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Novel Intramolecular [4 + 1] and [4 + 2] Annulation Reactions Employing Cascade Radical Cyclizations

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Tributyltin hydride and tris(trimethylsilyl)silane promote sequential/cascade free radical cyclization reactions of dienoate tethered vinyliodides or alkynes. These processes produce [4 + 1] and [4 + 2] annulated products. In contrast, the electrochemical reductions of the vinyliodides afford monocyclic compounds. Both the regiochemical and stereochemical courses of the sequential radical cyclizations strongly depend on substrate structure. Especially important is the balance between steric and stereoelectronic (Baldwin's rules) factors that serve to control cyclization regiochemistry.

Introduction

Formation of bi- and polycyclic structures from acyclic polyene precursors is a fundamentally important strategy used by synthetic organic chemists. Intramolecular cycloaddition reactions are perhaps the most common processes in this broad family.[1] Particularly illustrative of this family are Diels−Alder reactions, which have been fully explored and utilized as key elements in the synthesis of complex natural products.[2] Recently, several new annulation reactions of acyclic polyenes, based on transition metal catalyzed processes, have been developed.[3] These methods bring about annulation reactions that correspond to [$m + n$], and [$l + m + n$] cycloadditions.

Recently, cascade or domino reactions have shown great utility as attractive and highly effective methods to prepare polycyclic ring systems in one step from acyclic precursors.[4,5] Examples of this are found in the cascade-type, intramolecular double Michael and Michael-aldol reactions, which serve as efficient annulation processes.[6]

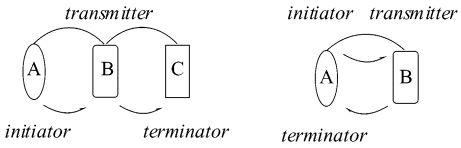

FIGURE 1. Typical cascade reaction (left), boomerang-type cascade reaction (right), and the concept of present study.

In these reactions, nucleophilic functions in the substrates are changed to electrophilic centers following the initial reaction steps and the original electrophilic groups become nucleophiles in the second steps of the cascade sequences. In each of these pathways, the reaction centers move in a "boomerang" fashion away from and then back to the same functional group via intervening functional groups (Figure 1).

We envisaged an extension of the boomerang concept to radical cascade reactions, in which a vinyl radical motif initially acts as a radical donor and then as an acceptor.[7,8] Previously, we reported the results of studies of a cascade radical reaction of this type, in which halopolyenes, undergo [2 + 1] annulations.[8a] Below, we describe the results of an investigation of novel, radical cascade, intramolecular [4 + 1] and [4 + 2] annulation reactions[9] of dienoate tethered iodoolefins (Figure 2). Factors con-

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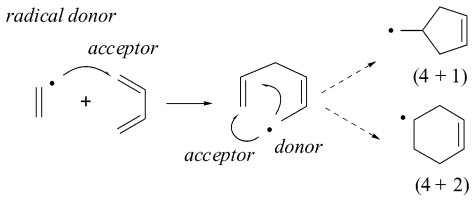
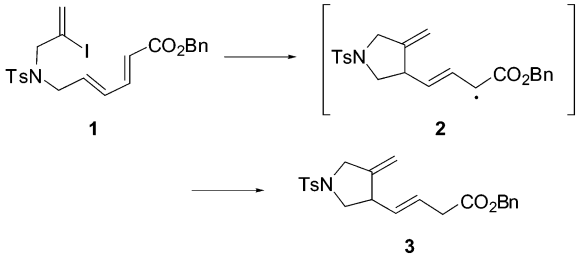


FIGURE 2. Boomerang-type [4 + 1] and [4 + 2] radical cascade reaction.

TABLE 1. Radical Reaction of 1 by Using TBTH or Electrolysis



run	conditions	yield (%) of **3**
1	TBTH, AIBN, benzene, reflux[a]	56
2	Ni(cyclam)$^{2+}$, DMF, −1.5 V, rt	65

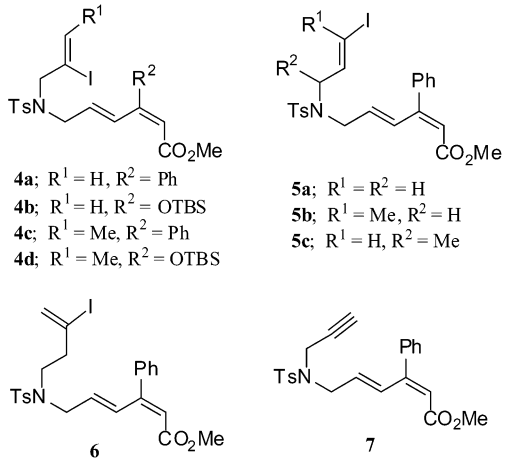
[a] TBTH (1.2 equiv) and AIBN (0.5 equiv) were added deopwise over 1 h.

trolling the regiochemical and stereochemical courses of these processes are also described.[10]

Results and Discussion

Reaction Design. In initial experiments, we examined the radical cyclization reactions of the linear trienoate ester **1**, mediated by either tributyltin hydride−azodiisobutyronitrile (TBTH−AIBN) or cathodic electrolysis[11] mediated by nickel(II) cyclam (Table 1). Trienoate **1** was chosen as a probe because the first radical cyclization step would generate intermediate **2**, a capto-dative (acyl-vinyl radical) stabilized radical expected to participate in a succeeding radical cyclization process. However, reaction of **1** under both initiation conditions described above affords only the monocyclic product **3** having *trans*-β,γ-unsaturated ester moiety. The results suggested that the capto-dative radical intermediate **2** was indeed formed in the first cyclization step but the ensuing cyclization process is prohibited by the *trans* geometry of the intermediate.

Our attention next focused on trienoate substrates that contain bulky substituents at the β-position in the dienoates in order to control the configuration of the olefinic moiety in the initially formed radical intermediate. For this purpose, several substrates possessing iodoolefinic and β-substituted dienoate moieties (e.g., **4a**−**d**, **5a**−**c**, **6**. and ω-alkynyldienoate **7**) were designed. Substances of general structure **4** all contain a 2-iodoallylic moiety, whereas substrates **5**, **6**, and **7** possess 3-iodoallylic, 3-iodohomoallylic and propargylic groupings, respectively. It is important note that these substances would be rather unsuitable Diels−Alder substrates because each contains *trans* geometry between an ester function and a bulky β-substituent that blocks adoption of the required *s-cis* diene conformation.



Substrate Preparation. The substrates **4**−**7** were synthesized by sequences involving coupling of the 1-bromo-2,4-dienoates **10** or **13** with iodoalkenes **15a**−**f** or alkyne **19** (Scheme 1). Dienoate **10**, having a β-phenyl substituent, was prepared from ketone **8**[12] by Peterson olefination to give (2*E*,4*E*)-**9**, followed by the allylic bromination. Siloxydienoate (2*Z*,4*E*)-**13** was prepared from the known ketoester **11**[13] by sequential enol silylation and allylic bromination. Whereas Peterson olefination of **8** affords a 3:2 mixture of (2*E*,4*E*)- and (2*Z*,4*E*)-**9**, enol silylation of **11** with TBSCl in the presence of NEt_3 furnishes (2*Z*,4*E*)-**12** as the sole stereoisomer. Separation by column chromatography was used to obtain pure (2*Z*,4*E*)-**9** and its (2*E*,4*E*) isomer.

The sulfonamide segments of **15a**−**c** were prepared by alkylation of *p*-toluenesulfonamide with the corresponding iodoalkenyl methanesulfonates **14a**−**c**. Substrates **15d**,**e** were synthesized by Mitsunobu reaction of the iodoalkenyl alcohol **16a**,**b**[14,15] with *N*-Boc-*p*-toluenesulfonyl amide, followed by the carbamate removal. The route employed to prepare **15f** starts with mesylation of **17**[14] followed by S_N2' reaction with sodium azide. This sequence produces the alkenyl azide **18**, which is transformed to **15f** by reduction followed by the treatment with *p*-toluenesulfonyl chloride. Coupling reactions of the halodienoates with the tosylamides give **4a**−**d**, **5a**−**c**, **6**, and **7**.

Radical Cyclization Reactions of the 2-Iodovinyldienoates 4. Cascade 5-*exo*,6-*endo* cyclization reactions of the 2-iodovinyl-dienoate ester **4a** were carried out under a variety of different conditions (Table 2). Reaction of **4a** by slow addition (1 h) of TBTH (1.2 equiv) and AIBN

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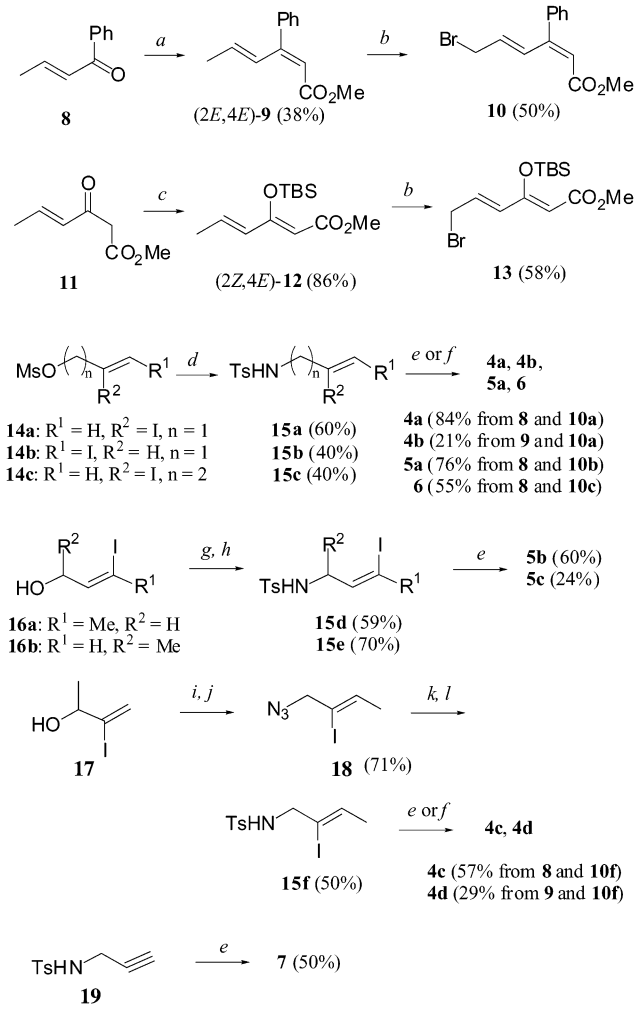
SCHEME 1. Synthetic Procedure for Substrates 4a−d, 5a−c, 6, and 7[a]



[a] (a) $TMSCH_2CO_2Me$, $^cHex_2NLi$, THF, −78 °C; (b) NBS, benzoyl peroxide, CCl_4, reflux; (c) TBSCl, NEt_3, DMAP, CH_2Cl_2, rt; (d) $TsNH_2$, K_2CO_3, acetone, reflux; (e) **10**, K_2CO_3, acetone, reflux; (f) **13**, NaH, DMF, rt; (g) TsNHBoc, DEAD, PPh_3, THF, rt; (h) TFA, CH_2Cl_2, rt; (i) MsCl, NEt_3, CH_2Cl_2, rt; (j) NaN_3, DMF, 60 °C; (k) $LiAlH_4$, Et_2O, rt; (l) TsCl, NEt_3, CH_2Cl_2, rt.

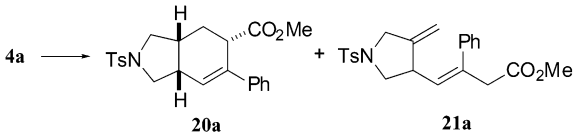
(0.5 equiv) at reflux in benzene affords the bicyclic and monocyclic products **20a** (40%) and **21a** (20%), respectively (run 1). When TBTH and AIBN are added more slowly (2 h) to a solution of **4a**, only **20a** is formed in 63% yield and as a single diastereomer (run 2). In addition, **20a** is formed as the sole product when tris(trimethylsilyl)silane ($(TMS)_3SiH$)[16] in the presence of AIBN is used as a radical source (run 3). Substrate **4a** is unreactive under benzene reflux conditions in the absence of a radical source (runs 4 and 5). This observation strongly suggests that the [4 + 2] annulation reactions are not the result of a Diels−Alder process.

In contrast to these results, when **4a** is subjected to indirect cathodic electrolysis,[12] no bicyclic products are produced. Instead, monocyclic product **21a** is formed under these conditions in 85% and 86% yield at ambient temperature or 100 °C (runs 6 and 7). Radical reaction of *β*-siloxy substituted from **4b** under the TBTH−AIBN slow addition conditions furnishes the *cis*-fused bicyclic [4 + 2] product **20b** (Scheme 2). Silyl enol ether **20b** is quantitatively transformed into the ketoester **22** by treatment with aqueous acetic acid.

Radical cyclization reactions of **4c** and **4d**, both of which possess methyl substitution on the terminal olefin center, follow a different regiochemical course (Scheme 3). For example, TBTH treatment of **4c** affords the azabicyclo[4.3.0]nonene **20c** as a minor product (11%) along with the predominant azabicyclo[3.3.0]nonenes **23c** and **24c** in respective yields of 25% and 36%. The [4 + 1] intramolecular annulated products **23c** and **24c** are formed through a pathway involving cascade 5-*exo*,5-*exo* cyclization. In the similar manner, **4d** also yields a mixture of regioisomers **20d**, **23d**, and **24d** under these radical cyclization conditions.

The differences in regiochemistry observed in reactions of **4a,b** vs **4c,d** appear to be the consequence of steric effects that govern the direction of the second radical

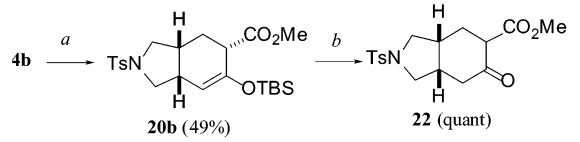
TABLE 2. Radical Reaction of 2-Iodoallylic Substrate 4a



		yield (%)	
run	conditions	**20a**	**21a**
1	TBTH, AIBN, benzene, reflux[a]	40	20
2	TBTH, AIBN, benzene, reflux[b]	63	0
3	$(TMS)_3SiH$, AIBN, benzene, reflux[b]	66	0
4	benzene, reflux	0	0
5	TBTH, benzene, reflux	0	0
6	$Ni(cyclam)^{2+}$, DMF, −1.5 V, rt	0	85
7	$Ni(cyclam)^{2+}$, DMF, −1.5 V, 100 °C	0	86

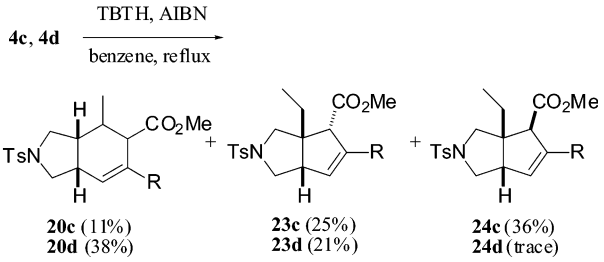
[a] TBTH (1.2 equiv) and AIBN (0.5 equiv) were added dropwise over 1 h. [b] Hydride (1.2 equiv) and AIBN (0.5 equiv) were added dropwise over 2 h.

SCHEME 2[a]



[a] (a) TBTH, AIBN, benzene, reflux; (b) AcOH, H_2O, THF, rt.

SCHEME 3[a]



[a] **c**, R = Ph; **d**, R = OTBS.

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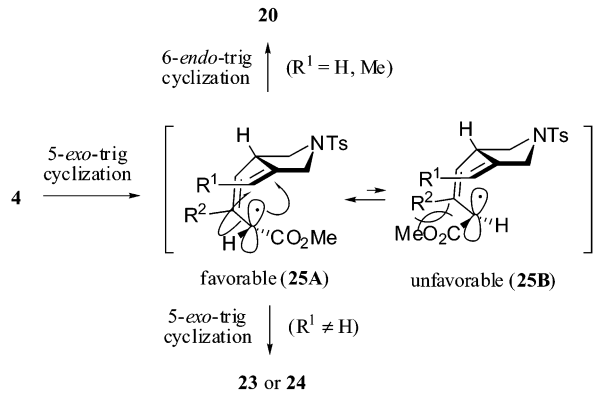
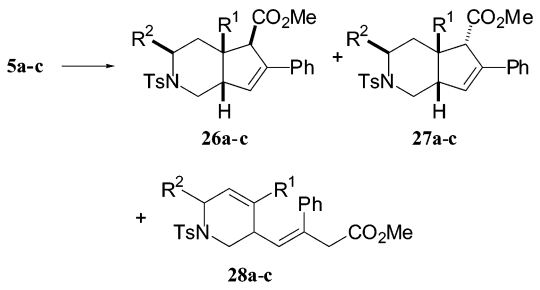


FIGURE 3. Transition-state model of **4** after the first cyclization.

cyclization step in the sequence (Figure 3). In the cases of **4a,b**, the capto-dative radical intermediates **25** (R′ = H), formed by initial 5-*exo-trig* cyclizations, cyclize by preferential addition to the unsubstituted terminal sp^2 carbons (6-*endo-trig*).[17] The stereochemistry of these processes results from the steric repulsion between phenyl substituent and ester moiety (i.e., **25A** leading to **20** is lower in energy than **25B** leading to **23** or **24**). In contrast, methyl substitution at the terminal olefinic carbons in the intermediates **25** (R^1 = Me), arising from **4c** and **4d** causes 5-*exo-trig* cyclization[17,18] leading to the production of **23** and **24**. On the other hand, the preference for formation of monocyclic products in the electrolytic processes is likely the result of rapid one-electron reduction of the radical intermediate **25** to form stable enolate anion.

Radical Cyclization Reactions of the 3-Iodoallyldienoates 5. The length of the chain between the radical donor and olefin radical acceptor influences the regiochemistry and stereochemistry of boomerang-type radical cascade reactions. The radical cyclization reactions of the 3-iodoallylic substrates **5a**−**c**, involving initial longer chain "outside" vinyl radical intermediates, were explored. Treatment of **5a** with TBTH or $(TMS)_3SiH$ in the presence of AIBN leads to formation of fused [4 + 1] products **26a** and **27a** in 25−28% and 40−42%, respectively (Table 3, runs 1 and 2). The regioselectivity of the second cyclization step in this case is controlled by a stereoelectronic effect in which the trajectory leading to 5-*exo* cyclization is favored over that giving [4 + 2] products by a 6-*endo* process. Under electrolytic reduction conditions, **5a** yields only the monocyclic piperidine **28a** (run 3). The reaction of **5b**, which contains a methyl substituent on the terminal olefinic carbon, also furnishes [4 + 1] internal adducts **26b** and **27b** along with **28b** (run 4). It is noteworthy that chirality at the allylic amide center of substrate **5c** induces chirality at the newly formed stereogenic center at the first cyclization stage in the product. Treatment of **5c** with TBTH−AIBN produces a mixture of **26c** and **27c**, both diastereomers having the same relative configurations at the chiral

TABLE 3. Radical Reaction of 3-Iodoallylic Substrates 5a−c



run	substrate	conditions[a]	yield (%) 26	27	28
1	**5a** ($R^1 = R^2 = H$)	A	25	40	0
2	**5a**	B	28	42	0
3	**5a**	C	0	0	47
4	**5b** (R^1 = Me, $R^2 = H$)	A	27	28	11
5	**5c** ($R^1 = H$, R^2 = Me)	A	20	39	0

[a] Condition A: TBTH (1.2 equiv), AIBN (0.5 equiv), benzene, reflux. Condition B: $(TMS)_3SiH$ (1.2 equiv), AIBN (0.5 equiv), benzene, reflux. Condition C: $Ni(cyclam)^{2+}$, DMF, −1.5 V, 100 °C

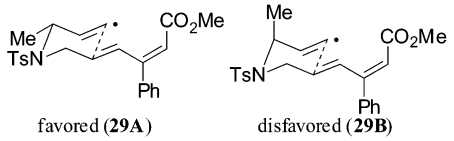


FIGURE 4. Transition-state model of **5c** at the first cyclization.

centers in the six-membered rings (run 5). Importantly, **26c** is quantitatively obtained as a sole diastereomer by treatment of a mixture of **26c** and **27c** with DBU. The presumed transition state model of the first radical cyclization step in the reaction of **5c** Figure 4) possesses conformation **29A** rather than **29B**, in which the methyl substituent and dienoate moiety are oriented equatorial in the forming six-membered ring.

Radical Cyclization Reactions of the 3-Iodohomoallyl-dienoate 6. Cascade 6-*exo*,5-*exo* radical cyclization reaction of iodotrienoate **6**, which has a longer tether as compared to **4**, with TBTH or $(TMS)_3SiH$ in the presence of AIBN leads to formation of the [4 + 1] internal adduct bicyclo[4.3.0]nonene **26b**, which is the same product leading from **5b**, as a single diastereomer (runs 1 and 2, Table 4). The source of regiochemical and stereochemical control in production of **26b** from **6** derives from repulsion between the phenyl ring and the ester group and the axially oriented hydrogen in the forming piperidine ring (see **31A** and **31B** in Figure 5). Electrolysis of **6** affords the monocyclic product **30** (run 3).

Radical Cyclization Reactions of Ynedienoate 7. In Table 5 are summarized the results obtained from studies with the ynedienoate substrate **7**. When **7** is treated with TBTH−AIBN in refluxing benzene for 4 h, two diastereomeric bicyclic [4 + 2] products, **32** and **33**, are generated in 40% and 10% yield, respectively (run 1). Although an intramolecular Diels−Alder process could produce these [4 + 2] products, reaction of **7** under similar conditions, in the absence of TBTH−AIBN, results in exclusive and low yielding formation of diastereomerically pure **33** (run 2). Thus, the annulation

(17) The radical addition of alkyl radical with intramolecular di- and trisubstituted olefin often predominates 6-*endo-trig* cyclization over the 5-*exo-trig* one. (a) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073−3100. (b) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925−3941.

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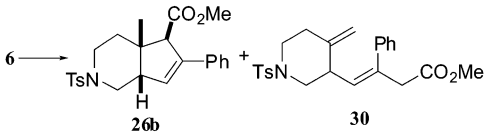
TABLE 4. Radical Reaction of 3-Iodohomoallylic Substrate 6



run	conditions	yield (%) 26b	30
1	TBTH, AIBN, benzene, reflux[a]	45	0
2	$(TMS)_3SiH$, AIBN, benzene, reflux[a]	36	0
3	$Ni(cyclam)^{2+}$, DMF, −1.5 V, rt	0	36

[a] Hydride (1.2 equiv) and AIBN (0.5 equiv) were added dropwise over 2 h.

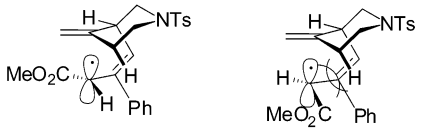
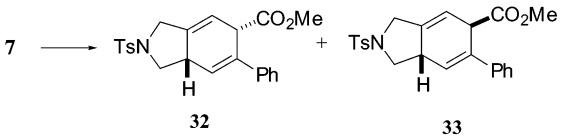


FIGURE 5. Transition-state model of **6** after the first cyclization.

TABLE 5. Radical Reaction of Propargylic Substrate 7



run	conditions	yield (%) 32	33
1	TBTH (2.0 equiv), AIBN, benzene, reflux, 4 h[a]	40	10
2	benzene, reflux, 48 h	0	20
3	TBTH (0.5 equiv), AIBN, toluene, reflux, 4 h[a]	56	22

[a] TBTH and AIBN (0.5 equiv) were added dropwise over 3 h.

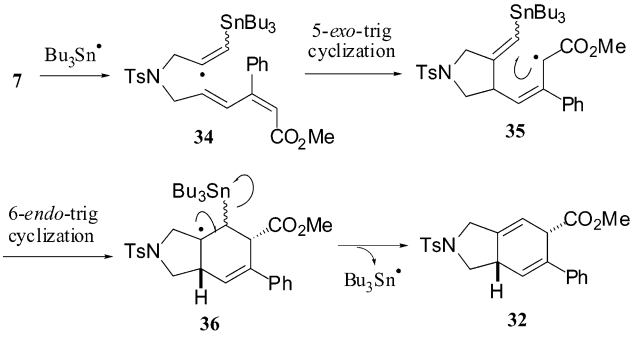
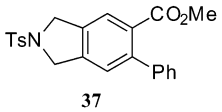


FIGURE 6. Plausible mechanism of the radical reaction of **7**.

reaction of **7** promoted by TBTH−AIBN is at least in part the consequence of a radical process. Actually, the stereochemistry of **32** is not in accord with its formation by a Diels−Alder reaction, whereas that of **33** is. A plausible mechanism for the formation of **32** from **7** is shown in Figure 6. It is well-known that vinyl radicals are generated from alkynes by the addition of stannyl radicals. Accordingly, tributyltin radical addition to the less hindered terminal sp carbon of **7** generates the vinyl radical **34**. This intermediate undergoes 5-*exo-trig* radical addition to furnish the intermediate radical **35**, whose conformation should be similar to **25B** (Figure 3). Subsequent 6-*endo* radical cyclization to give tertiary radical **36**, followed by β-stannyl radical elimination, then gives [4 + 2] internal adduct **32**. Thus, the process is catalytic in the stannyl radical. Although a higher reaction temperature is necessary to bring about complete consumption of the substrate, treatment of **7** with only 0.5 equiv of TBTH affords **32** and **33** in 56% and 22% yield, respectively (run 3 in Table 5). As an aside, both dienes **32** and **33** undergo slow oxidation to form the heteroaromatic compound **37**.



Conclusion

The investigation described above has led to the development a novel methodology for ring formation based on a boomerang-type cascade radical process. In these pathways, iodoalkenyl and alkynyl moieties can act as both radical donors and acceptors. The processes provide [4 + 2] or [4 + 1] annulated heterocyclic products, whose regiochemistry and stereochemistry are dependent on the structure of the substrate. Especially important in determining the regioselectivities and stereoselectivities of these reactions are steric and/or stereoelectronic effects on the transition states of the second radical cyclization steps, which govern whether 5-*exo-trig* or 6-*endo-trig* processes are preferred. In addition, the results show that the stepwise radical annulation method is effective in bringing about [4 + 2] intramolecular cycloadditions of *s-trans*-diene substrates, which resist Diels−Alder reactions.

Finally, the core ring systems of the nitrogen heterocycles, prepared in this study by using the boomerang-type cascade radical reaction, are classified as isoindoles, [2]pyrindines, and cyclopenta[*c*]pyrroles. Although these skeletal types are rarely found in nature, they have attracted interest as medicinally important targets.[19] Further studies are underway in this laboratory that are aimed at developing routes to biologically active heterocycles in these families.

Experimental Section

General. All reactions were carried out under an inert atmosphere, and the organic extracts obtained on workup were dried over $MgSO_4$ or Na_2SO_4, filtered, and concentrated in vacuo. Unless otherwise described, ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, and are reported in ppm downfield from TMS for the ^1H NMR and relative to the central $CDCl_3$ resonance for the ^{13}C NMR. The structures and stereochemistry of all new synthetic compounds

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were assigned based on 1D and/or 2D NMR spectroscopic data. All substance were isolated as oils, unless otherwise noted, and were >90% pure as judged by NMR analysis.

Methyl (2*E*,4*E*)-3-Phenyl-2,4-hexadienoate (9). Dicyclohexylamine (0.55 mL, 2.75 mmol) was dissolved in THF (5 mL). The solution was then cooled to −78 °C and treated with BuLi (1.53 M solution in hexanes; 1.8 mL, 2.75 mmol). To the mixture was added methyl (trimethylsilyl)acetate (0.45 mL, 2.75 mmol) dropwise at −78 °C. To the resulting solution was added phenylpropenyl ketone (**8**)[12] (134 mg, 0.92 mmol) in THF (2 mL) at −78 °C, and the mixture was stirred for 1 h at the same temperature. After addition of finely ground sodium bisulfate monohydrate (0.40 g), the mixture was stirred for 10 min and allowed to heat to room temperature. After the removal of the solids, the resulting solution was extracted with EtOAc. The combined organic extracts were washed with brine, dried, and concentrated. Chromatography of the residue on silica gel (5% EtOAc/hexane) furnished (2*E*,4*E*)-**9** (70. 0 mg, 38%) as colorless needles, and its geometrical (2*Z*,4*E*)-isomer (48.0 mg, 26%) as colorless oil.

(2*E*,4*E*)-9: mp 62−63 °C (colorless needles from Et_2O). IR (neat): ν 1720, 1700, 1590, 1430, 1230, 1160 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.40−7.33 (m, 3H), 7.12 (d, 2H, J = 7.7 Hz), 6.36 (d, 1H, J = 15.2 Hz), 5.86 (s, 1H), 5.59 (dt, 1H, J = 15.2, 6.9 Hz), 3.54 (s, 3H), 1.79 (d, 3H, J = 6.9 Hz). ^{13}C NMR ($CDCl_3$): δ 166.6, 156.0, 137.6, 137.4, 134.8, 128.3, 127.8, 127.6, 117.2, 50.9, 18.5. LRMS (*m*/*z*): 202 (M^+). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.88; H, 7.13.

(2*Z*,4*E*)-Isomer: IR (neat): ν 2950, 1710, 1630, 1590, 1490, 1300, 1160 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.70 (d, 1H, J = 15.7 Hz), 7.37−7.27 (m, 5H), 5.86 (dt, 1H, J = 15.7, 6.7 Hz), 5.67 (s, 1H), 3.75 (s, 3H), 1.88 (d, 3H, J = 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 166.7, 156.5, 140.5, 138.9, 129.0, 128.8, 128.3, 128.1, 115.4, 50.9, 18.8. LRMS (*m*/*z*): 202 (M^+). HRMS (*m*/*z*) calcd for $C_{13}H_{14}O_2$ 202.0993, found 202.0988.

Methyl (2*E*,4*E*)-6-Bromo-3-phenyl-2,4-hexadienoate (10). To a solution of (2*Z*,4*E*)-**9** (66 mg, 327 μmol) in CCl_4 (5 mL) were added NBS (52.0 mg, 294 μmol) and benzoyl peroxide (8.0 mg, 33 μmol) at room temperature, and the mixture was refluxed for 18 h. After concentration of the mixture under reduced pressure, the residue was subjected to silica gel chromatography (5% EtOAc/hexane) to give **10** (24 mg, 50%) as colorless oil. IR (neat): ν 2950, 1710, 1630, 1590, 1430, 1270, 1170 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.91 (d, 1H, J = 15.7 Hz), 7.40−7.26 (m, 5H), 5.97 (dt, 1H, J = 15.7, 7.7 Hz), 5.82 (s, 1H), 4.09 (d, 2H, J = 7.7 Hz), 3.77 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 166.4, 154.4, 139.4, 136.6, 130.0, 128.9, 128.8, 128.4, 118.9, 51.3, 32.2. LRMS (*m*/*z*): 282, 280 (M^+). HRMS (*m*/*z*) calcd for $C_{13}H_{13}{}^{79}BrO_2$ 280.0099, found 280.0116.

2-Iodo-2-propenyl Methanesulfonate (14a). To a solution of 2-iodo-2-propenol[21] (5.40 g, 29.4 mmol) in CH_2Cl_2 (80 mL) were added methanesulfonyl chloride (2.7 mL, 35 mmol) and Et_3N (4.9 mL, 35 mmol) at 0 °C. After being stirred for 2 h at 0 °C, the solution was concentrated and diluted with Et_2O and water. The mixture was extracted with Et_2O, washed with saturated NH_4Cl and brine, dried, and concentrated. Silica gel chromatography of the crude product yielded **14a** (6.82 g, 89%) as colorless oil. IR (neat): ν 3000, 1620, 1610, 1340, 1160, 820 cm^{-1}. ^1H NMR ($CDCl_3$): δ 6.53 (s, 1H), 6.05 (s, 1H), 4.78 (s, 2H), 3.10 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 129.8, 99.3, 75.5, 38.5. LRMS (*m*/*z*): 262 (M^+). HRMS (*m*/*z*): calcd for $C_4H_7IO_3S$ 261.9159, found 261.9140.

***N*-(2-Iodo-2-propenyl)-*p*-toluenesulfonamide (15a).** To a solution of **14a** (2.00 g, 7.64 mmol) and *p*-toluenesulfonamide (13.0 g, 76.4 mmol) in acetone (50 mL) was added K_2CO_3 (1.00 g, 7.64 mmol) at room temperature, and the reaction mixture was refluxed for 18 h. After removal of the solvent, the mixture was extracted with Et_2O, washed with brine, and dried. The residue was purified with column chromatography on silica gel (20% EtOAc/hexane) to give **15a** (1.46 g, 60%) as colorless needles (recrystallized from Et_2O), mp 62−63 °C. IR (neat): ν 3250, 1610, 1590, 1420, 1320, 800, 660 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.76 (d, 2H, J = 8.1 Hz), 7.30 (d, 2H, J = 8.1 Hz), 6.28 (d, 1H, J = 1.8 Hz), 5.74 (d, 1H, J = 1.8 Hz), 5.65 (t, 1H, J = 6.3 Hz), 3.78 (d, 2H, J = 6.3 Hz), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 143.7, 137.0, 129.8, 127.2, 104.8, 54.3, 21.4. LRMS (*m*/*z*): 338 (M^+ + 1), 336 (M^+ − 1). Anal. Calcd for $C_{10}H_{12}INO_2S$: C, 35.61; H, 3.59; N, 4.16. Found: C, 35.92; H, 3.74; N, 4.05.

***N*-(2-Iodo-2-propenyl)-*N*-[(2*E*,4*E*)-5-methoxycarbonyl-4-phenyl-2,4-pentadienyl]-*p*-toluenesulfonamide (4a).** To a solution of **10** (285 mg, 1.01 mmol) and **15a** (341 mg, 1.01 mmol) in acetone (20 mL) was added K_2CO_3 (140 mg, 1.01 mmol) at room temperature, and the reaction mixture was refluxed for 12 h. After concentration of the mixture, which was subjected to silica gel chromatography (10% EtOAc/hexane) to furnish **4a** (456 mg, 84%) as colorless needles (from Et_2O), mp 92−93 °C. IR (neat): ν 2930, 1700, 1580, 1340, 1150 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.70−7.64 (m, 3H), 7.38−7.14 (m, 7H), 6.39 (s, 1H), 5.93 (s, 1H), 5.76 (s, 1H), 5.52 (dt, 1H, J = 15.9, 6.9 Hz), 3.96 (s, 2H), 3.94 (s, 2H), 3.74 (s, 3H), 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 166.5, 154.6, 143.7, 139.4, 136.8, 134.9, 131.5, 129.8, 128.7, 128.5, 128.4, 127.4, 118.2, 105.1, 58.2, 51.3, 49.7, 21.5. LRMS (*m*/*z*): 537 (M^+). Anal. Calcd for $C_{23}H_{24}INO_4S$: C, 51.40; H, 4.50; N, 2.61; I, 23.61; S, 5.97. Found: C, 51.59; H, 4.63; N, 2.46; I, 23.43; S, 6.00.

General Procedure for TBTH and $(TMS)_3SiH$ Method. To a stirred solution of a reaction substrate (52.0 μmol) in degassed benzene or toluene (25 mL) were dropwise added Bu_3SnH (62.4 μmol) or $(TMS)_3SiH$ (62.4 μmol) and AIBN (26.0 μmol) or Et_3B (15.6 μmol) in benzene (4 mL) over 1 or 2 h using a syringe pump under reflux condition. After the mixture stirred under the same temperature for 2 h, the solvent was removed, and the residue was purified by chromatography on silica gel (20% EtOAc/hexane).

General Procedure for Electrolysis. A reaction substrate (40.0 μmol), NH_4ClO_4 (80.0 μmol), and [Ni(cyclam)]$(ClO_4)_2$ (4.0 μmol) were dissolved in DMF (13 mL) containing Et_4NClO_4 (0.1 M in DMF) in a H-shaped divided cell. The solution was electrolyzed potentiostatically using a graphite plate as a cathode at the redox potential of nickel complex at −1.5 V vs SCE at room temperature under inert gas. After the usual workup, the extracts were purified by column chromatography, affording cyclized products.

(1*S,4*S**,6*R**)-4-Methoxycarbonyl-3-phenyl-8-*p*-toluenesulfonyl-8-azabicyclo[4.3.0]non-2-ene (20a).** Colorless needles (recrystallized from Et_2O), mp 176−178 °C. IR (neat): ν 2950, 1730, 1340, 1160, 1090, 660 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, 2H, J = 8.5 Hz), 7.34−7.16 (m, 7H), 5.88 (dd, 1H, J = 4.9, 1.8 Hz), 3.69 (m, 2H), 3.53 (dd, 1H, J = 10.1, 6.7 Hz), 3.38 (s, 3H), 3.13 (dd, 1H, J = 10.1, 1.8 Hz), 3.05 (t, 1H, J = 9.7 Hz), 2.81 (m, 1H), 2.43 (s, 3H), 2.36 (m, 1H), 1.92 (dt, 1H, J = 13.4, 4.9 Hz), 1.54 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.1, 143.4, 140.7, 137.8, 133.7, 129.7, 128.3, 127.5, 127.3, 125.5, 53.1, 51.9, 51.7, 44.6, 38.3, 35.1, 28.6, 21.5. LRMS (*m*/*z*): 411 (M^+). Anal. Calcd for $C_{23}H_{25}NO_4S$: C, 67.13; H, 6.12; N, 3.42; S, 7.79. Found: C, 66.99; H, 6.28; N, 3.36; S, 7.88.

3-[(1*Z*)-3-Methoxycarbonyl-2-phenyl-1-propenyl]-4-methylene-1-*p*-toluenesulfonylpyrrolidine (21a). Colorless oil. IR (neat): ν 2950, 1730, 1590, 1490, 1340, 1160, 810, 660 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.65 (d, 2H, J = 8.0 Hz), 7.33−7.27 (m, 5H), 7.12 (dd, 2H, J = 7.4, 2.2 Hz), 5.25 (d, 1H, J = 9.5 Hz), 4.94 (m, 2H), 3.96 (d, 1H, J = 15.0 Hz), 3.69 (dd, 1H, J = 15.0, 1.9 Hz), 3.60−3.55 (m, 4H), 3.34 (s, 2H), 3.24 (m, 1H), 2.84 (t, 1H, J = 9.5 Hz), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 171.6, 147.4, 143.8, 139.0, 138.2, 132.9, 129.8, 128.6, 128.5, 128.0, 127.8, 127.7, 108.4, 53.4, 51.9, 51.8, 44.2, 43.2, 21.5. LRMS (*m*/*z*): 411 (M^+). HRMS (*m*/*z*): calcd for $C_{23}H_{25}NO_4S$ 411.1503, found 411.1483.

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Supporting Information Available: Detailed experimental section and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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