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Coarctate versus Pericyclic Reactivity in Naphthalene-Fused Azo–Ene–Ynes: Synthesis of Benzocinnolines and Benzoisoindazoles

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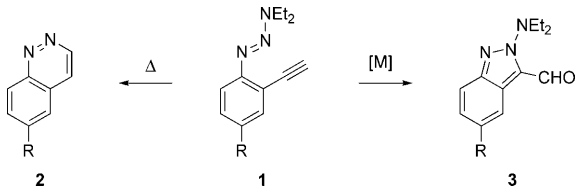
Dedicated to Prof. Dr. Henning Hopf on the occasion of his 70th birthday

Abstract: The cyclization reactions of naphthalene-fused azo–ene–yne compounds are explored both computationally and experimentally. Calculations reveal that naphtho-fusion to an azo–ene–yne scaffold does not significantly alter the transition state energies compared to the benzene-based systems; however, fusing the naphthalene in an angular fashion leads to lower energy intermediates due to the creation of arenes possessing greater aromaticity. Experimentally, the cyclization of the angular systems yields not only the expected monomeric benzocinnolines and benzoisoindazoles, but also several dimeric structures, including one that readily isomerizes in the presence of light and/or trace acid.

Keywords: alkenynes · coarctate · density functional calculations · heterocycles · pericyclic reaction

Introduction

Over the past decade there has been considerable interest in the cyclization reactions of conjugated 'ene–ene–yne' compounds as a versatile, high yielding, and efficient way to synthesize aromatic heterocycles.[1] In particular, we have been examining the dual reaction pathways of conjugated azo–ene–ynes (**1**, Scheme 1),[2] where under thermal conditions a pericyclic cyclization generates a new benzo-fused six-membered ring (**2**), or addition of a carbene stabilizer induces a coarctate cyclization[3,4] to form a new benzo-fused five-membered ring (**3**). Through these methodologies, a variety of substituted cinnolines and isoindazoles, respectively, are available from simple anilines in high yields and in only a few steps.[5–10] To date though, our synthetic and computational[11] studies have focused solely on benzo-fused heterocycles.



Scheme 1. Cyclization reactions of triazene–ene–yne **1**.

Acenes and closely related polycyclic aromatic hydrocarbons (PAHs) are molecules that have garnered tremendous attention over the last decade as they possess a number of properties that make them ideal for use in organic electronic devices.[12] They often possess low HOMO–LUMO gap energies, and upon functionalization, are typically robust and form highly ordered architectures in the solid state. More recently, nitrogen containing heteroacenes have emerged as materials that have properties complementary to typical acenes.[13] *N*-Heteroacenes have been investigated as electron-transport materials, whereas all-carbon acenes have seen more use as hole transport layers. Furthermore, incorporation of electronegative atoms within the acene core results in π-deficient aromatic heterocycles, which makes them more resistant to undesired oxidation.[13] With the increased electronic materials interest in larger acenes and PAHs, our focus has now turned to applying the pericyclic/coarctate cyclizations for the synthesis of larger aromatic heterocycles. Herein we describe our first steps toward this goal, namely the preparation of naphthalene-based 'azo–ene–yne' precursors and their conversion into a variety of benzocinnolines and benzoisoindazoles.

Results and Discussion

The strategy employed for heterocycle synthesis relies on the ability to form an *ortho*-ethynylaryl-*N,N*-dialkyltriazene.[2,10] Traditionally these triazenes are prepared from *ortho*-haloanilines such as **4** in good yields via three simple steps (Scheme 2).[2,7,8,10] Extension of this methodology to naphthalene derivatives would suggest three potential cycli-

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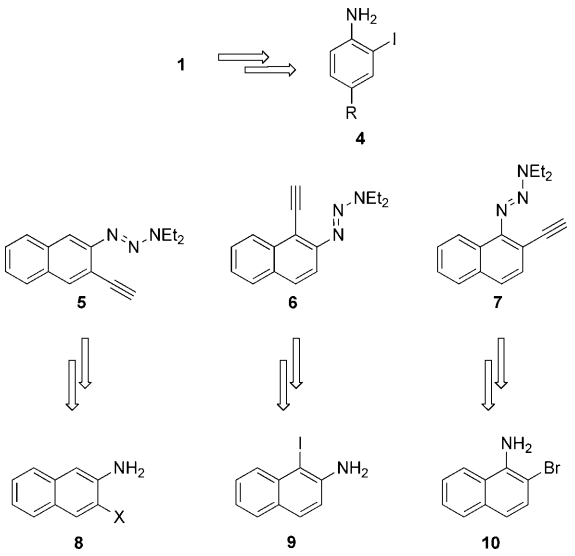


Scheme 2. Precursor targets **5–7** for the cyclization of naphthalene-fused azo–ene–yne compounds starting from substituted naphthalenes **8–10**.

zation precursors **5–7**, which would originate from the corresponding halonaphthalenamines **8–10** (Scheme 2). Examination of the literature revealed that related structures **9**[14] and **10**[15] are known compounds, whereas linear derivative **8** (X = I, Br) is unknown and therefore an alternate precursor is necessary. The conversion of aldehydes into alkynes has been well documented;[16] thus, known carbaldehyde **8** (X = CHO)[17] was identified as the potential starting point for the preparation of **5**.

Computational studies: Prior to synthesis, the cyclization profiles of naphthalenes **5–7** were examined by using density functional theory at the B3LYP level for a 6-31G* basis set,[18] as has been done with previous systems.[2,5,7–11] This level of theory has proven to give reliable results that are comparable to experimental findings in prior cyclization studies. To reduce the number of conformational degrees of freedom, the NEt_2 substitution on the triazene was replaced with an NMe_2 group. A representative energy diagram is shown in Figure 1, with full results in Table 1.

Table 1. DFT (B3LYP/6-31G* + ZPE) calculated energies [kcal mol^{-1}] for the cyclizations of dimethylamino analogues of **5–7**.

Mechanism/Orientation	**1**[a,b]	**5**[a]	**6**[a]	**7**[a]
pericyclic zwitterion	15.01	19.41	9.73	11.00
syn carbene	26.07	27.54	26.19	23.49
anti carbene	28.69	31.37	24.68	24.68
pericyclic TS	30.30	31.31	28.10	28.84
coarctate *syn* TS	30.60	30.77	30.70	29.28
coarctate *anti* TS	31.58	32.45	29.41	29.50

[a] NEt_2 replaced by NMe_2 in computations. [b] Values are 2.14 kcal mol^{-1} lower than in reference [10] as the reactive conformation is defined as 0 in Figure 3.

As depicted in Figure 1, there are two reaction pathways that have very similar activation barriers. As we have observed in the past, the pericyclic cyclization gives rise to the lowest energy cyclization intermediate which indicates that thermal treatment of **5** should afford the linear benzo[*g*]cinnoline. In comparison to the parent triazene–ene–yne **1**,[2,10] the zwitterionic intermediate is over 4 kcal mol^{-1} higher in energy, whereas the transition state is about 1 kcal mol^{-1} higher. The coarctate pathway features transition states that are similar or slightly higher (< 1 kcal mol^{-1}) than the parent, which indicates that **5** should be able to undergo the analogous cyclization. The *syn* intermediate (where *syn* refers to the orientation of the H atom to the original ring) is 1.5 kcal mol^{-1} higher in energy than the benzene system,

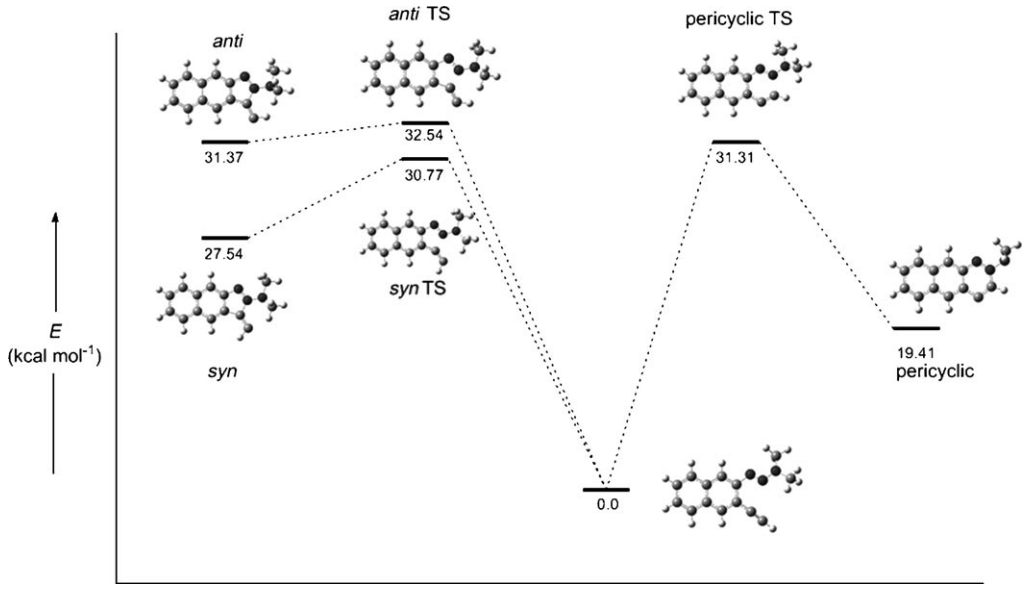


Figure 1. DFT (B3LYP/6-31G* + ZPE) calculated energies for the dual cyclization pathways of the dimethylamino derivatives of **5**.

whereas the *anti* intermediate is 2.7 kcal mol^{-1} higher. Taken as a whole, this indicates that fusing a naphthalene ring onto the ene–ene–yne scaffold in a "linear" fashion has a minimal effect on the cyclization energies and thus suggests that **5** is a viable candidate for experimental exploration.

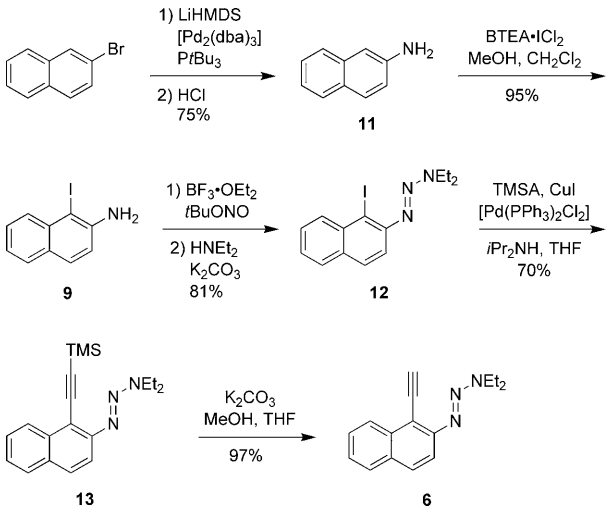
Interestingly, more dramatic differences can be seen in the computed reaction pathways of the "angular" systems, which would give rise to phenanthrene-like derivatives. The zwitterionic intermediates are much lower in energy (ca. 10 and 8 kcal mol^{-1} for **6** and **7**, respectively) than for linear **5**. One possible explanation for the difference could be related to the aromaticity of the resultant tricyclic arenes. In phenanthrene, the two outer rings have much more aromatic character than the center ring, where the C=C double bond possesses more double bond character and will undergo addition reactions not usually seen in aromatic systems. Conversely, in linear acenes, as more and more rings are fused together, the overall aromaticity decreases. It is therefore reasonable to assume that by cyclization of **5** we would generate an anthracene-like, linear benzocinnoline that would be less aromatic (one Clar sextet) than the corresponding phenanthrene-like, angular benzocinnolines produced upon the cyclization of **6** or **7** (two Clar sextets).

Examination of the coarctate cyclizations for **6** and **7** reveal that they too have lower intermediate energies than the parent and **5**, which is consistent with the aromaticity explanation of the pericyclic cyclizations. In the case of **6**, the *syn* intermediate is higher in energy than the *anti* intermediate, presumably due to the steric repulsion between the carbene hydrogen and the H-atom on the pendant aromatic ring. Because of the overall lower cyclization energies, isomers **6** and **7** were chosen as the first synthetic targets.

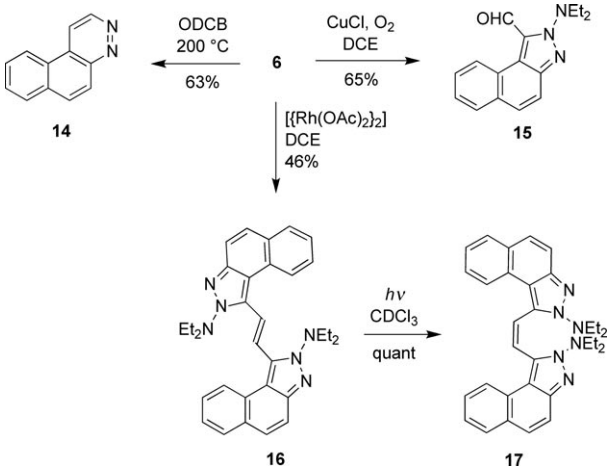
Synthetic investigations:

*Synthesis and cyclization of naphthalene **6***: The assembly of **6** begins with a Pd-catalyzed cross-coupling reaction between 2-bromonaphthalene and LiHMDS, which was subsequently desilated to give naphthylamine **11** (Scheme 3).[19] Amine **11** was halogenated by the mild iodinating agent BTEA·ICl_2[20] to furnish iodide **9**.[14] Triazene formation was then attempted with $NaNO_2$ and HCl followed by quenching with K_2CO_3 and $HNEt_2$ in aqueous MeCN. While **12** could be prepared under these conditions, yields were not optimal (ca. 50%), primarily due to the insolubility of the naphthalene derivative in the water/MeCN mixture. The yield could be improved to 81% by using $BF_3{\cdot}OEt_2$ and *t*BuONO in THF to generate the diazonium intermediate[21] followed by quenching with K_2CO_3 and $HNEt_2$ in DMF.[22] Sonogashira cross-coupling with (trimethylsilyl)acetylene (TMSA) gave **13**; subsequent protiodesilation afforded cyclization precursor **6**.

Thermolysis of **6** at 200 °C in *ortho*-dichlorobenzene (ODCB) generated the known benzo[*f*]cinnoline **14**[23] in 63% yield (Scheme 4). Treatment of **6** by CuCl in 1,2-dichloroethane (DCE) failed to provide aldehyde **15** cleanly; however, saturation of the solvent with O_2 prior to CuCl addition afforded **15** in 65% isolated yield. While attempting to optimize the coarctate product, catalytic [{$Rh(OAc)_2$}$_2$] was also examined as it has successfully promoted coarctate cyclizations.[10] Surprisingly, the reaction did not furnish the desired aldehyde, but instead bis(benzo[*e*]isoindazole) **16**, in which two carbenes had dimerized to form a double bond. Similar to other isoindazole dimers we have observed previously, the ^{1}H NMR spectrum of **16** showed the characteristic singlet of the alkene protons at $\delta = 8.46$ ppm. While the proton spectrum was initially clean, peaks of a second component began to appear within an hour, with a new singlet at $\delta = 7.41$ ppm. After about 24 h, the sample appeared to be approximately 95% converted to this new material; all traces of the starting dimer were gone after 48 h. Crystallization of the new molecule by slow evaporation of a CH_2Cl_2 solution produced single crystals suitable for X-ray diffraction. The crystal structure analysis revealed the new product to be the *cis* isomer **17** (Figure 2). Believing that the acidic



Scheme 3. Synthesis of cyclization precursor **6**.



Scheme 4. Cyclization of **6** to benzo[*f*]cinnoline **14** and benzo[*e*]isoindazoles **15**–**17**.

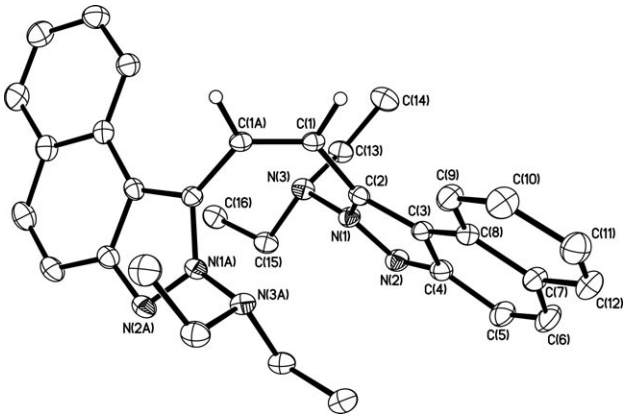
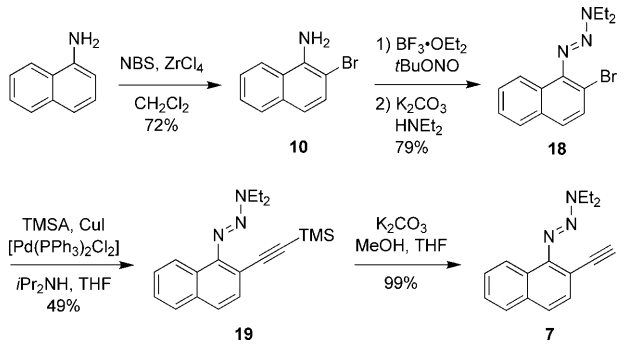


Figure 2. Molecular structure of *cis* dimer **17**; ellipsoids drawn at the 30% probability level; only H atoms at C(1) and its symmetrical equivalent are shown for clarity.

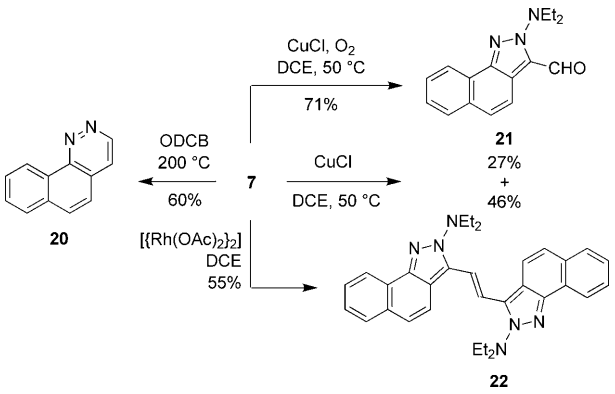
nature of the $CDCl_3$ was behind the isomerization, a freshly prepared sample of **16** was dissolved in CD_2Cl_2 and monitored by ^1H NMR spectroscopy. By keeping the sample in the instrument, no isomerization was detected after 48 h, which indicated that ambient light triggered the isomerization. Indeed, leaving the CD_2Cl_2 solution of **16** on the benchtop resulted in isomerization to **17** over the course of 10 days, which confirmed that the isomerization was photoinduced and greatly accelerated by trace acid in $CDCl_3$. DFT analysis of the *cis* and *trans* dimers revealed that the *cis* orientation is 2.6 kcal mol^{-1} lower in energy than the *trans*.

Synthesis and cyclization of naphthalene **7**: The synthesis of isomer **7** began with the selective bromination of 1-naphthalenamine with *N*-bromosuccinimide (NBS) and $ZrCl_4$ to afford bromide **10** in 72% yield (Scheme 5).[15] Anhydrous



Scheme 5. Synthesis of cyclization precursor **7**.

triazene formation using $BF_3{\cdot}OEt_2$ and *t*BuONO again provided superior yields of **18** compared to the aqueous HCl/$NaNO_2$ route. Cross-coupling **18** with TMSA at 50°C provided protected azo–ene–yne **19**, which was desilated to give **7** in 28% overall yield.



Scheme 6. Cyclization of **7** to benzo[*h*]cinnoline **20** and benzo[*g*]isoindazoles **21** and **22**.

Heating **7** to 200°C in ODCB provided the known benzo[*h*]cinnoline **20**[24] in 60% yield (Scheme 6). Analogous to **6**, treatment of a 0.002 M DCE solution of **7** with CuCl at 50°C provided a mixture of compounds, which upon purification were identified as aldehyde **21** (27%) and the highly blue fluorescent dimer **22** (46%). The exact isomeric form of **22** (*trans*) was conclusively provided by X-ray crystallography (Figure 3). This corroborates our hypothesis that the

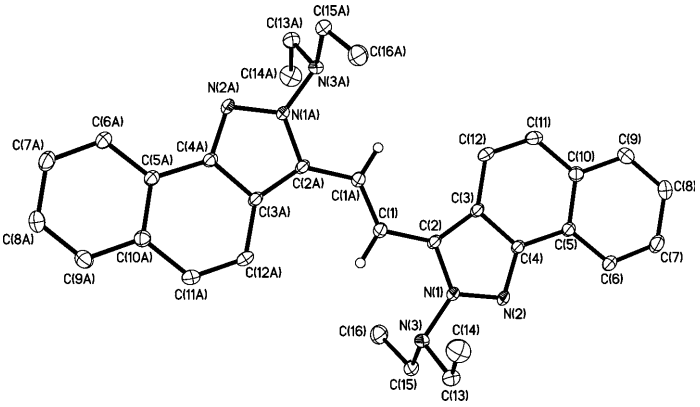
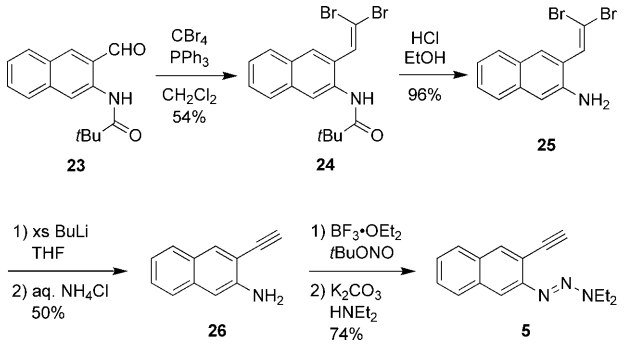


Figure 3. Molecular structure of *trans* dimer **22**; ellipsoids drawn at the 30% probability level; only H atoms at C(1) and its symmetrical equivalent are shown for clarity.

trans dimer initially forms preferentially to the *cis* isomer. Interestingly, leaving a $CDCl_3$ sample of **22** on the benchtop (and later in the window) resulted in no isomerization to the *cis* isomer. DFT analysis revealed that with this system, the *trans* dimer is 4.9 kcal mol^{-1} lower in energy than the *cis*. Cyclization using $[\{Rh(OAc)_2\}_2]$ under Ar improved the dimer yield slightly (55%), while also suppressing aldehyde formation. Alternatively, saturation of the DCE with O_2 prior to CuCl addition afforded **21** in 71% yield, with no evidence of dimer formation.

Synthesis and cyclization of naphthalene **5**: As discussed earlier, a requisite 3-halo-2-naphthalenamine to generate linear precursor **5** is unknown. Thummel et al. have previously re-

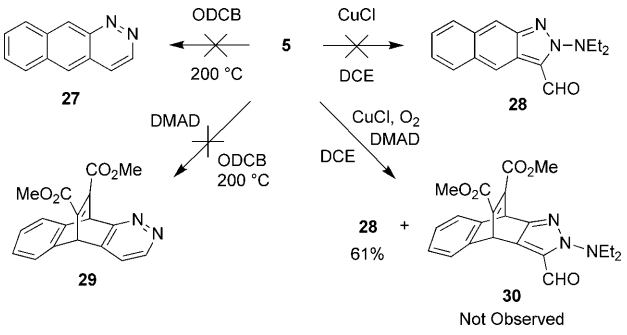
ported the synthesis of 3-amino-2-naphthaldehyde (**8**, X = CHO),[17] which seemed to be an appropriate starting material for **5**; however, all attempts to directly transform **8** into **26** met with failure. Deviating from the literature procedure, a Wittig reaction between **23**[17] and $Ph_3P{=}CBr_2$ gave dibromide **24** (Scheme 7). The amide was cleaved under acidic



Scheme 7. Synthesis of cyclization precursor **5**.

conditions to afford free amine **25**. Reaction with excess *n*BuLi completed the Corey–Fuchs procedure[16a] to afford terminal alkyne **26**. Treatment of **26** with $BF_3{\cdot}OEt_2$ and *t*BuONO followed by $HNEt_2$ and K_2CO_3 accomplished conversion of the amine to the triazene unit without destruction/cyclization of the alkyne moiety.

Examination of the reactivity of **5** proved intriguing. Heating **5** to 200 °C provided none of the expected benzo[*g*]-cinnoline (**27**, the only benzocinnoline isomer not known in the literature), but instead furnished what appeared to be polymeric products (Scheme 8). ^1H NMR analysis of what



Scheme 8. Reactivity of azo–ene–yne **5**.

little material that was soluble did not show the characteristic cinnoline doublet in the $\delta = 8.5$–9.5 ppm region of the spectrum. Shielding the reaction from light or rigorously excluding air had no effect and led to decomposition/polymerization every time, similar to previous attempts to prepare **27**.[25] The coarctate cyclization of **5** was also explored, and similarly only polymeric material was isolated; there was no evidence of the formation of either **28** or dimeric material analogous to **17** and **22**. These results suggested that the cyclized products were most likely unstable under the reaction conditions and thus prone to polymerization. Longer, linear acenes such as anthracene and pentacene are known to undergo dimerization and polymerization by cycloaddition reactions. In an attempt to intercept possible reactive species, the cyclization studies were repeated in the presence of dimethyl acetylenedicarboxylate (DMAD), as this would trap of the products immediately after cyclization. Heating **5** in ODCB with excess DMAD, however, led to the formation of a thick polymeric gum and not **29**. While DMAD is a good dieneophile, it is also an excellent Michael acceptor (a trait shared by most good dieneophiles). A likely explanation is that the zwitterionic intermediate reacted with/polymerized the DMAD in a Michael fashion instead of the desired Diels–Alder reaction. Surprisingly, the coarctate cyclization of **5** in the presence of DMAD led not to trapped product **30**, but rather inhibited the polymerization such that linear benzo[*f*]isoindazole **28** was isolated in 61% yield! Use of $[\{Rh(OAc)_2\}_2]$ also furnished **28** in low yield, and interestingly, only trace amounts of a dimeric compound. Based on these results, the cyclization reactions of the linear naphtho-fused azo–ene–yne **5** appear to yield compounds or intermediates that are very reactive/unstable under the reaction conditions studied; further work is ongoing.

Electronic absorption and emission spectroscopy: The electronic absorption and emission spectra for **16**, **17**, and **22** are presented in Figure 4. The emission profiles of the three

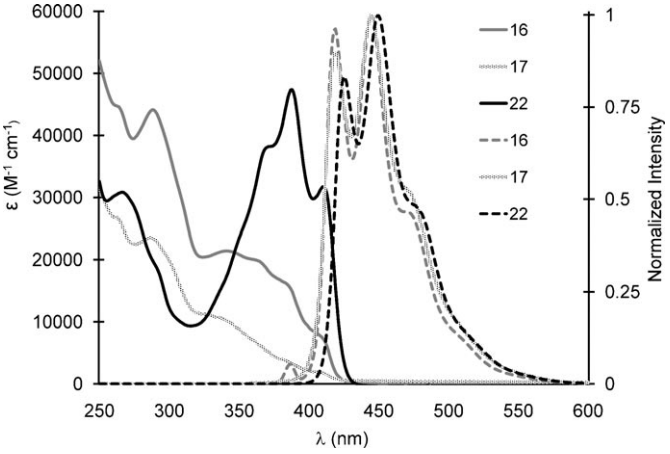


Figure 4. Electronic absorption (solid, left) and emission (dashed, right) spectra for dimers **16**, **17**, and **22**.

dimers are remarkably similar, although this is not unexpected as **16**, **17**, and **22** are structural isomers; however, their absorption spectra are much more unique. Dimer **22** has strong absorption from 350 nm to the λ_{max} at 411 nm. Indeed, excitation of **22** going from 411 to 370 nm and then to 280 nm results in only a 5 and 25% reduction of the fluorescent intensity, respectively. The *trans* dimer **16** displays a much weaker absorption and upon isomerization to *cis*-**17**

the absorption becomes almost non-existent. The increase in the absorption is most likely due to the planar nature of **22**, where it possesses a longer conjugation pathway than **16** and **17**, both of which are twisted out of planarity, confirmed by the X-ray structure in Figure 2 as well as by the DFT calculated structures.

Time-dependent DFT calculations (Table 2) corroborate these findings, as there is excellent agreement between the computed and experimental transition wavelengths. In addition, the transition dipole, which corresponds roughly to the extinction coefficient of that transition, faithfully replicate the absorption spectra in Figure 4: $f=1.242$ for **22** is a strong transition, $f=0.482$ for **16** is medium, and $f=0.191$ for **17** is weak.

Table 2. TD-DFT (B3LYP/6-31G* + ZPE) calculated transitions for dimers **16**, **17**, and **22**.

	16	**17**	**22**
HOMO/LUMO gap [eV]	3.195	3.267	3.028
absorbance (calcd) [nm]	388	380	410
absorbance (exp) [nm]	387(sh)	385(sh)	411
transition dipole *f* [Debye]	0.482	0.191	1.242

Conclusion

Three isomers of naphthalene-based ethynyltriazenes were synthesized and studied for the potential to undergo both pericyclic and coarctate cyclizations. Cyclization of 1,2-disubstituted naphthalenes **6** and **7** successfully yielded both benzocinnolines and benzoisoindazoles. Interestingly, the coarctate reaction of both isomers furnished significant amounts of dimerized material, which was unexpected because of the very dilute reaction conditions. In the case of **6**, the resultant *trans* dimer **16** was found to undergo light-mediated isomerization in solution to *cis* isomer **17**, a reaction that was significantly accelerated by the presence of trace acid. On the other hand, *trans* dimer **22** was unaffected by light and/or acid. The cyclization of **5** to afford the linear benzocinnoline/benzoisoindazole systems proved to be more problematic as the cyclized material appeared to be unstable under the reaction conditions examined, though **28** could be isolated in the presence of excess DMAD. While the results for **5** suggest that heteroacene-like structures might be difficult to prepare by pericyclic and coarctate azo–ene–yne cyclizations, recent work in our lab converting aminoanthraquinones ultimately to tetracene-like structures has been successful;[26] these new studies will be the subject of future reports.

Experimental Section

General methods: ^{1}H NMR spectra were recorded on a Varian Inova 300 MHz spectrometer (^{1}H, 299.95 MHz) and ^{13}C NMR spectra were recorder on either a Varian Inova 300 MHz or Varian Inova 500 MHz spectrometer (^{13}C, 75.43 or 125.76 MHz, respectively). Chemical shifts (δ) are expressed as ppm downfield from tetramethylsilane using residual solvent as an internal standard ($CHCl_3$; ^{1}H = 7.26 ppm and ^{13}C = 77.0 ppm; [D_6]DMSO; ^{1}H = 2.50 ppm and ^{13}C = 39.5 ppm). Coupling constants (*J*) are expressed in Hz. IR spectra were recorded by using a Nicolet Magna 550 FTIR spectrometer. THF, Et_2O, and toluene were distilled over Na/benzophenone ketal under N_2 prior to use. CH_2Cl_2 and 1,2-dichloroethane (DCE) were distilled over P_2O_5 under N_2 prior to use. All other chemicals were purchased at reagent grade quality and used as received. Reactions were carried out under an inert atmosphere (Ar) or by using medical-grade oxygen when necessary. Column chromatography was performed on 230–400 mesh silica gel. Preparative and analytical thin-layer chromatography was carried out on plastic-backed silica gel TLC plates with a UV indicator.

General procedure A—triazene formation:[21,22] To a flame-dried flask was added $BF_3{\cdot}OEt_2$ (4 equiv) under an Ar atmosphere and the flask was cooled to −15 °C. Slowly, a solution of the naphthalenamine (1 equiv) in dry THF (0.24 M) was added such that the internal temperature stayed below −10 °C. After complete addition, the reaction mixture was allowed to stir for 5 min, after which a 1 M solution of *t*BuONO in dry THF (3.5 equiv) was added over a 30 min period. The reaction mixture was then allowed to stir at −15 °C for 10 min before warming to 5 °C over 20 min. Pentane was added and the resultant red precipitate was isolated by filtration. The solid was then dissolved in DMF (0.06 M) and stirred at room temperature with $HNEt_2$ (10 equiv) and K_2CO_3 (20 equiv) for 2 h. The reaction mixture was then diluted with EtOAc, and washed with aqueous NH_4Cl (2×), water (3×) and brine. The organic layer was dried over $MgSO_4$, filtered through a short pad of silica; and concentrated in vacuo.

General procedure B—Sonogashira cross-coupling: A mixture of aryl halide (1 equiv), [$Pd(PPh_3)_2Cl_2$] (2 mol%), and CuI (4 mol%) was dissolved in a 1:1 solution of THF and iPr$_2$NH (0.05 M). The solution was purged with Ar for 45 min at room temperature, then TMSA (2 equiv) was added. Aryl iodides were stirred at room temperature, aryl bromides at 50 °C under an Ar atmosphere. Upon completion, the solvent was removed and the crude material was dissolved in minimal 10% CH_2Cl_2 in hexanes. The material was then filtered through a pad of silica eluting with 20% CH_2Cl_2 in hexanes. The solvent was then removed in vacuo.

General procedure C—protiodesilation: To a stirred solution of protected acetylene (1 equiv) in 5:1 THF/MeOH (0.05 M) was added K_2CO_3 (5 equiv). The reaction mixture was stirred at room temperature until completion, as which time it was diluted with EtOAc and washed with aq. NH_4Cl (2×), water (3×) and brine. The organic layer was then dried over $MgSO_4$, filtered through a pad of silica, and concentrated in vacuo to give the terminal acetylene.

General procedure D—pericyclic cyclization: In a screwtop pressure reaction vessel, a solution of azo–ene–yne (1 equiv) was dissolved in ODCB (0.005 M), capped, and placed in a preheated 200 °C sand bath. The reaction mixture was heated overnight, then cooled to room temperature. Removal of the ODCB in vacuo followed by purification by preparative TLC afforded pure benzocinnoline.

General procedure E—coarctate cyclization: A mixture of azo–ene–yne (1 equiv) and CuCl (5 equiv) in DCE (0.002 M) was stirred open to the air at room temperature until TLC indicated the reaction was complete. The reaction mixture was then filtered through a pad of silica eluting with 1:1 hexanes/EtOAc and the solvent was removed in vacuo.

Triazene 12: Iodoamine **9**[14] (0.85 g, 3.1 mmol) was allowed to react according to general Procedure A. Column chromatography (4:1 hexanes/CH_2Cl_2) furnished **12** (0.90 g, 81%) as a red oil. ^{1}H NMR ($CDCl_3$): $\delta=$ 8.38 (d, $J=8.7$ Hz, 1H), 7.80–7.68 (m, 3H), 7.57 (td, $J=7.5$ Hz, 1.5 Hz, 1H), 7.45 (td, $J=7.5$, 1.5 Hz, 1H), 4.0–3.8 (m, 4H), 1.39 ppm (t, $J=$ 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$): $\delta=148.5$, 135.6, 132.5, 132.0, 129.0, 128.0, 127.4, 125.2, 117.4, 100.6, 49.1, 42.3, 14.5, 10.9 ppm; IR (NaCl): $\tilde{\nu}=$ 3056, 2973, 2932, 2870, 1614, 1398, 1313, 1243 cm^{-1}; HRMS (ESI): *m*/*z*: calcd for $C_{14}H_{16}IN_3$: 353.0389, found 353.0401.

Alkyne 13: Iodotriazene **12** (0.71 g, 2.0 mmol) was allowed to react according to general procedure B at room temperature. Column chromatography (6:1 hexanes/CH_2Cl_2) gave **13** (0.45 g, 70%) as a red oil. ^{1}H NMR ($CDCl_3$): $\delta=8.38$ (d, $J=8.1$ Hz, 1H), 7.76 (d, $J=7.8$ Hz, 1H),

7.73–7.69 (m, 2H), 7.55–7.51 (m, 1H), 7.42–7.39 (m, 1H), 3.9–3.8 (m, 4H), 1.36 (t, J=7.2 Hz, 6H), 0.33 ppm (s, 9H); ^{13}C NMR ($CDCl_3$): δ= 151.4, 134.4, 131.2, 129.1, 127.9, 126.8, 126.1, 125.0, 116.5, 113.5, 104.0, 101,2, 49.2, 42.0, 14.5, 11.0 ppm; IR (NaCl): $\tilde{\nu}$=3057, 2963, 2934, 2139, 1617, 1588, 1405, 1329, 1247 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{19}H_{25}N_3Si$: 323.1818, found 323.1813.

Azo–ene–yne 6: Alkyne **13** (0.40 g, 1.2 mmol) was deprotected according to general procedure C. Terminal alkyne **6** (0.29 g, 97%) was isolated as a red oil and used without further purification. ^{1}H NMR ($CDCl_3$): δ= 8.48 (d, J=8.1 Hz, 1H), 7.82 (d, J=7.8 Hz, 1H), 7.81–7.78 (m, 2H), 7.59 (t, J=7.8 Hz, 1H), 7.45 (t, J=7.8 Hz, 1H), 4.0–3.8 (m, 4H), 3.78 (s, 1H), 1.36 ppm (t, J=6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ=151.8, 134.5, 131.0, 129.3, 127.9, 126.8, 125.8, 125.0, 116.7, 112.3, 86.4, 79.9, 49.0, 41.8, 14.4, 10.8 ppm; IR (NaCl): $\tilde{\nu}$=3290, 3057, 3974, 2933, 2871, 2094, 1616, 1588, 1451, 1403, 1328, 1243 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{17}N_3$: 251.1422, found 251.1433.

Benzo[*f*]cinnoline 14: Azo–ene–yne **6** (0.115 g, 0.45 mmol) was heated according to general procedure D. Purification by preparative TLC (2:1 EtOAc/hexanes) afforded **14** (0.051 g, 63%) as a tan solid. ^{1}H NMR ($CDCl_3$): δ=9.44 (d, J=6.0 Hz, 1H), 8.66–8.60 (m, 1H), 8.51 (d, J= 6.0 Hz, 1H), 8.28 (d, J=9.0 Hz, 1H), 8.03 (d, J=9.0 Hz, 1H), 7.98–7.92 (m, 1H), 7.82–7.70 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ=150.5, 146.7, 132.9, 132.3, 129.9, 128.9, 127.8, 127.7, 126.5, 125.5, 123.7, 118.2 ppm; IR (NaCl): $\tilde{\nu}$=2924, 2853, 1595, 1404, 1269 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{12}H_8N_2$: 180.0687, found 180.0701.

Benzo[*e*]isoindazole 15: Azo–ene–yne **6** (40 mg, 0.15 mmol) was dissolved in 1,2-dichloroethane (100 mL), and the solution was saturated with O_2 for 30 min. CuCl (200 mg) was added and the reaction was carried out according to general procedure E. Purification by preparative TLC (Et_2O) gave **15** (26 mg, 65%) as a red oil. ^{1}H NMR ($CDCl_3$): δ= 10.67 (s, 1H), 9.54 (dd, J=8.1, 1.2 Hz, 1H), 7.88 (dd, J=8.4, 1.2 Hz, 1H), 7.75–7.60 (m, 4H), 3.6–3.5 (m, 2H), 3.3–3.2 (m, 2H), 0.90 ppm (t, J= 7.5 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ=182.6, 145.0, 135.1, 132.0, 129.7, 128.6, 127.7, 127.2, 127.1, 126.9, 117.1, 116.9, 52.6, 12.0 ppm; IR (NaCl): $\tilde{\nu}$=2923, 2853, 1676, 1618, 1442 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{17}N_3O$: 267.1372, found 267.1394.

Dimers 16 and 17: Alkyne **6** (50 mg, 0.19 mmol) was dissolved in dry 1,2-dichloroethane (40 mL) and purged with Ar for 30 min. [{$Rh(OAc)_2$}$_2$] (5 mol%) was added and heated to 50°C with stirring. Upon completion, the reaction was cooled and filtered through a pad of silica. Concentration in vacuo and purification by preparative TLC (CH_2Cl_2) gave *trans* dimer **16** (22 mg, 46%) as a tan solid. ^{1}H NMR ($CDCl_3$): δ=8.82–8.79 (m, 2H), 8.46 (s, 2H), 7.88–7.85 (m, 2H), 7.70–7.62 (m, 4H), 7.52–7.44 (m, 4H), 3.6–3.5 (m, 4H), 3.35–3.25 (m, 4H), 0.98 ppm (t, J=7.2 Hz, 12H); ^{13}C NMR ($CDCl_3$): δ=145.3, 135.0, 131.1, 129.4, 128.7, 128.5, 126.5, 124.9, 123.1, 122.4, 117.9, 113.1, 52.6, 11.9 ppm; IR (NaCl): $\tilde{\nu}$= 2973, 2933, 2855, 1553, 1440 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{32}H_{34}N_6$: 502.2845, found 502.2869. The NMR sample of **16** in $CDCl_3$ (ca. 0.7 mL) was allowed to stand at room temperature for 36 h exposed to ambient light. Removal of the solvent afforded *cis* dimer **17** (22 mg, 100%) as a tan solid. ^{1}H NMR ($CDCl_3$): δ=8.13 (d, J=7.5 Hz, 2H), 7.72 (d, J= 7.5 Hz, 2H), 7.55–7.43 (m, 4H), 7.41 (s, 2H), 7.27 (m, 2H), 7.0–6.9 (br m, 2H), 3.0–2.6 (m, 8H), 0.65 ppm (t, J=7.2 Hz, 12H); ^{13}C NMR ($CDCl_3$): δ=144.8, 133.7, 130.5, 128.5, 128.3, 128.1, 125.8, 124.6, 123.9, 122.4, 117.5, 113.8, 51.1, 11.7 ppm; IR (NaCl): $\tilde{\nu}$=2973, 2933, 2856, 1452, 1379 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{32}H_{34}N_6$: 502.2845, found 502.2857.

Triazene 18: Bromoamine **10**[15] (1.0 g, 4.5 mmol) was allowed to react according to general procedure A. Purification by column chromatography (9:1 hexanes/CH_2Cl_2) furnished **18** (1.08 g, 79%) as a red oil. ^{1}H NMR ($CDCl_3$): δ=7.96–7.91 (m, 1H), 7.83–7.78 (m, 1H), 7.65 (d, J=8.7 Hz, 1H), 7.52–7.48 (m, 3H), 4.0–3.8 (m, 4H), 1.39 ppm (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ=146.2, 133.5, 130.4, 129.4, 127.9, 126.3, 126.1, 125.8, 124.0, 112.7, 49.1, 41.5, 14.9, 11.3 ppm; IR (NaCl): $\tilde{\nu}$=2974, 2932, 1580, 1466, 1409, 1339, 1242 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{14}H_{16}BrN_3$: 305.0528, found 305.0511.

Alkyne 19: Bromotriazene **18** (0.675 g, 2.1 mmol) was allowed to react according to general procedure B at 50°C. Alkyne **19** (0.635 g, 94%) was isolated as a yellow oil of sufficient purity. ^{1}H NMR ($CDCl_3$): δ=8.20–8.17 (m, 1H), 7.79–7.76 (m, 1H), 7.56–7.52 (m, 2H), 7.49–7.44 (m, 2H), 3.90 (q, J=7.2 Hz, 4H), 1.39 (t, J=7.2 Hz, 6H), 0.26 ppm (s, 9H); ^{13}C NMR ($CDCl_3$): δ=150.5, 133.8, 130.2, 128.4, 127.5, 126.5, 125.7, 124.2, 124.1, 109.8, 105.0, 95.9, 48.6, 41.1, 14.4, 11.0, 0.07 ppm; IR (NaCl): $\tilde{\nu}$=3055, 2963, 2933, 2142, 1466, 1413, 1337, 1247 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{19}H_{25}N_3Si$: 323.1818, found 323.1827.

Azo–ene–yne 7: Alkyne **19** (0.625 g, 1.91 mmol) was deprotected according to general procedure C. Terminal alkyne **7** (0.497 g, 99%) was isolated as a yellow oil and used without further purification. ^{1}H NMR ($CDCl_3$): δ=8.24–8.20 (m, 1H), 7.81–7.78 (m, 1H), 7.60–7.45 (m, 4H), 3.88 (q, J=7.2 Hz, 4H), 3.12 (s, 1H), 1.38 ppm (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ=151.0, 134.0, 130.2, 127.8, 127.6, 126.7, 125.9, 125.5, 124.3, 118.1, 83.7, 78.8, 52.5, 12.3 ppm; IR (NaCl): $\tilde{\nu}$=3289, 3053, 2974, 2933, 2871, 2095, 1672, 1448, 1340, 1242 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{17}N_3$: 251.1422, found 251.1412.

Benzo[*h*]cinnoline 20: Alkyne **7** (35 mg, 0.14 mmol) was cyclized according to general procedure D. Purification by preparative TLC (1:1 hexanes/EtOAc) afforded **20** (15 mg, 60%) as a light brown solid. ^{1}H NMR ($CDCl_3$): δ=9.61 (dd, J=7.2, 1.8 Hz, 1H), 9.46 (d, J=8.7 Hz, 1H), 7.99 (d, J=8.7 Hz, 1H), 7.95 (dd, J=7.2, 1.8 Hz, 1H), 7.90–7.77 (m, 3H), 7.63 ppm (d, J=8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ=147.3, 133.4, 133.2, 129.9, 129.6, 128.8, 128.2, 125.9, 124.4, 123.3, 122.8, 105.0 ppm; IR (NaCl): $\tilde{\nu}$=3053, 2923, 2853, 1607, 1579, 1499, 1414, 1366 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{12}H_8N_2$: 180.0687, found 180.0675.

Benzo[*g*]isoindazole 21 and dimer 22: Alkyne **7** (35 mg, 0.14 mmol) was cyclized according to general procedure E. Purification by preparative TLC (9:1 hexanes/ EtOAc) afforded **21** (10 mg, 27%) as a tan solid and **22** (16 mg, 46%) as a yellow solid. If the DCE solution was saturated with O_2 prior to CuCl addition, **21** was isolated in 71% yield, with no evidence of dimer formation. **21**: ^{1}H NMR ($CDCl_3$): δ=10.45 (s, 1H), 8.63–8.60 (m, 1H), 8.09 (d, J=9.3 Hz, 1H), 7.88 (dd, J=6.9, 1.8 Hz, 1H), 7.70–7.57 (m, 3H), 3.55 (br s, 2H), 3.28 (br s, 2H), 0.90 ppm (t, J= 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ=182.1, 143.3, 133.4, 132.4, 128.6, 128.1, 127.2, 127.1, 125.1, 122.5, 118.6, 117.2, 52.6, 12.1 ppm; IR (NaCl): $\tilde{\nu}$=3049, 2974, 2934, 2855, 1672, 1551, 1440 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{17}N_3O$ 267.1372, found 267.1387. **22**: ^{1}H NMR ($CDCl_3$): δ= 8.68–8.60 (m, 2H), 8.01 (s, 2H), 7.92–7.84 (m, 4H), 7.63–7.51 (m, 6H), 3.58 (br s, 4H), 3.28 (br s, 4H), 0.94 ppm (t, J=7.5 Hz, 12H); ^{13}C NMR ($CDCl_3$): δ=143.8, 134.9, 132.3, 128.2, 126.6, 126.5, 125.6, 124.0, 122.6, 118.8, 118.1, 113.9, 52.5, 12.3 ppm; IR (NaCl): $\tilde{\nu}$=3053, 2974, 2862, 1548, 1446 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{32}H_{34}N_6$: 502.2845, found 502.2832.

Dimer 22 using [{$Rh(OAc)_2$}$_2$]: Alkyne **7** (50 mg, 0.19 mmol) was dissolved in DCE (10 mL) and purged with Ar for 45 min. [{$Rh(OAc)_2$}$_2$] (5 mol%) was added and the reaction mixture was stirred at room temperature. Filtration through a pad of silica followed by purification by preparative TLC (9:1 hexanes/EtOAc) afforded **22** (27 mg, 55%) as a yellow solid whose spectral data matched those above.

Dibromide 24: CBr_4 (5.24 g, 7.8 mmol) was added to a solution of PPh_3 (8.2 g, 15.6 mmol) in CH_2Cl_2 (80 mL) at 0°C. The reaction mixture was stirred for 30 min then warmed to room temperature over 30 min. Aldehyde **23**[17] (1.0 g, 3.9 mmol) in DCM (25 mL) was added by cannula and the reaction mixture was stirred at room temperature. Upon completion, pentane (200 mL) was added. The resultant precipitate was filtered off and the solvent removed in vacuo. Purification by column chromatography (1:1 Et_2O/hexanes) provided **24** (0.86 g, 54%) as a yellow solid. ^{1}H NMR ($CDCl_3$): δ=8.54 (s, 1H), 7.80–7.74 (m, 3H), 7.59 (br s, 1H), 7.53 (s, 1H), 7.50–7.73 (m, 3H), 1.38 ppm (s, 9H); ^{13}C NMR ($CDCl_3$): δ= 176.7, 133.9, 133.4, 131.8, 130.0, 128.0, 127.7, 127.6, 127.5, 126.9, 125.5, 119.7, 95.3, 39.6, 27.4 ppm; IR (NaCl): $\tilde{\nu}$=3275, 2975, 2934, 2869, 1688, 1653, 1590, 1448, 1260 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{17}H_{17}Br_2NO$ 408.9677, found 408.9698.

Amine 25: A solution of **24** (0.5 g, 1.2 mmol) in EtOH (25 mL) and HCl (2 M, 45 mL) was refluxed overnight. Upon cooling, the resultant precipitate was removed by filtration. The filtrate was neutralized with aqueous $NaHCO_3$ solution to pH 8, then extracted twice with CH_2Cl_2. The combined organics were dried ($MgSO_4$), filtered through a short pad of silica, and concentrated in vacuo to give **25** (0.40 g, 96%) as a tan solid.

^{1}H NMR ($CDCl_3$): $\delta = 7.80$ (s, 1H), 7.72 (d, $J = 8.4$ Hz, 1H), 7.58 (d, $J = 8.1$ Hz, 1H), 7.48 (s, 1H), 7.39 (td, $J = 6.6$, 1.2 Hz, 1H), 7.28–7.21 (m, 1H), 7.04 (s, 1H), 3.48 ppm (br s, 2H); ^{13}C NMR ($CDCl_3$): $\delta = 141.4$, 134.5, 133.8, 129.0, 127.9, 127.4, 126.8, 125.5, 124.7, 122.9, 109.5, 93.7 ppm; IR (NaCl): $\tilde{\nu} = 3451$, 3375, 3052, 1632, 1611, 1506, 1465 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{12}H_9Br_2N$: 324.9102, found 324.9094.

Alkyne 26: Amine **25** (0.40 g, 1.2 mmol) in dry THF (60 mL) was cooled to −78 °C and then BuLi (1.6 M in hexanes, 4 mL, 6.0 mmol) was added. The reaction mixture was stirred at −78 °C for 30 min, then warmed to 0 °C and stirred for an additional hour. The reaction mixture was diluted with aqueous NH_4Cl solution and extracted three times with EtOAc. The combined organics were washed with brine, dried ($MgSO_4$), and concentrated. Purification by column chromatography (1:1 hexanes/CH_2Cl_2) afforded **26** (95 mg, 50 %) as a tan solid. ^{1}H NMR ($CDCl_3$): $\delta = 7.91$ (s, 1H), 7.64 (d, $J = 8.4$ Hz, 1H), 7.55 (d, $J = 8.7$ Hz, 1H), 7.37 (t, $J = 8.1$ Hz, 1H), 7.21 (t, 8.1 Hz, 1H), 7.00 (s, 1H), 4.34 (br s, 2H), 3.42 ppm (s, 1H); ^{13}C NMR ($CDCl_3$): $\delta = 144.4$, 134.9, 133.3, 127.6, 127.3, 127.0, 125.5, 122.8, 110.1, 107.9, 82.5, 80.3 ppm; IR (NaCl): $\tilde{\nu} = 3456$, 3370, 3287, 3050, 2096, 1626, 1608, 1502, 1364, 1182 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{12}H_9N$: 167.0735, found 167.0741.

Azo–ene–yne 5: Alkyne **26** (85 mg, 0.5 mmol) was allowed to react according to general procedure A, yielding **5** (90 mg, 74 %) as a red oil. ^{1}H NMR ($CDCl_3$): $\delta = 8.05$ (s, 1H), 7.80–7.69 (m, 3H), 7.45–7.33 (m, 2H), 3.85 (q, $J = 7.2$ Hz, 4H), 3.29 (s, 1H), 1.37–1.29 ppm (m, 6H); ^{13}C NMR ($CDCl_3$): $\delta = 149.5$, 133.9, 133.7, 130.9, 127.8, 127.3, 126.8, 125.0, 117.1, 113.4, 82.2, 80.5, 49.1, 42.3, 14.5, 11.0 ppm; IR (NaCl): $\tilde{\nu} = 3057$, 2963, 2934, 2139, 1588, 1405, 1329, 1247 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{17}N_3$: 251.1422, found 251.1441.

Benzo[*f*]isoindazole 28: Azo–ene–yne **5** (20 mg, 0.08 mmol) was allowed to react according to general procedure E with the addition of DMAD (4 mL). Purification by preparative TLC (CH_2Cl_2) afforded **28** (13 mg, 61 %) as a yellow oil. ^{1}H NMR ($CDCl_3$): $\delta = 10.50$ (s, 1H), 8.87 (s, 1H), 8.39 (s, 1H), 7.97–7.93 (m, 2H), 7.38–7.37 (m, 2H), 3.47 (br s, 4H), 0.92 ppm (t, $J = 7.2$ Hz. 6H); ^{13}C NMR ($CDCl_3$): $\delta = 180.4$, 144.4, 133.0, 132.8, 132.4, 128.8, 128.6, 125.4, 125.1, 120.1, 120.0, 115.3, 52.8, 11.9 ppm; IR (NaCl): $\tilde{\nu} = 3064$, 2975, 2934, 2870, 1685, 1561, 1466, 1223 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{17}N_3O$: 267.1372, found 267.1399.

Computational methods: All computations were performed by using the Gaussian 03[27] suite of programs at the B3LYP/6-31G* level of theory.[18] All stationary points were confirmed by harmonic frequency analysis and checked for stability for triplet and SCF convergence. The energies of the stationary points were determined, including zero point energies, at the same level of theory.

X-ray structure determinations: Diffraction intensities for **17** and **22** were collected at 173(2) K on a Bruker Apex CCD diffractometer using $Mo_{K\alpha}$ radiation $\lambda = 0.71073$ Å.[28] Space groups were determined based on systematic absences. Absorption corrections were applied by SADABS.[29] Structures were solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. All H atoms were found from the residual density maps and refined with isotropic thermal parameters. In the absence of atoms with significant anomalous scattering, an absolute configuration of **17** was indeterminate. All calculations were performed by the Bruker SHELXTL (v. 6.10) package.[30]

CCDC-784859 (**17**) and CCDC-784860 (**22**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystallographic Data for ***17***: $C_{32}H_{34}N_6$, $M = 502.65$, $0.38 \times 0.16 \times 0.10$ mm, $T = 173(2)$ K, orthorhombic, space group *Aba2*, $a = 22.550(7)$, $b = 9.826(3)$, $c = 12.140(4)$ Å, $V = 2689.9(14)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.241$ Mg m^{-3}, $\mu = 0.075$ mm^{-1}, $F(000) = 1072$, $2\theta_{max} = 54.00°$, 8468 reflections, 2824 independent reflections [$R_{int} = 0.0289$], $R1 = 0.0389$, $wR2 = 0.0953$ and GOF = 1.023 for 2504 reflections (240 parameters) with $I > 2\sigma(I)$, $R1 = 0.0462$, $wR2 = 0.1014$ and GOF = 1.023 for all 2824 reflections, max/min residual electron density +0.181/−0.130 e Å^3.

Crystallographic Data for ***22***: $C_{32}H_{34}N_6$, $M = 502.65$, $0.48 \times 0.12 \times 0.02$ mm, $T = 173(2)$ K, monoclinic, space group *C2/c*, $a = 25.653(10)$, $b = 8.777(4)$, $c = 12.795(5)$ Å, $\beta = 103.454(6)°$, $V = 2802(2)$ Å^3, $Z = 4$, $Z' = 0.5$, $\rho_{calcd} = 1.192$ Mg m^{-3}, $\mu = 0.072$ mm^{-1}, $F(000) = 1072$, $2\theta_{max} = 50.00°$, 10 639 reflections, 2473 independent reflections [$R_{int} = 0.0500$], $R1 = 0.0463$, $wR2 = 0.1088$ and GOF = 1.003 for 1759 reflections (240 parameters) with $I > 2\sigma(I)$, $R1 = 0.0766$, $wR2 = 0.1258$ and GOF = 1.003 for all 2473 reflections, max/min residual electron density +0.162/−0.218 e Å^3.

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