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7-*endo* Selective Aryl Radical Cyclization onto Enamides Leading to 3-Benzazepines: Concise Construction of a Cephalotaxine Skeleton

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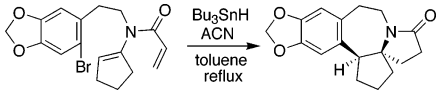
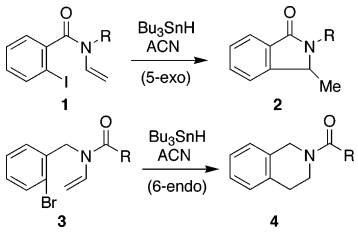


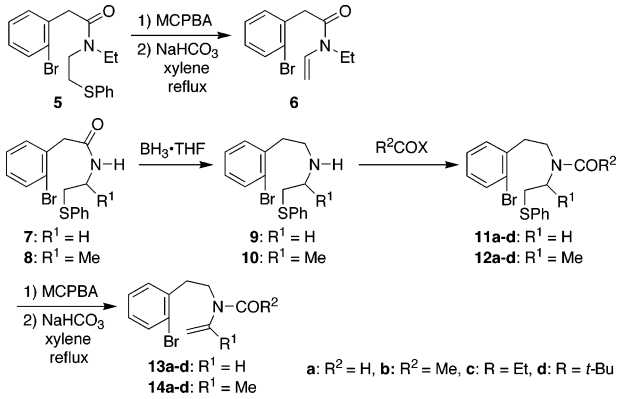
Bu_3SnH-mediated radical cyclizations of 2-(2-bromophenyl)-*N*-ethenylacetamide gave 6-*exo* cyclization product **15** as the major product, whereas *N*-[2-(2-bromophenyl)ethyl]-*N*-ethenylamides gave almost exclusively 7-*endo* cyclization products. These results indicated that the position of the carbonyl group on enamide played an important role in deciding the course of the cyclization. The 7-*endo* selective cyclization was applied to concise construction of a cephalotaxine skeleton.

Bu_3SnH-mediated cyclization of aryl radicals having a 3-butenyl group at the ortho position generally gave 5-*exo* cyclization products.[1,2] This was also the case for enamides **1** that gave 5-*exo* cyclization products, isoindolones **2** (Scheme 1).[3] We recently reported, however, that enamides **3** gave only 6-*endo* cyclization products, tetrahydroisoquinolines **4**.[4a] These results clearly indicated that the position of the carbonyl group played an important role in deciding the course of the cyclization.

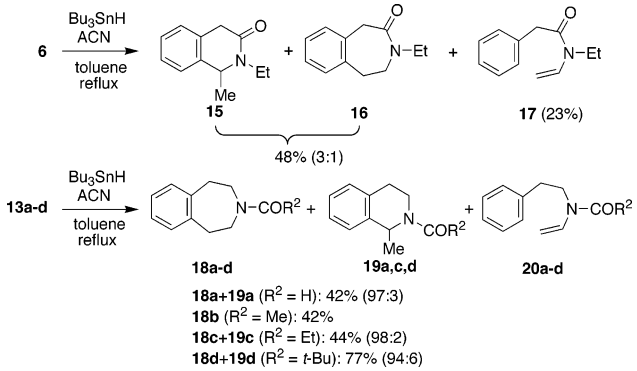
SCHEME 1. Aryl Radical Cyclizations of 1 and 3



SCHEME 2. Preparations of Radical Precursors 6, 13a−d, and 14a−d



SCHEME 3. Radical Cyclizations of 6 and 13a−d



We assumed that the alkenic bond and the carbonyl group of enamides **1** and **3** were opposite each other as depicted in Scheme 1 due to thier steric and electronic repulsion. Radicals generally attack the nearest cabon atoms of the alkenic bonds, and hence enamides **1** give 5-*exo* cyclization products **2** and enamides **3** give 6-*endo* cyclization products **4**.

As a continuation of our studies, we were interested in the modes of cyclization (6-*exo* vs 7-*endo*) of homologous congeners of **1** and **3**, and we found that enamide **6** underwent aryl radical cyclization in a 6-*exo* manner to give the isoquinolinone derivative **15** and that enamides **13** and **14** gave the 7-*endo* cyclization products **18** and **21** (Schemes 3 and 4), respectively. The present paper describes the results of our work in this area, including application of 7-*endo* selective aryl radical cyclization to concise construction of a cephalotaxine skeleton **30**.

The synthesis of enamide **6** was begun by condensation of *o*-bromophenylacetic acid and *N*-ethyl-2-(phenylthio)-

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(1) For radical cyclizations of 2-(3-butenyl)bromobenzene, see: (a) Abeywickrema, A. N.; Beckwith, A. L. J.; Gerba, S. *J. Org. Chem.* **1987**, *52*, 4072. For radical cyclizations of 2-(allyloxy)bromobenzene, see: (b) Chung, S.-K.; Chung, F.-F. *Tetrahedron Lett.* **1979**, 2473. (c) Togo, H.; Kikuchi, O. *Tetrahedron Lett.* **1988**, *29*, 4133. For radical cyclizations of 2-(*N*-acylallylamino)bromobenzene, see: (d) Dittami, J. P.; Ramanathan, H. *Tetrahedron Lett.* **1988**, *29*, 45. (e) Özlü, Y.; Cladingboel, D. E.; Parsons, P. J. *Tetrahedron* **1994**, *50*, 2183. For others, see: (f) Jones, K.; Thompson, M.; Wright, C. *J. Chem. Soc., Chem. Commun.* **1986**, 115. (g) Jones, K.; Storey, J. M. D. *Tetrahedron Lett.* **1993**, *34*, 7797.

(2) A limited example of 6-*endo* selective cyclization has been reported for palladium-mediated reaction of *N*-acryloyl-7-bromoindoline. See: Dankwardt, J. W.; Flippin, L. A. *J. Org. Chem*. **1995**, *60*, 2312.

(3) Ishibashi, H.; Ohata, K.; Niihara, M.; Sato, T.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 547.

(4) (a) Ishibashi, H.; Kato, I.; Takeda, Y.; Kogure, M.; Tamura, O. *Chem. Commun.* **2000**, 1527. For recent reference of radical cyclization onto enamide, see: (b) Okano, T.; Fumoto, M.; Kusukawa, T.; Fujita, M. *Org. Lett.* **2002**, *4*, 1571. See also refs 6c and 7d.

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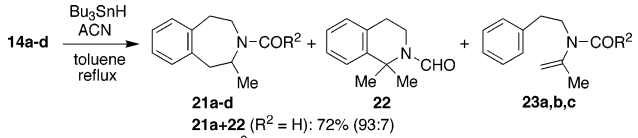
SCHEME 4. Radical Cyclizations of 14a−d



21a+22 (R^2 = H): 72% (93:7)
21b (R^2 = Me): 56%
21c (R^2 = Et): 79%
21d (R^2 = *t*-Bu): 80%

ethylamine, giving amide **5**. Treatment of **5** with *m*-chloroperbenzoic acid (MCPBA) followed by thermolysis of the resulting sulfoxide gave enamide **6** in 76% yield from **5** (Scheme 2). On the other hand, condensation of *o*-bromophenylacetic acid and 2-(phenylthio)ethylamine followed by reduction of the resulting amide **7** with BH_3 gave amine **9**. Acylation of amine **9** gave amides **11**, whose oxidation with MCPBA followed by thermolysis of the resulting sulfoxides afforded enamides **13a**−**d**. Similarly, enamides **14a**−**d** were prepared from *o*-bromophenylacetic acid and 1-methyl-2-(phenylthio)ethylamine.

When a mixture of Bu_3SnH and 1,1′-azobis(cyclohexanecarbonitrile) (ACN) in toluene was added dropwise to a boiling solution of **6** in toluene, a 3:1 mixture of the 6-*exo* cyclization product **15** and the 7-*endo* cyclization product **16** was obtained in 48% combined yield along with the simple reduction product **17** (23% yield) (Scheme 3).

The cyclizations of aryl radicals having a 4-pentenyl group at the ortho position usually gave a mixture of 6-*exo* and 7-*endo* cyclization products.[5] This was also the case for the cyclization of **6**.

On the other hand, Bu_3SnH-mediated cyclization of enamide **13a** gave the 7-*endo* cyclization product **18a** together with a small quantity of the 6-*exo* cyclization product **19a** in a ratio of 97:3 (by ^1H NMR) and in 42% combined yield. Enamide **13b** gave only the 7-*endo* cyclization product **18b** in 42% yield. Similar treatment of enamide **13c** gave a 98:2 (by ^1H NMR) mixture of the 7-*endo* cyclization product **18c** and the 6-*exo* cyclization product **19c** in 44% combined yield. Enamide **13d** gave a 94:6 (by ^1H NMR) mixture of **18d** and **19d** in 77% combined yield.[6,7] These results clearly indicated that the size of the substituent R^2 did not influence the product distribution of **18** and **19**. The reason the use of pivaloyl amide **13d** resulted in the increase in the yield of the products, however, is obscure at the moment.

The methyl-substituted enamide **14a** gave a 93:7 (by ^1H NMR) mixture of the 7-*endo* cyclization product **21a** and the 6-*exo* cyclization product **22** in 72% combined yield along with the reduction product **23a** (8%) (Scheme 4). Similar treatment of enamides **14b**−**d** gave only the 7-*endo* cyclization products **21b**−**d** in 56%, 79% and 80% yields, respectively. No 6-*exo* cyclization product was detected in the crude reaction mixtures of **14b**−**d**.

The high regioselectivity and the high yield of the 7-*endo* cyclization products **21a**−**d** may be due to the formation of the highly stabilized radical intermediate **27**.

One possible explanation for the formation of **27** from **14a**−**d** may be a consecutive 6-*exo* cyclization of aryl radicals **24** and a neophyl rearrangement of the resulting radicals **25**, through the radical intermediates **26** (Figure 1). This possibility, however, was ruled out by results of the following work to simultaneously examine the effects of various Bu_3SnH concentrations, addition times and reaction temperatures.[8] For example, treatment of **14b** (R^2 = Me) with 1.6 equiv of Bu_3SnH (not using the slow addition technique) in the presence of V-70 [2,2′-azobis-(2,4-dimethyl-4-methoxyvaleronitrile)] in toluene at room temperature for 10 h gave compound **21b** as a sole cyclization product (see Experimental Section).

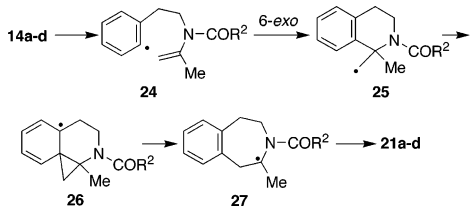


FIGURE 1. Excluded pathway to the radical intermediate **27**.

As described above, we found that the *exo* mode of cyclization could be shifted to the *endo* mode by a positional change of the carbonyl group of amides in the cyclizations of aryl radicals having a 4-pentenyl group at the ortho position.

We therefore next examined synthesis of a cephalotaxine skeleton using a radical cascade involving a 5-*endo-trig* cyclization of α-acylamino radicals such as **27**.[9]

Cephalotaxine (**31**)[10] is the predominant alkaloid of *Cephalotaxus* species and has attracted much attention from synthetic chemists due to its unique structral features as well as the antileukemic activity of its ester derivatives, harringtonine and homoharringtonine.[11]

(5) (a) Ishibashi, H.; Kobayashi, T.; Nakashima, S.; Tamura, O. *J. Org. Chem.* **2000**, *65*, 9022. (b) Yamauchi, T.; Sugiyama, J.; Higashiyama, K. *Heterocycles* **2002**, *58*, 431.

(6) For recent references on the synthesis of benzazepines, see: (a) Gerritz, S. W.; Smith, J. S.; Nanthakumar, S. S.; Uehling, D. E.; Cobb, J. E. *Org. Lett.* **2000**, *2*, 4099. (b) Martins, J. C.; Van Rampaey, K.; Wittmann, G.; Tömböly, C.; Tóth, G.; De Kimpe, N.; Tourwé, D. *J. Org. Chem.* **2002**, *66*, 2884. (c) Fuchs, J. R.; Funk, R. L. *Org. Lett.* **2001**, *3*, 3923. (d) Poschalko, A.; Welzig, S.; Treu, M.; Nerdinger, S.; Mereiter, K.; Jordis, U. *Tetrahedron* **2002**, *58*, 1513. (e) Van Rampaey, K.; Van den Eynde, I.; De Kimpe, N.; Tourwé, D. *Tetrahedron* **2003**, *59*, 4421.

(7) For a review on the synthesis of seven-membered ring compounds using radical cyclizations, see: (a) Yet, L. *Tetrahedron* **1999**, *55*, 9349. For recent references on the synthesis of benzazepines using radical cyclizations, see: (b) Gibson, S. E.; Guillo. N.; Tozer, M. J. *Chem. Commun.* **1997**, 637. (c) Kamimura, A.; Taguchi, Y.; Omata, Y.; Hagihara, M. *J. Org. Chem.* **2003**, *68*, 4996. (d) Cordes, M.; Franke, D. *Synlett* **2004**, 1917.

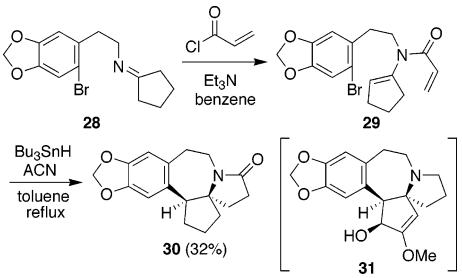
(8) Careful examinations on the effects of varying Bu_3SnH concentration, Bu_3SnH addition time, and reaction temperature have frequently shown that 6-*endo* cyclization products are formed by an initial 5-*exo* cyclization followed by neophyl rearrangement. See: (a) Parker, K. A.; Spero, D. M.; Inman, K. C. *Tetrahedron Lett.* **1986**, *27*, 2833. (b) Abeywickrema, A. N.; Beckwith, A. L. J.; S. Gerba, S. *J. Org. Chem.* **1987**, *52*, 4072. (c) Jones, K.; Brunton, S. A.; Gosain, R. *Tetrahedron Lett.* **1999**, *40*, 8935. See also refs 2, 3, and 5a.

(9) Ishibashi, H.; Ishita, A.; Tamura, O. *Tetrahedron Lett.* **2002**, *43*, 473.

(10) For the synthesis of cephalotaxine, see: Planas, L.; Pérard-Viret, J.; Royer, J. *J. Org. Chem.* **2004**, *69*, 3087 and references therein.

(11) For reviews, see: (a) Smith, C. R., Jr.; Mikolajczak, K. l.; Powell, R. G. *Anticancer Agents Based on Natural Product Models*; Cassady, J. M., Douros, J. D., Eds.; Academic Press: New York, 1980; Chapter 11. (b) Huang, L.; Xue, Z. *The Alkaloids-Chemistry and Pharmacology*; Brossi, A., Ed.; Academic Press: New York, 1984; Vol. 23, Chaper 3. (c) Hudlicky, T.; Kwart, L. D.; Reed, J. W. *Alkaloids, Chemical and Biological Perspectives*; Pelletire, S. W. J., Ed.; Wiley: New York, 1987; Vol. 5, Chapter 5.

SCHEME 5. Radial Cascade Leading to Cephalotaxine Skeleton 30



The requisite enamide **29** was readily prepared by condensation of *o*-bromophenylethylamine and cyclopentanone followed by acylation of the resulting imine **28** with acryloyl chloride (Scheme 5).

Treatment of **29** with Bu_3SnH in the presence of ACN in boiling toluene gave the expected radical cascade product **30** in 32% yield. The structure of **30** was confirmed by an X-ray crystallographic analysis, and its stereochemistry was found to be identical to that of the natural cephalotaxine (**31**).

In conclusion, *exo* cyclization of aryl radicals having a 4-pentenyl group at the ortho position can be shifted to the *endo* mode by a positional change of the carbonyl group of enamides.

Experimental Section

2-(2-Bromophenyl)-*N*-ethyl-*N*-(2-phenylthioethyl)acetamide (5). To a solution of (2-bromophenyl)acetic acid (3.65 g, 17.0 mmol) in CH_2Cl_2 (100 mL) was added *N*-ethyl-2-(phenylthio)ethylamine[12] (3.26 g, 14.2 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) (3.23 g, 16.8 mmol) at room temperature, and the mixture was stirred for 2 h. The reaction mixture was diluted with water and the whole was extracted with $CHCl_3$. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel ($CHCl_3$/MeOH, 100:1) to give **5** (5.72 g, 89%) as a yellow oil: IR ($CHCl_3$) ν 1640 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.11 (33/100 × 3 H, t, J = 7.1 Hz), 1.15 (67/100 × 3 H, t, J = 7.1 Hz), 3.06 (33/100 × 2 H, t, J = 7.4 Hz), 3.17 (67/100 × 2 H, t, J = 7.4 Hz) 3.38 (2 H, q, J = 7.1 Hz), 3.56 (2 H, t, J = 7.4 Hz), 3.71 (33/100 × 2 H, s), 3.77 (67/100 × 2 H, s), 7.09−7.54 (9 H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 12.9, 14.2, 30.5, 32.6, 40.6, 41.0, 44.0, 46.3, 47.4, 124.7, 125.9, 127.0, 127.5, 127.6, 128.5, 128.6, 128.7, 129.0, 129.2, 130.2, 130.8, 131.0, 132.6, 134.6, 135.2, 135.7, 169.3, 169.7. ^1H and ^{13}C NMR spectra of **5** showed it to be a mixture of rotamers. Anal. Calcd for $C_{18}H_{20}BrNOS$: C, 57.14; H, 5.33; N, 3.70. Found: C, 56.85; H, 5.29; N, 3.67.

2-(2-Bromophenyl)-*N*-ethenyl-*N*-ethylacetamide (6). To a solution of **5** (2.00 g, 5.29 mmol) in CH_2Cl_2 (100 mL) was added dropwise a solution of MCPBA (1.20 g, 5.55 mmol) in CH_2Cl_2 (100 mL) at 0 °C over 30 min. To the mixture was added 10% aqueous solution of $Na_2S_2O_3$, and the mixture was stirred at the same temperature for 10 min. The mixture was washed brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/AcOEt, 1:4 → 1:8 → AcOEt) to give 2-(2-bromophenyl)-*N*-ethyl-*N*-(2-phenylsulfinylethyl)acetamide (2.02 g, 97%) as an oil. A mixture of this sulfoxide (1.00 g, 2.54 mmol) and $NaHCO_3$ (1.07 g, 12.7 mmol) in xylene (200 mL) was heated at reflux for 14 h. The mixture was diluted with water and extracted with AcOEt. The organic phase was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/AcOEt, 15:1 → 2:1) to give **6** (530 mg 78%) as yellow crystals: mp 59−60 °C (hexane); IR ($CHCl_3$) ν 1670, 1620 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.16 (4/5 × 3 H, t, J = 7.1 Hz), 1.24 (1/5 × 3 H, t, J = 7.1 Hz), 3.64 (1/5 × 2 H, q, J = 7.1 Hz), 3.75 (4/5 × 2 H, q, J = 7.1 Hz) 3.93 (2 H, s), 4.37 (1 H, d, J = 9.0 Hz), 4.54 (1 H, d, J = 15.2 Hz), 6.79 (4/5 H, dd, J = 15.2, 9.0 Hz), 7.10−7.28 (3 H, m), 7.44 (1/5 H, dd, J = 15.2, 9.0 Hz), 7.58 (1 H, d, J = 7.9 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 11.8, 12.8, 37.1, 39.0, 41.1, 93.7, 94.2, 124.7, 127.6, 128.6, 130.7, 131.0, 132.3, 132.7, 134.7, 168.3. ^1H and ^{13}C NMR spectra of **6** showed it to be a mixture of rotamers. HRMS calcd for $C_{12}H_{14}{}^{79}BrNO$ 267.0259, found 267.0251.

***N*-[2-(2-Bromophenyl)ethyl]-*N*-(2-phenylthioethyl)-formamide (11a).** To a stirred solution of formic acid (581 mg, 12.6 mmol) in CH_2Cl_2 (20 mL) was added EDC (1.82 g, 9.47 mmol) at 0 °C, and the mixture was stirred at the same temperature for 15 min. To the mixture was added a solution of **9** (1.06 g, 3.16 mmol) and *N*-methylmorpholine (639 mg, 6.31 mmol) in CH_2Cl_2 (20 mL), and the mixture was stirred at the same temperature for 1 h. Compound **9** was not consumed, and therefore EDC (605 mg, 3.16 mmol) was added to the mixture, and the mixture was stirred for 1 h. The reaction mixture was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/AcOEt, 6:1 → 5:1 → 4:1) to give **11a** (1.05 g, 91%) as a colorless oil: IR ($CHCl_3$) ν 1670 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.88−3.02 [(2 + 1/2) x H, m], 3.13 (1/2 × 2 H, dd, J = 7.4, 5.9 Hz), 3.31 (1/2 × 2 H, t, J = 7.4 Hz), 3.45−3.57 [(2 H + 1/2) x H, m], 7.05−7.55 (9 H, m), 7.89 (1/2 H, s), 8.01 (1/2 H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 30.8, 33.1, 34.0, 36.2, 42.7, 42.9, 47.1, 48.0, 124.3, 126.3, 127.0, 127.7, 127.8, 128.4, 128.7, 129.1, 129.2, 129.3, 130.3, 131.0, 131.2, 132.8, 133.1, 134.3, 135.2, 136.8, 137.8, 162.8, 163.0. ^1H and ^{13}C NMR spectra of **11a** showed it to be a mixture of rotamers. Anal. Calcd for $C_{17}H_{18}BrNOS$: C, 56.05; H, 4.98; N, 3.84. Found: C, 56.11; H, 5.11; N, 3.84.

***N*-[2-(2-Bromophenyl)ethyl]-*N*-ethenylformamide (13a).** Using a procedure similar to that for the preparation of **6**, compound **11a** (858 mg, 2.36 mmol) was treated with MCPBA (533 mg, 2.47 mmol) in CH_2Cl_2 (160 mL) to give *N*-[2-(2-bromophenyl)ethyl]-*N*-(2-phenylsulfinylethyl)formamide as an oil. A mixture of this sulfoxide (660 mg, 1.74 mmol) and $NaHCO_3$ (729 mg, 8.68 mmol) in xylene (150 mL) was heated at reflux for 14 h. After workup, the crude material was purified by chromatography on silica gel (hexane/AcOEt, 7:1 → 6:1) to give **13a** (359 mg, 81%) as a colorless oil: IR ($CHCl_3$) ν 1690, 1635 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 3.01 (3/4 × 2 H, t, J = 7.8 Hz), 3.08 (1/4 × 2 H, t, J = 7.1 Hz), 3.74 (1/4 × 2 H, t, J = 7.1 Hz), 3.81 (3/4 × 2 H, t, J = 7.8 Hz) 4.45 (3/4 H, dd, J = 9.2, 1.7 Hz), 4.63 (1/4 H, d, J = 9.2 Hz), 4.79 (3/4 H, dd J = 15.5, 1.7 Hz), 4.80 (1/4 H, d, J = 16.5 Hz), 6.57 (3/4 H, dd, J = 15.5, 9.2 Hz), 7.07−7.30 [(1/4 + 3) H, m], 7.53−7.59 (1 H, m), 7.82 (1/4 H, s), 8.31 (3/4 H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 33.0, 34.2, 40.2, 44.8, 94.1, 95.4, 124.4, 127.7, 127.8, 128.4, 128.6, 128.8, 131.2, 131.3, 132.8, 133.0, 133.1, 137.1, 137.8, 161.1, 162.4. ^1H and ^{13}C NMR spectra of **13a** showed it to be a mixture of rotamers. Anal. Calcd for $C_{11}H_{12}BrNO$: C, 51.99; H, 4.76; N, 5.51. Found: C, 52.07; H, 4.81; N, 5.43.

2-Ethyl-1,2,3,4-tetrahydro-1-methylisoquinolin-2-one (15), 3-Ethyl-2,3,4,5-tetrahydro-1*H*-3-benzazepin-2-one (16), and *N*-Ethenyl-*N*-ethyl-2-phenylacetamide (17). General Procedure for Radical Cyclization. To a boiling solution of **6** (250 mg, 0.932 mmol) in toluene (50 mL) was added dropwise a solution of Bu_3SnH (407 mg, 1.40 mmol) and ACN (45.6 mg, 0.187 mmol) in toluene (50 mL) over 1.5 h, and the mixture was further heated at reflux for 1 h. The solvent was evaporated off, Et_2O (50 mL) and an 8% aqueous KF solution (50 mL) were added to the residue, and mixture was vigorously stirred at room temperature overnight. The organic phase was separated, and the aqueous phase was further extracted with Et_2O. The combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane → hexane/AcOEt, 10:1 → 5:1 → 3:1). The first fraction gave **17** (40.6 mg, 23%) as a colorless oil: IR ($CHCl_3$) ν 1665, 1620 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.13 (3 H, t, J = 7.1 Hz), 3.60−3.76 (total 2 H, q, J = 7.1 Hz), 3.83 (2 H, s), 4.30 (1 H, d, J = 9.2 Hz), 4.48 (1 H, d, J = 15.5 Hz), 6.80 (1 H, dd, J

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= 15.5, 9.2 Hz), 7.15−7.49 (5 H, m); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 11.7, 36.9, 41.1, 93.9, 126.9, 128.7, 132.6, 169.3. HRMS calcd for $C_{12}H_{15}NO$ 189.1154, found 189.1152. The second fraction gave a mixture of **15** and **16** (84.6 mg, 48%) in a ratio of ca. 3:1: IR ($CHCl_3$) ν 1640 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 0.85 (1/4 × 3 H, t, J = 7.1 Hz, for **16**), 0.92 (3/4 × 3 H, d, J = 6.8 Hz, for **15**), 0.96 (3/4 × 3 H, t, J = 7.3 Hz, for **15**), 2.48 (1/4 × 2 H, t, J = 5.9 Hz, for **16**) 2.75 (3/4 H, dq, J = 13.8, 6.9 Hz, for **15**), 2.86 (1/4 × 2 H, t, J = 9.2 Hz, for **16**), 3.20 (1/4 × 2 H, q J = 7.1 Hz, for **16**), 3.37 (3/4 H, d, J = 19.0 Hz, for **15**); 3.52 (3/4 H, d, J = 19.0 Hz, for **15**), 3.66 (1/4 × 2 H, s, for **16**), 3.84 (3/4 H, dq, J = 13.9, 7.0 Hz, for **15**), 3.90 (3/4 H, q, J = 6.7 Hz, for **15**), 6.71−7.32 (3/4 × 4 H + 1/4 × 4 H, m, for **15** and **16**). HRMS calcd for $C_{12}H_{15}NO$ 189.1154, found 189.1155. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.75; H, 7.96; N, 7.36.

3-Formyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine (18a),2-Formyl-1,2,3,4-tetrahydro-1-methylisoquinoline (19a), and *N*-Ethenyl-*N*-(2-phenylethyl)formamide (20a). Following the general procedure, a boiling solution of **13a** (100 mg, 0.394 mmol) in toluene (20 mL) was treated with Bu_3SnH (172 mg, 0.590 mmol) and ACN (19.2 mg, 0.0787 mmol) in toluene (20 mL). After workup, the crude material was chromatographed on silica gel (hexane/AcOEt, 6:1 → 2:1 → 3:2). The first fraction gave **20a** (11.1 mg, 16%) as a colorless oil: IR ($CHCl_3$) ν 1690, 1635 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.86 (3/4 × 2 H, t, J = 7.6 Hz), 2.92 (1/4 × 2 H, t, J = 6.9 Hz), 3.69 (1/4 × 2 H, t, J = 6.9 Hz), 3.79 (3/4 × 2 H, t, J = 7.6 Hz) 4.47 (1 H, dd, J = 9.2, 1.5 Hz), 4.64 (3/4 H, dd, J = 16.2, 1.5 Hz), 4.67 (1/4 H, dd J = 16.2, 1.5 Hz), 6.57 (3/4 H, dd, J = 16.2, 9.2 Hz), 7.12−7.37 [(1/4 + 5 H), m], 7.74 (1/4 H, s), 8.29 (3/4 H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 32.5, 33.6, 41.8, 47.0, 93.8, 95.3, 126.6, 127.0, 128.6, 161.1, 162.3. ^{1}H and ^{13}C NMR spectra of **20a** showd it to be a mixture of rotamers. HRMS calcd for $C_{11}H_{13}NO$ 175.0997, found 175.0991. The second fraction gave a mixture of **18a** and **19a** (29.0 mg, 42%) in a ratio of 97:3: IR ($CHCl_3$) ν 1670, 1660 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 0.94 (3/100 × 3 H, d, J = 6.8 Hz, for **19a**), 1.97 (97/100 × 2 H, t, J = 5.1 Hz, for **18a**), 2.13 (97/100 × 2 H, t, J = 5.1 Hz, for **18a**), 2.33 (97/100 × 2 H, t, J = 5.0 Hz, for **18a**), 3.14 (97/100 × 2 H, t, J = 5.0 Hz, for **18a**), 4.11 (3/100 H, dd, J = 13.2, 6.5 Hz, for **19a**), 5.24 (3/100 H, q, J = 6.8 Hz, for **19a**), 6.43−6.60 (97/100 × 2 H + 3/100 × 2 H, m, for **18a** and **19a**), 6.65−6.70 (97/100 × 2 H + 3/100 × 2 H, m, for **18a** and **19a**), 7.52 (97/100 H, s, for **18a**), 7.72 (3/100 H, s, for **19a**); ^{13}C NMR (125 MHz, C_6D_6 for **18a**) δ 37.7, 39.1, 42.6, 48.5, 127.0, 127.3, 130.0, 130.2, 140.8, 141.7, 161.5. HRMS calcd for $C_{11}H_{13}NO$ 175.0997, found 175.0996.

3-Formyl-2,3,4,5-tetrahydro-2-methyl-1*H*-3-benzazepine (21a), 2-Formyl-1,2,3,4-tetrahydro-1,1-dimethylisoquinoline (22), and *N*-(1-Methylethenyl)-*N*-(2-phenylethyl)-formamide (23a). Following the general procedure, a boiling solution of **14a** (100 mg, 0.373 mmol) in toluene (20 mL) was treated with Bu_3SnH (163 mg, 0.559 mmol) and ACN (18.2 mg, 0.0746 mmol) in toluene (20 mL). After workup, the crude material was chromatographed on silica gel (hexane/AcOEt, 6:1 → 3:2). The first fraction gave **23a** (5.5 mg, 8%) as a colorless oil: IR ($CHCl_3$) ν 1670, 1645, 1630 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.99 (3 H, s), 2.83 (2 H, t like, J = 7.9 Hz), 3.79 (2 H, t like, J = 7.9 Hz), 4.61 (1 H, s), 4.62 (1 H, s), 7.19−7.32 (5 H, m), 8.42 (1 H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 20.1, 33.6, 43.1, 102.8, 126.5, 128.5, 128.8, 138.5, 141.4, 160.8. HRMS calcd for $C_{12}H_{15}NO$ 189.1154, found 189.1153. The second fraction gave a mixture of **21a** and **22** (50.8 mg, 72%) in a ratio of 93:7: IR ($CHCl_3$) ν 1660 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.93 (93/200 × 3 H, d, J = 6.9, for **21a**), 1.04 (93/200 × 3 H, d, J = 6.9 Hz, for **21a**), 1.75 (7/100 × 6 H, s, for **22**), 2.72−3.00 (93/100 × 3 H + 93/200 H, m, for **21a**), 3.11−3.21 (93/100 H, m, for **21a**), 3.25−3.35 (93/200 H, m, for **21a**), 3.54−3.62 (93/200 H, m, for **21a**), 3.84 (7/100 × 2 H, t, J = 5.8 Hz, for **22**), 3.97−4.03 (93/200 H, m, for **21a**), 4.50−4.57 (93/200 H, m, for **21a**), 5.00−5.06 (93/200 H, m, for **21a**), 7.06−7.24 (93/100 × 4 H + 7/200 × 4 H, m, for **21a** and **22**), 8.08 (93/200 H, s, for **21a**), 8.17 (93/200 H, s, for **21a**), 8.63 (7/100 H, s, for **22**); ^{13}C NMR for **21a** (67.8 MHz, $CDCl_3$) δ 15.5, 17.1, 36.9, 37.9, 41.6, 43.1, 44.2, 52.2, 126.7, 126.9, 127.1, 129.2, 129.4, 130.6, 130.8, 136.7, 137.5, 139.5, 140.4, 161.7, 161.9. ^{1}H and ^{13}C NMR spectra of **21a** showed it to be a mixture of rotamers. HRMS calcd for $C_{12}H_{15}NO$ 189.1154, found 189.1152.

Radical Cyclization of 14b at Room Temperature. To a solution of **14b** (91 mg, 0.323 mmol) and V-70 (50.0 mg, 0.161 mmol) in toluene (20 mL) was added Bu_3SnH (155 mg, 0.532 mmol) at room temperature, and the mixture was stirred at the same temperature for 10 h. After workup, the crude material was chromatographed on silica gel (hexane/AcOEt, 4:1 → 3:1). The first fraction gave a mixture of **14b** and **23b** (31.1 mg) as a colorless oil. The second fraction gave **21b** (8.6 mg, 13%) as a colorless oil.

***N*-[2-(6-Bromobenzo[1,3]dioxol-5-yl)ethyl]-*N*-(cyclopent-1-enyl)acrylamide (29).** A mixture of 2-(6-bromo-1,3-benzodioxol-5-yl)ethylamine (491 mg, 2.01 mmol) and cyclopentanone (200 mg, 2.38 mmol) in benzene (10 mL) was heated under reflux with azeotropic removal of water for 2 h. After cooling, Et_3N (407 mg, 4.02 mmol) and acryloyl chloride (267 mg, 2.95 mmol) were added to the reaction mixture, and the mixture was stirred at room temperature for 20 min. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel (hexane/AcOEt, 5:1) to give **29** (467 mg, 64%) as colorless crystals, mp 96.5−97.5 °C (hexane); IR ($CHCl_3$) ν 1645 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.98 (2 H, quint., J = 7.6 Hz), 2.37−2.42 (4 H, m), 2.90−2.95 (2 H, m), 3.62−3.68 (2 H, m), 5.43 (1 H, s), 5.60 (1 H, dd, J = 9.9, 2.3 Hz), 5.95 (2 H, s), 6.36 (1 H, dd, J = 16.8, 2.3 Hz), 6.51 (1 H, dd, J = 16.8, 9.9 Hz), 6.78 (1 H, s), 6.97 (1 H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 22.4, 30.4, 32.8, 34.4, 45.9, 101.6, 110.7, 112.6, 114.4, 126.9, 129.0, 131.3, 142.2, 147.0, 147.4, 165.5. Anal. Calcd for $C_{17}H_{18}BrNO_3$: C, 56.06; H, 4.98; N, 3.85. Found: C, 56.28; H, 5.00; N, 3.79.

(3a*R,14b*S**)-1,2,3,8,9,14b-Hexahydro-4*H*-cyclopenta[*a*]-[1,3]dioxolo[4,5-*h*]pyrrolo[2,1-*b*][3]benzazepin-6(5*H*)-one (30).** Following the general procedure, a boiling solution of **29** (200 mg, 0.549 mmol) in toluene (50 mL) was treated with Bu_3SnH (238 mg, 0.818 mmol) and ACN (13.4 mg, 0.0548 mmol) in toluene (50 mL). The solvent was evaporated off and the residue was taken up in CH_3CN. This mixture was washed with hexane and concentrated. The residue was chromatographed on silica gel (hexane/AcOEt, 1:2) to give **30** (50.2 mg, 32%) as colorless crystals. A sample was recrystallized from hexane/AcOEt for X-ray crystallographic analysis (see Supporting Information): mp 176−179 °C; IR ($CHCl_3$) ν 1670 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.50−2.29 (10 H, m), 2.55−2.66 (1 H, m), 2.98 (1 H, dd, J = 10.9, 8.6 Hz), 3.07−3.24 (2 H, m), 3.96−4.09 (1 H, m), 5.89 (1 H, d, J = 1.7 Hz), 5.90 (1 H, d, J = 1.7 Hz), 6.59 (1 H, s), 6.62 (1 H, s); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 24.0, 29.7, 30.2, 33.7, 35.4, 38.5, 38.6, 57.8, 69.6, 100.9, 110.7, 111.0, 129.8, 133.0, 146.2, 146.5, 175.5. Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.37; H, 6.62; N, 4.89. Several byproducts were also formed, but their structures were unknown at the moment.

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Supporting Information Available: Experimental procedure for **7**, **8**, **9**, **10**, **11b−d**, **12a−d**, **13b−d**, **14a−d**, **18b−d**, **19c,d**, **20b−d**, **21b−d**, and **23b,c**; ^{1}H and ^{13}C NMR spectra for **6**, **9**, **11c,d**, **13c,d**, **14b**, **17**, **18a,b**, **18d**, **19a**, **19d**, **20a−d**, **21a−d**, **22**, and **23a−c** (^{1}H NMR spectrum only for **23b**); and X-ray crystallographic data for **30** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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