Biradicals/Zwitterions from Thermolysis of Enyne−Isocyanates. Application to the Synthesis of 2(1*H*)-Pyridones, Benzofuro[3,2-*c*]pyridin-1(2*H*)-ones, 2,5-Dihydro-1*H*-pyrido[4,3-*b*]indol-1-ones, and Related Compounds

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Thermolysis of benzannulated enyne−isocyanates **13** and enyne−isocyanates **36** and **37** promoted the cycloaromatization reactions to generate in situ *O*,4-didehydro-2-hydroxyquinolines and *O*,4-didehydro-2-hydroxypyridines, respectively, as reactive intermediates. These cycloaromatized intermediates could be captured either as biradicals and/or as zwitterions depending on the nature of the substituent at the alkynyl terminus. The intermediate derived from cycloaromatization of **13a** bearing a phenyl substituent could be regarded as biradical **14**, which then abstracts hydrogen atoms from *γ*-terpinene leading to 2(1*H*)-quinolinone **15**. Alternatively, the same intermediate could also be regarded as zwitterion **14′**, which then undergoes an initial hydride abstraction from *γ*-terpinene followed by protonation to produce **15**. The presence of a 2-phenylethyl substituent in **13b** and **37a** or a 2-methylphenyl substituent in **37b** also allowed the resulting intermediates to be captured intramolecularly either as biradicals or as zwitterions, producing 2(1*H*)-quinolinone **19**, 2(1*H*)-pyridone **39**, and benzopyranopyridine **43**, respectively. On the other hand, with a 2-methoxyphenyl, a 2-(dimethylamino)phenyl, or a 3-methoxypropyl substituent, the chemical behavior of the cycloaromatized adduct could be best accounted for in terms of a zwitterionic intermediate leading to benzofuro[3,2-*c*]quinolin-6(5*H*)-one (**20**), 5,11-dihydro-11-methyl-6*H*-indolo-[3,2-*c*]quinolin-6-one (**25**), benzofuro[3,2-*c*]pyridin-1(2*H*)-one **44**, 2,5-dihydro-2,5-dimethyl-1*H*-pyrido-[4,3-*b*]indol-1-one **46**, and related compounds. Interestingly, thermolysis of **37f** bearing a 2-(methoxymethyl)phenyl substituent at the alkynyl terminus produced the unexpected benzopyranopyridine **56** as the major product in a process involving the cleavage of the bond between the methoxyl oxygen and the adjacent methylene carbon. The efficiency and selectivity of the cycloaromatization reaction could also be enhanced by the introduction of 1.1 to 10 equiv of dimethylphenylsilyl chloride to the reaction mixture to capture the resulting zwitterion.

Introduction

The use of unsaturated compounds to generate biradicals has received considerable attention.[1] In the cases that contain only carbon atoms in the conjugated system, the Bergman cyclization reaction of (*Z*)-3-hexene-1,5-diynes (enediynes) to 1,4-didehydrobenzene biradicals[2] and the Myers−Saito cyclization reaction of (*Z*)-1,2,4-heptatrien-6-ynes (enyne−allenes) to α,3-didehydrotoluene[3] biradicals have been investigated extensively. A different mode of cyclization of enyne−allenes involving the formation of a bond between the C2 and the C6 carbon atoms leading to the five-membered-ring fulvene biradicals (Schmittel cyclization) has also been reported.[4] In general, enyne−allenes having an aryl substituent or a sterically demanding group, such as *tert*-butyl or trimethylsilyl, at the alkynyl terminus prefer the Schmittel cyclization pathway.

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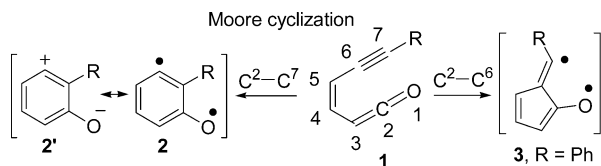
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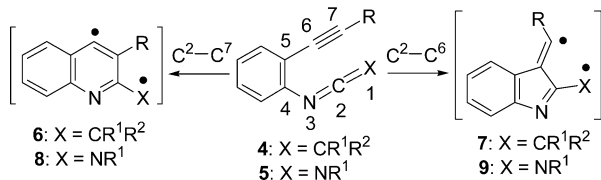
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SCHEME 1

Moore cyclization

2′   **2**   **1**   **3**, R = Ph

SCHEME 2

6: X = CR^{1}R^2
8: X = NR^1

4: X = CR^{1}R^2
5: X = NR^1

7: X = CR^{1}R^2
9: X = NR^1

The Moore cyclization reaction of enyne−ketene **1** having an oxygen atom in the conjugated system produces biradical **2** bearing an aryl radical center and a phenoxyl radical center (Scheme 1).[5] Under certain reaction conditions, the chemical behavior of biradical **2** could be best accounted for by regarding it as zwitterion **2′**. Examples of the C^2−C^6 cyclization reaction of the enyne−ketene system having a phenyl substituent or other radical-stabilizing groups at the alkynyl terminus to form the fulvene biradical **3** were also observed.[5a,c]

The conjugated systems bearing other heteroatoms have also been employed to generate biradicals. A case containing a sulfur atom was observed.[6] Recently, a potential aza-Bergman route from 3-aza-3-hexene-1,5-diynes and a related heterocyclic analogue to 2,5-dide-hydropyridine biradicals were reported.[7] Examples involving the enallene−nitrile[8] and the enallene−isonitrile[9] systems have also been investigated. The benzannulated enyne−ketenimines **4** were also found to undergo the C^2−C^7 cyclization reaction to form the quinoline biradicals **6** (R = H or Pr) and/or the C^2−C^6 cyclization reaction to form the putative indole biradicals **7** (R = Pr, Ph, *t*-Bu, or Me$_3$Si) (Scheme 2).[10] These cyclization reactions occurred readily under mild thermal conditions ranging from ambient temperature to 80 °C. In contrast, sub-

SCHEME 3

10   **11**   **11′**
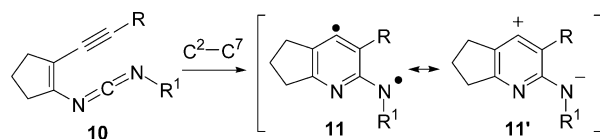
stantially higher temperatures (80−138 °C) were needed to promote the cyclization reactions of the benzannulated enyne−carbodiimides **5**.[11] In addition, with the only exception of R = H, cyclization gave exclusively the putative indole biradicals **9** (R = Me, Pr, Ph, *t*-Bu, or Me$_3$-Si) via the C^2−C^6 cyclization pathway.[11a] However, it is possible to redirect the reaction toward the C^2−C^7 pathway by incorporating the central carbon−carbon double bond of the enyne−carbodiimide system in a five-membered ring as depicted in **10** to form the pyridine biradical **11** (Scheme 3).[11e] As in the enyne−ketene system, under certain reaction conditions, the chemical behavior of biradical **11** could be best described in terms of zwitterion **11′**.

Our continued interest in the development of new conjugated systems for the thermal generation of biradicals/zwitterions and the use of these reactive intermediates for synthetic applications led us to investigate the enyne−isocyanate system. Several interesting features of this system and new synthetic pathways to the derivatives of 2(1*H*)-pyridone, benzofuro[3,2-*c*]pyridin-1(2*H*)-one,[12] 2,5-dihydro-1*H*-pyrido[4,3-*b*]indol-1-one,[13] and related compounds were discovered.

Results and Discussion

The benzannulated enyne−isocyanate **13a** (R = Ph) was previously synthesized as the precursor of an enyne−carbodiimide.[11a] Alternatively, it could also be efficiently synthesized by treatment of 2-(phenylethynyl)aniline (**12a**), derived from the palladium-catalyzed cross-coupling reaction between 2-iodoaniline and phenylacetylene,[10a] with triphosgene (Scheme 4) in 81% yield (Table 1). However, **13a** did not show any propensity to undergo cyclization in the presence of an excess of γ-terpinene under refluxing benzene (80 °C) for 4 h. This is in sharp contrast to the benzannulated enyne−ketenimine **4a** (R = Ph, X = CPh$_2$) and the benzannulated enyne−carbodiimide **5a** (R = Ph, X = NPh), which underwent facile C^2−C^6 cyclizations to generate **7a** (R = Ph, X = CPh$_2$) at ambient temperature[10a] and **9a** (R = Ph, X = NPh) under refluxing benzene,[11a] respectively. Heating **13a** under refluxing 1,2-dichlorobenzene at 180 °C for 24 h also failed to promote the cyclization reaction. It was necessary to heat **13a** in the presence of an excess of γ-terpinene in 1,2-dichlorobenzene in a sealed glass

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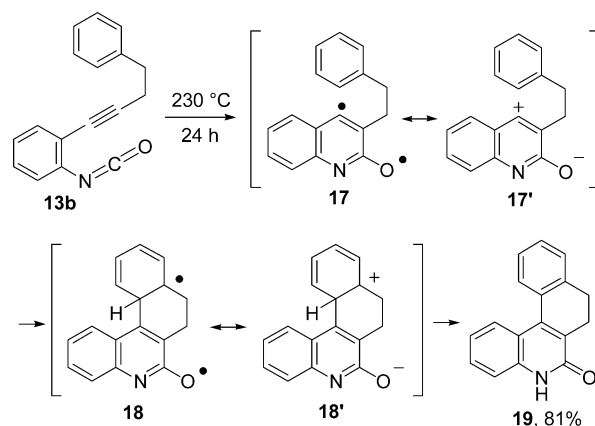
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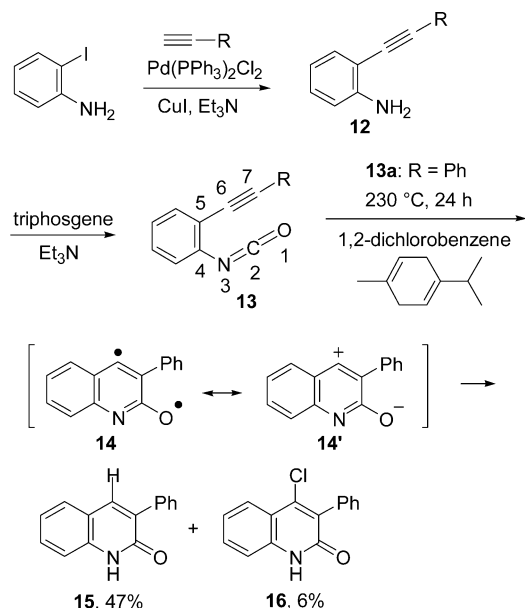
TABLE 1. Synthesis of the Benzannulated Enyne—Isocyanates 13

| R	**12** (yield, %)	**13** (yield, %)
phenyl	**12a** (89)	**13a** (81)
2-phenylethyl	**12b** (90)	**13b** (74)
2-methoxyphenyl	**12c** (89)	**13c** (88)
2-(dimethylamino)phenyl	**12d** (89)	**13d** (72)
3-methoxypropyl	**12e** (83)	**13e** (75)

tube at 230 °C for 24 h to produce 3-phenyl-2(1*H*)-quinolinone (**15**)[14] in 47% yield along with a small amount of the chlorinated adduct **16**[15] (6%). Presumably, the C^2—C^7 cyclization reaction of **13a** occurred to generate the quinoline biradical/zwitterion **14/14′**. Hydrogen atom abstractions from γ-terpinene by biradical **14** then produced **15**. Alternatively, an initial hydride abstraction from γ-terpinene by zwitterion **14′** followed by protonation could also lead to **15**. The chloro substituent in **16** presumably came from 1,2-dichlorobenzene. However, the reaction pathway that allowed the acquisition of the chloro substituent remained to be investigated. The preference for **13a** to undergo the C^2—C^7 cyclization reaction is also dramatically different from those of **4a** and **5a**, which favor the C^2—C^6 cyclization pathway. The reason for such a change is not clear at the present time.

Several other enyne—isocyanates were likewise synthesized from 2-iodoaniline (Table 1). Thermolysis of **13b** bearing a properly situated phenyl substituent at 230 °C in a sealed glass tube allowed the resulting aryl radical/cationic center in **17/17′** to be captured by the phenyl substituent to form **18/18′**. A subsequent prototropic rearrangement then furnished 7,8-dihydrobenzo[*k*]phenanthridin-6(5*H*)-one (**19**)[15,16] in 81% yield (Scheme 5). Again, it was necessary to conduct the reaction at 230 °C for 24 h. Thermolysis of **13b** under refluxing 1,2-dichloroben-

SCHEME 5

SCHEME 6
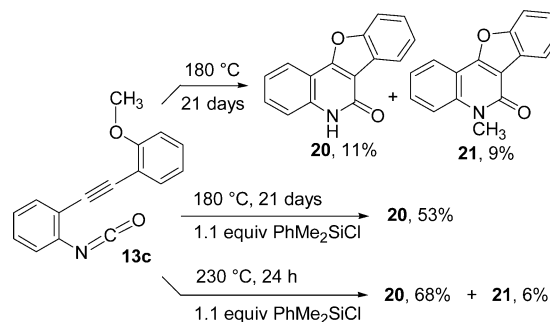
zene (180 °C) for 14 days produced **19** in only 27% yield. The ability of the phenyl substituent to capture the aryl radical/cationic center was also observed previously in the enyne—ketene[5e,f] and the enyne—carbodiimide[11e] systems.

Thermolysis of **13c** having a 2-methoxyphenyl substituent at the alkynyl terminus under refluxing 1,2-dichlorobenzene for 21 days produced benzofuro[3,2-*c*]quinolin-6(5*H*)-one (**20**)[17a—c] in 11% yield and the *N*-methylated adduct **21**[17d—f] in 9% yield (Scheme 6). The yield of **20** was improved to 53% when thermolysis was conducted in the presence of 1.1 equiv of dimethylphenylsilyl chloride. Dimethylphenylsilyl chloride instead of trimethylsilyl chloride was selected as the silylating agent because of its relatively high boiling point. Heating **13c** in the presence of 1.1 equiv of dimethylphenylsilyl chloride in 1,2-dichlorobenzene in a sealed glass tube at 230 °C for 24 h further improved the yield of **20** to 68% along with 6% of **21**. The formation of **20** and **21** could be best accounted for by regarding the initial formed *O*,4-didehydro-2-hydroxyquinoline biradical **22** as zwitterion **22′** (Scheme 7). The carbocationic center in **22′** was captured by the methoxyl group to give the oxonium ion in **23**. Subsequent hydrolysis of **23** then afforded **20**. It is worth noting that methylation of **23** or the corresponding demethylated anion occurred on the nitrogen to furnish **21**. The reactive methyl group of the oxonium

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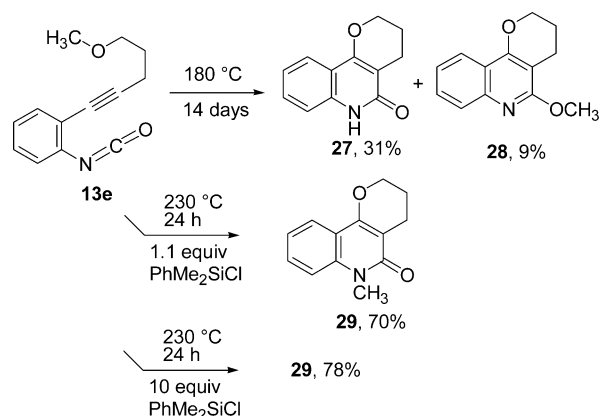
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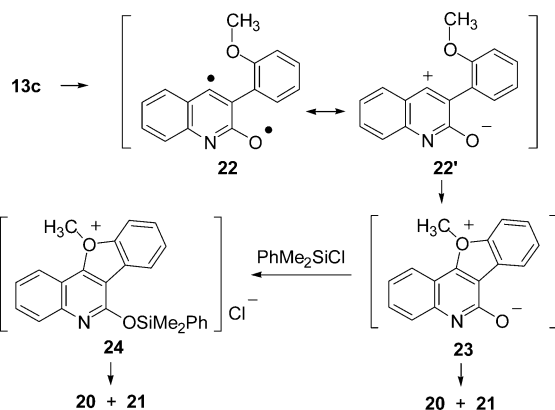
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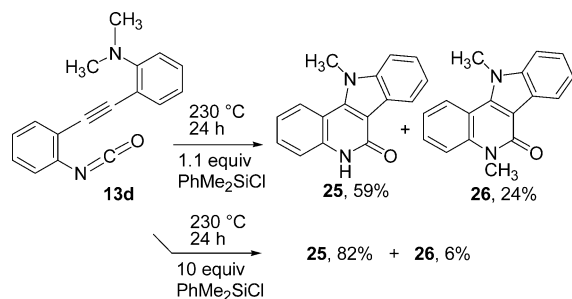
ion in **23** is presumably the source of the methyl group for methylation intermolecularly. The chemical behavior of **22** as zwitterion **22** is reminiscent of what were observed previously in the enyne−ketene,[5] the enyne−carbodiimide,[11e] and the enallene−isonitrile[9] systems. The favorable effect by either trimethylsilyl chloride or dimethylphenylsilyl chloride was also observed previously in several examples of the enyne−ketene[5b] and the enyne−carbodiimide[11e] systems. Presumably, the oxygen-centered anion in **23** was captured by dimethylphenylsilyl chloride to form **24**, enhancing the efficiency and selectivity of the cycloaromatization reaction.

The use of **13d** bearing a 2-(dimethylamino)phenyl group at the alkynyl terminus for thermolysis in the presence of 1.1 equiv of dimethylphenylsilyl chloride at 230 °C for 24 h furnished 5,11-dihydro-11-methyl-6*H*-indolo[3,2-*c*]quinolin-6-one (**25**)[15,18] in 59% yield and 5,11-dihydro-5,11-dimethyl-6*H*-indolo[3,2-*c*]quinolin-6-one (**26**) in 24% yield (Scheme 8). In the presence of 10 equiv of dimethylphenylsilyl chloride, **25** and **26** were isolated in 82% and 6% yields, respectively.

Interestingly, when **13e** was subjected to thermolysis at 180 °C for 14 days, 2(1*H*)-quinolinone **27** and the corresponding *O*-methylated adduct **28** were obtained (Scheme 9). On the other hand, in the presence of 1.1 or

SCHEME 9

SCHEME 10
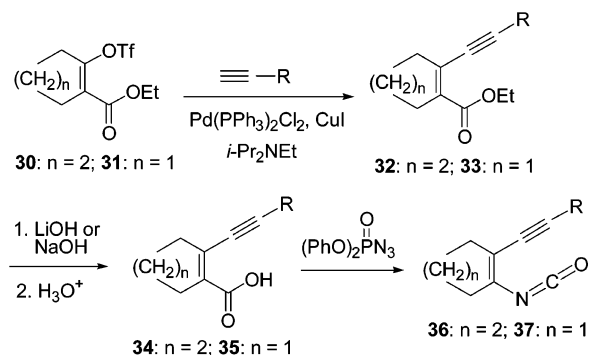
TABLE 2. Synthesis of Enyne−Isocyanates 36 and 37

R	32/33 (yield, %)	34/35 (yield, %)	36/37 (yield, %)
3-methoxypropyl	**32** (91)	**34** (87)	**36** (82)
2-phenylethyl	**33a** (98)	**35a** (92)	**37a** (86)
2-methylphenyl	**33b** (90)	**35b** (96)	**37b** (91)
2-methoxyphenyl	**33c** (92)	**35c** (92)	**37c** (84)
2-(dimethylamino)phenyl	**33d** (91)	**35d** (85)	**37d** (87)
3-methoxypropyl	**33e** (97)	**35e** (86)	**37e** (89)
2-(methoxymethyl)phenyl	**33f** (93)	**35f** (89)	**37f** (91)

10 equiv of dimethylphenylsilyl chloride at 230 °C, the *N*-methylated adduct **29** was produced.

Enyne−isocyanate **36** (R = 3-methoxypropyl) having the central carbon−carbon double bond incorporated in the cyclohexenyl ring was synthesized from **30**[19] as outlined in Scheme 10. The palladium-catalyzed cross-coupling reaction between **30** and 5-methoxy-1-pentyne produced carboxylic ester **32**, which was then hydrolyzed to give the corresponding carboxylic acid **34** (Table 2). Treatment of **34** with diphenyl phosphorazidate[20] (DPPA) then furnished enyne−isocyanate **36**. Enyne−isocyanates **37** bearing a cyclopentenyl ring were likewise synthesized from **31**[19] as reported previously.[11e]

Enyne−isocyanates **36** and **37** appeared to be more reactive than the benzannulated derivatives. Thermolysis

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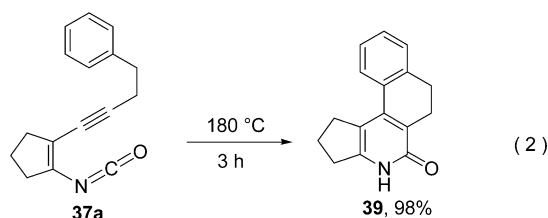
SCHEME 11
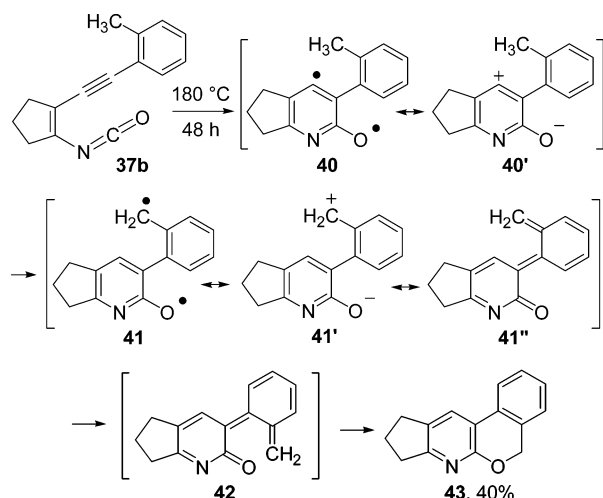
of **36** in the presence of 1.1 equiv of dimethylphenylsilyl chloride under refluxing 1,2-dichlorobenzene at 180 °C for 36 h was sufficient to produce 2(1*H*)-pyridone **38**[15] (eq 1). However, unlike **13e**, the *N*-methylated adduct of **38** was not detected.
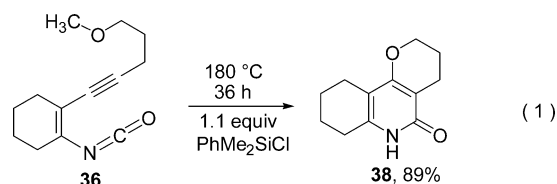

The chemical behavior of **37a** closely resembles that of the benzannulated analogue **13b** in producing **39**[15] in 98% yield (eq 2) except that heating at 180 °C for 3 h was also sufficient to promote the cyclization reaction. However, heating **37a** at 132 °C under refluxing chlorobenzene for 10 h resulted in only ca. 65% completion of reaction.


Biradical/zwitterion **40/40′**, generated from thermolysis of **37b** at 180 °C for 48 h, underwent a 1,5-hydrogen/hydride shift to form **41/41′**, which could also be regarded as *o*-quinodimethane **41″** (Scheme 11). A subsequent rotation around the central carbon–carbon bond of **41/41′** could give **42** for an electrocyclic reaction to produce **43**.[15] Such a cascade sequence was also observed previously in the enyne–allene,[21] the enyne–ketene,[5d] and the enyne–carbodiimide[11e] systems. Thermolysis of **37c** at 132 °C for 36 h furnished **44**[15] and **45** in 10% and 52% yields, respectively (Scheme 12). In the presence of 1.1 equiv of dimethylphenylsilyl chloride, **44** was produced exclusively. Similarly, cyclization of **37d** led to **46**[15] and

(21) Liu, B.; Wang, K. K.; Petersen, J. L. *J. Org. Chem.* **1996**, *61*, 8503–8507.
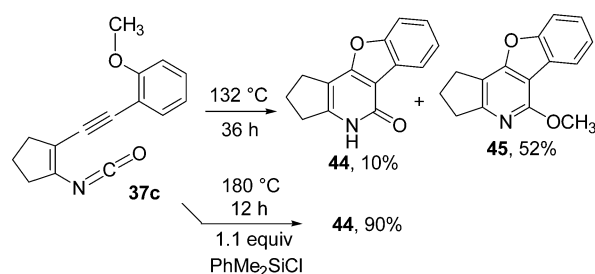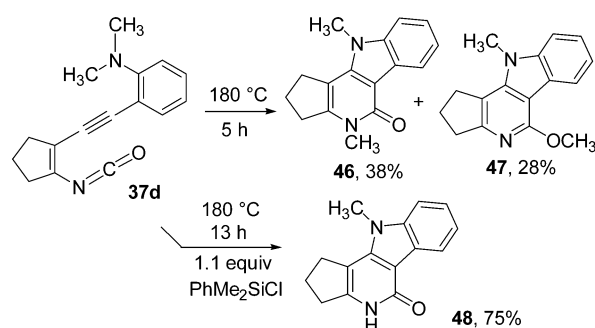
SCHEME 12

SCHEME 13

SCHEME 14
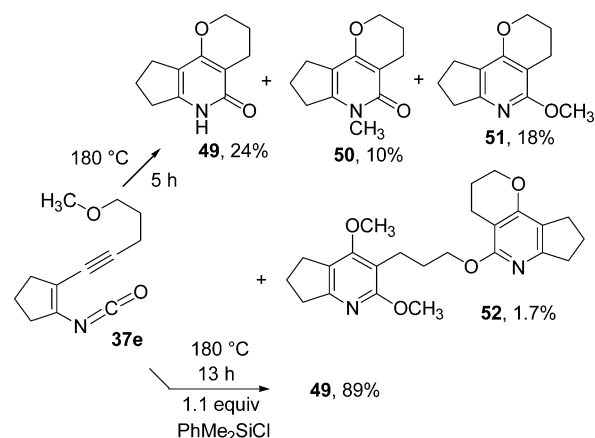
SCHEME 15
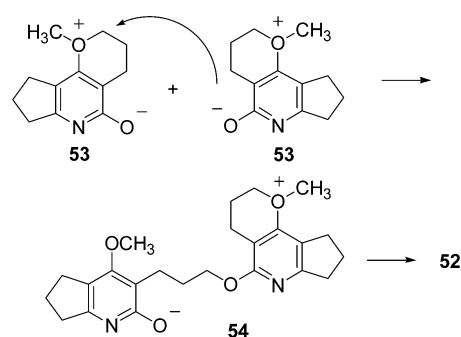
47[15] in 38% and 28% yields, respectively, and in the presence of 1.1 equiv of dimethylphenylsilyl chloride, **48**[15] in 75% yield (Scheme 13).

In addition to the cyclized products **49**–**51**, a small amount of **52** was isolated from thermolysis of **37e** (Scheme 14). Presumably, the initially formed zwitterion **53** or its methylated derivative was attacked by a second molecule of **53** or its demethylated derivative as depicted

SCHEME 16

SCHEME 17

in Scheme 15 leading to **52**. In the presence of 1.1 equiv of dimethylphenylsilyl chloride, **49** was produced exclusively in 89% yield.
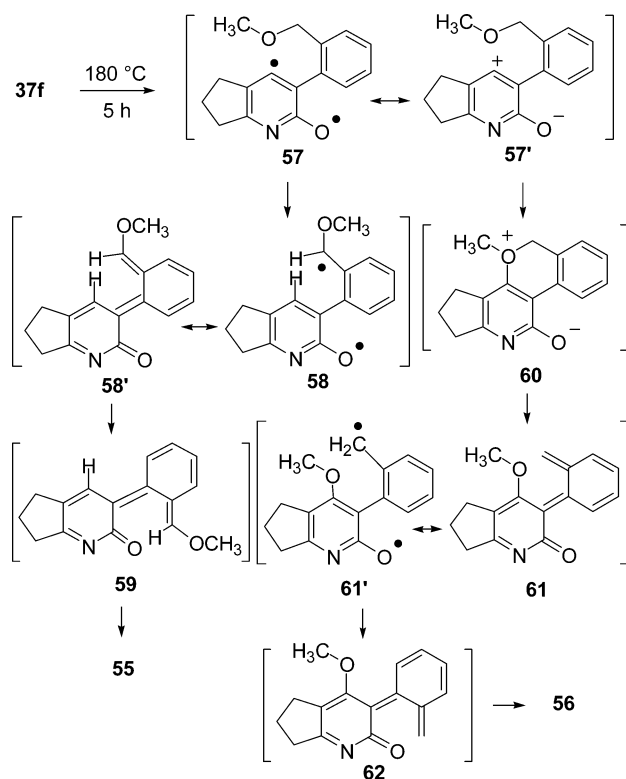
Surprisingly, thermolysis of **37f** at 180 °C for 5 h furnished **55** and the unexpected benzopyranopyridine **56**[15] (Scheme 16). As observed in the case of **40**, a 1,5-hydrogen shift of the initially formed biradical **57** could form **58**, which could also be regarded as *o*-quinodimethane **58′** (Scheme 17). A subsequent rotation around the central carbon−carbon bond of **58** could give **59** for an electrocyclic reaction to produce **55**. Alternatively, the carbocationic center in **57′** could be captured by the methoxyl oxygen to form **60**. The cleavage of the bond between the oxonium oxygen and the adjacent methylene carbon could lead to *o*-quinodimethane **61**, which could also be regarded as biradical **61′**. Rotation around the central carbon−carbon bond of **61′** could give **62**, which in turn could undergo an electrocyclic reaction to account for the formation of the unexpected **56**. Thermolysis of **37f** at 150 °C for 20 h produced **56** exclusively in 59% yield. In the presence of 1.1 equiv of

dimethylphenylsilyl chloride, **56** was also produced exclusively in 76% yield.

Conclusions

Thermolysis of enyne−isocyanates and the benzannulated analogues was successful in promoting the cycloaromatization reactions to generate *O*,4-didehydro-2-hydroxypyridines and *O*,4-didehydro-2-hydroxyquinolines as biradicals/zwitterions for subsequent synthetic applications. The presence of two reactive centers in the same molecule simultaneously provided many pathways for intramolecular decay to produce heteroaromatic compounds. A variety of 2(1*H*)-pyridones, 2(1*H*)-quinolinones, benzopyranopyridines, benzofuro[3,2-*c*]quinolin-6(5*H*)-ones,[17] 5,11-dihydro-11-methyl-6*H*-indolo[3,2-*c*]-quinolin-6-ones,[18] benzofuro[3,2-*c*]pyridin-1(2*H*)-ones,[12] 2,5-dihydro-5-methyl-1*H*-pyrido[4,3-*b*]indol-1-ones,[13] and related compounds were thus synthesized. Many derivatives of these heteroaromatic compounds were found to possess interesting biological activities. Compared to other conjugated systems, such as enyne−allene, enyne−ketene, enyne−ketenimine, enyne−carbodiimide, and enallene−isonitrile, the cycloaromatization reactions of enyne−isocyanates appear to require higher temperatures and are more in favor of the C^2−C^7 cyclization pathway.

Experimental Section

2-(4-Phenyl-1-butynyl)aniline (12b). The following procedure is representative for the preparation of anilines **12**. To a mixture of 2-iodoaniline (1.095 g, 5.0 mmol), triethylamine (0.84 mL, 6.0 mmol), Pd(PPh₃)₂Cl₂ (0.105 g, 0.15 mmol), and copper(I) iodide (0.049 g, 0.26 mmol) in 30 mL of DMF was added slowly a solution of 4-phenyl-1-butyne (0.710 g, 5.5 mmol) in 5 mL of DMF. After 2 h of stirring at room temperature, 50 mL of a saturated aqueous ammonium chloride solution and 50 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/50% diethyl ether in hexanes) afforded 0.997 g of **12b** (4.5 mmol, 90%) as a light yellow liquid: IR (neat) 3467, 3358, 749 cm⁻¹; ¹H δ 7.37−7.21 (6 H, m), 7.08 (1 H, ddd, *J* = 8.5, 7.7, 1.6 Hz), 6.69−6.63 (2 H, m), 3.93 (2 H, br s), 2.95 (2 H, t, *J* = 7.0 Hz), 2.81 (2 H, t, *J* = 7.0 Hz); ¹³C δ 147.7, 140.5, 131.9, 128.9, 128.5, 128.4, 126.3, 117.6, 114.0, 108.5, 94.6, 77.9, 35.0, 21.6.

Enyne−Isocyanate 13b. The following procedure is representative for the preparation of the benzannulated enyne−isocyanates **13** from anilines **12**. To a solution of 0.104 g of triphosgene (0.35 mmol) in 15 mL of anhydrous benzene was added a mixture of 0.208 g of aniline **12b** (0.94 mmol) and 0.28 mL of triethylamine (2.0 mmol) in 10 mL of benzene under a nitrogen atmosphere at room temperature. After 6 h of stirring, the white precipitate of triethylamine hydrochloride was removed by filtration, and the filtrate was concentrated in vacuo. Purification of the residue by flash column chromatography (silica gel/20% diethyl ether in hexanes) afforded 0.172 g of **13b** (0.70 mmol, 74%) as a pale yellow liquid: IR (neat) 2252, 755, 699 cm⁻¹; ¹H δ 7.40−7.25 (6 H, m), 7.21 (1 H, dd, *J* = 7.7, 1.6 Hz), 7.12 (1 H, td, *J* = 7.5, 1.4 Hz), 7.03 (1 H, dd, *J* = 7.8, 1.1 Hz), 3.00 (2 H, t, *J* = 7.5 Hz), 2.81 (2 H, t, *J* = 7.2 Hz); ¹³C δ 140.4, 135.2, 132.1, 128.7, 128.4, 127.4, 126.3, 125.2, 123.4, 121.3, 98.6, 76.9, 34.5, 21.8; MS *m/z* 247 (M⁺), 218, 156, 91.

3-Phenyl-2-(1*H*)-quinolinone (15)[14] **and 4-Chloro-3-phenyl-2-(1*H*)-quinolinone (16).** A solution of **13a** (0.038 g, 0.17 mmol) and γ-terpinene (0.48 g, 3.4 mmol) in 2 mL of 1,2-dichlorobenzene in a sealed glass tube was heated at 230 °C for 24 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica gel/25% ethyl acetate in methylene chloride) to afford 0.018 g of **15** (0.081 mmol, 47%) as white crystals and 0.0025 g (6%) of **16** as a solid. **15**: mp 230−231 °C (lit.[14a] mp 234 °C); IR 3446, 1659, 753, 696 cm^{-1}; ^{1}H δ 11.7 (1 H, br s), 7.92 (1 H, s), 7.84−7.79 (2 H, m), 7.61 (1 H, dd, J = 7.9, 1.0 Hz), 7.53−7.41 (4 H, m), 7.37 (1 H, d, J = 8.2 Hz), 7.23 (1 H, t, J = 7.2 Hz); ^{13}C δ 163.1, 138.5, 138.0, 136.2, 132.4, 130.3, 128.9, 128.3, 128.2, 127.8, 122.7, 120.3, 115.5. **16**: ^{1}H δ 11.4 (1 H, s), 8.05 (1 H, d, J = 7.4 Hz), 7.55−7.44 (6 H, m), 7.32 (1 H, t, J = 7.4 Hz), 7.26 (1 H, d, J = 7.6 Hz). The structure of **16** was established by X-ray structure analysis.

7,8-Dihydrobenzo[*k*]phenanthridin-6(5*H*)-one (19).[16] A solution of **13b** (0.186 g, 0.75 mmol) in 10 mL of 1,2-dichlorobenzene was heated under reflux for 14 days. The solvent was removed in vacuo, and the residue was purified by column chromatography to afford 0.050 g of **19** (0.20 mmol, 27%) as brown crystals. Similarly, a solution of **13b** (0.100 g, 0.40 mmol) in 2 mL of 1,2-dichlorobenzene in a sealed glass tube was heated at 230 °C for 24 h to afford 0.081 g of **19** (0.33 mmol, 81%): mp 245−246 °C (lit.[16a] mp 250−252 °C); IR 3430, 1646, 755 cm^{-1}; ^{1}H δ 12.04 (1 H, br s), 8.18 (1 H, d, J = 8.2 Hz), 7.90−7.85 (1 H, m), 7.52−7.50 (2 H, m), 7.44−7.33 (3 H, m), 7.27−7.21 (1 H, m), 2.94−2.81 (4 H, m); ^{13}C δ 163.4, 142.6, 140.3, 138.1, 131.8, 129.4, 129.3, 129.0, 128.3, 128.2, 126.2, 126.0, 122.2, 117.9, 116.9, 28.4, 21.9. The structure of **19** was established by X-ray structure analysis.

Benzofuro[3,2-*c*]quinolin-6(5*H*)-one (20)[17a−c] **and 5-Methylbenzofuro[3,2-*c*]quinolin-6(5*H*)-one (21).**[17d−f] A solution of **13c** (0.095 g, 0.38 mmol) in 4 mL of 1,2-dichlorobenzene was heated under reflux for 21 days. The solvent was removed in vacuo, and the residue was purified by column chromatography to afford 0.010 g of **20** (0.043 mmol, 11%) as a light brown solid and 0.009 g of **21** (0.036 mmol, 9%) as a white solid. Similarly, a solution of **13c** (0.150 g, 0.6 mmol) and dimethylphenylsilyl chloride (0.113 g, 0.66 mmol) in 6 mL of 1,2-dichlorobenzene was heated under reflux for 21 days to afford 0.076 g of **20** (0.32 mmol, 53%). Thermolysis of a solution of **13c** (0.050 g, 0.2 mmol) and dimethylphenylsilyl chloride (0.036 g, 0.21 mmol) in 2 mL of 1,2-dichlorobenzene in a sealed glass tube at 230 °C for 24 h produced 0.032 g of **20** (0.14 mmol, 68%) and 0.003 g of **21** (0.012 mmol, 6%). **20**: mp 294−295 °C (lit.[17a] mp 294−296 °C); IR 1685, 736 cm^{-1}; ^{1}H (DMSO-d_6) δ 12.01 (1 H, br s), 8.10 (1 H, dd, J = 6.9, 2.0 Hz), 8.05 (1 H, d, J = 7.9 Hz), 7.84 (1 H, dd, J = 7.1, 1.4 Hz), 7.61 (1 H, ddd, J = 8.4, 7.1, 1.3 Hz), 7.54−7.44 (3 H, m), 7.33 (1 H, td, J = 7.5, 0.9 Hz); ^{13}C (DMSO-d_6) δ 159.1, 157.9, 154.8, 138.4, 130.9, 126.3, 124.7, 123.8, 122.5, 121.3, 121.2, 116.2, 111.8, 110.7, 110.0. **21**: mp 201−202 °C (lit.[17d] mp 202−204 °C); IR 1660, 742 cm^{-1}; ^{1}H δ 8.32−8.27 (1 H, m), 8.17 (1 H, dd, J = 7.7, 1.4 Hz), 7.68−7.61 (2 H, m), 7.50 (1 H, d, J = 8.9 Hz), 7.47−7.41 (2 H, m), 7.37 (1 H, ddd, J = 8.0, 6.9, 1.1 Hz), 3.85 (3 H, s); ^{13}C δ 159.6, 157.3, 155.4, 139.3, 130.7, 126.1, 124.6, 124.4, 122.3, 122.2, 115.1, 112.8, 111.3, 110.3, 29.2.

5,11-Dihydro-11-methyl-6*H*-indolo[3,2-*c*]quinolin-6-one (25)[18] **and 5,11-Dihydro-5,11-dimethyl-6*H*-indolo[3,2-*c*]quinolin-6-one (26).** A solution of **13d** (0.050 g, 0.19 mmol) and dimethylphenylsilyl chloride (0.036 g, 0.21 mmol) in 2.5 mL of 1,2-dichlorobenzene in a sealed glass tube was heated at 230 °C for 24 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica gel/20% ethanol in methylene chloride, R_f 0.55) to afford 0.028 g of **25** (0.11 mmol, 59%) as a white solid and 0.012 g of **26** (0.046 mmol, 24%) as a yellow solid. Similarly, a solution of **13d** (0.139 g, 0.53 mmol) and dimethylphenylsilyl chloride (0.92 g, 5.3 mmol) in 2.5 mL of 1,2-dichlorobenzene in a sealed glass tube was heated at 230 °C for 24 h to afford 0.108 g of

25 (0.44 mmol, 82%) and 0.008 g of **26** (0.03 mmol, 6%). **25**: mp 335 °C dec with melting (lit.[18a] mp 323−326 °C); IR 3500, 1648 cm^{-1}; ^{1}H δ 9.88 (1 H, br s), 8.58 (1 H, d, J = 7.4 Hz), 8.36 (1 H, d, J = 8.4 Hz), 7.58−7.46 (4 H, m), 7.41 (1 H, ddd, J = 8.1, 6.4, 1.5 Hz), 7.33 (1 H, ddd, J = 8.4, 6.9, 1.5 Hz), 4.33 (3 H, s); ^{13}C (4% MeOH-d_4 in CDCl$_3$) δ 161.0, 140.8, 139.6, 137.6, 128.8, 124.5, 123.6, 122.4, 122.1, 121.8, 121.7, 116.9, 113.3, 109.0, 107.4, 33.3; MS m/z 248 (M$^+$), 232, 207. The structure of **25** was established by X-ray structure analysis. **26**: mp 207−208 °C; IR 1648, 744 cm^{-1}; ^{1}H δ 8.56 (1 H, d, J = 7.4 Hz), 8.30 (1 H, d, J = 8.2 Hz), 7.57 (1 H, ddd, J = 8.5, 6.6, 1.5 Hz), 7.48 (1 H, d, J = 7.9 Hz), 7.43−7.27 (4 H, m), 4.17 (3 H, s), 3.80 (3 H, s); ^{13}C (4% MeOH-d_4 in CDCl$_3$) δ 160.0, 139.6, 139.2, 138.9, 128.8, 124.4, 124.2, 122.9, 122.2, 121.8, 121.3, 115.6, 114.4, 108.9, 107.6, 33.5, 29.0; MS m/z 262 (M$^+$), 248, 233, 207.

Ethyl 2-(5-Methoxy-1-pentynyl)-1-cyclohexenecarboxylate (32). To a mixture of enol triflate **30**[19] (0.40 g, 1.32 mmol), *N,N*-diisopropylethylamine (0.23 mL, 1.32 mmol), Pd(PPh$_3$)$_2$-Cl$_2$ (0.027 g, 0.040 mmol), and copper(I) iodide (0.013 g, 0.066 mmol) in 5 mL of DMF was added slowly a solution of 5-methoxy-1-pentyne[22] (0.13 g, 1.32 mmol) in 2 mL of DMF. After 2 h of stirring at room temperature, 10 mL of a saturated aqueous ammonium chloride solution and 10 mL of diethyl ether were added. The organic layer was separated, and the aqueous layer was back extracted with diethyl ether. The combined organic layers were washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/ 50% diethyl ether in hexanes, R_f 0.45) afforded 0.30 g of **32** (1.2 mmol, 91%) as a yellow liquid: IR (neat) 2214, 1719, 1696 cm^{-1}; ^{1}H δ 4.21 (2 H, quartet, J = 7.2 Hz), 3.48 (2 H, t, J = 6.4 Hz), 3.34 (3 H, s), 2.47 (2 H, t, J = 6.9 Hz), 2.38−2.26 (4 H, m), 1.81 (2 H, quintet, J = 6.6 Hz), 1.65−1.58 (4 H, m), 1.30 (3 H, t, J = 7.2 Hz); ^{13}C δ 167.2, 133.3, 128.4, 96.8, 80.9, 71.2, 60.3, 58.6, 32.7, 28.7, 26.1, 21.8, 21.7, 16.6, 14.3; MS m/z 250 (M$^+$), 235, 222, 205, 192, 177, 164.

2-(5-Methoxy-1-pentynyl)-1-cyclohexenecarboxylic Acid (34). A mixture of 1.2 g of **32** (4.8 mmol) in 10 mL of 1,2-dimethoxyethane and 10 mL of a 1 M aqueous lithium hydroxide solution was stirred at room temperature for 36 h. Then 1,2-dimethoxyethane was removed in vacuo, and 10 mL of water was introduced. The solution was extracted with diethyl ether (3 × 10 mL), and the diethyl ether extracts were discarded. The aqueous solution was cooled in an ice−water bath, acidified with cold 10% sulfuric acid, and then extracted with Et$_2$O (3 × 30 mL). The combined diethyl ether layers were dried over sodium sulfate and concentrated in vacuo to give 0.93 g of **34** (4.19 mmol, 87%) as a colorless liquid: IR (neat) 3300−2600 (br), 2241, 1690 cm^{-1}; ^{1}H δ 3.49 (2 H, t, J = 6.2 Hz), 3.34 (3 H, s), 2.51 (2 H, t, J = 6.9 Hz), 2.38−2.30 (4 H, m), 1.82 (2 H, quintet, J = 6.6 Hz), 1.67−1.60 (4 H, m); ^{13}C δ 170.4, 132.7, 131.0, 100.4, 80.8, 71.0, 58.6, 33.1, 28.4, 25.9, 21.7, 16.6; MS m/z 222 (M$^+$), 190, 177.

Enyne−Isocyanate 36. To a solution of 0.42 g of **34** (1.89 mmol) in 15 mL of anhydrous benzene was added a solution of 0.29 mL of triethylamine (2.1 mmol) and 0.51 g of DPPA (1.85 mmol) in 2 mL of benzene. After 6 h of stirring at room temperature, the reaction mixture was then washed with brine and water, dried over sodium sulfate, and concentrated. Purification of the residue by flash column chromatography (silica gel/5% diethyl ether in hexanes, R_f 0.28) afforded 0.33 g of **36** (1.51 mmol, 82%) as a colorless liquid: IR (neat) 2248, 1458, 1120 cm^{-1}; ^{1}H δ 3.48 (2 H, t, J = 6.2 Hz), 3.34 (3 H, s), 2.47 (2 H, t, J = 6.9 Hz), 2.21−2.08 (4 H, m), 1.82 (2 H, quintet,

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J = 6.9 Hz), 1.70−1.53 (4 H, m); ^{13}C (C$_6$D$_6$) δ 133.9, 115.1, 98.3, 79.8, 71.8, 59.0, 30.3, 30.1, 29.8, 22.9, 22.5, 17.4; MS *m/z* 219 (M$^+$), 204, 187, 158.

2,3,4,6,7,8,9,10-Octahydro-5*H***-pyrano[3,2-***c***]quinolin-5-one (38).** A solution of **36** (0.23 g, 1.05 mmol) and dimethylphenylsilyl chloride (0.20 g, 1.15 mmol) in 10 mL of 1,2-dichlorobenzene was heated under reflux for 36 h. The solvent was removed in vacuo, and the residue was purified by column chromatography to afford 0.19 g of **38** (0.93 mmol, 89%) as a pale yellow solid: mp 261−263 °C; IR 1641, 1128 cm^{-1}; ^{1}H δ 11.3 (1 H, br), 4.17 (2 H, t, J = 5.0 Hz), 2.6−2.5 (4 H, m), 2.35 (2 H, t, J = 5.9 Hz), 1.94 (2 H, quintet, J = 5.2 Hz), 1.78−1.66 (4 H, m); ^{13}C δ 164.3, 162.4, 139.8, 107.6, 104.4, 66.8, 26.6, 22.1, 21.7, 21.3, 20.6, 18.8. The structure of **38** was established by X-ray structure analysis.

Benzoisoquinolinone 39. The following procedure is representative for thermolysis of enyne–isocyanates **37**. A solution of 0.237 g of **37a** (1.0 mmol) in 6 mL of 1,2-dichlorobenzene was heated under reflux for 3 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica gel/50% diethyl ether in hexanes) to afford 0.232 g of **39** (0.98 mmol, 98%) as light yellow crystals: mp 244−245 °C; IR (KBr) 3000−2300 (br), 1643, 764, 740 cm^{-1}; ^{1}H δ 13.51 (1 H, br s), 7.74−7.70 (1 H, m), 7.32−7.28 (3 H, m), 3.12 (2 H, t, J = 7.1 Hz), 2.99 (2 H, t, J = 7.5 Hz), 2.82 (4 H, s), 2.15 (2 H, quintet, J = 7.3 Hz); ^{13}C δ 164.5, 147.6, 143.3, 139.9, 133.2, 129.0, 128.1, 126.9, 126.3, 123.2, 116.7, 32.5, 31.0, 28.8, 23.7, 21.2; MS *m/z* 237 (M$^+$), 236, 207; HRMS calcd for C$_{16}$H$_{15}$NO 237.1154, found 237.1156. The structure of **39** was established by X-ray structure analysis.

Benzopyranopyridine 43. A solution of 0.178 g of **37b** (0.80 mmol) in 6 mL of 1,2-dichlorobenzene was heated under reflux for 48 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica gel/50% diethyl ether in hexanes, R_f 0.26) to afford 0.072 g of **43** (0.32 mmol, 40%) as a brown solid. Recrystallization of **43** from CH$_2$Cl$_2$/hexanes gave brown crystals: mp 103−104 °C; IR 1409, 782, 734 cm^{-1}; ^{1}H δ 7.82 (1 H, s), 7.61 (1 H, d, J = 7.7 Hz), 7.34 (1 H, td, J = 7.5, 1.4 Hz), 7.26 (1 H, td, J = 7.4, 1.3 Hz), 7.12 (1 H, d, J = 7.3 Hz), 5.27 (2 H, s), 2.92 (4 H, quartet, J = 7.6 Hz), 2.12 (2 H, quintet, J = 7.6 Hz); ^{13}C δ 164.4, 160.4, 131.5, 130.5, 129.8, 128.4, 127.8, 127.7, 124.5, 121.7, 114.1, 68.9, 34.0, 30.0, 23.2; MS *m/z* 223 (M$^+$), 222. Anal. Calcd for C$_{15}$H$_{13}$NO: C, 80.68; H, 5.87; N, 6.28. Found: C, 80.38; H, 5.89; N, 6.23. The structure of **43** was established by X-ray structure analysis.

Benzofuro[3,2-*c***]pyridin-1(2***H***)-one 44 and Benzofuro-[3,2-***c***]pyridine 45.** A solution of 0.104 g of **37c** (0.44 mmol) in 6 mL of chlorobenzene was heated under reflux at 132 °C for 36 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography to afford 0.010 g of **44** (0.044 mmol, 10%) as a white solid and 0.054 g of **45** (0.23 mmol, 52%) as a white solid. Similarly, a solution of **37c** (0.095 g, 0.40 mmol) and dimethylphenylsilyl chloride (0.076 g, 0.44 mmol) in 3.5 mL of 1,2-dichlorobenzene was heated under reflux for 12 h to afford 0.080 g of **44** (0.36 mmol, 90%) as a white solid. **44**: mp 305 °C dec with melting; IR 3421, 1656, 748 cm^{-1}; ^{1}H δ 10.74 (1 H, br s), 8.22−8.16 (1 H, m), 7.57−7.51 (1 H, m), 7.42−7.35 (2 H, m), 3.05 (4 H, t, J = 7.4 Hz), 2.30 (2 H, quintet, J = 7.4 Hz); ^{13}C (DMSO-d_6) δ 160.1, 159.7, 153.8, 150.2, 124.6, 124.1, 123.7, 120.1, 110.9, 106.9, 105.1, 30.9, 26.1, 22.0; MS *m/z* 225 (M$^+$) 191; HRMS calcd for C$_{14}$H$_{11}$NO$_2$ 225.0790, found 225.0779. The structure of **44** was established by X-ray structure analysis. **45**: recrystallization from CH$_2$Cl$_2$/hexanes gave brown crystals, mp 115−116 °C; IR 1594, 1067, 748 cm^{-1}; ^{1}H δ 8.02 (1 H, d, J = 6.7 Hz), 7.54 (1 H, d, J = 7.3 Hz), 7.43−7.33 (2 H, m), 4.17 (3 H, s), 3.11 (2 H, t, J = 7.3 Hz), 3.06 (2 H, t, J = 7.7 Hz), 2.24 (2 H, quintet, J = 7.5 Hz); ^{13}C δ 161.7, 160.1, 159.6, 155.2, 126.0, 123.5, 122.6, 122.1, 113.4, 111.1, 105.5, 53.6, 34.7, 26.8, 23.1; MS *m/z* 239 (M$^+$), 238, 210.

2,5-Dihydro-2,5-dimethyl-1*H***-pyrido[4,3-***b***]indol-1-one 46 and 1-Methoxy-5-methyl-5***H***-pyrido[4,3-***b***]indole 47.** A solution of 0.282 g of **37d** (1.12 mmol) in 5 mL of 1,2-dichlorobenzene was heated under reflux at 180 °C for 5 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography to afford 0.106 g of **46** (0.42 mmol, 38%) as brown crystals and 0.079 g of **47** (0.31 mmol, 28%) as yellow crystals. **46**: mp 238−240 °C; IR 1653, 1561, 747, 721 cm^{-1}; ^{1}H δ 8.40 (1 H, dd, J = 6.6, 1.9 Hz), 7.31 (1 H, td, J = 7.0, 1.6 Hz), 7.26 (1 H, td, J = 6.9, 1.6 Hz), 7.20 (1 H, dd, J = 6.6, 1.6 Hz), 3.70 (3 H, s), 3.50 (3 H, s), 3.05 (2 H, t, J = 7.4 Hz), 2.81 (2 H, t, J = 7.7 Hz), 2.13 (2 H, quintet, J = 7.5 Hz); ^{13}C δ 160.3, 147.5, 142.7, 138.9, 125.0, 123.3, 121.4, 121.0, 108.1, 105.3, 105.2, 32.0, 31.2, 30.4, 29.7, 22.0; MS *m/z* 252 (M$^+$), 251, 236. The structure of **46** was established by X-ray structure analysis. **47**: mp 205−206 °C; IR (KBr) 1622, 1595, 752 cm^{-1}; ^{1}H δ 8.21 (1 H, dd, J = 6.7, 2.0 Hz), 7.42 (1 H, td, J = 7.6, 1.2 Hz), 7.31−7.25 (2 H, m), 4.20 (3 H, s), 3.85 (3 H, s), 3.26 (2 H, t, J = 7.3 Hz), 3.04 (2 H, t, J = 7.7 Hz), 2.22 (2 H, quintet, J = 7.5 Hz); ^{13}C δ 159.7, 158.6, 144.6, 139.8, 124.5, 122.1, 121.9, 120.2, 111.1, 108.1, 103.6, 53.2, 34.2, 30.5, 29.0, 23.0; MS *m/z* 252 (M$^+$), 251, 223. The structure of **47** was established by X-ray structure analysis.

2,5-Dihydro-5-methyl-1*H***-pyrido[4,3-***b***]indol-1-one 48.** A solution of **37d** (0.038 g, 0.15 mmol) and dimethylphenylsilyl chloride (0.028 g, 0.16 mmol) in 5 mL of 1,2-dichlorobenzene was heated under reflux for 13 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography to afford 0.027 g of **48** (0.11 mmol, 75%) as a white solid: mp 318 °C dec with melting; IR 3385, 1636, 751 cm^{-1}; ^{1}H δ 9.35 (1 H, br s), 8.40 (1 H, d, J = 7.2 Hz), 7.38−7.32 (3 H, m), 3.95 (3 H, s), 3.25 (2 H, t, J = 7.2 Hz), 2.96 (2 H, t, J = 7.7 Hz), 2.29 (2 H, quintet, J = 7.7 Hz); ^{13}C (4% of MeOH-d_4 in CDCl$_3$) δ 161.3, 146.0, 144.6, 138.9, 124.1, 123.8, 121.3, 120.9, 108.5, 106.5, 105.2, 30.5, 29.1, 22.5. The structure of **48** was established by X-ray structure analysis.

Benzopyranopyridines 55 and 56. A solution of 0.372 g of **37f** (1.47 mmol) in 6 mL of 1,2-dichlorobenzene was heated under reflux at 180 °C for 5 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica gel/50% diethyl ether and 10% methylene chloride in hexanes) to afford 0.068 g of **55** (0.27 mmol, 18%) as a white solid and 0.215 g of **56** (0.85 mmol, 58%) as white crystals. Similarly, a solution of 0.306 g of **37f** (1.21 mmol) in 6 mL of 1,2-dichlorobenzene was heated at 150 °C for 20 h. The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica gel/50% diethyl ether and 10% methylene chloride in hexanes, R_f 0.30) to afford 0.182 g of **56** (0.72 mmol, 59%) as white crystals. Heating a solution of **37f** (0.021 g, 0.083 mmol) and dimethylphenylsilyl chloride (0.016 g, 0.090 mmol) in 4 mL of 1,2-dichlorobenzene under reflux at 180 °C for 13 h produced 0.016 g of **56** (0.063 mmol, 76%). **55**: mp 84−86 °C; IR 1607, 1408, 782, 753 cm^{-1}; ^{1}H δ 7.97 (1 H, s), 7.78 (1 H, d, J = 7.9 Hz), 7.47 (1 H, ddd, J = 7.7, 5.9, 3.0 Hz), 7.41−7.34 (2 H, m), 6.07 (1 H, s), 3.64 (3 H, s), 3.00 (2 H, td, J = 7.6, 2.6 Hz), 2.96 (2 H, t, J = 7.3 Hz), 2.17 (2 H, quintet, J = 7.6 Hz); ^{13}C δ 164.6, 156.7, 131.9, 129.6, 129.4, 128.6, 127.9, 127.7, 126.4, 121.8, 113.1, 100.2, 56.0, 34.1, 30.1, 23.2; MS *m/z* 253 (M$^+$), 222. **56**: mp 125−126 °C; IR 1584, 1558, 1080, 795, 748 cm^{-1}; ^{1}H δ 8.19 (1 H, d, J = 7.9 Hz), 7.34 (1 H, td, J = 7.5, 1.2 Hz), 7.26 (1 H, t, J = 7.0 Hz), 7.16 (1 H, d, J = 7.3 Hz), 5.15 (2 H, s), 4.01 (3 H, s), 3.12 (2 H, t, J = 7.3 Hz), 2.92 (2 H, t, J = 7.7 Hz), 2.12 (2 H, quintet, J = 7.6 Hz); ^{13}C δ 165.9, 163.1, 162.2, 131.2, 129.0, 128.1, 127.1, 126.3, 124.4, 120.8, 106.0, 69.1, 59.1, 34.3, 29.6, 23.0; MS *m/z* 253 (M$^+$), 252, 236. The structure of **56** was established by X-ray structure analysis.

Supporting Information Available: Experimental procedures and spectroscopic data for **12c**−**e**, **13a**, **13c**−**e**, **27**−**29**, **33e**, [[2-(methoxymethyl)phenyl]ethynyl]trimethylsilane, 1-ethynyl-2-(methoxymethyl)benzene, **33f**, **35e**,**f**, **37e**,**f**, and **49**−**52**; ^{1}H and ^{13}C NMR spectra of compounds **12b**−**e**, **13b**− e, **15**, **16**, **19**−**21**, **25**−**29**, **32**, **33e**, [[2-(methoxymethyl)phenyl]ethynyl]trimethylsilane,[23] 1-ethynyl-2-(methoxymethyl)benzene,[24] **33f**, **34**, **35e**,**f**, **36**, **37e**,**f**, **38**, **39**, **43**−**52**, **55**, and **56**; ORTEP drawings of the crystal structures of **16**, **19**, **25**, **38**, **39**, **43**, **44**, **46**−**48**, and **56** in PDF format; and X-ray crystallographic data of **16**, **19**, **25**, **38**, **39**, **43**, **44**, **46**−**48**, and **56** as CIF. This material is available free of charge via the Internet at http://pubs.acs.org.

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