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Thermal C^2-C^6 Cyclization of Enyne−Carbodiimides: Experimental Evidence Contradicts a Diradical and Suggests a Carbene Intermediate

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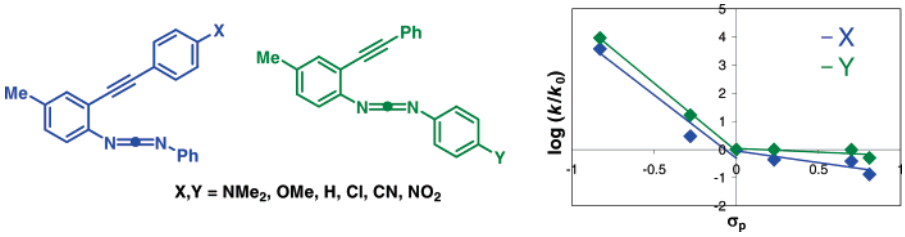

Mechanistic details of the thermal C^2-C^6 cyclization of enyne−carbodiimides are investigated. A variety of product and kinetic studies on solvent and substituent effects open the way for a deeper mechanistic understanding. Nonlinear Hammett correlations suggest that a change of mechanism takes place: the thermal C^2-C^6 cyclization of enyne−carbodiimides with electron-withdrawing substituents may be best described as a coarctate cyclization to a carbene and with electron-donating substituents as a polar cyclization to a carbene with strong zwitterionic character. Theoretical investigations had originally suggested a diradical intermediate. DFT computations and NBO analysis for the parent diazafulvenediyl are in agreement with a carbene intermediate. While any intermolecular trapping of the intermediate failed, the formation of the C−H insertion product **19** strongly supports the carbene hypothesis.

Introduction

Thermal cyclizations with concomitant formation of diradical intermediates have aroused enormous interest over the past two decades.[1] In particular, the efficient DNA cleaving properties of natural enediynes, e.g., neocarzinostatin, calicheamicin, or dynemicin,[2] ignited intense research efforts to understand the diradical process at the heart of their antitumor antibiotic activity. Depending on the structure of the reactive subunit, the natural enediynes cyclize either via the Bergman format[3] to 1,4-didehydrobenzene diradicals or by the Myers−Saito (C^2-C^7) reaction to α,3-didehydrotoluene diradicals.[4]

Interestingly, the Myers−Saito (C^2-C^7) reaction is not the only reaction mode for enyne−allenes/cumulenes. Over the past decade, we[5] and others[6] have demonstrated that the C^2-C^6 (Schmittel) cyclization of enyne−allenes **1** → **3** (A, B = carbon) (Scheme 1) can be triggered through the proper choice of

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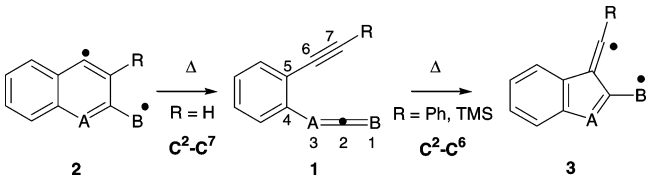
SCHEME 1. Postulated C^2-C^7 (2) and C^2-C^6 (3) Diradical Intermediates in the Thermal Cyclization of 1



substituents at the alkyne terminus, using electronic,[7] steric,[8] or ring strain effects.[9] According to kinetic isotope effect studies, the formulation of diradical intermediate **3** is clearly warranted, at least as long as one aryl group is present at center 1 or 7.[10] Depending on the substituents at the allene terminus, **3** has several options for efficient intramolecular follow-up reactions (to either formal [4 + 2][11] and [2 + 2][12] cycloadducts or ene products[13]), which make it a versatile compound for the construction of various ring systems.[14]

Herein, we will detail a kinetic study of the thermal cyclization of enyne−carbodiimides (A, B = nitrogen).[15] Other groups, in particular Wang et al.,[16] have exploited the thermal cyclization of enyne−carbodiimides for the preparation of pharmacologically interesting compounds such as indoloquinolines,[17] neocryptolepine[18] derivatives, and benzocarbazoles.[19] Previous computational and mechanistic studies suggested that **3** (for A, B = nitrogen) is a diradical as for A, B = carbon.[15a] The results of the present paper obtained through the kinetic evaluation of electronic and solvent effects, however, draw a different picture, proposing that the intermediate has either carbene (for electron-withdrawing substituents) or zwitterionic character (for electron-donating substituents).

Results

Synthesis of Enyne−Carbodiimides 7. Most of the required enyne−carbodiimides **7a**−**7e**, **7g**, and **7j** (Scheme 2) were synthesized along standard protocols.[15,20] Sonogashira coupling[21] of 2-iodo-4-methylaniline (**4**) with the corresponding acetylene led to anilines **5** in good to excellent yields. Reaction of **5** with isothiocyanates in the presence of a catalytic amount of DMAP in ethanol furnished the required thioureas **6** that were treated with methanesulfonyl chloride to afford enyne−carbodiimides **7**.

Because the synthesis of **7b** proved to be inexpedient due to the insolubility of thiourea **6b**, an alternative strategy was applied (Scheme 3). As a first step, thiourea **9** was prepared by the reaction of 2-ethynyl-4-methylaniline (**8**)[22] with phenyl isothiocyanate. After the reaction of **9** with methanesulfonyl chloride to yield enyne−carbodiimide **10**, cross-coupling with 4-iodonitrobenzene afforded the anticipated product **7b** in 73% yield.

All initial attempts to prepare **7f** and **7k** by the desulfonation of the corresponding thiourea according to the literature[15a] yielded directly the cyclized products **12f**,**k** (Scheme 5). As all efforts to isolate the thermolabile enyne−carbodiimides **7f** and **7k** at room temperature were unsuccessful, their characterization was effected spectroscopically at low temperature without purification.

The IR spectrum of crude **7k** showed the characteristic carbodiimide absorption at 2118 cm^{-1}, while the ^{13}C NMR spectrum (at 235 K) exhibited the two characteristic acetylenic signals at 86.3 and 96.5 ppm. The differential scanning calorimetry (DSC) study revealed an exothermic peak (T_{onset} = 18.4 °C) indicative of a low-temperature process, most likely C^2-C^6 cyclization, due to the formation of **12k** (Scheme 5). Equally, the DSC investigation of crude **7f** revealed an exothermic peak at T_{onset} = 29.1 °C, pointing again to a low-temperature C^2-C^6 cyclization. The IR spectrum of **7f** showed the existence of a carbodiimide unit by two strong signals at 2124 and 2142 cm^{-1}, while the ^{13}C NMR spectrum (at 236 K) confirmed the presence of the acetylene unit (C≡C) due to signals at 83.4 and 97.9 ppm.

For synthesis of **7h,i**, a method was used that had originally been explored by Wang et al.[16a] Accordingly, reaction of aniline **5a** with triphenylphosphonium dibromide furnished the aza-Wittig reagent **11** whose subsequent reaction with the corresponding isocyanates led to the formation of carbodiimides **7h,i** in 55% and 46% yield (Scheme 4).[16b]

X-ray Structure of 7b. 7b was obtained as a yellow crystalline solid from *n*-hexane/diethyl ether (10:1) and analyzed by X-ray diffraction. X-ray structural information on enyne−(hetero)allenes is presently limited to only one enyne−allene investigated by Dopico and Finn.[23] While the latter crystallized in the *s-trans* conformation, calculated to be the thermodynamically favored form,[24] **7b** was found to possess the *s-cis* conformation in the solid state (see the Supporting Information).

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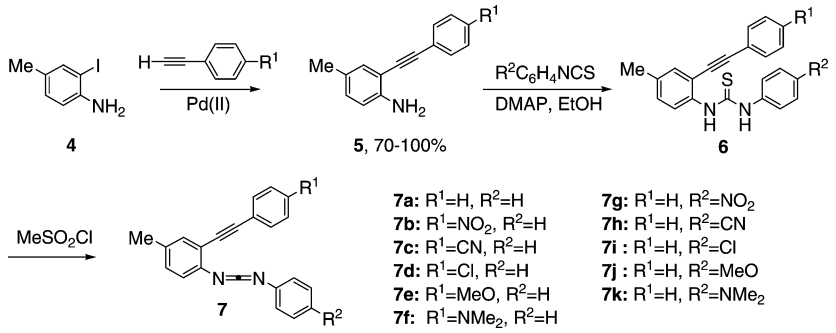
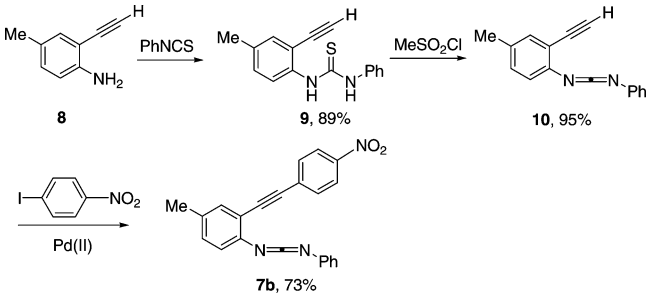
SCHEME 2. Synthesis of Enyne−Carbodiimides 7



SCHEME 3. Synthesis of Enyne−Carbodiimide 7b



In line with the X-ray results, DFT computations at the B3LYP/6-31G** level[25] suggest that *s-cis*-**7b** is more stable than the *trans* conformer by 0.88 kcal mol^{-1}. In the crystal, the carbodiimide unit (∠N3═C═N1 = 168.3°; for the numbering, see Scheme 1) has a bent geometry with an 11.7° deviation from linearity, agreeing well with the calculated data (∠N3═C═N1 = 167.8°, deviation 12.2°). The *s-cis* conformer in the solid is characterized by angles $\angle C_{Ar}-N3=C$ = 135.4° and $\angle C=N1-C_{Ph}$ = 128.5°, again in good agreement with the computed values ($\angle C_{Ar}-N3=C$ = 137.1°, $\angle C=N1-C_{Ph}$ = 132.2°). The phenyl group at the alkyne terminus arranges almost perpendicular to the phenyl group at the carbodiimide terminus. The nonbonding distance $N1-H_{PhNO_2}$ is 2.708 Å, somewhat shorter than in the computed structure (2.878 Å). On the basis of the computational and X-ray analysis data, *s-cis*-**7b** is the energetically favored conformer because of $N1-H_{PhNO_2}$ and CH/π hydrogen bonding and additional intermolecular π,π-stacking in the solid state.

Thermolysis of Enyne−Carbodiimides 7. To find optimum conditions for the thermolysis, enyne−carbodiimides were subjected to DSC measurements. While DSC kinetic investigations may not be well suited for reactions that are associated with significant amounts of side processes,[26] they are remarkably accurate for clean intramolecular reactions.[27] Kinetic data and onset temperatures, obtained from the analysis of the DSC signals,[27] are thus listed in Table 1.[28] For a better comparison, the rate constants at 120 °C (k_{120}) are also shown.

Conditions and appropriate solvents for the thermolysis were chosen depending on the onset temperatures (see Table 2). In general, a 20-fold excess of 1,4-cyclohexadiene (1,4-CHD) was added. All thermolysis reactions afforded as the main product the indoloquinolines **12** (Scheme 5) that were readily characterized by standard spectroscopic methods. The assignment had earlier been corroborated through X-ray crystallography.[29] The results are summarized in Table 2.

Moreover, thermolysis of enyne−carbodiimide **7h** was carried out in a flow experiment using a Cellular Process Chemistry (CPC) Systems microreactor[30,31] (flow rate at 150 °C, 0.25 mL min^{-1}), yielding 83% **12h** within 4 h.

Kinetic Studies on the Cyclization of 7a in Various Solvents. It is an important characteristic of radical reactions that their rates are remarkably independent of the polarity of the reaction medium.[32] Hence, the rate of the cyclization of **7a** was investigated in solvents with various polarities (C_6D_6, d_8-dioxane, CD_3CN, and CD_3OD) using ^1H NMR spectroscopy at 85 °C (Table 3). For methanol as solvent it was not possible to determine the rate at 85 °C since the reaction proceeded too fast for exact analysis. Therefore, the thermolysis was carried out at 45 °C and compared to the reaction in CD_3CN at the same temperature.

Discussion

As pointed out by various groups,[16−19,33] the thermal cyclization of enyne−carbodiimides provides pharmacologically interesting products. Hence, for more extended use of this thermal reaction, e.g., in combinatorial synthesis,[34] the influence of internal (electron-withdrawing and -donating groups) and external (polar and unpolar media) effects on the cyclization mode and their limitations should be well understood.

Solvent Effects on the Cyclization Rate. True radical and diradical cyclizations, as demonstrated for Myers−Saito[2a] and C^2-C^6 cyclizations[5,6] of enyne−allenes, do not depend significantly on the polarity or donor number (DN) of the solvent.[32] For enyne−carbodiimides not necessarily the same situation was expected, as the nitrogen atoms are potential donor centers and the central carbodiimide carbon atom is well-known for its high

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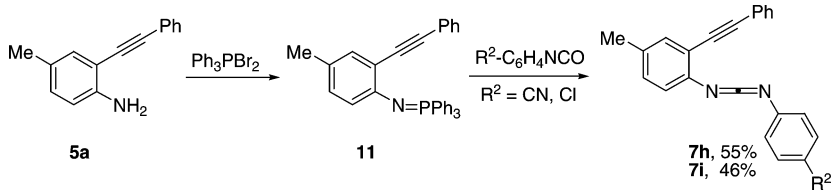
SCHEME 4. Synthesis of 7h,i via Aza-Wittig Reaction



SCHEME 5. Thermolysis of Enyne−Carbodiimides 7

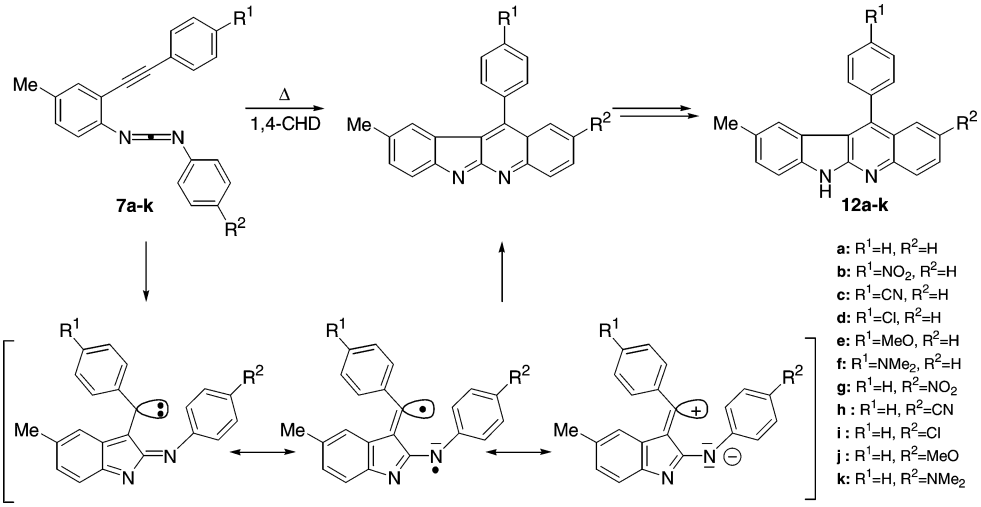


TABLE 1. Onset Temperatures and Kinetic Data of Enyne−Carbodiimide Cyclizations from DSC Measurements

enyne−carbodiimide **7**	onset temp T_c[a]/°C	activation energy E_a[b]/kcal mol^{-1}	rate constant $k_{120}/10^{-3}$ s^{-1}
a	97	27.7	2.60
b	126	29.5	0.33
c	110	28.7	0.98
d	106	28.6	1.14
e	73	27.2	7.71
f[c]	29	21.6	9660
g	115	28.4	1.29
h	111	27.9	2.56
i	99	27.9	2.59
j	64	25.7	43.0
k[c]	18	20.8	23700

[a] Obtained from DSC graphs. [b] Accuracy ±0.2 kcal mol^{-1}. [c] DSC data were obtained without purification of the enyne−carbodiimide.

TABLE 2. Conditions for the Thermolysis of 7 Yielding Product 12

enyne−carbodiimide **7**	solvent	cyclization conditions	yield of **12**/%
a	toluene	111 °C, 4 h	78[b]
b	toluene	111 °C, 10 h	63
c	toluene	111 °C, 6.5 h	65
d	toluene	111 °C, 6 h	52
e	toluene	75 °C, 7 h	79
g	toluene	111 °C, 5 h	75
h	toluene	111 °C, 12 h	98
i	toluene	111 °C, 5 h	54
j	toluene	111 °C, 0.5 h[a]	76

[a] Because of slow decomposition, **7j** was subjected to thermolysis directly after isolation. [b] Reference 15a.

electrophilicity.[35] Indeed, the kinetic study of the thermolysis of **7a** showed a significant dependence of the cyclization rate constant on the solvent. At 85 °C the reaction proceeded 7 times faster in dioxane ($k = 5.30 \times 10^{-4}$ s^{-1}) and 9 times faster in acetonitrile ($k = 6.93 \times 10^{-4}$ s^{-1}) than in benzene ($k = 7.83 \times 10^{-5}$ s^{-1}). A further acceleration by about a factor of 4, as compared to the reaction in acetonitrile, was found in methanol ($k = 9.16 \times 10^{-5}$ s^{-1} vs 2.33×10^{-5} s^{-1} at 45 °C). As the rate constants correlate best with the DN and not with the dielectric constant ϵ or $E_T(30)$,[36] the reactive species in the rate-determining step of the thermal C^2−C^6 cyclization of enyne−carbodiimides may be different from that of enyne−allenes.[15] Hence, a discussion about the mechanism has to invoke alternative pathways (Scheme 5).

TABLE 3. Rate Constants of the C^2−C^6 Cyclization of 7a in Various Solvents Measured by ^{1}H NMR Spectroscopy

solvent	temp/°C	$k/10^{-5}$ s^{-1}	half-life $t_{1/2}$/min	R^2
C_6D_6	85	7.83	147	0.999
d_8-dioxane	85	53.0	22	0.999
CD_3CN	85	69.3	17	0.998
CD_3CN	45	2.33	495	0.999
CD_3OD	45	9.16	126	0.993

Influence of Substituents on the Kinetics of the Cyclization. Interesting information about the nature of the transition state and the involved intermediate was obtained from the influence of electron-withdrawing and -donating groups at the alkyne and carbodiimide termini on the cyclization kinetics. Figure 1 shows that there is a clear trend in the cyclization rate constants and the activation energies as a function of the electronic properties of the substituents: incorporation of electron-donating groups, e.g., methoxy and dimethylamino, leads to an acceleration of the cyclization, whereas electron-withdrawing groups, e.g., chloro, cyano and nitro, decelerate

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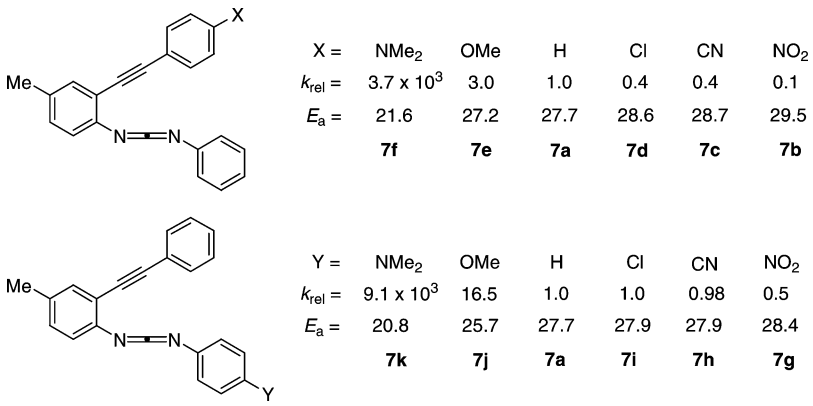

FIGURE 1. Summarized kinetic data of the enyne−carbodiimide cyclization at 120 °C. Substituents are varied at either the alkyne or carbodiimide terminus (k, s^{-1}; E_a, kcal mol^{-1}).

TABLE 4. Comparison of the Experimental log(k/k_0) Values of 7 with Various σ Constants ($k_0 = k_{X,Y=H}$)[38]

	log(k/k_0) (X)	log(k/k_0) (Y)	σ_p	σ_p^+	σ_p^-	$\sigma_p^\bullet$
NO_2	−0.88	−0.30	0.81	0.79	1.27	0.57
CN	−0.42	−0.01	0.70	0.66	1.00	0.46
Cl	−0.36	−0.002	0.23	0.11	0.19	0.12
OMe	0.47	1.22	−0.28	−0.78	−0.26	0.24
NMe_2	3.57	3.96	−0.63	−1.7	−0.12	0.90

the reaction independent of the position of the substituent. The rate increase is about 29000-fold for substituent X at the alkyne terminus and about 18000-fold for substituent Y at the allene unit. This has to be compared to the minor electronic influence of the 4-C_6H_4R substitution at the alkyne terminus on the thermal C^2-C^6 cyclization of enyne−allenes (with R = OMe, Me, H, F, CN, and NO_2) as manifested by a maximum rate acceleration of 2.6 (at 60 °C) on going from R = F to R = NO_2.[37]

Although the substituents X and Y in the thermal cyclization of **7** are numerically somewhat limited, their wide diversity from donor to acceptor character should still allow for a meaningful quantitative correlation with Hammett σ values[38] to receive helpful information about the character of the transition state.

From the data in Table 4 it is obvious that the log(k/k_0) values of enyne−carbodiimides **7** do not correlate straightforward with the $\sigma_p^\bullet$ values for radical reactions (see also the Supporting Information). This is particularly noteworthy, as the rate constants of the enyne−allene thermolysis correlate very well with the radical substituent constant $\sigma_p^\bullet$, thus lending strong support for a diradical mechanism. While in radical processes the attachment of electron-withdrawing groups, such as nitro or cyano, leads to an acceleration due to the developing radical center in the transition state (positive $\sigma_p^\bullet$ value), the cyclization of enyne−carbodiimides is decelerated with both substituents (as X and Y).

Correlations of the rate constants, separated for the series X and Y (see Figure 1), with substituent constants provided the best correlations with σ_p (and slightly worse with σ_p^+), but *only* when we allowed for a changeover in the mechanism separating electron-donating (X, Y = NMe_2, OMe, H) and electron-withdrawing (X, Y = NO_2, CN, Cl, H) substituents. Correlations with σ_p are shown in Figure 2; for all the others see the Supporting Information. For the electron-withdrawing substituents X, Y = NO_2, CN, Cl, H both series X and Y display only a very small negative ρ on the order of −0.83 (X) and −0.26 (Y), while for the electron-donating ones the ρ values are much more negative (−4.49 and −4.80 for X and Y, respectively). The same picture, though with a slightly worse correlation coefficient, is received for σ_p^+. Remarkably, ρ values for both series X and Y exhibit the same sign and almost identical magnitude. Moreover, for both series the correlation lines meet at the same point of intersection (at X, Y = H). This suggests that (i) a change in the mechanism and the nature of the intermediate may take place for both series at X, Y = H, (ii) the activation energy is lowered by electron-donating groups X and Y independent of their location in **7**, and (iii) their quantitative electronic influence operates along the same line.

What Do These Data Suggest for the Mechanism? A concerted mechanism, **7** → **12**, which has already been excluded earlier by the almost identical rate constants for 2,6-dimethylphenyl vs phenyl groups at the carbodiimide terminus,[15a] is no plausible option for the formation of **12**. Accordingly, in line with Engels's computational results, a stepwise mechanism should apply.[15a] As the observed substituent effect on the rate constant of up to 29 000, however, is much too pronounced to be rationalized by a radical process, a diradical intermediate is not very plausible. Moreover, whatever the intermediate, it must profit equally from donor substituents at both sites X and Y and for both mechanisms to the same extent as indicated by the similar slope in the Hammett correlation. This strongly proposes the intermediacy of a carbene-like intermediate. Actually, computational results from Engels and co-workers on the C^2-C^6 cyclization of enyne−allenes[39] and enyne−ketenes[40] suggest that the attachment of an amino group at the alkyne terminus may lead to intermediate **15** that no longer possesses diradical character (as **14**) but the character of a polar carbene (Scheme 6).

How can one reconcile the findings of a nonlinear Hammett correlation[41] with carbene-type intermediates? The notable acceleration in the thermolysis of **7** for both electron-donating

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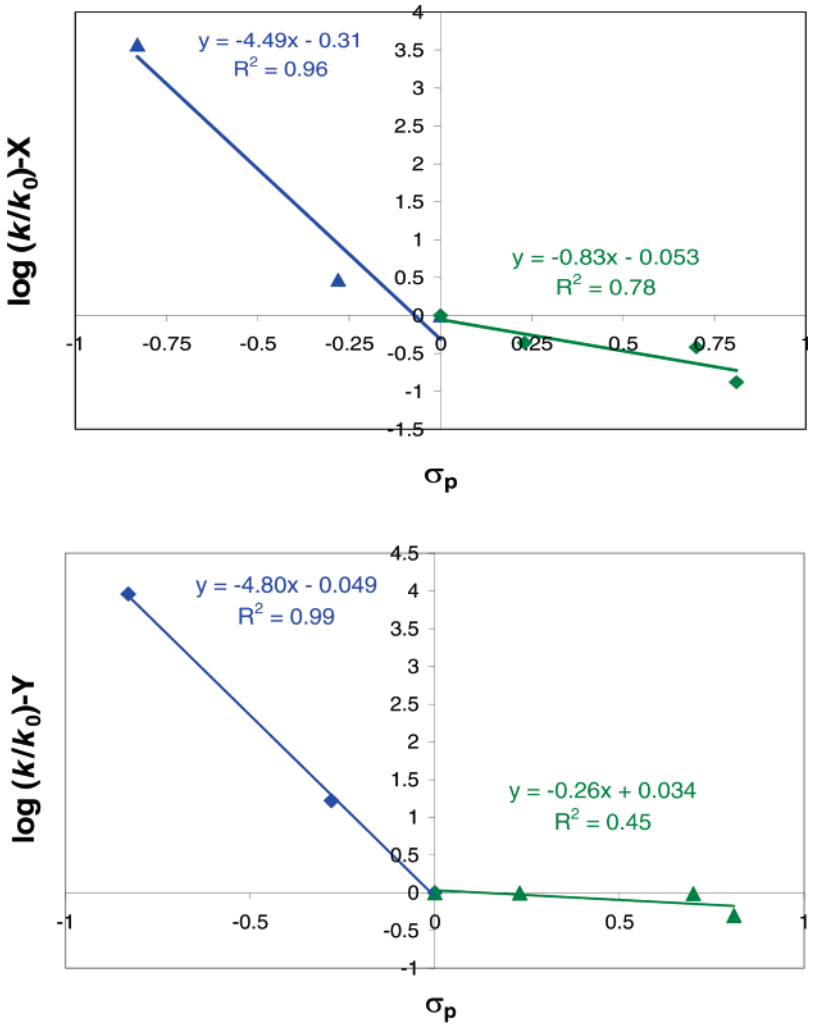
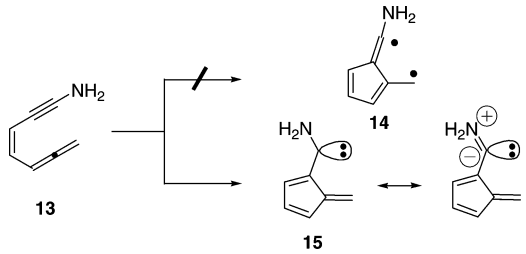


FIGURE 2. Correlation of the rate constants of the thermolysis of **7** with σ_p.

SCHEME 6. Diradical 14 vs Carbenoide 15 Intermediate in the Cyclization of Amino-Substituted Enyne−Allene 13[39b]



substituents X and Y = NMe_2, OMe suggests to invoke a polar cyclization resulting in the formation of a strongly zwitterionic carbene. The assumption of a carbene, **16f,k**, with strong zwitterionic character as an intermediate in the C^2-C^6 cyclization of enyne−carbodiimides **7f,k** is indeed in line with both the observed substituent effects, as (i) the dipole moment is expected to be enlarged against that in the reactant and (ii) the electron-deficient carbene center should be stabilized by the attachment of electron-donating groups at both positions X and Y (Scheme 7). The analogous polar mechanism should apply for X, Y = OMe and to a small extent even with X, Y = H. The odds of a polar mechanism for X, Y = H receives some support from the observed solvent effect, as the rate strongly increases with the donor quality DN of the solvent.

For enyne−carbodiimides with X, Y = H, Cl, CN, NO_2, a much less polar transition state must apply for the thermal cyclization. A reasonable mechanistic hypothesis that is in full agreement with all experimental results is a coarctate transition[42] state leading directly to carbene **17** (Scheme 8), in which the zwitterionic contributions are rather small. Formation of carbene intermediates has been discussed in the coarctate cyclizations of (2-ethynylphenyl)phenyldiazenes[43b,c] and pseudocoarctate cyclizations of (2-ethynylphenyl)triazenes.[43]

Altogether, the Hammett plot indicates a break in the mechanism that may be rationalized by a changeover from a polar (with X, Y = NMe_2, OMe) to a coarctate mechanism. The real molecule **7**, however, possibly experiences all electronic interactions at once, so that within the series an allocation of the two mechanistic scenarios may depend on the donor quality of X and Y.

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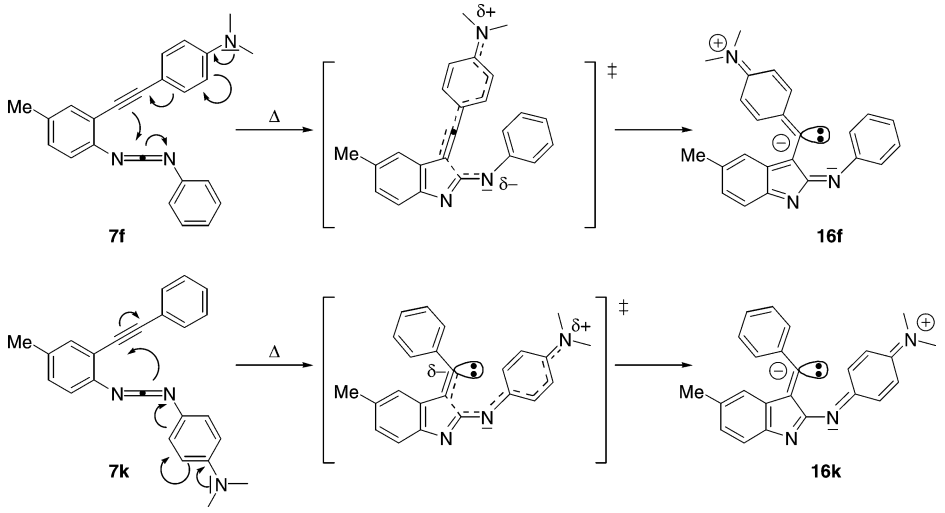
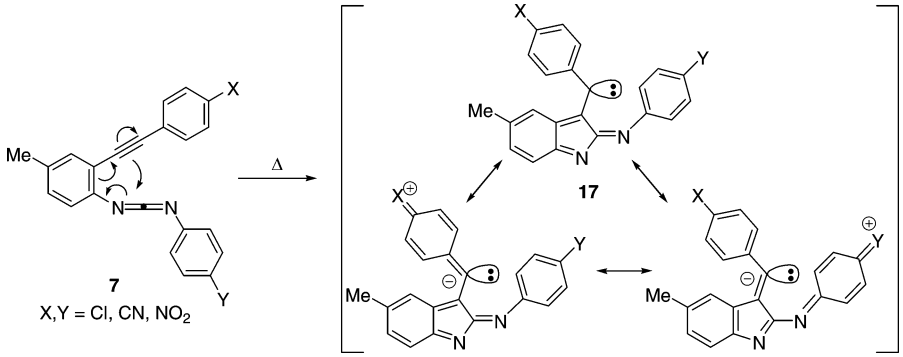
SCHEME 7. Postulated Polar Cyclization Leading to Zwitterionic Carbene Intermediates 16



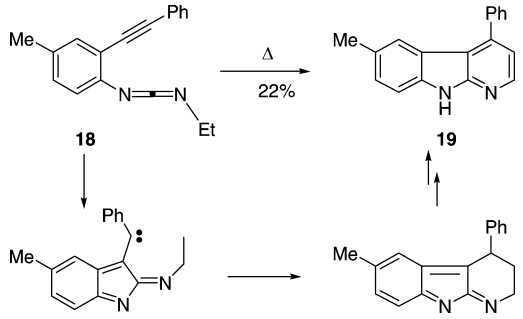
SCHEME 8. Postulated Coarctate Cyclization Leading to Carbene Intermediates 17



Despite the suggested intermediacy of carbenes **16** and **17**, all intermolecular trapping experiments involving enyne−carbodiimides **7a**, **7g**, and **7k** with tetramethylethene, 1,4-CHD, and MeOH were met with failure. Evidently, intermolecular trapping of **16** and **17** cannot compete with their cyclization to **12**. Recent evidence has exposed that the thermolysis of enyne−allenes, although depending on the substituent pattern, is dominated by nonstatistical dynamic intramolecular follow-up reactions that should render intermolecular trapping of an intermediate practically impossible.[44] The thermal cyclization of enyne−carbodiimides **7** may equally be influenced by dynamic effects, but ongoing work in our group has not yet resulted in clear-cut evidence.

If nonstatistical dynamic effects are operative in the thermal cyclization of enyne−carbodiimides, then an alternative intramolecular trapping reaction has to be conceived, which is strongly evocative of a carbene intermediate. To avoid a cyclization onto the aryl group, we have prepared enyne−carbodiimide **18** carrying an ethyl group at the carbodiimide terminus. While intermolecular trapping was again unsuccessful, the detection of product **19** (Scheme 9) furnished strong indirect evidence for the occurrence of a carbene intermediate, as otherwise formation of **19** cannot readily be rationalized. It seems that insertion into a CH bond via a six-membered transition state dominates over other reaction options, strongly suggestive of a carbene intermediate.

SCHEME 9. Formation of 19 and the Postulated Reaction Pathway via an Intermediate Carbene



Finally, computations on the parent diazafulvenediyl intermediate and its NBO analysis (on the CISD/6-31(d) level of theory) corroborate our assignment of a carbene-type intermediate (see the Supporting Information), suggesting that the thermal cyclization of enyne−carbodiimides proceeds similarly to the cyclization of triazenes and diazenes.[42b,c,43] Despite notable efforts, a diradical intermediate could not be located on the energy hypersurface constructed as a function of the bond angle and the bond length at the carbene center.

Conclusions

From the nonlinear correlation of $\log(k/k_0)$ of **7** with Hammett σ_p values, indicative of a change of the mechanism, it can be proposed that the C^2-C^6 cyclization of enyne−carbodiimides generates a carbene intermediate by either a coarctate or a polar

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cyclization. Electron-donating groups X and Y lead to a highly zwitterionic carbene and electron-withdrawing groups X and Y to a rather unpolar carbene. The incidence of a polar cyclization mechanism is additionally supported by the notable rate increase with augmentation of the DN of the solvent, as observed for enyne−carbodiimide **7a**. While intermolecular trapping of the intermediate was unsuccessful, an intramolecular CH insertion, as derived indirectly from the formation of **19,** and computational evidence support the carbene hypothesis. As a consequence, further mechanistic studies on the nature of the intermediate are now also warranted for the thermal cyclization of enyne−ketenimines[45] (see Scheme 1, A = nitrogen, B = carbon) and alternative hetero-enyne−allenes and −cumulenes.[46]

Experimental Section

(4-Methoxyphenyl)acetylene, (4-chlorophenyl)acetylene, and 4-ethynyl-*N*,*N*-dimethylaniline were prepared as described by Sonogashira et al.[21] 2-Iodo-4-methylaniline (**4**), [47] 4-methyl-2-(phenylethynyl)aniline (**5a**),[48] and 2-ethynyl-4-methylaniline (**8**)[22] were prepared according to reported procedures.

2-[(4-Cyanophenyl)ethynyl]-4-methylaniline (5c). 5c was prepared from **4** (1.38 g, 5.92 mmol) and (4-cyanophenyl)acetylene (830 mg, 6.53 mmol) in 35 mL of dry triethylamine with $Pd(PPh_3)_2Cl_2$ (83.0 mg, 118 μmol) and copper(I) iodide (11.0 mg, 57.8 μmol) as the catalyst. The reaction was finished after 3 d. The crude product was purified by column chromatography (silica gel, *n*-hexane:ethyl acetate = 3:1), yielding **5c** as a yellow solid (1.21 g, 5.21 mmol, 88%): mp 99−100 °C; IR (KBr) $\tilde{\nu}$ = 3457 (m, N−H), 3367 (m, N−H), 3051 (w), 2928 (w), 2857 (m), 2228 (s, C≡N), 2188 (s, C≡C), 1622 (s), 1599 (s), 1570, 1497 (s), 1403 (m), 1312 (m), 1255 (s), 1157 (s), 855 (s), 837 (s), 818 (s), 556 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.24 (3H, s), 4.32 (2H, br s, NH), 6.67 (1H, d, J = 8.3 Hz), 7.00 (1H, dd, J = 8.3 and 1.9 Hz), 7.18 (1H, d, J = 1.9 Hz), 7.55−7.63 (4H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.2, 90.8, 92.9, 106.8, 111.2, 114.8, 118.5, 127.5, 128.3, 131.6, 131.8, 132.0, 132.4, 145.6. Anal. Calcd for $C_{16}H_{12}N$ (232.28): C, 82.73; H, 5.21; N, 11.87. Found: C, 82.26; H, 4.83; N, 11.81.

2-[(4-Chlorophenyl)ethynyl]-4-methylaniline (5d). 5d was prepared from **4** (1.55 g, 6.66 mmol) and (4-chlorophenyl)acetylene (1.00 g, 7.32 mmol) in 40 mL of dry triethylamine with $Pd(PPh_3)_2Cl_2$ (93.0 mg, 133 μmol) and copper(I) iodide (50.0 mg, 266 μmol) as the catalyst at 50 °C. The reaction was finished after 3 h. The crude product was purified by column chromatography (silica gel, *n*-hexane:ethyl acetate = 4:1), yielding **5d** as a bright yellow solid (1.46 g, 6.04 mmol, 91%): mp 127−129 °C; IR (KBr) $\tilde{\nu}$ = 3435 (m, N−H), 3345 (m, N−H), 2914 (w), 2856 (w), 2197 (w, C≡C), 1622 (m), 1498 (s), 1396 (w), 1317 (m), 1250 (m), 1155 (m), 1010 (m), 887 (w), 817 (C−Cl), 810 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.23 (3H, s), 4.12 (2H, br s, NH), 6.65 (1H, d, J = 8.3 Hz), 6.96 (1H, dd, J = 8.3 and 1.6 Hz), 7.18 (1H, d, J = 1.6 Hz), 7.32 (2H, d, J = 8.5 Hz), 7.44 (2H, d, J = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.2, 87.1, 93.2, 107.5, 114.6, 121.8, 127.2, 128.6, 130.8, 132.2, 132.5, 134.0, 145.4. Anal. Calcd for $C_{15}H_{12}ClN\cdot 0.1H_2O$ (241.72): C, 73.98; H, 5.05; N 5.75. Found: C, 73.82; H, 4.89; N, 5.78.

2-[(4-Methoxyphenyl)ethynyl]-4-methylaniline (5e). 5e was prepared from **4** (1.42 g, 6.09 mmol) and (4-methoxyphenyl)-acetylene (804 mg, 6.08 mmol) in 30 mL of dry triethylamine with copper(I) iodide (17.7 mg, 92.9 μmol) and $Pd(PPh_3)_2Cl_2$ (64.4 mg, 91.7 μmol) as the catalyst. After 5 h the reaction was finished. Crystallization from cyclohexane yielded 1.01 g of a brown solid (4.25 mmol, 70%): mp 82−84 °C; IR (KBr) $\tilde{\nu}$ = 3468 (m, N−H), 3376 (m, N−H), 3041 (w), 3019 (w), 2961 (m), 2916 (m), 2837 (w), 2196 (w, C≡C), 1606 (s), 1563 (m), 1510 (s), 1500 (s), 1457 (m), 1441 (s), 1414 (m), 1315 (m), 1287 (s), 1246 (s), 1170 (m), 1154 (m), 1104 (m), 1027 (s), 832 (s), 816 (s), 575 (m), 529 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.23 (3H, s), 3.83 (3H s), 4.13 (2H, br s, NH), 6.65 (1H, d, J = 8.3 Hz), 6.88 (2H, d, J = 8.8 Hz), 6.94 (1H, dd, J = 8.3 and 1.6 Hz), 7.18 (1H, d, J = 1.6 Hz), 7.46 (2H, d, J = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.3, 55.3, 84.6, 94.3, 108.3, 113.9, 114.5, 115.5, 127.2, 130.2, 132.1, 132.9, 145.2, 159.5. Anal. Calcd for $C_{16}H_{15}NO$ (237.30): C, 80.98; H, 6.37; N, 5.90. Found: C, 80.96; H, 6.41; N, 5.92.

2-[[4-(*N*,*N*-Dimethylamino)phenyl]ethynyl]-4-methylaniline (5f). To a solution of **4** (3.52 g, 15.1 mmol) and 4-ethynyl-*N*,*N*-dimethylaniline (2.40 g, 16.6 mmol) in 50 mL of dry NEt_3 were added $PdCl_2(PPh_3)_2$ (110 mg, 15.0 μmol) and copper(I) iodide (60.0 mg, 30.0 μmol) at room temperature under a nitrogen atmosphere. After the black reaction mixture had been stirred for 2 h, the crude product was purified by column chromatography (silica gel, *n*-hexane:ethyl acetate = 6:1), yielding **5f** as a brown solid (2.59 g, 10.3 mmol, 68%): mp 136−138 °C dec; IR (KBr) $\tilde{\nu}$ = 3452 (m, N−H), 3363 (m, N−H), 2910 (m), 2192 (w, C≡C), 1611 (s), 1525 (s), 1499 (w), 1446 (w), 1316 (w), 1229 (m), 1188 (m), 1067 (w), 944 (w), 815 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.23 (3H, s), 2.99 (6H, s), 4.12 (2H, br s, NH_2), 6.61−6.68 (3H, m), 6.91 (1H, dd, J = 8.1 Hz, J = 1.5 Hz), 7.16 (1H, d, J = 1.5 Hz), 7.39 (2H, d, J = 9.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.3, 40.2, 83.7, 95.5, 108.9, 110.2, 111.8, 114.3, 127.1, 129.7, 131.9, 132.5, 145.0, 149.9.

General Procedure for the Preparation of Thioureas. To a solution of the appropriate aniline in ethanol (0.15−0.30 M, depending on the solubility of the aniline) were added an equimolar amount of the corresponding isothiocyanate and a catalytic amount of 4-(dimethylamino)pyridine (DMAP).[49] The mixture was stirred at room temperature for several days, after which the thioureas were directly isolated by filtration.

Data for *N*-(2-ethynyl-4-methylphenyl)-*N*′-phenylthiourea (9): yield 89%; white solid; mp 144.5−147 °C dec; IR (KBr) $\tilde{\nu}$ = 3307 (s, C≡C−H), 3164 (s, N−H), 3021 (w), 2973 (w), 2108 (w, C≡C), 1588 (m), 1574 (w), 1532 (s), 1502 (s), 1449 (m), 1358 (m), 1314 (m), 1291 (m), 1263 (m), 1230 (m), 1200 (s), 850 (w), 750 (m), 693 (m), 638 (m), 611 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.29 (3H, s), 3.11 (1H, s), 7.19 (1H, dd, J = 8.6 and 1.6 Hz), 7.25 (1H, semicovered), 7.32−7.46 (5H, m), 8.11 (1H, br s, NH), 8.18 (1 H, br s, NH), 8.24 (1H, d, J = 8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.7, 79.1, 83.7, 115.2, 123.4, 126.1, 127.7, 129.9, 130.2, 132.8, 135.2, 136.2, 137.3, 179.0. Anal. Calcd for $C_{16}H_{14}N_2S$ (266.37): C, 72.15; H, 5.30; N, 10.52; S, 12.04. Found: C, 72.20; H, 5.49; N, 10.48; S, 11.84.

Data for *N*-[4-methyl-2-(phenylethinyl)phenyl]-*N*′-phenylthiourea (6a): yield 89%; white solid; mp 135−137 °C; IR (KBr) $\tilde{\nu}$ = 3320 (m, N−H), 3180 (s, N−H), 3097 (m), 3033 (m), 3006 (m), 2950 (m), 2199 (w, C≡C), 1587 (s), 1534 (s), 1445 (m), 1360 (s), 1313 (m), 1294 (m), 1254 (s), 1182 (m), 822 (m), 754 (s), 698 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.32 (3H, s), 7.10−7.39 (12H, m), 8.15 (1H, d, J = 8.4 Hz), 8.22 (1H, br s, NH), 8.29 (1H, br s, NH); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 20.7, 84.5, 95.8, 116.9, 122.2, 124.2, 125.2, 127.2, 128.2, 128.7, 129.7, 129.8, 131.6, 132.4, 135.4 (2C), 136.4, 178.9. Anal. Calcd for $C_{22}H_{18}N_2S$ (342.46): C, 77.16; H, 5.30; N, 8.13; S, 9.36. Found: C, 76.83; H, 5.35; N, 7.88; S, 9.05.

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Data for *N*-[2-[(*p*-chlorophenyl)ethinyl]-4-methylphenyl]-*N′*-phenylthiourea (6d): yield 67%; yellow solid; mp 139−141 °C; IR (KBr) $\tilde{\nu}$ = 3324 (s, N−H), 3119 (s, N−H), 2973 (m), 2196 (w, C≡C), 1634 (m), 1586 (s), 1544 (s), 1488 (s), 1362 (m), 1294 (m), 1179 (m), 1086 (m), 823 (s, C−Cl), 763 (m), 694 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.31 (3H, s), 7.12 (1H, t, J = 7.4 Hz), 7.23 (1H, dd, J = 8.3 and 1.6 Hz), 7.29−7.33 (2H, m), 7.39 (1H, s), 7.48−7.56 (6H, m), 7.60 (1H, d, J = 8.3 Hz), 9.47 (1H, br s, NH), 10.0 (1H, br s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 20.3, 87.7, 92.8, 118.4, 121.3, 123.9, 124.7, 127.0, 128.5, 128.9, 129.8, 132.2, 133.0, 133.6, 135.1, 137.9, 139.2, 179.9. Anal. Calcd for $C_{22}H_{17}ClN_2S$ (376.90): C, 70.11; H, 4.55; N, 7.43; S, 8.51. Found: C, 70.30; H, 4.46; N, 7.47; S, 8.51.

Data for *N*-[2-[(*p*-methoxyphenyl)ethinyl]-4-methylphenyl]-*N′*-phenylthiourea (6e): yield 73%; light brown solid; mp 136−137.5 °C; IR (KBr) $\tilde{\nu}$ = 3315 (s, N−H), 3190 (s, N−H), 3100 (m), 3019 (m), 2963 (m), 2201 (m, C≡C), 1601 (s), 1591 (s), 1540 (s), 1513 (s), 1451 (m), 1365 (m), 1318 (m), 1301 (s), 1253 (s), 1170 (m), 1031 (m), 832 (m), 754 (w), 712 (w), 702 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.32 (3H, s), 3.84 (3H, s), 6.81−6.85 (2H, m), 7.12−7.31 (7H, m), 7.36 (2H, d, J = 7.5 Hz), 7.89 (1H, br s, NH), 8.11 (1H, d, J = 8.1 Hz), 8.32 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.8, 55.3, 83.2, 96.0, 113.9, 114.3, 124.1, 125.2, 127.2, 129.2, 129.4, 129.8, 130.7, 132.4, 133.2, 135.6, 136.4, 159.9, 178.9. Anal. Calcd for $C_{23}H_{20}N_2S$ (372.49): C, 74.16; H, 5.41; N, 7.52; S, 8.61. Found: C, 74.00; H, 5.66; N, 7.35; S, 8.34.

Data for *N*-[4-methyl-2-[[*p*-(*N*,*N*-dimethylamino)phenyl]ethynyl]phenyl]-*N′*-phenylthio urea (6f): yield 63%; orange solid; mp 158−162 °C; IR (KBr) $\tilde{\nu}$ = 3314 (s, N−H), 3163 (m, N−H), 3041 (m), 2991 (m), 2187 (m, C≡C), 1603 (s), 1592 (s), 1543 (s), 1525 (s, C−N), 1509 (s), 1444 (m), 1365 (s, N−H), 1293 (m), 1256 (s), 1181 (s, C═S), 811 (s), 759 (m), 697 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.32 (3H, s), 3.01 (6H, s, NMe_2), 6.60 (2H, d, J = 9.1 Hz), 7.11−7.40 (9H, m), 7.90 (1H, br s, NH), 8.08 (1H, d, J = 8.4 Hz), 8.26 (1H, br s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 20.3, 39.7, 82.3, 95.9, 108.4, 111.8, 119.4, 123.8, 123.9, 124.7, 126.8, 128.5, 131.7, 132.6, 134.9, 137.1, 139.2, 150.2, 179.7. Anal. Calcd for $C_{24}H_{23}N_3S$ (385.53): C, 74.77; H, 6.01; N, 10.90; S, 8.32. Found: C, 74.44; H, 6.17; N, 10.86; S, 8.19.

Data for *N*-[4-methyl-2-(phenylethinyl)phenyl]-*N′*-(*p*-nitrophenyl)thiourea (6g): yield 75%; pale yellow solid; mp 208−210 °C dec; IR (KBr) $\tilde{\nu}$ = 3318 (m, N−H), 3081 (w), 3020 (w), 2923 (w), 1631 (m), 1582 (s), 1545 (s), 1504 (s), 1327 (s), 1302 (s), 1271 (m), 1228 (m), 1180 (w), 1142 (m), 1109 (m), 849 (m), 821 (m), 750 (m), 698 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.37 (3H, s), 7.23 (1H, dd, J = 8.4 and 1.8 Hz), 7.29−7.42 (6H, m), 7.64 (2H, d, J = 9.1 Hz), 7.72 (1H, d, J = 8.4 Hz), 8.06−8.13 (3H, m), 8.44 (1H, br s, NH); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.8, 84.3, 96.5, 118.5, 121.8, 123.2, 124.6, 124.8, 128.4, 129.1, 130.3, 131.5, 133.2, 134.8, 137.2, 143.4, 144.5, 178.4. Anal. Calcd for $C_{22}H_{17}N_3O_2S$ (387.46): C, 68.20; H, 4.42; N, 10.85; S, 8.28. Found: C, 67.95; H, 4.50; N, 10.59; S, 7.78.

Data for *N*-(*p*-methoxyphenyl)-*N′*-[4-methyl-2-(phenylethinyl)phenyl]thiourea (6j): yield 76%; light brown solid; mp 139−141 °C; IR (KBr) $\tilde{\nu}$ = 3332 (s, N−H), 3152 (s, N−H), 3013 (w), 2948 (m), 2831 (w), 1605 (w), 1583 (m), 1538 (m), 1510 (s), 1461 (m), 1361 (m), 1301 (m), 1260 (s), 1248 (s), 1166 (m), 1026 (m), 834 (m), 815 (m), 760 (m), 696 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.31 (3H, s), 3.64 (3H, s), 6.71 (2H, d, J = 8.9 Hz), 7.19 (1H, dd, J = 8.6 and 2.0 Hz), 7.23−7.38 (8H, m), 7.99 (1H, br s, NH), 8.22−8.26 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.7, 55.2, 84.5, 95.6, 114.9, 122.3, 123.9, 127.5, 128.2, 128.6, 128.6, 129.6, 131.6, 132.4, 135.1 (2C), 136.5, 158.8, 178.4. Anal. Calcd for $C_{23}H_{20}N_2OS$ (372.49): C, 74.16; H, 5.41; N, 7.52; S, 8.61. Found: C, 73.86; H, 5.51; N, 7.81; S, 8.25.

Data for *N*-[4-methyl-2-(phenylethynyl)phenyl]-*N′*-[*p*-(*N*,*N*-dimethylamino)phenyl]thiourea (6k): yield 97%; light yellow solid; mp 172−174 °C; IR (KBr) $\tilde{\nu}$ = 3286 (m, N−H), 3161 (m, N−H), 3045 (m), 2987 (m), 2203 (w, C≡C), 1607 (m), 1588 (s), 1543 (s), 1520 (s, C−N), 1440 (m), 1359 (m, N−H), 1275 (m), 1260 (s), 1191 (m), 1168 (s, C═S), 826 (m), 750 (s), 687 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.31 (3H, s), 2.82 (6H, s), 6.46 (2H, d, J = 8.9 Hz), 7.14−7.20 (3H, m), 7.28−7.33 (6H, m), 7.67 (1H, br s, NH), 8.16 (1H, br s, NH), 8.36 (1H, d, J = 7.4 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 20.2, 40.2, 86.1, 94.3, 112.4, 117.4, 122.2, 126.0, 126.1, 128.7 (2C), 128.9, 129.5, 131.4, 132.0, 134.4, 138.0, 148.5, 179.3. Anal. Calcd for $C_{24}H_{23}N_3S$ (385.53): C, 74.77; H, 6.01; N, 10.90; S, 8.32. Found: C, 74.69; H, 6.27; N, 10.96; S, 8.25.

General Procedure for the Preparation of Enyne−Carbodiimides 7. According to the reported procedure,[50] methanesulfonyl chloride (200 mol %) was added via syringe over a period of 10−15 min to a solution of thiourea **6** (0.05−0.10 M), dry triethylamine (300 mol %), and DMAP (catalytic amount) in dry dichloromethane, cooled in an ice bath. The resulting mixture was stirred for an additional 10−15 min. Then the solvent was removed in vacuo, and **7** was isolated from the crude mixture by column chromatography.

Data for *N*-[4-methyl-2-(phenylethynyl)phenyl]-*N′*-phenylcarbodiimide (7a): yield 89%; pale yellow oil (silica gel, *n*-hexane: diethyl ether = 10:1) that crystallizes on standing at −30 °C; mp 29 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3060 (w), 3024 (w), 2921 (w), 2861 (w), 2318 (w), 2147 (s, N═C═N), 2124 (s, N═C═N), 1593 (s), 1566 (w), 1518 (w), 1493 (s), 1485 (s), 1443 (w), 1396 (w), 1283 (w), 1261 (m), 1213 (s), 1071 (m), 1026 (w), 821 (m), 754 (s), 689 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.36 (3H, s), 7.07−7.16 (3H, m), 7.20−7.30 (7H, m), 7.37−7.42 (3H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.7, 85.7, 96.2, 119.7, 122.7, 124.2, 124.4, 125.0, 128.0, 128.2, 129.2, 130.1, 131.5, 133.2, 133.5, 135.1, 135.9, 139.0. Anal. Calcd for $C_{22}H_{16}N_2$ (308.38): C, 85.69; H, 5.23; N, 9.08. Found: C, 85.37; H, 5.33; N, 9.06.

***N*-[4-Methyl-2-[(*p*-nitrophenyl)ethynyl]phenyl]-*N′*-phenylcarbodiimide (7b)** was prepared by a Sonogashira coupling from *N*-(2-ethynyl-4-methylphenyl)-*N′*-phenylcarbodiimide (**10**).

10 was prepared along the general procedure: yield 95%; colorless oil (silica gel, dichloromethane) that crystallizes on standing at −30 °C; mp 60 °C (DSC); IR (neat) $\tilde{\nu}$ = 3294 (m, C≡C−H), 3063 (w), 3021 (w), 2923 (w), 2856 (w), 2129 (s, N═C═N), 2105 (s, N═C═N), 2077 (s, N═C═N), 1591 (m), 1560 (w), 1528 (w), 1484 (s), 1450 (w), 1280 (w), 1216 (s), 1072 (m), 822 (s), 758 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.31 (3H, s), 3.24 (1H, s), 7.04 (1H, d, J = 8.1 Hz), 7.09−7.24 (4H, m), 7.29−7.38 (3H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.7, 80.3, 83.5, 118.0, 124.2, 124.4, 125.4, 129.3, 130.8, 133.7, 133.9, 135.1, 137.8, 138.7. Anal. Calcd for $C_{16}H_{12}N_2$ (232.28): C, 82.73; H, 5.21; N, 12.06. Found: C, 82.49; H, 5.31; N, 11.98.

To prepare **7b**, 4-iodonitrobenzene (122 mg, 490 μmol) and **10** (125 mg, 538 μmol) were dissolved in a mixture of dry triethylamine and dry tetrahydrofuran (5 mL each) under nitrogen and protection from light. After addition of 17.0 mg of $PdCl_2(PPh_3)_2$ (24.0 μmol) and 5.0 mg of copper(I) iodide (24 μmol), the resulting suspension was stirred at room temperature for 90 min. Then the solvent was removed in vacuo, and **7b** was isolated by column chromatography (silica gel, *n*-hexane:ethyl acetate = 9:1) to yield 127 mg (359 μmol, 73%) of a yellow solid: mp 104 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3104 (w), 3069 (w), 2922 (w), 2851 (m), 2206 (m, C≡C), 2169 (s, N═C═N), 2131 (s, N═C═N), 1592 (s), 1561 (w), 1516 (s, N═O), 1482 (m), 1340 (s, N═O), 1218 (w), 1106 (w), 852 (m), 827 (w), 762 (m), 748 (w), 690 (w) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.35 (3H, s), 7.05−7.29 (7H, m), 7.35−7.37 (1H, m), 7.42 (2H, d, J = 9.0 Hz), 8.04 (2H, d, J = 9.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.8, 90.9, 94.0, 118.6, 123.3, 124.3, 124.6, 125.4, 129.5, 129.6, 131.3, 132.1, 133.2, 133.8, 135.5, 136.4, 138.8, 146.9. Anal. Calcd for $C_{22}H_{15}N_3O_2$ (353.38): C, 74.78; H, 4.28; N, 11.89. Found: C, 74.63; H, 4.58; N, 11.63.

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***N*-[2-[(*p*-Cyanophenyl)ethynyl]-4-methylphenyl]-*N*′-phenylcarbodiimide (7c).** As *N*-[2-[(*p*-cyanophenyl)ethynyl]-4-methylphenyl]-*N*′-phenylthiourea (**6c**) was not obtained in pure form, the crude thiourea was directly used. The reaction of 100 mg of crude **6c** (max 272 μmol), suspended in 5 mL of dry dichloromethane, with 54 μL of methanesulfonyl chloride (79.4 mg, 549 μmol) and 115 μL of triethylamine (84.0 mg, 830 μmol) yielded 41.0 mg of **7c** (123 μmol, 45% over two steps) as a yellow solid after column chromatography (silica gel, *n*-hexane:ethyl acetate = 5:1): mp 118 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3052 (w), 2922 (w), 2860 (w), 2222 (w, C≡N), 2208 (m, N═C═N), 2173 (s, N═C═N), 2124 (m, N═C═N), 1594 (m), 1487 (m), 1401 (w), 1263 (w), 1221 (m), 1074 (w), 847 (m), 814 (m), 756 (m), 690 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.34 (3H, s), 7.04−7.18 (5H, m), 7.19−7.28 (2H, m), 7.33−7.38 (3H, m), 7.44−7.48 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.7, 89.9, 94.2, 111.4, 118.4, 118.6, 124.2, 124.5, 125.3, 127.5, 129.4, 131.0, 131.6, 131.8, 133.1, 133.6, 135.4, 136.3, 138.7. Anal. Calcd for $C_{23}H_{15}N_3$ (333.39): C, 82.86; H, 4.54; N, 12.60. Found: C, 82.54; H, 4.67; N, 12.30.

Data for *N*-[2-[(*p*-chlorophenyl)ethynyl]-4-methylphenyl]-*N*′-phenylcarbodiimide (7d): yield 74%; white solid (silica gel, *n*-hexane:ethyl acetate = 9:1); mp 68 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3065 (w), 3031 (w), 2925 (w), 2862 (w), 2253 (m, C≡C), 2126 (s, N═C═N), 1594 (m), 1493 (s), 1398 (w), 1262 (w), 1213 (m), 1091 (m), 908 (s), 828 (m), 740 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.33 (3H, s), 7.06 (1H, d, J = 8.1 Hz), 7.08−7.12 (2H, m), 7.15−7.17 (4H, m), 7.22−7.24 (4H, m), 7.34 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.7, 86.6, 95.1, 119.4, 121.2, 124.2, 124.4, 125.1, 128.3, 129.3, 130.4, 132.7, 133.3, 133.5, 134.3, 135.2, 135.9, 138.9. Anal. Calcd for $C_{22}H_{15}ClN_2$ (333.39): C, 77.08; H, 4.41; N, 8.17. Found: C, 76.66; H, 4.29; N, 8.16.

Data for *N*-[2-[(*p*-methoxyphenyl)ethynyl]-4-methylphenyl]-*N*′-phenylcarbodiimide (7e): yield 82%; pale yellow oil (silica gel, *n*-hexane:ethyl acetate = 6:1); IR (neat) $\tilde{\nu}$ = 3062 (w), 3001 (w), 2956 (w), 2933 (w), 2836 (w), 2313 (w), 2124 (s, N═C═N), 1604 (s), 1595 (s), 1511 (s), 1487 (s), 1464 (m), 1398 (w), 1290 (m), 1250 (s), 1213 (m), 1173 (m), 1032 (m), 831 (m), 757 (m), 690 (w) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ = 1.96 (3H, s), 3.81 (3H, s), 6.57 (2H, d, J = 9.0 Hz), 6.72 (1H, dd, J = 8.2 and 2.2 Hz), 6.76−6.84 (1H, m), 6.88−7.02 (3H, m), 7.10−7.17 (2H, m), 7.28−7.29 (1H, m), 7.38 (2H, d, J = 9.0 Hz); ^{13}C NMR (50 MHz, C_6D_6) δ = 20.6, 54.7, 85.3, 97.5, 114.2, 114.6, 115.4, 120.9, 124.6, 124.8, 125.1, 129.6, 130.1, 133.4, 133.9, 135.3, 136.4, 139.8, 160.2; MS (EI, 70 eV) *m*/*z* (rel intens) = 338 (100, M$^+$), 323 (13, M$^+$ − CH_3), 293 (14), 279 (10); HR-MS ($C_{23}H_{18}N_2O$) *m*/*z* calcd for [M]$^+$ 338.1419, found 338.1415.

Data for *N*-[4-methyl-2-(phenylethynyl)phenyl]-*N*′-(*p*-nitrophenyl)carbodiimide (7g): yield 78%; white solid (silica gel, *n*-hexane:ethyl acetate = 9:1); mp 115 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3057 (w), 2922 (w), 2835 (w), 2182 (m, N═C═N), 2135 (s, N═C═N), 2079 (m, N═C═N), 1602 (m), 1586 (s), 1517 (s, N═O), 1490 (m), 1336 (s, N═O), 1217 (m), 1169 (w), 1109 (m), 859 (m), 848 (m), 831 (m), 759 (m), 748 (m), 687 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.35 (3H, s), 7.06 (1H, d, J = 8.4 Hz), 7.11−7.31 (8H, m), 7.36−7.37 (1H, m), 8.00 (2H, d, J = 9.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.8, 85.2, 96.8, 120.4, 122.3, 124.4 (2C), 124.9, 128.1, 128.7, 130.3, 131.3, 132.0, 133.5, 134.0, 136.3, 144.3, 146.6. Anal. Calcd for $C_{22}H_{15}N_3O_2$ (353.38): C, 74.78; H, 4.28; N, 11.89. Found: C, 74.42; H, 4.40; N, 12.03.

***N*-(*p*-Cyanophenyl)-*N*′-[4-methyl-2-(phenylethynyl)phenyl]-carbodiimide (7h).** To 4-methyl-2-(phenylethynyl)-*N*-(triphenylphosphoranylidene)aniline (**11**)[16a] (0.730 g, 1.61 mmol) in 15 mL of dry benzene was added a solution of *p*-cyanophenyl isocyanate (231 mg, 1.61 mmol) in 10 mL of dry benzene at room temperature under a nitrogen atmosphere. After the reaction mixture was stirred for 3 h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, *n*-hexane:diethyl ether = 4:1), yielding 310 mg of **7h** (890 μmol, 55%) as white needles: mp 112 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3155, 2934 (w), 2253 (m, C≡N), 2228 (m, C≡C), 2137 (s, N═C═N), 1600 (m), 1566 (w), 1496 (m), 1383 (m), 1263 (m), 1218 (m), 1096 (w), 841 (m), 734 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.36 (3H, s), 7.07 (1H, d, J = 8.2 Hz), 7.14 (1H, dd, J = 8.2 Hz, 1.5 Hz), 7.19 (2H, d, J = 8.4 Hz), 7.22 (2H, m), 7.29 (3H, m), 7.38 (1H, m), 7.43 (2H, d, J = 8.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 20.8, 85.2, 96.7, 107.9, 118.7, 120.3, 122.3, 124.4, 124.8, 128.1, 128.7, 130.3, 131.3, 133.2, 133.5, 133.5, 134.3, 136.1, 144.4. Anal. Calcd for $C_{23}H_{15}N_3$ (333.39): C, 82.86; H, 4.54; N, 12.60. Found: C, 82.83; H, 4.51; N, 12.80.

***N*-(*p*-Chlorophenyl)-*N*′-[4-methyl-2-(phenylethynyl)phenyl]-carbodiimide (7i).** To **11**[16a] (1.00 g, 2.21 mmol) in 25 mL of dry toluene was added a solution of *p*-chlorophenyl isocyanate (339 mg, 2.21 mmol) in 15 mL of dry toluene at room temperature under a nitrogen atmosphere. After the reaction mixture was stirred for 2 h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, *n*-hexane"ethyl acetate = 4:1) followed by recrystallization from *n*-hexane/diethyl ether (9:1), yielding 350 mg of **7i** (1.02 mmol, 46%) as a white solid: mp 56−58 °C; IR (KBr) $\tilde{\nu}$ = 3207 (w), 3055 (w), 2862 (w), 2262 (m, C≡C), 2150 (s, N═C═N), 1500 (s), 1483 (s), 1442 (m), 1262 (s), 1214 (s), 1091 (s), 1013 (m), 828 (s, C−Cl), 755 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.34 (3H, s), 7.06 (1H, d, J = 8.0 Hz), 7.07 (2H, d, J = 8.8 Hz), 7.09−7.12 (1H, m), 7.14 (2H, d, J = 8.8 Hz), 7.22−7.24 (2H, m), 7.27−7.33 (3H, m), 7.37 (1H, d, J = 1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.7, 85.5, 96.4, 119.8, 122.5, 124.3, 125.3, 128.0, 128.4, 129.2, 130.1, 130.3, 131.4, 133.2, 133.5, 135.4, 135.5, 137.7; MS (EI, 70 eV) *m*/*z* (rel intens) = 342 (24, M$^+$), 341 (15), 308 (25), 307 (100, M$^+$ − Cl), 292 (24), 75 (38); ESI-MS ($C_{22}H_{16}ClN_2^+$) *m*/*z* calcd 343.1, found 343.1.

Data for *N*-(*p*-methoxyphenyl)-*N*′-[4-methyl-2-(phenylethynyl)phenyl]carbodiimide (7j): yellow oil that is not stable and rapidly assumes a dark green hue (silica gel, *n*-hexane:ethyl acetate = 5:2); IR (neat) $\tilde{\nu}$ = 3033 (m), 2923 (m), 2835 (m), 2270 (w), 2129 (s, N═C═N), 1582 (m), 1520 (s), 1499 (s), 1464 (m), 1442 (m), 1350 (m), 1291 (m), 1246 (s), 1213 (s), 1144 (m), 1034 (m), 954 (m), 830 (s), 757 (s), 691 (m) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ = 2.04 (3H, s), 3.29 (3H, s), 6.60 (2H, d, J = 8.9 Hz), 6.81 (1H, dd, J = 7.9, 1.8 Hz), 7.00−7.05 (3H, m), 7.12 (1H, d, J = 7.9 Hz), 7.15 (2H, d, J = 8.9 Hz), 7.37 (1H, d, J = 1.8 Hz), 7.51−7.57 (2H, m); ^{13}C NMR (50 MHz, C_6D_6) δ = 19.5, 53.8, 85.7, 95.9, 113.9, 119.2, 122.5, 123.8, 124.6, 127.3, 127.4, 128.2, 128.8, 129.5, 130.9, 133.1, 134.0, 136.4, 156.6.

Thermolyses of Enyne−Carbodiimides 7. To a degassed solution of **7** in the appropriate solvent (3−5 mM) was added a 20-fold excess of 1,4-CHD. The reaction mixture was heated under nitrogen until the reaction control by TLC showed the full disappearance of **7**. After evaporation of the solvent and of 1,4-CHD, the residue was purified by column chromatography, furnishing the cyclized products **12** in yields between 60% and 98% (for the thermolysis of **7a**, see ref 15a, and for data for **12a**, see ref 20).

9-Methyl-11-(*p*-nitrophenyl)-6*H*-indolo[2,3-*b*]quinoline (12b). **7b** was heated in toluene at reflux temperature for 10 h. Column chromatography (silica gel, *n*-pentane:ethyl acetate = 1:1) yielded **12b** as a yellow solid: yield 63%; mp > 328 °C dec; IR (KBr) $\tilde{\nu}$ = 3103 (br, m), 3072 (br, m), 2921 (m), 2849 (m), 1619 (m), 1599 (m), 1586 (m), 1520 (s, N═O), 1484 (m), 1399 (w), 1382 (w), 1344 (s, N═O), 1302 (w), 1292 (w), 1249 (m), 1230 (m), 1219 (w), 860 (w), 846 (w), 826 (w), 801 (w), 754 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.21 (3H, s), 6.71 (1H, s), 7.29 (1H, d, J = 8.0 Hz), 7.38−7.42 (2H, m), 7.51 (1H, d, J = 7.5 Hz), 7.75 (1H, td, J = 8.3 and 1.3 Hz), 7.88 (2H, d, J = 8.6 Hz), 8.05 (1H, d, J = 8.3 Hz), 8.56 (2H, d, J = 8.6 Hz), 11.81 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 21.1, 111.0, 115.0, 119.8, 122.1, 122.3, 123.2, 124.4, 125.3, 127.4, 128.3, 128.8, 129.5, 130.9, 138.9, 139.9, 143.1, 146.2, 147.8, 152.5. Anal. Calcd for $C_{22}H_{15}N_3O_2 \cdot 1/$

$_{10}C_4H_8O_2$ (353.38): C, 74.28; H, 4.40; N, 11.60. Found: C, 74.29; H, 3.99; N, 11.54.

11-(*p*-Cyanophenyl)-9-methyl-6*H*-indolo[2,3-*b*]quinoline (12c). Thermolysis of **7c** was carried out in toluene at reflux temperature for 6.5 h. Column chromatography (silica gel, *n*-hexane:ethyl acetate = 4:1) yielded **12c** as a yellow solid: yield 65%; mp > 323 °C dec; IR (KBr) $\tilde{\nu}$ = 3122 (br, m), 3027 (br, m), 2922 (w), 2852 (w), 2228 (m, C≡N), 1620 (m), 1606 (m), 1588 (m), 1486 (m), 1402 (m), 1384 (m), 1354 (m), 1301 (w), 1250 (w), 1233 (w), 1218 (w), 1023 (w), 843 (w), 783 (m) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6) δ = 2.21 (3H, s), 6.65 (1H, s), 7.28 (1H, dd, J = 8.5, 1.2 Hz), 7.39 (1H, ddd, J = 8.5, 6.8, 1.2 Hz), 7.40 (1H, d, J = 8.2 Hz), 7.51 (1H, dd, J = 8.5, 1.2 Hz), 7.73 (1H, ddd, J = 8.5, 6.8, 1.2 Hz), 7.79 (2H, d, J = 8.4 Hz), 8.04 (1H, d, J = 8.2 Hz), 8.19 (2H, d, J = 8.4 Hz), 11.80 (1 H, br s, NH); ^{13}C NMR (50 MHz, DMSO-d_6) δ = 21.1, 110.9, 111.7, 115.1, 118.9, 119.8, 122.2, 122.3, 123.2, 125.4, 127.4, 128.2, 128.8, 129.5, 130.5, 133.2, 139.4, 139.9, 141.2, 146.2, 152.5. Anal. Calcd for $C_{23}H_{15}N_3 \cdot {}^1/_{12}C_4H_8O_2$ (333.39): C, 82.25; H, 4.63; N, 12.33. Found: C, 82.29; H, 4.41; N, 12.36.

11-(*p*-Chlorophenyl)-9-methyl-6*H*-indolo[2,3-*b*]quinoline (12d). Thermolysis of **7d** was carried out in toluene at reflux temperature for 6 h. Purification of the product by column chromatography (silica gel, *n*-hexane:ethyl acetate = 7:3) yielded **12d** as a yellow solid: yield 52%; mp 278−280 °C; IR (KBr) $\tilde{\nu}$ = 3135 (m), 3061 (m), 2915 (w), 2852 (w), 1598 (s), 1485 (s), 1379 (m), 1354 (m), 1249 (m), 1228 (m), 1089 (s), 839 (s), 816 (m), 757 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.32 (3H, s), 6.91 (1H, s), 7.24 (1H, d, J = 8.3 Hz), 7.38−7.42 (2H, m), 7.49 (2H, d, J = 8.5 Hz), 7.67 (2H, d, J = 8.5 Hz), 7.70 (1H, dd, J = 8.3 and 0.8 Hz), 7.75 (1H, ddd, J = 7.5, 6.4, 1.3 Hz), 8.21 (1H, d, J = 8.1 Hz), 11.41 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.5, 110.5, 116.5, 120.9, 123.0, 123.1, 123.5, 126.2, 126.7, 128.9, 129.2 (2C), 130.9 (2C), 134.7, 134.9, 139.5, 141.1, 146.2, 153.3; MS (EI, 70 eV) *m*/*z* (rel intens) = 342 (100, M^+), 341 (41), 305 (20), 153 (30), 75 (39), 63 (34), 52 (43), 50 (44), 39 (84), 28 (47), 27 (93); ESI-MS ($C_{22}H_{16}ClN_2^+$) *m*/*z* calcd 343.1, found 343.1.

11-(*p*-Methoxyphenyl)-9-methyl-6*H*-indolo[2,3-*b*]quinoline (12e). Thermolysis of **7e** was carried out in toluene at 75 °C for 7 h. Column chromatography (silica gel, *n*-hexane:ethyl acetate = 3:1) afforded **12e** as a yellow solid: yield 79%; mp 284−286 °C; IR (KBr) $\tilde{\nu}$ = 3131 (br, m), 2997 (br, m), 2960 (m), 2930 (m), 2833 (m), 1607 (s), 1507 (m), 1486 (w), 1439 (w), 1381 (w), 1355 (w), 1293 (m), 1249 (s), 1178 (m), 1036 (m), 841 (w), 803 (w), 758 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.21 (3H, s), 3.92 (3H, s), 6.84 (1H, s), 7.24−7.27 (3H, m), 7.36 (1H, d, J = 7.8 Hz), 7.37 (1H, dd, covered), 7.47 (2H, d, J = 7.5 Hz), 7.64−7.61 (2H, m), 8.00 (1H, d, J = 8.6 Hz), 11.68 (1H, br s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 21.2, 55.4, 110.6, 114.5, 115.6, 120.5, 121.7, 122.5, 122.6, 123.2, 125.9, 127.2, 127.8, 128.5, 129.0, 130.6, 139.7, 141.4, 146.4, 152.7, 159.5. Anal. Calcd for $C_{23}H_{18}N_2O$ (338.41): C, 81.63; H, 5.36; N, 8.28. Found: C, 81.41; H, 5.44; N, 8.39.

9-Methyl-11-[4-(*N*,*N*-dimethylamino)phenyl]-6*H*-indolo[2,3-*b*]quinoline (12f). Crude **7f**, synthesized from **6f** (100 mg, 260 μmol) in 5 mL of dry dichloromethane, was allowed to warm to room temperature for 30 min. After washing with water, the solvent was removed under reduced pressure. Column chromatography (silica gel, *n*-hexane:diethyl ether 1:4) yielded 41.0 mg of **12f** (120 μmol, 45%) as a dark yellow solid: mp 306 °C (DSC); IR (KBr) $\tilde{\nu}$ = 3019 (s, N−H), 2400 (m, N−H), 1605 (m), 1524 (m), 1482 (w), 1444 (w), 1358 (m), 1216 (s), 1126 (m), 1053 (m), 929 (w), 756 (s), 668 (s) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.32 (3H, s), 3.12 (6H, s), 6.98 (2H, d, J = 7.8 Hz), 7.16 (1H, s), 7.24 (1H, m), 7.35−7.45 (4H, m), 7.73 (1H, t, J = 7.5 Hz), 7.91 (1H, d, J = 8.5, 1.2 Hz), 8.18 (1H, d, J = 8.5 Hz), 10.81 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.5, 42.0, 110.2, 112.4, 116.7, 121.7, 122.5, 123.5, 123.7, 124.4, 126.6, 126.9, 128.6, 128.8, 128.9, 130.4, 139.2, 143.6, 146.5, 150.6, 153.5; MS (EI, 70 eV) *m*/*z* (rel intens) = 351 (100, M^+), 350 (20, $M^+ - H$), 335 (12, $M^+ - H - CH_3$), 175 (30), 153 (11); ESI-MS ($C_{24}H_{22}N_3^+$) *m*/*z* calcd 352.2, found 352.2. Anal. Calcd for $C_{24}H_{21}N_3 \cdot 0.2H_2O$ (351.44): C, 81.19; H, 6.08; N, 11.84. Found: C, 81.37; H, 6.07; N, 11.82.

9-Methyl-2-nitro-11-phenyl-6*H*-indolo[2,3-*b*]quinoline (12g). Heating of **7g** for 5 h under reflux in toluene led to complete conversion of the reactant. Upon cooling, **12g** was isolated by crystallization as a yellow solid: yield 75%; mp > 340 °C dec; IR (KBr) $\tilde{\nu}$ = 3145 (br, m), 3088 (br, m), 2923 (m), 2856 (m), 1598 (s), 1503 (m), 1406 (w), 1380 (w), 1330 (s, N═O), 1290 (w), 1250 (m), 1229 (m), 1216 (m), 1093 (m), 841 (w), 830 (w), 704 (m) cm^{-1}; ^{1}H NMR (100 MHz, DMSO-d_6) δ = 2.21 (3H, s), 6.74 (1H, s), 7.34 (1H, d, J = 8.2 Hz), 7.43 (1H, d, J = 8.2 Hz), 7.62−7.65 (2H, m), 7.77−7.79 (3H, m), 8.16 (1H, d, J = 9.3 Hz), 8.38 (1H, dd, J = 9.3 and 2.5 Hz), 8.63 (1H, d, J = 2.5 Hz), 12.22 (1H, br s, NH); ^{13}C NMR (50 MHz, DMSO-d_6) δ = 21.2, 111.3, 117.2, 119.8, 121.4, 121.9, 122.7, 123.0, 128.7, 129.1, 129.2, 129.4, 129.5, 130.1, 134.6, 139.9, 141.9, 143.2, 148.9, 154.5; MS (EI, 70 eV) *m*/*z* (rel intens) = 353 (100, M^+), 323 (18), 307 (23), 292 (43, $M^+ - NO_2 - CH_3$); HR-MS ($C_{22}H_{15}N_3O_2$) *m*/*z* calcd for $[M]^+$ 353.1164, found 353.1161.

2-Cyano-9-methyl-11-phenyl-6*H*-indolo[2,3-*b*]quinoline (12h). To 25 mL of toluene was added **7h** (26.0 mg, 77.9 μmol). After the reaction mixture was refluxed for 12 h, the product was purified by column chromatography (silica gel, *n*-hexane:diethyl ether = 1:1), yielding 25.7 mg of **12h** (77.1 μmmol, 98%) as a yellow solid; mp > 340 °C dec; IR (KBr) $\tilde{\nu}$ = 3302 (br s), 3057 (w), 2919 (w), 2854 (w), 2224 (s, C≡N), 1069 (m), 1595 (s), 1577 (m), 1483 (m), 1402 (m), 1378 (m), 1356 (m), 1287 (m), 1257 (m), 1234 (w), 1123 (w), 1033 (w), 822 (m), 805 (m) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.28 (3H, s), 6.85 (1H, s), 7.20−7.26 (1H, m), 7.32 (1H, d, J = 8.1 Hz), 7.46−7.50 (2H, m), 7.70−7.73 (3H, m), 7.82 (1H, dd, J = 8.8, 1.8 Hz), 8.11 (1H, d, J = 1.8 Hz), 8.15 (1H, d, J = 8.8 Hz), 10.58 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.4, 106.0, 110.6, 117.7, 119.6, 120.8, 123.4, 123.6, 128.2, 129.2 (2C), 129.3 (2C), 129.9, 130.3, 133.2, 134.9, 138.9, 142.9, 147.7, 154.1; MS (EI, 70 eV) *m*/*z* (rel intens) = 333 (100, M^+), 332 (41), 330 (13), 317 (11), 51(21), 39(12). Anal. Calcd for $C_{23}H_{15}N_3$ (333.39): C, 82.86; H, 4.54; N, 12.60. Found: C, 82.24; H, 4.65; N, 12.42.

2-Chloro-9-methyl-11-phenyl-6*H*-indolo[2,3-*b*]quinoline (12i). **12i** was obtained from thermolysis of **7i** in refluxing toluene (5 h). **12i** was isolated by column chromatography (silica gel, *n*-hexane: ethyl acetate = 7:3) as a yellow solid: yield 54%; mp 256−258 °C; IR (KBr) $\tilde{\nu}$ = 3140 (br, m), 3022 (m), 2917 (m), 2855 (w), 1616 (s), 1484 (m), 1401 (m), 1350 (m), 1290 (w), 1245 (s), 1215 (w), 1176 (w), 1081 (w), 817 (m), 703 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.24 (3H, s), 6.73 (1H, s), 7.00 (1H, d, J = 8.2 Hz), 7.15 (1H, d, J = 8.2 Hz), 7.38−7.41 (2H, m), 7.48 (1H, dd, J = 8.9 and 2.3 Hz), 7.58 (1H, d, J = 2.3 Hz), 7.65−7.68 (3H, m), 7.97 (1H, J = 8.9 Hz), 12.55 (1 H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.3, 110.4, 117.0, 120.4, 123.1, 123.9, 124.9, 127.6, 128.0, 128.8, 128.9, 129.0, 129.1 (2C), 129.4, 135.6, 139.6, 141.4, 144.4, 153.1; MS (EI, 70 eV) *m*/*z* (rel intens) = 342 (100, M^+), 341 (36), 305 (21, $M^+ - Cl$), 51 (15); ESI-MS ($C_{22}H_{16}ClN_2^+$) *m*/*z* calcd 343.1, found 343.1.

2-Methoxy-9-methyl-11-phenyl-6*H*-indolo[2,3-*b*]quinoline (12j). **12j** could be obtained from thermolysis of **7j** in refluxing toluene (30 min). **12j** was isolated by column chromatography (silica gel, *n*-hexane:ethyl acetate = 1:1) as a yellow solid: yield 76%; mp 249−251 °C; IR (KBr) $\tilde{\nu}$ = 3144 (br, s), 3054 (br, m), 2922 (m), 2832 (w), 1622 (s), 1586 (m), 1516 (m), 1485 (m), 1469 (m), 1450 (m), 1399 (m), 1351 (m), 1296 (m), 1250 (m), 1235 (s), 1225 (s), 1163 (m), 1116 (w), 1036 (s), 883 (w), 819 (s), 795 (m), 732 (s), 702 (m) cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6) δ = 2.15 (3H, s), 3.64 (3H, s), 6.66 (1H, m), 6.91 (1H, d, J = 2.8 Hz), 7.22 (1H, d, J = 8.2 Hz), 7.35 (1H d, J = 8.2 Hz), 7.40 (1H, dd, J = 9.4, 2.8 Hz), 7.51−7.56 (2H, m), 7.65−7.76 (3H, m), 7.94 (1H, d, J = 9.4 Hz), 11.56 (1 H, s, NH); ^{13}C NMR (50 MHz, DMSO-d_6) δ = 21.1, 55.1, 104.0, 110.2, 115.5, 120.1, 120.2, 122.4, 123.2, 127.6, 128.6,

128.7, 128.9, 129.0, 129.2, 136.2, 139.7, 140.1, 142.1, 151.5, 154.7. Anal. Calcd for $C_{23}H_{18}N_2O$ (338.41): C, 81.63; H, 5.36; N, 8.28. Found: C, 81.39; H, 5.38; N, 8.07.

9-Methyl-2-(*N*,*N*-dimethylamino)-11-phenyl-6*H*-indolo[2,3-*b*]-quinoline (12k). Crude **7k**, freshly synthesized from desulfonation of **6k** (100 mg, 260 μmol) in 5 mL of dry dichloromethane at 0 °C, was allowed to warm to room temperature for 30 min. The crude product was purified by column chromatography (silica gel, *n*-hexane:diethyl ether = 1:4) to yield 11.0 mg of **12k** (31.0 μmol, 12%) as a brown solid: mp 252−254 °C; IR (KBr) $\tilde{\nu}$ = 3019 (br s, N−H), 2400 (m, N−H), 1733 (s), 1619 (s), 1520 (m), 1478 (m), 1444 (w), 1375 (m), 1216 (s), 1128 (m), 1046 (m), 929 (m), 879 (w) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.27 (3H, s), 2.93 (6H, s), 6.79 (1H, m), 6.83 (1H, d, J = 2.8 Hz), 7.20 (1H, dd, J = 8.1, 1.2 Hz), 7.40 (1H, d, J = 8.1 Hz), 7.47 (1H, dd, J = 9.2, 2.8 Hz), 7.53−7.68 (5H, m), 8.13 (1H, d, J = 9.2 Hz), 11.68 (1H, br s); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 21.4, 41.2, 105.5, 110.3, 116.7, 119.7, 121.3, 123.0, 124.6, 127.1, 128.2, 128.3, 128.6, 128.9, 129.3, 137.1, 139.6, 140.5, 140.7, 146.5, 151.9; ESI-MS ($C_{24}H_{22}N_3^+$) *m*/*z* calcd 352.2, found 352.2. Anal. Calcd for $C_{24}H_{21}N_3$ (351.44): C, 82.02; H, 6.02; N, 11.96. Found: C, 81.44; H, 5.96; N, 11.87.

***N*-Ethyl-*N*′-[4-methyl-2-(phenylethynyl)phenyl]carbodiimide (18).** For details of the synthesis, see the Supporting Information: yield 17%; colorless oil (silica gel, *n*-hexane:diethyl ether = 9:1); IR (neat) $\tilde{\nu}$ = 3054 (w), 3025 (w), 2976 (w), 2923 (w), 2869 (w), 2135 (s, N=C=N), 1598 (w), 1507 (m), 1490 (m), 1443 (w), 1379 (w), 1340 (m), 1258 (w), 1171 (m), 1098 (m), 821 (m), 756 (m), 691 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.26 (3H, t, J = 7.2 Hz), 2.31 (3H, s), 3.38 (2H, q, J = 7.2 Hz), 6.99 (1H, d, J = 8.1 Hz), 7.06 (1H, dd, J = 8.1 and 1.7 Hz), 7.32 (1H, m), 7.34−7.38 (3H, m), 7.59−7.62 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 16.5, 20.6, 41.7, 86.4, 94.9, 118.5, 123.2, 123.8, 128.2, 128.3, 130.1, 131.4, 133.5, 133.9, 134.6, 138.3; MS (EI, 70 eV) *m*/*z* (rel intens) = 260 (29, M^+), 259 (100, $M^+ - H$), 244 (10, $M^+ - H - CH_3$), 232 (11), 231 (14), 218 (15), 217 (11), 203 (18), 183 (62), 176 (12), 168 (12).

Thermolysis of 18, Furnishing 19. A degassed solution of enyne−carbodiimide (14.0 mg, 53.9 μmol) and 20 equiv of CHD in 25 mL of dry toluene was heated at 100 °C for 20 h. Thereafter, the solvent was removed, and the resulting residue was purified by preparative TLC (*n*-hexane:ethyl acetate = 4:1), furnishing 6-methyl-4-phenyl-9*H*-pyrido[2,3-*b*]indole[51] (**19**; 3.00 mg, 11.6 μmol) in 22% yield as a yellow solid: mp > 340 °C dec; IR (KBr) $\tilde{\nu}$ = 3132 (m), 3060 (m), 2961 (m), 2921 (m), 2274 (w), 2254 (m), 1595 (s), 1475 (s), 1391 (m), 1302 (s), 1266 (m), 1215 (m), 1176 (w), 1028 (w), 821 (m), 797 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.35 (3H, s), 7.09 (1H, d, J = 5.1 Hz), 7.26 (1H, dd, J = 8.2 and 1.4 Hz), 7.40 (1H, d, J = 8.2 Hz), 7.44 (1H, s), 7.53−7.60 (3H, m), 7.69 (2H, dd, J = 8.1 and 1.9 Hz), 8.47 (1H, d, J = 5.1 Hz), 9.29 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.5, 110.6, 113.5, 116.6, 120.9, 122.7, 128.1 (2C), 128.6 (2C), 128.7 (2C), 129.0, 136.6, 138.9, 145.4, 145.5, 152.6; ESI-MS ($C_{18}H_{15}N_2^+$) *m*/*z* calcd 259.3, found 259.5; MS (EI, 70 eV) *m*/*z* (rel intens) = 258 (100, M^+), 257 (64, $M^+ - H$), 255 (18), 128 (12), 51 (13), 39 (14), 28 (15), 27 (18), 14 (10).

Procedure for the CPC Systems Reactor. The cyclization reaction of **7h** (10 mg, 3.00 mM in mesitylene) was performed in a CPC Cytos reactor at 150 °C for 4 h with a flow rate of 0.25 mL min^{-1}, furnishing the product **12h** in 83% yield.

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Supporting Information Available: Carbene trapping experiments, kinetic data, Hammett correlations, computational data, ^{1}H and ^{13}C NMR data of all compounds, and X-ray structural data of **7b**. This material is available free of charge via the Internet at http://pubs.acs.org

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