Articles

Aryl Radical Additions to Aldehydes and Oxime Ethers: The Tandem Enediyne-Radical Cyclization

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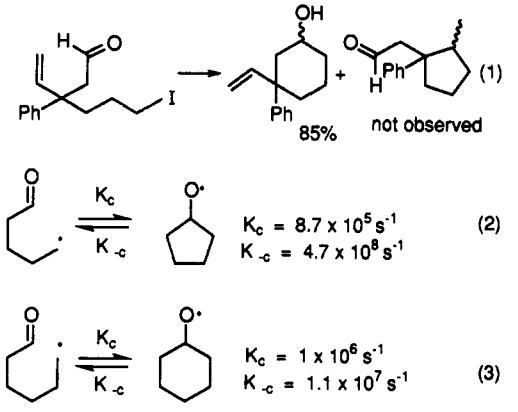
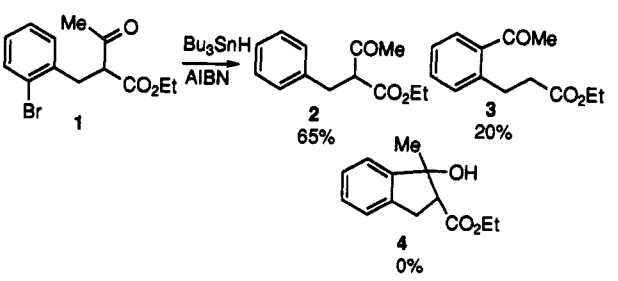
The previously unreported cyclization of aryl radicals onto aldehyde and oxime ether acceptors is described. The aryl radicals were generated from a cyclization of enediyne substrates. The aldehydes **6** and **9** and the oxime ethers **7** and **10** were heated to 190 °C in chlorobenzene in the presence of 1,4-cyclohexadiene as a hydrogen atom source to yield the tandem enediyne-radical cyclization products **11a, 11b, 14, 21,** and **22,** and the simple enediyne cyclization products **12, 13, 15, 16,** and **23.** For the enediyne aldehyde substrates tandem enediyne-radical cyclization does not appear to be a synthetically useful process and a mixture of products was obtained. The aryl radicals generated in these enediyne cyclizations subsequently undergo either a radical cyclization or other reactions such as hydrogen abstraction from 1,4-cyclohexadiene, decarbonylation, or intramolecular 1,5- and 1,6-hydrogen abstractions. In contrast, the reactions with oxime ether precursors provide the tandem enediyne-radical cyclization products in good yield and provide a useful alternative to the tandem enediyne-6-*exo*-radical cyclization onto olefins.

Recently there has been increased interest in the cyclization of alkyl radicals into ketone and aldehyde acceptors.[1-5] Fraser-Reid was the first to observe that a 6-*exo*-hexenyl radical cyclization into an aldehyde acceptor could compete successfully with a 5-*exo* cyclization into an alkene (Scheme I, eq 1).[3] The 5-*exo* radical cyclization into aldehydes is not nearly as favorable as the corresponding 5-*exo* alkene radical cyclizations.[3] Beckwith carried out kinetic studies on these systems and found that while the forward rate of the radical addition is similar for the two systems, it is the slower β-scission of the cyclohexyloxy radical that makes the 6-*exo* radical cyclization into aldehydes a synthetically useful process (Scheme I, eqs 2 and 3).[4a] Beckwith has reported the free radical reactions of an aryl radical with a β-carbomethoxy ketone resulting in an aryl bromide reduction product **2** and an addition/fragmentation product **3** where a formyl group is transferred from the alkyl chain to the aromatic ring. None of the cyclization product **4** was observed (Scheme II).[4c] Both Beckwith[4] and Dowd[5] have reported success with a similar reaction of alkyl radical ketone additions and they have used this reaction as a useful ring-expansion process.

Scheme I



Scheme II



Although the above-mentioned workers have completed some very elegant work, we have been unable to find any

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(1) For general references on free radical cyclizations see: (a) Curran, D. P. *Synlett* **1991**, 63. (b) Hart, D. J. *Science* **1984**, *223*, 883. (c) Giese, B. *Radicals in Organic Synthesis*; Pergamon Press: New York, 1986. (d) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (e) Curran, D. P. *Synthesis* **1988**, 417. (f) Curran, D. P. *Synthesis* **1988**, 489. (g) Neumann, W. P. *Synthesis* **1987**, 665. (h) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (i) *Houben-Weyl Methoden der Organischen Chemie*, Band 19a; Regitz, M., Giese, B.; Thieme: Stuttgart, 1989.

(2) (a) Tsai, Y.-M.; Cherng, C.-D. *Tetrahedron Lett.* **1991**, *32*, 3515. (b) Knapp, S.; Gibson, F. S. *J. Org. Chem.* **1992**, *57*, 4802. (c) Maillard, B.; Gardrat, C.; Bourgeois, M.-J. *J. Organomet. Chem.* **1982**, *236*, 61. (d) Flies, F.; Lalande, R.; Maillard, B. *Tetrahedron Lett.* **1976**, 439.

(3) (a) Fraser-Reid, B.; Walton, R. *J. Am. Chem. Soc.* **1991**, *113*, 5791. (b) Tsang, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1986**, *108*, 8102. (c) Tsang, R.; Dickson, J. K.; Pak, H.; Walton, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1987**, *109*, 3484. (d) Fraser-Reid, B.; Vite, G. D.; Yeung, B.-W. A.; Tsang, R. *Tetrahedron Lett.* **1988**, *29*, 1645.

(4) (a) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674. (b) Beckwith, A. L. J.; Raner, K. D. *J. Org. Chem* **1992**, *57*, 4954. (c) Beckwith, A. L. J.; O'Shea, D. M.; Westwood, S. W. *J. Am. Chem. Soc.* **1988**, *110*, 2565. (d) Beckwith A. L. J.; O'Shea, D. M.; Gerba, S.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666.

(5) (a) Dowd, P.; Zhang, W. *Tetrahedron Lett.* **1992**, *33*, 7307. (b) Dowd, P.; Zhang, W. *J. Am. Chem. Soc.* **1991**, *113*, 9875. (c) Dowd, P.; Choi, S.-C. *Tetrahedron Lett.* **1991**, *32*, 565. (d) Dowd, P.; Choi, S.-C. *Tetrahedron* **1991**, *47*, 4847. (e) Dowd, P.; Choi, S.-C. *Tetrahedron Lett.* **1989**, *30*, 6129. (f) Dowd, P.; Choi, S.-C. *Tetrahedron Lett.* **1989**, *30*, 77. (g) Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 3493. (h) Dowd, P.; Choi, S.-C. *J. Am. Chem. Soc.* **1987**, *109*, 6548.

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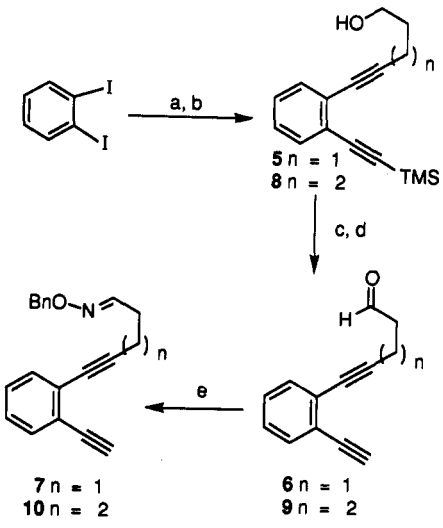
Scheme III[a]

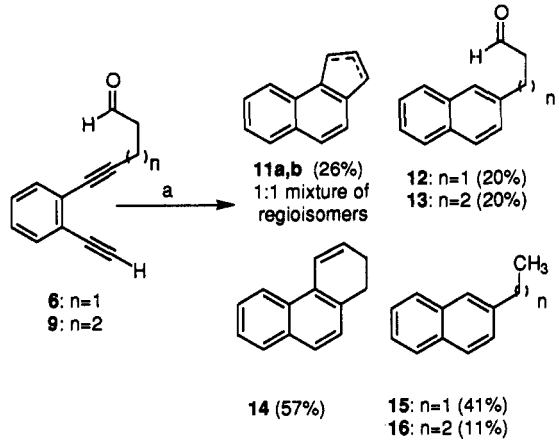


[a](a) 1.5 equiv of 4-pentynol or 5-hexynol, 0.03 equiv of $(Ph_3P)_2PdCl_2$, 0.1 equiv of CuI, 3.0 equiv of NEt_3, THF; (b) 1.2 equiv of (trimethylsilyl)acetylene, same as a; (c) K_2CO_3 (cat.), MeOH; (d) 1.2 equiv of PCC, CH_2Cl_2; (e) $BnONH_3Cl$, pyridine, CH_2Cl_2.

examples of aryl radical additions to aldehydes and oxime ethers. Aryl radicals are inherently less stable and undergo radical cyclizations with pendent alkenes more rapidly than their corresponding alkyl analogues.[6] Thus, we would expect aryl radicals to add successfully to carbonyl and oxime ether π-acceptors. In this paper we report the expansion of the scope of aryl radical cyclizations by employing aryl radicals generated from our recently described[7] tandem enediyne-radical cyclization[8] in radical additions to aldehydes and oxime ethers. The success of these reactions demonstrates not only the further synthetic usefulness of the tandem enediyne-radical cyclization reaction, but also the interesting mechanistic facets of these aryl radical addition reactions.

Synthesis of Aldehyde and Oxime Ether Cyclization Precursors. We have synthesized the aldehydes **6** and **9**, as well as the oxime ethers **7** and **10**, in a straightforward manner as shown in Scheme III.[7] The palladium-catalyzed coupling of *o*-diiodobenzene to 4-pentynol proceeded in 56% yield and the same coupling of *o*-diiodobenzene to 5-hexynol gave a 48% yield. These reactions were followed by a second palladium catalyzed coupling with (trimethylsilyl)acetylene to give the aromatic enediynes **5** and **8** in 90% yield.[9] The acetylenic trimethylsilyl group was removed in 97% yield using potassium carbonate/methanol, followed by PCC oxidation of the alcohol (88%) to yield the aldehyde cyclization precursors **6** and **9**. Treatment of the aldehydes with the hydrochloride salt of *O*-benzylhydroxylamine afforded the oxime ether **7** in 76% yield as a 1:1 mixture of *E*/*Z* oxime isomers and **10** in 82% yield as a 2:3 mixture of *E*/*Z* oxime isomers.

Scheme IV[a]



[a](a) 1,4-Cyclohexadiene (0.5 mol/L), chlorobenzene, 190 °C, 8 h.

Radical Cyclizations to Aldehyde Acceptors. Subjecting the enediyne aldehydes to thermolysis at 190 °C in the presence of 1,4-cyclohexadiene (1,4-CHD) as a hydrogen atom donor yields a mixture of tandem enediyne-radical cyclization and enediyne cyclization products. When aldehyde **6** was heated to 190 °C in chlorobenzene in the presence of 1,4-CHD, four products were obtained. The major product was β-ethylnaphthalene (**15**) (41%), formed along with the aldehyde **12** (20%) and the tricyclic tandem enediyne-radical cyclization products **11a** and **11b** (26%) as a 1:1 mixture of double bond regioisomers (Scheme IV). Overall, the desired tandem enediyne-radical cyclization products **11a** and **11b** were formed in a disappointing ratio of 1:2.5, relative to the simple enediyne cyclization products **12** and **15**.

A mechanism to account for the formation of these products is shown in Scheme V. The expected tandem enediyne-radical cyclization product **17** was not directly observed, but is presumably converted to tricycles **11a,b** *via* dehydration and double bond isomerization. Aldehyde **12** could be formed by an enediyne cyclization followed by hydrogen abstraction from 1,4-CHD. Given the inherent stability of acyl radicals over aryl radicals,[10] an alternative pathway would involve intramolecular 1,5-hydrogen abstraction followed by hydrogen abstraction from 1,4-CHD.[8] β-Ethylnaphthalene (**15**) arises from an enediyne cyclization followed by an intramolecular 1,5-hydrogen abstraction, CO-elimination, and hydrogen abstraction from 1,4-CHD. The decarbonylation of acyl radicals is a well-precedented process.[12]

Thermolysis of the homologous aldehyde **9** under the same conditions resulted in a dramatic increase of tandem enediyne-radical cyclization product formation (Scheme IV). The desired 6-*exo* tandem enediyne cyclization product **14**, which seems to be the dehydration product of the initially formed (but not observed) alcohol **18**, was formed as the major product (57%) along with the simple enediyne cyclized aldehyde **13** (20%) and the CO-elimination product **16** (11%; Scheme IV). It was encouraging to see that in the 6-*exo* radical cyclization the tandem

(6) (a) Johnston, L. J.; Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 4877. (b) Beckwith, A. L. J.; Gara, W. B. *J. Chem. Soc., Perkin Trans. 2* **1975**, 593. (c) Beckwith, A. L. J.; Gara, W. B. *J. Chem. Soc., Perkin Trans. 2* **1975**, 795. (d) Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.* **1981**, 136. (e) Abeywickrema, A. N.; Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.* **1986**, 464.

(7) (a) Grissom, J. W.; Calkins, T. L. *Tetrahedron Lett.* **1992**, 33, 2315. (b) Boger, D. L.; Zhou, J. *J. Org. Chem.* **1993**, *58*, 3018.

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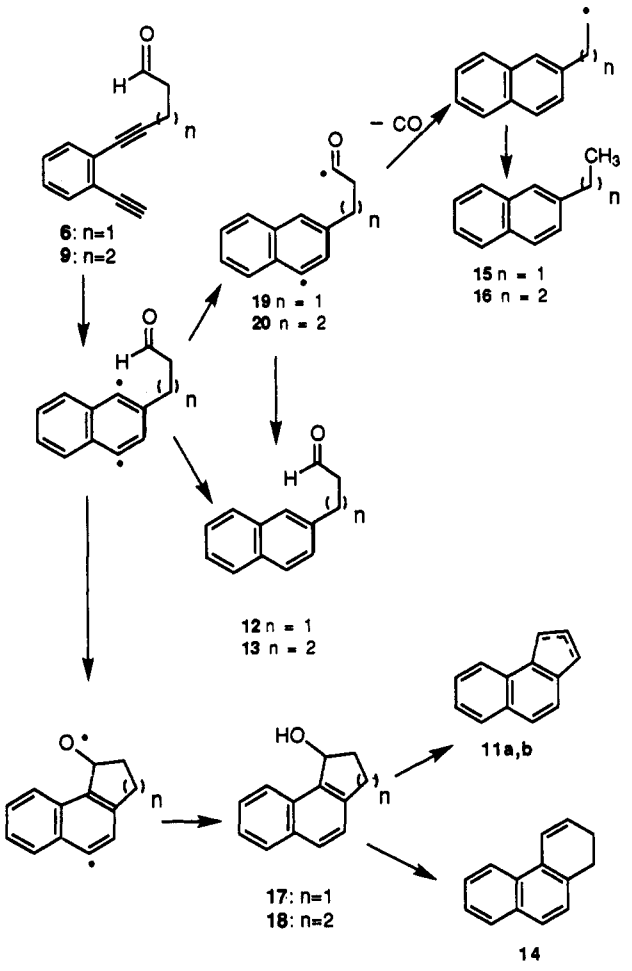
(9) (a) Singh, R.; Just, G. *Tetrahedron Lett.* **1990**, *31*, 185. (b) Guillerm, D.; Linstrumelle, G. *Tetrahedron Lett.* **1985**, *26*, 3811. (c) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

(10) Golden, B. M.; Benson, S. W. *Chem. Rev.* **1969**, *69*, 125.

(11) For examples of acyl radical additions to olefins see: (a) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1992**, *57*, 1429. (b) Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4003. (c) Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4008. (d) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1989**, *54*, 1777. (e) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1988**, *53*, 3377.

(12) Winstein, S.; Suebold, F. H. *J. Am. Chem. Soc.* **1947**, *69*, 2916.

Scheme V

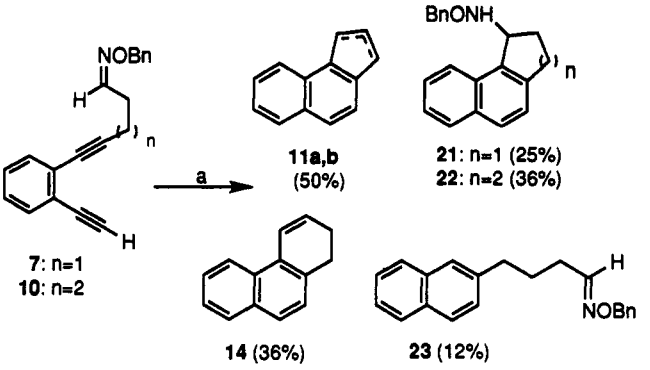


enediyne-radical cyclization product **14** is favored in a ratio of 2:1 over the simple enediyne cyclization products **13** and **16**.

Presumably the products in the reaction with the homologous enediyne aldehyde **9** arise by the same pathways as described for aldehyde **6**, but the observation of β-propylnaphthalene deserves comment (Scheme V). Again this product appears to arise from the decarbonylation of radical **20**. Given the high concentration of 1,4-CHD (0.5–1.0 M), it seems unlikely that the intermolecular abstraction of the aldehyde hydrogen would be a significant competing process. A more likely scenario involves an intramolecular 1,6-hydrogen abstraction by the aryl radical.[13] Theoretical calculations suggest that this mode of hydrogen transfer should be geometrically allowed.[14]

The 6-*exo* alkyl radical cyclization onto aldehydes ($k = 1.0 \times 10^6$ s^{-1} [80 °C]) is known to be kinetically favored over the respective 5-*exo* cyclization ($k = 8.7 \times 10^5$ s^{-1} [80 °C]), and the β-scission of the resulting oxy-radical is faster in the five-membered ring ($k = 4.7 \times 10^8$ s^{-1} [80 °C]) than in the six-membered ring ($k = 1.1 \times 10^7$ s^{-1} [80 °C]).[3] Although rates for the cyclization of aryl radicals onto aldehydes or the β-scission of the resulting oxy-radicals have not been measured, our observed results show that

Scheme VI[a]



[a](a) 1,4-Cyclohexadiene (0.5 mol/L), chlorobenzene, 190 °C, 8 h.

presumably the same trend is followed as in the alkyl radical cyclization. Clearly the 6-*exo* radical cyclizations are favored over the 5-*exo* cases. We did not observe any formyl transfer product.[3b]

Radical Cyclizations to Oxime Ether Acceptors. Since oxime ethers are known to be better radical acceptors than aldehydes,[15] we employed the oxime ethers **7** and **10** as substrates in the tandem enediyne-radical cyclization (Scheme VI). When oxime ether **7** (*E*/*Z* = 1:1) was thermolyzed under the same conditions as outlined above for aldehydes **6** and **9**, there was no evidence for any simple enediyne cyclization product. The only products formed were tandem enediyne-radical cyclization products consisting of hydrocarbons **11a,b** (50%) and *O*-benzylhydroxylamine **21** (25%). Hydrocarbons **11a,b** were isolated as a mixture of double bond isomers in a 1:1 ratio (Scheme VI).

Employing oxime ether **10** (*E*/*Z* = 3:2) as the substrate in the tandem enediyne-radical cyclization resulted in the formation of four products (Scheme VI). In addition to the tricyclic products **14** and **22**, which were formed in a 72% yield as a 1:1 mixture, we also isolated the enediyne cyclization product oxime ether **23** in a 12% yield as a 1:1 mixture of *E*/*Z* isomers. In this case, the tandem enediyne-radical cyclization products are favored over the simple enediyne cyclization product in a 6:1 ratio.

We have investigated the mechanism for the formation of the elimination product in the tandem enediyne-radical cyclization of starting enediynes **6**, **7**, **9**, and **10**. Control experiments suggest that the formation of the elimination products **11a,b** and **14** increases with reaction time. A sample of alcohol **17** synthesized by an alternative method underwent elimination to form **11a,b** when subjected to the reaction conditions for the tandem enediyne-radical cyclization. Subjecting a pure sample of tandem enediyne cyclization product **21** to the reaction conditions also resulted in the formation of hydrocarbons **11a** and **11b**. A catalytic amount of acid, which can always be present in the glassware or originate from chlorobenzene decomposition, might suffice to catalyze both the elimination of water and *O*-benzylhydroxylamine at the high temperatures employed in these reactions. The observation that the tandem enediyne-radical cyclized amines **21** and **22**

(13) (a) For an example of a 1,6-hydrogen abstraction see: Little, R. D.; Billera, C. F. *Abstract of Papers*; 205th National Meeting of the American Chemical Society, Denver, CO; American Chemical Society: Washington, D.C., 1993; Abstract ORG. 103. (b) For an example of a 1,9-hydrogen transfer see: Kraus, G. A.; Wu, Y. *J. Am. Chem. Soc.* **1990**, *114*, 8705.

(14) Huang, X. L.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 5421.

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can be detected and isolated, while the respective alcohols 17 and 18 cannot, and that the elimination of water took only 1 h while the alkoxy amine elimination took 3–4 h, supports the fact that water is eliminated much more readily than alkoxy amines.

The results of the two oxime ether experiments render both systems synthetically useful for the formation of both the dihydrobenz[*e*]indene and dihydrophenanthrene systems. Both the aldehyde **9** and the oxime ether **10** provide a useful alternative for the 6-*exo* aryl radical cyclization onto an olefin acceptor, in which the tandem enediyne cyclization product formation was limited to a 1:1 ratio with respect to the competing formation of simple enediyne cyclization products.[7a] In addition, if the elimination problem can be solved, there would be a heteroatom functionality on the five- or six-membered rings that could be further elaborated.

Conclusion

In conclusion, we have employed enediyne-generated aryl radicals in both the 5-*exo* and 6-*exo* radical cyclization onto aldehydes and oxime ethers. The results with the enediyne aldehyde cyclizations, while not synthetically useful, are mechanistically interesting. In particular, we have noted an intramolecular 1,6-hydrogen shift and an elimination of water or alkoxy amines. We have found that oxime ethers are synthetically useful precursors for the tandem enediyne-radical cyclization to form either a dihydrobenz[*e*]indene or a dihydrophenanthrene system. This methodology should prove to be useful in the synthesis of multicyclic natural products.

Experimental Section

General. All reactions were carried out in flame-dried flasks under nitrogen. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl; ethyl acetate, dichloromethane, pyridine, and triethylamine were distilled from calcium hydride and hexanes from calcium chloride prior to use. Chlorobenzene was distilled from phosphorus pentoxide and stored over molecular sieves (Linde type 4 Å). EM Science silica gel 60 (230–400 mesh) was used for column chromatography. Thin-layer chromatography (TLC) was carried out using E. Merck precoated silica gel F-254 plates (thickness 0.25 mm). IR spectra were recorded on a Mattson FT-IR spectrometer. Peaks are reported in cm^{-1}. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian Unity spectrometer in $CDCl_3$ with chemical shifts (δ) reported in ppm relative to tetramethylsilane as an internal standard. Mass spectra were obtained on a Finnigan-MAT 95 high resolution gas chromatograph/mass spectrometer with Finnigan MAT ICIS II operating system using electron impact (EI) at 70 eV unless otherwise noted.

Preparation of 5-(2-Iodophenyl)pent-4-yn-1-ol and 6-(2-Iodophenyl)hex-5-yn-1-ol: *o*-Diiodobenzene (1.00 g, 3.0 mmol) was dissolved in 30 mL of THF. After the addition of triethylamine (1.470 mL, 920 mg, 9.10 mmol) and bis(triphenylphosphine)palladium(II) chloride (64 mg, 0.09 mmol), the reaction mixture was stirred for 10 min. Then copper(I) iodide (57 mg, 0.30 mmol) was added and the reaction mixture stirred for an additional 10 min, before 4-pentynol/5-hexynol (4.50 mmol) was added in one portion *via* syringe. The reaction was allowed to stir at room temperature until the starting material was consumed (TLC). The solvent was removed *in vacuo* and the residue filtered through silica gel using a 1:1 mixture of hexanes/diethyl ether. Purification of the product was accomplished by flash chromatography with an 85:15 mixture of hexanes/diethyl ether.

5-(2-Iodophenyl)pent-4-yn-1-ol: 486 mg (56%) of a yellow oil; TLC R_f 0.25 (2:1 hexanes/ethyl acetate); IR (neat) ν 3374 (br), 3059, 2230 cm^{-1}; ^1H NMR δ 1.52 (s, br, 1H, OH), 1.89 (quintet, 2H, J = 6.3 Hz), 2.59 (t, 2H, J = 6.3 Hz), 3.87 (t, 2H, J = 6.3 Hz), 6.94 (td, 1H, J = 7.5, 1.5 Hz), 7.24 (td, 1H, J = 7.5, 1.5 Hz), 7.38 (dd, 1H, J = 7.8, 1.5 Hz), 7.79 (dd, 1H, J = 7.8, 1.5 Hz); ^{13}C NMR δ 16.1, 31.0, 61.7, 83.4, 93.6, 101.0, 127.7, 128.9, 130.2, 132.5, 138.6; HRMS (EI) calcd for $C_{11}H_{11}IO$ (M^+) 285.9853, found 285.9849.

6-(2-Iodophenyl)hex-5-yn-1-ol: 437 mg (48%) of a yellow oil; TLC R_f 0.27 (2:1 hexanes/ethyl acetate); IR (neat) ν 3376 (br), 3059, 2232 cm^{-1}; ^1H NMR δ 1.35 (t, br, 1H, OH), 1.75(m, 4H), 2.50 (t, 2H, J = 6.9 Hz), 3.71 (q, 2H, J = 5.7 Hz), 6.93 (td, 1H, J = 7.8, 1.5 Hz), 7.24 (td, 1H, J = 7.8, 1.2 Hz), 7.37 (dd, 1H, J = 7.8, 1.5 Hz), 7.79 (dd, 1H, J = 7.8, 1.2 Hz); ^{13}C NMR δ 19.3, 24.7, 31.9, 62.5, 83.2, 94.2, 101.0, 127.7, 128.8, 130.3, 132.5, 138.6; HRMS (EI) calcd for $C_{12}H_{13}IO$ (M^+) 300.0010, found 300.0016.

Preparation of 5 and 8. 5-(2-Iodophenyl)pent-4-yn-1-ol or 6-(2-iodophenyl)hex-5-yn-1-ol (1.50 mmol) and triethylamine (0.727 mL, 455 mg, 4.50 mmol) were dissolved in 20 mL of THF. After the addition of bis(triphenylphosphine)palladium(II) chloride (35 mg, 0.05 mmol), the reaction mixture was stirred for 10 min, before copper(I) iodide (29 mg, 0.15 mmol) was added and the heterogeneous mixture was stirred for an additional 10 min. After that, (trimethylsilyl)acetylene (0.254 mL, 177 mg, 1.80 mmol) was added in one portion *via* syringe. The reaction was allowed to stir for 30 min at room temperature. Then the solvent was removed *in vacuo* and the residue passed through a short silica gel column with a 1:1 mixture of hexanes/diethyl ether. The crude product was purified by flash chromatography with an 85:15 mixture of hexanes/diethyl ether.

5: 346 mg (90%) of a yellow oil; TLC R_f 0.33 (2:1 hexanes/ethyl acetate); IR (neat) ν 3351 (br), 3060, 2230, 2158 cm^{-1}; ^1H NMR δ 0.30 (s, 9H), 1.74 (t, br, 1H, OH), 1.91 (quintet, 2H, J = 6.3 Hz), 2.63 (t, 2H, J = 6.3 Hz), 3.88 (q, 2H, J = 6.3 Hz), 7.24 (m, 2H), 7.40 (m, 1H), 7.47 (m, 1H); ^{13}C NMR δ 0.0, 16.2, 31.3, 61.8, 79.8, 93.6, 97.9, 103.8, 125.4, 126.4, 127.3, 128.2, 131.8, 132.3; HRMS (EI) calcd for $C_{16}H_{20}OSi$ (M^+) 256.1283, found 256.1269.

8: 365 mg (90%) of a yellow oil; TLC R_f 0.31 (2:1 hexanes/ethyl acetate); IR (neat) ν 3354 (br), 3061, 2232, 2158 cm^{-1}; ^1H NMR δ 0.30 (s, 9H), 1.41 (s, br, 1H, OH), 1.78 (m, 4H), 2.55 (t, 2H, J = 6.6 Hz), 3.75 (t, 2H, J = 6.0 Hz), 7.25 (m, 2H), 7.41 (m, 1H), 7.47 (m, 1H); ^{13}C NMR δ 0.0, 19.3, 25.0, 31.9, 62.4, 79.6, 94.2, 97.8, 103.8, 125.4, 126.7, 127.2, 128.1, 131.8, 132.2; HRMS (EI) calcd for $C_{17}H_{22}OSi$ (M^+) 270.1440, found 270.1424.

Preparation of 5-(2-Ethynylphenyl)pent-4-yn-1-ol and 6-(2-Ethynylphenyl)hex-5-yn-1-ol. 5-[2-[(Trimethylsilyl)-ethynyl]phenyl]pent-4-yn-1-ol (**5**) or 6-[2-[(trimethylsilyl)ethynyl]phenyl]hex-5-yn-1-ol (**8**) (1.00 mmol) was dissolved in 5 mL of methanol. A catalytic amount of potassium carbonate was added and the reaction mixture stirred for 30 min. The solvent was then removed *in vacuo* and the residue passed through a short silica gel column with diethyl ether. The crude product was purified by flash chromatography with an 85:15 mixture of hexanes/diethyl ether.

5-(2-Ethynylphenyl)pent-4-yn-1-ol: 179 mg (97%) of a clear yellow oil; TLC R_f 0.21 (2:1 hexanes/ethyl acetate); IR (neat) ν 3375 (br), 3285, 3063, 2228, 2106 cm^{-1}; ^1H NMR δ 1.71 (s, br, 1H, OH), 1.87 (quintet, 2H, J = 6.3 Hz), 2.59 (t, 2H, J = 6.3 Hz), 3.27 (s, 1H), 3.86 (t, 2H, J = 6.3 Hz), 7.24 (m, 2H), 7.39 (m, 1H), 7.46 (m, 1H); ^{13}C NMR δ 16.2, 31.1, 61.7, 79.7, 80.5, 82.4, 93.8, 124.4, 126.7, 127.4, 128.5, 131.8, 132.5; HRMS (EI) calcd for $C_{13}H_{12}O$ (M^+) 184.0888, found 184.0886.

6-(2-Ethynylphenyl)hex-5-yn-1-ol: 192 mg (97%) of a clear yellow oil; TLC R_f 0.19 (2:1 hexanes/ethyl acetate); IR (neat) ν 3374 (br), 3285, 3063, 2232, 2106 cm^{-1}; ^1H NMR δ 1.43 (s, br, 1H, OH), 1.74 (m, 4H), 2.50 (t, 2H, J = 6.6 Hz), 3.27 (s, 1H), 3.69 (t, 2H, J = 6.0 Hz), 7.22 (td, 2H, J = 7.2, 1.8 Hz), 7.38 (dd, 1H, J = 7.2, 1.8 Hz), 7.46 (dd, 1H, J = 7.2, 1.8 Hz); ^{13}C NMR δ 19.3, 24.8, 31.7, 62.4, 79.4, 80.5, 82.5, 94.4, 124.3, 126.9, 127.3, 128.5, 131.9, 132.5; HRMS (EI) calcd for $C_{14}H_{14}O$ (M^+) 198.1045, found 198.1044.

Preparation of 6 and 9. 5-(2-Ethynylphenyl)pent-4-yn-1-ol or 6-(2-ethynylphenyl)hex-5-yn-1-ol (1.00 mmol) was dissolved in dichloromethane and pyridinium chlorochromate (259 mg, 1.20 mmol) was added portionwise under vigorous stirring. After the addition was completed, the reaction mixture was allowed to stir at room temperature until the alcohol was no longer visible by TLC (5–8 h). The mixture was passed through a short Florisil

column. Purification was accomplished by flash chromatography with a 95:5 mixture of hexanes/ethyl acetate.

6: 160 mg (88%) of a slightly yellow oil; TLC R_f 0.35 (3:1 hexanes/ethyl acetate); IR (neat) ν 3283, 3063, 2236, 2106, 1728 cm^{-1}; ^{1}H NMR δ 2.78 (s, 4H), 3.27 (s, 1H), 7.24 (m, 2H), 7.38 (dd, 1H, J = 6.9, 1.8 Hz), 7.47 (dd, 1H, J = 6.9, 1.8 Hz), 9.87 (s, 1H); ^{13}C NMR δ 12.9, 42.5, 80.0, 80.7, 82.2, 92.2, 124.5, 126.3, 127.6, 128.5, 131.9, 132.5, 200.6; HRMS (EI) calcd for $C_{13}H_{10}O$ (M^+) 182.0732, found 182.0733.

9: 173 mg (88%) of a slightly yellow oil; TLC R_f 0.38 (3:1 hexanes/ethyl acetate); IR (neat) ν 3283, 3063, 2232, 2106, 1723 cm^{-1}; ^{1}H NMR δ 1.94 (quintet, 2H, J = 6.9 Hz), 2.55 (t, 2H, J = 6.9 Hz), 2.72 (td, 2H, J = 6.9, 1.2 Hz), 3.27 (s, 1H), 7.24 (m, 2H), 7.39 (dd, 1H, J = 6.9, 2.4 Hz), 7.47 (dd, 1H, J = 6.9, 2.4 Hz), 9.83 (t, 1H, J = 1.2 Hz); ^{13}C NMR δ 18.9, 21.0, 42.7, 80.2, 80.5, 82.5, 93.2, 124.4, 126.6, 127.5, 128.5, 131.8, 132.5, 202.0; HRMS (EI) calcd for $C_{14}H_{12}O$ (M^+) 196.0888, found 196.0880.

Preparation of 7 and 10. 5-(2-Ethynylphenyl)-4-pentynal (**6**) or 6-(2-ethynylphenyl)-5-hexynal (**9**) (0.50 mmol) was dissolved in 8 mL of dichloromethane. After adding *O*-benzylhydroxylamine hydrochloride (88 mg, 0.55 mmol) and pyridine (0.044 mL, 44 mg, 0.55 mmol), the reaction mixture was allowed to stir at room temperature until the aldehyde was no longer visible by TLC (7–8 h). The reaction mixture was then passed through a short silica gel column with dichloromethane. Purification of the crude product was accomplished by flash chromatography with a 95:5 mixture of hexanes/ethyl acetate.

7: 120 mg (76%) of a pale yellow oil (1:1 mixture of *E* and *Z* isomers); TLC R_f 0.48 (3:1 hexanes/ethyl acetate); IR (neat) ν 3283, 3063, 3032, 2234, 2108 cm^{-1}; ^{1}H NMR δ 2.53 (m, 1H), 2.66 (m, 3H), 3.24 (s, 0.5H), 3.28 (s, 0.5H), 5.07 (s, 1H), 5.13 (s, 1H), 6.95 (t, 0.5H, J = 7.8 Hz), 7.19–7.49 (m, 9H), 7.68 (t, 0.5H, J = 5.7 Hz); ^{13}C NMR δ 16.7, 17.4, 25.1, 28.8, 75.7, 75.9, 80.1, 80.2, 80.8, 82.2, 82.3, 92.5, 92.7, 124.5, 124.6, 126.5, 126.6, 127.5, 127.5, 127.8, 128.0, 128.2, 128.4, 128.4, 131.9, 132.5, 137.6, 137.9, 149.8, 150.4 (some signals of both isomers coincide); HRMS (CI) calcd for $C_{20}H_{18}NO$ (M^+ + 1) 288.1388, found 288.1383.

10: 136 mg (82%) of a pale yellow oil (3:2 mixture of *E* and *Z* isomers); TLC R_f 0.48/0.53 (3:1 hexanes/ethyl acetate); IR (neat) ν 3283, 3063, 3032, 2232, 2108 cm^{-1}; ^{1}H NMR δ 1.81 (m, 2H), 2.42 (m, 1H), 2.51 (t, 2H, J = 6.9 Hz), 2.61 (m, 1H), 3.21 (s, 0.4H), 3.25 (s, 0.6H), 5.05 (s, 1.2H), 5.11 (s, 0.8H), 6.75 (t, 0.4H, J = 5.4 Hz), 7.18–7.48 (m, 9H), 7.50 (t, 0.6H, J = 5.7 Hz); ^{13}C NMR δ 19.1, 19.4, 25.2, 25.3, 25.6, 28.6, 75.6, 75.7, 79.8, 79.9, 80.6, 80.7, 82.3, 82.4, 93.5, 93.6, 124.4, 126.8, 127.3, 127.8, 127.8, 127.9, 128.3, 128.4, 128.4, 131,8, 132.5, 137.6, 138.0, 150.6, 151.5 (some signals of both isomers coincide).

General Procedure for the Tandem Enediyne-Radical Cyclization. The starting enediyne (**6**, **7**, **9**, or **10**) (0.30 mmol) was dissolved in 7.5 mL of chlorobenzene and transferred into a tube with Teflon screw cap. The solution was purged with nitrogen for 30 min, and 1,4-cyclohexadiene (0.355 mL, 300 mg, 3.75 mmol) was added *via* syringe. The vial was sealed and slowly heated up to 190 °C and kept at this temperature for 8 h, and then it was allowed to cool to room temperature. The solvent was removed *in vacuo* and the residue passed through a short silica gel column with a 3:1 mixture of ethyl acetate/hexanes. The products were separated by flash chromatography, eluting with pentane and slowly increasing the polarity with ethyl acetate.

Tandem Enediyne-Radical Cyclization of Aldehyde 6. 1*H*-Benz[*e*]indene/3*H*-benz[*e*]indene (11a,b): colorless oil (26%), 1:1 mixture; ^{1}H NMR δ 3.56 (dd, 1H, J = 0.1, 1.8 Hz), 3.71 (dd, 1H, J = 0.1, 1.8 Hz), 6.65 (dt, 0.5H, J = 5.4, 1.8 Hz), 6.73 (td, 0.5H, J = 5.4, 1.8 Hz), 6.99 (td, 0.5H, J = 5.4, 1.8 Hz), 7.34–8.21 (m, 6.5H); HRMS (EI) calcd for $C_{13}H_{10}$ (M^+) 166.0783, found 166.0799 (1*H*), 166.0787 (3*H*).

Naphthalene-2-propanal (12): slightly yellow oil (20%); IR (neat) ν 3054, 1722 cm^{-1}; ^{1}H NMR δ 2.86 (t, 2H, J = 7.5 Hz), 3.11 (t, 2H, J = 8.4 Hz), 7.31 (d, 1H, J = 8.4 Hz), 7.43 (m, 2H), 7.62 (s, 1H), 7.77 (m, 3H), 9.85 (s, 1H); ^{13}C NMR δ 28.2, 45.2, 125.5, 126.1, 126.5, 126.9, 127.5, 127.6, 128.3, 132.1, 133.6, 137.8, 201.6; HRMS (EI) calcd for $C_{13}H_{12}O$ (M^+) 184.0888, found 184.0888.

2-Ethylnaphthalene (15): colorless oil (41%); ^{1}H NMR δ 1.31 (t, 3H, J = 7.5 Hz), 2.80 (q, 2H, J = 7.5 Hz), 7.34 (dd, 1H, J = 8.7, 1.8 Hz), 7.41 (m, 2H), 7.61 (s, 1H), 7.77 (m, 3H); ^{13}C NMR δ 15.5, 29.0, 125.0, 125.5, 125.8, 127.1, 127.4, 127.6, 127.8, 131.9, 133.7, 141.8; HRMS (EI) calcd for $C_{12}H_{12}$ (M^+) 156.0939, found 156.0939.

Tandem Enediyne-Radical Cyclization of Aldehyde 9. Naphthalene-2-butanal (13): slightly yellow oil (20%); IR (neat) ν 3054, 1721 cm^{-1}; ^{1}H NMR δ 2.04 (quintet, 2H, J = 7.5 Hz), 2.47 (td, 2H, J = 7.5, 1.5 Hz), 2.81 (t, 2H, J = 7.5 Hz), 7.30 (dd, 1H, J = 8.4, 1.8 Hz), 7.43 (m, 2H), 7.59 (s, 1H), 7.77 (m, 3H), 9.76 (t, 1H, J = 1.5 Hz); ^{13}C NMR δ 23.4, 35.1, 43.1, 125.3, 126.0, 126.6, 127.1, 127.4, 127.6, 128.1, 132.1, 133.6, 138.7, 202.3; HRMS (EI) calcd for $C_{14}H_{14}O$ (M^+) 198.1045, found 198.1055.

3,4-Dihydrophenanthrene (14): colorless oil (57%); IR (neat) ν 3046, 1618, 1589 cm^{-1}; ^{1}H NMR δ 2.37 (tdd, 2H, J = 8.7, 4.5, 1.8 Hz), 2.92 (t, 2H, J = 8.1 Hz), 6.25 (dt, 1H, J = 9.9, 4.5 Hz), 7.27 (m, 2H), 7.42 (m, 2H), 7.64 (d, 1H, J = 8.1 Hz), 7.77 (d, 1H, J = 8.1 Hz), 8.08 (d, 1H, J = 8.1 Hz); ^{13}C NMR δ 22.9, 28.4, 122.3, 123.1, 124.8, 125.9, 126.8, 126.8, 128.4, 128.9, 129.2, 129.4, 132.8, 133.1; HRMS (EI) calcd for $C_{14}H_{12}$ (M^+) 180.0939, found 180.0938.

2-Propylnaphthalene (16): colorless oil (11%); ^{1}H NMR δ 0.96 (t, 3H, J = 7.5 Hz), 1.72 (sextet, 2H, J = 7.5 Hz), 2.73 (t, 2H, J = 7.5 Hz), 7.32 (dd, 1H, J = 7.8, 1.8 Hz), 7.42 (m, 2H), 7.59 (s, 1H), 7.76 (m, 3H); HRMS (EI) calcd for $C_{13}H_{14}$ (M^+) 170.1096, found 170.1107.

Tandem Enediyne-Radical Cyclization of Oxime Ether 7. 1*H*-Benz[*e*]indene/3*H*-benz[*e*]indene (11a,b): colorless oil (50%), 1:1 mixture; ^{1}H NMR δ 3.56 (dd, 1H, J = 0.1, 1.8 Hz), 3.71 (dd, 1H, J = 0.1, 1.8 Hz), 6.65 (dt, 0.5H, J = 5.4, 1.8 Hz), 6.73 (td, 0.5H, J = 5.4, 1.8 Hz), 6.99 (td, 0.5H, J = 5.4, 1.8 Hz), 7.34–8.21 (m, 6.5H); HRMS (EI) calcd for $C_{13}H_{10}$ (M^+) 166.0783, found 166.0799 (1*H*), 166.0787 (3*H*).

***N*-(Benzyloxy)-2,3-dihydro-1*H*-benz[*e*]inden-1-amine (21)**: yellow oil (25%); IR (neat) ν 3248, 3053, 1445 cm^{-1}; ^{1}H NMR δ 2.27–2.48 (m, 2H), 2.95 (ddd, 1H, J = 16.5, 9.0, 2.4 Hz), 3.26 (dt, 1H, J = 16.5, 8.1 Hz), 4.66 (s, 2H), 5.08 (d, 1H, J = 6.6 Hz), 5.63 (s, br, 1H, NH), 7.27–7.48 (m, 8H), 7.74 (d, 1H, J = 8.4 Hz), 7.83 (d, 1H, J = 8.4 Hz), 7.95 (d, 1H, J = 8.4 Hz); ^{13}C NMR δ 30.4, 31.4, 65.2, 76.6, 123.4, 124.1, 124.8, 126.3, 127.8, 128.3, 128.4, 128.6, 129.0, 130.6, 132.8, 135.8, 138.0, 143.1; HRMS (EI) calcd for $C_{20}H_{17}NO$ (M^+ – 2) 287.1310, found 287.1302.

Tandem Enediyne-Radical Cyclization of Oxime Ether 10. 3,4-Dihydrophenanthrene (14): colorless oil (36%); IR (neat) ν 3046, 1618, 1589 cm^{-1}; ^{1}H NMR δ 2.37 (tdd, 2H, J = 8.7, 4.5, 1.8 Hz), 2.92 (t, 2H, J = 8.1 Hz), 6.25 (dt, 1H, J = 9.9, 4.5 Hz), 7.27 (m, 2H), 7.42 (m, 2H), 7.64 (d, 1H, J = 8.1 Hz), 7.77 (d, 1H, J = 8.1 Hz), 8.08 (d, 1H, J = 8.1 Hz); ^{13}C NMR δ 22.9, 28.4, 122.3, 123.1, 124.8, 125.9, 126.8, 126.8, 128.4, 128.9, 129.2, 129.4, 132.8, 133.1; HRMS (EI) calcd for $C_{14}H_{12}$ (M^+) 180.0939, found 180.0938.

***N*-(Benzyloxy)-1,2,3,4-tetrahydrophenanthren-1-amine (22)**: yellow oil (36%); ^{1}H NMR δ 1.68 (tt, 1H, J = 13.8, 3.4 Hz), 1.76–1.85 (m, 1H), 2.05–2.21 (m, 1H), 2.49–2.57 (m, 1H), 2.86–2.91 (m, 2H), 4.80 (AB q, 2H, J = 11.5 Hz), 4.81 (hidden by AB q, 1H), 5.73 (s, br, 1H, NH), 7.16 (d, 1H, J = 8.5 Hz), 7.29–7.48 (m, 7H), 7.64 (d, 1H, J = 8.5 Hz), 7.73 (dd, 1H, J = 8.4, 1.4 Hz), 8.00 (d, 1H, J = 8.0 Hz); ^{13}C NMR δ 16.9, 25.3, 30.2, 54.2, 76.9, 122.5, 124.8, 126.6, 127.9, 128.0, 128.0, 128.4, 128.6, 128.7, 132.4, 132.4, 136.9, 138.2 (one carbon not detected); HRMS (EI) calcd for $C_{21}H_{21}NO$ (M^+) 303.1623, found 303.1617.

***syn*-*N*-(Benzyloxy)naphthalene-2-butanimine (23a)**: yellow oil (5%); IR (neat) ν 3055, 3032, 2928, 1632, 1601 cm^{-1}; ^{1}H NMR δ 1.89 (quintet, 2H, J = 7.8 Hz), 2.44 (td, 2H, J = 7.5, 5.6 Hz), 2.80 (t, 2H, J = 7.6 Hz), 5.10 (s, 2H), 6.72 (t, 1H, J = 5.6 Hz), 7.30 (dd, 1H, J = 8.5, 1.7 Hz), 7.32–7.35 (m, 5H), 7.41–7.45 (m, 2H), 7.60 (s, 1H), 7.74–7.81 (m, 3H); ^{13}C NMR δ 25.4, 27.7, 35.6, 75.7, 125.2, 125.9, 126.5, 127.2, 127.4, 127.6, 127.7, 127.9, 128.0, 128.4, 132.0, 133.6, 138.1, 139.1, 151.9; HRMS (EI) calcd for $C_{21}H_{21}NO$ (M^+) 303.1623, found 303.1611.

***anti*-*N*-(Benzyloxy)naphthalene-2-butanimine (23b)**: yellow oil (7%); IR (neat) ν 3055, 3032, 2928, 1632, 1601 cm^{-1}; ^{1}H NMR δ 1.90 (quintet, 2H, J = 7.5 Hz), 2.22–2.29 (m, 2H), 2.79 (t, 2H, J = 7.5 Hz), 5.07 (s, 2H), 7.30 (dd, 1H, J = 8.5, 1.7 Hz), 7.35–7.38 (m, 5H), 7.41–7.45 (m, 2H), 7.48 (t, 1H, J = 6.1 Hz), 7.58 (s, 1H), 7.75–7.81 (m, 3H); ^{13}C NMR δ 28.1, 29.0, 35.2, 75.5, 125.2, 125.9, 126.6, 127.2, 127.4, 127.6, 127.8, 127.9, 128.2, 128.4, 132.0, 133.6, 137.7, 139.1, 151.0; HRMS (EI) calcd for $C_{21}H_{21}NO$ (M^+) 303.1623, found 303.1614.

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Supplementary Material Available: ^{1}H NMR or ^{13}C NMR spectra of **5–10**, **11a,b**, **12–17**, and **21–23** were taken (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.