A Study of Aryl Radical Cyclization in Enaminone Esters†

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Aryl radical cyclization in *N*-phenyl, *N*-benzyl, and *N*-phenethyl enaminone esters **1a**−**f** was studied. *N*-Benzyl and *N*-phenethyl enaminones afforded 5-exo and 6-exo cyclization products, respectively, but radical cyclization did not occur in *N*-phenyl enaminones. The rate constants for the 5-exo and 6-exo cyclization processes in secondary enaminones were estimated as being on the order of 10^7 s^{-1} at 353 K; since DNMR experiments showed the rate constant for rotation around the enaminone C3−N bond to be on the order of 10^4 s^{-1} at this temperature, the initial enaminone configuration is maintained throughout the cyclization process. PM3 calculations suggested that the nonoccurrence of endo and 4-exo cyclizations is due to the corresponding transition structures involving significant distortion of the conjugated enaminone system.

Introduction

Radical cyclizations of highly reactive aryl radicals onto double and triple bonds have proven to be very useful for construction of both carbocycles and heterocycles,[1] aza heterocycles in particular.[1c] Aza heterocycles of various sizes have been obtained by radical addition to *N*-vinyl amides (enamides).[2,3] The use of other compounds containing the *N*-vinyl unit such as enamines,[4] *N*-sulfonylenamines,[5] and enaminones[6,7] has been less frequent.

Electronically, enaminone esters can be described as push−pull systems with extensive charge donation from the nitrogen to the carbonyl group. Their structure is accordingly best represented as a resonance hybrid of the neutral and zwitterionic forms depicted in Figure 1. Due to this extended conjugation, their reactivities are very different from those of simple enamides or enamines.[8] To investigate whether these differences might make them of interest as radical acceptors, we explored the synthetic potential and mechanistic features of intramolecular aryl radical cyclization onto enaminone esters.

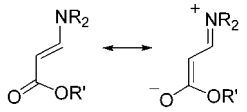
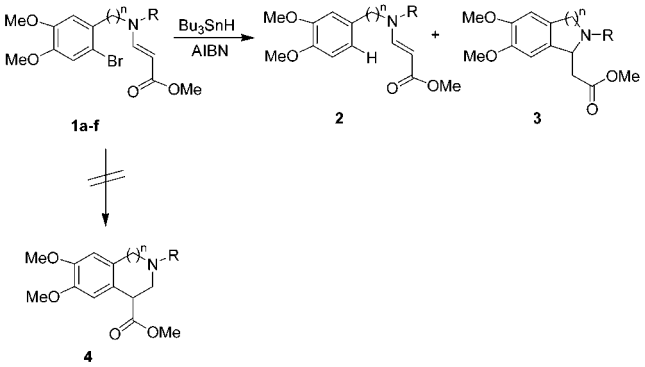


Figure 1.

Scheme 1



Results and Discussion

As part of our study, we chose the enaminone esters **1a**−**f** (Scheme 1, Table 1), which were prepared by condensation of the appropriate amine with methyl propiolate. The *N*-benzyl and *N*-phenethyl compounds **1c**−**f** were easily obtained in very good yields at room temperature,[9] but high temperatures and acetic acid

† Dedicated to Prof. Michael P. Cava on the occasion of his 75th birthday.

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(2) For some recent examples of the use of enamides as radicalofiles, see the following papers and references therein: (a) D'Annibale, A.; Nanni, D.; Trogolo, C.; Umani, F. *Org. Lett.* **2000**, *2*, 401−402. (b) Davies, D. T.; Kapur, N.; Parsons, A. F. *Tetrahedron Lett.* **1999**, *40*, 8615−8618. (c) Clark, A. J.; Dell, C. P.; Ellard, J. M.; Hunt, N. A.; McDonagh, J. P. *Tetrahedron Lett.* **1999**, *40*, 8619−8623. (d) Baker, S. R.; Burton, K. I.; Parsons, A. F.; Pons, J. F.; Wilson, M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 427−436. (e) Ishibashi, H.; Inomata, M.; Ohba, M.; Ikeda, M. *Tetrahedron Lett.* **1999**, *40*, 1149−1152. (f) Ishibashi, H.; Oata, K.; Niihara, M.; Sato, T.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **2000**, 547−553. (g) Ishibashi, H.; Kato, I.; Takeda, Y.; Kogure, M.; Tamura, O. *Chem. Commun.* **2000**, 1527−1528.

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Scheme 2

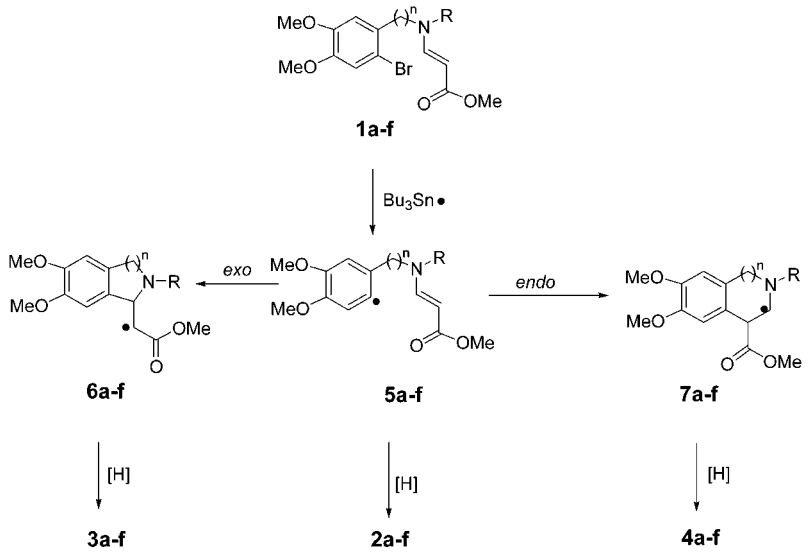

Table 1. Product Yields upon Cyclization of Enaminone Esters 1[a]

enaminone **1**	*n*	R	**2** (%)	**3** (%)
a	0	H	43	
b	0	Me	55	
c	1	H		71
d	1	Me	12	56
e	2	H	49	42[b]
				82
f	2	Me	19	51

[a] Reaction conditions: syringe pump addition, over 3 h, of a solution of 2 equiv of Bu_3SnH and AIBN (20% w/w) in benzene to a refluxing 0.01 M solution of enaminone **1** in the same solvent. [b] Refluxing of a 0.01 M solution of enaminone **1** in benzene containing 1.1 equiv of Bu_3SnH and AIBN (20% w/w).

catalysis[10] were required in order to obtain the *N*-phenyl derivatives **1a** and **1b** in even moderate yields.

Formation of the aryl radicals of compounds **1a**−**f** (radicals **5**) could in principle be followed by several reaction pathways (Scheme 2). Direct reduction of **5** by tributyltin hydride leads to the reduced products **2** (the *N*-methyl compounds **2d** and **2f** could also be formed via a stabilized α-amino radical produced by a [1−5] or [1−6] hydrogen shift, [11] followed by Bu_3SnH reduction). The other reaction paths are exo and endo cyclizations onto the enaminone double bond, furnishing radicals **6** and **7**, respectively, followed by reduction to compounds **3** and **4**.

Radical Cyclization: Experimental Results. When the enaminone esters **1a**−**f** were subjected to standard conditions for aryl radical formation (Bu_3SnH/AIBN), the only reaction products isolated were those formed by reduction of the aryl radical by tin hydride, **2**, and for **1c**−**f**, the corresponding exo cyclization products **3** (Scheme 1). The latter were distinguished from the alternative endo products **4**, by mass spectrometry and 2D NMR spectroscopy (HMBC).[12] The mass spectra of all the cyclized compounds showed the loss of a $\cdot CH_2CO_2Me$ fragment, and all the HMBC spectra showed a three-bond correlation between the methine proton and the methylene carbon α to the nitrogen (the lowest-field methylene in the ^{13}C spectrum); the HMBC spectra of the *N*-methyl compounds also showed a three-bond correlation between the *N*-methyl carbon and the methine proton.

The phenethyl compounds **1e** and **1f** furnished the isoquinolines **3e** and **3f** in moderate to good yields (Table 1). Since not using slow addition techniques for addition of the tin hydride/AIBN solution halved the yield of the first reaction examined, **1e** → **3e** (Table 1), syringe pump addition was used for all the other experiments. The yields of the isoindoles **3c** and **3d** were comparable to those of the isoquinolines **3e** and **3f**, and the phenyl compounds **1a** and **1b** completely failed to furnish any cyclized product. The *N*-methyl compounds **1d** and **1f** furnished lower yields of the cyclization products than the secondary enaminones **1c** and **1e**, accompanied by higher amounts of reduced products (**2d** and **2f**, respectively) that are associated with [1−5] or [1−6] hydrogen shifts.

NMR Experiments to Determine Rates and Conformations. We surmised that the outcome of the intramolecular reaction was probably influenced by the rigidity imparted on enaminone esters by their large conjugated systems. The enaminones are known to exist in several conformations;[13] in the case under study, the most relevant conformations are those obtained by the rotation around the C3−N bond and the cis and trans isomerization of the double bond (Figure 2). Taking this into account, if compounds **1** existed largely in a conformation favoring the exo reaction, and if the entire cyclization reaction was faster than any relevant process of conformational change, then no endo reaction would take place. Note that the s-(*E*) conformation of the C3−N bond leads to a geometry that certainly favors the exo reaction, while for the s-(*Z*) conformation, both endo and exo processes might be possible. Furthermore, rotation around the C3−N bond seemed likely to be slower than

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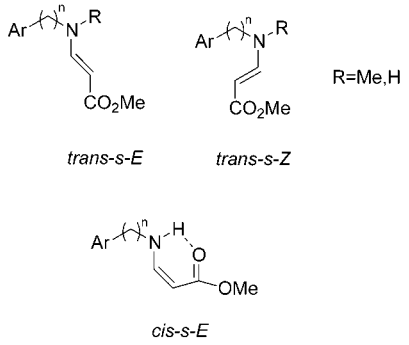
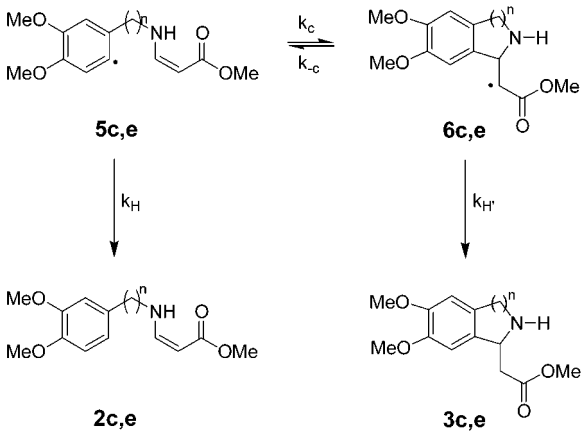


Figure 2. Principal conformers on secondary and tertiary enaminone esters.

Scheme 3



cyclization because rotation around the amide bond is known to be slower than aryl radical cyclization of amides.[14]

To support this interpretation of our synthetic results, we carried out NMR experiments to determine the predominant conformations of **1a**−**f** in benzene and estimate the orders of the rate constants for cyclization and for rotation around the C3−N bond.

Rates of Cyclization. The rates of the 5-exo and 6-exo cyclization processes, relative to that of direct abstraction of hydrogen from tributyltin hydride by the aryl radicals, were determined by performing experiments with **1c** and **1e** at different Bu_3SnH concentrations. On the basis of the mechanism shown in Scheme 3, the steady-state approximation leads to eq 1,[15] which gives the ratio [**2**]/[**3**] as a linear function of the initial tributyltin hydride concentration, $[Bu_3SnH]_0$. The slope of the line is k_H/k_c, and the intercept is an estimate of the constant k_{-c}/k_c governing the equilibrium between the open-chain radical **5** and the cyclized radical **6**.

$$\frac{[\mathbf{2}]}{[\mathbf{3}]} = \frac{k_H}{k_c}[Bu_3SnH]_0 + \frac{k_H k_{-c}}{k_{H'} k_c} \qquad (1)$$

A 6.0×10^{-3} M solution of enaminone **1c** in benzene containing 25% (w/w) of AIBN was treated with four different initial concentrations of tributyltin hydride, and the ratio of **2c** and **3c** in the resulting mixture of reduced and cyclized products was measured by integration of the ^{1}H NMR spectra. From the slope of the line so obtained (Figure 3), and assuming a value of 10^9 M^{-1} s^{-1} for k_H,[16] we calculated the 5-exo cyclization rate constant k_c at 80 °C as $(3.5 \pm 0.1) \times 10^7$ s^{-1}. A similar kinetic study for the phenethyl enaminone **1e** gave a 6-exo rate constant k_c of $(7.1 \pm 0.5) \times 10^7$ s^{-1}, likewise at 80 °C. In both cases, the intercept was close to zero to within the experimental error, indicating that the cyclization is fundamentally irreversible ($k_{-c} \approx 0$) as expected for a highly exothermic aryl radical cyclization. The k_c values found show that enaminones are only moderate radical acceptors in comparison to enamines; for example, the relative rate constants for 5-exo and 6-endo aryl radical cyclization of *N*-butyl-*N*-(2-bromobenzyl)-1-cyclohexenylamine obtained by Warkentin are 4.0×10^8 s^{-1} and 1.3×10^9 s^{-1}, respectively.[17]

Rotation Around the C3−N Bond. We determined the barrier to rotation around the C3−N bond by means of dynamic ^{1}H NMR experiments carried out between 248 and 303 K on a 0.08 M solution of the *N*,*N*-dimethyl tertiary enaminone **8** in $CDCl_3$ (Figure 4). The broad *N*-methyl signal observed at room temperature split into two singlets upon cooling. Full line shape analysis[18] optimized both the chemical shifts of the methyl groups and the rate constants for C3−N rotation (Table 2), the latter of which were used to construct a plot of $\ln(k/T)$ against $1/T$ (Figure 4). Fitting these data with the Eyring equation[19] (eq 2; we assume transmission coefficients of unity) then afforded the values $\Delta H^{\ddagger} = 15.6 \pm 0.6$ kcal/mol and $\Delta S^{\ddagger} = 7.6 \pm 0.3$ e.u., which imply a rate constant $k = 7.1 \times 10^4$ s^{-1} at 353 K. Therefore, since we saw in the previous section that for exo cyclizations of **1c** and **1e** $k_c \approx 10^7$ s^{-1}, rotation around the enaminone C3−N bond is ca. 1000-fold slower than the cyclization process, which must occur without alteration of the configuration with respect to this bond.

$$\ln \frac{k}{T} = \ln \frac{k_B}{h} e^{\Delta S^{\ddagger}/R} - \frac{\Delta H^{\ddagger}}{RT} \qquad (2)$$

*Conformations of **1a**−**f** in Benzene*. To determine the predominant conformations of **1a**−**f** in benzene, in which rotation around the C3−N bond is fast on the NMR time scale at the temperature of interest, we performed NOE experiments in deuterated benzene (for instrumental safety, these experiments were carried out at 343 rather than 353 K). Note that the conformational distribution in radicals **5a**−**f** will be dictated by that of the parent bromide compounds **1a**−**f** since, as we have seen in the previous section, thermal equilibration between conformers is a much slower process than radical reactions. All the tertiary enaminones **1b**, **1d**, and **1f** exist exclusively in the trans form with respect to the enaminone double bond, as shown by the large coupling constants between the olefinic protons (J = 13.1, 13.0, and 12.9 Hz, respectively). Irradiation of the vinylic C3 and C2 protons of **1b**, respectively, induced NOE of 1.8% with the

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(17) In the original paper (ref 4) a different k_H value was used (3.52×10^8 M^{-1} s^{-1}); therefore, for the purpose of comparison, we recalculated the reported values using the new k_H from ref 16.

(18) Line shape analysis was performed using Gnmr3.6: Budzeelar, P. H. M.; Cherwell Scientific Publishing: Oxford, 1995.

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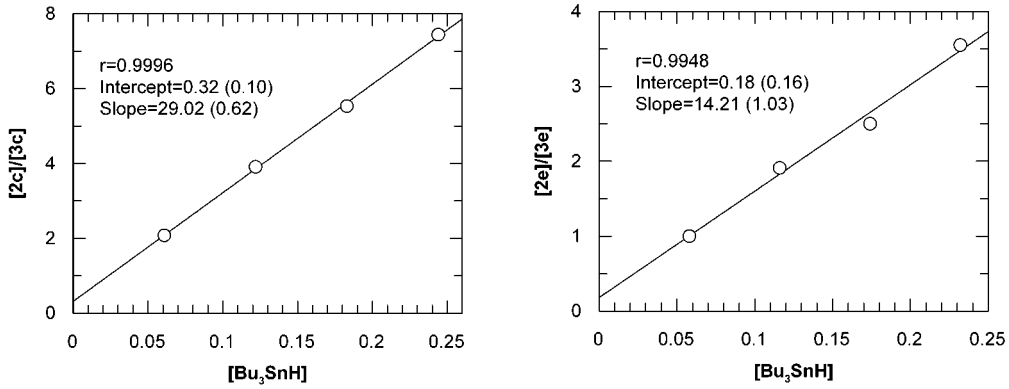

Figure 3. Kinetic measurements of the aryl radical cyclization of enaminone esters **1c** and **1e** (standard errors in parentheses).

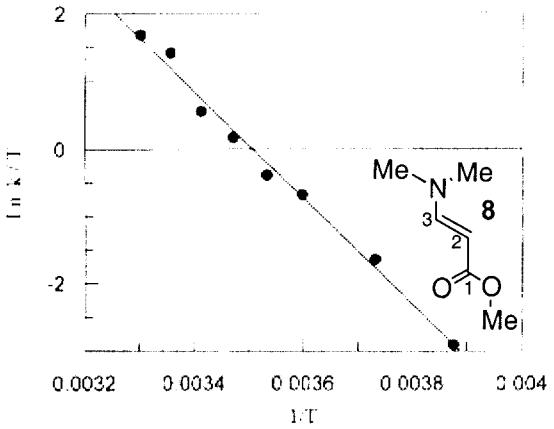

Figure 4. Plots of ln(k/T) vs $1/T$ data for rotation about the C_3−N bond of enaminone ester **8** obtained by DNMR rate constant measurements.

Table 2. Chemical Shifts of *N*-Methyl Protons in Enaminone Ester 8 and Corresponding Rate Constants for Rotation around the C3−N Bond, as Calculated by Lineshape Analysis of DNMR Data Obtained between 248 and 303 K

T (K)	k (s^{-1})	$\delta 1$	$\delta 2$
248	0[a]	2.75	3.04
258	14	2.75	3.03
268	52	2.74	3.03
278	141	2.74	3.02
283	193	2.74	3.02
288	344	2.74	3.02
293	513	2.74	3.02
298	1230	2.71	3.05
303	1630	2.71	3.04

[a] Assumed to be zero.

aromatic protons and 5.0% with the *N*-methyl protons (Scheme 4), showing that **1b** had mainly adopted the s-(*E*) conformation around the C3−N bond. Irradiation of the C3 proton of **1d** induced NOE with the methylene group (5.7%) and the methyl group (ca 1%), and irradiation of the C3 and C2 protons in the phenethyl compound **1f**, respectively, induced NOE of 5.0% with one of the methylene groups and 5.1% with the *N*-methyl protons. Thus the s-(*E*) conformation also seems to be preferred by **1d** and **1f**.

The ^{1}H NMR spectra of the secondary enaminones **1a**, **1c**, and **1e** in benzene show all three to be mixtures of cis and trans forms with respect to the enaminone double bond, as determined by ^{1}H NMR analysis (for **1a** J_{cis} = 8.3 and J_{trans} = 12.9, for **1c** J_{cis} = 8.2 and J_{trans} = 13.5, and for **1e** J_{cis} = 7.9 and J_{trans} = 12.9, all in Hz). For **1a**, the cis:trans ratio is 7.5:1 at 300 K and 24:1 at 343 K; for **1c**, 2.8:1 at 300 K and 4.1:1 at 343 K; and for **1e**, 2.2:1 at 300 K and 4.80:1 at 343 K. The cis form necessarily adopts an s-(*E*) conformation around the C3−N bond due to the hydrogen bond, while the trans form may in principle adopt both s-(*E*) and s-(*Z*) conformations. Irradiation of the methylene protons of the trans form of **1c** at 343 K induced NOE of 3.6% on the C2 proton and 2.9% on the C3 proton, showing a mixture of s-(*Z*) and s-(*E*) conformations, whereas, as expected, irradiation of the methylene protons of the cis form, induced NOE only with the C3−H proton (2.7%). Similarly, with enaminone **1e**, irradiation of the CH_2N protons of the trans form gave NOE of 2.6% with C2−H and 1.0% with C3−H, and irradiation of those of the cis form gave NOE of 1.9% with C3−H. Taken together, these results show that, like the tertiary enaminones, the secondary enaminones exist mainly in the s-(*E*) conformation, since this is the one adopted by the more abundant cis form of secondary enaminones.

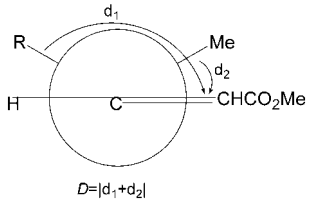

Figure 5. Definition of the enaminone distortion parameter *D*.

PM3 Calculations on the Cyclization Reactions. To get a theoretical support of the synthetic results, we carried out PM3[20] calculations, using an unrestricted formalism, on the cyclization of the *N*-methyl radicals **5b**, **5d**, and **5f** (the methoxy groups on the aryl ring, which should not affect the reaction course significantly, were supressed for simplicity). Minima and transition state structures were identified, by means of numerical Hessian calculations, (although only the latter will be presented in this work, structures and energies of the former are available as Supporting Information) for both s-(*E*) and s-(*Z*) conformations with respect to the C3−N bond. The connection between the transition structures and products was verified by IRC[21] calculations. Since

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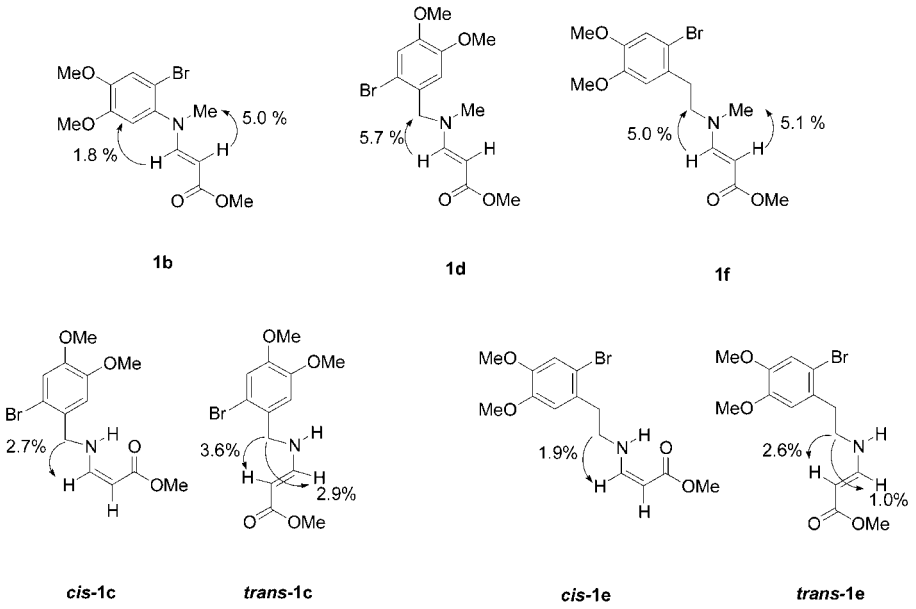
Scheme 4



in all structures discussed here the nitrogen is to some degree pyramidal, distortion of the C3−N bond can be measured in terms of the quantity *D* defined by the absolute value of the algebraic sum of the dihedral angles R−N−C═C (d1) and Me-N−C═C (d2). *D* is close to 180° in an undistorted enaminone and close to 0° when C3−N conjugation is completely disrupted.

*Cyclization of **5b.*** For both s-(*E*) and s-(*Z*) rotamers of radical **5b** (**5bi** and **5bii**, respectively; see Supporting Information), 4-exo cyclization requires passing through transition structure TS-**5biii** (Figure 6), which involves almost complete disruption of conjugation in the enaminone moiety (*D* = 24°, see Table 3). The activation barriers are accordingly high, 17.91 kcal/mol from the s-(*E*) rotamer and 19.52 kcal/mol from **5bii**. 5-Endo cyclization, which takes place through TS-**5biv**, can proceed only from the s-(*Z*) rotamer, **5bii**. This involves much less distortion of the enaminone moiety (*D* = 202°), and the activation barrier is accordingly much lower, 9.62 kcal/mol (Figure 7); this barrier is mainly due to the poor alignment of the aryl radical center with the C═C double bond, as the dihedral angle ·C− C═C−N is only 25° instead of the optimal 90°. Our failure to obtain either 4-exo or 5-endo cyclization products from **1b** is attributed to the activation barrier for the 4-exo process still being large compared to those of the other cyclizations studied (see below) and the lack of the s-(*Z*) conformation in solution as seen by NOE experiments.

*Cyclization of **5d.*** The s-(*E*) rotamer **5di** (see Supporting Information) can cyclize in a 5-exo fashion via transition state TS-**5diii**, in which the alkyl chain is equatorial (Figure 6), the activation barrier for this process being 4.46 kcal/mol. 5-Exo cyclization is also possible from the s-(*Z*) rotamer **5dii**; this process has just a slightly higher activation barrier, 4.72 kcal/mol, and passes through TS-**5div**, with an axial alkyl chain. Endo cyclization is impossible from the s-(*E*) conformer **5di** because the reaction centers are too far apart, and in fact no TS could be located, but can proceed from the s-(*Z*) rotamer **5dii** via TS-**5dv**. This process has an activation barrier of 5.87 kcal/mol (Figure 7), 1.1 kcal/mol higher than that for exo cyclization of **5dii**. The barrier preventing 6-endo cyclization of **5d**, like that preventing 5-endo cyclization of **5b**, is a consequence of the nonoptimal alignment of the radical center with the double bond (·C−C═C−N = 47°). To sum up, both rotamers can in principle undergo exo cyclization, whereas only the s-(*Z*) rotamer can undergo endo cyclization, which also has a higher activation barrier.

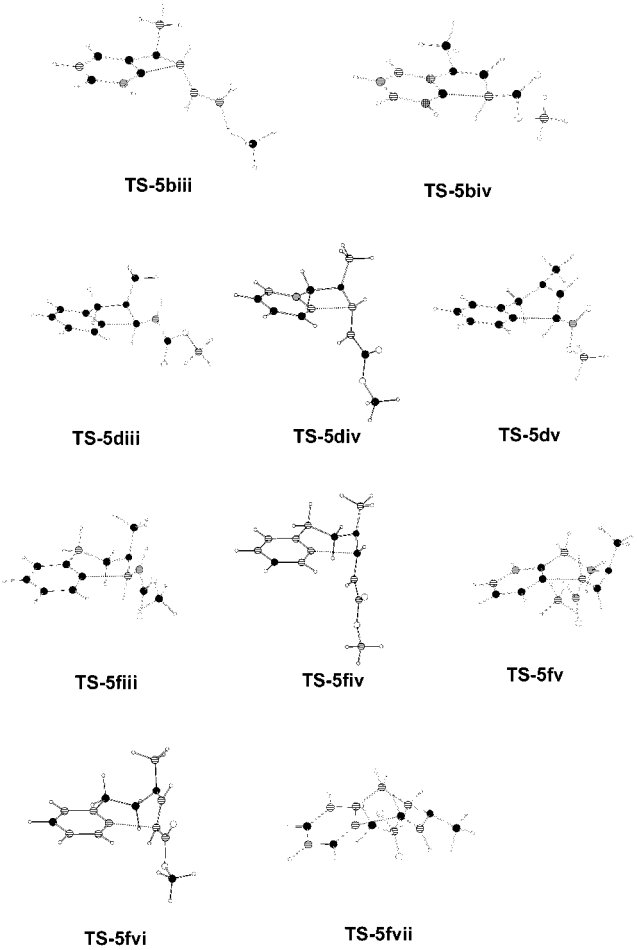


Figure 6. Geometries for transition structures calculated at the UPM3 level.

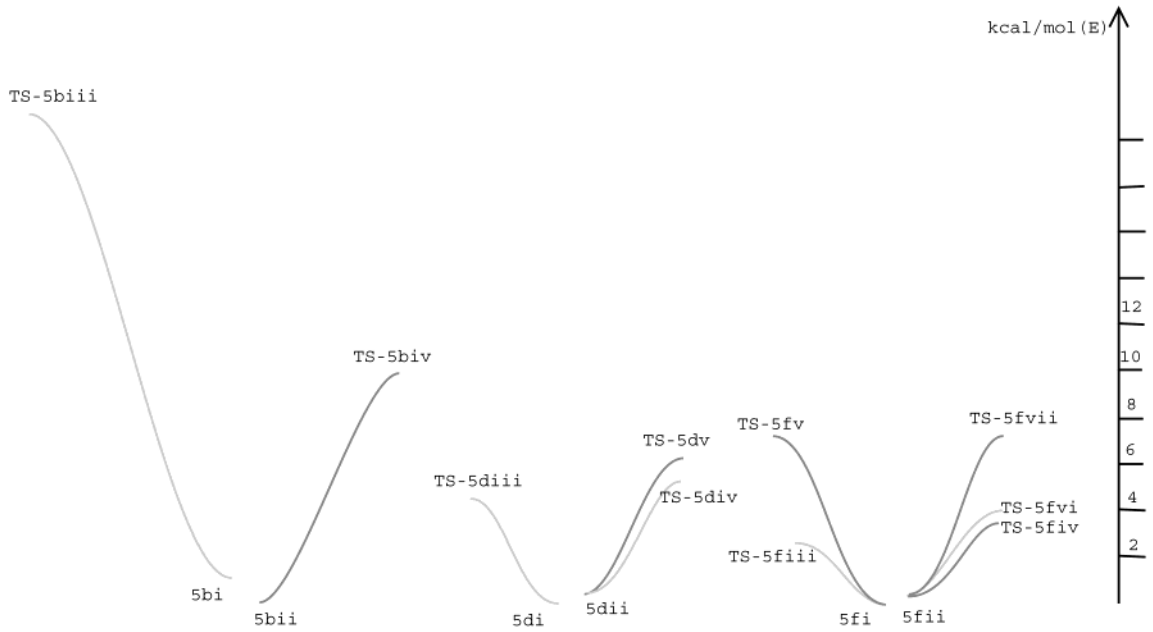
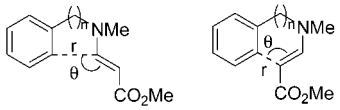


Figure 7. Calculated UPM3 activation energies for radical cyclization of **5b**,**d**,**f** species. Grey: exo cyclizations. Black: endo cyclizations.

Table 3. Relevant Geometrical Parameters of the Cyclization Transition Structures of Radicals 5 Calculated at the PM3 Level of Theory



	parameters		
TS	*r* (Å)	*θ* (deg)	*D* (deg)
TS-**5biii**	2.016	105.5	24
TS-**5biv**	2.085	92.7	202
TS-**5diii**	2.244	102.3	145
TS-**5div**	2.342	91.5	107
TS-**5dv**	2.144	99.8	139
TS-**5fiii**	2.256	102.2	175
TS-**5fiv**	2.431	88.9	136
TS-**5fv**	2.270	91.6	66
TS-**5fvi**	2.287	95.4	188
TS-**5fvii**	2.431	97.8	106

*Cyclization of **5f***. Now, both the s-(*E*) and s-(*Z*) rotamers, **5fi** and **5fii**, respectively, readily cyclize in an exo fashion, the former via the chairlike transition structure TS-**5fiii** (Figure 6) with a barrier of only 2.75 kcal/mol and the latter via the likewise chairlike TS-**5fiv** with a barrier of 3.58 kcal/mol (Figure 7). In the case of **5f**, endo cyclization is in principle possible for both rotamers. For the s-(*E*) rotamer, endo cyclization requires passage through the chair form TS-**5fv**, which involves considerable distortion of the enaminone ($D = 66°$) and, therefore, has a significant activation barrier, 7.58 kcal/mol. For the s-(*Z*) rotamer **5fii**, there are two endo cyclizations. One proceeds via the 7-endo chair TS-**5fvii**, in which distortion of the enaminone ($D = 106°$) again creates a significant barrier, 7.26 kcal/mol; however, the other proceeds via a half-boat structure, TS-**5fvi**, for which $D = 188°$, allowing the conjugation of the enaminone system to be mantained throughout the cyclization process. The barrier to the latter process is only 3.36 kcal/mol, lower than that for the 6-exo cyclization of **5fii**. To sum up, the s-(*E*) rotamer **5fi** must cyclize in a 6-exo fashion for kinetic reasons, whereas the s-(*Z*) rotamer **5fii** can cyclize via either a 6-exo or a half-boat 7-endo transition structure; however, since the preferred conformation in solution for **5f** is s-(*E*), as previously shown by NOE studies in precursor **1f**, no significant amounts of product **7f**, derived from an endo cyclization of s-(*Z*) rotamer **5fii**, were expected.

Conclusions

6-Exo cyclization onto *N*-phenethyl enaminones is a useful method for synthesis of functionalized isoquinolines, although high-dilution techniques are required. 5-Exo radical cyclization of *N*-benzyl enaminones affords isoindoles in good yield. In both cases, yields are moderate for tertiary enaminones. No cyclized product was obtained from *N*-phenyl enaminones. Measurement of relative rate constants for the cyclization of *N*-phenethyl and *N*-benzyl enaminones showed them to be only moderate radical acceptors allowing estimation of the rate constant for this process to be on the order of 10^7 s^{-1}. Since the rate constant for rotation around the C3−N enaminone bond was 7.1×10^4 s^{-1}, as estimated by means of DNMR experiments, configuration with respect to this bond is maintained throughout the cyclization process, as in the case of amides.

PM3 studies confirmed that the course of the reaction is strongly dependent on the initial configuration of the starting enaminones with respect to the C3−N bond, endo-type cyclizations requiring the s-(*Z*) conformation. Since our secondary and tertiary enaminones were shown by NMR experiments to exist mainly in the s-(*E*) conformation, only exo cyclization products were obtained.

Experimental Section[22]

All spectra were recorded in $CDCl_3$ unless otherwise stated. The ^{13}C NMR spectra for tertiary enaminones **1b**, **2b**, **1d**, **2d**, **1f**, and **2f** were recorded in C_6D_6 at 75 °C in order to achieve

(22) For general procedures and protocols, see ref 3b.

fast exchange between the s-(*E*) and s-(*Z*) rotamers. ^{1}H NMR coupling constants are given in hertz.

Methyl 3-[(2-Bromo-4,5-dimethoxyphenyl)amino]prop-2-enoate (1a). 2-Bromo-4,5-dimethoxyaniline (0.27 g, 1.13 mmol), methyl propiolate (0.11 mL, 1.21 mmol), and AcOH (0.050 mL) were dissolved in 4 mL of dry benzene, and the solution was heated at 110 °C for 4 days with an extra 0.11 mL of methyl propiolate being added every 24 h. After the mixture was cooled, the solvent was evaporated and the residue chromatographed (SiO_2, 70:30 hexane/EtOAc), affording 0.25 g (74%) of **1a** as a yellowish oil. ^{1}H NMR analysis showed only the cis (2*Z*) conformer. IR (film CsI): 3366, 3219, 3010−2840, 1677, 1640, 1521, 1477, 1209 cm^{-1}. ^{1}H NMR: δ 10.17 (d, J = 12.4, 1H), 7.15 (dd, J = 12.4, J = 8.3, 1H), 7.02 (s, 1H), 6.61 (s, 1H), 4.92 (d, J = 8.3, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.75 (s, 3H). ^{13}C NMR: δ 170.7 (CO), 149.9 (C), 145.3 (C), 142.7 (CH), 132.8 (C), 116.3 (CH), 102.1 (C), 99.2 (CH), 88.3 (CH), 56.8 (OCH_3), 56.5 (OCH_3), 51.2 (OCH_3). MS: *m*/*z* (%) 317 (38), 315 (38), 285 (19), 283 (19), 270 (24), 268 (24), 204 (53), 176 (100). HRMS: calcd for $C_{12}H_{14}BrNO_4$, 315.0106; found, 315.0113.

Methyl 3-[(2-Bromo-4,5-dimethoxyphenyl)(methyl)amino]prop-2-enoate (1b). *N*-Methyl-2-bromo-4,5-dimethoxyaniline (1.1 g, 4.47 mmol), methyl propiolate (0.50 mL, 5.58 mmol), and AcOH (0.10 mL) were dissolved in 15 mL of dry toluene, and the solution was heated at 150 °C for 4 days with an extra 0.50 mL of methyl propiolate being added every 24 h. After the mixture was cooled, the solvent was evaporated and the residue chromatographed (SiO_2, 70:30 hexane/EtOAc), affording 0.73 g (50%) of **1b** as a yellowish solid. ^{1}H NMR analysis showed only the trans (2*E*) conformer. Mp: 93−95 °C. IR (film CsI): 3000−2840, 1692, 1593, 1505, 1232, 1157 cm^{-1}. ^{1}H NMR: δ 7.54 (d, J = 13.1, 1H), 7.04 (s, 1H), 6.70 (s, 1H), 4.80 (broad, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.67 (s, 3H), 3.15 (broad s, 3H). ^{13}C NMR (C_6D_6, 75 °C): 169.0 (CO), 151.7 (CH), 150.7 (C), 150.4 (C), 138.9 (C), 117.6 (CH), 113.0 (CH), 112.0 (C), 89.7 (CH), 56.4 (OCH_3), 56.4 (OCH_3), 50.4 (OCH_3), 39.7 (NCH_3). MS: *m*/*z* (%) 331 (19), 329 (19), 300 (5), 298 (5), 250 (83), 218 (100), 191 (57), 176 (68). HRMS: calcd for $C_{13}H_{16}BrNO_4$, 329.0262; found, 329.0271.

Methyl 3-[(2-Bromo-4,5-dimethoxybenzyl)amino]prop-2-enoate (1c). 2-Bromo-4,5-dimethoxybenzylamine (3.48 g, 14.08 mmol) and methyl propiolate (1.37 mL, 15.48 mmol) were dissolved in 30 mL of dry THF, and the solution was stirred at room temperature for 30 min. After evaporation of the solvent, the crude was beaten with Et_2O and filtered, giving **1c** as a white solid of mp 70−73 °C in almost quantitative yield. ^{1}H NMR analysis showed an approximately 2:1 mixture of cis (2*Z*) and trans (2*E*) conformers. IR (film CsI): 3381, 3346, 2999−2841, 1673, 1615, 1504 cm^{-1}. ^{1}H NMR: δ 8.15 (broad, 2/3H), 7.60 (dd, J = 13.3, 8.1, 1/3H), 7.02 (s, 1H), 6.79 (s, 1H), 6.70 (dd, J = 13.0, 8.0, 2/3H), 4.81 (d, J = 13.3, 1/3H), 4.75 (broad s, 1/3H), 4.56 (d, J = 8.0, 2/3H), 4.34 (d, J = 6.2, 2 × 2/3H), 4.23 (d, J = 5.6, 2 × 1/3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.65 (s, 3H). ^{13}C NMR (major cis conformer): 171.4 (C), 152.4 (CH), 149.6 (C), 149.4 (C), 130.0 (C), 116.1 (CH), 113.6 (C), 112.6 (CH), 84.3 (CH), 56.6 (OCH_3), 56.4 (OCH_3), 52.5 (CH_2), 50.6 (OCH_3). MS: *m*/*z* (%) 331 (23), 329 (24), 316 (8), 314 (9), 300 (14), 298 (26), 296 (13), 251 (49), 250 (93), 232 (34), 231 (100), 230 (39), 229 (98), 218 (23), 190 (56), 151 (41). Anal. Calcd for $C_{13}H_{16}BrNO_4$: C, 47.29; H, 4.88; N, 4.24. Found: C, 47.53; H, 5.15; N, 4.28.

Methyl 3-[(2-Bromo-4,5-dimethoxybenzyl)(methyl)amino]prop-2-enoate (1d). *N*-Methyl-2-bromo-4,5-dimethoxybenzylamine (1.1 g, 4.19 mmol) and methyl propiolate (0.41 mL, 4.61 mmol) were dissolved in 20 mL of dry THF, and the solution was stirred at room temperature for 30 min. After evaporation of the solvent, the crude was chromatographed (SiO_2, 1:1 hexane/EtOAc), affording an 88% yield of **1d** as a solid. ^{1}H NMR analysis showed only the trans (2*E*) conformer. Mp: 97−100 °C. IR (film CsI): 3000−2840, 1689, 1613, 1507, 1260, 1147 cm^{-1}. ^{1}H NMR: δ 7.65 (d, J = 13.0, 1H), 7.02 (s, 1H), 6.62 (s, 1H), 4.64 (d, J = 13.0, 1H), 4.34 (s, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 3.67 (s, 3H), 2.78 (broad s, 3H). ^{13}C NMR (C_6D_6, 75 °C): 169.4 (CO), 152.7 (CH), 151.0 (C), 150.5 (C), 127.9 (C), 117.8 (CH), 113.9 (C), 113.0 (CH), 87.0 (CH), 58.7 (CH_2), 56.4 (OCH_3), 56.2 (OCH_3), 50.3 (OCH_3), 36.5 (NCH_3). MS: *m*/*z* (%) 328(3), 326(3), 278(57), 264(42), 231 (97), 229-(100), 218(33). HRMS: calcd for $C_{14}H_{18}BrNO_4$, 343.0419; found, 343.0410.

Methyl 3-{[2-(2-Bromo-4,5-dimethoxyphenyl)ethyl]amino}prop-2-enoate (1e). 2-Bromo-4,5-dimethoxyphenethylamine (0.88 g, 3.07 mmol) and methyl propiolate (0.30 mL, 3.37 mmol) were dissolved in 20 mL of dry THF, and the solution was stirred at room temperature for 30 min. Evaporation of the solvent gave **1e** as a solid in almost quantitative yield. Recrystallization from CH_2Cl_2/hexane afforded a white solid of mp 58−61 °C, which ^{1}H NMR analysis showed to be an approximately 4:1 mixture of cis (2*Z*) and trans (2*E*) conformers at room temperature. IR (film CsI): 3378, 3341, 2999−2841, 1668, 1616, 1509, 1383 cm^{-1}. ^{1}H NMR: δ 7.88 (broad, 4/5H), 7.47 (dd, J = 13.4, 8.4, 1/5H), 7.00 (s, 1H), 6.67 (s, 1H), 6.49 (dd, J = 14.1, 8.0, 4/5H), 4.83 (d, J = 13.4, 1/5H), 4.51 (broad, 1/5H), 4.43 (d, J = 8.0, 4/5H), 3.85 (s, 3H), 3.83 (s, 3H), 3.62 (s, 3H), 3.42−3.28 (m, 2H), 2.96−2.85 (m, 2H). ^{13}C NMR (major cis conformer): 171.4 (CO), 152.6 (CH), 152.5 (C), 148.7 (C), 129.7 (C), 116.0 (CH), 114.4 (C), 114.3 (CH), 82.1 (CH), 56.5 (OCH_3), 56.3 (OCH_3), 50.5 (OCH_3), 48.7 (CH_2), 38.3 (CH_2). MS: *m*/*z* (%) 328(3), 326 (3), 278 (57), 264 (42), 231 (97), 229 (100), 218 (33). Anal. Calcd for $C_{14}H_{18}BrNO_4$: C, 48.85; H, 5.27; N, 4.07. Found: C, 48.85; H, 5.37; N, 4.11.

Methyl 3-{[2-(2-Bromo-4,5-dimethoxyphenyl)ethyl](methyl)amino}prop-2-enoate (1f). *N*-Methyl-2-bromo-4,5-dimethoxyphenethylamine (1.20 g, 4.35 mmol) and methyl propiolate (0.32 mL, 3.68 mmol) were dissolved in 20 mL of dry THF, and the solution was stirred at room temperature for 30 min. Evaporation of the solvent gave an almost quantitative yield of **1f** as a solid that was recrystallized from Et_2O (0 °C); mp 71−73 °C. ^{1}H NMR analysis showed only the trans (2*E*) conformer. IR (film CsI): 2996−2913, 1678, 1612, 1509, 1219 cm^{-1}. ^{1}H NMR: δ 7.46 (d, J = 12.9, 1H), 7.00 (s, 1H), 6.65 (s, 1H), 4.57 (d, J = 12.9, 1H), 3.85 (s, 6H), 3.66 (s, 3H), 3.37 (t, J = 7.5, 2H), 2.90 (t, J = 7.5, 2H), 2.80 (broad s, 3H). ^{13}C NMR (C_6D_6, 75 °C): 169.4 (CO), 152.0 (CH), 150.4 (2C), 130.5 (C), 118.0 (CH), 116.1 (CH), 115.0 (C), 86.4 (CH), 56.7 (OCH_3), 56.4 (OCH_3), 55.2 (CH_2), 50.2 (OCH_3), 37.6 (CH_2), 34.9 (NCH_3). MS: *m*/*z* (%) 328 (52), 326 (53), 279 (67), 278 (95), 244 (53), 242 (53), 129 (48), 128 (100). Anal. Calcd for $C_{15}H_{20}BrNO_4$: C, 50.29; H, 5.63; N, 3.91. Found: C, 50.29; H, 5.78; N, 3.93.

Methyl 3-[(3,4-Dimethoxybenzyl)amino]prop-2-enoate (2c). 3,4-Dimethoxybenzylamine (0.66 g, 3.98 mmol) and methyl propiolate (0.39 mL, 4.37 mmol) were dissolved in 20 mL of dry THF, and the solution was stirred at room temperature for 30 min. Evaporation of the solvent gave an almost quantitative yield of **2c** as a solid that was pure according to TLC and ^{1}H NMR and, after recrystallization from Et_2O, was shown by ^{1}H NMR analysis to consist of an approximately 1.5:1 ratio mixture of cis (2*Z*) and trans (2*E*) conformers. Mp: 81−83 °C. IR (film CsI): 3311, 3000−2837, 1656, 1610, 1513 cm^{-1}. ^{1}H NMR: δ 8.07 (broad s, 3/5H), 7.58 (dd, J = 13.3, 8.1, 2/5H), 6.83−6.75 (m, 18/5H), 4.81 (d, J = 13.3, 2/5H), 4.68 (broad s, 2/5H), 4.55 (d, J = 8.0, 3/5H), 4.29 (d, J = 5.8, 6/5H), 4.15 (d, J = 5.2, 4/5H), 3.87 (s, 6H), 3.67 (s, 6/5H), 3.65 (s, 9/5H). ^{13}C NMR (major cis conformer): 170.3 (C), 152.3 (CH), 149.6 (C), 149.0 (C), 129.8 (C), 120.3 (CH), 111.6 (CH), 111.1 (CH), 86.6 (CH), 56.3 (2OCH_3), 52.3 (CH_2), 50.9 (CH_3). MS: *m*/*z* (%) 251 (74), 236 (20), 218 (21), 152 (53), 151 (100), 107 (25), 106 (19). Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.13; H, 7.10; N, 5.67.

Methyl 3-{[2-(3,4-Dimethoxyphenyl)ethyl]amino}prop-2-enoate (2e). 3,4-Dimethoxyphenethylamine (0.76 g, 4.19 mmol) and methyl propiolate (0.41 mL, 4.61 mmol) were dissolved in 20 mL of dry THF, and the solution was stirred at room temperature for 30 min. Evaporation of the solvent gave an almost quantitative yield of **2e** as an oil, which ^{1}H NMR analysis showed to consist of a mixture of an approximately 1:1 ratio of cis (2*Z*) and trans (2*E*) conformers. IR (film CsI): 3367, 2997−2836, 1668, 1615, 1516 cm^{-1}. ^{1}H NMR: δ 7.86 (broad s, 1/2H), 7.48 (dd, J = 13.3, 8.2, 1/2H), 6.82 (d, J = 8.0, 1H), 6.72 (d, J = 8.0, 1H), 6.69 (s, 1H), 6.49 (dd, J = 13.2, 8.0, 1/2H), 4.79 (d, J = 13.3, 1/2H), 4.45 (broad s, 1/2H), 4.43 (d, J = 8.0, 1/2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.66 (s, 3/2H), 3.63 (s, 3/2H), 3.40−3.25 (m, 2H), 2.87−2.70 (m, 2H).

^{13}C NMR: δ 171.4 (C), 170.4 (C), 152.6 (2CH), 149.3 (C), 149.2 (C), 148.1 (C), 148.0 (C), 131.3 (C), 131.2 (C), 121.1 (CH), 120.9 (CH), 112.5 (CH), 112.1 (CH), 111.7 (2CH), 85.4 (CH), 81.7 (CH), 56.2 ($2OCH_3$), 56.1 ($2OCH_3$), 50.8 ($2OCH_3$), 50.4 ($2CH_2$), 37.8 ($2CH_2$). MS: *m*/*z* (%) 265 (77), 234 (26), 165 (27), 164 (69), 152 (55), 151 (84), 114 (100), 82 (98). HRMS: calcd for $C_{14}H_{19}NO_4$, 265.1314; found, 265.1311.

Methyl (2*E*)-3-(3-Dimethylamino)prop-2-enoate (8). To a solution of methyl propiolate (0.18 mL, 0.82 mmol) in 2 mL of dry THF was added a 2 M solution of *N*,*N*-dimethylamine in the same solvent (0.42 mL, 0.84 mmol), and the mixture was stirred at room temperature for 30 min. Evaporation of the solvent gave a quantitative yield of **8**[23] as a white solid that was pure according to TLC and ^{1}H NMR and further purified by sonication in hexane and subsequent filtration. ^{1}H NMR: δ 7.44 (d, J = 12.9, 1H), 4.52 (d, J = 12.6, 1H), 3.66 (s, 3H), 2.88 (broad s, 6H).

Bu_3SnH-Mediated Radical Reactions: General Procedure. At the 0.10 g scale, a 0.07 M benzene solution of Bu_3SnH (200% mol) containing AIBN (20% w:w) was added over 3 h to a refluxing 0.01 M solution of the enaminone ester bromide. After the mixture was cooled, the solvent was evaporated and the residue dissolved in acetonitrile and extracted with hexane (3 × 10 mL). The acetonitrile fraction was concentrated and chromatographed on a SiO_2 column.

From Enaminone 1a. Eluent for chromatography: (70:30, hexane/AcOEt). **2a** was obtained in 43% yield as a yellowish oil, identical to an authentic sample prepared from 3,4-dimethoxyaniline and methyl propiolate. IR (CsI): 3316, 3000−2835, 1668, 1639, 1595, 1520, 1208 cm^{-1}. ^{1}H NMR: δ 9.80 (d, J = 12.6, 1H), 7.16 (dd, J = 12.6, 8.2, 1H), 6.81 (d, J = 9.2, 1H), 6.53 (m, 2H), 4.79 (d, J = 8.2, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.70 (s, 3H). MS: *m*/*e* (%) 237 (65), 205 (90), 190 (100), 162 (33), 120 (19). ^{13}C NMR: δ 171.2 (CO), 150.3 (C), 145.4 (C), 144.5 (CH), 135.2 (C), 112.7 (CH), 107.1 (CH), 101.4 (CH), 86.2 (CH), 56.7 (OCH_3), 56.3 (OCH_3), 50.9 (OCH_3). HRMS: calcd for $C_{12}H_{15}NO_4$, 237.1001; found 237.1001.

From Enaminone 1b. Eluent for chromatography: (70:30, hexane/AcOEt). **2b** was obtained in 55% yield as a yellowish solid, mp 53−56 °C, identical to an authentic sample prepared from *N*-methyl-3,4-dimethoxyaniline and methyl propiolate. IR (KBr): 3007−2839, 1694, 1593, 1516, 1246, 1150 cm^{-1}. ^{1}H NMR: δ 7.83 (d, J = 13.1, 1H), 6.83 (d, J = 9.4, 1H), 6.66 (m, 2H), 4.86 (d, J = 13.1, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.69 (s, 3H), 3.21 (s, 3H). ^{13}C NMR (C_6D_6, 75 °C): δ 169.2 (CO), 151.5 (C), 149.5 (CH), 148.1 (C), 141.6 (C), 114.4 (CH), 113.6 (CH), 107.5 (CH), 90.6 (CH), 56.7 (OCH_3), 56.3 (OCH_3), 50.5 (OCH_3), 37.3 (NCH_3). MS: *m*/*e* (%) 251 (100), 236 (39), 220 (37), 204 (32), 192 (61), 176 (37), 134 (51), 79 (54). HRMS: calcd for $C_{13}H_{17}NO_4$, 251.1157; found 251.1153.

From Enaminone 1c. Eluent for chromatography: (90:10, CH_2Cl_2/MeOH). Isoindole **3c** was obtained as a colorless oil in 71% yield. IR (film CsI): 3371, 2995−2871, 1733, 1608, 1506 cm^{-1}. ^{1}H NMR: δ 6.77 (s, 1H), 6.70 (s, 1H), 4.88 (m, 1H), 4.27 (s, 2H), 3.87 (s, 6H), 3.73 (s, 3H), 3.15 (broad s, NH), 2.85 (dd, J = 15.9, 3.2, 1H), 2.67 (dd, J = 15.9, 8.9, 1H). ^{13}C NMR: δ 172.7 (CO), 149.4 (C), 149.0 (C), 133.7 (C), 132.2 (C), 105.9 (CH), 105.5 (CH), 60.5 (CH), 56.5 (OCH_3), 56.4 (OCH_3), 52.2 (OCH_3), 51.7 (CH_2), 41.4 (CH_2). MS: *m*/*z* (%) 251 (14), 250 (5), 236 (5), 190 (6), 179 (22), 178 (100), 163 (8), 162 (8), 147 (12). HRMS: calcd for $C_{13}H_{17}NO_4$, 251.1157; found, 251.1153.

From Enaminone 1d. Eluent for chromatography: (96:4, CH_2Cl_2/MeOH). Isoindole **3d** was obtained as a brownish solid in 56% yield; mp 62−66 °C. IR (film CsI): 3004−2789, 1726, 1509, 1456 cm^{-1}. ^{1}H NMR: δ 6.73 (s, 1H), 6.71 (s, 1H), 4.21 (d, J = 12.4, 1H), 4.13 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.74 (s, 3H), 3.65 (d, J = 12.4, 1H), 2.74 (m, 1H) 2.67 (m, 1H), 2.55 (s, 3H). ^{13}C NMR: δ 172.7 (CO), 148.8 (C), 148.5 (C), 134.3 (C), 131.1 (C), 105.7 (CH), 105.5 (CH), 67.3 (CH), 60.5 (CH_2), 56.0 ($2OCH_3$), 51.6 (OCH_3), 41.0 (NCH_3), 40.0 (CH_2). MS: *m*/*z* (%) 264 (3), 250 (5), 206 (23), 192 (100). HRMS: calcd for $C_{14}H_{19}NO_4$, 265.1314; found 265.1310.

The reduction product, **2d**, was obtained in 12% yield as a white solid, mp 90−92 °C, identical to an authentic sample prepared from *N*-methyl-3,4-dimethoxybenzylamine and methyl propiolate. IR (CsI): 3020−2833, 1686, 1613, 1518 cm^{-1}. ^{1}H NMR: δ 7.67 (d, J = 12.9, 1H), 6.83 (d, J = 8.1, 1H), 6.73 (dd, J = 8.1, 1.9, 1H), 6.67 (d, J = 1.9, 1H), 4.65 (d, J = 12.9, 1H), 4.28 (s, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.68 (s, 3H), 2.72 (broad s, 3H). ^{13}C NMR: δ 169.5 (CO), 152.7 (CH), 151.2 (C), 150.6 (C), 130.1 (C), 120.6 (CH), 113.8 (CH), 113.0 (CH), 86.5 (CH), 59.1 (CH_2), 56.3 ($2OCH_3$), 50.2 (OCH_3), 36.2 (NCH_3). MS: *m*/*e* (%) 265 (93), 250 (42), 234 (54), 206 (29), 191 (29), 152 (75), 151 (100), 107 (50). HRMS calcd for $C_{14}H_{19}NO_4$, 265.1314; found 265.1315.

From Enaminone 1e. Eluent for chromatography: (90:10, CH_2Cl_2/MeOH). Isoquinoline **3e** was obtained as a colorless oil in 82% yield. IR (film CsI): 3350, 3060−2836, 1721, 1612, 1520 cm^{-1}. ^{1}H NMR: δ 6.57 (s, 1H), 6.56 (s, 1H), 4.40 (m, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.75 (s, 3H), 3,15 (m, 1H), 3.04 (m, 1H), 2.80−2.68 (m, 4H). ^{13}C NMR (CD_3OD): δ 174.3 (CO), 149.9 (C), 149.5 (C), 129.6 (C), 128.4 (C), 113.8 (CH), 111.2 (CH), 57.0 (OCH_3), 56.8 (OCH_3), 53.7 (CH), 52.8 (OCH_3), 41.4 (CH_2), 41.3 (CH_2), 29.2 (CH_2). MS: *m*/*z* (%) 265 (48), 250 (18), 232 (20), 192 (100), 177 (56), 176 (78), 148 (47). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.13; H, 7.35; N, 5.30.

From Enaminone 1f. Eluent for chromatography: (95:5, CH_2Cl_2/MeOH). Isoquinoline **3f** was obtained as an oil in 51% yield. IR (film CsI): 2951−2852, 1733, 1668, 1609, 1515 cm^{-1}. ^{1}H NMR: δ 6.54 (s, 2H), 4.05 (t, J = 6.6, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.69 (s, 3H), 3.10 (m, 1H), 2.90−2.70 (m, 3H), 2.60−2.45 (m, 2H), 2.44 (s, 3H). ^{13}C NMR: δ 173.2 (CO), 148.1 (C), 147.8 (C), 129.1 (C), 126.3 (C), 111.8 (CH), 110.4 (CH), 59.9 (CH), 56.3 (OCH_3), 56.2 (OCH_3), 52.1 (OCH_3), 46.2 (CH_2), 42.4 (NCH_3), 41.1 (CH_2), 24.5 (CH_2). MS: *m*/*z* (%) 206 (100), 190 (19), 162 (7). HRMS: calcd for $C_{15}H_{21}NO_4$, 279.1470; found 279.1474.

The reduction product, **2f**, was obtained in 19% yield as a white solid, mp 59−61 °C, identical to an authentic sample prepared from *N*-methyl-3,4-dimethoxyphenethylamine and methyl propiolate. IR (KBr): 3009−2839, 1684, 1609, 1512, 1358, 1247, 1234, 1143 cm^{-1}. ^{1}H NMR: δ 7.45 (d, J = 13.0, 1H), 6.81 (d, J = 8.1, 1H), 6.69 (d, J = 8.1, 1H), 6.66 (s, 1H), 4.55 (d, J = 13.0, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.66 (s, 3H), 3.36 (t, J = 7.4, 2H), 2.77 (s, 3H), 2.76 (t, J = 7.4, 2H). ^{13}C NMR (C_6D_6, 75 °C): δ 169.4 (CO), 152.1 (CH), 151.1 (C), 149.9 (C), 132.0 (C), 121.6 (CH), 114.8 (CH), 114.2 (CH), 86.1 (CH), 57.0 (CH_2), 56.6 (OCH_3), 56.5 (OCH_3), 50.2 (OCH_3), 37.5 (NCH_3), 34.5 (CH_2). MS: *m*/*e* (%) 279 (2), 248 (5), 165 (7), 164 (29), 151 (8), 128 (100). HRMS: calcd for $C_{15}H_{21}NO_4$, 279.1470; found 279.1461.

Kinetic Measurements. Determination of k_c for Radicals 5c and 5e. For kinetic measurements, Bu_3SnH was distilled under a vacuum and 10, 20, 30, and 40 equiv were reacted with compound **1c** (for **3c**) and **1e** (for **3e**) as follows. Compound **1c** or **1e** (15 mg) was dissolved in 7.5 mL of dry benzene along with 4 mg of AIBN. The solution was heated to reflux, and Bu_3SnH was added at once. After 3 h of refluxing, the reaction mixture was allowed to cool; the solvent was evaporated, and the crude was analyzed by ^{1}H NMR ($CDCl_3$) to determine the **2c**/**3c** and **2e**/**3e** ratios (in the former case, deconvolution of the signals of **2c** and **3c** was performed before integration).

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Supporting Information Available: Cartesian coordinates and energies of all calculated structures, copies of the ^{1}H and ^{13}C NMR spectra of compounds **1a**−**f**, **2a**, **2b**, **2d**−**f**, **3c**, **3d**, and **3f**, and NOE of compounds **1a**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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