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Synthesis of benzocarbazoles, indoloquinolines and indolonaphthridines from thermolysis of benzoenynyl ketenimines and carbodiimides

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Synthesis of Benzocarbazoles, Indoloquinolines and Indolonaphthridines from Thermolysis of Benzoenynyl Ketenimines and Carbodiimides

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ABSTRACT

Synthesis of Benzocarbazoles, Indoloquinolines and Indolonaphthridines from Thermolysis of Benzoenynyl Ketenimines and Carbodiimides

Chongsheng Shi

The development of a general route to the *N*-[2-(1-alkynyl)phenyl]ketenimines (enyne-ketenimines) and *N*-[2-(1-alkynyl)phenyl]carbodiimides (enyne-carbodiimides) and their subsequent thermal behavior are described. Like enyne-allene and enyne-ketene systems, these enyne-hetereocumulenes undergo cycloaromatization through two competing biradical mechanisms under thermal conditions and therefore could serve as potential DNA cleaving agents. The resultant nitrogen-containing hetereocyclic compounds are also biologically interesting. The research described herein provides a easy access to the synthesis of benzo[*b*]carbazole, indoloquinoline and indolonaphthyridine alkaloids. In addition, the new synthetic strategies for these compounds are very versatile, providing access to a diverse array of analogs of these alkaloids.

DEDICATION

To my wife, Lingyun, and daughter, Yi.

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1. Introduction

1.1 Background of the Biradical-Forming Cycloaromatizations

The biradical-forming cycloaromatization reactions have attracted considerable attention in recent years.[1,2] This is due mainly to the discovery of several very potent antitumor antibiotics such as calicheamicins **1**,[3] esperamicins **2**,[4] dynemicin **3**,[5] C-1027 chromophore **4**,[6] kedarcidin **5**,[7] and neocarzinostatin (NCS) chromophore **6**,[8] which cleave DNA via generation of biradicals under mild conditions (Figure 1). Among these thermally-induced biradical-forming reactions,

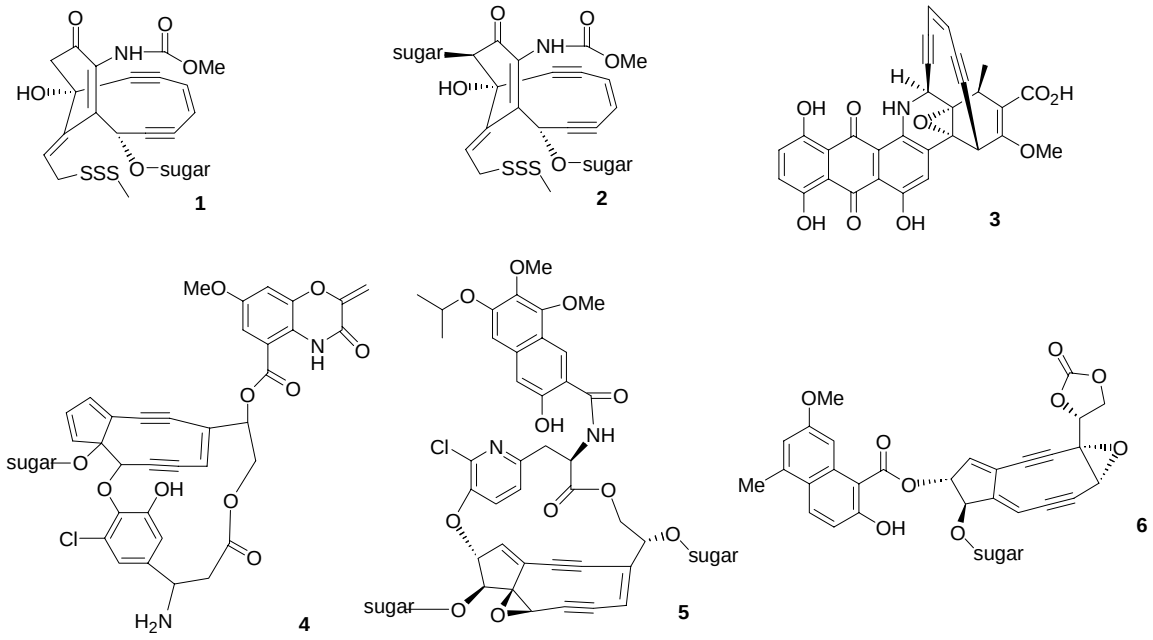
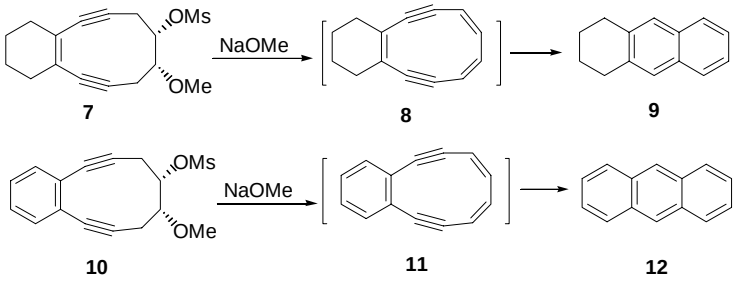


Figure 1. Structures of Enediyne Antitumor Antibiotics **1-6**.

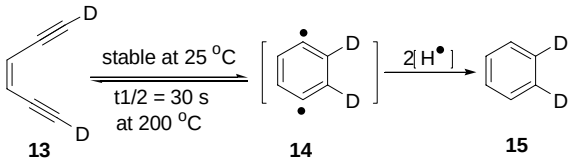
the Bergman cyclization of (*Z*)-3-hexene-1,5-diynes (enediynes) to 1,4-didehydrobenzenes and the Myers cyclization of (*Z*)-1,2,4-heptatrien-6-ynes (enyne-allenes) to α,3-didehydrotoluenes have been investigated extensively.[9,10]

As for as enediyne cyclization, in 1971, Masamune et al. reported the conversion of the two cyclic enediynes (**7** and **10**) into the corresponding benzenoid systems (**9** and **12**), but they did not mention the involvement of a biradical intermediate in the process (Scheme 1).[11]



Scheme 1. Observations by Masamune et al. Ms = mesyl

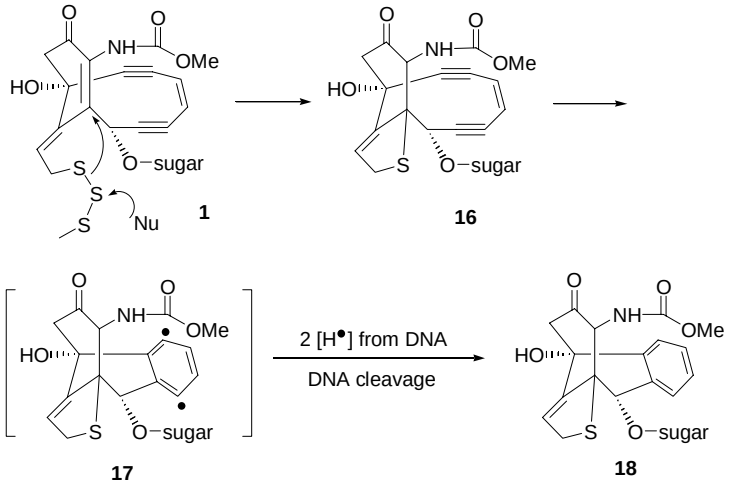
The cycloaromatization of endiynes via the 1,4-didehydrobenzene biradicals was clearly demonstrated with the elegantly designed studies by Bergman in 1972 (Scheme 2).[9a]



Scheme 2. The Bergman Cycloaromatization Reaction.

It was in 1987 that the enediyne chemistry did arouse much interest in chemical community when two very potent naturally occurring antitumor antibiotics, calicheamicins (**1**) and esperamicins (**2**) bearing an enediyne moiety, were discovered by researchers from the Lederle Laboratories[3] and Bristol-Myers[4], respectively. In the proposed mechanisms for DNA cleavage by these enediyne antibiotics, the 1,4-benzenoid biradicals generated by the Bergman cyclization attack DNA deoxyribose by hydrogen atom abstraction (Scheme 3).[1d] A nucleophile attacks the middle sulfur atom of the trisulfide group in **1**. The resulting thiolate reacts with the α,β-unsaturated ketone intramolecularly to give the corresponding addition product **16**. The

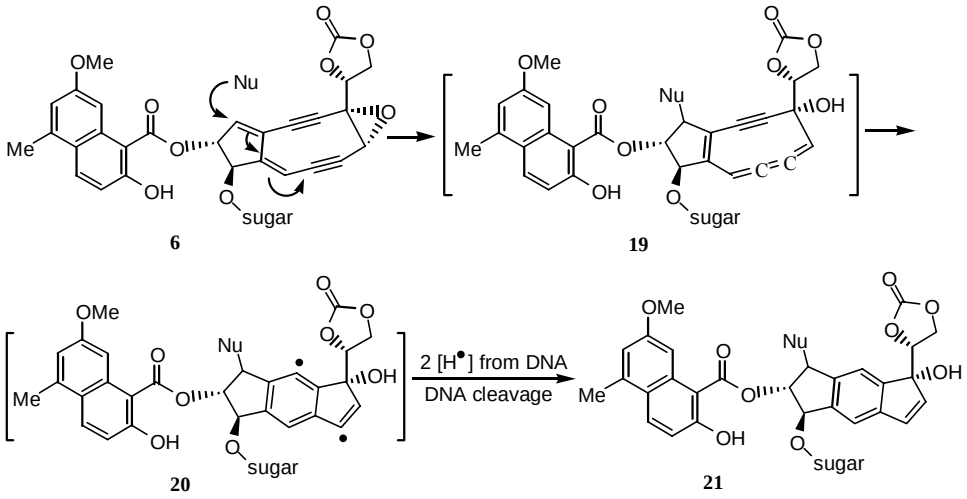
biradical **17** produced from the following Bergman cyclization reaction of **16** cleaves DNA by abstracting two hydrogen atoms, giving **18**.



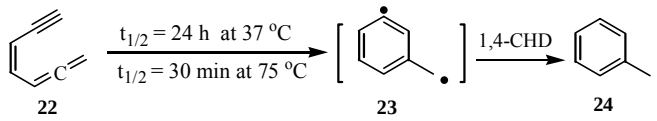
Scheme 3. Mechanism of DNA Cleavage by Calicheamicin γ^1_1 **1**.

It is believed that the NCS chromophore **6** causes DNA damage in a similar way (Scheme 4).[12] According to the hypothesis, a nucleophile stereospecifically attacks at C12, resulting in the ring skeleton rearrangement with epoxide opening and formation of the highly strained and labile cyclic enyne-cumulene **19**. The 3,7-dehydroindene derivative **20** formed from the very reactive intermediate **19**, which rapidly undergoes cycloaromatization, proceeds to attack DNA by hydrogen abstraction, resulting in the formation of **21**.

The involvement of the biradical **20** in the action of the NCS chromophore **6** was demonstrated with the parent (*Z*)-1,2,4-heptatrien-6-yne (**22**) by Myers and co-workers in 1989. This cycloaromatization leads to toluene (**24**) via α,3-didehydrotoluene (**23**) by hydrogen atom abstraction from 1,4-cyclohexadiene (1,4-CHD) (Scheme 5).[10a] A fundamental distinction between the 3,7-dehydroindene derivative **20** and the putative α,3-didehydrotoluene species **23** is that the former is almost certainly constrained as a σ-radical pair, while the latter is a σ,π-biradical capable of full benzylic resonance.

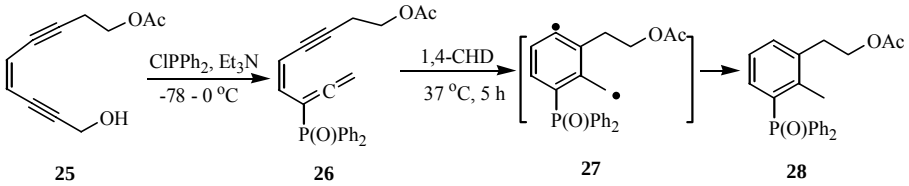


Scheme 4. Mechanism of DNA Cleavage by the NCS Chromophore **6**.



Scheme 5. The Myers Cycloaromatization Reaction.

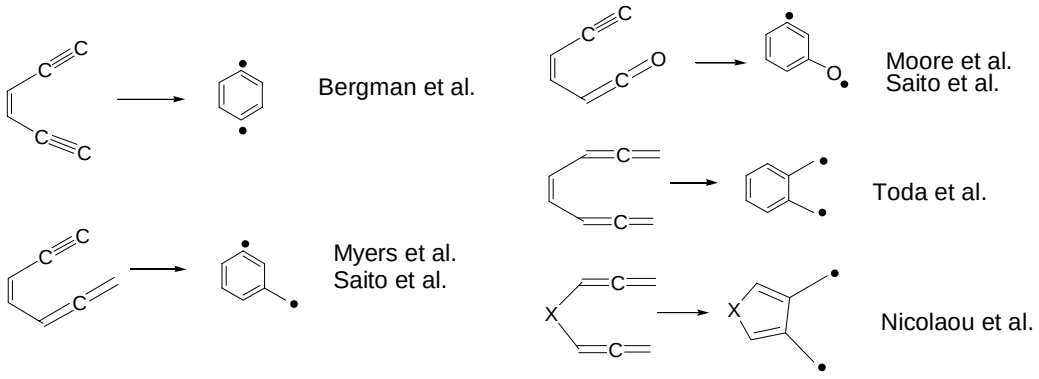
Similarly, Saito and co-workers also demonstrated independently that the enyne-allene system **26** with a substituent at C-3 position undergoes facile cycloaromatization to produce biradical species **27**, which mimics to some extent the action of neocarzinostatin and causes clean scission of double stranded DNA at 37 ºC in the absence of any additives (Scheme 6).[10c,10d]



Scheme 6. Saito's Study Related to the NCS.

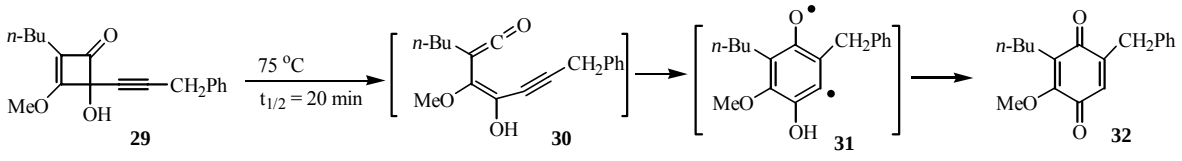
Because the naturally occuring enediyne antibiotics still rank amongst the most potent antitumor agents known so far, it is therefore not surprising that many choices of various

precursors which can lead to the characteristic biradical intermediates have been used to mimic the DNA-cleaving ability of these enediyne antibiotics. Some basic systems that are widely used for the model studies of enediyne prodrugs are listed in Scheme 7.[1c,9b,10b,10c,10d,13,14,15] In addition to parent system, each of the unsaturated groups in the (*Z*)-enediynes could be substituted with an isoelectronic group.



Scheme 7. Systems for the Biradical-Forming Reactions.

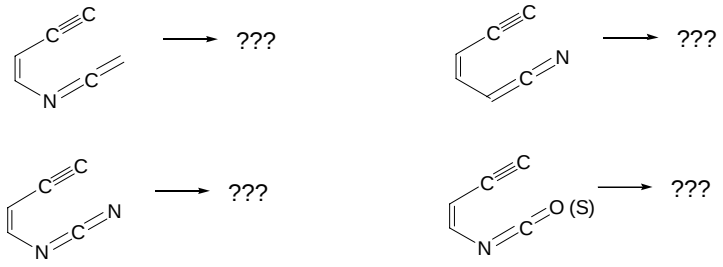
Moore and co-workers successfully incorporated an oxygen atom into the conjugated enyne-allene systems with a very imaginative and skillful choice of "masked" enyne-ketene precursors. Similarly, the Moore cyclization of enyne-ketenes provides easy access to biradicals having an aryl and a phenoxy radical center.[16] For example, thermolysis of 4-alkynylcyclobutenone **29** in acetonitrile gave the quinone **32** (Scheme 8).[13b] The reaction is believed to proceed through an electrocyclic ring opening of **29** to form the enyne-ketene **30**.



Scheme 8. The Moore Cyclization.

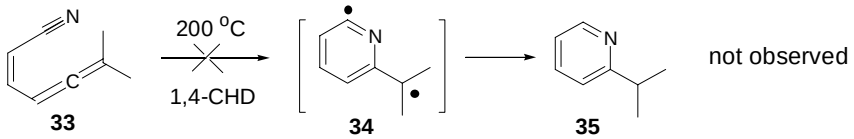
The highly reactive **30** then undergoes a Moore cyclization to give the biradical **31**, which in turn leads to **32** via an intermolecular hydrogen-atom transfer.

As for the conjugated enyne-heterocumulenes, while several synthetic pathways to enyne-ketenes and their versatility as reactive intermediates have been reported, the biradical-forming reactions involving other hetero atoms in the conjugated systems such as enyne-ketenimines, enyne-carbodiimides, enyne-isocyanates, and enyne-thioisocyanates remained virtually unexplored (Scheme 9). Compounds with these heteroanalogous functionalities might prove to be viable medicinal agents and useful biological probes.



Scheme 9. The Unexplored Conjugated Enyne-Heterocumulene Systems.

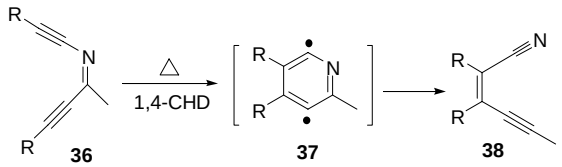
In an effort toward demonstrating the use of a nitrile group as a substituent for the alkynyl group of enyn-allenes, compound **33** was synthesized. However, attempts to generate biradical **34** and subsequently 2-isopropylpyridine **35** by thermolysis of **33** containing an excess of 1,4-CHD as a hydrogen-atom donor were unsuccessful (Scheme 10).[17a]



Scheme 10. Wang's Early Attempts to Generate the Biradical **34**.

A similar attempt to involve the nitrile group in a biradical-forming reaction also failed.[17b] Interestingly, when *C*,*N*-dialkynyl imines **36** were heated in refluxing benzene, enynyl

nitriles **38** were produced in excellent yields presumably through the putative 2,5-didehydropyridines **37**, which could not be captured by 1,4-CHD or, in the case of **38b**, by the carbon-carbon double bond intramolecularly (Scheme 11).[18a] Recently, it was observed that very small amount of **37a** could be captured to produce 2-methyl-4,5-diphenylpyridine when the reaction was conducted in the presence of moderate amounts of a protic acid (HBF_4).[18b]



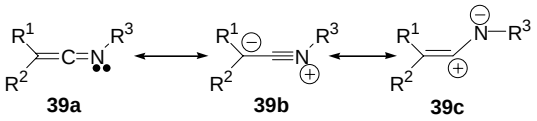
a: R = Ph; **b**: R = CH_2CH_2CH=CHPh

Scheme 11. Studies about the 2,5-Didehydropyridine Biradicals.

1.2 Research Objectives

Although only a trace amount of putative 2,5-didehydropyridines **37a**[18b] are trapped in the presence of a protic acid (HBF_4), the high-yielding conversions of *C*,*N*-dialkynyl imines **36** to (*Z*)-β-alkynylacrylonitriles **38** under mild thermal condition[18a] are in good agreement with the proposed mechanism of the aza-Bergman rearrangement as depicted in Scheme 11. We reasoned that the radical site at the *ortho* position of *N*-atom involving pyridine biradicals might be the cause of pyridine ring opening, leading to the nitriles. However, the enyne-azacumulene systems could avoid this problem. As a part of our continuing efforts in the study of enyne-allene chemistry, we envisioned that enyne-ketenimines having a nitrogen atom in the conjugated system and enyne-carbodiimides having two nitrogen atoms in the conjugated system could serve as precursors for the generation of biradicals via cyclization reaction similar to enyne-allenes and enyne-ketenes. The resulting biradicals from cycloaromatization of enyne-ketenimines and enyne-carbodiimides could also behave as potentially potent DNA cleaving

agents and find applications for the synthesis of biologically interesting alkaloids, such as quinolines, benzocarbazoles, indoloquinolines, indolonaphthridines, benzopyridoindoles, and pyridopyrroloquinolines. Unlike allenes and ketenes, ketenimines have three major resonant structures: the 1-azaallene form **39a**, and the zwitterionic forms **39b** and **39c** as outlined in Scheme 12. The nucleophilicity of the β-carbon atom and the electrophilicity of the central carbon atom may play a different role in the reaction.



Scheme 12. The Resonance Structures of Ketenimines.

The objectives of this research are: (i) to develop a new biradical forming reaction system; (ii) to synthesize and isolate enyne-ketenimines and enyne-carbodiimides; (iii) to investigate the general thermal behaviors, the influence of the substituents at the alkyne terminus in the conjugated systems on the cyclization mode and the relevant mechanisms of enyne-ketenimines and enyne-carbodiimides; (iv) to exploit a new efficient route to the synthesis of quinolines and 5*H*-benzo[*b*]carbazoles by intermolecular and/or intramolecular trapping the biradicals produced from thermolysis of the corresponding benzoenynyl ketenimines; and (v) to develop a convenient and flexible methodology for the synthesis of 2-aminoquinolines, 6*H*-indolo[2,3-*b*]quinolines and indolonaphthyridines by intermolecular and/or intramolecular trapping the biradicals produced from thermolysis of the corresponding benzoenynyl carbodiimides.

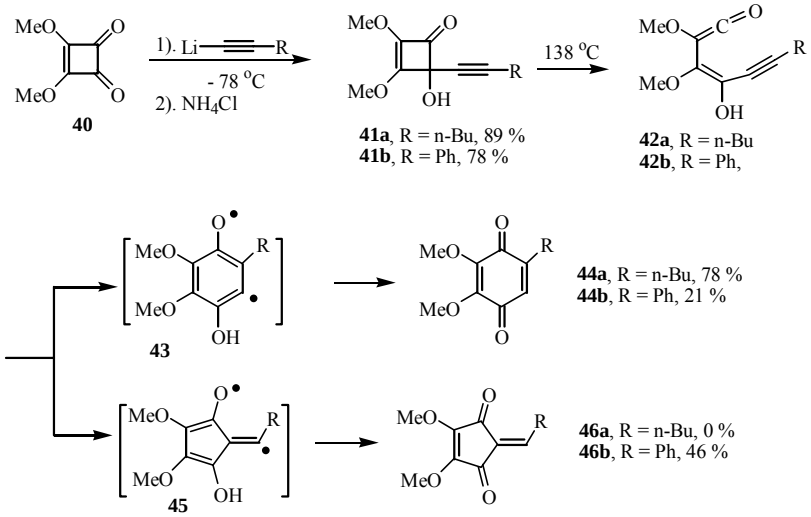
2. Literature Survey for the Synthesis of Enyne-Ketenimines and Enyne-Carbodiimides and the Related Cycloaromatization Reactions

2.1 Competing Pathways for the Cycloaromatization Reactions

To begin this research, it is instructive to first consider the extensive research efforts in this area by other groups. Since the disclosure of the biradical-forming mechanisms of the Bergman and the Myers reactions, the research interests on the thermal cycloaromatization of enediynes, enyne-cumulenes, enyne-allenes and enyne-ketenes have been focused on the synthesis of model compounds to mimic the naturally-occuring enediyne antibiotics as well as on the utilization of the biradical cyclization for the construction of polycyclic compounds by the intramolecular trapping strategies. [1a] Furthermore, the attention was drawn on the influence of the substituents at the alkyne terminus in the conjugated systems on the cyclization mode and on the further exploitation of the new alternative pathways for synthetic and biological applications.

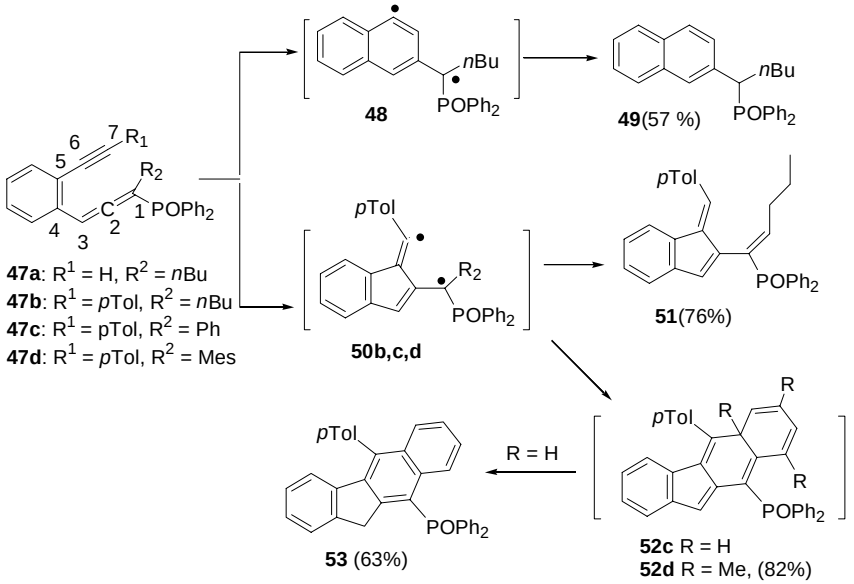
In 1989, the Moore group reported that the enyne-ketenes could undergo two competing routes to produce two different biradicals for the ring closure.[19] For example, treatment of dimethyl squarate **40** with 1-lithio-1-hexyne followed by quenching the reaction mixture with ammonium chloride furnished cyclobutenone **41a**. Thermolysis of **41a** in refluxing *p*-xylene gave the 1,4-benzoquinone **44a** as the sole product (Scheme 13). The reaction is considered to proceed through a stereoselective ring opening of **41a** in which the electron-donating hydroxyl group rotates outward to give the Z geometric enyne-ketene **42a.**[19] Subsequent cycloaromatization to form biradical **43** followed by an intermolecular or intramolecular hydrogen-atom transfer process results in the formation of **44a**. [13b,20] When the R group is phenyl, the enyne-ketene **42b** also undergoes a competing ring closure to form the five-

membered ring biradical **45** in which the phenyl group stablizes the adjacent vinyl radical. As a result, a mixture of **44b** and **46b** was produced from **41b**.



Scheme 13. A Competing Pathway to the Moore Cyclization.

The Schmittel group discovered an alternative C^2-C^6 cyclization pathway which replaces the well-known C^2-C^7 Myers-Saito cycloaromatization when an aryl substituent is attached at the alkyne terminus in the enyne-allene system (Scheme 14).[21] The enyne-allenes **47a-d** were heated

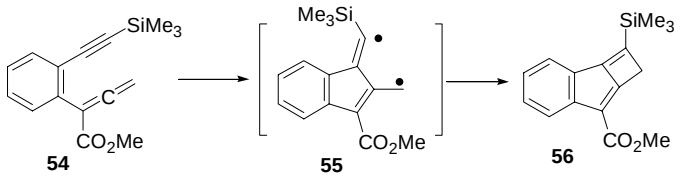


Scheme 14. An Alternative Pathway to the Myers-Saito Cycloaromatization.

with an excess of 1,4-CHD as hydrogen-atom donor in toluene. Compound **47a** gave the C^2-C^7 Myers-Saito cycloaromatization product **49**, whereas the thermal reaction of **47b-d** provided the C^2-C^6 cyclization products **51**, **52d** and **53**.[21]

Although they were not able to trap the postulated biradical **50** by an intermolecular reaction (O_2, PhSH, $(Me_3Si)_3SiH$, 1,4-CHD, 2,2,6,6-tetramethylpiperidine N-oxide),[22] they could exclude a zwitterion as an alternative intermediate because the rates of the transformations of the formal ene reaction **47b** → **51** and the Diels-Alder reaction **47c-d** → **52** were not affected by the change from a non-polar solvent (mesitylene or benzene) to a very polar solvent, such as DMSO. The very similar activation data for the formal ene reaction (**47b** → **51**) and the Diels-Alder reaction (**47c-d** → **52**) and the almost identical activation energies for the formal Diels-Alder reactions of **47c** and **47d** supported the proposed stepwise biradical mechanism instead of the concerted ene reaction or the Diels-Alder reaction. The activation energy of **47d** would be expected to be much higher than that of **47c** because of the steric effect of the bulky mesityl group. Moreover, intramolecular vinyl radical cyclizations onto the aromatic rings are well documented.[23]

Gillmann and co-workers also independently reported their observation of the new behavior of enyne-allenes (Scheme 15). Thermolysis of enyne-allene ester **54** in chlorobenzene



Scheme 15. Observations by Gillmann and Co-workers.

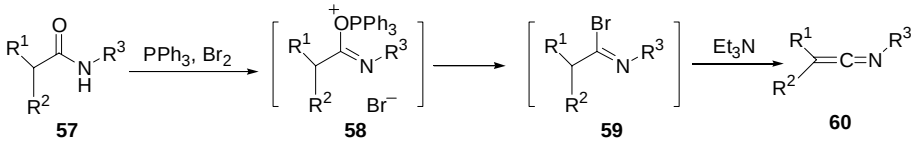
in the presence of 1,4-CHD gave the tricyclic 1*H*-cyclobuta[*a*]indene **56** in 62% yield. The 1-silylvinyl radical **55** was proposed to be the intermediate in the process, but a polar mechanism involving a 1-silylvinyl carbenium ion could not be ruled out.[24]

The methods for preparation of enyne-ketenimines and enyne-carbodiimides are rarely recorded in literature.[25] No isolated enyne-ketenimines or enyne-carbodiimides was reported when we started this project. To the best of our knowledge, only one example regarding the reaction of enyne-ketenimine was reported in the literature.[25a] Introduction of the ketenimine and carbodiimide functionalities in conjugation with the enyne system is obviously a key step. There are many synthetic methods reported in the literature for ketenimines and carbodiimides.[26] The following is a brief review of the methods for the preparation of ketenimines and carbodiimides.

2.2 Methods for the Synthesis of Ketenimines

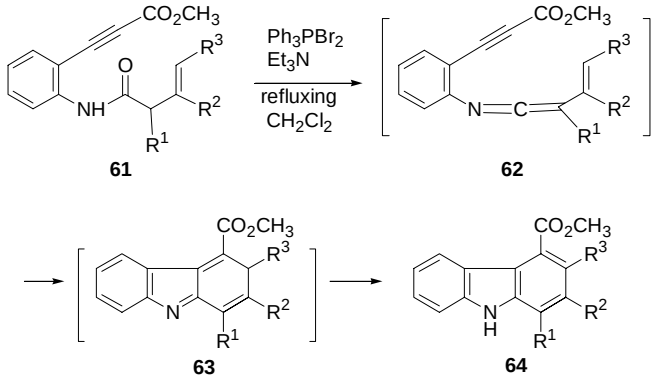
2.2.1 Synthesis of Ketenimines by Dehydration of Secondary Amides

Synthesis of ketenimines by dehydration of secondary amides is a general method that was introduced in 1964 by Stevens and Singhal.[27] Originally, phosphorus pentoxide was employed as dehydrating reagent and Florisil or sand was used to facilitate stirring and to accelerate the reaction. Pyridine or triethylamine was used as solvent. Later, Bestmann and co-workers introduced the use of dibromotriphenylphosphorane (prepared *in situ* from triphenylphosphine and bromine) as the dehydrating reagent and provided convenient access to trisubstituted ketenimines under mild reaction conditions.[28a] The putative intermediate in this reaction is **58**. It is conceivable that the ketenimine **60** was produced from the dehydrobromonation of the imidoyl bromide **59** which was formed from **58** (Scheme 16).



Scheme 16. The Bestmann Method for the Dehydration of Secondary Amides.

Differding and Ghosez made the carbazole **64** by treatment of the anilide **61** with Ph_3PBr_2 in the presence of triethylamine in refluxing CH_2Cl_2 (Scheme 17).[25a] In the proposed mechanism, the vinylketenimine **62** acts as electron-rich dienes in the Diels-Alder reaction. The adduct **63** undergoes tautomerization to give **64** under the reaction conditions. In fact, this is the only reported example involving enyne-ketenimines.



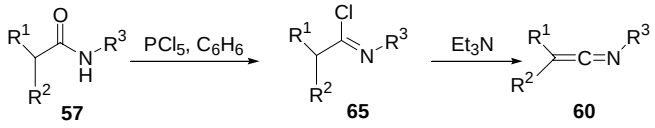
Scheme 17. Observations by Differding and Ghosez.

A different variation uses dichlorotriphenylphosphorane, prepared *in situ* from triphenylphosphine and tetrachloromethane, as the dehydration agent.[28b]

2.2.2 Synthesis of Ketenimines by Dehydrohalogenation of Imidoyl Halides

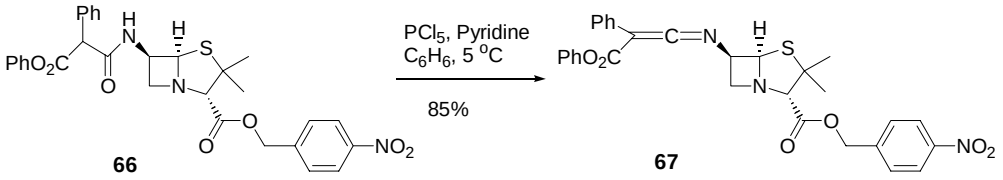
This frequently used method for the preparation of ketenimines was introduced by Stevens and French in 1954.[29] Treatment of the secondary amides **57** with phosphorus pentachloride in refluxing benzene gave the imidoyl chloride **65** as isolatable intermediate in most cases. When **65** was treated with triethylamine, dehydrochlorination occurred to afford the

ketenimine **60** (Scheme 18). This method is suitable for the preparation of the trialkyl ketenimines and ketenimines bearing chiral substituents on nitrogen. For example, the ketenimine **67** was obtained from the penicillin derivative **66** using this method (eq 1).[30]



57 65 60

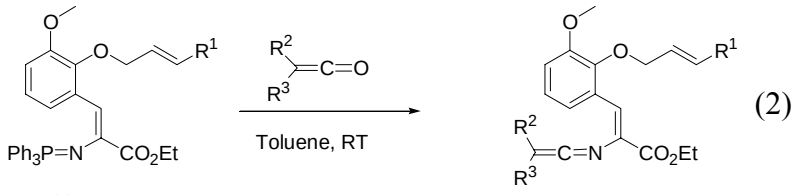
Scheme 18. Dehydration of Secondary Amides Using PCl_5.



66 67 (1)

2.2.3 From Ketenes and Iminophosphoranes[31]

In the early 1920s, Staudinger and co-workers prepared ketenimines by the reaction of iminotriphenylphosphorane (Ph_3P=NR, *N,P*-ylide) with ketenes under mild conditions. This method is especially useful for the preparation of the thermally labile ketenimines. The key factor in this method is actually the preparation of ketenes. The *N*-vinyl ketenimine **69** was prepared from the *N,P*-ylide **68** using this approach (eq 2).[32]

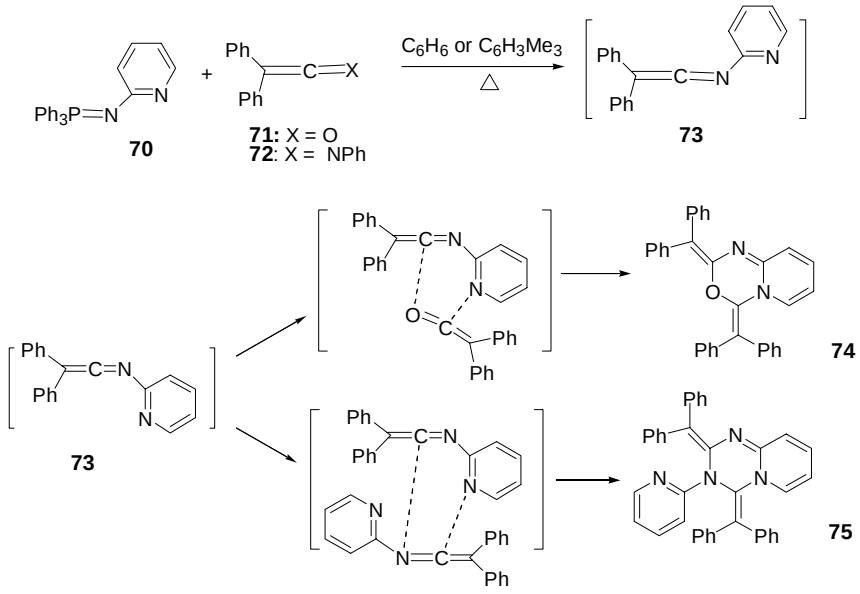


68 69 (2)

R^1 = H, Me, Ph; R^2 = Ph, *p*-Tol; R^3 = Et, Ph, *p*-Tol

It is interesting to note that *N*-pyridyl iminophosphorane **70** reacts with both diphenylketene (**71**) and *N*- phenyl-diphenylketenimine (**72**) to give the *N*-(2-pyridyl)ketenimine **73** (Scheme 19).[33] Under the reaction conditions, the ketenimine **73** spontaneously dimerized to

afford the heterocyclic products **74** and **75**. The relative yields of **74** and **75** depend on the molar ratio of the *N*-*P* ylide **70** and the ketene **71** or the ketenimine **72** in the reaction (1:1 of **70** to **71** gave **75** in 60% yield; 1:3 of **70** to **72** afforded **75** in 38% yield; 1:3 of **70** to **71** afforded **74** in 88% yield).

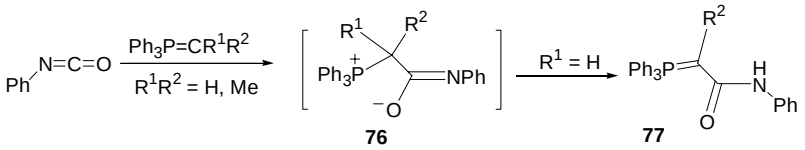


Scheme 19 Reactions of *N*-(2-Pyridyl)Ketenimine **73**.

2.2.4 From Phosphorus Ylides and Isocyanates or Related Compounds

Historically, the first ketenimine, $Ph_2C{=}C{=}NPh$, was synthesized by Staudinger and Meyer from the reaction between phenyl isocyanate and diphenylmethylenetriphenyl-phosphorane. However, there is a potential problem about this methodology when the nonstablized ylides were used. For instance, the reaction between the isocyanate with $Me_2C{=}PPh_3$ stopped at the bataine stage (**76**) (Scheme 20). Furthermore, bataines from nonstablized ylides bearing hydrogen(s) on the methylene carbon then rearranged to yield new ylides **77**. Generally speaking, this method is not suitable for the reactions involving

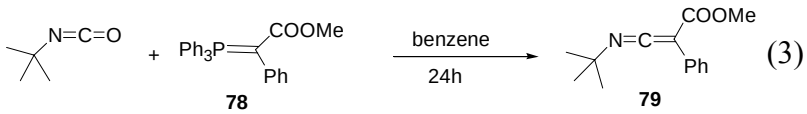
nonstablized ylides due to difficulty in inducing an elimination of triphenylphosphine oxide from the betaine intermediates.



76 77

Scheme 20. The Rearrangement of the Bataine Intermediates.

Phenylmethoxycarbonylketene-*N*-*t*-butylimine (**79**) was prepared in 92% yield by the reaction of methyl triphenylphosphoranylidenephenylacetate (**78**) with *t*-butyl isocyanate at 103 ^{o}C for 24 hours (eq 3).[34]



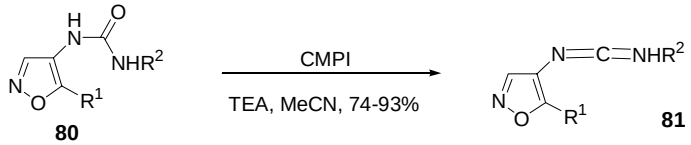
78 79 (3)

2.3 Methods for the Synthesis of Carbodiimides

For the preparation of carbodiimides, the usual starting materials are ureas, thioureas, isocyanates and isothiocyanates. The following are most widely cited methods.

2.3.1 Dehydration of Ureas

The widely used dehydrating agents include Ph_3PBr_2, Ph_3PCl_2, PCl_5, *p*-toluenesulfonyl chloride, phosgene, and 2-chloro-1-methylpyridinium iodide (CMPI). The carbodiimides **81** were prepared from ureas **80** in good yields using this method (eq 4).[35]

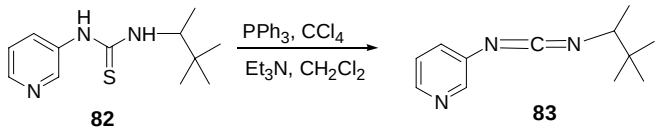


80 81 (4)

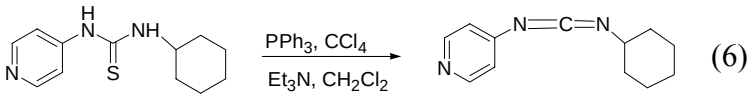
R^1 = H, Me; R^2 = Me, Pr, ^{i}Pr, ^{t}Bu, 4-MeC_6H_4, 2,6-$Me_2C_6H_3$

2.3.2 Elimination of Hydrogen Sulfide from Thioureas

The extrusion of hydrogen sulfide from *N,N'*-disubstituted thioureas is one of the most commonly used methods for the preparation of carbodiimides. Pyridin-3-yl-[(1,2,2-trimethyl-propylimino)methylene]amine (**82**) was prepared by the reaction of 1-pyridin-3-yl-3-(1,2,2-trimethyl-propyl)thiourea (**83**) with PPh_3/CCl_4 in the presence of triethylamine (eq 5).[36a] The carbodiimide **85** was also prepared from urea **84** in quantitative yield using this method (eq 6).[36b]

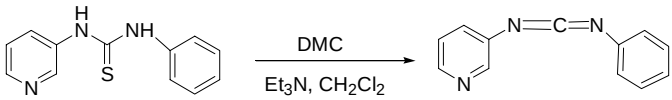


82 **83** (5)



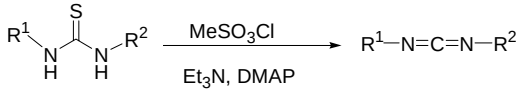
84 **85** (6)

Recently, Isobe and Ishikawa synthesized phenyl-pyridin-3-yl-carbodiimide (**87**) by treatment of 1-phenyl-3-pyridin-3-yl-thiourea (**86**) with 2-chloro-1,3-dimethylimidazolinium chloride (DMC) in the presence of triethylamine (eq 7).[37]



86 **87** (7)

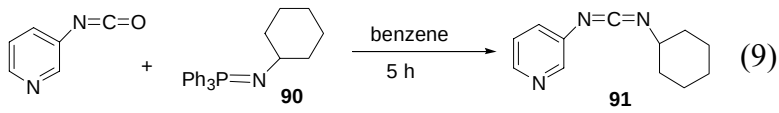
Fell and Coppola developed a mild, efficient, and rapid method for the conversion of mono- or diarylthioureas **88** to the corresponding carbodiimides **89** by treatment of the thiourea with methylsulfonyl chloride in the presence of triethylamine and a catalytic amount of 4-dimethylaminopyridine (DMAP) (eq 8).[38]



88 **89** (8)

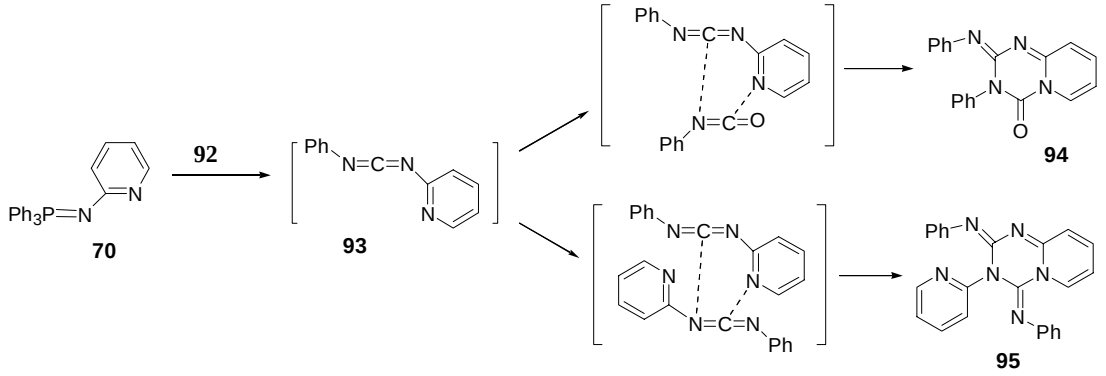
2.3.3 Aza-Wittig Reactions of Iminophosphoranes with Isocyanates or Isothiocyanates[39]

This is another most common approach to the synthesis of carbodiimides. *N*-Cyclohexyl-*N*'-(3-pyridyl)carbodiimide (**91**) was prepared by the reaction of 3-isocyanatopyridine with cyclohexyliminotriphenylphosphorane (**90**) in 83% yield (eq 9).[40]



(9)

It is noteworthy that the pyridyl carbodiimides can be used as part of a diene or dienophile component in the Diels-Alder reaction. A very interesting example is the competition of the [4+2] cycloadditions of phenyl isocyanate (**92**) with *N*-Phenyl-*N'*-(2-Pyridyl)carbodiimide

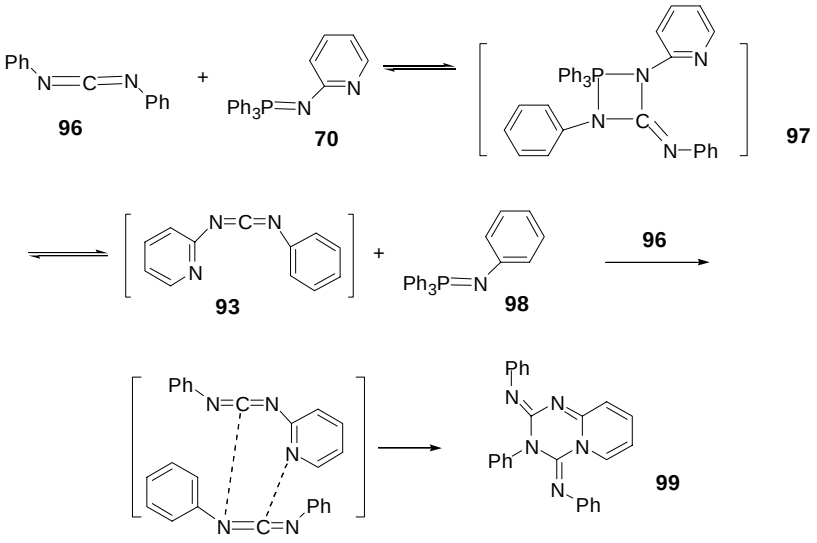


Scheme 21. Reactions of *N*-Phenyl-*N'*-(2-Pyridyl)carbodiimide **93**.

(**93**) and **93** with itself, resulting in the formation of two heterocyclic products **94** and **95** as outlined in Scheme 21. The relative yields of **94** and **95** depend on the molar ratio of the *N*-*P* ylide **70** and phenyl isocyanate (**92**) in the reaction mixture (1:3.5 ratio of **70** to **92** gave **94** in 83% yield; 1:1.5 ratio of **70** to **92** furnished **94** in 24% yield and **95** in 50% yield).[41]

It is interesting to note that *N*-pyridyl iminophosphorane **70** (1 equiv) also reacts with diphenylcarbodiimide **96** (2 equiv), via the intermediate **97**, to give the *N*-(2-pyridyl)ketenimine

93 and *N-P* ylide **98**. The reactive **93** in turn undergoes a [4+2] cycloaddition with **96** to furnish **99** in 52% yield (Scheme 22).[42]



Scheme 22. Dimerization of the Mixed Carbodiimides.

3. Results and Discussion

3.1 Generation of Biradicals and Subsequent Formation of Quinolines and 5*H*-Benzo[*b*]carbazoles from *N*-[2-(1-Alkynyl)phenyl]ketenimines

3.1.1 Retrosynthetic Analysis

It should be emphasized that ketenimines (1-alkenylideneamines) with a hydrogen-substituent or with a small-unbranched alkyl substituent are elusive substances. Ketenimines are reasonably stable when substituted with a stabilizing group such as an aryl,[43] a phosphonium ylide group[44] or a trimethylsilyl group.[45,46] We reasoned that it would be a wise choice to start with relatively stable enyne-ketenimines in our model studies. Since incorporation of the central carbon-carbon double bond of acyclic enediynes into a benzene ring has little effect on the rate of the Bergman cyclization reaction,[47] such system was chosen for the enyne-ketenimine system. This system is easy to construct and provides a variety of enyne-ketenimine systems for subsequent studies.

There are two kinds of enyne-ketenimines **100** and **101** for this system (Figure 2). We selected **100** in our study. For the preparation of ketenimines, the reasonably versatile and

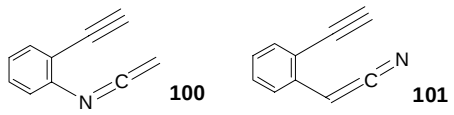
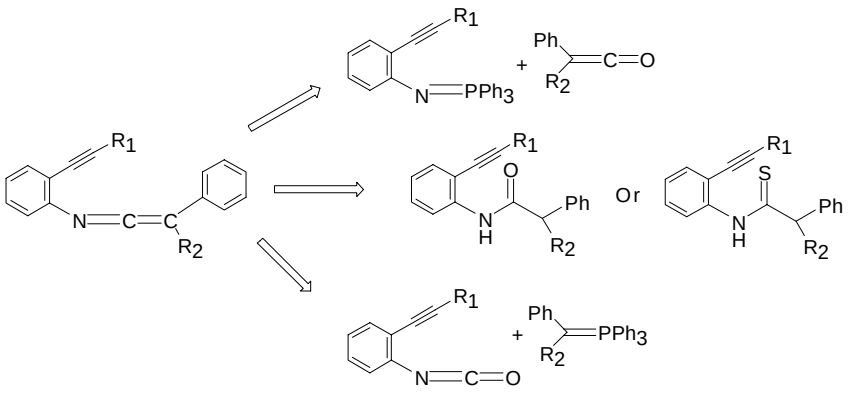


Figure 2. Two Type of Enyne-Ketenimines.

general reactions are dehydration of secondary amides and elimination of hydrogen sulfide from thioamides and their derivatives. From the retrosynthetic viewpoint, ketenimines can also be disconnected in two ways: scission of the N=C bond and excision of the C=C bond in N=C=C systems. In other words, enyne-ketenimines **100** could also be synthesized by the aza-Wittig reaction of the corresponding iminophosphoranes with ketenes and by the reaction of phosphorus

ylides with isocyanates or related compounds. The retrosynthetic analysis is summerized in Scheme 23. Among these, the aza-Wittig reaction is most appealing because of its mild reaction condition and easy accessibility, and therefore provides the great opportunity to isolate the key intermediates in the process.



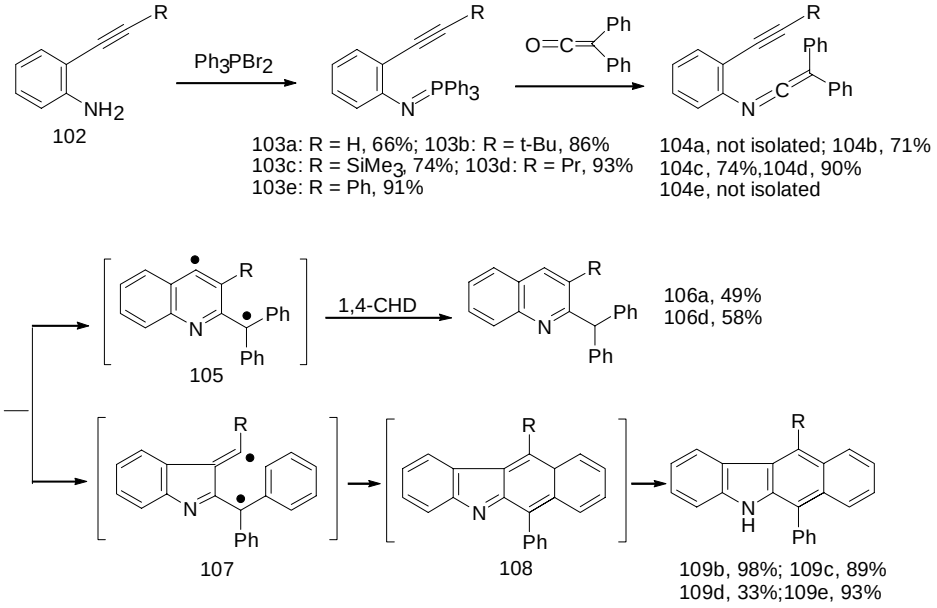
Scheme 23. Retrosynthetic Analysis.

Diphenylketene was selected in this preliminary study because it would allow interamolecular coupling of the biradical intermediates. Moreover, diphenylketene is relatively stable and can be easily isolated and purified.

3.1.2 Results and Discussions

The Pd-catalyzed cross-coupling reactions between 2-iodoaniline and 1-alkynes furnished **102** in nearly quantitative yields.[48] Treatment of **102** with Ph_3PBr_2 gave the iminophosphoranes **103** (Scheme 25).[49a] The aza-Wittig reaction between **103a** (R = H) [49b] and diphenylketene[50] was carried out in benzene containing a large excess of 1,4-CHD at 0 ºC followed by reflux for 2 hours to furnish the quinoline **106a** (R = H) in 49% yield. Apparently, the reaction proceeded through an initial formation of the ketenimine **104a** followed by cycloaromatization to produce the biradical **105a** and subsequently **106a**. Attempts to isolate **104a** resulted in its decomposition after the solvent was removed. However, the IR spectrum taken immediately after **103a** was

treated with diphenylketene (strong absorptions at 2105 cm^{-1} in IR spectrum)[50] in C_6D_6 containing an excess of 1,4-CHD exhibited an intense absorption at 2002 cm^{-1}, attributable to



Scheme 24. Thermolysis of Enyne-Ketenimine **104**.

104a.[43] The ^{1}H NMR spectrum of the same solution also showed the disappearance of the acetylenic C-H signal of **103a**[49b] at δ 3.26 and the appearance of a new signal at δ 2.86, attributable to the acetylenic C-H of **104a**. The assignments of the signals were based on the systematic observation of the appearance and disappearance of the signals at δ 2.86 and 3.86, and on the comparison of the signal at δ 2.51 for **103d** and the signal at δ 2.10 for **104d** of the proparagylic protons. The rate of disappearance of **104a** and appearance of **106a** was monitored with IR and ^{1}H NMR. The reaction exhibited clean first-order behavior over three half-lives with $k = 1.87 \pm 0.04$ h^{-1} ($t_{1/2} = 0.37$ h) at 22 ºC (Figure 3).[51]

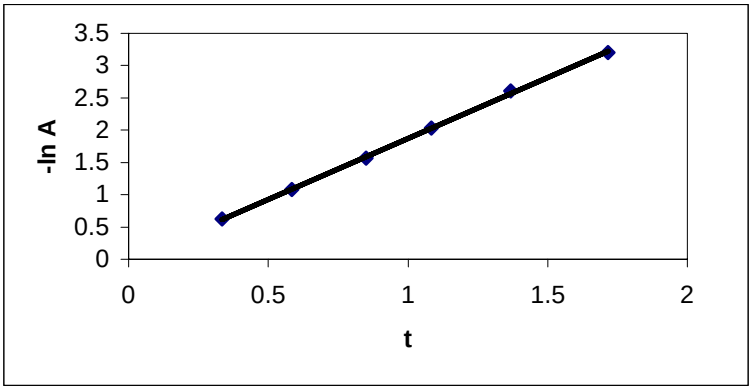


Figure 3. A Plot of -ln A versus Reaction Time t (hr) in the Case of **104a**.
A: IR absorbance at 2002 cm^{-1}

Treatment of **103b** with diphenylketene furnished **104b**, which was isolated in 71% yield. Interestingly, thermolysis of **104b** in refluxing benzene gave the benzocarbazole **109b** in 98% yield. The cascade sequence outlined in Scheme 24 with an initial formation of a five-membered ring to produce biradical **107b** followed by an intramolecular radical-radical combination to form **108b** and a subsequent tautomerization could account for the formation of **109b**. The severe nonbonded steric interactions between the *tert*-butyl group at the C-3 position and the substituent at the C-2 position of the quinoline biradical **105b** (R = *tert*-butyl) (figure 4) is probably responsible for directing the reaction toward **107b**. Such a preference resembles the formation of the five-membered ring biradicals in several analogous cases of ring closures of enyne-ketenes[19a] and enyne-allenes.[21, 51]

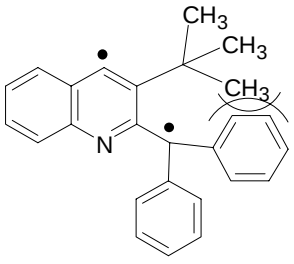


Figure 4. The Nonbonded Steric Interactions in **105b**.

Alternatively, a one-step intramolecular Diels-Alder reaction of **104b** could also produce **108b**[49b,25a,52] as reported previously by Differding and Ghosez in an elegant synthesis of carbazoles **64** by using **61** to generate in situ the acetylenic vinylketenimines **62** (Scheme 17).[25a] However, unlike **62**, a sterically demanding *tert*-butyl group is at the acetylenic terminus of **104b**. Examination of the molecular model for the transformation from **104b** to **108b** via the Diels-Alder mechanism reveals the severe nonbonded steric interactions in the transition state between the *tert*-butyl group and the phenyl group at the ketenimine terminus, making a concerted process highly unlikely (Figure 5). On the other hand, the two-step biradical

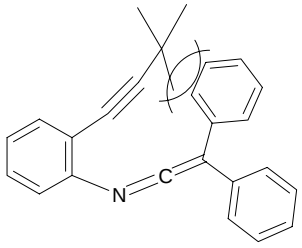


Figure 5. The Nonbonded Steric Interactions in the Diels-Alder Reaction.

mechanism permits the sterically demanding *tert*-butyl group to bend away in the first step, greatly reducing the steric interactions and allowing the reaction to occur under relatively mild thermal conditions ($k = 0.186 \pm 0.004$ h^{-1}, $t_{1/2} = 3.73$ h at 72 ºC.) (Figure 6). With the absence of an apparent proton source, it is also unlikely that the reaction could proceed through a cationic reaction mechanism involving an initial protonation of the nitrogen atom in **104b**.

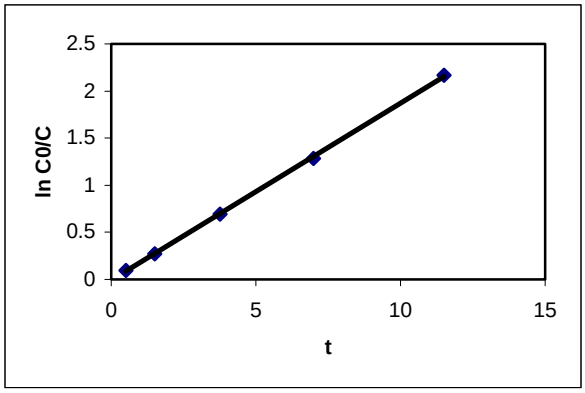


Figure 6. A Plot of ln C_0/C versus Reaction Time t (hr) in the Case of **104b**.
C_0 and C are the concentrations of reactant **104b** at t = 0 and t = t, respectively.

When **104c** (R = $SiMe_3$) was heated under refluxing benzene, the benzocarbazole **109c** was produced (k = 0.78 ± 0.06 h^{-1}, $t_{1/2}$ = 0.89 h at 72 ºC) (Figure 7).[55] The ability of the trimethylsilyl group in stabilizing the adjacent radical site in **107c**[56] along with the arising of nonbonded interactions in **105c** direct the reaction toward **109c**.

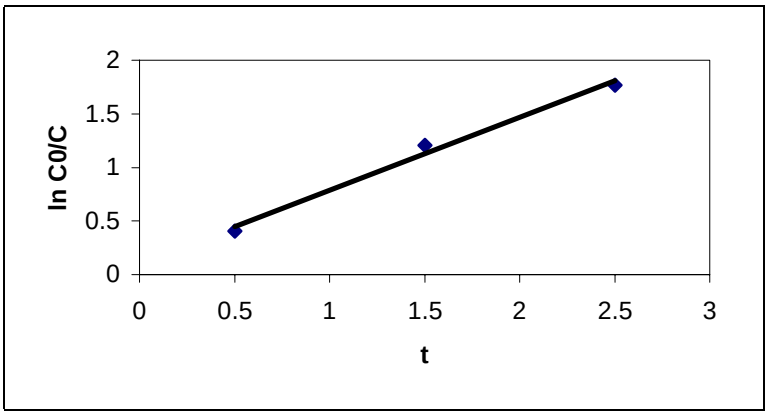


Figure 7. A Plot of ln C_0/C versus Reaction Time t (hr) in the Case of **104c**.
C_0 and C are the concentrations of reactant **104c** at t = 0 and t = t, respectively.

Thermolysis of **104d** (R = Pr) in refluxing 1,4-CHD furnished the quinoline **106d** (58%) and the benzocarbazole **109d** (33%) (*k* of the disappearance of **104d** = 1.01 ± 0.11 h^{-1}, $t_{1/2}$ = 0.69 h at 52 ºC) (Figure 8).[57] Apparently, the reaction could proceed through biradicals **105d** and

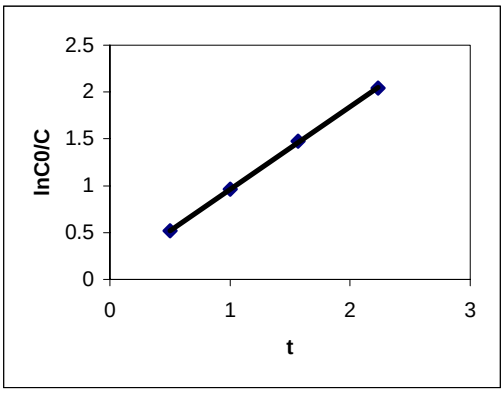
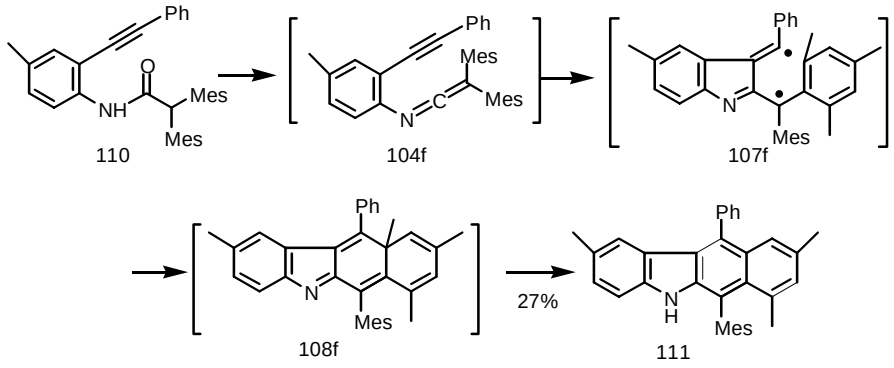


Figure 8. A Plot of ln C_0/C versus Reaction Time t (hr) in the Case of **104d**. C_0 and C are the concentrations of reactant **104d** at t = 0 and t = t, respectively.

107d with comparable efficiency. If one compares the rate of formation of **109d** (*k* = 0.36 h^{-1}, $t_{1/2}$ = 1.93 h at 52 ºC) with that of **109b**, the steric factors do not appear to affect the rate of reaction dramatically, again contrary to what would be expected of a concerted Diels-Alder mechanism. When **103e** (R = Ph) was treated with diphenylketene at room temperature for one hour, the benzocarbazole **109e** (93%) was produced exclusively. Presumably, because the phenyl substituent can further stabilize the vinyl radical site[58] in **107e**, the ketenimine **104e** was thermally labile and was readily converted to **109e**.

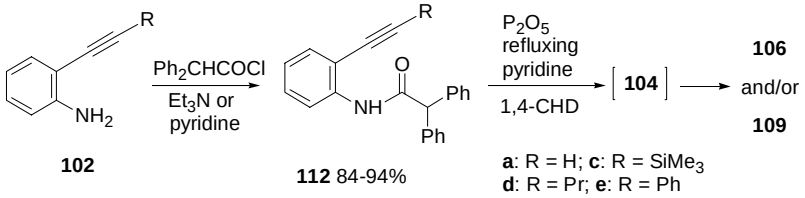
A similar study was also reported by Schmittel, Engels, and co-workers recently.[25f] To demonstrate experimentally that biradical **107f** is an intermediate, they replaced two phenyl groups at the ketenimine terminus with two bulky mesityl substituents in **104f**. The product was **111** with the loss one of the methyl groups at the ortho position (Scheme 25). The stepwise

biradical route is most likely the reaction pathway because the concerted Diels-Alder reaction suffers from severe steric hindrance.



Scheme 25. Schmittel's Observation.

Alternatively, the ketenimines **104** could also be produced in situ by dehydration of **112** with P_2O_5 in refluxing pyridine,[27] leading to **106a** (34%), **106d** (35%), **109d** (31%), and **109e** (70%) (Scheme 26). In the case of **112c** (R = $SiMe_3$), the resulting benzocarbazole **109c** is prone

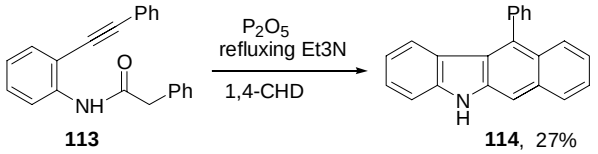


Scheme 26. One Pot Reactions Involving Ketenimine Intermediates.

to protodesilylation under the reaction condition, and a significant amount of the desilylated adduct **109a** (R = H) was produced. Treatment of the reaction mixture with 1 *N* HCl at 40 ºC for one hour completely converted **109c** to **109a**, which was isolated in an overall yield of 81% from **112c**. It is interesting to note that benzo[*b*]carbazole **109a** could not be prepared directly from the corresponding amide **112a** or the iminophosphorane **103a**, which leads to the quinoline **106a** because the corresponding key intermediate **104a** only undergoes Myers' cycloaromatization.

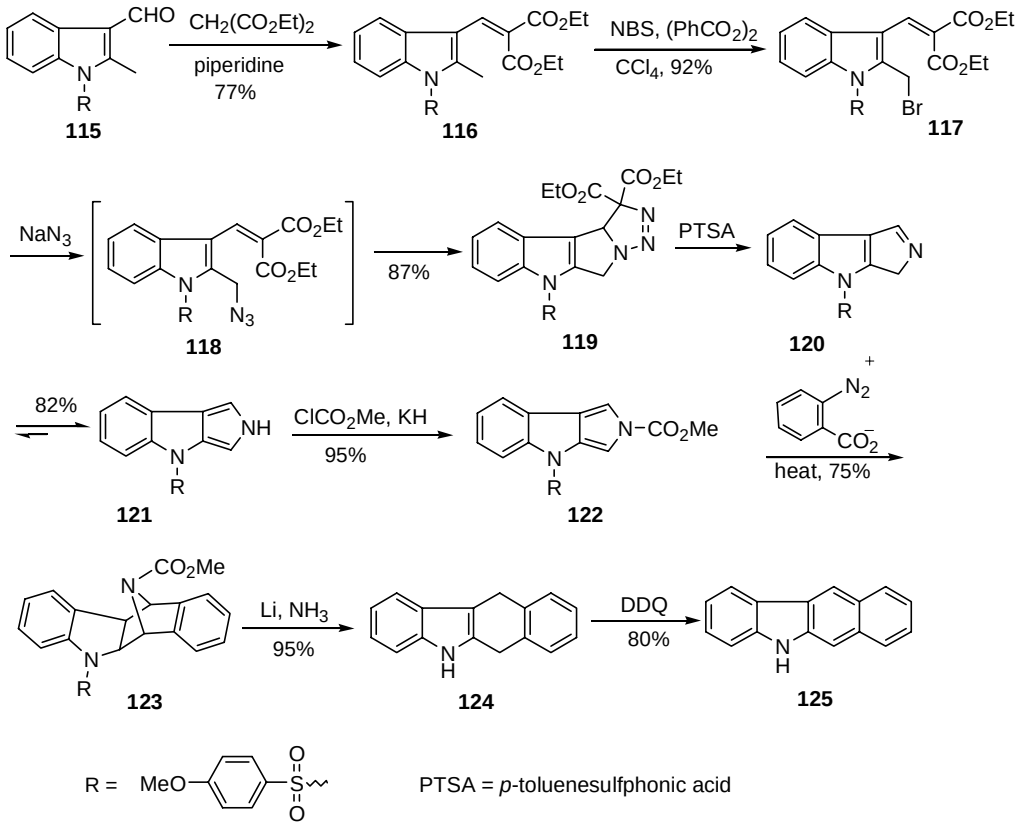
By starting from **113**, derived from acylation of **102e** with phenylacetyl chloride (97%

yield), the benzocarbazole **114** was produced in 27% isolated yield (eq 10).



113 **114**, 27% (10)

The synthetic methods for benzo[*b*]carbazoles outlined in Scheme 24 and 26 represent new and efficient routes to these heterocyclic compounds. Compared with the other reported methods, the ready availability of the starting materials and the short pathways are especially attractive features. For example, a multi-step synthetic route to benzo[*b*]carbazoles involving an intermolecular Diels-Alder reaction of 2,4-dihydropyrrolo[3,4-*b*]indole derivatives[59] (**122**) with highly reactive dienophiles, such as benzyne, was reported by Sha and co-workers (Scheme 27).[59d]



Scheme 27. Synthesis of 5*H*-Benzo[*b*]carbazole.

The structures of **103a**[49b], **104d**, **106d**, **109d**, the other quinolines and benzo[*b*]carbazoles were fully characterized by spectroscopic methods.

The ^{1}H NMR spectrum of **103a** showed a characteristic acetylenic proton signal at δ 3.34 (1 H, s) along with nineteen hydrogens in the aromatic region between δ 7.88 and 6.47. The ^{13}C NMR spectrum gave expected 12 signals as reported previously[49b]: δ 153.57 (C_1), 133.57 (C_3), 132.61 (d, $^{2}J_{P\text{-}C}$ = 9.8 Hz, C_{10}), 131.63 (d, $^{4}J_{P\text{-}C}$ = 2.6 Hz, C_{12}), 130.92 (d, $^{1}J_{P\text{-}C}$ = 99.7 Hz, C_9), 128.82 (C_4), 128.49 (d, $^{3}J_{P\text{-}C}$ = 11.9 Hz, C_{11}), 121.19 (d, $^{3}J_{P\text{-}C}$ = 9.8 Hz, C_6), 117.23 (d, $^{3}J_{P\text{-}C}$ = 23.2 Hz, C_2), 116.80 (C_5), 85.12 (C_7), 79.22 (C_8).

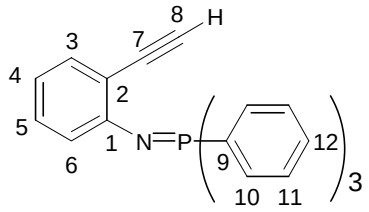


Figure 9. Numbering of **103a**.

The ketenimine intermediates exhibit characteristic IR absorption at 2000-2050 cm^{-1} (N=C=C) and ^{13}C NMR signal at δ 190-200 ppm for the central carbon of the ketenimine moiety (N=C*=C). For **104d**, a strong absorption at 2004 cm^{-1} (N=C=C) in the IR spectrum and signals at δ 189.41 (N=C*=C), 97.30 (C≡C) and 76.78 (C≡C) ppm in the ^{13}C NMR spectrum. The ^{1}H NMR spectrum of **104d** showed the characteristic propyl signals at δ 2.10 (2 H, t, *J* = 7.2 Hz), 1.47 (2 H, sextet, *J* = 7.3 Hz) and 0.94 (3 H, t, *J* = 7.4 Hz) and exhibited signals for fourteen aromatic hydrogens in the aromatic region between δ 7.49 and 7.16.

Thermolysis of **104d** gave two isolated products **106d** and **109d**. For **106d**, the mass spectrum showed the molecular ion with two mass units higher than that of the starting material **104d**, in agreement the proposed hydrogen-atom abstraction mechanism. The ^{1}H NMR spectrum showed fifteen hydrogens in the aromatic region (δ 7.49-7.16). In addition, the ^{1}H-^{13}C COSY

and ^{13}C APT NMR spectra showed eight C-H and five quaternary carbon signals in the aromatic region. The ^{1}H NMR signal at δ 7.91 (1 H, s, C_4-H) and a new alkyl C-H signal at δ 6.03 (1 H, s, C_{11}-H) as well as a ^{13}C NMR signal at δ 54.85 (C_{11}) are consistent with the structure of **106d**. The tentative assignments of chemical shifts are listed in Table 1.

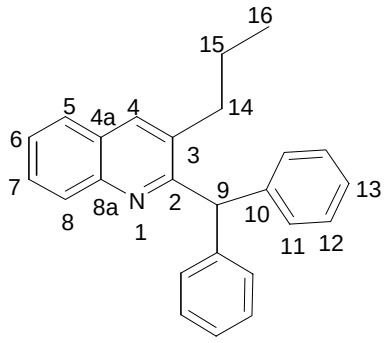


Figure 10. Numbering of **106d**.

No.	2	3	4	4a	5	6	7	8	8a
CHn	C	C	CH	C	CH	CH	CH	CH	C
H			7.91		8.03	7.62	7.48	7.76	
C	161.46	134.28	135.38	127.08	129.48	128.07	126.66	125.95	146.41
No.	9	10	11	12	13	14	15	16	
CHn	CH	C	CH	CH	CH	CH2	CH2	CH3	
H	6.03		7.4-7.2	7.4-7.2	7.4-7.2	2.85	1.74	1.05	
C	54.85	142.95	128.07	129.68	126.25	34.63	23.78	14.13	

Table 1. Tentative Chemical-Shift Assignments of NMR Spectra of **106d**.

The molecular ion of the benzo[*b*]carbazole **109d** has the same mass as the starting material **104d** (m/z 335, M^+). Except the three propyl carbons, all other carbon signals are located in the aromatic region. In the ^{1}H NMR spectrum, **109d** has one less aromatic proton, but one extra N-H signal at δ 7.82 (1 H, br s) compared with the starting material **104d**. The benzylic methylene group exhibited a triplet (δ 3.75) which was shifted downfield. The IR

spectrum also showed the N-H absorption at 3402 cm^{-1}. The tentative assignments of NMR signals are listed in Table 2 based on the ^{1}H-^{13}C COSY and ^{13}C APT NMR spectra.

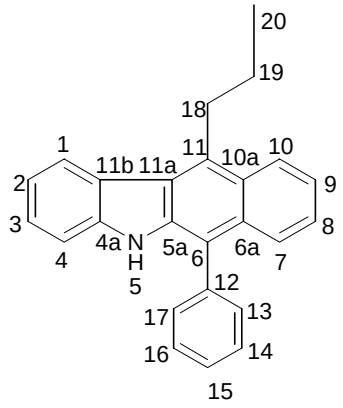


Figure 11. Numbering of **109d**.

No.	1	2	3	4	4a	5	5a	6	6a
CHn	CH	CH	CH	CH	C	NH	C	C	C
H	7.83	7.7-7.2	7.7-7.2	7.7-7.2		7. 82			
C	125	119.44	122. 39	110.05	137.39		137.05	122.61	126.88
No.	7	8	9	10	10a	11	11a	11b	12
CHn	CH	CH	CH	CH	C	C	C	C	C
H	8.38	7.7-7.2	7.7-7.2	8.28					
C	124.15	126.67	124.81	123.61	141.99	133.87	122.61	130.83	123.61
No.	13	14	15	16	17	18	19	20	
CHn	CH	CH	CH	CH	CH	CH2	CH2	CH3	
H	7.7-7.2	7.7-7.2	7.7-7.2	7.7-7.2	7.7-7.2	3.75	2.02	1.3	
C	129.22	130. 99	127.7	130.99	129.22	31.37	23.18	14.8	

Table 2. Tentative Chemical-Shift Assignments of NMR Signals of **109d**.

3.1.3 Summary

Similar to the enyne-allene system, the enyne-ketenimines **104** having a nitrogen atom in the conjugated system could serve as excellent precursors for generation of biradicals. Because of prevalence of the amide functionality in biological systems, structures similar to those of **112** are particularly attractive for the development of new DNA-cleaving agents. The cascade

sequences outlined in Schemes 24 and 26 also provide efficient and flexible alternative pathways to quinolines and 5*H*-benzo[*b*]carbazoles.[49b,59]

3.2 Biradicals from Thermolysis of *N*-[2-(1-Alkynyl)phenyl]-*N'*-phenylcarbodiimides and Their Subsequent Transformations to 6*H*-Indolo[2,3-*b*]quinolines

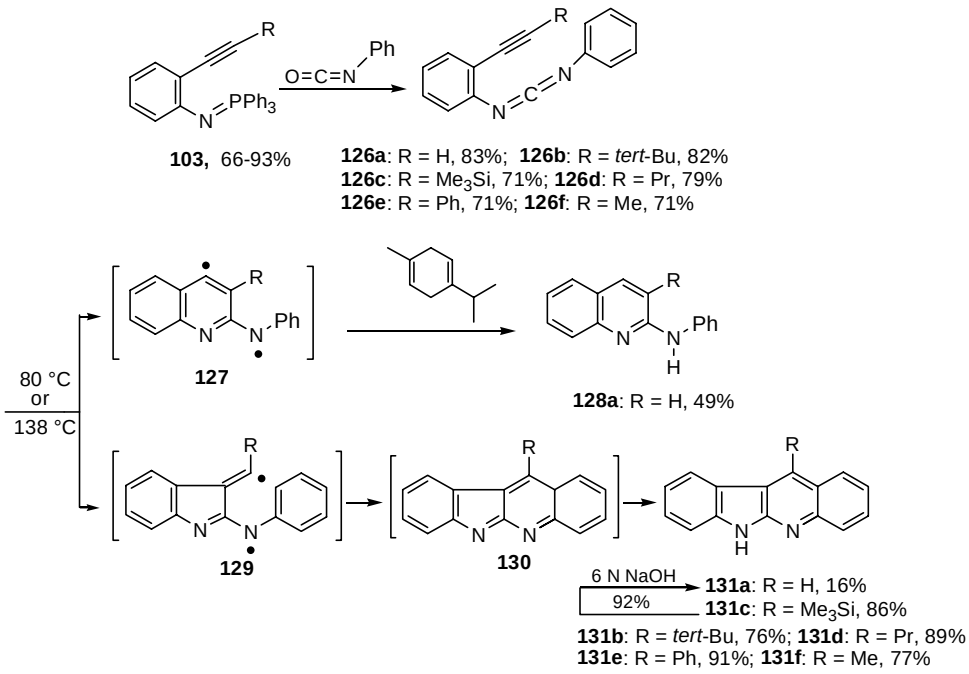
3.2. 1 General Strategy

The successful study of using the enyne-ketenimine system for biradical formation and Schmittel, Engels and co-workers' similar results demonstrate the feasibility of placing a nitrogen atom in the conjugated system for the generation of biradicals under mild thermal conditions, providing a new avenue for the design of novel DNA-cleaving agents.[1c,1d] A logical extension of this work involves replacing the ketenimine moiety in the conjugated system with other heterocumulenes. Carbodiimide appears to be an excellent candidate for such a substitution. A success of using such a system would add a new example of a growing list of the thermally-induced biradical-forming cycloaromatization reactions and provide a new approach to the synthesis of indolo[2,3-*b*]quinolines and 2-aminoquinolines. There has been a surge of interest in developing new synthetic pathways to 6*H*-indolo[2,3-*b*]quinolines[49,60] recently because several members of this group of compounds have been found to possess interesting biological activities.[61]

As mentioned earlier, many practical synthetic routes for the synthesis of carbodiimides are well documented in the literature. Among the widely cited methods, the aza-Wittig reaction between the iminophosphoranes and isocyanates is one of the most effective approaches. Condensation between the iminophosphoranes **103** and isocyanates could thus lead to the enyne-carbodiimide systems.

3.2.2 Results and Discussion

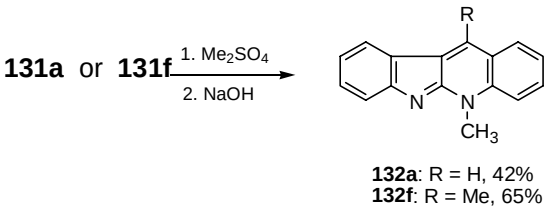
The aza-Wittig reaction between **103** and phenyl isocyanate in anhydrous benzene furnished enyne-carbodiimide **126** in good yields. Thermolysis of isolated **126** gave the 2-aminoquinoline **128** and the 6*H*-indolo[2,3-*b*]quinolines **131**.



Scheme 28. Thermolysis of Enyne-Carbodiimide **126**.

It was interesting to learn that carbodiimide **126a** had already been prepared previously by treatment of iminophosphorane **103a** (R = H) with phenyl isocyanate.[25b] Thermolysis of **126a** in toluene at 160 ºC in a sealed tube furnished 2-(phenylamino)quinoline (**128a**, 40%) and the parent 6*H*-indolo[2,3-*b*]quinoline (**131a**, 19%).[25b] We were able to reproduce similar results by heating **126a**, isolated in 83% yield from treatment of **103a** with phenyl isocyanate, in γ-terpinene at 138 ºC to afford **128a** (49%) and **131a** (16%). Apparently, **128a** was produced via the biradical **127a** followed by hydrogen-atom abstraction from γ-terpinene. A two-step biradical pathway through **129a** or a one-step intramolecular Diels-Alder reaction could furnish **130a**, which then underwent tautomerization to give **131a**. Several analogous examples in which

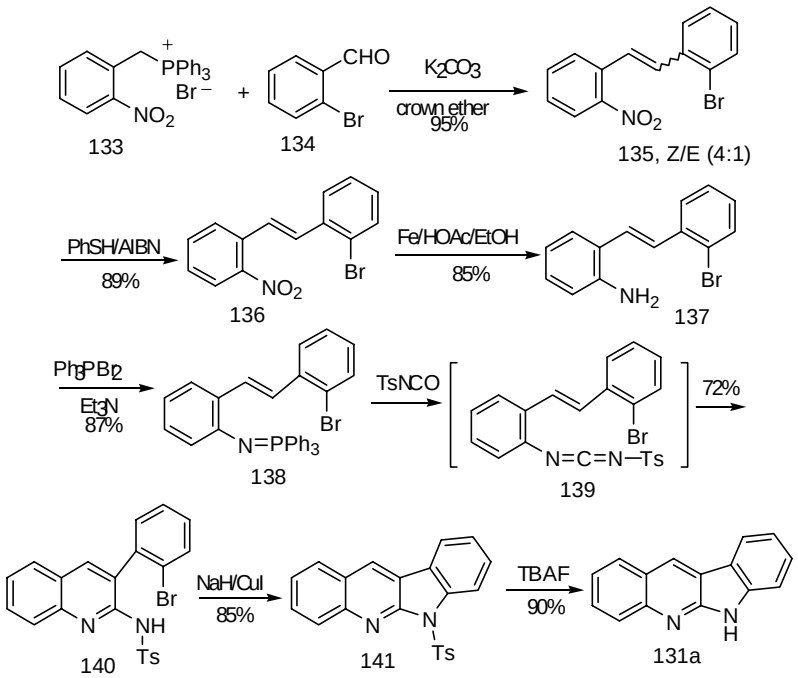
a carbon-carbon double bond replaces the triple bond in **126** for the intramolecular Diels-Alder reaction have been reported.[49,60] The indoloquinoline **131a** was used as an immediate precursor for the synthesis of a naturally occurring alkaloid, 5-methyl-5*H*-indolo[2,3-*b*]quinoline (**132a**) (eq 11),[25b,61] which was isolated from the roots of the West African plant *Cryptolepis sanguinolenta*[62] and was found to possess interesting biological activities.[61]



(11)

132a: R = H, 42%
132f: R = Me, 65%

Molina and co-workers reported a useful and efficient synthesis of **131a** (Scheme 29)[63] as an alternative to the synthetic method outlined in Scheme 28. However, it is lengthy, involving multiple steps.



Scheme 29. Molina's Synthesis of **131a**.

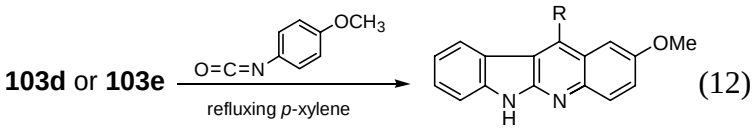
The reaction sequence outlined in Scheme 28 could provide a more efficient route to the indoloquinoline **131a** if the competing pathway toward the quinoline **128a** could be suppressed. The result with **126c** suggests that a trimethylsilyl group at the acetylenic terminus could serve as a surrogate for the hydrogen atom in directing the reaction toward the indoloquinoline **131c**. A subsequent protodesilylation reaction could lead to **131a**. It was gratifying to observe that thermolysis of **126c**, obtained in 71% from **103c** and phenyl isocyanate, in refluxing *p*-xylene at 138 ºC produced **131c** in 86% yield. Similarly, heating the reaction mixture of **103c** and phenyl isocyanate in refluxing *p*-xylene without isolation of **126c** also gave **131c** (61%) in a single operation. Treatment of **131c** with 6 N NaOH in refluxing ethanol for 12 h then furnished **131a** in 92% yield.

When **126f** was subjected to thermolysis in *p*-xylene at 138 ºC for 4 h, the indoloquinoline **131f** (77%) was produced exclusively, indicating a preferential formation of **130f** for subsequent tautomerization to **131f**. The corresponding quinoline **128f** (R = Me) was not detected. Direct thermolysis of the reaction mixture of **103f** and phenyl isocyanate in refluxing *p*-xylene without isolation of **126f** also afforded **131f** (59%) in a single operation. It was reported that **131f** could serve as the immediate precursor of 5,11-dimethyl-5*H*-indolo[2,3-*b*]quinoline (**132f**) (eq 10), which was found to display a strong antibacterial, antimycotic, and cytotoxic activity *in vitro*, as well as significant antitumor properties *in vivo*.[61]

Similarly, when **126d** having a propyl group at the acetylenic terminus was heated either in refluxing *p*-xylene or in γ-terpinene at 138 ºC, the indoloquinoline **131d** (89%) was produced exclusively, in sharp contrast to the ketenimine **104d** (R = Pr) which furnished the quinoline **106d** preferentially. In addition, the carbodiimide **126d** is thermally less labile than the ketenimine **104d**, and a higher temperature is needed to promote the reaction. Treatment of

103d with phenyl isocyanate in refluxing *p*-xylene without isolation of **126d** also afforded **131d** directly in a one-step operation in 72% yield. With **126b** having a sterically very demanding *tert*-butyl group, thermolysis in refluxing *p*-xylene for 14 h produced the indoloquinoline **131b** (76%). Again, the presence of a *tert*-butyl group at the acetylenic terminus of **126b** makes the formation of **130b** via the concerted intramolecular Diels-Alder reaction unlikely. With a phenyl substituent at the acetylenic terminus of **126e**, thermolysis under refluxing benzene (80 ºC) for 4 h was sufficient to induce the transformation to **131e**[58] in 91% yield. Direct thermolysis of the reaction mixture of **103e** and phenyl isocyanate in refluxing benzene without isolation of **126e** also afforded **131e** in 67% yield.

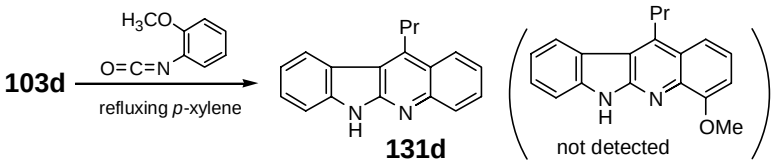
4-Methoxyphenyl isocyanate was also used for the aza-Wittig reaction with **103d** and **103e**. Thermolysis of the reaction mixtures furnished the indoloquinolines **142d** and **142e**[49b] having a methoxy substituent at the C-2 position (eq 12).



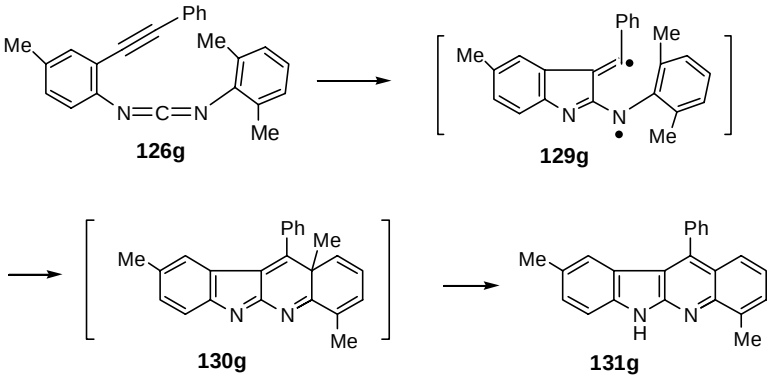
(12)

142d: R = Pr, 47%
142e: R = Ph, 55%

Surprisingly, when 2-methoxyphenyl isocyanate was used for the aza-Wittig reaction with **103d**, the thermolysis product was **131d** C- with the loss of the methoxyl group. The indoloquinoline product having a methoxyl substituent at the 4 position was not detected (eq 13). The observation of the loss of the methoxyl group is consistent with the report by Schmittel, Engels and co-workers as outlined in Scheme 30.[25g] Thermolysis of enyne-carbodiimide **126g** in toluene in the presence of 1,4-CHD afforded **131g** with the loss of one methyl group.

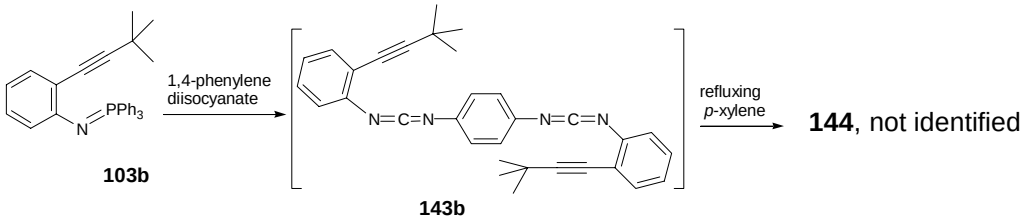


(13)

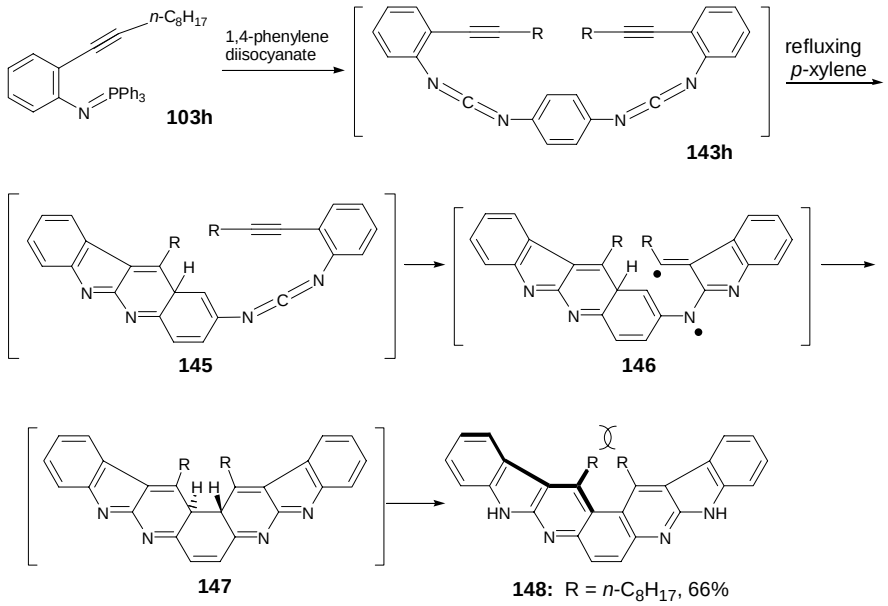


Scheme 30. Thermolysis of Enyne-Carbodiimide **126g**.

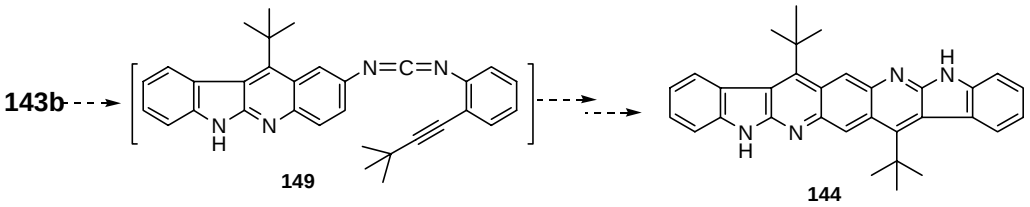
Treatment of 1,4-phenylene diisocyanate with two equiv of **103b** for the aza-Wittig reaction produced **143b** in situ, which on thermolysis in refluxing *p*-xylene furnished a solid product **144** (Scheme 31). A signal at *m/z* = 470.2464, corresponding to a rearranged product of **143b**, was detected on a high-resolution mass spectrometer. Because of its extremely poor solubility in organic solvents (DMSO, CF_3CO_2H, DMF, MeOH, etc.), we were not able to identify its structure. In an analogous study, Quan Zhang of our group synthesized **148** (Scheme 32).[25d] The presence of the two *n*-octyl groups in **148** greatly enhances its solubility in organic solvents. However, because the *tert*-butyl groups in **143b** are sterically more demanding, it is not clear whether a structure similar to **148** with R being *tert*-butyl is possible from thermolysis of **143b**. Another possible structure for **144** is shown in Scheme 33. Tautomerization of **145** (R= *t*-Bu) could lead to **149**, which could lead to the linearly fused system **144**.



Scheme 31. Thermolysis of **143b**.



Scheme 32. Thermolysis of **143h**.



Scheme 33. Proposed Structure of **144**.

The structures of **126** and **131** were characterized by spectroscopic methods.

Generally speaking, the characteristic signals for carbodiimides include IR absorptions around 2150-2100 cm^{-1} for N=C=N and the ^{13}C NMR signal around δ 140 ppm for N=C=N. For **126d**, it showed strong absorptions at 2143 and 2107 cm^{-1} (N=C=N) in the IR spectrum. The HRMS (m/z 260.1312, M^+) indicates that it has a molecular formula of $C_{18}H_{16}N_2$. The ^1H NMR spectrum of **126d** showed the characteristic propyl signals at δ 2.10 (2 H, t, J = 7.2 Hz), 1.46 (2 H, sextet, J = 7.3 Hz) and 0.93 (3 H, t, J = 7.3 Hz) and signals for nine aromatic hydrogens between δ 7.44 and 7.08. The tentative chemical-shift assignments for the ^{13}C NMR spectrum of **126d** are as following: δ 139.16 (C_1), 138.72 (C_8), 133.65 (C_7), 133.01 (C_3), 129.25 (C_{10}), 128.39

(C_5), 125.12 (C_4), 125.05 (C_6), 124.25 (C_{11}), 124.19 (C_9), 120.78 (C_2), 98.70 (C_{13}), 76.87 (C_{12}), 21.69 (C_{14}), 21.53 (C_{15}), 13.40 (C_{16}).

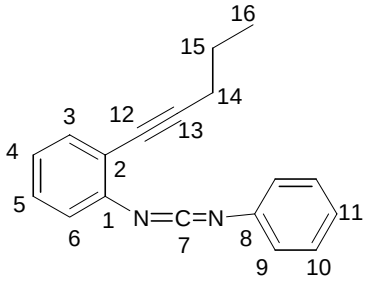


Figure 12. Numbering of **126d**.

The molecular ion of the 6*H*-indolo[2,3-*b*]quinoline **131d** has the same mass as the starting material **126d** (m/z 260, M^+). The elemental also analysis indicated its molecular formula as $C_{18}H_{16}N_2$. The IR spectrum showed the N-H absorption at 3455 cm^{-1}. In the ^1H NMR spectrum, **131d** has one less aromatic hydrogen, but one extra N-H signal at δ 12.23 (1 H, br s) ppm compared with the starting material **126d**. The benzylic methylene group exhibited a triplet at δ 3.65 ppm, which was shifted downfield. Except the three propyl carbons, all other carbon signals are located in the aromatic region. The tentative assignments of NMR signals are listed in Table 3 based on the ^1H and ^{13}C APT NMR spectra.

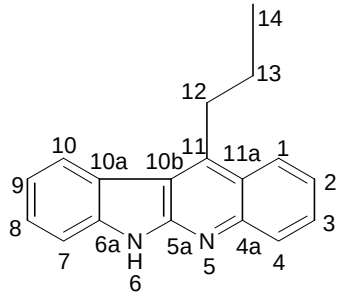


Figure 13. Numbering of **131d**.

No.	1	2	3	4	4a	5a	6
CHn	CH	CH	CH	CH	C	C	NH
H	8.22	7.6-7.48	7.6-7.48	8.3			12.23
C	128.71	123.41	124.17	127.45	146.26	153.44	
No.	6a	7	8	9	10	10a	10b
CHn	C	CH	CH	CH	CH	C	C
H		8.17	7.6-7.48	7.31	7.77		
C	144.31	110.93	127.04	119.99	122.67	121.39	116.63
No.	11	11a	12	13	14		
CHn	C	C	CH2	CH2	CH3		
H			3.65	1.98	1.24		
C	141.38	123.41	30.93	22.92	14.7		

Table 3. Tentative Chemical-Shift Assignments of NMR Spectra of **131d**.

3.2.3 Summary

Thermolysis of the carbodiimides 126 represents a new way of generating biradicals from unsaturated molecules having two nitrogen atoms in the conjugated system. The cascade sequence outlined in Scheme 28 also provides a general and efficient pathway to 6*H*-indolo[2,3-*b*]quinolines. The possibility of placing a wide variety of substituents at various positions of the 6*H*-indolo[2,3-*b*]quinoline structure by selecting suitable fragments for assembly is an especially attractive feature of this synthetic route.

3.3 Synthesis of 6*H*-Indolo[2,3-*b*][1,6]naphthyridines and Related Compounds as the 5-Aza Analogues of Ellipticine Alkaloids

3.3.1 General Strategy

Ellipticine **150** and 9-methoxyellipticine **151** are two naturally occurring 6*H*-pyrido[4,3-*b*]carbazole alkaloids isolated from the leaves of *Ochrosia elliptica* Labill (family Apocynaceae) (Figure 13).[65] The discovery of their antitumor activities in 1967[66] has led to an explosion of synthetic, biological, and pharmacological studies of ellipticine and its derivatives.[67] Several

ellipticine derivatives have been used in clinical trials.[67a–c] More recently, 5-methyl-5*H*-indolo[2,3-*b*]quinoline **132a**, an indoloquinoline alkaloid isolated from the West African plant *Cryptolepis sanguinolenta*,[68] was reported to display a strong antiplasmodial activity.[69] Similarly, **132f** having a methyl substituent at the C11 position exhibited a strong

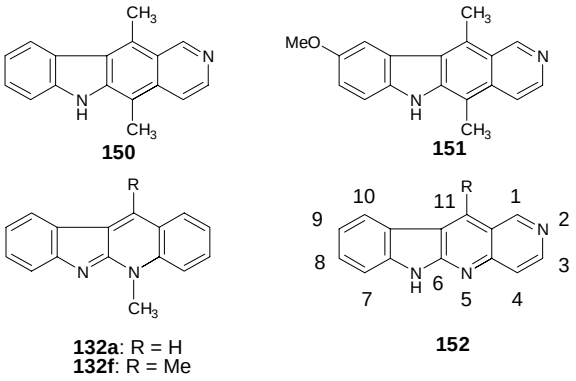
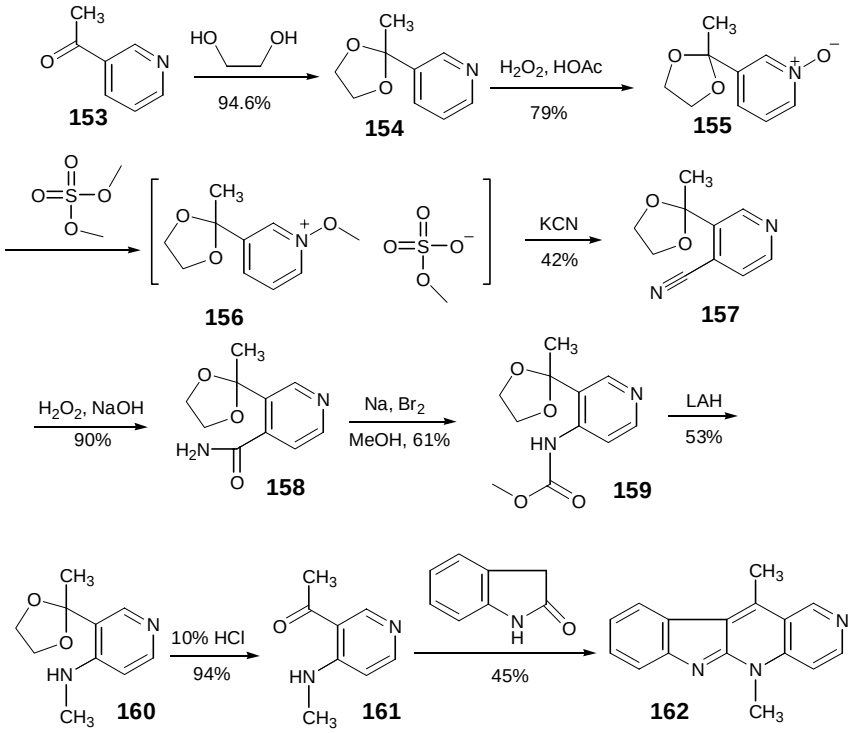


Figure 14. Structure Comparison.

antibacterial, antimycotic, and cytotoxic activity *in vitro* as well as significant antitumor properties *in vivo*.[61a] Methylation of 6*H*-indolo[2,3-*b*]quinolines **131** with dimethyl sulfate followed by treatment with sodium hydroxide led to **132** directly (eq 11).[25b,61,63] The interesting biological activities of ellipticines and indoloquinolines prompted us to develop a new synthetic route to the 6*H*-indolo[2,3-*b*][1,6]naphthyridines **152**, which could be regarded as the 5-aza analogues of ellipticines merging the heterocyclic frameworks of both ellipticine and indoloquinoline. Only one synthetic route involving a seven-step synthesis of 3-acetyl-4-(methylamino)pyridine from 3-acetylpyridine followed by condensation with oxindole to form 5,11-dimethyl-*5H*-indolo[2,3-*b*][1,6]naphthyridine as the 5-aza analogue of ellipticine had been reported previously (Scheme 34).[70]

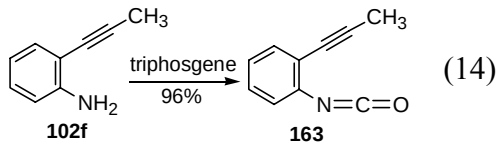


Scheme 34. Synthesis of 5,11-Dimethyl-5*H*-indolo[2,3-*b*][1,6]naphthyridine.

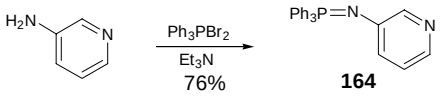
The efficient synthetic route to the 6*H*-indolo[2,3-*b*]quinolines **131** via thermolysis of the benzoenynyl carbodiimides **126** outlined in Scheme 28 could be adopted for the synthesis of **152** and related compounds.[25d] We envisioned that by replacing the phenyl group in the iminophosphorane with a pyridyl group, the similar synthetic sequence could lead to a variety of indolonaphthyridines as the 5-aza analogues of ellipticines and the much less studied isoellipticines[71] in which the pyridine nitrogen is at a different ring D position.

3.3.2 Results and Discussion

Treatment of **102f** with triphosgene provided 2-(1-propynyl)phenyl isocyanate **163** in 96% yield (eq 14).[72] The iminophosphorane **164** was prepared by treatment of 3-aminopyridine with dibromotriphenylphosphorane (Ph_3PBr_2) in 76% yield in a single step (eq 15).[73]

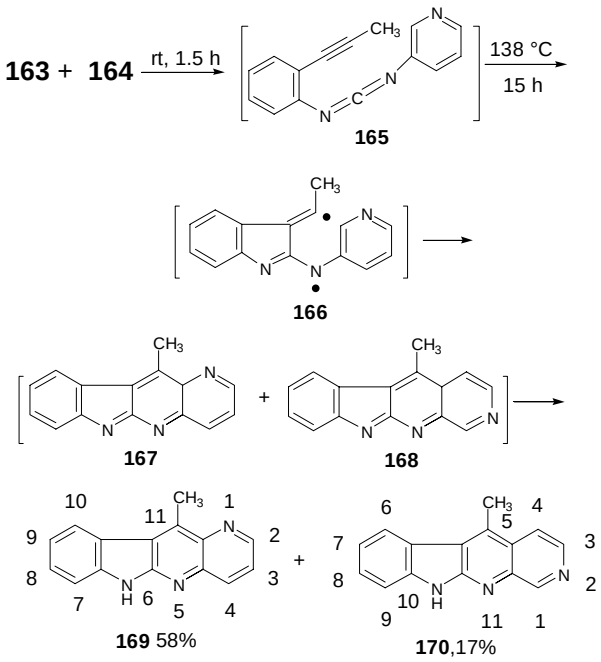


102f **163** (14)



164 (15)

The aza-Wittig reaction between **163** and **164** produced in situ the benzoenynyl carbodiimides **165** (Scheme 35). Thermolysis of **165** under refluxing *p*-xylene then furnished the

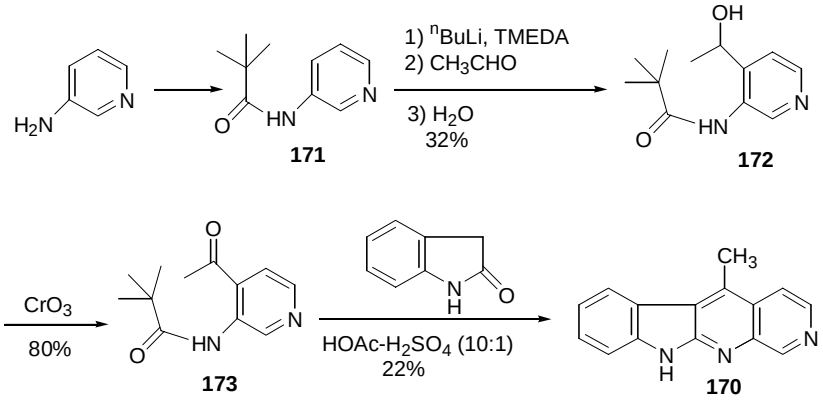


Scheme 35. Thermolysis of of Benzoenynyl Carbodiimides **165**.

6*H*-indolo[2,3-*b*][1,5]naphthyridines **169** as the major isomer and the 10*H*-indolo[2,3-*b*][1,7]naphthyridines **170** as the minor isomer. Apparently, cyclization of **165** furnished the formal Diels-Alder adducts **167** preferentially, leading to **169** as the major isomer. The reason for such a preference is not clear at this time. The structures of **169** and **170** represent two rare heterocyclic systems that could be regarded as the aza analogues of isoellipticines.

There was only one earlier report of a indolonaphthyridine derivative having the

heterocyclic structure of **169**.[74] The indolonaphthyridine **170** was previously synthesized by condensation of 4-acetyl-3-pivaloylaminopyridine (**171**) with oxindole (Scheme 36).[75]



Scheme 36. Synthesis of Indolonaphthyridine **170**.

Similarly, Quan Zhang successfully synthesized **152** by treatment of **163** and its analogues with *N*-(4-pyridylimino)triphenylphosphorane.[25e] It is worth noting that the synthetic sequence outlined in Scheme 35 allows easy introduction of a variety substituents as the R group at the C11 position of **169** or at the C5 position of **170** and similarly at the C11 position of **152** by using *N*-(4-pyridylimino)triphenylphosphorane for condensation.

The structures of **169** and **170** were characterized by spectroscopic methods. For **169**, both elemental analysis and HRMS (m/z 233.0954, M^+) indicated its molecular formula as $C_{15}H_{11}N_3$. The ^{1}H NMR spectrum of **169** clearly showed nine aromatic hydrogens and a methyl group at δ 3.37 (3 H, s) ppm, which was shifted downfield. The ^{13}C NMR spectrum of **169** indicated fourteen carbons in the aromatic region and one methyl group. The tentative assignments of the NMR signals are listed in Table 4 based on the ^{1}H and ^{13}C APT NMR spectra.

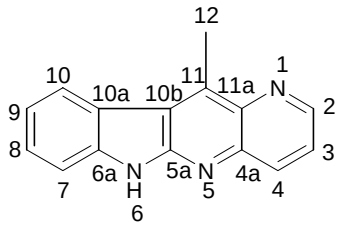


Figure 15. Numbering of **169**.

No.	2	3	4	4a	5a	6
CHn	CH	CH	CH	C	C	NH
H	8.95	7.62	8.33			9.73
C	146.2	124	128.1	139	152.1	
No.	6a	7	8	9	10	
CHn	C	CH	CH	CH	CH	
H		7.5	7.35	7.55	8.3	
C	140	110.9	135	120	123.5	
No.	10a	10b	11	11a	12	
CHn	C	C	C	C	CH3	
H					3.37	
C	121	118.6	141.7	141.3	13.4	

Table 4. Tentative Chemical-Shift Assignments of NMR Spectra of **169**.

Compound **170** is the isomer of **169** and the signal at δ 9.32 (1 H, s) ppm in its ^{1}H NMR spectrum distinguished **170** from **169**. The tentative chemical-shifts assignments are listed in Table 5 based on the ^{1}H and ^{13}C APT NMR spectra.

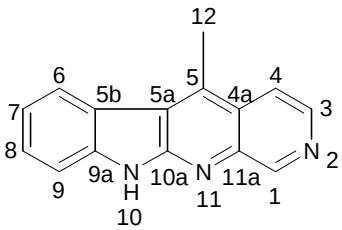


Figure 16. Numbering of **170**.

No.	1	3	4	4a	5	5a
CHn	CH	CH	CH	C	C	C
H	9.32	8.51	8.21			
C	151.7	139.6	120.1	120.4	137.8	117
No.	5b	6	7	8	9	
CHn	C	CH	CH	CH	CH	
H		7.54	7.32	7.6	8.39	
C	119.1	124.5	120.1	128.7	111	
No.	9a	10	10a	11a	12	
CHn	C	NH	C	C	CH3	
H		11.97			3.18	
C	142		152.8	126.3	14.4	

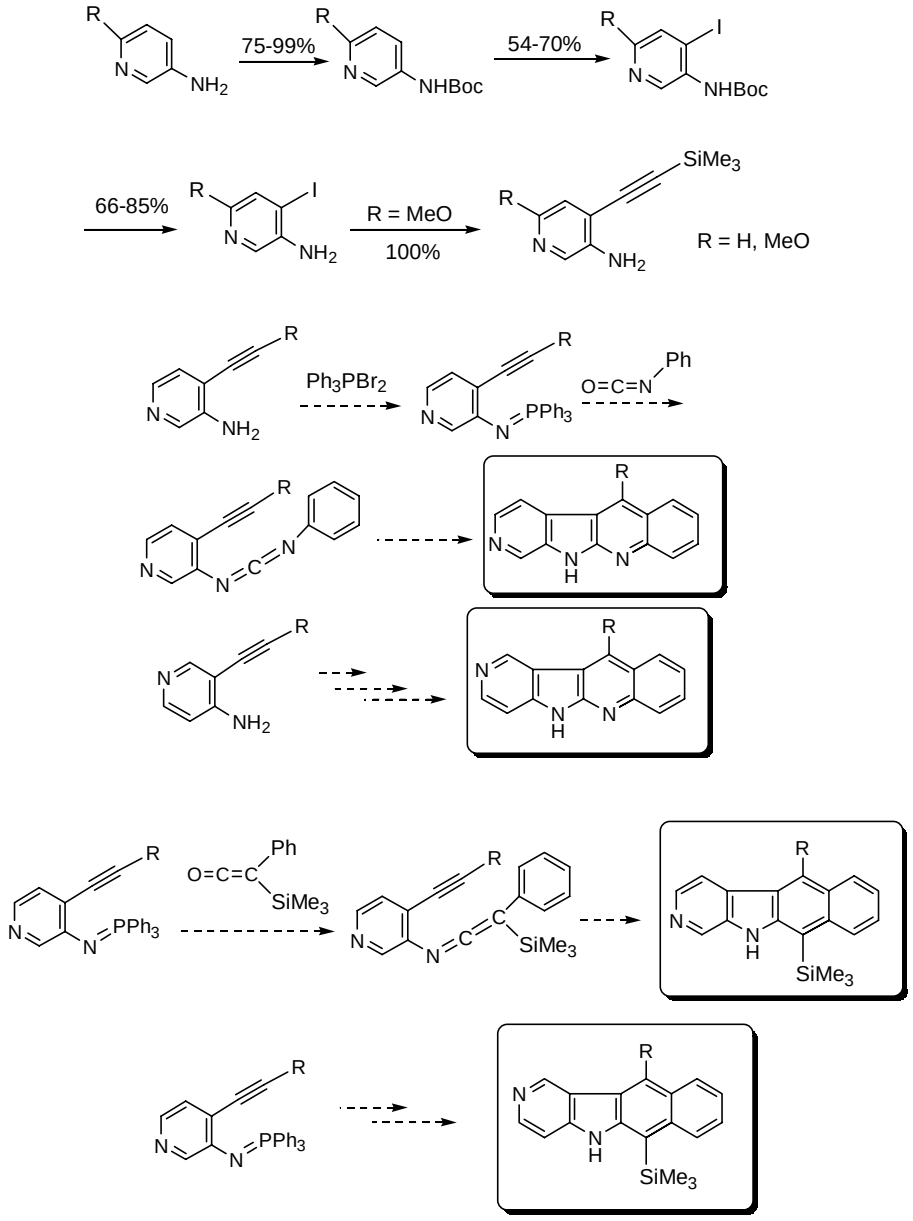
Table 5. Tentative Chemical-Shift Assignments of NMR Spectra of **170**.

3.3.3 Summary

A new and efficient synthetic pathway to indolonaphthyridines has been developed. The synthetic route is convergent and allows easy placement of a variety of substituents around the periphery of the heterocyclic ring system. The structures of indolonaphthyridines resemble those of ellipticine alkaloids, making them good candidates as DNA intercalating agents with potentially interesting biological activities.

4. Conclusion

The thermal behaviors of enyne-ketenimines and enyne-carbodiimides are very similar to those of the corresponding enyne-allenes and enyne-ketenes. There are two competing pathways for the biradical cyclization reaction mainly depending on the nature of substitution at the alkyne terminus. On the bases of our preliminary studies, the enyne-ketenimines and enyne-carbodiimides without substitution at the alkyne terminus tend to undergo Myers-like cycloaromatization reactions and give the quinoline derivatives as the major products. With a small and unbranched alkyl group attached to the alkyne terminus, such as methyl and propyl groups, the benzoenynyl ketenimines favor the Myers-like cycloaromatization. On the other hand, the benzoenynyl carbodiimides are thermally more inert and favor the formation of biradicals **129**. The biradical-forming reactions of enyne-ketenimines and enyne-carbodiimides provide efficient synthetic routes to: (i) the quinolines and 5*H*-benzo[*b*]carbazoles **109** via thermolysis of benzoenynyl ketenimines; (ii) 6*H*-indolo[2,3-*b*]quinolines **131** via thermolysis of benzoenynyl carbodiimides and (iii) indolonaphthyridines. In addition, the flexible nature of the synthesis plan should provide access to a diverse array of alkaloids. The methodology described herein could also find potential applications for the synthesis of other biologically interesting heterocycles, such as benzo[*f*]pyridoindoles[76] and pyridopyrrolo[5,4-*b*]quinolines[77,78] as outlined in Scheme 37.



Scheme 37. Potential Applications in the Synthesis of Benzo[*f*]pyridoindoles and Pyridopyrroloquinolines.

5. Experimental Section

General procedures. Diethyl ether and tetrahydrofuran (THF) were distilled from benzophenone ketyl prior to use. Pyridine and triethylamine were distilled over CaH_2 prior to use. The 2-(1-alkynyl)anilines **102** (83-100% yield),[48] iminophosphoranes **103**[49a] and **164**[67] were prepared according to the reported procedure. Diphenylketene was prepared by dehydrochlorination of diphenylacetyl chloride as reported previously.[50] 2-Iodoaniline was purchased from Oakwood Products, Inc. and was used as received. 1-Alkynes were obtained from Farchan Laboratories, Inc. and were used without further purification. Dibromotriphenylphosphorane (Ph_3PBr_2), phenylacetyl chloride, diphenylacetyl chloride, triphosgene, 3-aminopyridine, $Pd(PPh_3)_2Cl_2$, 1,4-CHD, phenyl isocyanate, 4-methoxyphenyl isocyanate, 1,4-phenylene diisocyanate, $Pd(PPh_3)_4$, *p*-xylene (anhydrous), *N*,*N*-dimethylformamide (DMF), *N*,*N*-diisopropylethylamine, and γ-terpinene were purchased from Aldrich. The kinetic studies were carried out in a constant-temperature bath (± 0.5 ºC) and error bounds are quoted as 2σ. Melting points were uncorrected. ^{1}H (270 MHz) and ^{13}C (67.9 MHz) NMR spectra were recorded in $CDCl_3$ on a JEOL-GX-270 NMR spectrometer using $CHCl_3$ (^{1}H δ 7.26) or $CDCl_3$ (^{13}C δ 77.00) as the internal standard. IR spectra were taken on Perkin-Elmer 1600 FT-IR spectrometer. Mass-spectra were obtained on Hewlett Packard 5970B GC/MSD instrument at 70 eV.

All reactions were conducted in oven-dried (120 ^{o}C) glassware under a nitrogen atmosphere.

2-(1-Propynyl)aniline (102f). A suspension of 2.190 g of 2-iodoaniline (10.0 mmol), 0.190 g of copper(I) iodide (1.00 mmol), and 0.562 g of $Pd(PPh_3)_2Cl_2$ (0.800 mmol) in 50 mL of triethylamine was cooled to -78 ^{o}C under a nitrogen atmosphere and degassed by freeze-pump-

thaw. After the reaction mixture was allowed to warm to rt, 672 mL of gaseous propyne (27 mmol) was introduced with a gas-tight syringe, and the resulting mixture was stirred at rt for 27 h. The reaction mixture was then concentrated, and 200 mL of diethyl ether was added. The solid suspension was removed by filtration, and the filtrate was washed with water, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/10% diethyl ether in hexanes) to furnish 1.310 g of **102f** (10.0 mmol, 100%) as a yellow oil: IR (neat) 3469, 3374, 2044, 1614, 749 cm^{-1}; ^1H δ 7.25 (1 H, dd, *J* = 8.2 and 1.5 Hz), 7.08 (1 H, td, *J* = 7.7 and 1.5 Hz), 6.69-6.64 (2 H, m), 4.18 (2 H, br s), 2.11 (3 H, s); ^{13}C δ 147.61, 131.92, 128.74, 117.76, 114.10, 108.85, 90.96, 76.13, 4.51; MS *m/z* 131 (M^+), 130, 103, 77.

2-Ethynyl-*N*-(triphenylphosphoranylidene)benzenamine (103a).[49b] Iminophosphorane **103a** was prepared according to the reported procedure.[49a] To 3.798 g of Ph_3PBr_2 (9.00 mmol) was added a mixture of 1.053 g of 2-ethynylaniline (**102a**, 9.00 mmol) and 2.5 mL of anhydrous triethylamine in 100 mL of anhydrous benzene via cannula under a nitrogen atmosphere. The reaction mixture was heated under reflux for 4 hours. The white triethylammonium bromide precipitate was removed by filtration, and the filtrate was concentrated *in vacuo*. The residue was purified through a short column (silica gel/40-60% diethyl ether in hexanes) to furnish 2.239 g (5.94 mmol, 66%) of **103a** as colorless crystals: mp 142-143 ºC (lit.[49b] 141 ºC); IR (KBr) 3279, 2094, 1584, 1479, 1436, 1368, 1110, 750, 715 cm^{-1}; ^1H δ 7.88-7.80 (6 H, m), 7.56-7.39 (10 H, m), 6.87 (1 H, td, *J* = 7.7 and 1.6 Hz), 6.59 (1 H, t, *J* = 7.4 Hz), 6.47 (1 H, d, *J* = 8.1 Hz), 3.34 (1 H, s); ^{13}C δ 153.57, 133.57, 132.61 (d, *J* = 9.8 Hz), 131.63 (d, *J* = 2.6 Hz), 130.92 (d, *J* = 99.7 Hz), 128.82, 128.49 (d, *J* = 11.9 Hz), 121.19 (d, *J* = 9.8 Hz), 117.23 (d, *J* = 23.2 Hz), 116.80, 85.12, 79.22.

2-(3,3-Dimethyl-1-butynyl)-*N*-(triphenylphosphoranylidene)benzenamine (103b). The same procedure was repeated as described for **103a** except that a mixture of 1.557 g of 2-(3,3-dimethyl-1-butynyl)aniline (**102b**, 9.00 mmol), 3.798 g of Ph_3PBr_2 (9.00 mmol), and 2.5 mL of anhydrous triethylamine in 100 mL of anhydrous benzene was heated under reflux for 4 hours to afford 3.352 g of **103b** (7.74 mmol, 86%) as colorless crystals: mp 111-112 ^oC; IR (KBr) 1583, 1477, 1438, 1347, 1112, 748, 714, 694 cm^{-1}; ^1H δ 7.91-7.82 (6 H, m), 7.56-7.40 (9 H, m), 7.32 (1 H, dt, *J* = 7.7 and 2.1 Hz), 6.79 (1 H, tm, *J* = 7.7 and 1.7 Hz), 6.57 (1 H, tt, *J* = 7.4 and 1 Hz), 6.44 (1 H, dt, *J* = 7.9 and 1.1 Hz), 1.41 (9 H, s); ^{13}C δ 152.13, 133.19, 132.72 (d, *J* = 9.3 Hz), 131.48 (d, *J* = 2.6 Hz), 131.45 (d, *J* = 100.0 Hz), 128.37 (d, *J* = 12.4 Hz), 127.55, 121.27 (d, *J* = 8.8 Hz), 119.34 (d, *J* = 22.8 Hz), 117.01, 100.28, 79.78, 31.48, 28.24.

2-[(Trimethylsilyl)ethynyl]-*N*-(triphenylphosphoranylidene)benzenamine (103c). The same procedure was repeated as described for **103a** except that a mixture of 1.890 g of 2-[(trimethylsilyl)ethynyl]aniline (**102c**, 10.0 mmol), 4.220 g of Ph_3PBr_2 (10.0 mmol), and 2.8 mL of anhydrous triethylamine in 100 mL of anhydrous benzene was heated under reflux for 4 hours to afford 3.323 g of **103c** (7.40 mmol, 74%) as colorless crystals: mp 107-108 ^oC; IR (KBr) 2146, 1583, 1475, 1437, 1348, 1108, 870, 741, 714, 691 cm^{-1}; ^1H δ 7.88-7.80 (6 H, m), 7.56-7.36 (10 H, m), 6.83 (1 H, ddd, *J* = 7.7, 7.3, and 1.7 Hz), 6.56 (1 H, t, *J* = 7.4 Hz), 6.44 (1 H, d, *J* = 7.9 Hz), 0.30 (9 H, s); ^{13}C δ 153.29, 133.67, 132.72 (d, *J* = 9.8 Hz), 131.61 (d, *J* = 2.6 Hz), 131.16 (d, *J* = 100.5 Hz), 128.69, 128.47 (d, *J* = 11.9 Hz), 121.27 (d, *J* = 9.3 Hz), 118.31 (d, *J* = 23.3 Hz), 116.89, 106.86, 95.48, 0.44.

2-(1-Pentynyl)-*N*-(triphenylphosphoranylidene)benzenamine (103d). The same procedure was repeated as described for **103a** except that a mixture of 1.590 g of 2-(1-pentynyl)aniline (**102d**, 10.0 mmol), 4.220 g of Ph_3PBr_2 (10.0 mmol), and 2.8 mL of anhydrous triethylamine in

100 mL of anhydrous benzene was heated under reflux for 4 hours to afford 3.897 g of **103d** (9.30 mmol, 93%) as colorless crystals: mp 141-142 ^{o}C; IR (KBr) 2136, 1582, 1476, 1438, 1348, 1109, 749, 719, 693 cm^{-1}; ^{1}H δ 7.88-7.80 (6 H, m), 7.55-7.40 (9 H, m), 7.33 (1 H, dt, *J* = 7.7 and 2.0 Hz), 6.81 (1 H, td, *J* = 7.7 and 1.7 Hz), 6.58 (1 H, t, *J* = 7.4 Hz), 6.48 (1 H, d, *J* = 7.9 Hz), 2.51 (2 H, d, *J* = 7.1 Hz), 1.71 (2 H, sextet, *J* = 7.3 Hz), 1.08 (3 H, t, *J* = 7.3 Hz); ^{13}C δ 152.38, 132.92, 132.69 (d, *J* = 9.3 Hz), 131.51 (d, *J* = 2.6 Hz), 131.36 (d, *J* = 100.5 Hz), 128.40 (d, *J* = 11.9 Hz), 127.60, 121.45 (d, *J* = 9.3 Hz), 119.36 (d, *J* = 22.3 Hz), 117.04, 92.19, 81.55, 22.62, 22.10, 13.82.

2-(Phenylethynyl)-*N*-(triphenylphosphoranylidene)benzenamine (103e). The same procedure was repeated as described for **103a** except that a mixture of 1.930 g of 2-(phenylethynyl)aniline (**102e**, 10.0 mmol), 4.220 g of Ph_3PBr_2 (10.0 mmol), and 2.8 mL of anhydrous triethylamine in 100 mL of anhydrous benzene was heated under reflux for 4 hours to afford 4.124 g of **103e** (9.10 mmol, 91%) as pale yellow crystals: mp 123-124 ^{o}C; IR (KBr) 2195, 1585, 1472, 1441, 1354, 1103, 749, 713, 687 cm^{-1}; ^{1}H δ 7.91-7.83 (6 H, m), 7.62-7.29 (15 H, m), 6.88 (1 H, td, *J* = 7.7 and 1.8 Hz), 6.63 (1 H, t, *J* = 7.3 Hz), 6.50 (1 H, d, *J* = 8.1 Hz); ^{13}C δ 152.93, 132.90, 132.70 (d, *J* = 9.8 Hz), 131.63 (d, *J* = 2.6 Hz), 131.42, 131.19 (d, *J* = 100.5 Hz), 128.59, 128.51 (d, *J* = 11.9 Hz), 128.11, 127.20, 125.00, 121.41 (d, *J* = 9.3 Hz), 118.53 (d, *J* = 22.3 Hz), 117.11, 91.91, 91.45. Anal. Calcd for $C_{32}H_{24}NP$: C, 84.75; H, 5.33; N, 3.09. Found: C, 84.93; H, 5.36; N, 3.05.

2-(1-Propynyl)-*N*-(triphenylphosphoranylidene)benzenamine (103f). To 4.220 g of Ph_3PBr_2 (10.0 mmol) were added 1.310 g of **102f** (10.0 mmol), 2.78 mL of anhydrous triethylamine, and 100 mL of anhydrous benzene under a nitrogen atmosphere. The reaction mixture was heated under reflux for 4 h. The white triethylammonium bromide precipitate was removed by

filtration, and the filtrate was concentrated. The residue was purified by column chromatography (silica gel/40-60% diethyl ether in hexanes) to furnish 2.776 g (7.10 mmol, 71%) of **103f** as colorless crystals: IR (KBr) 3088, 1605, 734 cm^{-1}; ^{1}H δ 7.9-7.77 (6 H, m), 7.6-7.4 (9 H, m), 7.30 (1 H, dt, *J* = 7.4 and 2.0 Hz), 6.82 (1 H, td, *J* = 7.7 and 1.6 Hz), 6.58 (1 H, t, *J* = 7.4 Hz), 6.49 (1 H, d, *J* = 8.2 Hz), 2.16 (3 H, s); ^{13}C δ 152.48, 132.68 (d, *J* = 9.8 Hz), 132.65, 131.54 (d, *J* = 2.6 Hz), 131.38 (d, *J* = 100.5 Hz), 128.43 (d, *J* = 11.9 Hz), 127.68, 121.58 (d, *J* = 9.3 Hz), 119.32 (d, *J* = 21.2 Hz), 117.08, 87.70, 80.76, 4.95.

Ketenimine 104b. To a solution of 0.433 g of **103b** (1.00 mmol) in 30 mL of anhydrous diethyl ether was introduced 0.194 g of diphenylketene (1.00 mmol) in 5 mL of anhydrous diethyl ether via cannula at 0 ºC under a nitrogen atmosphere. The reaction mixture was stirred for 10 min before it was allowed to warm to room temperature. After one hour, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel/5-10% diethyl ether in hexanes) to furnish 0.248 g (0.71 mmol, 71%) of **104b** as a yellow oil: IR (neat) 2000, 1594, 1491, 758, 693 cm^{-1}; ^{1}H δ 7.49-7.16 (14 H, m), 1.25 (9 H, s); ^{13}C δ 188.80, 141.29, 134.16, 133.73, 128.74, 128.42, 127.89, 126.91, 126.21, 123.43, 119.68, 105.25, 76.47, 75.70, 30.78, 28.19; MS *m/z* 349 (M^{+}).

Ketenimine 104c. The same procedure was repeated as described for **104b** except that 0.449 g of **103c** (1.00 mmol) in 20 mL of anhydrous diethyl ether was treated with 0.194 g of diphenylketene (1.00 mmol) in 20 mL of anhydrous diethyl ether to afford 0.271 g (0.74 mmol, 74%) of **104c** as a yellow oil: IR (neat) 2154, 1997, 1248, 865, 840, 759 cm^{-1}; ^{1}H δ 7.59 (1 H, d, *J* = 7.2 Hz), 7.47-7.21 (13 H, m), 0.25 (9 H, s); ^{13}C δ 189.81, 142.08, 134.11, 133.95, 129.50, 128.78, 127.97, 126.93, 126.36, 123.20, 118.81, 101.26, 101.10, 76.96, -0.13; MS *m/z* 365 (M^{+}).

Ketenimine 104d. The same procedure was repeated as described for **104b** except that 0.419 g of **103d** (1.00 mmol) in 20 mL of anhydrous diethyl ether was treated with 0.194 g of diphenylketene (1.00 mmol) in 20 mL of anhydrous diethyl ether and 0.38 mL of 1,4-CHD to afford 0.302 g (0.90 mmol, 90%) of **104d** as a yellow oil: IR (neat) 2004, 1453, 750, 699 cm^{-1}; ^{1}H δ 7.49-7.16 (14 H, m), 2.10 (2 H, t, *J* = 7.2 Hz), 1.47 (2 H, sextet, *J* = 7.3 Hz), 0.94 (3 H, t, *J* = 7.4 Hz); ^{13}C δ 189.41, 141.44, 134.34, 133.65, 128.71, 128.42, 128.00, 126.94, 126.20, 123.75, 119.61, 97.30, 76.78, 22.02, 21.45, 13.51.

2-(Diphenylmethyl)quinoline (106a). To 0.189 g of **103a** (0.50 mmol) was added a mixture of 0.097 g of diphenylketene (0.50 mmol) and 2.9 mL of 1,4-CHD in 4 mL of anhydrous benzene via cannula at 0 ºC under a nitrogen atmosphere. After 10 min, the reaction mixture was allowed to warm to room temperature for one hour and then was heated under reflux for 2 hours. The reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel/5-20% of diethyl ether in hexanes). The eluent was allowed to evaporate slowly to furnish 0.072 g of **106a** (0.244 mmol, 49%) as yellow crystals.

The rate of reaction was determined by using a solution obtained from treatment of 0.189 g of **103a** (0.50 mmol) with a solution of 0.097 g of diphenylketene (0.50 mmol) in 2.0 mL of C_6D_6 and 1.5 mL of 1,4-CHD at 22 ºC. The rate of disappearance of **104a** and appearance **106a** was monitored with IR (cell thickness = 0.11 mm) and ^{1}H NMR.

Preparation of **106a** by the dehydration method was carried out in a 100-mL flask containing 0.400 g of **112a** (1.29 mmol), 2 g of Florisil, 1.10 g of P_2O_5 (7.72 mmol), 30 mL of pyridine, and 1.66 mL of γ-terpinene (10.3 mmol), and the reaction flask was flushed with nitrogen. The mixture was stirred vigorously and heated under reflux (oil bath temperature 135 ºC) for 16 hours before it was allowed to cool to room temperature. The liquid phase was

filtered through a short Florisil column using dry pyridine as eluent. The residue in the flask was extracted with dry pyridine (3 x 15 mL), and the combined pyridine extracts were passed through the same Florisil column. The combined pyridine solutions were concentrated *in vacuo*. The residue was purified by column chromatography (silica gel/5-20% of diethyl ether in hexanes). The eluent was allowed to evaporate slowly to furnish 0.128 g of **106a** (0.434 mmol, 34%) as yellow crystals: mp 104-105 ºC; IR (KBr) 1594, 1495, 824, 756, 719, 698 cm^{-1}; ^{1}H δ 8.09 (1 H, d, *J* = 8.3 Hz), 8.07 (1 H, d, *J* = 8.3 Hz), 7.79 (1 H, dd, *J* = 8.2 and 1.1 Hz), 7.70 (1 H, tm, *J* = 7.7 and 1.6 Hz), 7.51 (1 H, tm, *J* = 7.5 and 1.1 Hz), 7.35-7.20 (11 H, m), 5.94 (1 H, s); ^{13}C δ 163.07, 147.85, 142.59 (2 carbons), 136.29, 129.41, 129.34, 128.40, 127.44, 126.78, 126.55, 126.20, 121.91, 60.08; MS *m*/*z* 295 (M^{+}), 294, 218, 217, 216, 165. Anal. Calcd for $C_{22}H_{17}N$: C, 89.46; H, 5.80; N, 4.74. Found: C, 89.26; H, 5.79; N, 4.73.

2-(Diphenylmethyl)-3-propylquinoline (106d) and 6-Phenyl-11-propyl-5*H*-benzo[*b*]carbazole (109d). A solution of 0.268 g of **104d** (0.80 mmol) in 3.0 mL of 1,4-CHD (31.8 mmol) was heated under reflux for 24 hours. The solution was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel/5-20% diethyl ether in hexanes). The eluent was allowed to evaporate slowly to furnish 0.155 g of **106d** (0.46 mmol, 58%) and 0.087 g of **109d** (0.26 mmol, 33%) as pale yellow crystals. The rate of reaction was determined by conducting the reaction in C_6D_6 containing a large excess of 1,4-CHD and using ^{1}H NMR to monitor the disappearance of **104d** and the appearance of **106d** and **109d** at 52 ^{o}C.

Preparation of **106d** and **109d** by the dehydration method was carried out by using the same procedure described for **106a** except that a mixture of 0.706 g of **112d** (2.00 mmol), 3.5 g of Florisil, 1.70 g of P_2O_5 (12.0 mmol), 50 mL of pyridine, and 0.76 mL of 1,4-CHD (8.0 mmol) was used. The reaction mixture was heated under vigorous reflux for 18 hours. Purification by

column chromatography followed by recrystallization furnished 0.236 g of **106d** (0.700 mmol, 35%) and 0.208 g of **109d** (0.621 mmol, 31%) as pale yellow crystals. **106d**: mp 99-100 ^{o}C; IR (KBr) 1598, 1560, 753, 697 cm^{-1}; ^{1}H δ 8.03 (1 H, d, *J* = 8.1 Hz), 7.91 (1 H, s), 7.76 (1 H, d, *J* = 8.1 Hz), 7.62 (1 H, tm, *J* = 7.7 and 1.4 Hz), 7.48 (1 H, tm, *J* = 7.5 and 1.3 Hz), 7.39-7.22 (10 H, m), 6.03 (1 H, s), 2.85 (2 H, t, *J* = 7.7 Hz), 1.74 (2 H, sextet, *J* = 7.6 Hz), 1.05 (3 H, t, *J* = 7.3 Hz); ^{13}C δ 161.46, 146.41, 142.95 (2 carbons), 135.38, 134.28, 129.68, 129.48, 128.07, 127.08, 126.66, 126.25, 125.95, 54.85, 34.63, 23.78, 14.13; MS *m*/*z* 337 (M^{+}), 336, 322, 309, 308, 307, 306, 294, 260, 246. Anal. Calcd for $C_{25}H_{23}N$: C, 88.98; H, 6.87; N, 4.15. Found: C, 88.78; H, 6.82; N, 4.09. **109d**: mp 124-125 ^{o}C; IR (KBr) 3402, 756, 700 cm^{-1}; ^{1}H δ 8.38 (1 H, d, *J* = 9.1 Hz), 8.28 (1 H, d, *J* = 7.9 Hz), 7.83 (1 H, d, *J* = 8.7 Hz), 7.82 (1 H, br s, NH), 7.66-7.29 (10 H, m), 3.75 (2 H, t, *J* = 8.1 Hz), 2.02 (2 H, sextet, *J* = 7.7 Hz), 1.30 (3 H, t, *J* = 7.3 Hz); ^{13}C δ 141.99, 137.39, 137.05, 133.87, 130.99, 130.83, 129.22, 127.70, 126.88, 126.67, 125.00, 124.81, 124.15, 123.61, 122.61, 122.39, 119.44, 116.29, 110.05, 31.37, 23.18, 14.80; MS *m*/*z* 335 (M^{+}), 306, 291, 146.

6-Phenyl-5*H*-benzo[*b*]carbazole (109a). Preparation of **109a** by the dehydration method was carried out by using the same procedure described for **106a** except that a mixture of 0.766 g of **112c** (2.00 mmol), 4 g of Florisil, 1.70 g of P_2O_5 (12.0 mmol), 50 mL of pyridine, and 0.80 mL of 1,4-CHD (8.5 mmol) was used. A mixture of **109c** and **109a** was isolated by column chromatography (silica gel/5-20% diethyl ether in hexanes). Treatment of the mixture of **109c** and **109a** in 5 mL of dichloromethane with 3.0 mL of 1 *N* HCl at 40 ºC for one hour converted all of **109c** to the corresponding desilylated adduct **109a**. Purification by column chromatography (silica gel/20% diethyl ether in hexanes) followed by recrystallization from 10% of diethyl ether in hexanes furnished 0.475 g of **109a** (1.62 mmol, 81%) as pale yellow crystals:

IR (KBr) 3400, 751, 693 cm^{-1}; ^1H δ 8.60 (1 H, s), 8.24 (1 H, d, *J* = 7.7 Hz), 8.15-8.10 (1 H, m), 7.87-7.84 (1 H, m), 7.82 (1 H, br s, NH), 7.68-7.52 (5 H, m), 7.50-7.41 (3 H, m), 7.34-7.25 (2 H, m); ^{13}C δ 141.84, 137.64, 136.76, 130.74, 130.64, 129.22, 128.75, 128.61, 127.81, 127.34, 125.16, 124.96, 124.44, 123.35, 122.63, 121.15, 119.44, 118.32, 118.10, 110.22; MS *m*/*z* 293 (M^+), 146.

6-Phenyl-11-*tert*-butyl-5*H*-benzo[*b*]carbazole (109b). A solution of 0.150 g of **104b** (0.43 mmol) in 3 mL of anhydrous benzene was heated under reflux for 24 hours. Benzene was allowed to evaporate slowly to afford 0.147 g of **109b** (0.42 mmol, 98%) as yellow crystals: mp 132-133 ºC; IR (KBr) 3410, 1601, 1462, 747, 699 cm^{-1}; ^1H δ 8.81 (1 H, dd, *J* = 8.0 and 2.2 Hz), 8.43 (1 H, d, *J* = 8.1 Hz), 7.78 (1 H, br, NH), 7.75-7.71 (1 H, m), 7.67-7.54 (5 H, m), 7.44-7.20 (5 H, m), 2.06 (9 H, s); ^{13}C δ 143.17, 141.79, 138.44, 137.08, 131.46, 131.00, 129.27, 128.68, 127.77, 127.32, 127.07, 126.33, 124.60, 124.12, 124.06, 123.66, 120.07, 118.31, 116.93, 109.93, 38.55, 33.63; MS *m*/*z* 349 (M^+), 334, 293, 241, 146, 57; HRMS calcd for $C_{26}H_{23}N$ 349.1831, found 349.1827. The rate of reaction was determined by conducting the reaction in C_6D_6 and using ^1H NMR to monitor the disappearance of **104b** and the appearance of **109b** at 72 ºC.

6-Phenyl-11-(trimethylsilyl)-5*H*-benzo[*b*]carbazole (109c). A mixture of 0.183 g of **104c** (0.50 mmol) in 3 mL of anhydrous benzene was heated under reflux for 24 hours. The reaction mixture was then concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel/5-20% diethyl ether in hexanes). The eluent was allowed to evaporate slowly to afford 0.163 g of **109c** (0.447 mmol, 89%) as pale yellow crystals: mp 153-154 ºC; IR (KBr) 3403, 1260, 847, 769, 748, 702 cm^{-1}; ^1H δ 8.60-8.53 (1 H, m), 8.33 (1 H, d, *J* = 7.9 Hz), 7.83 (1 H, br s, NH), 7.82-7.77 (1 H, m), 7.67-7.52 (5 H, m), 7.47-7.36 (3 H, m), 7.32 (1 H, d, *J* = 7.9 Hz), 7.23 (1 H, tm, *J* = 7.9 and 1.1 Hz), 0.78 (9 H, s); ^{13}C δ 142.27, 137.01, 136.82, 133.31, 132.29.

131.40, 130.77, 130.20, 129.53, 129.27, 127.92, 126.92, 126.53, 124.89, 124.53, 123.81, 121.67, 119.73, 118.33, 110.06, 3.47; MS *m*/*z* 365 (M^+), 350. Anal. Calcd for $C_{25}H_{23}NSi$: C, 82.14; H, 6.34; N, 3.83. Found: C, 82.26; H, 6.42; N, 3.80. The rate of reaction was determined by conducting the reaction in C_6D_6 and using ^1H NMR to monitor the disappearance of **104c** and the appearance of **109c** at 72 ºC.

6,11-Diphenyl-5*H*-benzo[*b*]carbazole (109e). To a solution of 0.453 g of **103e** (1.00 mmol) in 30 mL of anhydrous diethyl ether was introduced 0.194 g of diphenylketene (1.00 mmol) in 5 mL of anhydrous diethyl ether at 0 ºC. The reaction mixture was allowed to warm to room temperature and was stirred for one hour. At this point, the benzocarbazole **109e** had already formed. The reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel/5-20% diethyl ether in hexanes). The eluent was allowed to evaporate slowly to afford 0.343 g of **109e** (0.93 mmol, 93%) as pale yellow crystals.

Preparation of **109e** by the dehydration method was carried out by using the same procedure described for **106a** except that a mixture of 0.724 g of **112e** (1.87 mmol), 3 g of Florisil, 1.59 g of P_2O_5 (11.2 mmol), 40 mL of pyridine, and 0.71 mL of 1,4-CHD (7.5 mmol) was used. Purification by column chromatography afforded 0.483 g of **109e** (1.31 mmol, 70%) as pale yellow crystals: mp 241-242 ºC; IR (KBr) 3451, 754, 702 cm^{-1}; ^1H δ 7.88 (1 H, d, *J* = 8.7 Hz), 7.85 (1 H, br s, NH), 7.80 (1 H, d, *J* = 8.5 Hz), 7.70-7.53 (10 H, m), 7.42 (1 H, tm, *J* = 7.5 and 1.3 Hz), 7.37-7.27 (3 H, m), 6.92-6.90 (2 H, m); ^{13}C δ 141.99, 139.06, 137.11, 136.83, 133.42, 130.89, 130.53, 130.23, 129.29, 128.95, 127.86, 127.81, 127.65, 126.99, 126.56, 125.01, 124.41, 123.45, 123.20, 122.94, 122.50, 119.14, 117.57, 109.87; MS *m*/*z* 369 (M^+), 291, 183, 146. Anal. Calcd for $C_{28}H_{19}N$: C, 91.03; H, 5.18; N, 3.79. Found: C, 90.75; H, 5.27; N, 3.71.

***N*-(2-Ethynylphenyl)diphenylacetamide (112a).** To 0.351 g of 2-ethynylaniline (**102a**, 3.00 mmol) in a 50-mL flask were added 0.762 g of diphenylacetyl chloride (3.30 mmol), 5 mL of anhydrous diethyl ether, and 0.8 mL of anhydrous triethylamine under a nitrogen atmosphere. The reaction mixture was heated under reflux for 2 hours and then was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel/10-20% diethyl ether in hexanes) to furnish 0.803 g (2.58 mmol, 86%) of **112a** as yellow crystalline needles: IR (KBr) 3290, 3219, 2107, 1665, 755, 701, 656 cm^{-1}; ^{1}H δ 8.55 (1 H, d, *J* = 8.1 Hz), 8.24 (1 H, br s), 7.43-7.29 (12 H, m), 7.03 (1 H, td, *J* = 7.6 and 1.1 Hz), 5.21 (1 H, s), 3.01 (1 H, s); ^{13}C δ 170.25, 139.45, 138.83, 131.81, 130.13, 129.19, 128.96, 127.45, 123.48, 118.98, 110.84, 84.18, 78.25, 60.63; MS *m*/*z* 311 (M^{+}), 194, 168, 167, 165, 152, 116.

***N*-[2-(Trimethylsilylethynyl)phenyl]diphenylacetamide (112c).** The same procedure was repeated as described for **112a** except that a mixture of 0.756 g of 2-[(trimethylsilyl)ethynyl]aniline (**102c**, 4.00 mmol), 1.015 g of diphenylacetyl chloride (4.40 mmol), and 1.1 mL of triethylamine in 5 mL of diethyl ether was heated under reflux for 15 hours to afford 1.411 g (3.68 mmol, 92%) of **112c** as colorless crystalline needles: IR (KBr) 3370, 2151, 1708, 1251, 842, 745, 698 cm^{-1}; ^{1}H δ 8.45 (1 H, d, *J* = 8.5 Hz), 8.18 (1 H, br s), 7.41-7.25 (12 H, m), 7.01 (1 H, td, *J* = 7.6 and 1.1 Hz), 5.07 (1 H, s), 0.20 (9 H, s); ^{13}C δ 170.05, 139.10, 138.64, 131.94, 129.83, 128.86, 128.84, 127.49, 123.40, 119.26, 111.95, 102.00, 99.85, 60.50, -0.09; MS *m*/*z* 383 (M^{+}), 368, 216, 215, 200, 168, 167, 165, 152, 115, 73.

***N*-[2-(1-Pentynyl)phenyl]diphenylacetamide (112d).** The same procedure was repeated as described for **112a** except that a mixture of 0.340 g of 2-(1-pentynyl)aniline (**102d**, 2.14 mmol), 0.544 g of diphenylacetyl chloride (2.35 mmol), and 0.7 mL of triethylamine in 5 mL of diethyl ether was heated under reflux for 15 hours to afford 0.635 g (1.80 mmol, 84%) of **112d** as

colorless crystals: IR (KBr) 3301, 2234, 1663, 743, 701 cm^{-1}; ^{1}H δ 8.48 (1 H, d, *J* = 8.3 Hz), 8.15 (1 H, br s), 7.41-7.24 (12 H, m), 7.00 (1 H, td, *J* = 7.5 and 1.2 Hz), 5.15 (1 H, s), 2.14 (2 H, t, *J* = 7.1 Hz), 1.47 (2 H, sextet, *J* = 7.3 Hz), 0.97 (3 H, t, *J* = 7.4 Hz); ^{13}C δ 170.22, 138.88, 138.61, 131.67, 129.11, 128.87, 128.78, 127.46, 123.45, 118.96, 112.83, 97.59, 75.38, 60.67, 22.06, 21.31, 13.54; MS *m*/*z* 353 (M^{+}), 325, 310, 296, 186, 167, 165, 152.

***N*-[2-(Phenylethynyl)phenyl]diphenylacetamide (112e).** The same procedure was repeated as described for **112a** except that a mixture of 0.386 g of 2-(phenylethynyl)aniline (**102e**, 2.00 mmol), 0.461 g of diphenylacetyl chloride (2.00 mmol), and 0.3 mL of anhydrous pyridine in 10 mL of diethyl ether was heated under reflux for four hours to afford 0.724 g (1.87 mmol, 94%) of **112e** as colorless crystals: IR (KBr) 3222, 1654, 749, 702, 692 cm^{-1}; ^{1}H δ 8.51 (1 H, d, *J* = 8.3 Hz), 8.20 (1 H, br s), 7.45 (1 H, dd, *J* = 7.7 and 1.4 Hz), 7.39-7.22 (14 H, m), 7.16 (2 H, tt, *J* = 7.1 and 1.6 Hz), 7.07 (1 H, td, *J* = 7.6 and 1.2 Hz), 5.17 (1 H, s); ^{13}C δ 170.27, 138.73, 138.68, 131.81, 131.72, 129.67, 128.94, 128.91, 128.81, 128.25, 127.50, 123.66, 122.13, 119.42, 112.19, 96.08, 83.62, 60.64; MS *m*/z 387 (M^{+}), 310, 296, 220, 219, 193, 167, 165, 152.

***N*-[2-(phenylethynyl)phenyl]phenylacetamide (113).** The same procedure was repeated as described for **112a** except that a mixture of 0.965 g of 2-(phenylethynyl)aniline (**102e**, 5.00 mmol), 0.70 mL of phenylacetyl chloride (0.82 g, 5.3 mmol), and 1.4 mL of triethylamine in 20 mL of diethyl ether was stirred at room temperature for three hours to afford 1.512 g (4.86 mmol, 97%) of **113** as colorless crystals: IR (KBr) 3300, 1664, 756, 688 cm^{-1}; ^{1}H δ 8.45 (1 H, d, *J* = 8.3 Hz), 7.96 (1 H, br s), 7.44-7.29 (9 H, m), 7.15 (2 H, tm, *J* = 7.2 and 1.0 Hz), 7.09-7.01 (2 H, m), 3.80 (2 H, s); ^{13}C δ 169.21, 138.67, 133.86, 131.87, 131.79, 129.64, 129.50, 129.18, 128.85, 128.28, 127.65, 123.52, 122.19, 119.29, 112.00, 95.92, 83.60, 45.39; MS *m*/*z* 311 (M^{+}), 220, 193, 165, 91.

11-Phenyl-5*H*-benzo[*b*]carbazole (114). The same dehydration procedure was repeated as described for **106a** except that a mixture of 0.622 g of **113** (2.00 mmol), 3 g of Florisil, 1.42 g of P_2O_5 (10.0 mmol), 30 mL of triethylamine, and 0.57 mL of 1,4-CHD (6.0 mmol) was used. The reaction mixture was heated under reflux for 40 hours. Purification by column chromatography followed by recrystallization afforded 0.157 g of **114** (0.54 mmol, 27%) as pale yellow crystals: IR (KBr) 3408, 748, 704 cm^{-1}; ^1H δ 8.00 (1 H, br s, NH), 7.97 (1 H, d, *J* = 8.3 Hz), 7.79 (1 H, s), 7.73 (1 H, d, *J* = 8.5 Hz), 7.68-7.60 (3 H, m), 7.55-7.45 (3 H, m), 7.39-7.36 (2 H, m), 7.31 (1 H, tm, *J* = 7.6 and 1.2 Hz), 6.96-6.87 (2 H, m); ^{13}C δ 142.15, 138.92 (2 carbons), 133.87, 132.55, 130.13, 128.90, 127.78, 127.51, 126.97, 126.90, 126.34, 125.00, 123.60, 123.29, 123.11, 122.68, 119.15, 109.87, 104.73; MS *m*/*z* 293 (M^+), 146.

***N*-(2-Ethynylphenyl)-*N'*-phenylcarbodiimide (126a).**[25b] The following procedure for the preparation of **126a** is representative. To 0.377 g of **103a** (1.00 mmol) was introduced a solution of 0.119 g of phenyl isocyanate (1.00 mmol) in 15 mL of anhydrous benzene via cannula under a nitrogen atmosphere at rt. After 1 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel/5% diethyl ether in hexanes) to furnish 0.181 g (0.83 mmol, 83%) of **126a** as a yellow oil: IR (neat) 3285, 2258, 2139, 2103, 1592, 754, 689 cm^{-1}; ^1H δ 7.49 (1 H, dd, *J* = 7.6 and 1.4 Hz), 7.37-7.28 (3 H, m), 7.25-7.10 (5 H, m), 3.26 (1 H, s); ^{13}C δ 140.58, 138.34, 133.60, 129.90, 129.37, 125.50, 125.14, 124.47, 124.40, 118.30, 83.88, 80.19; MS *m/z* 218 (M^+), 190, 114, 89, 77; HRMS calcd for $C_{15}H_{10}N_2$ 218.0844, found 218.0837.

***N*-[2-(3,3-Dimethyl-1-butynyl)phenyl]-*N'*-phenylcarbodiimide (126b).** The same procedure was repeated as described for **126a** except that 0.866 g of **103b** (2.00 mmol) was treated with 0.238 g of phenyl isocyanate (2.00 mmol) in 20 mL of anhydrous benzene to afford 0.449 g

(1.64 mmol, 82%) of **126b** as a pale yellow oil: IR (neat) 2244, 2141, 2106, 1590, 755 cm^{-1}; ^{1}H δ 7.42 (1 H, dd, *J* = 7.9 and 1.6 Hz), 7.38-7.07 (8 H, m), 1.21 (9 H, s); ^{13}C δ 139.37, 137.95, 133.49, 129.39, 128.37, 125.21, 125.09, 124.56, 124.28, 120.89, 106.34, 75.30, 30.49, 28.18; MS *m/z* 274 (M^+), 273, 259, 243, 218; HRMS calcd for $C_{19}H_{17}N_2$ (M^+ - 1) 273.1392, found 273.1381.

***N*-[2-(Trimethylsilylethynyl)phenyl]-*N'*-phenylcarbodiimide (126c).** The same procedure was repeated as described for **126a** except that 0.746 g of **103c** (1.66 mmol) was treated with 0.198 g of phenyl isocyanate (1.66 mmol) in 20 mL of anhydrous benzene to afford 0.339 g (1.17 mmol, 71%) of **126c** as a yellow oil: IR (neat) 2142, 2107, 1590, 1249, 864, 843, 755, 689 cm^{-1}; ^{1}H δ 7.47 (1H, dd, *J* = 8.0 and 1.5 Hz), 7.37-7.08 (8 H, m), 0.08 (9 H, s); ^{13}C δ 139.02, 138.90, 133.87, 129.49, 129.44, 125.26, 125.19, 124.61, 124.46, 119.75, 102.48, 100.68, -0.48; MS *m/z* 290 (M^+), 289, 275, 259, 245, 218, 183, 73; HRMS calcd for $C_{18}H_{17}N_2Si$ (M^+ - 1) 289.1161, found 289.1148.

***N*-[2-(1-Pentynyl)phenyl]-*N'*-phenylcarbodiimide (126 d).** The same procedure was repeated as described for **126a** except that 0.871 g of **103d** (2.08 mmol) was treated with 0.248 g of phenyl isocyanate (2.08 mmol) in 30 mL of anhydrous benzene to afford 0.427 g (1.64 mmol, 79%) of **126d** as a yellow oil: IR (neat) 2247, 2143, 2107, 1592, 756, 689 cm^{-1}; ^{1}H δ 7.44 (1H, dd, *J* = 7.9 and 1.5 Hz), 7.4-7.08 (8 H, m), 2.10 (2 H, t, *J* = 7.2 Hz), 1.46 (2 H, sextet, *J* = 7.3 Hz), 0.93 (3 H, t, *J* = 7.3 Hz); ^{13}C δ 139.16, 138.72, 133.65, 133.01, 129.25, 128.39, 125.12, 125.05, 124.25, 124.19, 120.78, 98.70, 76.87, 21.69, 21.53, 13.40; MS *m/z* 260 (M^+), 245, 231, 218; HRMS calcd for $C_{18}H_{16}N_2$ 260.1314, found 260.1312.

***N*-[2-(2-Phenylethynyl)phenyl]-*N'*-phenylcarbodiimide (126e).** The same procedure was repeated as described for **126a** except that 0.622 g of **103e** (1.37 mmol) was treated with 0.164 g of phenyl isocyanate (1.37 mmol) in 15 mL of anhydrous benzene to afford 0.286 g (0.973

mmol, 71%) of **126e** as a pale yellow oil: IR (neat) 2138, 1590, 754, 689 cm^{-1}; ^{1}H δ 7.53 (1 H, dm, *J* = 7.7 and 1.5 Hz), 7.37-7.06 (13 H, m); ^{13}C δ 138.75, 138.68, 133.25, 132.88, 131.54, 129.31, 129.27, 128.36, 128.05, 125.27, 125.19, 124.60, 124.31, 122.69, 119.99, 96.22, 85.56; MS *m/z* 294 (M^{+}), 264, 216, 190, 176, 147, 77; HRMS calcd for $C_{21}H_{14}N_2$ 294.1157, found 294.1171.

***N*-[2-(1-Propynyl)phenyl]-*N'*-phenylcarbodiimide (126f).** The same procedure was repeated as described for **126a** except that 0.782 g of **103f** (2.00 mmol) was treated with 0.238 g of phenyl isocyanate (2.00 mmol) in 20 mL of anhydrous benzene to afford 0.330 g (1.42 mmol, 71%) of **126f** as a pale yellow oil: IR (neat) 2138, 1590, 756, 686 cm^{-1}; ^{1}H (C_6D_6) δ 7.35 (1 H, dd, *J* = 7.7 and 1.5 Hz), 7.13 (2 H, m), 6.99-6.91 (3 H, m), 6.86-6.77 (2 H, m), 6.71 (1 H, td, *J* = 7.5 and 1.4 Hz), 1.39 (3 H, s); ^{13}C (C_6D_6) δ 139.93, 139.66, 134.33, 133.10, 129.59, 128.78, 125.42, 125.19, 124.75, 124.64, 121.55, 94.98, 76.75, 4.27; MS *m/z* 232 (M^{+}), 231.

2-(Phenylamino)quinoline (128a)[25b, 49b] and 6*H*-Indolo[2,3-*b*]quinoline (131a).[25b,56] A solution of 0.182 g (0.835 mmol) of **126a** in 2.0 mL of γ-terpinene was heated under a nitrogen atmosphere at 138 °C for 14 h. After the reaction mixture was cooled to rt, a pale yellow solid precipitated out of the solution and coated the inside wall of the flask. The γ-terpinene solution was removed with a pipet, and the remaining solid was washed with benzene and dried *in vacuo* to give 0.029 g (0.13 mmol, 16%) of **131a** (mp 338-340 °C, lit.[25b] 342-346 °C) as a pale yellow solid. The combined solution of benzene and γ-terpinene was concentrated *in vacuo*, and the residue was purified by preparative thin layer chromatography (silica gel/40% diethyl ether in hexanes) to furnish 0.090 g (0.41 mmol, 49%) of **128a** (mp 101-103 °C, lit.[49b] 103-104 °C) as a yellow solid.

The indoloquinoline **131a** was also obtained by heating a suspension of 0.076 g of **131c** (0.26 mmol) over 0.5 mL of a 6 N sodium hydroxide solution and 0.5 mL of ethanol under reflux for 12 h. Then, the reaction mixture was cooled to rt, and 0.5 mL of water was added. The supernatant liquid was removed with a pipette, and the residue was washed with water and dichloromethane to give 0.053 g of **131a** (0.24 mmol, 92%).

11-(1,1-Dimethylethyl)-6*H*-indolo[2,3-*b*]quinoline (131b). A solution of 0.289 g of **126b** (1.05 mmol) in 3.0 mL of *p*-xylene was heated under reflux for 14 h. The reaction mixture was then concentrated, and the residue was purified by flash chromatography (silica gel/20-50% diethyl ether in hexanes) to afford 0.220 g (0.803 mmol, 76%) of **131b** as bright yellow crystals: mp 237-239 ^{o}C; IR (KBr) 1590, 741 cm^{-1}; ^{1}H δ 10.9 (1 H, br s, NH), 8.88 (1 H, dd, *J* = 9.0 and 0.9 Hz), 8.36 (1 H, d, *J* = 8.2 Hz), 8.15 (1 H, d, *J* = 8.4 Hz), 7.71 (1 H, ddd, *J* = 8.3, 6.8, and 1.2 Hz), 7.55-7.46 (2 H, m), 7.39 (1 H, ddd, *J* = 8.9, 6.7, and 1.5 Hz), 7.29 (1 H, ddd, *J* = 8.2, 5.9, and 2.5 Hz), 2.04 (9 H, s); ^{13}C δ 154.23, 153.63, 147.12, 140.99, 128.64, 128.17, 127.25, 127.00, 123.69, 121.42, 121.19, 119.28, 117.99, 110.68, 39.12, 32.99; MS *m/z* 274 (M^{+}), 259, 243, 219, 190, 122; HRMS calcd for $C_{19}H_{18}N_2$ 274.1470, found 274.1475.

11-(Trimethylsilyl)-6*H*-indolo[2,3-*b*]quinoline (131c). A solution of 0.216 g of **126c** (0.745 mmol) in 3.0 mL of *p*-xylene was heated under reflux for 5 h. The reaction mixture was then concentrated, and the residue was purified by flash chromatography (silica gel/20-50% diethyl ether in hexanes) to afford 0.186 g (0.641 mmol, 86%) of **131c** as bright pale yellow crystals: mp 247-248 ^{o}C; IR (KBr) 3060, 1252, 864, 842, 743 cm^{-1}; ^{1}H δ 11.79 (1 H, br s, NH), 8.53 (1 H, d, *J* = 8.4 Hz), 8.26 (1 H, d, *J* = 7.9 Hz), 8.24 (1 H, dd, *J* = 7.9 and 1.1 Hz), 7.78 (1 H, ddd, *J* = 8.2, 6.8, and 1.3 Hz), 7.60-7.46 (3 H, m), 7.28 (1 H, ddd, *J* = 8.2, 6.9, and 1.6 Hz), 0.80 (9 H, s); ^{13}C δ 152.14, 145.15, 144.57, 141.81, 129.21, 128.46, 128.38, 127.81, 127.12, 126.44, 125.18,

122.21, 121.54, 119.17, 110.87, 2.57; MS *m/z* 290 (M^+), 275, 259, 245, 231, 218, 73; HRMS calcd for $C_{18}H_{18}N_2Si$ 290.1239, found 290.1242.

The indoloquinoline **131c** (61% yield) was also synthesized in a one-pot operation from **103c** and phenyl isocyanate without isolation of **126c**.

11-Propyl-6*H*-indolo[2,3-*b*]quinoline (131d). A solution of 0.368 g of **126d** (1.42 mmol) in 4.0 mL of *p*-xylene was heated under reflux for 5 h. The reaction mixture was then concentrated, and the residue was purified by flash chromatography (silica gel/20-50% diethyl ether in hexanes) to afford 0.329 g (1.27 mmol, 89%) of **131d** as golden yellow crystals: mp 245-246 ^oC IR (KBr) 3455, 1611, 739 cm^{-1}; ^1H δ 12.23 (1 H, br s, NH), 8.30 (1 H, d, *J* = 8.4 Hz), 8.22 (1 H, d, *J* = 8.2 Hz), 8.17 (1 H, d, *J* = 7.9 Hz), 7.77 (1 H, d, *J* = 7.6 Hz), 7.6-7.48 (3 H, m), 7.31 (1 H, t, *J* = 7.6 Hz), 3.65 (2 H, t, *J* = 8.0 Hz), 1.98 (2 H, sextet, *J* = 7.6 Hz), 1.24 (3 H, t, *J* = 7.4 Hz); ^{13}C δ 153.44, 146.26, 144.31, 141.38, 128.71, 127.45, 127.04, 124.17, 123.41, 122.67, 121.39, 119.99, 116.63, 110.93, 30.93, 22.92, 14.70; MS *m/z* 260 (M^+), 231. Anal. Calcd for $C_{18}H_{16}N_2$: C, 83.05; H, 6.19; N, 10.76. Found: C, 82.86; H, 6.16; N, 10.67.

The indoloquinoline **131d** (72% yield) was also synthesized in a one-pot operation from **103d** and phenyl isocyanate without isolation of **126d**.

11-Phenyl-6*H*-indolo[2,3-*b*]quinoline (131e).[58] A solution of 0.188 g of **126e** (0.639 mmol) in 2.0 mL of anhydrous benzene was heated under reflux for 4 h. The reaction mixture was then concentrated, and the residue was purified by flash chromatography (silica gel/20-50% diethyl ether in hexanes) to furnish 0.171 g (0.582 mmol, 91%) of **131e** as bright pale yellow crystals: mp 266-268 ^oC (lit.[58] 269-271 ^oC); IR (KBr) 1593, 743 cm^{-1}; ^1H δ 12.46 (1 H, br s, NH), 8.28 (1 H, d, *J* = 8.4 Hz), 7.81-7.73 (3 H, m), 7.7-7.65 (3 H, m), 7.57-7.52 (3 H, m), 7.44-7.37 (2 H, m), 7.08 (1 H, d, *J* = 7.4 Hz), 6.98 (1 H, td, *J* = 7.5 and 1.1 Hz); ^{13}C δ 153.36, 146.18, 142.80,

141.55, 136.37, 129.35, 128.95, 128.55, 127.87, 126.59, 126.40, 123.69, 123.06, 122.85, 121.04, 119.70, 116.75, 110.79; MS *m/z* 294 (M^+), 293, 264, 146. Anal. Calcd for $C_{21}H_{14}N_2$: C, 85.69; H, 4.79; N, 9.52. Found: C, 85.74; H, 4.84; N, 9.50.

The indoloquinoline **131e** (67% yield) was also synthesized in a one-pot operation from **103e** and phenyl isocyanate without isolation of **126e**.

11-Methyl-6*H*-indolo[2,3-*b*]quinoline (131f).[56] A solution of 0.160 g of **126f** (0.690 mmol) in 1.0 mL of *p*-xylene was heated at 138 °C for 4 h. The reaction mixture was then concentrated, and the residue was purified by flash chromatography (silica gel/40-60% diethyl ether in hexanes) to furnish 0.123 g (0.530 mmol, 77%) of **131f** as pale yellow crystals: IR (KBr) 3423, 1476, 1398, 1171, 1036, 805 cm^{-1}; ^1H δ 10.16 (1 H, br s, NH), 8.30 (2 H, d, *J* = 7.9 Hz), 8.14 (1 H, d, *J* = 8.4 Hz), 7.77 (1 H, ddd, *J* = 8.2, 6.9, and 1.4 Hz), 7.57-7.51 (3 H, m), 7.33 (1 H, dd, *J* = 7.7 and 4.0 Hz), 3.24 (3 H, s); ^1H δ (DMSO-d_6) 11.66 (1 H, br s, NH), 8.34 (1 H, d, *J* = 7.7 Hz), 8.32 (1 H, d, *J* = 7.7 Hz), 7.95 (1 H, d, *J* = 8.4 Hz), 7.71 (1 H, td, *J* = 7.7 and 1.1 Hz), 7.55-7.46 (3 H, m), 7.27 (1 H, td, *J* = 7.2 and 2.0 Hz), 3.17 (3 H, s); ^{13}C δ (DMSO-d_6) 152.33, 146.19, 141.32, 138.68, 128.45, 127.49 (two overlapping signals), 124.44, 123.72, 123.46, 122.46, 121.05, 119.62, 115.95, 110.71, 14.87; MS *m/z* 232 (M^+), 231.

The indoloquinoline **131f** (59%) was also synthesized in a one-pot operation from **103f** and phenyl isocyanate without isolation of **126f**.

2-Methoxy-11-propyl-6*H*-indolo[2,3-*b*]quinoline (142d). To a solution of 0.650 g of **103d** (1.55 mmol) in 10 mL of anhydrous *p*-xylene was added via cannula a solution of 0.231 g of 4-methoxyphenyl isocyanate (1.55 mmol) in 10 mL of anhydrous *p*-xylene under a nitrogen atmosphere. The reaction mixture was heated under reflux for 5 h and then concentrated. The residue was purified by flash chromatography (silica gel/20-50% diethyl ether in hexanes) to

afford 0.212 g (0.731 mmol, 47%) of **142d** as a pale yellow solid: mp 236-238 ^{o}C; IR (KBr) 3417, 1633, 1613, 1232, 823, 724 cm^{-1}; ^{1}H δ 9.66 (1 H, br s, NH), 8.18 (1 H, d, *J* = 7.9 Hz), 8.04 (1 H, d, *J* = 9.2 Hz), 7.56-7.49 (3 H, m), 7.45 (1 H, dd, *J* = 9.2 and 2.6 Hz), 7.34-7.28 (1 H, m), 4.01 (3 H, s), 3.62 (2 H, t, *J* = 8.0 Hz), 1.98 (2 H, sextet, *J* = 7.6 Hz), 1.23 (3 H, d, *J* = 7.4 Hz); ^{13}C (DMSO-d_6) δ 154.70, 151.30, 142.14, 141.53, 141.34, 128.97, 127.31, 123.25, 120.56, 120.27, 119.44, 115.43, 110.68, 102.60, 55.37, 29.95, 22.27, 14.21; MS *m/z* 290 (M^+), 275, 261, 246, 218; HRMS calcd for $C_{19}H_{18}N_2O$ 290.1419, found 290.1420.

2-Methoxy-11-phenyl-6*H*-indolo[2,3-*b*]quinoline (**142e**).[49b] The same procedure was repeated as described for **142d** except that 0.500 g of 56e (1.10 mmol) in 6 mL of anhydrous benzene and 0.164 g of 4-methoxyphenyl isocyanate (1.10 mmol) in 9 mL of anhydrous benzene were used to afford 0.194 g (0.599 mmol, 55%) of **142e** as bright pale yellow crystals: IR (KBr) 3431, 3077, 1630, 1608, 821, 744 cm^{-1}; ^{1}H δ 11.46 (1 H, br s, NH), 8.15 (1 H, d, *J* = 9.2 Hz), 7.72-7.64 (3 H, m), 7.57-7.53 (2 H, m), 7.50 (1 H, s), 7.47-7.39 (2 H, m), 7.07 (1 H, d, *J* = 2.9 Hz), 7.04 (1 H, dm, *J* = 7.6 and 0.8 Hz), 6.97 (1 H, ddd, *J* = 8.4, 6.9, and 1.1 Hz), 3.78 (3 H, s); ^{13}C δ 155.29, 152.09, 142.15, 141.47, 141.39, 136.59, 129.26, 129.10, 128.56, 127.96, 127.81, 124.28, 123.11, 121.14, 120.99, 119.59, 116.72, 110.63, 104.77, 55.44; MS *m/z* 324 (M^+), 309, 292. Anal. Calcd for $C_{22}H_{16}N_2O$: C, 81.46; H, 4.97; N, 8.64. Found: C, 81.55; H, 5.00; N, 8.57.

2-(1-Propynyl)phenyl Isocyanate (163). To a solution of 1.089 g of triphosgene (3.67 mmol) in 20 mL of anhydrous benzene was added dropwise a mixture of 1.310 g of **102f** (10.0 mmol) and 2.78 mL of anhydrous triethylamine (20.0 mmol) in 30 mL of anhydrous benzene under a nitrogen atmosphere at rt. After 2 h at 70 ^{o}C, the white precipitate of triethylamine hydrochloride was removed by filtration and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel/10-20% of diethyl ether in hexanes) to give

1.507 g of **163** (9.60 mmol, 96%) as a light yellow liquid: IR (neat) 2241, 1723, 755 cm^{-1}; ^{1}H δ 7.37 (1 H, dd, *J* = 7.5 and 1.6 Hz), 7.21 (1 H, td, *J* = 7.7 and 1.7 Hz), 7.10 (1 H, td, *J* = 7.5 and 1.3 Hz), 7.00 (1 H, dd, *J* = 7.9 and 1.5 Hz), 2.13 (3 H, s); ^{13}C δ 135.4, 131.8, 128.6, 127.7, 125.2, 123.3, 121.5, 95.4, 75.7, 4.4; MS *m/z* 157 (M^+), 129, 102; HRMS calcd for $C_{10}H_7NO$ 157.0528, found 157.0525.

11-Methyl-6*H*-indolo[2,3-*b*][1,5]naphthyridine (169) and 5-Methyl-10*H*-indolo[2,3-b][1,7]naphthyridine (170).[69] To a solution of 0.708 g of **164** (2.00 mmol) in 3 mL of anhydrous benzene was added 0.314 g of **163** (2.00 mmol) in 7 mL of anhydrous benzene via cannula under a nitrogen atmosphere at rt. After 2 h at rt, the reaction mixture was filtered through a short silica gel column to remove triphenylphosphine oxide. The column was further eluded with *p*-xylene. The combined benzene and *p*-xylene solutions were concentrated in vacuo to remove benzene. The remaining *p*-xylene solution was heated to reflux under a nitrogen atmosphere for 12 h. The reaction mixture was concentrated in vacuo, and the residue was purified by flash chromatography (silica gel/12:7:1 of hexanes : diethyl ether : methanol) followed by preparative thin layer chromatography to furnish 0.272 g (1.17 mmol, 58%) of **169** and 0.081 g (0.35 mmol, 17%) of **170** as pale yellow crystals. **169**: IR (KBr) 1610, 1407, 734 cm^{-1}; ^{1}H δ 9.73 (1 H, br, s, NH), 8.95 (1 H, dd, *J* = 4.0 and 1.7 Hz), 8.33 (1 H, dd, *J* = 8.6 and 1.7 Hz), 8.30 (1 H, d, *J* = 7.7 Hz), 7.62 (1 H, dd, *J* = 8.5 and 4.1 Hz), 7.55 (1 H, td, *J* = 7.5 and 1.1 Hz), 7.50 (1 H, d, *J* = 7.2 Hz), 7.35 (1 H, ddd, *J* = 7.5, 6.9, and 1.6 Hz), 3.37 (3 H, s); ^{13}C δ (DMSO-d_6) 152.1, 146.2, 141.7, 141.3, 140.0, 139.0, 135.0, 128.1, 124.0, 123.5, 121.0, 120.0, 118.6, 110.9, 13.4; MS *m/z* 233 (M^+), 205, 152; HRMS calcd for $C_{15}H_{11}N_3$ 233.0953, found 233.0954. Anal. Calcd for $C_{15}H_{11}N_3$: C, 77.23; H, 4.75; N, 18.01. Found: C, 76.95; H, 4.83; N, 17.76. **170**: IR (KBr) 1615, 742 cm^{-1}; ^{1}H δ (DMSO-d_6) 11.97 (1 H, s), 9.32 (1 H, s), 8.51 (1 H, d,

J = 5.7 Hz), 8.39 (1 H, d, *J* = 7.7 Hz), 8.21 (1 H, d, *J* = 5.7 Hz), 7.60 (1 H, t, *J* = 7.5 Hz), 7.54 (1 H, d, *J* = 7.2 Hz), 7.32 (1 H, t, *J* = 7.3 Hz), 3.18 (3 H, s); ^{13}C δ (DMSO-d_6) 152.8, 151.7, 142.0, 139.6, 137.8, 128.7, 126.3, 124.5, 120.4, 120.1, 119.1, 117.0, 111.0, 14.4; MS *m*/*z* 233 (M^+), 205, 151; HRMS calcd for $C_{15}H_{11}N_3$ 233.0953, found 233.0950.

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(51) IR absorbance (A) at 2002 cm^{-1} at different reaction time was recorded in the following Table.

A	Time, min	Time, hr	-ln A
0.5366	20	0.33333	0.6225
0.339	35	0.58333	1.0818
0.2079	51	0.85	1.5707
0.1305	65	1.08333	2.0364
0.07405	82	1.36667	2.603
0.04072	103	1.71667	3.201

Lambert-Beer law establishes a relationship between the transmittance, the sample thickness, and the concentration of the absorbing species. This relationship is expressed as

$$\log (1/T) = \log_{10} (I_0/I) = abC = A$$

where T = transmittance,

I_0 = the intensity of the radiant energy striking the sample,

I = the intensity of the radiation emerging from the sample,

a = a constant characteristic of the solute,

b = path length through the sample,

C = concentration of solute,

A = absorbance.

For the first-order reaction, the relationship between the concentration of the reactant and the reaction time is expressed as: $\ln (C_0/C) = kt$ or $\ln C = -kt + \ln C_0$

Where t = reaction time,

C_0 = initial concentration of the reactant,

C = the concentration of the reactant at time t.

We can combine the above two equations and get the following new equation:

$$-\ln C = \ln A + \ln (ab) = kt + \ln C_0$$

$$\text{or } -\ln A = kt + \ln (abC_0)$$

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(54) The relative concentration C_0/C of reactant **104b** was represented as (A + B)/A:

A and B were the integrations of ^{1}H NMR absorptions at δ 1.25 (A) and at δ 2.06 (B), respectively (A: attributable to *tert*-butyl of **104b**; B: attributable to *tert*-butyl of **109b**).

diminishing A	developing B	(A + B)/A	Time, hr	ln [(A + B)/A]
9	0.909	1.1010	0.5	0.0962
9	2.831	1.3146	1.5	0.2735
9	9.011	2.0012	3.75	0.6938
3.446	9	3.6117	7	1.2842
1.163	9	8.7386	11.5	2.1678

(55) The relative concentration C_0/C of reactant **104c** was represented as (A + B)/A: A and B were the integrations of ^{1}H NMR absorptions at δ 0.25 (A) and at δ 0.78 (B), respectively (A: attributable to trimethylsilyl of **104c**; B: attributable to trimethylsilyl of **104c)**.

diminishing A	developing B	(A + B)/A	Time, hr	ln [(A + B)/A]
9	4.54	1.5044	0.5	0.4084
3.84	9	3.3438	1.5	1.2071
1.85	9	5.8649	2.5	1.7690

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diminishing A	developing B	developing C	(A+B+2C)/A	Time, hr	ln [(A+B+2C)/A]
1.812	0.4633	0.3849	1.6805	0.5	0.5191
1.2757	0.7752	0.6425	2.6149	1	0.9612
1.7063	2	1.8735	4.3681	1.5667	1.4743
0.8914	2	1.9899	7.7083	2.233	2.0423

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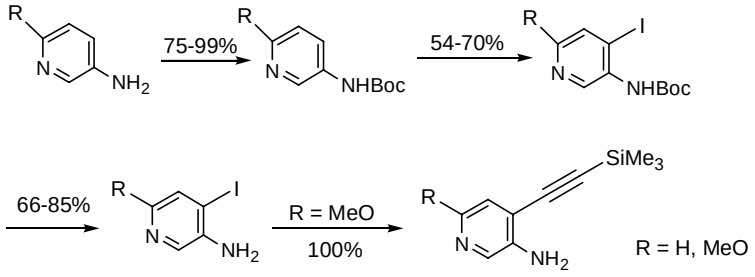
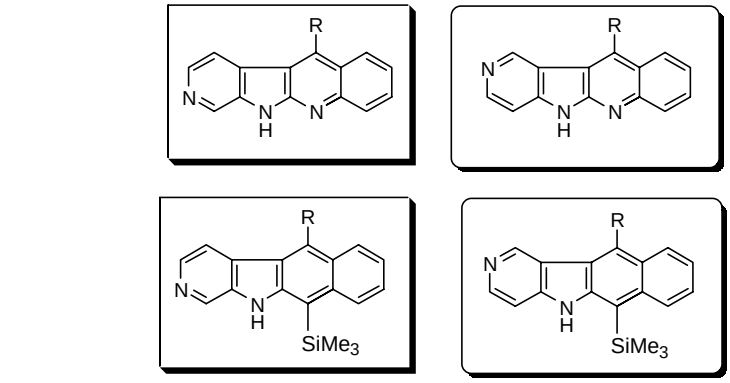
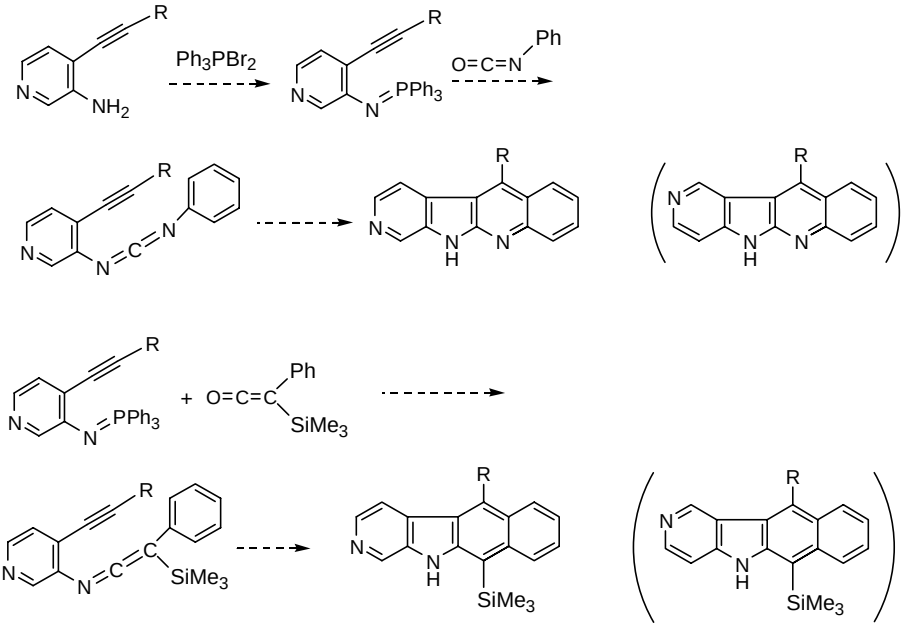
Appendix: Graphical Preview of Future Work

Synthesis of 4-amino-3-iodopyridine (and 3-amino-4-iodopyridine) derivatives[72]



Plan





Publications:

1. Zhang, Q.; Shi, C.; Zhang, H.-R.; Wang, K. K., "*Synthesis of 6H-Indolo[2,3-b][1,6]naphthyridines and Related Compounds as the 5-Aza Analogues of Ellipticine Alkaloids*", *J. Org. Chem.* **2000**, *65*, 7977–7983.

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