253, 1229, 1170, 1113, 1030, 989, 909, 840, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.8 Hz, 2H),

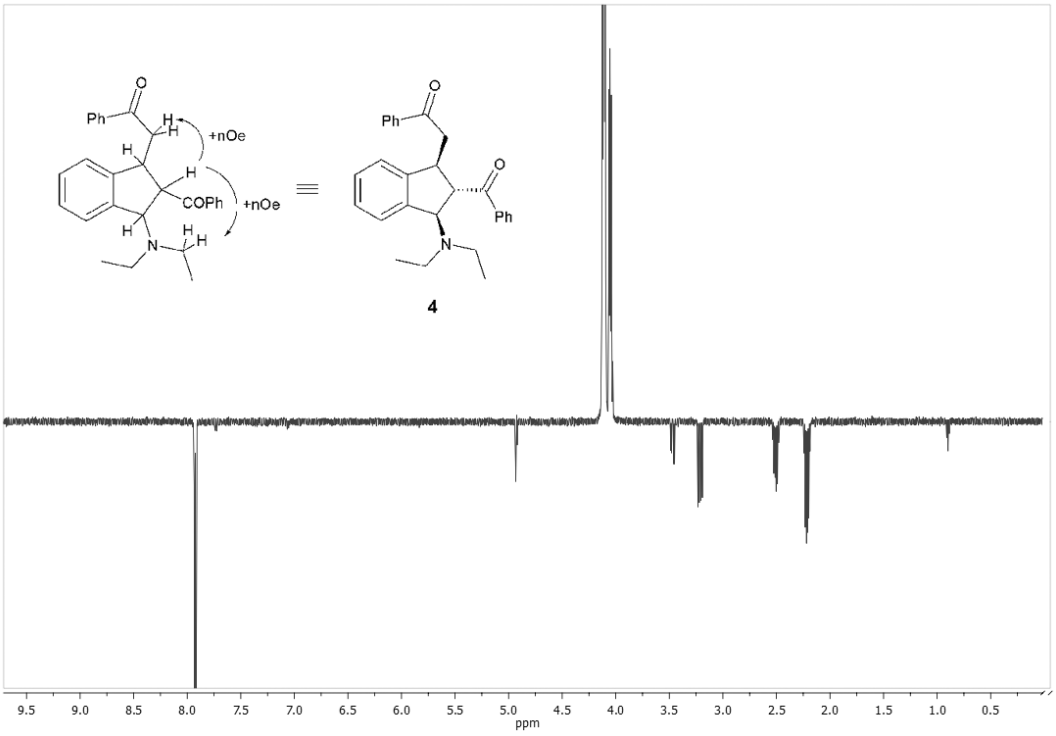
7.80 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 6.2 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.13 (d, *J* = 6.1 Hz, 1H), 6.87 (dt, *J* = 23.7, 11.9 Hz, 4H), 4.99 (d, *J* = 7.5 Hz, 1H), 4.17 (t, *J* = 7.9 Hz, 1H), 4.08 (d, *J* = 6.6 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.45 (dd, *J* = 16.7, 5.5 Hz, 1H), 3.23 (dd, *J* = 16.6, 7.5 Hz, 1H), 2.59 (dq, *J* = 14.6, 7.3 Hz, 2H), 2.30 (dq, *J* = 13.8, 7.0 Hz, 2H), 1.03 – 0.93 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 201.80, 197.09, 163.59, 163.50, 143.87, 143.31, 131.05, 130.88, 130.47, 130.20, 127.92, 127.27, 124.82, 123.35, 113.81, 71.78, 55.60, 55.56, 54.26, 45.18, 44.54, 43.26, 14.67; HRMS (CI): Exact mass calcd for $C_{30}H_{34}NO_2$ $[M+H]^+$: 472.2488, found: 472.2489.

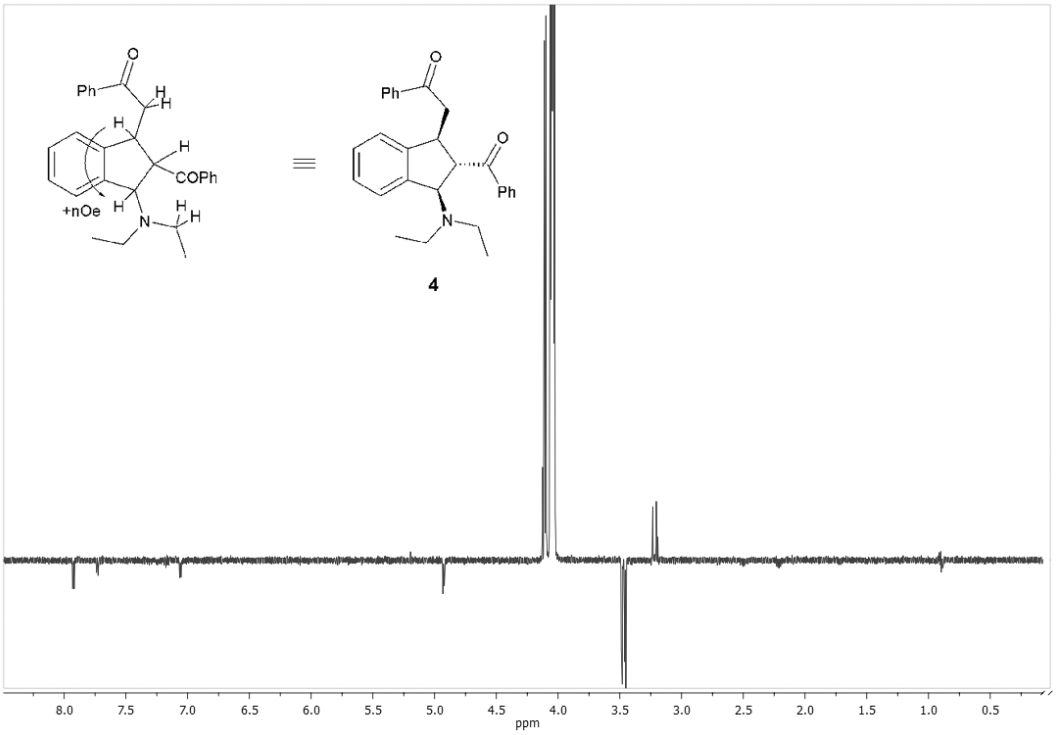
2-((1S,2S,3R)-2-benzoyl-3-(methyl((R)-1-phenylethyl)amino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone and 2-((1R,2R,3S)-2-benzoyl-3-(methyl((R)-1-phenylethyl)amino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (20a and 20b). The general procedure was used to afford an inseparable mixture of **20a** and **20b** in 96% yield (0.268 g, red oil) after flash chromatography on silica using 20% acetone/hexanes as eluent. Rf = 0.21 (20% Acetone/Hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07 – 8.02 (m, 2H), 8.02 – 7.97 (m, 4H), 7.90 – 7.83 (m, 6H), 7.65 – 7.39 (m, 20H), 7.38 – 7.32 (m, 10H), 7.31 – 7.23 (m, 14H), 7.23 – 7.12 (m, 14H), 7.11 – 7.07 (m, 4H), 5.17 (d, *J* = 7.1 Hz, 1H), 4.86 (d, *J* = 6.8 Hz, 2H), 4.31 (t, *J* = 7.4 Hz, 1H), 4.26 (t, *J* = 7.0 Hz, 2H), 4.15 (ddd, *J* = 20.6, 12.9, 7.8 Hz, 3H), 3.69 (q, *J* = 6.6 Hz, 3H), 3.65 – 3.48 (m, 6H), 3.31 (ddd, *J* = 17.2, 8.2, 2.0 Hz, 3H), 2.34 (s, 8H), 2.30 (s, 6H), 2.13 (s, 3H), 1.40 (d, *J* = 6.6 Hz, 8H), 1.25 (dd, *J* = 6.6, 2.4 Hz, 8H).

2-((1R,2R,3S)-2-benzoyl-3-((S)-2-(hydroxymethyl)pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (21b). The general procedure was used to afford **21b** in 83% yield (0.166 g, yellow oil) after flash chromatography on silica using 50% ethyl acetate/hexanes as eluent. Rf = 0.25 (50% EtOAc /Hexanes). IR (NaCl, neat): 3356, 3063, 2923, 1683, 1634, 1596, 1579, 1447, 1356, 1224, 750, 730, 689 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.90 – 7.84 (m, 2H), 7.77 – 7.73 (m, 2H), 7.47 (td, *J* = 7.4, 1.2 Hz, 2H), 7.35 (dd, *J* = 16.0, 8.3 Hz, 4H), 7.24 – 7.19 (m, 3H), 7.08 (d, *J* = 7.3 Hz, 1H), 5.04 (d, *J* = 6.9 Hz, 1H), 4.26 (t, *J* = 7.4 Hz, 1H), 4.05 (dd, *J* = 12.8, 7.7 Hz, 1H), 3.49 (ddd, *J* = 13.3, 6.6, 3.4 Hz, 2H), 3.28 (dd, *J* = 17.4, 7.9 Hz, 1H), 3.15 (d, *J* = 11.2 Hz, 1H), 2.80 – 2.75 (m, 1H), 2.61 (dd, *J* = 15.8, 8.5 Hz, 1H), 2.53 (s, 1H), 2.39 (br s, 1H), 1.70 – 1.55 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 203.33, 198.43, 143.26, 142.28, 137.52, 136.93, 133.41, 133.27, 128.91, 128.77, 128.60, 128.40, 128.16, 127.71, 124.91, 123.42, 68.92, 61.16, 60.98, 53.09, 47.33, 44.70, 43.53, 28.42, 24.03; HRMS (CI): Exact mass calcd for $C_{29}H_{30}NO_3$ $[M+H]^+$: 440.2226, found: 440.2220.

B.2. Nuclear Overhauser Effect Spectroscopy

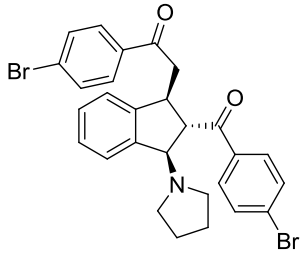
B.2.1. *Trans-trans*-2-(2-benzoyl-3-(diethylamino)-2,3-dihydro-1H-inden-1-yl)-1-phenylethanone (4).





B.3. Crystal Structures

B.3.1. Table 1. Crystal data and structure refinement for *trans*-*trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17).

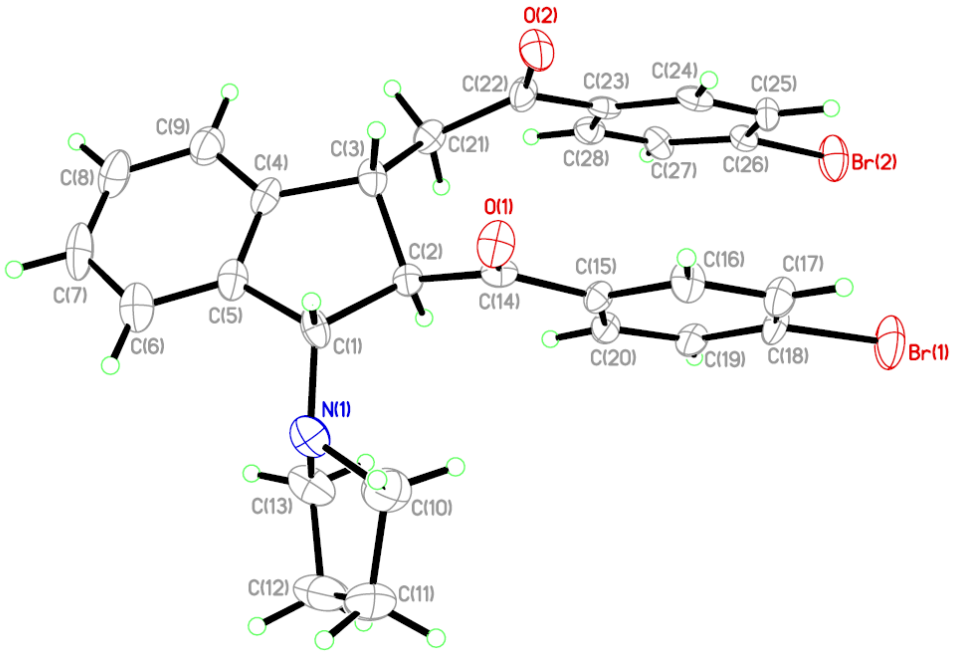


17

Empirical formula	C29.50 H27 Br2 N O2.50	
Formula weight	595.34	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 14.426(2) Å	□= 90°.
	b = 33.454(5) Å	□= 99.614(3)°.
	c = 10.8712(17) Å	□ = 90°.
Volume	5173.0(14) Å^3	
Z	8	
Density (calculated)	1.529 Mg/m^3	
Absorption coefficient	3.164 mm^{-1}	
F(000)	2408	
Crystal size	0.37 x 0.15 x 0.02 mm^3	
Theta range for data collection	1.22 to 27.00°.	
Index ranges	-18<=h<=18, -42<=k<=42, -13<=l<=13	
Reflections collected	57115	
Independent reflections	11295 [R(int) = 0.1160]	
Completeness to theta = 27.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9394 and 0.3873	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	11295 / 0 / 595	
Goodness-of-fit on F^2	0.978	

Final R indices [I>2sigma(I)]	R1 = 0.0786, wR2 = 0.1838
R indices (all data)	R1 = 0.1754, wR2 = 0.2176
Largest diff. peak and hole	1.035 and -0.909 e.Å^{-3}

B.3.2. Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for *trans-trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.



	x	y	z	U(eq)
Br(1)	7417(1)	8798(1)	2824(1)	70(1)
Br(2)	7045(1)	7711(1)	4793(1)	57(1)
O(1)	3273(3)	8926(2)	-1182(4)	42(1)
O(2)	3499(3)	7961(2)	-146(4)	46(1)
N(1)	1798(4)	9604(2)	413(6)	46(2)
C(1)	1726(4)	9186(2)	55(6)	35(2)
C(2)	2537(4)	8898(2)	627(6)	30(2)
C(3)	2078(4)	8478(2)	497(6)	35(2)
C(4)	1067(5)	8573(2)	646(6)	35(2)
C(5)	871(5)	8975(2)	369(6)	40(2)
C(6)	-12(5)	9121(3)	377(7)	54(2)
C(7)	-686(6)	8862(3)	690(9)	74(3)
C(8)	-493(5)	8470(3)	1002(8)	60(2)
C(9)	394(5)	8325(3)	943(7)	51(2)
C(10)	2563(7)	9826(3)	35(9)	67(3)

C(11)	2538(8)	10228(3)	680(11)	85(3)
C(12)	2074(8)	10141(3)	1811(10)	82(3)
C(13)	1845(6)	9702(2)	1736(8)	60(2)
C(14)	3369(5)	8916(2)	-50(6)	30(2)
C(15)	4351(4)	8911(2)	688(6)	29(2)
C(16)	5108(5)	8889(2)	49(6)	39(2)
C(17)	6029(5)	8862(2)	666(7)	42(2)
C(18)	6171(4)	8851(2)	1939(7)	38(2)
C(19)	5452(5)	8868(2)	2622(6)	37(2)
C(20)	4542(5)	8903(2)	2010(6)	32(2)
C(21)	2591(5)	8168(2)	1380(6)	35(2)
C(22)	3459(4)	8007(2)	943(7)	37(2)
C(23)	4320(5)	7917(2)	1903(6)	28(2)
C(24)	5184(5)	7903(2)	1523(6)	35(2)
C(25)	6003(5)	7842(2)	2362(7)	35(2)
C(26)	5933(5)	7793(2)	3613(6)	33(2)
C(27)	5075(5)	7791(2)	3992(6)	36(2)
C(28)	4274(5)	7860(2)	3164(6)	36(2)
Br(1')	-1360(1)	8870(1)	6013(1)	81(1)
Br(2')	-1210(1)	7651(1)	7849(1)	70(1)
O(1')	2775(3)	8933(2)	3720(4)	42(1)
O(2')	2375(3)	8001(2)	4612(4)	46(1)
N(1')	4386(4)	9561(2)	6007(5)	40(2)
C(1')	4364(4)	9145(2)	5676(6)	32(2)
C(2')	3509(4)	8892(2)	5849(6)	27(2)
C(3')	3859(4)	8457(2)	5950(6)	28(2)
C(4')	4869(5)	8515(2)	6597(6)	34(2)
C(5')	5173(5)	8898(2)	6398(6)	35(2)
C(6')	6061(5)	9022(3)	6848(7)	46(2)
C(7')	6685(5)	8749(3)	7527(7)	53(2)
C(8')	6385(5)	8365(3)	7724(7)	50(2)
C(9')	5500(5)	8247(2)	7264(7)	42(2)
C(10')	3712(6)	9820(2)	5241(7)	54(2)
C(11')	3807(7)	10214(3)	5912(8)	64(3)
C(12')	4171(8)	10105(3)	7279(8)	78(3)
C(13')	4308(7)	9667(2)	7308(7)	59(2)

C(14')	2661(5)	8935(2)	4804(6)	30(2)
C(15')	1700(5)	8945(2)	5129(6)	34(2)
C(16')	929(5)	8915(2)	4171(6)	42(2)
C(17')	24(6)	8897(3)	4417(7)	59(2)
C(18')	-128(5)	8910(3)	5644(7)	49(2)
C(19')	604(5)	8952(3)	6620(7)	54(2)
C(20')	1512(5)	8965(2)	6344(6)	40(2)
C(21')	3278(4)	8167(2)	6594(6)	34(2)
C(22')	2394(4)	8029(2)	5749(6)	30(2)
C(23')	1531(5)	7933(2)	6277(6)	37(2)
C(24')	669(5)	7940(2)	5489(7)	43(2)
C(25')	-143(5)	7857(3)	5952(7)	54(2)
C(26')	-97(5)	7770(2)	7207(7)	40(2)
C(27')	753(5)	7761(2)	7996(7)	44(2)
C(28')	1577(5)	7850(2)	7554(6)	37(2)

B.3.3. Table 3. Bond lengths [Å] and angles [°] for *trans-trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17).

Br(1)-C(18)	1.900(7)
Br(2)-C(26)	1.899(7)
O(1)-C(14)	1.215(7)
O(2)-C(22)	1.205(8)
N(1)-C(10)	1.445(10)
N(1)-C(1)	1.450(9)
N(1)-C(13)	1.466(9)
C(1)-C(5)	1.508(9)
C(1)-C(2)	1.562(9)
C(1)-H(1A)	1.0000
C(2)-C(14)	1.510(9)
C(2)-C(3)	1.551(9)
C(2)-H(2A)	1.0000
C(3)-C(21)	1.520(9)
C(3)-C(4)	1.527(9)
C(3)-H(3A)	1.0000
C(4)-C(9)	1.355(10)
C(4)-C(5)	1.399(10)
C(5)-C(6)	1.364(10)
C(6)-C(7)	1.385(12)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.372(12)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.380(11)
C(8)-H(8A)	0.9500
C(9)-H(9A)	0.9500
C(10)-C(11)	1.521(12)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.523(14)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900

C(12)-C(13)	1.504(12)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-C(15)	1.506(9)
C(15)-C(16)	1.391(9)
C(15)-C(20)	1.417(9)
C(16)-C(17)	1.388(9)
C(16)-H(16A)	0.9500
C(17)-C(18)	1.365(10)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.374(9)
C(19)-C(20)	1.374(9)
C(19)-H(19A)	0.9500
C(20)-H(20A)	0.9500
C(21)-C(22)	1.510(9)
C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(23)	1.514(9)
C(23)-C(24)	1.377(9)
C(23)-C(28)	1.397(9)
C(24)-C(25)	1.382(9)
C(24)-H(24A)	0.9500
C(25)-C(26)	1.390(9)
C(25)-H(25A)	0.9500
C(26)-C(27)	1.369(9)
C(27)-C(28)	1.359(9)
C(27)-H(27A)	0.9500
C(28)-H(28A)	0.9500
Br(1')-C(18')	1.892(7)
Br(2')-C(26')	1.897(7)
O(1')-C(14')	1.217(7)
O(2')-C(22')	1.235(7)
N(1')-C(1')	1.439(9)
N(1')-C(10')	1.455(9)

N(1')-C(13')	1.480(9)
C(1')-C(5')	1.533(10)
C(1')-C(2')	1.533(9)
C(1')-H(1'A)	1.0000
C(2')-C(14')	1.530(9)
C(2')-C(3')	1.538(9)
C(2')-H(2'A)	1.0000
C(3')-C(4')	1.520(9)
C(3')-C(21')	1.528(9)
C(3')-H(3'A)	1.0000
C(4')-C(5')	1.383(9)
C(4')-C(9')	1.393(10)
C(5')-C(6')	1.357(9)
C(6')-C(7')	1.401(11)
C(6')-H(6'A)	0.9500
C(7')-C(8')	1.385(11)
C(7')-H(7'A)	0.9500
C(8')-C(9')	1.351(10)
C(8')-H(8'A)	0.9500
C(9')-H(9'A)	0.9500
C(10')-C(11')	1.501(11)
C(10')-H(10C)	0.9900
C(10')-H(10D)	0.9900
C(11')-C(12')	1.535(12)
C(11')-H(11C)	0.9900
C(11')-H(11D)	0.9900
C(12')-C(13')	1.481(11)
C(12')-H(12C)	0.9900
C(12')-H(12D)	0.9900
C(13')-H(13C)	0.9900
C(13')-H(13D)	0.9900
C(14')-C(15')	1.487(9)
C(15')-C(20')	1.394(9)
C(15')-C(16')	1.395(9)
C(16')-C(17')	1.378(10)
C(16')-H(16B)	0.9500

C(17')-C(18')	1.388(10)
C(17')-H(17B)	0.9500
C(18')-C(19')	1.373(10)
C(19')-C(20')	1.391(9)
C(19')-H(19B)	0.9500
C(20')-H(20B)	0.9500
C(21')-C(22')	1.514(9)
C(21')-H(21C)	0.9900
C(21')-H(21D)	0.9900
C(22')-C(23')	1.490(9)
C(23')-C(24')	1.388(9)
C(23')-C(28')	1.407(9)
C(24')-C(25')	1.377(10)
C(24')-H(24B)	0.9500
C(25')-C(26')	1.386(10)
C(25')-H(25B)	0.9500
C(26')-C(27')	1.374(10)
C(27')-C(28')	1.387(9)
C(27')-H(27B)	0.9500
C(28')-H(28B)	0.9500

C(10)-N(1)-C(1)	116.4(6)
C(10)-N(1)-C(13)	104.5(7)
C(1)-N(1)-C(13)	118.0(6)
N(1)-C(1)-C(5)	114.5(6)
N(1)-C(1)-C(2)	118.1(6)
C(5)-C(1)-C(2)	102.1(6)
N(1)-C(1)-H(1A)	107.2
C(5)-C(1)-H(1A)	107.2
C(2)-C(1)-H(1A)	107.2
C(14)-C(2)-C(3)	110.7(5)
C(14)-C(2)-C(1)	112.7(5)
C(3)-C(2)-C(1)	104.0(5)
C(14)-C(2)-H(2A)	109.8
C(3)-C(2)-H(2A)	109.8
C(1)-C(2)-H(2A)	109.8

C(21)-C(3)-C(4)	116.6(5)
C(21)-C(3)-C(2)	114.0(5)
C(4)-C(3)-C(2)	101.7(5)
C(21)-C(3)-H(3A)	108.0
C(4)-C(3)-H(3A)	108.0
C(2)-C(3)-H(3A)	108.0
C(9)-C(4)-C(5)	120.8(7)
C(9)-C(4)-C(3)	129.3(7)
C(5)-C(4)-C(3)	109.8(6)
C(6)-C(5)-C(4)	119.8(7)
C(6)-C(5)-C(1)	129.4(8)
C(4)-C(5)-C(1)	110.8(6)
C(5)-C(6)-C(7)	118.2(9)
C(5)-C(6)-H(6A)	120.9
C(7)-C(6)-H(6A)	120.9
C(8)-C(7)-C(6)	122.4(8)
C(8)-C(7)-H(7A)	118.8
C(6)-C(7)-H(7A)	118.8
C(7)-C(8)-C(9)	118.4(8)
C(7)-C(8)-H(8A)	120.8
C(9)-C(8)-H(8A)	120.8
C(4)-C(9)-C(8)	120.2(8)
C(4)-C(9)-H(9A)	119.9
C(8)-C(9)-H(9A)	119.9
N(1)-C(10)-C(11)	104.2(7)
N(1)-C(10)-H(10A)	110.9
C(11)-C(10)-H(10A)	110.9
N(1)-C(10)-H(10B)	110.9
C(11)-C(10)-H(10B)	110.9
H(10A)-C(10)-H(10B)	108.9
C(12)-C(11)-C(10)	104.5(7)
C(12)-C(11)-H(11A)	110.8
C(10)-C(11)-H(11A)	110.8
C(12)-C(11)-H(11B)	110.8
C(10)-C(11)-H(11B)	110.8
H(11A)-C(11)-H(11B)	108.9

C(13)-C(12)-C(11)	105.3(8)
C(13)-C(12)-H(12A)	110.7
C(11)-C(12)-H(12A)	110.7
C(13)-C(12)-H(12B)	110.7
C(11)-C(12)-H(12B)	110.7
H(12A)-C(12)-H(12B)	108.8
N(1)-C(13)-C(12)	104.3(7)
N(1)-C(13)-H(13A)	110.9
C(12)-C(13)-H(13A)	110.9
N(1)-C(13)-H(13B)	110.9
C(12)-C(13)-H(13B)	110.9
H(13A)-C(13)-H(13B)	108.9
O(1)-C(14)-C(15)	118.6(6)
O(1)-C(14)-C(2)	121.9(6)
C(15)-C(14)-C(2)	119.5(5)
C(16)-C(15)-C(20)	118.0(6)
C(16)-C(15)-C(14)	118.8(6)
C(20)-C(15)-C(14)	123.2(6)
C(17)-C(16)-C(15)	122.0(6)
C(17)-C(16)-H(16A)	119.0
C(15)-C(16)-H(16A)	119.0
C(18)-C(17)-C(16)	117.5(6)
C(18)-C(17)-H(17A)	121.3
C(16)-C(17)-H(17A)	121.3
C(17)-C(18)-C(19)	123.2(6)
C(17)-C(18)-Br(1)	119.0(5)
C(19)-C(18)-Br(1)	117.8(5)
C(18)-C(19)-C(20)	119.2(6)
C(18)-C(19)-H(19A)	120.4
C(20)-C(19)-H(19A)	120.4
C(19)-C(20)-C(15)	120.1(6)
C(19)-C(20)-H(20A)	120.0
C(15)-C(20)-H(20A)	120.0
C(22)-C(21)-C(3)	112.7(5)
C(22)-C(21)-H(21A)	109.0
C(3)-C(21)-H(21A)	109.0

C(22)-C(21)-H(21B)	109.0
C(3)-C(21)-H(21B)	109.0
H(21A)-C(21)-H(21B)	107.8
O(2)-C(22)-C(23)	118.9(6)
O(2)-C(22)-C(21)	122.2(6)
C(23)-C(22)-C(21)	118.9(6)
C(24)-C(23)-C(28)	118.9(6)
C(24)-C(23)-C(22)	118.6(6)
C(28)-C(23)-C(22)	122.4(6)
C(23)-C(24)-C(25)	121.6(6)
C(23)-C(24)-H(24A)	119.2
C(25)-C(24)-H(24A)	119.2
C(24)-C(25)-C(26)	118.0(6)
C(24)-C(25)-H(25A)	121.0
C(26)-C(25)-H(25A)	121.0
C(27)-C(26)-C(25)	120.8(6)
C(27)-C(26)-Br(2)	120.0(5)
C(25)-C(26)-Br(2)	119.1(5)
C(28)-C(27)-C(26)	120.7(6)
C(28)-C(27)-H(27A)	119.6
C(26)-C(27)-H(27A)	119.6
C(27)-C(28)-C(23)	119.9(6)
C(27)-C(28)-H(28A)	120.1
C(23)-C(28)-H(28A)	120.1
C(1')-N(1')-C(10')	116.6(6)
C(1')-N(1')-C(13')	117.9(6)
C(10')-N(1')-C(13')	104.8(6)
N(1')-C(1')-C(5')	114.2(5)
N(1')-C(1')-C(2')	119.2(5)
C(5')-C(1')-C(2')	101.6(5)
N(1')-C(1')-H(1'A)	107.1
C(5')-C(1')-H(1'A)	107.1
C(2')-C(1')-H(1'A)	107.1
C(14')-C(2')-C(1')	114.6(5)
C(14')-C(2')-C(3')	110.8(5)
C(1')-C(2')-C(3')	105.5(5)

C(14')-C(2')-H(2'A)	108.6
C(1')-C(2')-H(2'A)	108.6
C(3')-C(2')-H(2'A)	108.6
C(4')-C(3')-C(21')	115.3(5)
C(4')-C(3')-C(2')	101.0(5)
C(21')-C(3')-C(2')	115.8(5)
C(4')-C(3')-H(3'A)	108.1
C(21')-C(3')-H(3'A)	108.1
C(2')-C(3')-H(3'A)	108.1
C(5')-C(4')-C(9')	118.9(7)
C(5')-C(4')-C(3')	110.5(6)
C(9')-C(4')-C(3')	130.5(7)
C(6')-C(5')-C(4')	122.0(7)
C(6')-C(5')-C(1')	127.8(7)
C(4')-C(5')-C(1')	110.1(6)
C(5')-C(6')-C(7')	118.5(8)
C(5')-C(6')-H(6'A)	120.8
C(7')-C(6')-H(6'A)	120.8
C(8')-C(7')-C(6')	119.7(7)
C(8')-C(7')-H(7'A)	120.1
C(6')-C(7')-H(7'A)	120.1
C(9')-C(8')-C(7')	121.0(8)
C(9')-C(8')-H(8'A)	119.5
C(7')-C(8')-H(8'A)	119.5
C(8')-C(9')-C(4')	119.9(8)
C(8')-C(9')-H(9'A)	120.0
C(4')-C(9')-H(9'A)	120.0
N(1')-C(10')-C(11')	104.2(7)
N(1')-C(10')-H(10C)	110.9
C(11')-C(10')-H(10C)	110.9
N(1')-C(10')-H(10D)	110.9
C(11')-C(10')-H(10D)	110.9
H(10C)-C(10')-H(10D)	108.9
C(10')-C(11')-C(12')	104.6(7)
C(10')-C(11')-H(11C)	110.8
C(12')-C(11')-H(11C)	110.8

C(10')-C(11')-H(11D)	110.8
C(12')-C(11')-H(11D)	110.8
H(11C)-C(11')-H(11D)	108.9
C(13')-C(12')-C(11')	106.1(7)
C(13')-C(12')-H(12C)	110.5
C(11')-C(12')-H(12C)	110.5
C(13')-C(12')-H(12D)	110.5
C(11')-C(12')-H(12D)	110.5
H(12C)-C(12')-H(12D)	108.7
C(12')-C(13')-N(1')	104.3(7)
C(12')-C(13')-H(13C)	110.9
N(1')-C(13')-H(13C)	110.9
C(12')-C(13')-H(13D)	110.9
N(1')-C(13')-H(13D)	110.9
H(13C)-C(13')-H(13D)	108.9
O(1')-C(14')-C(15')	120.8(6)
O(1')-C(14')-C(2')	119.9(6)
C(15')-C(14')-C(2')	119.1(5)
C(20')-C(15')-C(16')	117.0(6)
C(20')-C(15')-C(14')	124.3(6)
C(16')-C(15')-C(14')	118.6(6)
C(17')-C(16')-C(15')	121.4(7)
C(17')-C(16')-H(16B)	119.3
C(15')-C(16')-H(16B)	119.3
C(16')-C(17')-C(18')	119.4(7)
C(16')-C(17')-H(17B)	120.3
C(18')-C(17')-H(17B)	120.3
C(19')-C(18')-C(17')	121.4(7)
C(19')-C(18')-Br(1')	118.2(6)
C(17')-C(18')-Br(1')	120.4(6)
C(18')-C(19')-C(20')	117.8(7)
C(18')-C(19')-H(19B)	121.1
C(20')-C(19')-H(19B)	121.1
C(19')-C(20')-C(15')	122.8(7)
C(19')-C(20')-H(20B)	118.6
C(15')-C(20')-H(20B)	118.6

C(22')-C(21')-C(3')	112.8(5)
C(22')-C(21')-H(21C)	109.0
C(3')-C(21')-H(21C)	109.0
C(22')-C(21')-H(21D)	109.0
C(3')-C(21')-H(21D)	109.0
H(21C)-C(21')-H(21D)	107.8
O(2')-C(22')-C(23')	119.3(6)
O(2')-C(22')-C(21')	120.3(6)
C(23')-C(22')-C(21')	120.3(6)
C(24')-C(23')-C(28')	120.2(7)
C(24')-C(23')-C(22')	118.6(6)
C(28')-C(23')-C(22')	121.2(6)
C(25')-C(24')-C(23')	120.0(7)
C(25')-C(24')-H(24B)	120.0
C(23')-C(24')-H(24B)	120.0
C(24')-C(25')-C(26')	119.9(7)
C(24')-C(25')-H(25B)	120.1
C(26')-C(25')-H(25B)	120.1
C(27')-C(26')-C(25')	120.7(7)
C(27')-C(26')-Br(2')	119.2(5)
C(25')-C(26')-Br(2')	120.1(6)
C(26')-C(27')-C(28')	120.4(7)
C(26')-C(27')-H(27B)	119.8
C(28')-C(27')-H(27B)	119.8
C(27')-C(28')-C(23')	118.8(7)
C(27')-C(28')-H(28B)	120.6
C(23')-C(28')-H(28B)	120.6

B.3.4. Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for *trans-trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	27(1)	115(1)	64(1)	-12(1)	-1(1)	-1(1)
Br(2)	36(1)	95(1)	39(1)	4(1)	3(1)	9(1)
O(1)	38(3)	68(4)	21(3)	2(2)	5(2)	-3(3)
O(2)	39(3)	71(4)	28(3)	-12(3)	5(2)	9(3)
N(1)	52(4)	48(5)	40(4)	10(3)	10(3)	9(3)
C(1)	31(4)	47(5)	26(4)	8(3)	7(3)	14(3)
C(2)	29(4)	36(5)	23(3)	-2(3)	3(3)	1(3)
C(3)	29(4)	51(5)	24(4)	0(3)	6(3)	5(3)
C(4)	27(4)	52(6)	26(4)	0(3)	4(3)	-11(4)
C(5)	30(4)	63(6)	27(4)	-5(4)	6(3)	0(4)
C(6)	38(5)	78(7)	47(5)	6(4)	8(4)	6(4)
C(7)	23(4)	112(9)	88(7)	5(7)	11(4)	2(5)
C(8)	32(5)	76(7)	71(6)	11(5)	7(4)	-14(5)
C(9)	40(5)	62(6)	53(5)	-10(4)	11(4)	-9(4)
C(10)	74(6)	55(6)	80(7)	1(5)	34(5)	-6(5)
C(11)	80(7)	38(6)	133(10)	5(6)	8(7)	-5(5)
C(12)	110(9)	43(7)	87(8)	-12(5)	2(7)	11(6)
C(13)	80(7)	51(6)	48(5)	1(4)	10(4)	19(5)
C(14)	44(4)	28(4)	19(4)	-2(3)	9(3)	-3(3)
C(15)	27(3)	33(4)	27(4)	1(3)	8(3)	-6(3)
C(16)	40(4)	58(5)	22(4)	2(3)	13(3)	0(4)
C(17)	32(4)	54(5)	43(5)	-1(4)	10(3)	-7(4)
C(18)	22(3)	52(5)	40(4)	-2(4)	1(3)	-10(3)
C(19)	37(4)	50(5)	25(4)	-14(3)	6(3)	-9(4)
C(20)	31(4)	40(5)	27(4)	-7(3)	10(3)	-4(3)
C(21)	36(4)	40(5)	31(4)	5(3)	11(3)	-8(3)
C(22)	27(4)	47(5)	38(4)	-3(4)	11(3)	-7(3)
C(23)	43(4)	20(4)	24(4)	-5(3)	12(3)	-1(3)

C(24)	54(5)	26(4)	28(4)	-6(3)	14(3)	2(4)
C(25)	24(3)	41(5)	43(4)	0(3)	9(3)	1(3)
C(26)	35(4)	32(4)	33(4)	-7(3)	9(3)	1(3)
C(27)	41(4)	40(5)	29(4)	7(3)	15(3)	8(3)
C(28)	42(4)	28(4)	39(4)	0(3)	11(3)	-2(3)
Br(1')	32(1)	157(1)	56(1)	-15(1)	11(1)	-1(1)
Br(2')	37(1)	127(1)	49(1)	9(1)	12(1)	-18(1)
O(1')	38(3)	71(4)	17(2)	6(2)	6(2)	6(3)
O(2')	44(3)	66(4)	29(3)	-16(3)	11(2)	-13(3)
N(1')	49(4)	47(4)	23(3)	2(3)	8(3)	-9(3)
C(1')	29(4)	44(5)	21(3)	-5(3)	5(3)	-3(3)
C(2')	25(3)	37(5)	20(3)	0(3)	5(3)	-5(3)
C(3')	22(3)	37(4)	23(3)	-7(3)	1(3)	6(3)
C(4')	31(4)	47(5)	25(4)	-12(3)	6(3)	3(4)
C(5')	31(4)	47(5)	29(4)	-15(3)	12(3)	-10(4)
C(6')	31(4)	71(6)	36(4)	-6(4)	8(3)	-8(4)
C(7')	29(4)	93(8)	38(5)	-5(5)	15(4)	-1(5)
C(8')	37(4)	68(6)	46(5)	-12(4)	6(4)	24(4)
C(9')	34(4)	44(5)	45(5)	-7(4)	3(3)	9(4)
C(10')	72(6)	46(6)	46(5)	2(4)	12(4)	2(5)
C(11')	79(6)	48(6)	73(6)	2(5)	33(5)	-6(5)
C(12')	140(10)	48(7)	52(6)	-8(5)	34(6)	-21(6)
C(13')	97(7)	41(6)	41(5)	-13(4)	19(5)	-19(5)
C(14')	33(4)	32(4)	24(4)	-6(3)	3(3)	-5(3)
C(15')	37(4)	46(5)	21(3)	-4(3)	9(3)	5(3)
C(16')	30(4)	70(6)	26(4)	1(4)	3(3)	9(4)
C(17')	48(5)	90(7)	34(5)	-2(4)	-9(4)	-3(5)
C(18')	35(4)	73(6)	44(5)	-4(4)	18(4)	4(4)
C(19')	30(4)	96(7)	37(5)	-11(4)	6(3)	4(4)
C(20')	32(4)	66(6)	21(4)	-10(3)	1(3)	-1(4)
C(21')	33(4)	38(5)	29(4)	5(3)	2(3)	4(3)
C(22')	30(4)	26(4)	33(4)	-5(3)	5(3)	-4(3)
C(23')	40(4)	31(4)	36(4)	1(3)	0(3)	6(3)
C(24')	32(4)	66(6)	29(4)	5(4)	2(3)	-5(4)
C(25')	41(5)	75(6)	40(5)	5(4)	-7(4)	-8(4)
C(26')	41(4)	47(5)	33(4)	0(4)	10(3)	-14(4)

C(27')	48(5)	58(6)	29(4)	6(4)	12(4)	-4(4)
C(28')	39(4)	42(5)	30(4)	0(3)	5(3)	-11(3)

B.3.5. Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for *trans-trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17).

	x	y	z	U(eq)
H(1A)	1682	9175	-872	41
H(2A)	2744	8963	1529	36
H(3A)	2071	8383	-377	42
H(6A)	-160	9392	172	65
H(7A)	-1304	8960	689	89
H(8A)	-959	8303	1254	72
H(9A)	533	8051	1110	61
H(10A)	2465	9859	-883	81
H(10B)	3171	9689	310	81
H(11A)	3181	10334	940	102
H(11B)	2166	10424	121	102
H(12A)	2508	10203	2593	98
H(12B)	1495	10302	1783	98
H(13A)	2342	9545	2261	72
H(13B)	1236	9649	2009	72
H(16A)	4991	8893	-837	47
H(17A)	6541	8852	220	51
H(19A)	5582	8856	3507	44
H(20A)	4041	8922	2473	38
H(21A)	2774	8289	2215	42
H(21B)	2158	7943	1460	42
H(24A)	5217	7936	664	42
H(25A)	6596	7834	2092	42
H(27A)	5038	7741	4842	43
H(28A)	3685	7869	3443	43
H(1'A)	4423	9129	4773	38
H(2'A)	3312	8969	6656	33
H(3'A)	3872	8356	5088	33

H(6'A)	6255	9287	6706	55
H(7'A)	7310	8828	7851	63
H(8'A)	6809	8182	8190	61
H(9'A)	5307	7981	7395	50
H(10C)	3066	9714	5178	65
H(10D)	3866	9847	4391	65
H(11C)	3192	10351	5828	77
H(11D)	4258	10390	5578	77
H(12C)	4773	10244	7582	93
H(12D)	3709	10184	7814	93
H(13C)	3766	9529	7572	71
H(13D)	4888	9593	7887	71
H(16B)	1031	8907	3330	50
H(17B)	-493	8876	3752	71
H(19B)	495	8970	7456	65
H(20B)	2025	8989	7013	48
H(21C)	3668	7930	6882	41
H(21D)	3102	8298	7338	41
H(24B)	638	8002	4631	51
H(25B)	-733	7860	5412	64
H(27B)	776	7693	8849	53
H(28B)	2163	7854	8105	45

B.3.6. Table 6. Torsion angles [°] for *trans*-*trans*-2-(2-(4-bromobenzoyl)-3-(pyrrolidin-1-yl)-2,3-dihydro-1H-inden-1-yl)-1-(4-bromophenyl)ethanone (17).

C(10)-N(1)-C(1)-C(5)	-174.9(7)
C(13)-N(1)-C(1)-C(5)	59.6(8)
C(10)-N(1)-C(1)-C(2)	64.8(8)
C(13)-N(1)-C(1)-C(2)	-60.7(8)
N(1)-C(1)-C(2)-C(14)	-81.8(7)
C(5)-C(1)-C(2)-C(14)	151.7(5)
N(1)-C(1)-C(2)-C(3)	158.3(5)
C(5)-C(1)-C(2)-C(3)	31.8(6)
C(14)-C(2)-C(3)-C(21)	79.7(7)
C(1)-C(2)-C(3)-C(21)	-159.0(5)
C(14)-C(2)-C(3)-C(4)	-153.9(5)
C(1)-C(2)-C(3)-C(4)	-32.6(6)
C(21)-C(3)-C(4)-C(9)	-36.2(10)
C(2)-C(3)-C(4)-C(9)	-160.8(7)
C(21)-C(3)-C(4)-C(5)	146.5(6)
C(2)-C(3)-C(4)-C(5)	21.9(7)
C(9)-C(4)-C(5)-C(6)	-1.0(10)
C(3)-C(4)-C(5)-C(6)	176.5(6)
C(9)-C(4)-C(5)-C(1)	-179.3(6)
C(3)-C(4)-C(5)-C(1)	-1.8(8)
N(1)-C(1)-C(5)-C(6)	34.1(10)
C(2)-C(1)-C(5)-C(6)	162.9(7)
N(1)-C(1)-C(5)-C(4)	-147.9(6)
C(2)-C(1)-C(5)-C(4)	-19.0(7)
C(4)-C(5)-C(6)-C(7)	1.4(11)
C(1)-C(5)-C(6)-C(7)	179.3(8)
C(5)-C(6)-C(7)-C(8)	0.7(14)
C(6)-C(7)-C(8)-C(9)	-3.1(14)
C(5)-C(4)-C(9)-C(8)	-1.5(11)
C(3)-C(4)-C(9)-C(8)	-178.4(7)
C(7)-C(8)-C(9)-C(4)	3.5(12)
C(1)-N(1)-C(10)-C(11)	-172.6(7)

C(13)-N(1)-C(10)-C(11)	-40.6(9)
N(1)-C(10)-C(11)-C(12)	25.2(10)
C(10)-C(11)-C(12)-C(13)	-1.1(11)
C(10)-N(1)-C(13)-C(12)	39.9(9)
C(1)-N(1)-C(13)-C(12)	171.0(7)
C(11)-C(12)-C(13)-N(1)	-23.1(10)
C(3)-C(2)-C(14)-O(1)	73.3(8)
C(1)-C(2)-C(14)-O(1)	-42.7(9)
C(3)-C(2)-C(14)-C(15)	-105.2(6)
C(1)-C(2)-C(14)-C(15)	138.8(6)
O(1)-C(14)-C(15)-C(16)	-4.5(10)
C(2)-C(14)-C(15)-C(16)	174.1(6)
O(1)-C(14)-C(15)-C(20)	179.3(6)
C(2)-C(14)-C(15)-C(20)	-2.1(10)
C(20)-C(15)-C(16)-C(17)	-0.2(11)
C(14)-C(15)-C(16)-C(17)	-176.6(7)
C(15)-C(16)-C(17)-C(18)	1.0(11)
C(16)-C(17)-C(18)-C(19)	-0.5(12)
C(16)-C(17)-C(18)-Br(1)	178.1(5)
C(17)-C(18)-C(19)-C(20)	-0.8(12)
Br(1)-C(18)-C(19)-C(20)	-179.4(5)
C(18)-C(19)-C(20)-C(15)	1.6(10)
C(16)-C(15)-C(20)-C(19)	-1.2(10)
C(14)-C(15)-C(20)-C(19)	175.1(6)
C(4)-C(3)-C(21)-C(22)	163.5(6)
C(2)-C(3)-C(21)-C(22)	-78.3(7)
C(3)-C(21)-C(22)-O(2)	-34.9(10)
C(3)-C(21)-C(22)-C(23)	142.7(6)
O(2)-C(22)-C(23)-C(24)	19.4(10)
C(21)-C(22)-C(23)-C(24)	-158.3(6)
O(2)-C(22)-C(23)-C(28)	-162.8(7)
C(21)-C(22)-C(23)-C(28)	19.6(10)
C(28)-C(23)-C(24)-C(25)	-1.3(10)
C(22)-C(23)-C(24)-C(25)	176.7(6)
C(23)-C(24)-C(25)-C(26)	0.2(10)
C(24)-C(25)-C(26)-C(27)	2.3(10)

C(24)-C(25)-C(26)-Br(2)	-179.7(5)
C(25)-C(26)-C(27)-C(28)	-3.8(11)
Br(2)-C(26)-C(27)-C(28)	178.2(5)
C(26)-C(27)-C(28)-C(23)	2.7(10)
C(24)-C(23)-C(28)-C(27)	-0.2(10)
C(22)-C(23)-C(28)-C(27)	-178.1(6)
C(10')-N(1')-C(1')-C(5')	172.1(6)
C(13')-N(1')-C(1')-C(5')	-61.8(8)
C(10')-N(1')-C(1')-C(2')	-67.8(8)
C(13')-N(1')-C(1')-C(2')	58.3(9)
N(1')-C(1')-C(2')-C(14')	80.7(7)
C(5')-C(1')-C(2')-C(14')	-152.9(5)
N(1')-C(1')-C(2')-C(3')	-157.0(5)
C(5')-C(1')-C(2')-C(3')	-30.7(6)
C(14')-C(2')-C(3')-C(4')	157.6(5)
C(1')-C(2')-C(3')-C(4')	32.9(6)
C(14')-C(2')-C(3')-C(21')	-77.2(6)
C(1')-C(2')-C(3')-C(21')	158.2(5)
C(21')-C(3')-C(4')-C(5')	-148.8(6)
C(2')-C(3')-C(4')-C(5')	-23.2(6)
C(21')-C(3')-C(4')-C(9')	34.7(10)
C(2')-C(3')-C(4')-C(9')	160.3(7)
C(9')-C(4')-C(5')-C(6')	-1.0(10)
C(3')-C(4')-C(5')-C(6')	-178.0(6)
C(9')-C(4')-C(5')-C(1')	-178.7(6)
C(3')-C(4')-C(5')-C(1')	4.3(7)
N(1')-C(1')-C(5')-C(6')	-31.3(9)
C(2')-C(1')-C(5')-C(6')	-160.9(7)
N(1')-C(1')-C(5')-C(4')	146.2(6)
C(2')-C(1')-C(5')-C(4')	16.6(7)
C(4')-C(5')-C(6')-C(7')	0.4(10)
C(1')-C(5')-C(6')-C(7')	177.7(6)
C(5')-C(6')-C(7')-C(8')	-0.1(11)
C(6')-C(7')-C(8')-C(9')	0.4(11)
C(7')-C(8')-C(9')-C(4')	-1.1(11)
C(5')-C(4')-C(9')-C(8')	1.3(10)

C(3')-C(4')-C(9')-C(8')	177.6(7)
C(1')-N(1')-C(10')-C(11')	172.1(6)
C(13')-N(1')-C(10')-C(11')	39.7(8)
N(1')-C(10')-C(11')-C(12')	-25.7(9)
C(10')-C(11')-C(12')-C(13')	2.7(10)
C(11')-C(12')-C(13')-N(1')	21.0(10)
C(1')-N(1')-C(13')-C(12')	-169.6(7)
C(10')-N(1')-C(13')-C(12')	-37.9(9)
C(1')-C(2')-C(14')-O(1')	44.2(9)
C(3')-C(2')-C(14')-O(1')	-75.1(8)
C(1')-C(2')-C(14')-C(15')	-140.8(6)
C(3')-C(2')-C(14')-C(15')	99.9(7)
O(1')-C(14')-C(15')-C(20')	-177.2(7)
C(2')-C(14')-C(15')-C(20')	7.9(10)
O(1')-C(14')-C(15')-C(16')	5.8(10)
C(2')-C(14')-C(15')-C(16')	-169.1(6)
C(20')-C(15')-C(16')-C(17')	-1.3(11)
C(14')-C(15')-C(16')-C(17')	175.9(7)
C(15')-C(16')-C(17')-C(18')	0.2(13)
C(16')-C(17')-C(18')-C(19')	1.7(13)
C(16')-C(17')-C(18')-Br(1')	-178.0(6)
C(17')-C(18')-C(19')-C(20')	-2.3(13)
Br(1')-C(18')-C(19')-C(20')	177.4(6)
C(18')-C(19')-C(20')-C(15')	1.1(13)
C(16')-C(15')-C(20')-C(19')	0.7(11)
C(14')-C(15')-C(20')-C(19')	-176.3(7)
C(4')-C(3')-C(21')-C(22')	-163.5(5)
C(2')-C(3')-C(21')-C(22')	79.0(7)
C(3')-C(21')-C(22')-O(2')	30.7(9)
C(3')-C(21')-C(22')-C(23')	-148.1(6)
O(2')-C(22')-C(23')-C(24')	-20.3(10)
C(21')-C(22')-C(23')-C(24')	158.5(7)
O(2')-C(22')-C(23')-C(28')	161.7(7)
C(21')-C(22')-C(23')-C(28')	-19.4(10)
C(28')-C(23')-C(24')-C(25')	-1.3(12)
C(22')-C(23')-C(24')-C(25')	-179.3(7)

C(23')-C(24')-C(25')-C(26')	0.5(12)
C(24')-C(25')-C(26')-C(27')	-0.7(12)
C(24')-C(25')-C(26')-Br(2')	-179.4(6)
C(25')-C(26')-C(27')-C(28')	1.8(12)
Br(2')-C(26')-C(27')-C(28')	-179.5(6)
C(26')-C(27')-C(28')-C(23')	-2.6(11)
C(24')-C(23')-C(28')-C(27')	2.3(11)
C(22')-C(23')-C(28')-C(27')	-179.7(7)

APPENDIX C

SUPPORTING INFORMATION FOR CHAPTER IV

C.1. Experimental Details

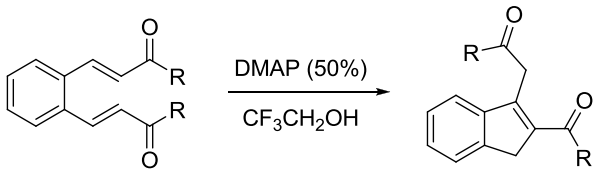
C.1.1. General Methods. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using either a Varian Inova 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) or 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz) or Agilent VNMRS 600 (^{1}H: 600 MHz, ^{13}C: 151 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm relative to the residual chloroform (^{1}H: 7.26 ppm, ^{13}C: 77.160 ppm) reference. Coupling constants are given in Hertz (Hz). Melting points were recorded on a Melt-Temp II melting point apparatus in open-end capillary tubes. IR spectra were recorded using a Nicolet Magna FTIR 550 spectrometer. High resolution mass spectra were recorded on a Waters Micromass MALDI Q-ToF or JEOL MS Route Magnetic Sector mass mpectrometer.

Diffraction intensities for **3a** was collected at 173(2) K on a Bruker Apex CCD diffractometer using MoKα radiation λ= 0.71073 Å. Space groups were determined based on systematic absences. Absorption corrections were applied by SADABS[G. M. Sheldrick, *Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, 1998.]. Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms in **3a** were found on residual density maps and refined with isotropic thermal parameters except those in a disordered Ph ring in **3a** which were refined in calculated positions. All H atoms in **3a** were refined in calculated positions in a rigid group model. Terminal Ph group in **3a** is disordered in

ratio 1:1 over two positions up and down from the average plane. All calculations were performed by the Bruker SHELXTL (v. 6.10) package [SHELXTL-6.10 "Program for Structure Solution, Refinement and Presentation" BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA].

C.1.2. Starting Materials. All reagents and solvents were purchased from Aldrich or TCI. Unless otherwise stated, all reagents were used as received. The preparation of bis(enones) **1a-g** is described in chapter II.

C.1.3. Amine-Catalyzed Intramolecular Rauhut-Currier Reaction.



1a: R=Ph
1b: R=4-Br-C_6H_4
1c: R=4-Me-C_6H_4
1d: R=Me
1e: R=Et
1f: R=H
1g: R=OEt

3a: R=Ph
3b: R=4-Br-C_6H_4
3c: R=4-Me-C_6H_4
3d: R=Me
3e: R=Et
3f: R=H
3g: R=OEt

To a stirred 0.03 M solution of **1a-g** (0.15 mmol) in 5 mL of CF_3CH_2OH, 0.090 g of DMAP (0.075 mmol, 50%) was added. The solution was stirred at ambient or elevated temperatures and held there for the specified time. When thin layer chromatography showed complete conversion of starting material, the reaction was then quenched by pouring it over a mixture of 10 mL of Et_2O and 10 mL of 10% HCl. The aqueous fraction was extracted twice more with ether, and the combined organic layers were then washed with 30 mL portions of 10% HCl, water (twice), and finally a saturated NaCl solution. The organic fraction was dried over sodium sulfate and the solvent removed by rotary evaporation. The

resulting residue was purified by silica column chromatography, to yield the 2,3-disubstituted indenes **3a-e** or compound **4**.

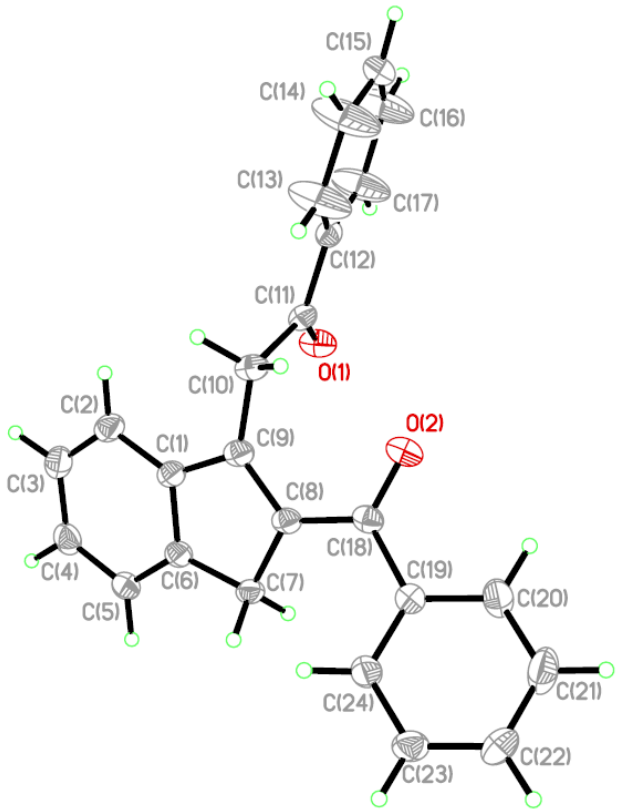
The characterization data for indenes **3a-e** and **4** matches that reported in chapter II.

C.2. Crystal Structures

C.2.1. Table 1. Crystal data and structure refinement for 2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (3a).

Empirical formula	C24 H18 O2	
Formula weight	338.38	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 18.113(2) Å	a= 90°
	b = 4.8074(6) Å	b= 105.403(2)°
	c = 20.617(2) Å	g = 90°
Volume	1730.7(4) $Å^3$	
Z	4	
Density (calculated)	1.299 Mg/m^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	712	
Crystal size	0.34 x 0.21 x 0.18 mm^3	
Theta range for data collection	1.17 to 25.00°.	
Index ranges	-21<=h<=21, -5<=k<=5, -24<=l<=24	
Reflections collected	15683	
Independent reflections	3051 [R(int) = 0.0224]	
Completeness to theta = 25.00°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9855 and 0.9728	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3051 / 0 / 307	
Goodness-of-fit on F^2	1.007	
Final R indices [I>2sigma(I)]	R1 = 0.0514, wR2 = 0.1355	
R indices (all data)	R1 = 0.0579, wR2 = 0.1435	
Largest diff. peak and hole	0.303 and -0.310 $e.Å^{-3}$	

C.2.2. Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (3a). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.



	x	y	z	U(eq)
O(1)	2669(1)	7113(3)	3620(1)	48(1)
O(2)	3199(1)	6246(3)	5327(1)	48(1)
C(1)	1206(1)	10093(4)	4097(1)	38(1)
C(2)	978(2)	11937(5)	3557(1)	45(1)
C(3)	207(2)	12100(5)	3226(1)	50(1)
C(4)	-327(2)	10460(5)	3423(1)	49(1)
C(5)	-104(1)	8661(5)	3969(1)	43(1)
C(6)	666(1)	8491(4)	4305(1)	37(1)
C(7)	1070(1)	6779(4)	4904(1)	37(1)
C(8)	1905(1)	7505(4)	4990(1)	35(1)

C(9)	1966(1)	9421(4)	4521(1)	37(1)
C(10)	2679(1)	10694(5)	4421(1)	42(1)
C(11)	3020(1)	9038(4)	3945(1)	35(1)
C(12)	3782(1)	9914(4)	3871(1)	35(1)
C(13)	4224(2)	11872(9)	4264(2)	94(1)
C(14)	4924(2)	12620(10)	4169(2)	112(2)
C(15)	5186(1)	11475(5)	3680(1)	51(1)
C(16)	4751(2)	9595(9)	3281(2)	92(1)
C(17)	4053(2)	8803(8)	3376(2)	90(1)
C(18)	2577(1)	6209(4)	5460(1)	36(1)
C(19)	2521(1)	4789(4)	6090(1)	35(1)
C(20)	3056(2)	2775(6)	6356(1)	54(1)
C(21)	3055(2)	1500(7)	6953(1)	75(1)
C(22)	2532(2)	2247(6)	7303(1)	55(1)
C(23)	2008(1)	4263(6)	7048(1)	51(1)
C(24)	2000(1)	5541(6)	6443(1)	49(1)

C.2.3. Table 3. Bond lengths [Å] and angles [°] for 2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (3a).

O(1)-C(11)	1.218(2)
O(2)-C(18)	1.229(2)
C(1)-C(2)	1.396(3)
C(1)-C(6)	1.399(3)
C(1)-C(9)	1.457(3)
C(2)-C(3)	1.384(4)
C(2)-H(2)	0.96(3)
C(3)-C(4)	1.389(4)
C(3)-H(3)	1.00(3)
C(4)-C(5)	1.392(3)
C(4)-H(4)	1.01(2)
C(5)-C(6)	1.386(3)
C(5)-H(5)	0.99(3)
C(6)-C(7)	1.503(3)
C(7)-C(8)	1.516(3)
C(7)-H(7A)	0.99(2)
C(7)-H(7B)	0.99(2)
C(8)-C(9)	1.361(3)
C(8)-C(18)	1.477(3)
C(9)-C(10)	1.492(3)
C(10)-C(11)	1.516(3)
C(10)-H(10A)	1.01(3)
C(10)-H(10B)	0.99(2)
C(11)-C(12)	1.489(3)
C(12)-C(17)	1.355(3)
C(12)-C(13)	1.356(4)
C(13)-C(14)	1.380(4)
C(13)-H(13)	0.87(5)
C(14)-C(15)	1.341(4)
C(14)-H(14)	0.87(5)
C(15)-C(16)	1.330(4)
C(15)-H(15)	0.94(3)
C(16)-C(17)	1.383(4)

C(16)-H(16)	0.93(4)
C(17)-H(17)	0.87(5)
C(18)-C(19)	1.494(3)
C(19)-C(20)	1.377(3)
C(19)-C(24)	1.383(3)
C(20)-C(21)	1.376(4)
C(20)-H(20)	1.02(3)
C(21)-C(22)	1.383(4)
C(21)-H(21)	0.96(4)
C(22)-C(23)	1.360(4)
C(22)-H(22)	0.96(3)
C(23)-C(24)	1.387(3)
C(23)-H(23)	0.96(3)
C(24)-H(24)	0.97(3)

C(2)-C(1)-C(6)	120.7(2)
C(2)-C(1)-C(9)	130.6(2)
C(6)-C(1)-C(9)	108.64(18)
C(3)-C(2)-C(1)	118.4(2)
C(3)-C(2)-H(2)	122.7(15)
C(1)-C(2)-H(2)	118.9(15)
C(2)-C(3)-C(4)	120.9(2)
C(2)-C(3)-H(3)	121.0(14)
C(4)-C(3)-H(3)	118.1(14)
C(3)-C(4)-C(5)	120.9(2)
C(3)-C(4)-H(4)	119.6(14)
C(5)-C(4)-H(4)	119.5(14)
C(6)-C(5)-C(4)	118.6(2)
C(6)-C(5)-H(5)	121.6(14)
C(4)-C(5)-H(5)	119.7(14)
C(5)-C(6)-C(1)	120.4(2)
C(5)-C(6)-C(7)	130.52(19)
C(1)-C(6)-C(7)	109.04(18)
C(6)-C(7)-C(8)	102.87(16)
C(6)-C(7)-H(7A)	112.4(12)
C(8)-C(7)-H(7A)	112.6(12)

C(6)-C(7)-H(7B)	110.1(13)
C(8)-C(7)-H(7B)	114.0(13)
H(7A)-C(7)-H(7B)	105.0(18)
C(9)-C(8)-C(18)	123.00(18)
C(9)-C(8)-C(7)	109.83(18)
C(18)-C(8)-C(7)	126.96(17)
C(8)-C(9)-C(1)	109.56(18)
C(8)-C(9)-C(10)	127.7(2)
C(1)-C(9)-C(10)	122.73(19)
C(9)-C(10)-C(11)	112.97(17)
C(9)-C(10)-H(10A)	111.7(15)
C(11)-C(10)-H(10A)	106.8(14)
C(9)-C(10)-H(10B)	112.1(14)
C(11)-C(10)-H(10B)	107.1(14)
H(10A)-C(10)-H(10B)	106(2)
O(1)-C(11)-C(12)	121.36(18)
O(1)-C(11)-C(10)	120.85(18)
C(12)-C(11)-C(10)	117.76(17)
C(17)-C(12)-C(13)	116.6(2)
C(17)-C(12)-C(11)	119.9(2)
C(13)-C(12)-C(11)	123.5(2)
C(12)-C(13)-C(14)	121.1(3)
C(12)-C(13)-H(13)	120(3)
C(14)-C(13)-H(13)	119(3)
C(15)-C(14)-C(13)	121.3(3)
C(15)-C(14)-H(14)	118(3)
C(13)-C(14)-H(14)	119(3)
C(16)-C(15)-C(14)	118.4(3)
C(16)-C(15)-H(15)	122.6(16)
C(14)-C(15)-H(15)	119.0(16)
C(15)-C(16)-C(17)	120.8(3)
C(15)-C(16)-H(16)	119(3)
C(17)-C(16)-H(16)	120(3)
C(12)-C(17)-C(16)	121.8(3)
C(12)-C(17)-H(17)	116(3)
C(16)-C(17)-H(17)	122(3)

O(2)-C(18)-C(8)	119.41(18)
O(2)-C(18)-C(19)	118.59(19)
C(8)-C(18)-C(19)	121.99(17)
C(20)-C(19)-C(24)	118.8(2)
C(20)-C(19)-C(18)	117.66(19)
C(24)-C(19)-C(18)	123.40(19)
C(21)-C(20)-C(19)	120.1(2)
C(21)-C(20)-H(20)	120.6(18)
C(19)-C(20)-H(20)	119.2(18)
C(20)-C(21)-C(22)	121.0(3)
C(20)-C(21)-H(21)	119(2)
C(22)-C(21)-H(21)	120(2)
C(23)-C(22)-C(21)	119.1(2)
C(23)-C(22)-H(22)	121.3(18)
C(21)-C(22)-H(22)	119.4(18)
C(22)-C(23)-C(24)	120.2(2)
C(22)-C(23)-H(23)	119.1(16)
C(24)-C(23)-H(23)	120.6(16)
C(19)-C(24)-C(23)	120.8(2)
C(19)-C(24)-H(24)	119.2(17)
C(23)-C(24)-H(24)	119.8(17)

C.2.4. Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (3a). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	53(1)	49(1)	47(1)	-16(1)	23(1)	-15(1)
O(2)	40(1)	59(1)	50(1)	-8(1)	21(1)	-5(1)
C(1)	52(1)	31(1)	35(1)	-3(1)	22(1)	1(1)
C(2)	67(2)	37(1)	40(1)	1(1)	27(1)	2(1)
C(3)	71(2)	47(1)	37(1)	5(1)	21(1)	16(1)
C(4)	56(1)	54(1)	42(1)	-1(1)	19(1)	16(1)
C(5)	47(1)	45(1)	42(1)	-1(1)	20(1)	6(1)
C(6)	47(1)	34(1)	36(1)	-3(1)	20(1)	3(1)
C(7)	43(1)	35(1)	37(1)	1(1)	20(1)	-1(1)
C(8)	43(1)	32(1)	34(1)	-6(1)	19(1)	-2(1)
C(9)	50(1)	32(1)	36(1)	-7(1)	22(1)	-3(1)
C(10)	53(1)	36(1)	43(1)	-6(1)	24(1)	-10(1)
C(11)	43(1)	32(1)	30(1)	2(1)	12(1)	-2(1)
C(12)	38(1)	34(1)	34(1)	5(1)	10(1)	2(1)
C(13)	70(2)	128(3)	103(2)	-76(2)	54(2)	-51(2)
C(14)	72(2)	146(4)	137(3)	-90(3)	64(2)	-62(2)
C(15)	35(1)	55(2)	66(2)	7(1)	18(1)	2(1)
C(16)	71(2)	125(3)	100(2)	-59(2)	58(2)	-39(2)
C(17)	74(2)	119(3)	98(2)	-70(2)	57(2)	-50(2)
C(18)	39(1)	35(1)	39(1)	-10(1)	16(1)	-4(1)
C(19)	35(1)	35(1)	35(1)	-6(1)	7(1)	-3(1)
C(20)	56(1)	62(2)	43(1)	1(1)	11(1)	19(1)
C(21)	98(2)	74(2)	50(2)	16(1)	15(2)	42(2)
C(22)	71(2)	53(1)	38(1)	8(1)	8(1)	-3(1)
C(23)	47(1)	70(2)	37(1)	7(1)	14(1)	2(1)
C(24)	49(1)	61(2)	41(1)	10(1)	17(1)	14(1)

C.2.5. Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (3a).

	x	y	z	U(eq)
H(2)	1358(14)	13040(60)	3432(12)	56(7)
H(3)	19(13)	13400(50)	2840(12)	54(7)
H(4)	-886(14)	10590(50)	3170(12)	53(7)
H(5)	-490(14)	7490(50)	4096(12)	52(7)
H(7A)	967(12)	4760(50)	4832(10)	37(5)
H(7B)	878(12)	7260(50)	5299(11)	41(6)
H(10A)	2584(14)	12640(60)	4230(13)	58(7)
H(10B)	3082(13)	10880(50)	4848(12)	47(6)
H(13)	4080(30)	12630(110)	4590(20)	146(17)
H(14)	5140(30)	14170(110)	4350(30)	154(18)
H(15)	5660(15)	12080(50)	3622(12)	55(7)
H(16)	4910(20)	8900(90)	2920(20)	127(14)
H(17)	3790(30)	7440(110)	3150(30)	151(18)
H(20)	3439(18)	2200(70)	6097(15)	83(9)
H(21)	3434(19)	100(80)	7136(17)	98(11)
H(22)	2529(16)	1280(60)	7709(15)	76(9)
H(23)	1657(15)	4820(60)	7298(13)	64(8)
H(24)	1658(16)	7090(60)	6284(14)	72(8)

C.2.6. Table 6. Torsion angles [°] for 2-(2-benzoyl-1H-inden-3-yl)-1-phenylethanone (3a).

C(6)-C(1)-C(2)-C(3)	-1.3(3)
C(9)-C(1)-C(2)-C(3)	178.0(2)
C(1)-C(2)-C(3)-C(4)	-0.3(3)
C(2)-C(3)-C(4)-C(5)	1.7(3)
C(3)-C(4)-C(5)-C(6)	-1.4(3)
C(4)-C(5)-C(6)-C(1)	-0.2(3)
C(4)-C(5)-C(6)-C(7)	179.6(2)
C(2)-C(1)-C(6)-C(5)	1.6(3)
C(9)-C(1)-C(6)-C(5)	-177.82(18)
C(2)-C(1)-C(6)-C(7)	-178.28(18)
C(9)-C(1)-C(6)-C(7)	2.3(2)
C(5)-C(6)-C(7)-C(8)	177.7(2)
C(1)-C(6)-C(7)-C(8)	-2.4(2)
C(6)-C(7)-C(8)-C(9)	1.7(2)
C(6)-C(7)-C(8)-C(18)	-173.07(18)
C(18)-C(8)-C(9)-C(1)	174.63(17)
C(7)-C(8)-C(9)-C(1)	-0.4(2)
C(18)-C(8)-C(9)-C(10)	-4.6(3)
C(7)-C(8)-C(9)-C(10)	-179.56(19)
C(2)-C(1)-C(9)-C(8)	179.5(2)
C(6)-C(1)-C(9)-C(8)	-1.2(2)
C(2)-C(1)-C(9)-C(10)	-1.3(3)
C(6)-C(1)-C(9)-C(10)	178.01(18)
C(8)-C(9)-C(10)-C(11)	89.1(3)
C(1)-C(9)-C(10)-C(11)	-90.0(2)
C(9)-C(10)-C(11)-O(1)	9.5(3)
C(9)-C(10)-C(11)-C(12)	-172.75(18)
O(1)-C(11)-C(12)-C(17)	8.4(4)
C(10)-C(11)-C(12)-C(17)	-169.3(3)
O(1)-C(11)-C(12)-C(13)	-173.8(3)
C(10)-C(11)-C(12)-C(13)	8.4(4)
C(17)-C(12)-C(13)-C(14)	-1.7(6)
C(11)-C(12)-C(13)-C(14)	-179.5(4)

C(12)-C(13)-C(14)-C(15)	1.1(8)
C(13)-C(14)-C(15)-C(16)	0.4(7)
C(14)-C(15)-C(16)-C(17)	-1.2(6)
C(13)-C(12)-C(17)-C(16)	0.8(6)
C(11)-C(12)-C(17)-C(16)	178.8(3)
C(15)-C(16)-C(17)-C(12)	0.6(7)
C(9)-C(8)-C(18)-O(2)	-19.7(3)
C(7)-C(8)-C(18)-O(2)	154.4(2)
C(9)-C(8)-C(18)-C(19)	161.63(18)
C(7)-C(8)-C(18)-C(19)	-24.3(3)
O(2)-C(18)-C(19)-C(20)	-23.4(3)
C(8)-C(18)-C(19)-C(20)	155.2(2)
O(2)-C(18)-C(19)-C(24)	151.5(2)
C(8)-C(18)-C(19)-C(24)	-29.8(3)
C(24)-C(19)-C(20)-C(21)	1.6(4)
C(18)-C(19)-C(20)-C(21)	176.8(3)
C(19)-C(20)-C(21)-C(22)	-1.4(5)
C(20)-C(21)-C(22)-C(23)	0.5(5)
C(21)-C(22)-C(23)-C(24)	0.2(4)
C(20)-C(19)-C(24)-C(23)	-1.0(4)
C(18)-C(19)-C(24)-C(23)	-175.9(2)
C(22)-C(23)-C(24)-C(19)	0.1(4)

APPENDIX D

SUPPORTING INFORMATION FOR CHAPTER V

D.1. Experimental Details

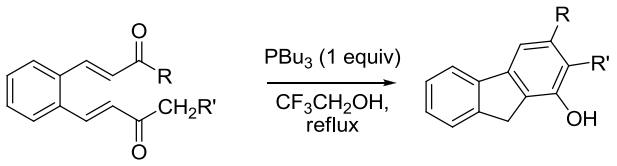
D.1.1. General Methods. Reactions were carried out under an Ar atmosphere using standard Schlenk techniques and, when necessary, glassware was flame-dried (under vacuum) before use. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using either a Varian Inova 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) or 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz) or Agilent VNMRS 600 (^{1}H: 600 MHz, ^{13}C: 151 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm relative to residual chloroform (^{1}H: 7.26 ppm, ^{13}C: 77.160 ppm). Coupling constants are given in Hertz (Hz). Melting points were recorded on a Melt-Temp II melting point apparatus in open-end capillary tubes. IR spectra were recorded using a Nicolet Magna FTIR 550 spectrometer. High resolution mass spectra were recorded on a Waters Micromass MALDI Q-ToF or JEOL MS Route Magnetic Sector mass spectrometer.

D.1.2. Starting Materials. All reagents and solvents were purchased from Aldrich or TCI. Unless otherwise stated, all reagents were as received. The preparation of bis(enones) **1a** and **1b** and indene **2a** is described in chapter II.

(E)-4,4-dimethyl-1-(2-((E)-3-oxobut-1-enyl)phenyl)pent-1-en-3-one (**1c**). To a solution of phthalaldehyde (1.690 g, 13.6 mmol) in dry THF (50 mL) was added (triphenylphosphoranylidene)pinacolone (4.595 g, 12.7 mmol) in 10 mL of dichloromethane. After 24 hours of stirring, (triphenylphosphoranylidene)acetone was

added (7.270 g, 19.06 mmol). After an additional 48 hours, the solvent was removed on a rotary evaporator. The resulting residue was purified by passing through a 10 cm diameter plug of 100 grams of silica, eluting with 33% EtOAc in hexanes (Rf = 0.23), affording **1c** (0.74 g, 23%) as a white solid, mp 76-80 °C. IR (NaCl, neat): 2967, 2868, 1682, 1607, 1593, 1476, 1359, 1322, 1254, 1075, 1007, 975 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.01 (d, *J* = 15.4 Hz, 1H), 7.88 (d, *J* = 16.1 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.44 – 7.38 (m, 2H), 7.00 (d, *J* = 15.4 Hz, 1H), 6.62 (d, *J* = 16.1 Hz, 1H), 2.41 (s, 3H), 1.24 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 203.84, 198.18, 140.42, 139.66, 135.37, 134.75, 130.55, 130.26, 130.12, 128.18, 127.84, 125.03, 43.45, 27.68, 26.36; HRMS (CI): Exact mass calcd for $C_{17}H_{21}O_2$ $[M+H]^+$: 257.1542, found: 257.1546

D.1.3. Synthesis of Hydroxyfluorenes.



1a: R=CH_3, R'=H
1b: R=CH_2CH_3, R'=CH_3
1c: R=*t*-Bu, R'=H

3a: R=CH_3,R'=H
3b: R=CH_2CH_3, R'=CH_3
3c: R=*t*-Bu, R'=H

To a stirred 0.05 M solution of **1a-c** (0.14 mmol) in 3 mL of CF_3CH_2OH under argon, 0.14 mL of a PBu_3 solution (1.0 M in toluene, 0.14 mmol, 1 equiv.) was added. The solution was heated to reflux and held there for the specified time. When thin layer chromatography showed complete conversion of starting material, the reaction was then quenched by pouring it over a mixture of 10 mL of Et_2O and 10 mL of a 10% HCl solution. The aqueous fraction was extracted twice more with ether, and the combined organic layers were then washed with

30 mL portions of 10% HCl, water (twice), and finally a saturated NaCl solution. The organic fraction was dried over sodium sulfate and the solvent removed by rotary evaporation. The resulting residue was purified by silica column chromatography, to yield hydroxy-fluorenes **3a-c**.

1-hydroxy-3-methyl-9*H*-fluorene (3a). Following the general procedure, 0.03 g of **1a** (0.14 mmol) and 0.14 mL of a 1.0 M solution of PBu_3 (0.14 mmol, 1 equivalent) in 3 mL of 3,3,3-trifluoroethanol were brought to reflux under an argon atmosphere. After stirring for 15 hours, the reaction was worked up as described in the general procedure, producing 0.0274 g of a white solid (94% yield), mp=120-123 °C. Rf = 0.4 (33% EtOAc/Hexanes); IR (NaCl, neat): 3384, 3028, 2920, 1627, 1582, 1450, 1421, 1274, 1223, 1081, 765, 728 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.30 (td, *J* = 7.4, 1.0 Hz, 1H), 7.24 (s, 1H), 6.60 (s, 1H), 4.68 (s, 1H), 3.80 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.97, 144.06, 143.37, 141.84, 138.93, 126.93, 126.85, 125.48, 125.27, 120.24, 114.61, 113.80, 33.40, 21.65; HRMS (CI): Exact mass calcd for $C_{14}H_{13}O$ $[M+H]^+$: 197.0966, found: 197.0957.

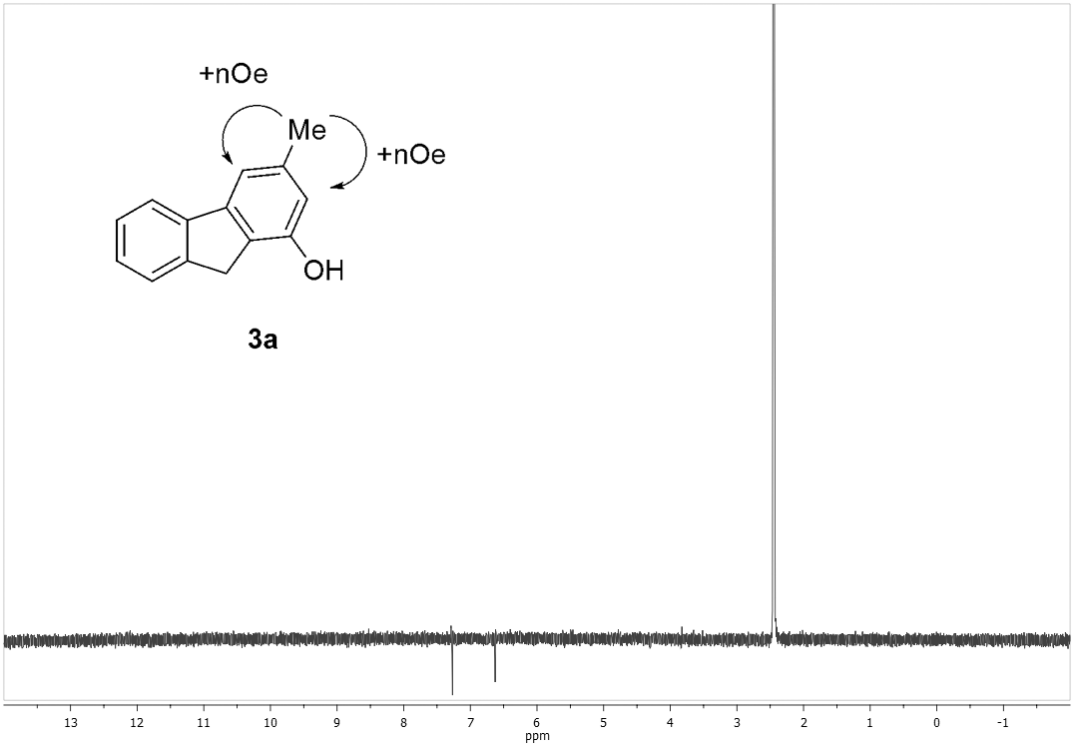
1-hydroxy-3-ethyl-2-methyl-9*H*-fluorene (3b). Following the general procedure, 0.05 g of **1b** (0.21 mmol) and 0.21 mL of a 1.0 M solution of PBu_3 (0.21 mmol, 1 equivalent) in 3 mL of 3,3,3-trifluoroethanol were brought to reflux under an argon atmosphere. After stirring for 15 hours, the reaction was worked up as described in the general procedure, producing 0.041 g of a pink solid, mp = 118-122 °C (89% yield). Rf = 0.6 (50% Et_2O/Hexanes); IR (NaCl, neat): 3395, 2963, 2931, 1574, 1455, 1429,

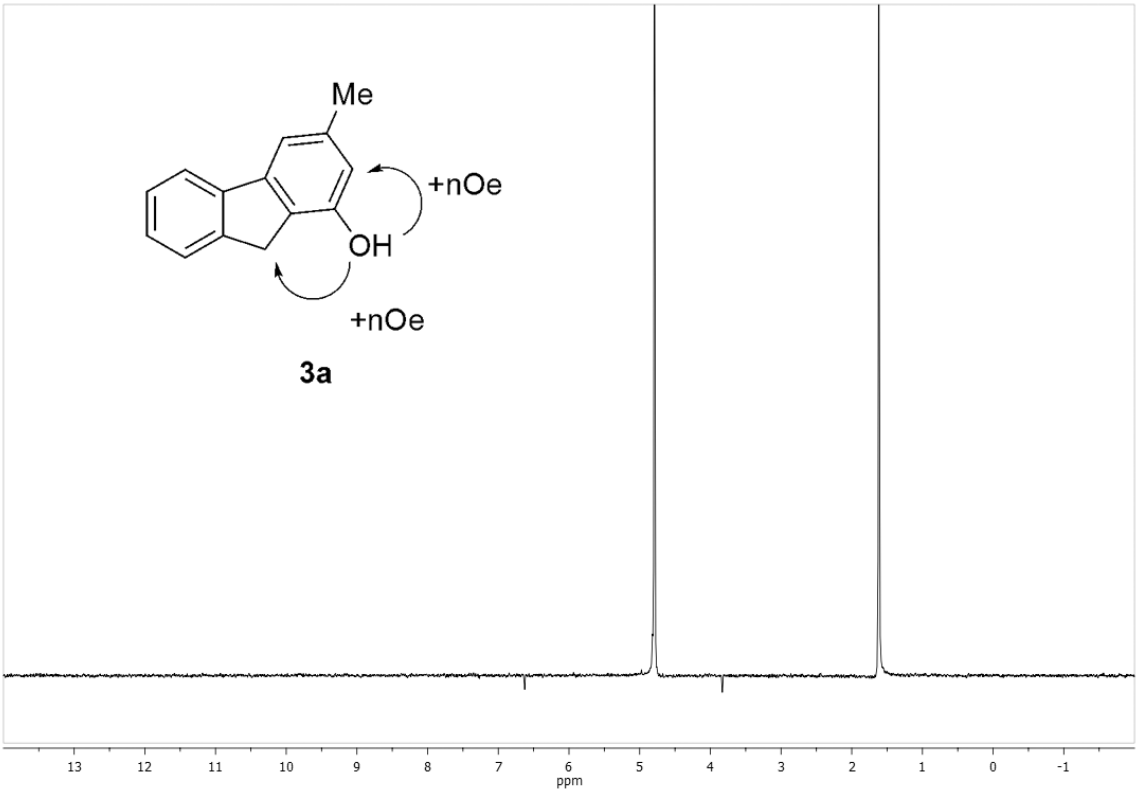
1263, 1222, 1093, 1039, 765, 734 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 8.2 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.27 (dt, *J* = 12.8, 3.3 Hz, 2H), 4.91 (s, 1H), 3.77 (s, 2H), 2.73 (q, *J* = 7.56 Hz, 2H), 2.28 (s, 3H), 1.27 (t, *J* = 7.57 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.51, 143.37, 142.85, 142.21, 140.72, 126.81, 126.42, 125.67, 125.15, 120.30, 119.89, 112.69, 33.57, 27.33, 15.20, 11.25; HRMS (MALDI): Exact mass calcd for $C_{16}H_{17}O$ $[M+H]^+$: 225.1279, found: 225.1270.

3-*tert*-butyl-1-hydroxy-9*H*-fluorene (3c). Following the general procedure, 0.040 g of **1c** (0.16 mmol) and 0.16 mL of a 1.0 M solution of PBu_3 (0.16 mmol, 1 equivalent) in 3 mL of 3,3,3-trifluoroethanol were brought to reflux under an argon atmosphere. After stirring for 48 hours, the reaction was worked up as described in the general procedure and purified by silica column chromatography (eluting with 1:2 Et_2O/Hexanes), producing 0.022 g of a colorless oil (59% yield). Rf = 0.35 (33% Et_2O/Hexanes); IR (NaCl, neat): 3381, 2962, 2905, 1628, 1586, 1479, 1420, 1362, 1276, 1245, 1209, 1080, 959, 765, 728, 700, 646 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.45 (d, *J* = 1.4 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.30 (dt, *J* = 7.4, 3.7 Hz, 1H), 6.82 (d, *J* = 1.5 Hz, 1H), 4.70 (s, 1H), 3.80 (s, 2H), 1.54 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 152.87, 151.82, 143.76, 143.32, 142.06, 126.88, 126.82, 125.51, 125.26, 120.19, 111.35, 109.97, 35.03, 33.34, 31.76; HRMS (MALDI): Exact mass calcd for $C_{17}H_{19}O$ $[M+H]^+$: 239.1436, found: 239.1428.

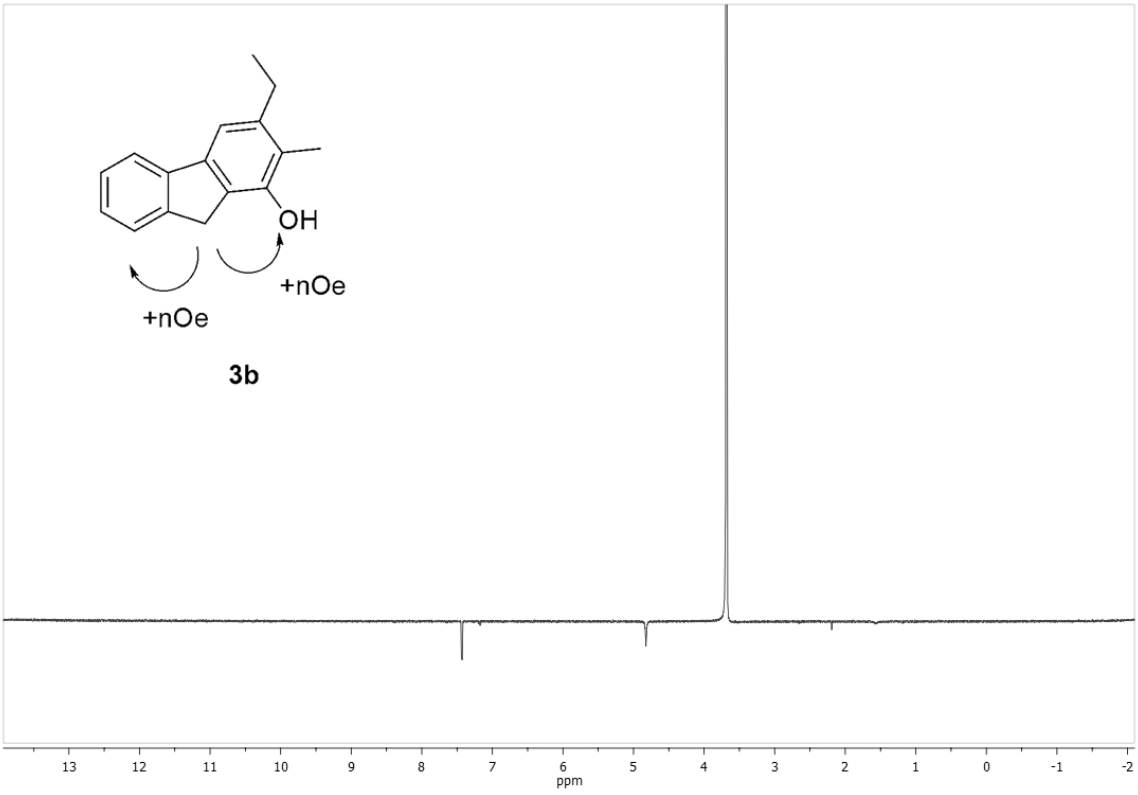
D.2. Nuclear Overhauser Effect Spectroscopy

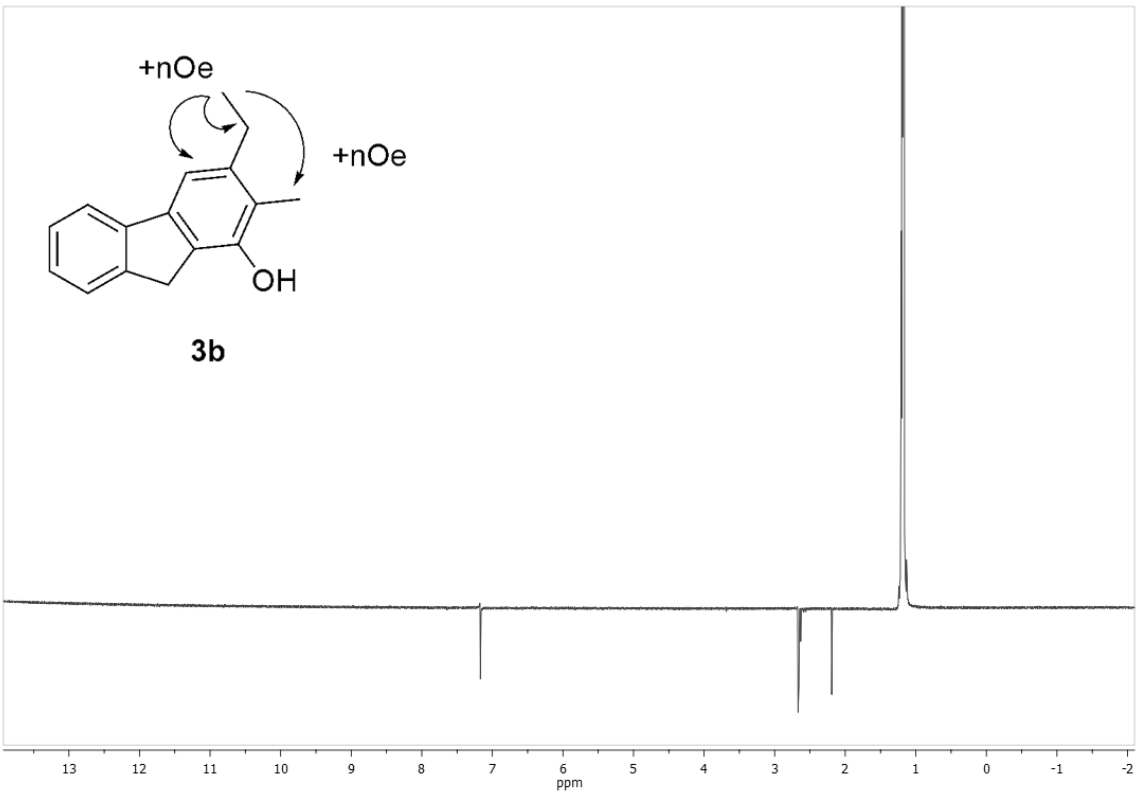
D.2.1. 1-hydroxy-3-methyl-9*H*-fluorene (3a).





D.2.2. 1-hydroxy-3-ethyl-2-methyl-9*H*-fluorene (3b)





APPENDIX E

SUPPORTING INFORMATION FOR CHAPTER VI

E.1. Experimental Details

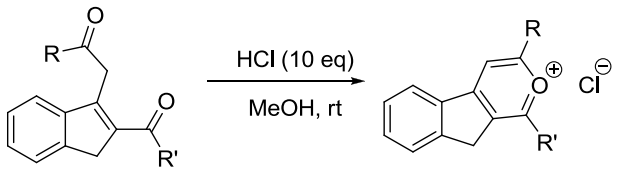
E.1.1. General Methods. ^{1}H and ^{13}C NMR spectra were recorded in CD_3OD using either a Varian Inova 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) or 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz) or Agilent VNMRS 600 (^{1}H: 600 MHz, ^{13}C: 151 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm relative to residual methanol (^{1}H: 3.31 ppm, ^{13}C: 49.00 ppm). Coupling constants are given in Hertz (Hz). Melting points were recorded on a Melt-Temp II melting point apparatus in open-end capillary tubes. IR spectra were recorded using a Nicolet Magna FTIR 550 spectrometer. High resolution mass spectra were recorded on a Waters Micromass MALDI Q-ToF or JEOL MS Route Magnetic Sector mass spectrometer.

Diffraction intensities for **4a** were collected at 173(2) K on a Bruker Apex CCD diffractometer using MoKα radiation λ= 0.71073 Å. Space groups were determined based on systematic absences and intensity statistics. Absorption corrections were applied by SADABS[G. M. Sheldrick, *Bruker/Siemens Area Detector Absorption Correction Program*, Bruker AXS, Madison, WI, 1998.]. Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms in **3a** were found on residual density maps and refined with isotropic thermal parameters. All calculations were performed by the Bruker SHELXTL (v. 6.10) package [SHELXTL-6.10 "Program for Structure Solution, Refinement and Presentation" BRUKER AXS Inc.,

5465 East Cheryl Parkway, Madison, WI 53711-5373 USA].

E.1.2. Starting Materials. All reagents and solvents were purchased from Aldrich or TCI. Unless otherwise stated, all reagents were used as received. The preparation of indenes **2a-d** is described in chapter II and **2e** in chapter V.

E.1.3. Synthesis of Indenopyrylium Salts



2a: R,R'=Me
2b: R,R'=Et
2c: R,R'=*i*-Pr
2d: R,R'=Ph
2e: R=*t*-Bu, R'=Me

4a: R,R'=Me
4b: R,R'=Et
4c: R,R'=*i*-Pr
4d: R,R'=Ph
4e: R=*t*-Bu, R'=Me

To a stirred 0.04 M solution of **2a-e** (0.23 mmol) in methanol, 0.2 mL of concentrated hydrochloric acid (12M, 2.30 mmol, 10 equiv.) was added. The solution was allowed to stir at room temperature for the required time.[xv] When thin layer chromatography showed complete conversion of starting material, the reaction was placed under vacuum to remove the methanol and remaining acid. When further purification was needed, the solid product was suspended in ethyl ether and filtered to yield pure indenopyrylium salts **4a-e**.

1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a). Following the general procedure, 0.19 mL of concentrated hydrochloric acid (12M, 2.23 mmol, 10 equiv.) was added to a solution of 0.05 g of **2a** (0.223 mmol) in 6 mL of

[xv] No attempt to exclude water or oxygen was made.

methanol. After stirring for 24 hours, the solvent was removed *in vacuo* and the solid material was suspended in ethyl ether before vacuum filtration produced **4a** in quantitative yield (0.054g, pale orange solid), mp = 160 °C (decomp). Rf = 0.0 (50% EtOAc/Hexanes); IR (NaCl, neat): 3016, 2881, 1641, 1605, 1552, 1574, 1518, 1475, 1441, 1332, 1240, 1090, 871, 787, 749, 650, 584 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD): δ 8.29 (s, 1H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.71 (dd, *J* = 6.2, 1.0 Hz, 2H), 7.52 (s, 1H), 4.16 (s, 2H), 2.82 (s, 3H), 2.80 (s, 3H); ^{13}C NMR (126 MHz, CD_3OD): δ 178.51, 173.71, 168.78, 151.81, 137.48, 136.79, 135.76, 130.17, 127.61, 127.53, 113.97, 35.72, 21.57, 19.53.; HRMS (CI): Exact mass calcd for $C_{14}H_{13}O$ $[M\text{-}Cl]^+$: 197.0966, found: 197.0970.

1,3-diethyl-9*H*-indeno[2,1-c]pyrylium chloride (4b). Following the general procedure, 0.18 mL of concentrated hydrochloric acid (12M, 2.0 mmol, 10 equiv.) was added to a solution of 0.05 g of **2b** (0.206 mmol) in 7 mL of methanol. After stirring for 24 hours, the solvent was removed *in vacuo* and the solid material was suspended in ethyl ether before vacuum filtration produced **4b** in 95% yield (0.051 g, white solid, mp 115-118 º C (decomp). Rf = 0.0 (50% Et_2O/Hexanes); IR (NaCl, neat): 3390, 2979, 2940, 2881, 1630, 1606, 1546, 1505, 1741, 1383, 1246, 787 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD): δ 8.47 (s, 1H), 8.40 (d, *J* = 7.9 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.71 (dd, *J* = 11.3, 4.8 Hz, 1H), 4.36 (s, 2H), 3.35 (q, *J* = 7.5 Hz, 2H), 3.30 (q, *J* = 7.6 Hz, 2H), 1.54 (t, *J* = 7.6, 3H), 1.53 (t, *J* = 7.6, 3H); ^{13}C NMR (151 MHz, CD_3OD): δ 182.48, 177.02, 169.22, 151.82, 137.55, 136.98, 135.28, 130.21, 127.59, 127.52, 112.74, 35.50, 29.37, 27.55, 11.23, 10.74; HRMS (CI): Exact mass calcd for $C_{16}H_{17}O$ $[M\text{-}Cl]^+$: 225.1279, found: 225.1277.

1,3-diisopropyl-9*H*-indeno[2,1-c]pyrylium chloride (4c). Following the general procedure, 0.09 mL of concentrated hydrochloric acid (12M, 1.04 mmol, 10 equiv.) was added to a solution of 0.030 g of **2c** (0.104 mmol) in 3 mL of methanol. After stirring for 12 hours, the solvent was removed *in vacuo* and the solid material was suspended in ethyl ether before vacuum filtration produced **4c** in 97% yield (0.031 g, white oil). Rf = 0.0 (66% Et_2O/Hexanes); ^{1}H NMR (300 MHz, CD_3OD): δ 8.44 (s, 1H), 8.36 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 5.4 Hz, 2H), 7.71 – 7.58 (m, 1H), 4.33 (s, 2H), 3.64 (sep, *J* = 7.0 Hz, 1H), 3.48 (sep, *J* = 7.1 Hz, 1H), 1.48 (d, *J* = 6.9 Hz, 12H); ^{13}C NMR (126 MHz, CD_3OD): δ 185.33, 179.36, 170.02, 169.95, 151.91, 137.67, 137.13, 134.63, 130.24, 127.61, 127.52, 111.84, 35.92, 35.47, 34.35, 20.58, 20.13; HRMS (CI): Exact mass calcd for $C_{18}H_{21}O$ $[M-Cl]^+$: 253.1592, found: 253.1601.

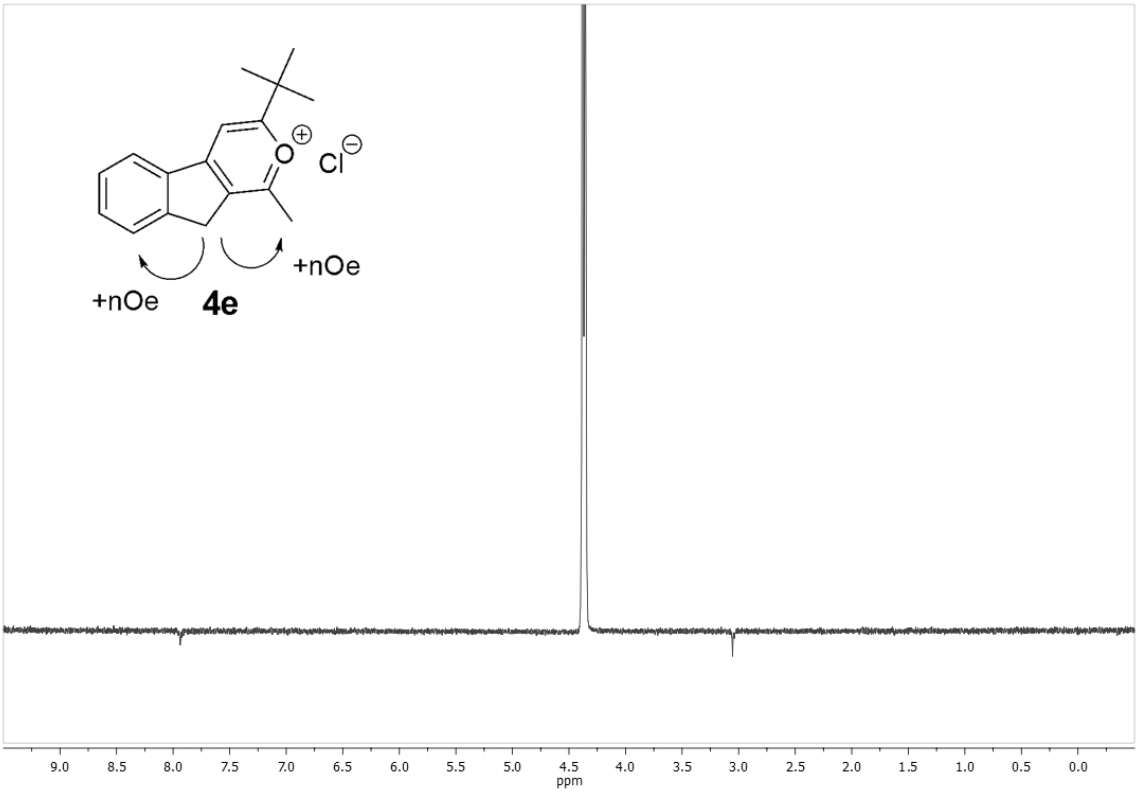
1,3-diphenyl-9*H*-indeno[2,1-c]pyrylium chloride (4d). Following the general procedure, 0.12 mL of concentrated hydrochloric acid (12M, 1.50 mmol, 10 equiv.) was added to a solution of 0.05 g of **2d** (0.150 mmol) in 4 mL of methanol. After stirring for 47 hours, the solvent was removed *in vacuo* and the solid material was suspended in ethyl ether before vacuum filtration produced **4d** in 81% yield (0.043 g, bright yellow solid), mp 212-220º C (decomp). Rf = 0.0 (50% Et_2O/Hexanes); IR (NaCl, neat): 3005, 2859, 1619, 1574, 1533, 1512, 1470, 1438, 1400, 1351, 1265, 1190, 1099, 1037, 995, 863, 779, 744, 708, 687, 624 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD): δ 9.27 (s, 1H), 8.57 (d, *J* = 7.8 Hz, 1H), 8.52 – 8.48 (m, 2H), 8.41 (dd, *J* = 8.1, 1.4 Hz, 2H), 7.99 – 7.91 (m, 2H), 7.89 – 7.71 (m, 7H), 4.76 (s, 2H); ^{13}C NMR (151 MHz, CD_3OD): δ 172.18, 170.18, 170.11, 166.70, 152.06, 152.01, 137.60, 137.19, 136.02, 135.35, 134.57, 131.23, 131.15, 130.88,

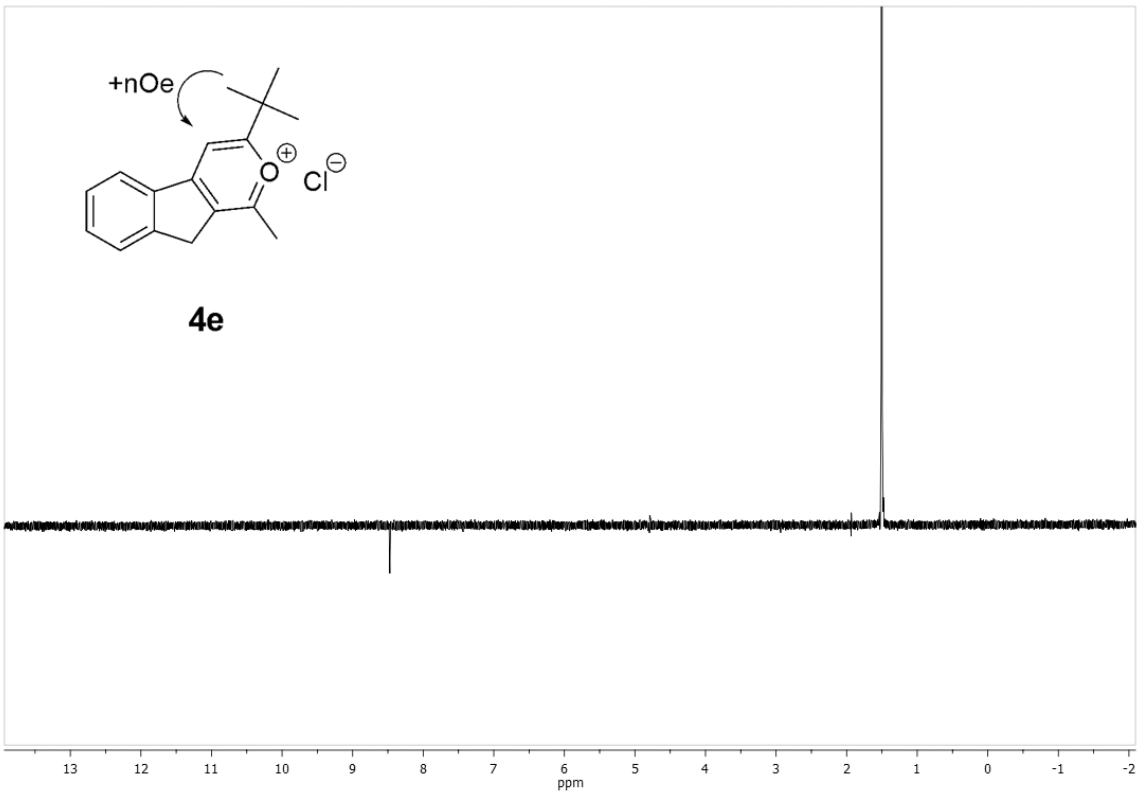
130.72, 130.31, 129.48, 127.52, 127.34, 110.85, 38.15; HRMS (CI): Exact mass calcd for $C_{24}H_{17}O$ $[M\text{-}Cl]^+$: 321.1279, found: 321.1270.

3-*tert*-butyl-1-methyl-9*H*-indeno[2,1-c]pyrylium chloride (4e). Following the general procedure, 0.06 mL of concentrated hydrochloric acid (12M, 0.78 mmol, 10 equiv.) was added to a solution of 0.02 g of **2e** (0.078 mmol) in 2 mL of methanol. After stirring for 45 hours, the solvent was removed *in vacuo* and the solid material was suspended in ethyl ether before vacuum filtration produced **4e** in 92% yield (0.0214 g, pink solid), mp = 152 °C (decomp). Rf = 0.0 (50% Et_2O/Hexanes); IR (NaCl, neat): 3304, 3302, 2960, 2865, 1629, 1604, 1546, 1502, 1469, 1448, 1375, 1328, 1239, 1210, 1032, 891, 783, 702, 577 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 8.57 (s, 1H), 8.48 (d, J = 7.9 Hz, 1H), 7.95 – 7.86 (m, 2H), 7.71 (dd, J = 10.4, 3.9 Hz, 1H), 4.35 (s, 2H), 3.03 (s, 3H), 1.60 (s, 9H); ^{13}C NMR (151 MHz, CD_3OD): δ 187.25, 173.75, 169.37, 151.80, 137.50, 137.23, 135.98, 130.21, 127.84, 127.51, 110.71, 39.71, 35.70, 28.64, 19.39; HRMS (CI): Exact mass calcd for $C_{17}H_{19}O$ $[M\text{-}Cl]^+$: 239.1436, found: 239.1432.

E.2. Nuclear Overhauser Effect Spectroscopy

E.2.1. 3-*tert*-butyl-1-methyl-9*H*-indeno[2,1-c]pyrylium chloride (4e)



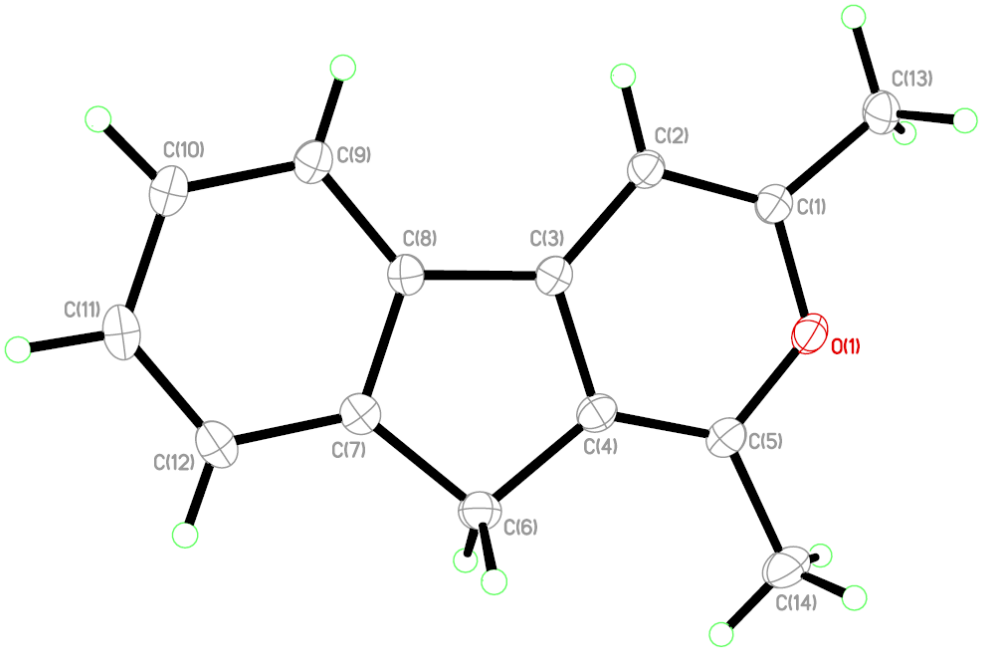


E.3. Crystal Structures

Table E.3.1. Crystal data and structure refinement for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a).

Empirical formula	C14 H15 Cl O2	
Formula weight	250.71	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.1739(15) Å	a= 81.438(3)°
	b = 8.9822(17) Å	b= 65.030(3)°
	c = 9.3921(17) Å	g = 80.900(3)°
Volume	614.6(2) $Å^3$	
Z	2	
Density (calculated)	1.355 Mg/m^3	
Absorption coefficient	0.297 mm^{-1}	
F(000)	264	
Crystal size	0.32 x 0.24 x 0.10 mm^3	
Theta range for data collection	2.31 to 27.00°.	
Index ranges	-10<=h<=10, -11<=k<=11, -11<=l<=11	
Reflections collected	6518	
Independent reflections	2575 [R(int) = 0.0181]	
Completeness to theta = 27.00°	96.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9709 and 0.9109	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2575 / 0 / 214	
Goodness-of-fit on F^2	1.075	
Final R indices [I>2sigma(I)]	R1 = 0.0362, wR2 = 0.1030	
R indices (all data)	R1 = 0.0392, wR2 = 0.1064	
Largest diff. peak and hole	0.227 and -0.336 $e.Å^{-3}$	

E.3.2. Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.



	x	y	z	U(eq)
Cl(1)	2472(1)	2176(1)	5835(1)	40(1)
O(1)	-14(1)	8871(1)	7110(1)	28(1)
O(2)	4760(2)	9591(2)	7122(2)	54(1)
C(1)	-869(2)	9061(2)	8664(2)	25(1)
C(2)	-378(2)	8125(2)	9740(2)	24(1)
C(3)	1035(2)	6974(2)	9173(2)	23(1)
C(4)	1921(2)	6814(2)	7541(2)	25(1)
C(5)	1356(2)	7775(2)	6529(2)	28(1)
C(6)	3362(2)	5501(2)	7218(2)	29(1)
C(7)	3180(2)	4898(2)	8857(2)	25(1)
C(8)	1822(2)	5782(2)	9989(2)	23(1)
C(9)	1386(2)	5443(2)	11600(2)	26(1)
C(10)	2351(2)	4200(2)	12058(2)	30(1)
C(11)	3704(2)	3317(2)	10930(2)	32(1)

C(12)	4125(2)	3642(2)	9333(2)	31(1)
C(13)	-2339(2)	10324(2)	8996(2)	31(1)
C(14)	2036(3)	7759(2)	4799(2)	43(1)

E.3.3. Table 3. Bond lengths [Å] and angles [°] for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a).

O(1)-C(5)	1.3479(18)
O(1)-C(1)	1.3502(17)
O(2)-H(1S)	0.83(3)
O(2)-H(2S)	0.83(3)
C(1)-C(2)	1.3680(19)
C(1)-C(13)	1.478(2)
C(2)-C(3)	1.3977(19)
C(2)-H(2)	0.936(18)
C(3)-C(4)	1.4105(19)
C(3)-C(8)	1.4498(17)
C(4)-C(5)	1.363(2)
C(4)-C(6)	1.496(2)
C(5)-C(14)	1.480(2)
C(6)-C(7)	1.506(2)
C(6)-H(6A)	0.99(2)
C(6)-H(6B)	0.979(18)
C(7)-C(12)	1.391(2)
C(7)-C(8)	1.403(2)
C(8)-C(9)	1.3968(19)
C(9)-C(10)	1.3852(19)
C(9)-H(9)	0.941(18)
C(10)-C(11)	1.399(2)
C(10)-H(10)	0.929(19)
C(11)-C(12)	1.385(2)
C(11)-H(11)	0.96(2)
C(12)-H(12)	0.91(2)
C(13)-H(13A)	1.00(2)
C(13)-H(13B)	0.97(2)
C(13)-H(13C)	0.96(2)
C(14)-H(14A)	0.91(3)
C(14)-H(14B)	0.94(3)
C(14)-H(14C)	0.96(3)

C(5)-O(1)-C(1)	122.72(11)
H(1S)-O(2)-H(2S)	111(2)
O(1)-C(1)-C(2)	120.86(13)
O(1)-C(1)-C(13)	112.17(12)
C(2)-C(1)-C(13)	126.96(14)
C(1)-C(2)-C(3)	117.68(13)
C(1)-C(2)-H(2)	118.1(11)
C(3)-C(2)-H(2)	124.2(11)
C(2)-C(3)-C(4)	120.26(12)
C(2)-C(3)-C(8)	131.29(12)
C(4)-C(3)-C(8)	108.42(12)
C(5)-C(4)-C(3)	119.22(13)
C(5)-C(4)-C(6)	130.02(13)
C(3)-C(4)-C(6)	110.72(12)
O(1)-C(5)-C(4)	119.24(13)
O(1)-C(5)-C(14)	112.88(13)
C(4)-C(5)-C(14)	127.86(15)
C(4)-C(6)-C(7)	101.82(11)
C(4)-C(6)-H(6A)	112.2(11)
C(7)-C(6)-H(6A)	111.1(11)
C(4)-C(6)-H(6B)	111.7(10)
C(7)-C(6)-H(6B)	111.8(10)
H(6A)-C(6)-H(6B)	108.2(15)
C(12)-C(7)-C(8)	119.83(13)
C(12)-C(7)-C(6)	129.19(13)
C(8)-C(7)-C(6)	110.98(12)
C(9)-C(8)-C(7)	121.79(13)
C(9)-C(8)-C(3)	130.14(13)
C(7)-C(8)-C(3)	108.04(12)
C(10)-C(9)-C(8)	117.83(14)
C(10)-C(9)-H(9)	119.6(10)
C(8)-C(9)-H(9)	122.5(10)
C(9)-C(10)-C(11)	120.43(14)
C(9)-C(10)-H(10)	122.5(12)
C(11)-C(10)-H(10)	117.1(11)
C(12)-C(11)-C(10)	121.81(14)

C(12)-C(11)-H(11)	120.3(12)
C(10)-C(11)-H(11)	117.9(12)
C(11)-C(12)-C(7)	118.30(14)
C(11)-C(12)-H(12)	121.1(12)
C(7)-C(12)-H(12)	120.6(12)
C(1)-C(13)-H(13A)	112.3(12)
C(1)-C(13)-H(13B)	109.4(12)
H(13A)-C(13)-H(13B)	108.7(17)
C(1)-C(13)-H(13C)	112.1(12)
H(13A)-C(13)-H(13C)	106.9(16)
H(13B)-C(13)-H(13C)	107.3(17)
C(5)-C(14)-H(14A)	111.2(16)
C(5)-C(14)-H(14B)	110.6(18)
H(14A)-C(14)-H(14B)	107(2)
C(5)-C(14)-H(14C)	109.0(16)
H(14A)-C(14)-H(14C)	111(2)
H(14B)-C(14)-H(14C)	109(2)

E.3.4. Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	45(1)	40(1)	33(1)	-8(1)	-16(1)	8(1)
O(1)	31(1)	28(1)	23(1)	3(1)	-12(1)	-4(1)
O(2)	66(1)	57(1)	29(1)	-5(1)	-19(1)	21(1)
C(1)	28(1)	25(1)	24(1)	-1(1)	-12(1)	-5(1)
C(2)	25(1)	26(1)	23(1)	-1(1)	-11(1)	-3(1)
C(3)	22(1)	24(1)	23(1)	0(1)	-10(1)	-6(1)
C(4)	24(1)	27(1)	23(1)	-1(1)	-8(1)	-6(1)
C(5)	28(1)	30(1)	24(1)	1(1)	-9(1)	-6(1)
C(6)	27(1)	31(1)	26(1)	-4(1)	-9(1)	-2(1)
C(7)	24(1)	25(1)	28(1)	-2(1)	-11(1)	-4(1)
C(8)	22(1)	23(1)	26(1)	-1(1)	-11(1)	-3(1)
C(9)	26(1)	28(1)	26(1)	2(1)	-12(1)	-5(1)
C(10)	31(1)	30(1)	31(1)	6(1)	-17(1)	-8(1)
C(11)	31(1)	25(1)	44(1)	4(1)	-22(1)	-4(1)
C(12)	26(1)	25(1)	40(1)	-3(1)	-13(1)	0(1)
C(13)	36(1)	29(1)	32(1)	-1(1)	-19(1)	2(1)
C(14)	45(1)	54(1)	23(1)	0(1)	-11(1)	1(1)

E.3.5. Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a).

	x	y	z	U(eq)
H(2)	-1040(20)	8267(19)	10810(20)	28(4)
H(6A)	4590(30)	5820(20)	6560(20)	42(5)
H(6B)	3140(20)	4750(20)	6680(20)	32(4)
H(9)	480(20)	6031(19)	12370(20)	25(4)
H(10)	2140(20)	3910(20)	13110(20)	35(5)
H(11)	4350(20)	2470(20)	11300(20)	37(5)
H(12)	4990(30)	3050(20)	8610(20)	33(4)
H(13A)	-3020(30)	10430(20)	10150(30)	45(5)
H(13B)	-1820(30)	11260(20)	8490(20)	47(5)
H(13C)	-3210(30)	10200(20)	8600(20)	41(5)
H(14A)	2680(30)	8560(30)	4280(30)	66(7)
H(14B)	2830(40)	6880(40)	4460(30)	85(9)
H(14C)	1020(40)	7770(30)	4530(30)	77(8)
H(1S)	4100(30)	10260(30)	6840(30)	60(7)
H(2S)	5450(30)	9090(30)	6380(30)	61(7)

E.3.6. Table 6. Torsion angles [°] for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a).

C(5)-O(1)-C(1)-C(2)	-0.36(19)
C(5)-O(1)-C(1)-C(13)	-179.12(12)
O(1)-C(1)-C(2)-C(3)	0.09(19)
C(13)-C(1)-C(2)-C(3)	178.65(13)
C(1)-C(2)-C(3)-C(4)	0.78(19)
C(1)-C(2)-C(3)-C(8)	-177.43(13)
C(2)-C(3)-C(4)-C(5)	-1.40(19)
C(8)-C(3)-C(4)-C(5)	177.18(12)
C(2)-C(3)-C(4)-C(6)	-179.29(11)
C(8)-C(3)-C(4)-C(6)	-0.71(15)
C(1)-O(1)-C(5)-C(4)	-0.27(19)
C(1)-O(1)-C(5)-C(14)	178.08(13)
C(3)-C(4)-C(5)-O(1)	1.13(19)
C(6)-C(4)-C(5)-O(1)	178.55(12)
C(3)-C(4)-C(5)-C(14)	-176.94(15)
C(6)-C(4)-C(5)-C(14)	0.5(3)
C(5)-C(4)-C(6)-C(7)	-176.43(14)
C(3)-C(4)-C(6)-C(7)	1.16(14)
C(4)-C(6)-C(7)-C(12)	177.81(13)
C(4)-C(6)-C(7)-C(8)	-1.24(14)
C(12)-C(7)-C(8)-C(9)	0.3(2)
C(6)-C(7)-C(8)-C(9)	179.45(12)
C(12)-C(7)-C(8)-C(3)	-178.26(12)
C(6)-C(7)-C(8)-C(3)	0.89(15)
C(2)-C(3)-C(8)-C(9)	-0.1(2)
C(4)-C(3)-C(8)-C(9)	-178.51(13)
C(2)-C(3)-C(8)-C(7)	178.25(13)
C(4)-C(3)-C(8)-C(7)	-0.11(14)
C(7)-C(8)-C(9)-C(10)	0.46(19)
C(3)-C(8)-C(9)-C(10)	178.67(13)
C(8)-C(9)-C(10)-C(11)	-0.5(2)
C(9)-C(10)-C(11)-C(12)	-0.2(2)
C(10)-C(11)-C(12)-C(7)	0.9(2)

C(8)-C(7)-C(12)-C(11)	-1.0(2)
C(6)-C(7)-C(12)-C(11)	-179.96(13)

E.3.7. Table 7. Hydrogen bonds for 1,3-dimethyl-9*H*-indeno[2,1-c]pyrylium chloride (4a).

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(1S)...Cl(1)#1	0.83(3)	2.34(3)	3.1697(15)	175(2)
O(2)-H(2S)...Cl(1)#2	0.83(3)	2.37(3)	3.1974(16)	176(2)

Symmetry transformations used to generate equivalent atoms:
#1 x,y+1,z #2 -x+1,-y+1,-z+1

APPENDIX F

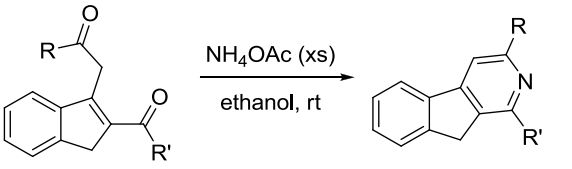
SUPPPORTING INFORMATION FOR CHAPTER VII

F.1. Experimental Details

F.1.1. General Methods. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using either a Varian Inova 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) or 500 (^{1}H: 500 MHz, ^{13}C: 126 MHz) or Agilent VNMRS 600 (^{1}H: 600 MHz, ^{13}C: 151 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm relative to residual chloroform (^{1}H: 7.26 ppm, ^{13}C: 77.160 ppm). Coupling constants are given in Hertz (Hz). Melting points were recorded on a Melt-Temp II melting point apparatus in open-end capillary tubes. IR spectra were recorded using a Nicolet Magna FTIR 550 spectrometer. High resolution mass spectra were recorded on a Waters Micromass MALDI Q-ToF or JEOL MS Route Magnetic Sector mass spectrometer.

F.1.2. Starting Materials. All reagents and solvents were purchased from Aldrich or TCI. Unless otherwise stated, all reagents were used as received. The preparation of indenes **1a-c** is described in chapter II and **1d** is described in chapter V.

F.1.3. General Procedure for the Synthesis of Indenopyridines



1a: R,R'=Me
1b: R,R'=Ph
1c: R,R'=Et
1d: R=*t*-Bu, R'=Me

2a: R,R'=Me
2b: R,R'=Ph
2c: R,R'=Et
2d: R=*t*-Bu, R'=Me

To a stirred 0.12 M solution of **1a-d** (0.23 mmol) in 2 mL of ethanol, 0.4 grams of ammonium acetate (0.47 mmol, 2 equivalents) was added. The solution was allowed to stir at room temperature for the required time.[xvi] When thin layer chromatography showed complete conversion of starting material, the reaction was then quenched by it pouring over a mixture of Et_2O and 10% HCl. The aqueous fraction was extracted twice more with ether, and the combined organic layers were then washed with 30 mL portions of 10% HCl, water (twice), and finally a saturated NaCl solution. The organic fraction was dried over sodium sulfate and the solvent removed by rotary evaporation. The residue was then purified via column chromatography or crystallization.

1,3-dimethyl-9*H*-indeno[2,1-c]pyridine (2a). Following the general procedure, 0.036 g of ammonium acetate (0.46 mmol, 2 equiv.) was added to a solution of 0.05 g of **1a** (0.223 mmol) in 2 mL ethanol. After stirring for 1.5 hours, the reaction was worked up and produced **2a** in 63% yield (0.023g, white solid), mp = 79-80 °C. Rf = 0.09 (50% EtOAc/Hexanes); IR (NaCl, neat): 3073, 2917, 2897, 1607, 1568, 1435, 1393, 1168, 1019, 875, 773, 742 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 7.70 – 7.66 (m, 1H), 7.47 (ddd,

[xvi] No attempt to exclude water or oxygen was made.

J = 5.1, 2.5, 0.8 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.13 (s, 1H), 3.70 (s, 2H), 2.51 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 156.40, 153.53, 149.79, 144.35, 140.13, 133.24, 128.92, 127.14, 125.53, 121.50, 112.20, 35.38, 24.84, 22.11; HRMS (CI): Exact mass calcd for $C_{14}H_{14}N$ $[M+H]^+$: 196.1126, found: 196.1135.

1,3-diphenyl-9*H*-indeno[2,1-c]pyridine (2b). Following the general procedure, 0.052 g of ammonium acetate (0.67 mmol, 4.5 equiv.) was added to a solution of 0.05 g of **1b** (0.148 mmol) in 2 mL of ethanol. After stirring for 48 hours, the reaction was worked up and produced **2b** in 88% yield (0.043 g, yellow solid, mp = 78-80º C) after column chromatography, eluding with 33% Et_2O/Hexanes. Rf = 0.72 (50% Et_2O/Hexanes); IR (NaCl, neat): 3058, 2971, 2930, 1713, 1653, 1600, 1576, 1548, 1494, 1417, 1396, 1310, 1186, 1074, 1022, 913, 867, 765, 737, 693, 629 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.23 (d, *J* = 7.2 Hz, 2H), 8.17 – 8.04 (m, 3H), 8.03 – 7.91 (m, 1H), 7.62 (d, *J* = 3.5 Hz, 1H), 7.59 – 7.35 (m, 9H), 4.22 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 156.19, 154.13, 151.73, 144.57, 140.37, 140.12, 139.69, 133.94, 129.30, 128.88, 128.81, 128.80, 128.70, 128.60, 127.30, 125.37, 121.42, 110.39, 37.33; HRMS (CI): Exact mass calcd for $C_{24}H_{18}N$ $[M+H]^+$: 320.1439, found: 320.1432.

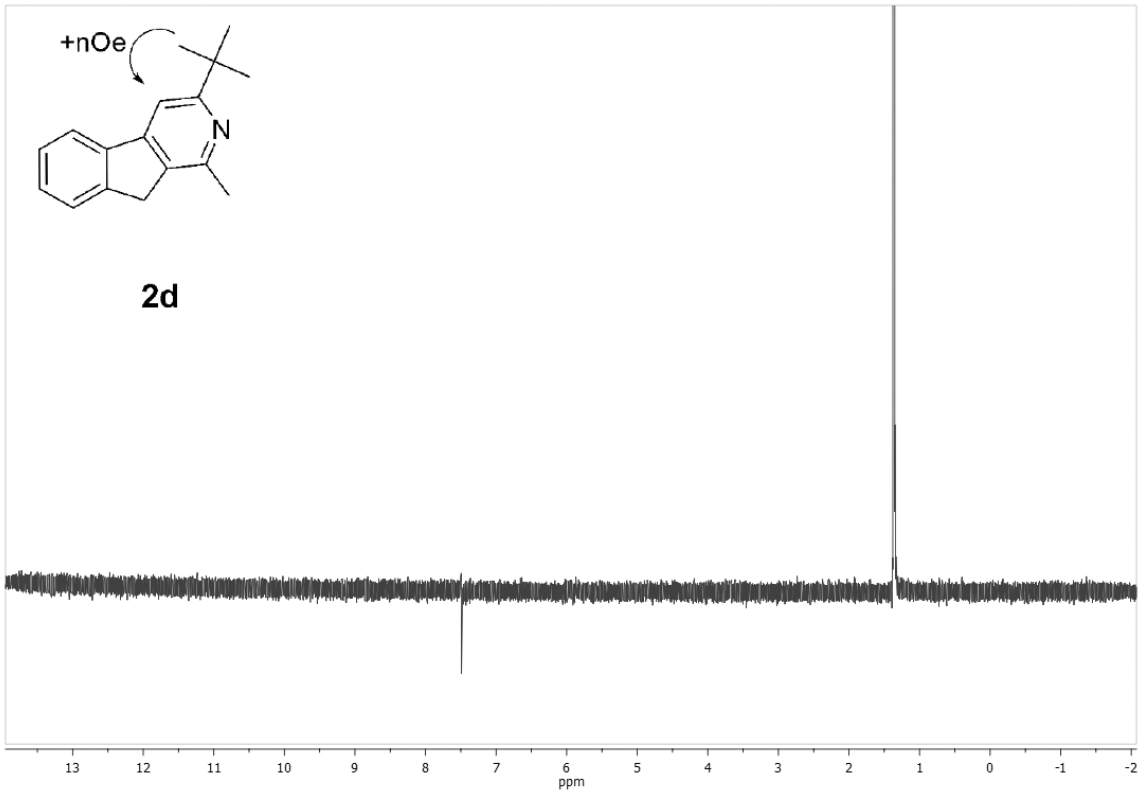
1,3-diethyl-9*H*-indeno[2,1-c]pyridine (2c). Following the general procedure, 0.036 g of ammonium acetate (0.46 mmol, 2.8 equiv.) was added to a solution of 0.04 g of **1c** (0.165 mmol) in 2 mL of ethanol. After stirring for 4 hours, the reaction was worked up and produced **2c** in 96% yield (0.036 g, white solid), 76-80 °C. Rf = 0.69 (50% EtOAc/Hexanes); IR (NaCl, neat): 2970, 2931, 2882, 2870, 1645, 1604, 1566,

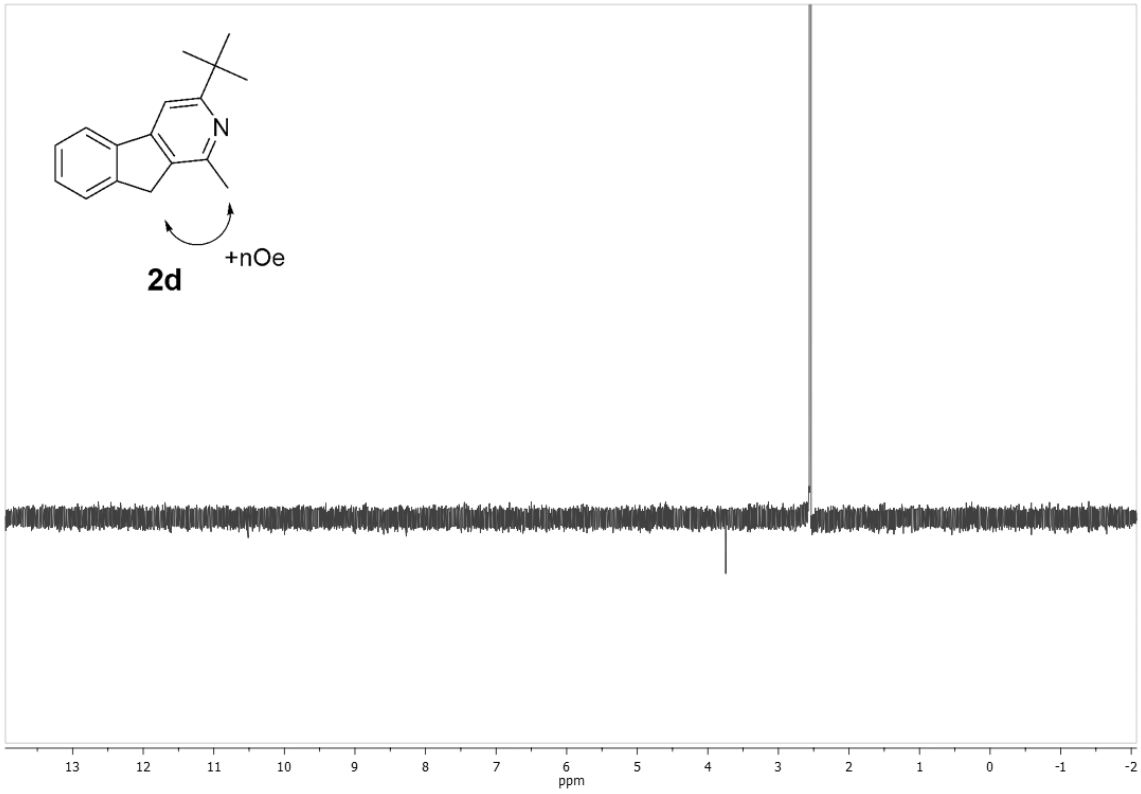
1458, 1433, 1402, 1369, 1270, 1193, 875, 755, 749 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 – 7.66 (m, 1H), 7.45 (d, *J* = 3.8 Hz, 1H), 7.32 – 7.23 (m, 2H), 7.12 (s, 1H), 3.73 (s, 2H), 2.89 – 2.70 (m, 4H), 1.31 – 1.16 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 162.03, 158.65, 150.06, 144.30, 140.31, 132.64, 128.81, 127.06, 125.46, 121.37, 110.76, 34.99, 31.84, 29.38, 14.73, 13.62; HRMS (CI): Exact mass calcd for $C_{16}H_{18}N$ $[M+H]^+$: 224.1439, found: 224.1426.

3-*tert*-butyl-1-methyl-9*H*-indeno[2,1-c]pyridine (2d). Following the general procedure, 0.012 g of ammonium acetate (0.156 mmol, 2 equiv.) was added to a solution of 0.020 g of **1d** (0.078 mmol) in 2 mL of ethanol. After stirring for 45 hours, the reaction was worked up and produced **2d** in 91% yield (0.017 g, white solid), mp = 104-106 °C. Rf = 0.86 (50% EtOAc/Hexanes); IR (NaCl, neat): 2939, 2856, 1600, 1569, 1459, 1395, 1351, 1216, 1089, 945, 853, 771, 752, 722 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.88 – 7.83 (m, 1H), 7.61 – 7.58 (m, 1H), 7.57 (s, 1H), 7.43 – 7.38 (m, 2H), 3.82 (s, 2H), 2.62 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 167.76, 153.00, 149.33, 144.29, 140.67, 133.08, 128.62, 127.02, 125.49, 121.33, 107.74, 37.56, 35.37, 30.69, 22.40; HRMS (CI): Exact mass calcd for $C_{17}H_{20}N$ $[M+H]^+$: 238.1596, found: 238.1594.

F.2. Nuclear Overhauser Effect Spectroscopy

F.2.1. 3-*tert*-butyl-1-methyl-9*H*-indeno[2,1-c]pyridine (2d)





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