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Regiochemistry in radical cyclizations (5-*endo* versus 4-*exo*) of *N*-(2-phenylthio- and 2-phenylcyclohex-1-enyl)-α-halo amides

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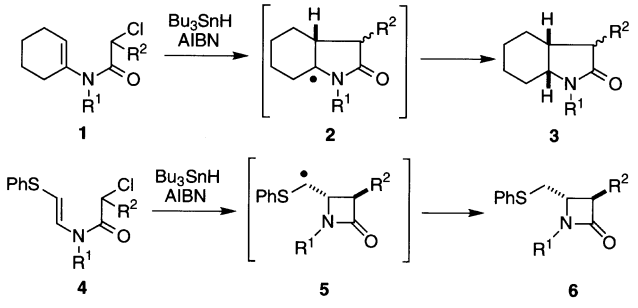
Abstract—Bu_3SnH-mediated radical cyclization of *N*-(2-phenylthiocyclohex-1-enyl)-α-halo amides was examined. Bromoacetamide **9a** having no substituent α to the halogen atom cyclized exclusively in a 4-*exo-trig* manner, whereas the fully substituted haloamides **9c** and **9e** gave 5-*endo-trig* cyclization products. The mono-substituted haloamides **9b** and **9d** showed an intermediate behavior to give a mixture of 4-*exo* and 5-*endo* cyclization products. The results of experiments on the effect of reaction temperature indicated that at a low temperature, i.e. under kinetically controlled conditions, 4-*exo-trig* cyclization predominated. On the other hand, the 2-phenylcyclohex-1-enyl congeners **22b** and **22c** gave exclusively 5-*endo* cyclization products.

1. Introduction

Previous studies in our laboratory have revealed that *N*-(cyclohex-1-enyl)-α-halo amides **1**, upon treatment with Bu_3SnH in the presence of AIBN, undergo radical cyclization in a 5-*endo-trig* manner to give five-membered lactams **3** via the intermediate radicals **2**.[1] α-Halo amides **4** having a phenylthio group at the terminus of their *N*-vinylic bond, however, cyclized in a 4-*exo-trig* manner to give β-lactams **6**.[2] Formation of **6** from **4** may be explained in terms of the high stability of the intermediary sulfur-substituted radicals **5**. As part of our program concerned with regioselection of radical cyclizations, we became interested in the modes of cyclization (5-*endo* versus 4-*exo*) of a series of *N*-(2-phenylthiocyclohex-1-enyl)-α-halo amides **9a–e** and their 2-phenyl congeners **22a–c**. This paper describes the results of our work in this area[3] (Scheme 1).

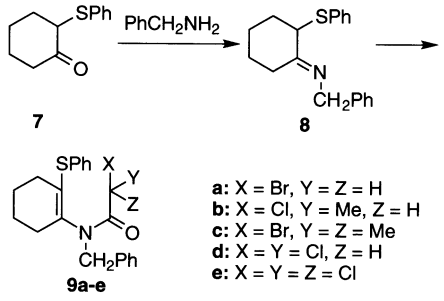


Scheme 1.

2. Results and discussion

2-Phenythio-substituted radical precursors **9a–e** were prepared by condensation of 2-(phenylthio)cyclohexanone (**7**) with benzylamine followed by acylation of the resulting imine **8** with appropriate acyl halides (Scheme 2).

Treatment of α-bromoacetamide **9a** with Bu_3SnH in the presence of AIBN in boiling toluene gave a complex mixture of products, from which the unexpected product



Scheme 2.

Keywords: radicals and radical reactions; azetidinones; lactams; electron transfer.

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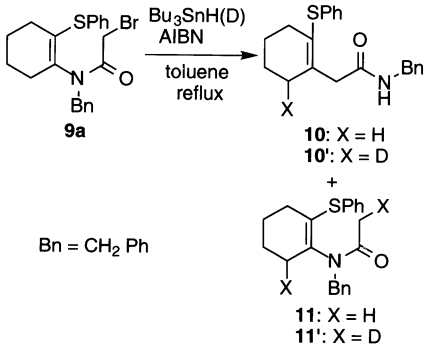
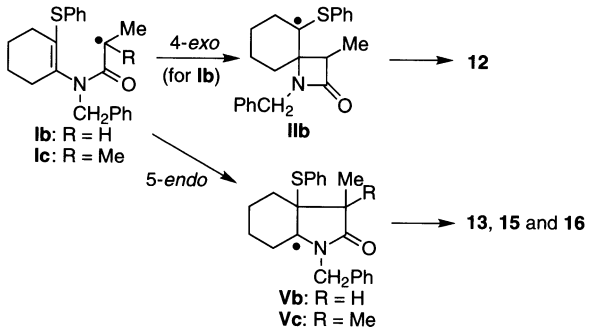


Scheme 3.



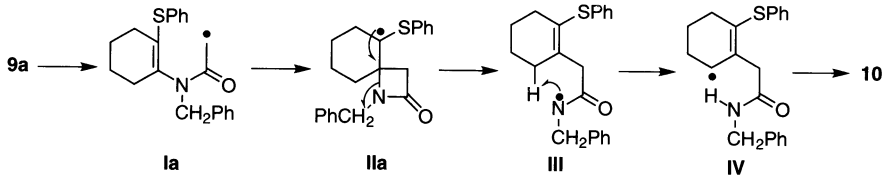
Scheme 6.

10 and simple reduction product **11** were isolated in 16 and 8% yields, respectively (Scheme 3).[†]

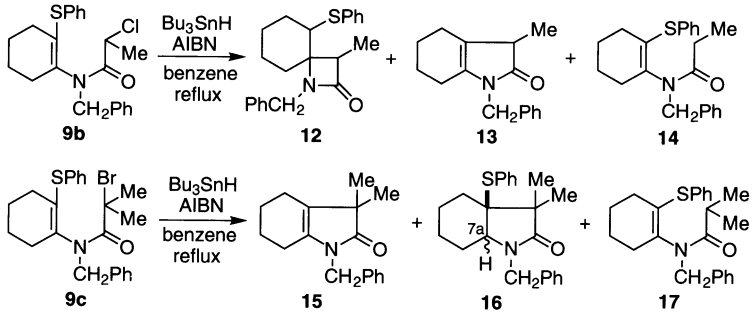
The IR spectrum of **10** showed bands at 3420 and 1660 cm^{-1}, which were clearly indicative of a secondary amide. The ^1H NMR spectrum of **10** exhibited a signal due to the protons α to the carbonyl group at δ 3.40 as a singlet and that due to the benzylic protons at δ 4.39 as a doublet (J=5.6 Hz). When **9a** was treated with Bu_3SnD, the deuterated compound **10′** was obtained as a mixture containing **10** in a ratio of ca. 3:2, together with the deuterated reduction product **11′**. Formation of **10** from **9a** may therefore be explained as outlined in Scheme 4. Thus, the carbamoylmethyl radical **Ia**, formed from **9a**, cyclizes in a 4-*exo-trig* manner to give the sulfur-stabilized radical **IIa**. This step is then followed by a ring-opening to give amidyl radical **III**. A subsequent 1,5-hydrogen shift gives the allylic radical **IV**, which is then trapped by Bu_3SnH to give **10**. A partial, direct attack of Bu_3SnH on **III** also gives **10**.

2-Chloropropanamide **9b** was next treated with Bu_3SnH–AIBN in boiling benzene[‡] to give β-lactam **12** and γ-lactam **13** in 31 and 13% yields, respectively, along with the reduction product **14** (40%) (Scheme 5). On the other hand, 2-bromo-2-methylpropanamide **9c** gave only the five-membered lactams **15** and **16** in 39 and 24% yields, respectively, together with the reduction product **17** (3%).

The structures of **12**, **13**, **15** and **16** were deduced from their spectroscopic evidence. The IR spectrum of **12** showed a band at 1730 cm^{-1} ascribable to β-lactam, and its ^1H NMR spectrum exhibited three doublets (J=7.6 Hz) due to methyl protons at δ 1.31, 1.32 and 1.59, respectively, indicating that compound **12** is a mixture of three diastrereoisomers. On the other hand, the IR spectrum of **13** showed bands at 1700 and 1670 cm^{-1} and the IR spectrum of **15** showed bands at 1700 and 1675 cm^{-1}, and their ^1H NMR spectrum exhibited a signal due to methyl protons of **13** as a doublet (J=7.9 Hz) at δ 1.27 and that due to two methyl protons of **15** as a singlet at δ 1.18. The IR spectrum of **16** showed bands at 1715 and 1675 cm^{-1}, and its ^1H NMR spectrum exhibited signals due to two methyl protons at δ 1.00 and 1.26 as a singlet, respectively, and that due to 7a-H as



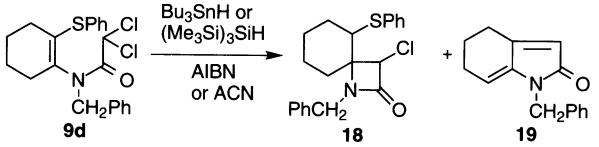
Scheme 4.



Scheme 5.

[†] Another unidentified product was also obtained.

[‡] The reactions of **9b**,**c** in boiling toluene afforded a complex mixture of products.



Scheme 7.

double doublets (J=6.3 and 3.0 Hz) at δ 4.79. However, the exact stereochemistry of the ring-juncture is unknown (probably *cis*).

Formation of **12** from enamide **9b** can be explained simply in terms of an attack of Bu_3SnH on the sulfur-substituted intermediate radical **IIb** formed by a 4-*exo-trig* cyclization of carbamoylmethyl radical **Ib** (Scheme 6). On the other hand, 5-*endo-trig* cyclization of radical **Ib** provides radical **Vb**, which then undergoes an elimination of benzenethiyl radical to give **13**. A similar sequence of the reactions of radical **Vc**, generated from **9c** via **Ic**, gives **15**. An attack of Bu_3SnH on the radical center of **Vc** gives **16**.

The above results suggest that the size of the substituents around the radical center strongly affects the mode of cyclization. Thus, radicals **Ia** (formed from **9a**) and **Ib** (formed from **9b**) having no substituent or a small substituent, cyclizes predominantly in a 4-*exo-trig* manner, whereas radical **Ic** (formed from **9c**) with sterically more-demanding groups, cyclizes exclusively in a 5-*endo-trig* manner to give five-membered lactams **15** and **16**.

Treatment of dichloroacetamide **9d** with Bu_3SnH and AIBN in boiling toluene gave β-lactam **18** and tetrahydroindolone **19** in 18 and 39% yields, respectively, (Scheme 7). The ^1H NMR spectrum of **18** exhibited a signal due to the proton α to the sulfur atom at δ 3.36 as double doublets (J=12.5 and 3.6 Hz) and a signal due to the proton α to the chlorine atom at δ 5.13 as a singlet, indicating that it is a single diastereoisomer, though the exact stereochemistry is unknown. The ^1H NMR spectrum of **19** exhibited signals due to two olefinic protons at δ 5.51 as double triplets (J=4.6 and 1.7 Hz, 7-H) and at δ 5.81 as a broad singlet (3-H), respectively.

Formation of **19** would involve 5-*endo-trig* cyclization of radical **Id** formed from **9d**, leading to the intermediate radical **Vd** (Scheme 8). This step is then followed by an elimination of benzenethiyl radical to give hexahydroindolone **VId**. An attack of tributyltin radical ($Bu_3Sn\cdot$) on the chlorine atom of **VId** followed by a single electron transfer (SET) reaction of the resulting radical **VIId** (or **VIId′**) would give acyliminium ion **VIIId**. A subsequent deprotonation gives the observed **19**. The SET reaction of **VIId** (or **VIId′**) probably occurs toward dichloroacetamide **9d**, which then produces new carbamoylmethyl radical **Id**.[4]

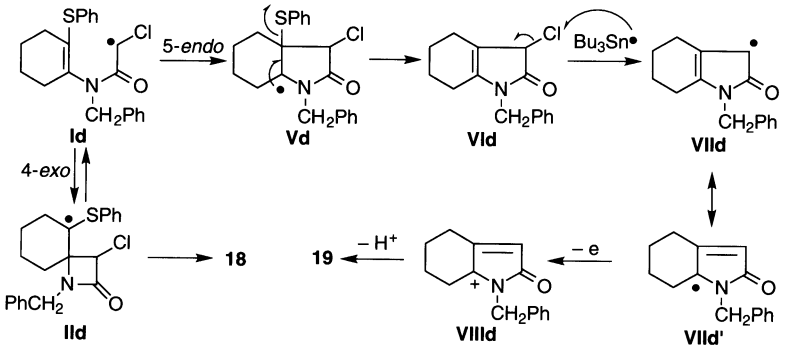
Table 1. Formation of **18** and **19** from **9d**

Entry[a]	Hydride	Solvent	Temperature (°C)	Yield (%)		**18**:**19**
				18	**19**	
1	Bu_3SnH	Toluene	110	18	39	1:2.2
2	Bu_3SnH	Benzene	80	43	35	1.2:1
3	$(Me_3Si)_3SiH$	Toluene	110	19	32	1:1.7
4[b]	$(Me_3Si)_3SiH$	Benzene	80	29	14	2.1:1

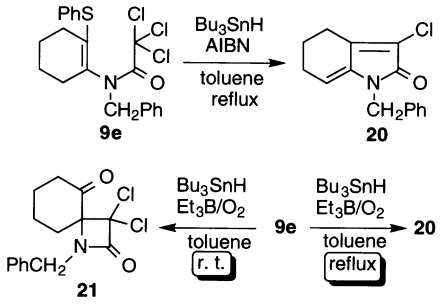
[a] AIBN was used as a radical initiator except for in entry 3 [ACN, azobis(cyclohexanecarbonitrile), was used].
[b] 35% of **9d** was recovered.

Interestingly, when the reaction of **9d** with Bu_3SnH–AIBN was carried out in benzene in place of toluene as a solvent, an increase in the yield of the 4-*exo* cyclization product **18** was observed with a decrease in the amount of the 5-*endo* cyclization product **19** (compare entries 1 and 2 in Table 1). This was also the case for the use of $(Me_3Si)_3SiH$ as a hydride in boiling toluene or benzene (compare entries 3 and 4 in Table 1). These results suggest that the radical cyclization of **9d** at a low temperature (in boiling benzene) occurs preferentially in a 4-*exo-trig* manner, whereas at much higher temperature (in boiling toluene), 5-*endo-trig* cyclization predominates. Strong support for this assumption was obtained by the cyclization of trichloroacetamide **9e**.

Compound **9e**, upon treatment with Bu_3SnH–AIBN in boiling toluene, gave the 5-*endo* cyclization product **20** as a sole product in 84% yield (Scheme 9). On the other hand, when compound **9e** was treated with Bu_3SnH at room temperature using triethylborane as a radical initiator, only β-lactam **21** was obtained in 35% yield along with the recovered **9e** (15%) and its partially dechlorinated product **9d** (10%). The IR spectrum of **21** showed two carbonyl bands at 1790 (β-lactam) and 1725 cm^{-1} (ketone). A similar reaction of **9e** with Bu_3SnH–Et_3B in boiling toluene,



Scheme 8.



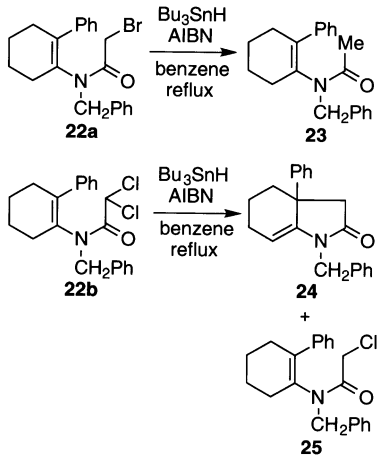
Scheme 9.

however, gave, again, the 5-*endo* cyclization product **20** in 51% yield along with the recovered **9e** (24%).[§]

Compound **20** might arise from the radical intermediate **Ve**, formed by 5-*endo* cyclization of carbamoylmethyl radical **Ie** (Scheme 10), by a sequence of reactions similar to that described above for the formation of **19** from **Vd** (Scheme 8). Formation of **21** may be explained as proceeding via the 4-*exo* cyclization of radical **Ie** followed by an attack of molecular oxygen on the intermediate radical **IIe**. A subsequent reduction of the resulting hydroperoxide **IX** with Bu_3SnH gives ketone **21**.

One possible explanation for the results observed for **9e** may be derived from consideration of the reversibility of 4-*exo* cyclization. At a low temperature, i.e. under kinetically controlled conditions, radical **Ie** cyclizes predominantly in a 4-*exo-trig* manner to give radical **IIe**. However, at a high temperature, ring-opening of radical **IIe** rapidly occurs, and the resulting radical **Ie** cyclizes in a 5-*endo-trig* manner to give radical **Ve**.[5,6] Subsequent elimination of benzenethiyl radical from **Ve** would immediately occur, and hence the 5-*endo* cyclization of **Ie** to **Ve** might be irreversible. This may also be the case for radical **Id** generated from **9d** (Scheme 8). The 4-*exo* cyclization product **18**, however, was formed from **9d** in substantial quantity even at a higher temperature. This is probably because the starting monochloro-substituted radical **Id** is less stable than the dichloro-substituted radical **Ie**, thereby reducing the ability of ring-opening of **IId**–**Id**. This assumption might be applicable to rationalization for the difference between the modes of cyclization of the monomethyl substituted halide **9b** and dimethyl substituted halide **9c**.

Carbon radicals are also stabilized by an adjacent phenyl



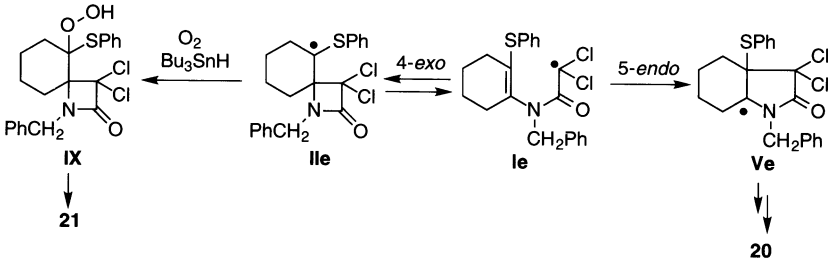
Scheme 11.

group.[7] We therefore turned our attention to the behavior of the reactions of enamide **22a**–**c** having a phenyl group at the 2-position of the *N*-cyclohex-1-enyl group.

When monobromo enamide **22a** was treated with Bu_3SnH–AIBN in boiling benzene, no cyclization product was detected, and only the simple reduction product **23** was obtained in 48% yield (Scheme 11). On the other hand, a similar reaction of dichloro enamide **22b** afforded the 5-*endo* cyclization product **24** and the reduction product **25** in 63 and 29% yields, respectively.

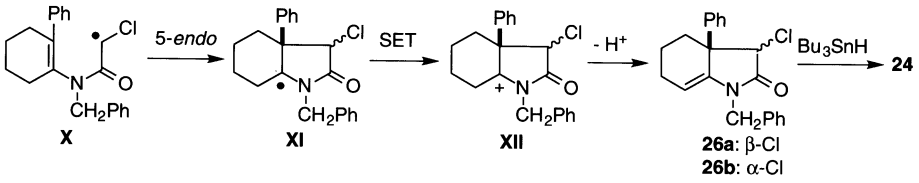
Formation of **24** from **22b** may involve 5-*endo* cyclization of the carbamoylmethyl radical **X** followed by a SET reaction of the resulting radical **XI**, yielding the cation **XII** (Scheme 12). This step is then followed by deprotonation and subsequent reductive dechlorination of the resulting unsaturated lactam **26** with Bu_3SnH to give **24**.

If the above mechanism for the formation of **24** is correct, Bu_3SnH would work mainly for the dechlorination of **26**. We therefore examined a similar reaction using a reduced amount (0.5 equiv.) of Bu_3SnH in the hope that compound **26** would be produced. These conditions, however, resulted in recovery of a large amount (64%) of the starting material **22b**, although a small amount of the expected product **26a** (2% yield) was obtained with the formation of **24** (22% yield) and **25** (6% yield). This result indicates that Bu_3SnH is rapidly consumed for reducing chlorides **26**.



Scheme 10.

[§] Treatment of **9d** with Bu_3SnH in the presence of Et_3B at room temperature resulted in recovery of the starting material.



Scheme 12.

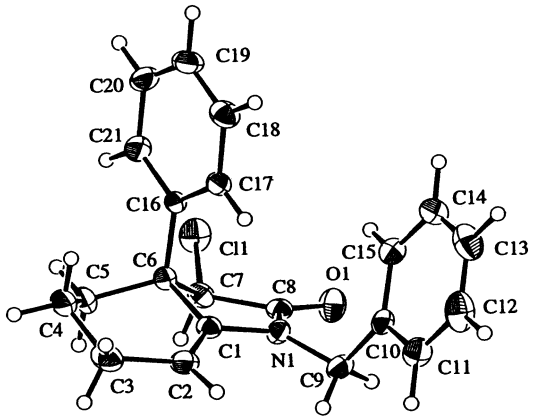


Figure 1. X-Ray structure of compound **26a**.

The structure of **26a** was established by X-ray crystallographic analysis. This compound seems to be an unstable form because the relative stereochemistry between the chlorine atom and the angular phenyl group is a *cis*-relationship. This result can be explained by assuming that the *trans*-isomer **26b** must be also formed in the course of the reaction and that reductive dechlorination of **26b** with Bu_3SnH occurs much faster than does that of **26a**. An Attack of tributyltin radical on the chlorine atom of the *cis*-isomer **26a** must be retarded by the presence of the adjacent angular phenyl group, whereas no remarkable steric hindrance is present in compound **26b** (Fig. 1).

The reaction of trichloroacetamide **22c** with Bu_3SnH–AIBN in boiling benzene gave the 5-*endo* cyclization product **26a** in a high yield (89%) (Scheme 13). Formation of **26a** from **22c** can be considered to proceed via a pathway similar to that described above for **24** from **22b** via radical **X** (Scheme 12). When Bu_3SnH attacks the radical center of **XIII** so as to avoid a steric repulsion between the phenyl group at the 3a-position of **XIII**, this might result in the formation of the observed **26a**.

In order to determine the effect of temperature on the mode of cyclization of **22c**, compound **22c** was next treated with Bu_3SnH at room temperature using triethylborane as a radical initiator. These conditions gave a complex mixture of products, from which 5-*endo* cyclization product **26a** (20%) and its stereoisomer **26b** (7%) and small quantities of the reduction products **22b** and **25** were identified. No 4-*exo* cyclization product was detected in the reaction mixture. No formation of the 4-*exo* cyclization product is probably because the intermediate radical like **IIb** (Scheme 6) is not sufficiently stabilized by an adjacent phenyl group due to free rotation of its aromatic π-system. The reason for the formation of the stereoisomer **26b** together with **26a** at room temperature in the presence of Et_3B is obscure at the moment.

In summary, the results described herein suggest that a 4-*exo* cyclization is essentially a favored process over a 5-*endo* cyclization for the ring-closure of carbamoylmethyl radicals, regardless of the nature of the substituent on the radical center. The product distributions, however, appear to depend on the relative stability between the initial carbamoylmethyl radicals and cyclized intermediate radicals.

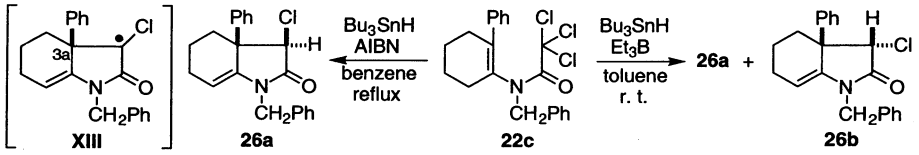
3. Experimental

3.1. General

Melting points are uncorrected. IR spectra were recorded with a Shimadzu FTIR-8100 spectrophotometer for solutions in $CHCl_3$. ^1H NMR spectra were measured on a JEOL JNM-EX 270 spectrometer for solutions in $CDCl_3$. δ Values quoted are relative to tetramethylsilane. High resolution mass spectra (HRMS) were obtained with a JEOL JMS-SX 102 instrument. Column chromatography was performed on Silica gel 60 PF_{254} (Nacalai Tesque) under pressure.

3.2. Preparation of *N*-benzyl-2-halo-*N*-(2-phenylthiocyclohex-1-enyl)acetamides 9a–e

3.2.1. *N*-Benzyl-2-bromo-*N*-(2-phenylthiocyclohex-1-enyl)-acetamide (9a). A mixture of 2-(phenylthio)cyclohexanone (**7**) (1.53 g, 7.42 mmol), benzylamine (662 mg, 6.18 mmol) and a catalytic amount of *p*-toluenesulfonic acid in toluene (70 mL) was heated under reflux with azeotropic removal of water for 4 h. After the solvent had been evaporated off, the residue containing the imine **8** was dissolved in Et_2O (70 mL). DMAP (79 mg, 0.65 mmol) and Et_3N (626 mg, 6.19 mmol) were added to the mixture, and then



Scheme 13.

bromoacetyl bromide (1.39 g, 6.88 mmol) was added slowly to the mixture at 0°C. After the mixture was stirred at room temperature for 15 h, the reaction mixture was washed with water. The organic phase was dried ($MgSO_4$) and concentrated, and the residue was chromatographed on silica gel [hexane–AcOEt (10:1)] to give **9a** (1.74 g, 68%) as an oil: IR ν 1655 cm^{-1}; ^1H NMR δ 1.40–1.66 (m, 4H), 1.87–2.24 (m, 4H), 3.93 (d, J=11.4 Hz, 1H, one of $COCH_2$), 4.08 (d, J=11.4 Hz, 1H, one of $COCH_2$), 4.50 (d, J=14.5 Hz, 1H, one of NCH_2), and 5.05 (d, J=14.5 Hz, 1H, one of NCH_2), 7.19–7.40 (m, 10H). HRMS Calcd for $C_{21}H_{22}{}^{79}BrNOS$: 415.0605. Found: 415.0609.

3.2.2. *N*-Benzyl-2-chloro-*N*-(2-phenylthiocyclohex-1-enyl)-propanamide (9b). Using a procedure similar to that described above for **9a**, the crude imine **8**, prepared from 2-(phenylthio)cyclohexanone (1.48 g, 7.17 mmol) and benzylamine (846 mg, 7.17 mmol), was treated with 2-chloropropionyl chloride (1.0 g, 7.89 mmol) in the presence of DMAP (96 mg, 0.79 mmol) and Et_3N (799 mg, 7.89 mmol). After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)] to give **9b** (1.56 g, 58%) as a mixture of two rotamers in a ratio of 5:1, mp 94–95°C (from hexane–AcOEt): IR ν 1665 cm^{-1}; ^1H NMR δ 1.40–1.66 (m, 4H), 1.71 (d, J=6.4 Hz, 1/6×3H, Me), 1.76 (d, J=6.4 Hz, 5/6×3H, Me), 1.90–2.08 [m, (3+1/6)H], 2.25–2.33 (m, 5/6H), 4.31 (d, J=14.2 Hz, 1/6H, one of NCH_2), 4.46 (d, J=14.2 Hz, 5/6H, one of NCH_2), 4.64 (q, J=6.6 Hz, 1/6H, COCH), 4.74 (q, J=6.6 Hz, 5/6H, COCH), 5.09 (d, J=14.2 Hz, 5/6H, one of NCH_2), 5.36 (d, J=14.2 Hz, 1/6H, one of NCH_2), 7.18–7.38 (m, 10H). Anal. Calcd for $C_{22}H_{24}ClNOS$: C, 68.46; H, 6.27; N, 3.63. Found: C, 68.52; H, 6.27; N, 3.40.

3.2.3. *N*-Benzyl-2-bromo-2-methyl-*N*-(2-phenylthiocyclohex-1-enyl)propanamide (9c). Using a procedure similar to that described above for **9a**, the crude imine **8**, prepared from 2-(phenylthio)cyclohexanone (5.0 g, 24.2 mmol) and benzylamine (1.6 mg, 15.0 mmol), was treated with 2-bromoisobutyryl bromide (4.48 g, 19.5 mmol) in the presence of DMAP (200 mg, 1.64 mmol) and Et_3N (1.66 mg, 16.5 mmol). After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (20:1)] to give **9c** (4.60 g, 69%) as an oil: IR ν 1630 cm^{-1}; ^1H NMR δ 1.20–1.70 (m, 4H), 2.0–2.7 (br, 4H), 2.11 (s, 6H), 4.11 (br, 1/2H, one of NCH_2), 4.80 (br, 1/2H, one of NCH_2), 5.62 (br d, J=14.2 Hz, 1H, one of NCH_2), 7.20–7.50 (m, 10H). HRMS (FAB) Calcd for $C_{23}H_{27}{}^{79}BrNOS$ [$(M+H)^+$]: 444.0997. Found: 444.0969.

3.2.4. *N*-Benzyl-2,2-dichloro-*N*-(2-phenylthiocyclohex-1-enyl)acetamide (9d). Using a procedure similar to that described above for **9a**, the crude imine **8**, prepared from 2-(phenylthio)cyclohexanone (2.99 g, 14.5 mmol) and benzylamine (1.20 g, 11.2 mmol), was treated with dichloroacetyl chloride (2.15 g, 14.6 mmol) in the presence of DMAP (178 mg, 1.46 mmol) and Et_3N (1.48 g, 14.6 mmol). After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)] to give **9d** (1.94 g, 47%), mp 81–82°C (from hexane–AcOEt): IR ν 1680 cm^{-1}; ^1H NMR δ 1.40–1.65 (m, 4H), 1.85–2.20 (m, 4H), 4.51 (d, J=14.2 Hz, 1H, one of NCH_2), 5.09 (d, J=14.2 Hz, 1H, one of NCH_2), 6.41 (s, 1H, COCH), 7.25–7.40 (m, 10H). Anal. Calcd for $C_{21}H_{21}Cl_2NOS$: C, 62.07; H, 5.21; N, 3.45. Found: C, 62.12; H, 5.18; N, 3.45.

3.2.5. *N*-Benzyl-2,2,2-trichloro-*N*-(2-phenylthiocyclohex-1-enyl)acetamide (9e). Using a procedure similar to that described above for **9a**, the crude imine **8**, prepared from 2-(phenylthio)cyclohexanone (2.70 g, 13.1 mmol) and benzylamine (1.0 g, 9.33 mmol), was treated with trichloroacetyl chloride (2.54 g, 14.0 mmol) in the presence of DMAP (113 mg, 0.93 mmol) and Et_3N (1.42 g, 14.0 mmol). After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (5:1)] to give **9e** (1.94 g, 47%), mp 80–81°C (from hexane): IR ν 1675 cm^{-1}; ^1H NMR δ 1.30–1.60 (m, 4H), 1.95–2.1 (m, 4H), 4.93 (br d, J=14.4 Hz, 1H, one of NCH_2), 5.48 (br d, J=14.4 Hz, 1H, one of NCH_2), 7.22–7.52 (m, 10H). Anal. Calcd for $C_{21}H_{20}Cl_3NOS$: C, 57.22; H, 4.57; N, 3.18. Found: C, 57.24; H, 4.55; N, 2.99.

3.3. Radical cyclization of 9a–c

3.3.1. Radical cyclization of 9a with Bu_3SnH–AIBN. General procedure. To a boiling solution of **9a** (289 mg, 0.69 mmol) in toluene (300 mL) was added dropwise a solution of Bu_3SnH (222 mg, 0.76 mmol) and AIBN (37 mg, 0.08 mmol) in toluene (100 mL) via a syringe during 5 h, and the mixture was further heated under reflux for 3 h. After evaporation of the solvent, Et_2O (50 mL) and 8% aqueous KF (20 mL) were added to the residue, and the whole was vigorously stirred at room temperature for 1 h. The organic layer was separated and the aqueous layer was further extracted with Et_2O. The combined organic phase was dried ($MgSO_4$) and concentrated, and the residue was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave *N*-benzyl-2-(2-phenylthiocyclohex-1-enyl)acetamide (**10**) (38 mg, 16%) as an oil: IR ν 3420, 1660 cm^{-1}; ^1H NMR δ 1.54–1.77 (m, 4H), 2.20 (br s, 2H), 2.34 (br s, 2H), 3.40 (s, 2H, $COCH_2$), 4.39 (d, J=5.6 Hz, 2H, NCH_2), 6.00 (br, 1H, NH), 7.11–7.45 (m, 10H). HRMS Calcd for $C_{21}H_{23}NOS$: 337.1501. Found: 337.1501. The second fraction gave *N*-benzyl-*N*-(2-phenylthiocyclohex-1-enyl)acetamide (**11**) (19 mg, 8%) as an oil: IR ν 1645 cm^{-1}; ^1H NMR δ 1.50–1.62 (m, 4H), 1.85–2.20 (m, 4H), 2.11 (s, 3H, COMe), 4.37 (d, J=14.4 Hz, 1H, one of NCH_2), 5.15 (d, J=14.4 Hz, 1H, one of NCH_2), 7.16–7.40 (m, 10H). HRMS Calcd for $C_{21}H_{23}NOS$: 337.1500. Found: 337.1492.

3.3.2. Radical cyclization of 9a with Bu_3SnD–ACN. Following the general procedure, compound **9a** (149 mg, 0.36 mmol) was treated with Bu_3SnD (126 mg, 0.43 mmol) and azobis(cyclohexanecarbonitrile) (ACN) (22 mg, 0.09 mmol) in boiling toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (4:1)]. The first fraction gave a mixture of *N*-benzyl-2-(2-phenylthiocyclohex-1-enyl)acetamide (**10**) and its 2-phenylthio-6-deuterocyclohex-1-enyl derivative **10′** (16 mg) as an oil. The ^1H NMR spectrum of the mixture showed a decrese in an integrated intensity of the peak height of a broad singlet at δ 2.34 due to the 6-position of 2-phenylthiocyclohex-1-enyl group of **10**, which indicated the ratio of **10** and **10′** to be ca. 2:3. The second fraction

gave *N*-benzyl-2-deutero-*N*-(2-phenylthiocyclohex-1-enyl)-acetamide (**11′**) (31 mg) as an oil, whose ^{1}H NMR spectrum indicated that an integrated intensity of the peak height of the signal due to the acetyl methyl protons of **11** at δ 2.11 was reduced to two-thirds.

3.3.3. Radical cyclization of 9b with Bu_3SnH–AIBN. Following the general procedure, compound **9b** (150 mg, 0.39 mmol) was treated with Bu_3SnH (125 mg, 0.43 mmol) and AIBN (20 mg, 0.12 mmol) in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (4:1)]. The first fraction gave *N*-benzyl-*N*-(2-phenylthiocyclohex-1-enyl)-propanamide (**14**) (55 mg, 40%): IR ν 1645 cm^{-1}; ^{1}H NMR δ 1.21 (t, J=7.4 Hz, 3H), 1.40–1.64 (m, 4H), 1.83–2.05 (m, 4H), 2.16–2.32 (m, 1H, one of $COCH_2$), 2.36–2.52 (m, 1H, one of $COCH_2$), 4.35 (d, J=14.3 Hz, 1H, one of NCH_2), 5.20 (d, J=14.3 Hz, 1H, one of NCH_2), 7.20–7.40 (m, 10H). HRMS Calcd for $C_{22}H_{25}NOS$: 351.1657. Found: 351.1653. The second fraction gave 1-benzyl-1,3,4,5,6,7-hexahydro-3-methylindol-2-one (**13**) (12 mg, 13%) as an oil: IR ν 1700, 1670 cm^{-1}; ^{1}H NMR δ 1.27 (d, J=7.9 Hz, 3H, Me), 1.60–1.75 (m, 4H), 1.90–2.15 (m, 4H), 2.83–2.98 (m, 1H, 3-H), 4.62 (s, 2H, NCH_2), 7.15–7.40 (m, 5H). HRMS Calcd for $C_{16}H_{19}NO$: 241.1466. Found: 241.1464. The third fraction gave one isomer of 1-benzyl-3-methyl-5-phenylthio-1-azaspiro[3.5]nonan-2-one (**12**) (20 mg, 15%) as an oil: IR ν 1730 cm^{-1}; ^{1}H NMR δ 1.10–1.80 (m, 7H), 1.32 (d, J=7.6 Hz, 3H, Me), 2.10–2.20 (m, 1H), 3.29 (dd, J=11.9, 3.6 Hz, 1H, 5-H), 3.44 (q, J=7.6 Hz, 1H, 3-H), 3.46 (d, J=15.7 Hz, 1H, one of NCH_2), 4.33 (d, J=15.7 Hz, 1H, one of NCH_2), 7.20–7.45 (m, 10H). HRMS Calcd for $C_{22}H_{25}NOS$: 351.1657. Found: 351.1657. The fourth fraction gave a ca. 1:1 mixture of two stereoisomers of **12** (23 mg, 16%) as an oil: IR ν 1730 cm^{-1}; ^{1}H NMR δ 1.10–1.90 (m, 7H), 1.31 (d, J=7.6 Hz, 1/2×3H), 1.59 (d, J=7.6 Hz, 1/2×3H), 2.10–2.25 (m, 1H), 3.02 (q, J=7.6 Hz, 1/2H, 3-H), 3.08 (q, J=7.6 Hz, 1/2H, 3-H), 3.32 (dd, J=12.2, 4.0 Hz, 1/2H, 5-H), 3.38–3.43 (m, 1/2H, 5-H), 3.66 (d, J=15.5 Hz, 1/2H, one of NH_2), 4.50 (d, J=15.5 Hz, 1/2H, one of NH_2), 4.65 (d, J=15.5 Hz, 1/2H, one of NH_2), 4.81 (d, J=15.5 Hz, 1/2H, one of NH_2), 7.10–7.50 (m, 10H). HRMS Calcd for $C_{22}H_{25}NOS$: 351.1657. Found: 351.1659.

3.3.4. Radical cyclization of 9c with Bu_3SnH–AIBN. Following the general procedure, compound **9c** (186 mg, 0.42 mmol) was treated with Bu_3SnH (134 mg, 0.46 mmol) and AIBN (20 mg, 0.12 mmol) in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave 1-benzyl-octahydro-3,3-dimethyl-3a-(phenylthio)indol-2-one (**16**) 836 mg, 24%) as an oil: IR ν 1715, 1675 cm^{-1}; ^{1}H NMR δ 1.00 (s, 3H, one of Me), 1.26 (s, 3H, one of Me), 1.40–2.10 (m, 7H), 2.35–2.50 (m, 1H), 4.56, 4.65 (AB q, J=15.2 Hz, 2H, NCH_2), 4.79 (dd, J=6.3, 3.0 Hz, 1H, 7a-H), 7.15–7.35 (m, 10H). HRMS Calcd for $C_{23}H_{27}NOS$: 365.1813. Found: 365.1815. The second fraction *N*-benzyl-2-methyl-*N*-(2-phenylthiocyclohex-1-enyl)-propanamide (**17**) (5 mg, 3%) as an oil: IR ν 1650 cm^{-1}; ^{1}H NMR δ 1.17 (d, J=6.6 Hz, 3H, one of Me), 1.25 (d, J=6.6 Hz, 3H, one of Me), 1.45–2.15 (m, 8H), 2.76 (septet, J=6.6 Hz, 1H, COCH), 4.26 (d, J=14.5 Hz, 1H, one of NCH_2), 5.31 (d, J=14.5 Hz, 1H, one of NCH_2), 7.25–7.45 (m, 10H). HRMS Calcd for $C_{23}H_{27}NOS$: 365.1813. Found: 365.1792. The third fraction gave 1-benzyl-1,3,4,5,6,7-hexahydro-3,3-dimethylindol-2-one (**15**)[8] (36 mg, 39%) as an oil: IR ν 1700, 1675 cm^{-1}; ^{1}H NMR δ 1.18 (s, 6H, 2×Me), 1.60–1.70 (m, 4H), 1.90–2.10 (m, 4H), 4.63 (s, 2H, NCH_2), 7.15–7.40 (m, 5H). HRMS Calcd for $C_{17}H_{21}NO$: 255.1623. Found: 255.1623.

3.4. Radical cyclization of 9d

3.4.1. Entry 1 in Table 1. Following the general procedure, compound **9d** (300 mg, 0.74 mmol) was treated with Bu_3SnH (236 mg, 0.81 mmol) and AIBN (40 mg, 0.24 mmol) in boiling toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave 1-benzyl-3-chloro-5-phenylthio-1-azaspiro[3.5]nonan-2-one (**18**) (50 mg, 18%) as a single stereoisomer, mp 110.5–111.5°C (from hexane–AcOEt): IR ν 1760 cm^{-1}; ^{1}H NMR δ 1.10–1.30 (m, 2H), 1.35–1.62 (m, 3H), 1.68–1.80 (m, 1H), 1.85–1.96 (m, 1H), 2.15–2.30 (m, 1H), 3.22 (d, J=15.7 Hz, 1H, one of NCH_2), 3.36 (dd, J=12.5, 3.6 Hz, 1H, 5-H), 4.22 (d, J=15.7 Hz, 1H, one of NCH_2), 5.13 (s, 1H, 3-H), 7.10–7.55 (m, 10H). Anal. Calcd for $C_{21}H_{22}ClNOS$: C, 67.82; H, 5.96; N, 3.77. Found: C, 68.09; H, 6.00; N, 3.73. The second fraction gave 1-benzyl-1,4,5,6-tetrahydro-2*H*-indol-2-one (**19**)[5] (65 mg, 39%), mp 92–92.5°C (from hexane–AcOEt) (lit.[5] mp 94°C): IR ν 1680 cm^{-1}; ^{1}H NMR δ 1.79 (quintet, J=6.2 Hz, 2H, 5-H), 2.26 (q, J=5.5 Hz, 2H, 6-H), 2.63 (td, J=6.4, 1.7 Hz, 2H, 4-H), 4.76 (s, 2H, NCH_2), 5.51 (td, J=4.6, 1.7 Hz, 1H, 7-H), 5.81 (br s, 1H, 3-H), 7.15–7.35 (m, 5H).

3.4.2. Entry 2 in Table 1. Following the general procedure, compound **9d** (153 mg, 0.38 mmol) was treated with Bu_3SnH (131 mg, 0.45 mmol) and AIBN (8 mg, 0.05 mmol) in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave **18** (60 mg, 43%). The second fraction gave **19** (30 mg, 35%).

3.4.3. Entry 3 in Table 1. Following the general procedure, compound **9d** (147 mg, 0.36 mmol) was treated with $(Me_3Si)_3SiH$ (131 mg, 0.45 mmol) and azobis(cyclohexanecarbonitrile) (ACN) (30 mg, 0.12 mmol) in boiling toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave **18** (26 mg, 19%). The second fraction gave **19** (26 mg, 32%).

3.4.4. Entry 4 in Table 1. Following the general procedure, compound **9d** (150 mg, 0.37 mmol) was treated with $(Me_3Si)_3SiH$ (99 mg, 0.40 mmol) and AIBN (20 mg, 0.12 mmol) in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave the recovered **9d** (43 mg, 35%). The second fraction gave **18** (40 mg, 29%). The third fraction gave **19** (12 mg, 14%).

3.5. Radical cyclization of 9e

3.5.1. Radical cyclization of 9e with Bu_3SnH and AIBN in boiling toluene. Following the general procedure,

compound **9e** (200 mg, 0.45 mmol) was treated with Bu_3SnH (173 mg, 0.6 mmol) and AIBN (23 mg, 0.14 mmol) in boiling toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)] to give 1-benzyl-3-chloro-1,4,5,6-tetrahydro-2*H*-indol-2-one (**20**)[4a,8] (99 mg, 84%) as an oil: IR ν 1700 cm^{-1}; ^1H NMR δ 1.81 (quintet, J=6.3 Hz, 2H, 5-H), 2.28 (q, J=5.5 Hz, 2H, 6-H), 2.62 (t, J=6.6 Hz, 2H, 4-H), 4.80 (s, 2H, NCH_2), 5.58 (t, J=4.6 Hz, 1H, 7-H), 7.20–7.25 (m, 5H). HRMS Calcd for $C_{15}H_{14}{}^{35}ClNO$: 259.0764. Found: 259.0758.

3.5.2. Radical cyclization of 9e with Bu_3SnH and Et_3B at room temperature in toluene. To a solution of **9e** (104 mg, 0.24 mmol) and Bu_3SnH (76 mg, 0.26 mmol) in toluene (15 mL) was added Et_3B (1 M solution in hexane) (0.03 mL, 0.03 mmol) at 0°C, and the mixture was stirred at room temperature for 3 h. Stirring was continued for about 2 days with occasional addition of Et_3B. After usual work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave the recovered **9e** (16 mg, 15%). The second fraction gave **9d** (10 mg, 10%), whose spectrospopic data were identical with those described above. The third fraction gave 1-benzyl-3,3-dichloro-1-azaspiro[3.5]nonane-2,5-dione (**21**) (26 mg, 35%) as an oil: IR ν 1790, 1725 cm^{-1}; ^1H NMR δ 1.40–1.90 (m, 4H), 2.00–2.15 (m, 2H), 2.55–2.80 (m, 2H, 6-H_2), 4.21 (d, J=15.5 Hz, 1H, one of NCH_2), 4.97 (d, J=15.5 Hz, 1H, one of NCH_2), 7.15–7.45 (m, 5H). HRMS Calcd for $C_{15}H_{15}{}^{35}Cl_2NO_2$: 311.0479. Found: 311.0458.

3.5.3. Radical cyclization of 9e with Bu_3SnH and Et_3B in boiling toluene. To a boiling solution of **9e** (100 mg, 0.23 mmol) and Bu_3SnH (73 mg, 0.25 mmol) in toluene (15 mL) was added Et_3B (1 M solution in hexane) (0.13 mL, 0.13 mmol), and the mixture was heated under reflux for 10 min. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)]. The first fraction gave the recovered **9e** (24 mg, 24%). The second fraction gave **20** (30 mg, 51%), whose spectrospopic data were identical with those obtained above.

3.6. Preparation of *N*-benzyl-2-halo-*N*-(2-phenylcyclohex-1-enyl)acetamides 22a–c

3.6.1. *N*-Benzyl-2-bromo-*N*-(2-phenylcyclohex-1-enyl)acetamide (22a). Using a procedure similar to that described above for **9a**, 2-phenylcyclohexanone (871 mg, 5.00 mmol) was condenced with benzylamine (540 mg, 5.00 mmol), and the resulting imine was treated with bromoacetyl bromide (1.11 g, 5.50 mmol) in the presence of Et_3N (1.52 g, 15.0 mmol) in toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (10:1)] to give **22a** (452 mg, 24%) as an oil: IR ν 1645 cm^{-1}; ^1H NMR (270 MHz) δ 1.50–2.50 (m, 8H), 3.71 (d, J=11.2 Hz, 1H, one of $COCH_2$), 3.76 (d, J=14.5 Hz, 1H, one of NCH_2), 4.08 (d, J=11.2 Hz, 1H, one of $COCH_2$), 5.16 (d, J=14.5 Hz, 1H, one of NCH_2), 7.06–7.38 (m, 10H). Anal. Calcd for $C_{21}H_{22}BrNO$: C, 65.63; H, 5.77; N, 3.64. Found: C, 65.53; H, 5.82; N, 3.79.

3.6.2. *N*-Benzyl-2,2-dichloro-*N*-(2-phenylcyclohex-1-enyl)acetamide (22b). Using a procedure similar to that described above for **9a**, 2-phenylcyclohexanone (871 mg, 5.00 mmol) was condensed with benzylamine (540 mg, 5.00 mmol), and the resulting imine was treated with dichloroacetyl chloride (0.93 g, 6.39 mmol) in the presence of Et_3N (1.52 g, 15.0 mmol) in toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (20:1)] to give **22b** (1.06 g, 57%): mp 101–103°C (hexane–AcOEt): IR ν 1680 cm^{-1}; ^1H NMR (270 MHz) δ 1.60–2.50 (m, 8H), 3.74 (d, J=14.5 Hz, 1H, one of NCH_2), 5.14 (d, J=14.5 Hz, 1H, one of NCH_2), 6.45 (s, 1H, $CHCl_2$), 7.09–7.37 (m, 10H). Anal. Calcd for $C_{21}H_{21}Cl_2NO$: C, 67.39; H, 5.65; N, 3.74. Found: C, 67.54; H, 5.79; N, 3.73.

3.6.3. *N*-Benzyl-2,2,2-trichloro-*N*-(2-phenylcyclohex-1-enyl)acetamide (22c). Using a procedure similar to that described above for **9a**, 2-phenylcyclohexanone (871 mg, 5.00 mmol) was condensed with benzylamine (540 mg, 5.00 mmol), and the resulting imine was treated with trichloroacetyl chloride (1.00 g, 5.50 mmol)in the presence of Et_3N (1.52 g, 15.0 mmol) in toluene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (20:1)] to give **22c** (1.59 g, 78%): mp 108–109°C (hexane–AcOEt): IR ν 1670 cm^{-1}; ^1H NMR (270 MHz) δ 1.07–2.48 (m, 8H), 3.56 (d, J=14.2 Hz, 1H, one of NCH_2), 5.17 (d, J=14.2 Hz, 1H, one of NCH_2), 7.21–7.41 (m, 10H). Anal. Calcd for $C_{21}H_{20}Cl_3NO$: C, 61.71; H, 4.93; N, 3.43. Found: C, 61.81; H, 4.98; N, 3.49.

3.7. Radical cyclization of 22a–c

3.7.1. Radical cyclization of 22a. Following the general procedure, compound **22a** (192 mg, 0.50 mmol) was treated with Bu_3SnH (189 mg, 0.65 mmol) and AIBN (24.6 mg, 0.15 mmol) during 2 h in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (5:1)] to give *N*-benzyl-*N*-(2-phenylcyclohex-1-enyl)acetamide (**23**) (73.8 mg, 48%) as an oil: IR ν 1630 cm^{-1}; ^1H NMR (270 MHz) δ 1.50–1.72 (m, 6H), 2.11 (s, 3H, COMe), 2.36–2.41 (m, 2H), 3.52 (d, J=14.2 Hz, 1H, one of NCH_2), 5.11 (d, J=14.2 Hz, 1H, one of NCH_2), 7.10–7.33 (m, 10H). Anal. Calcd for $C_{21}H_{23}NO$: C, 82.59; H, 7.59; N, 4.59. Found: C, 82.34; H, 7.74; N, 4.58.

3.7.2. Radical cyclization of 22b. Following the general procedure, compound **22b** (187 mg, 0.50 mmol) was treated with Bu_3SnH (189 mg, 0.65 mmol) and AIBN (24.6 mg, 0.15 mmol) during 2 h in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (8:1)]. The first fraction gave *N*-benzyl-2-chloro-*N*-(2-phenylcyclohex-1-enyl)acetamide (**25**) (48.5 mg, 29%) as an oil: IR ($CHCl_3$) ν 1660 cm^{-1}; ^1H NMR (270 MHz) δ 1.59–2.43 (m, 8H), 3.77 (d, J=14.5 Hz, 1H, one of NCH_2), 3.94 (d, J=12.9 Hz, 1H, one of $COCH_2$), 4.17 (d, J=12.9 Hz, 1H, one of $COCH_2$), 5.15 (d, J=14.5 Hz, 1H, one of NCH_2), 7.05–7.35 (m, 10H). Anal. Calcd for $C_{21}H_{22}ClNO$: C, 74.22; H, 6.52; N, 4.12. Found: C, 73.87; H, 6.57; N, 4.19. The second fraction gave 1-benzyl-1,3,3a,4,5,6-hexahydro-3a-phenylindol-2-one (**24**) (94.9 mg, 63%) as an oil: IR ν 1715, 1680 cm^{-1}; ^1H NMR (270 MHz) δ 0.96–1.15 (m, 1H), 1.45–1.57 (m, 1H), 1.75–1.90 (m, 1H), 2.06–2.13 (m, 2H), 2.24 (dt, J=12.2, 3.6 Hz, 1H), 2.73 (d, J=16.0 Hz, 1H, one of $COCH_2$), 2.86 (d, J=16.0 Hz, 1H, one of $COCH_2$), 4.41 (d, J=15.2 Hz, 1H,

one of NCH_2), 4.93 (d, J=15.2 Hz, 1H, one of NCH_2), 5.14 (t, J=3.6 Hz, 7-H), 7.14–7.34 (m, 10H). HRMS Calcd for $C_{21}H_{21}NO$: 303.1623. Found: 303.1626.

3.7.3. Radical cyclization of 22b with 0.5 equiv. of Bu_3SnH. Following the general procedure, compound **22b** (187 mg, 0.50 mmol) was treated with Bu_3SnH (75.6 mg, 0.26 mmol) and AIBN (8.2 mg, 0.05 mmol) during 2 h in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (20:1→8:1→5:1)]. The first fraction gave **22b** (120 mg, 64%). The second fraction gave **25** (9.5 mg, 6%). The third fraction gave (3R^*,3aS^*)-1-benzyl-3-chloro-1,3,3a,4,5,6-hexahydro-3a-phenylindol-2-one (**26a**) (4.2 mg, 2%): mp 178–180°C (from AcOEt); IR ν 1730, 1685 cm^{-1}; ^1H NMR (270 MHz) δ 1.07–1.23 (m, 1H, one of 5-H), 1.58–1.67 (m, 1H, one of 5-H), 1.77 (td, J=13.4, 3.3 Hz, 1H, one of 6-H), 2.04–2.12 (m, 2H, 4-H), 2.68 (dt, J=13.4, 3.3 Hz, 1H, one of 6-H), 4.62 (d, J=14.7 Hz, 1H, one of NCH_2), 4.65 (s, 1H, CHCl), 4.91 (d, J=14.7 Hz, 1H, one of NCH_2), 5.27 (t, J=3.3 Hz, 1H, 7-H), 6.98–7.42 (m. 10H). Anal. Calcd for $C_{21}H_{20}ClNO$: C, 74.66; H, 5.97; N, 4.15. Found: C, 74.41; H, 5.96; N, 4.13. The fourth fraction gave the starting material **24** (32.9 mg, 22%).

3.7.4. Radical cyclization of 22c in boiling benzene in the presence of AIBN. Following the general procedure, compound **22c** (204 mg, 0.50 mmol) was treated with Bu_3SnH (189 mg, 0.65 mmol) and AIBN (24.6 mg, 0.15 mmol) during 2 h in boiling benzene. After work-up, the crude material was chromatographed on silica gel [hexane–AcOEt (8:1)] to give **26a** (151 mg, 89%).

3.7.5. Radical cyclization of 22c in toluene at room temparature in the presence of Et_3B. Accoring to a procedure similar to that described above for Section 3.5.2, a mixture of compound **22c** (167 mg, 0.41 mmol) and Bu_3SnH (179 mg, 0.62 mmol) in toluene (15 mL) was treated with occasional addition of Et_3B (1 M solution in hexane) (total 0.56 mL, 0.56 mmol) at room temperature for 43 h. After usual work-up, the crude material was chromatographed on silica gel. The first fraction gave **22b** (28 mg, 18%). The second fraction gave (3S^*,3aS^*)-1-benzyl-3-chloro-1,3,3a,4,5,6-hexahydro-3a-phenylindol-2-one (**26b**) (9 mg, 7%): IR ν 1725, 1680 cm^{-1}; ^1H NMR (270 MHz) δ 1.02–1.23 (m, 1H, one of 5-H), 1.52–1.62 (m, 1H, one of 5-H), 2.01–2.15 (m, 3H), 2.28–2.39 (m, 1H), 4.61 (s, 1H, CHCl), 4.65 (d, J=15.2 Hz, 1H, one of NCH_2), 4.81 (d, J=15.2 Hz, 1H, one of NCH_2), 5.34 (t, J=3.6 Hz, 1H, 7-H), 7.00–7.38 (m. 10H). HRMS Calcd for $C_{21}H_{20}{}^{35}ClNO$: 337.1233. Found: 337.1242. The third fraction gave **25** as a mixture of an unidentified product (total 6 mg). The fourth fraction gave **26a** (27 mg, 20%). The fifth fraction gave an unidentified product (27 mg): IR ν 1730, 1680 cm^{-1}.

3.8. Crystal data for compound 26a

$C_{21}H_{20}ClNO$, M=337.85, monoclinic (from AcOEt), space group $P2_1/c$, a=14.183(2), b=7.403(2), c=16.561(3) Å, β=91.42(2)°, V=1738.2(6) $Å^3$, Z=4, μ(MoKα)=2.26 cm^{-1}, $F(000)$=712, D_c=1.291 g cm^{-3}, crystal dimensions: 0.10×0.14×0.20 mm. A total of 4473 reflections (4307 unique) were collected using the ω-2θ scan technique to a maximum 2θ value of 55°, and 1393 reflections with $I>3\sigma(I)$ were used in the structure determination. Final R and Rw values were 0.041 and 0.043, respectively. The maximum and minimum peaks in the difference map were 0.15 and −0.19 e $Å^{-3}$, respectively. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication and the deposition number 167494.

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