Preparation of α-(2,2-Diphenylhydrazino)lactones and Related Compounds by Radical Cyclization: Use of Glyoxylic Acid Hydrazone Derivatives

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Received September 14, 2000

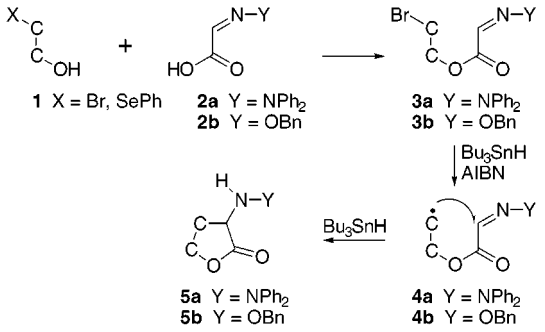
Glyoxylic acid diphenylhydrazone (**2a**) and the corresponding *O*-benzyloxime (**2b**) are easily esterified in high yield by *β*-bromo alcohols. The resulting esters undergo radical cyclization to α-(2,2-diphenylhydrazino)- or α-[(phenylmethoxy)amino]lactones on treatment with tributyltin hydride. Esters for radical cyclization were also made using a *β*-(phenylseleno) alcohol and an enol ether. Several derivatives of glyoxylic acid were evaluated, but none was as effective as **2a** or **2b**. The imine **28** was prepared by an indirect route; it undergoes radical cyclization with displacement of the nitrogen substituent (**28** → **30**) so that an α-amino lactone can be generated by acid hydrolysis of the cyclization product.

A previous report from this laboratory[1] described the preparation of α-(2,2-diphenylhydrazino)- and α-[(phenylmethoxy)amino]lactones **5a** and **5b**, respectively (Scheme 1), by acylation of alcohols (**1** → **3a**,**b**), using reagents **2a** or **2b**, followed by radical cyclization (**3a**,**b** → **4a**,**b** → **5a**,**b**). In subsequent publications, the method was applied to alcohols of the carbohydrate series[2] and was used to synthesize the amino acid antibiotic furanomycin.[3] Here we describe in detail the methodological aspects of the reactions summarized in Scheme 1.

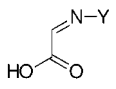
Our studies were undertaken with a view to using radical cyclization methods as a route to α-amino acids. In the event, although the equivalency between α-hydrazino lactones and amino acids was demonstrated,[2,3] the conversion, in the cases we examined,[2,3] was not straightforward.

The cyclization of radicals onto carbon−nitrogen double bonds, especially as in *O*-alkyl oximes[4,5] and diphenylhydrazones,[5−7] is a well-established process, and such imine-like radical acceptors were easily incorporated into reagents that were appropriate for our plans. Thus, glyoxylic acid reacts readily with *N*,*N*-diphenylhydrazine to afford crystalline **2a**, which had actually been reported before[8] but had not been used in radical chemistry. Reagent **2b** was accessible just as easily, using *O*-benzyl hydroxylamine, and was also a known compound;[9] it has seen extensive use in ionic reactions[10] and, recently (in the form of its esters and amides), in radical processes.[11]

Scheme 1



After the preliminary report,[1] we made a number of related reagents (**2c**[12]−**2h**) by the same process of condensation between glyoxylic acid and the appropriate amine derivative. These compounds were prepared so that we could examine the effect of reagent structure on the efficiency of the radical cyclization and on the opportunities for manipulating the hydrazino group in the cyclization products.



2c Y = NMe_2
2d Y = $NHCONH_2$
2e Y = $NHCONMe_2$
2f Y = $N(C_6H_4OMe\text{-}p)_2$
2g Y = N(Ph)COPh
2h Y = $NHCO_2Me$

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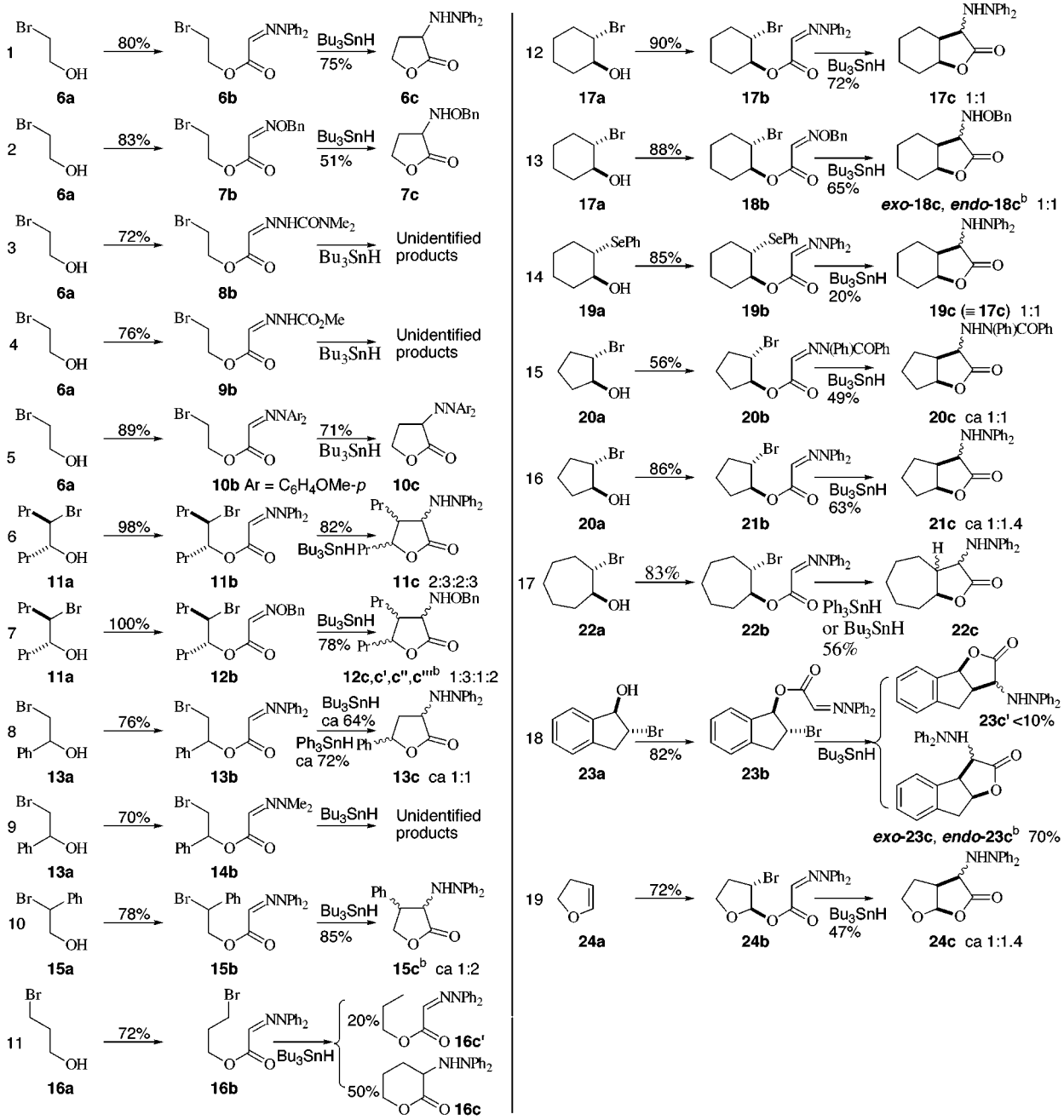
10.1021/jo0013655 CCC: $20.00
Published on Web 01/25/2001

Table 1[a]



[a] Isomer ratios given after compound numbers. [b] The individual isomers were separated.

With **2a** and **2b** in hand—and, later, the other reagents **2c**−**2h**, as well—we prepared the esters listed in Table 1. These were easily made by DCC-mediated coupling of the reagents with *β*-bromo- or *β*-(phenylseleno) alcohols[13] or, in the case of compound **24b**, by adding NBS to a mixture of 4,5-dihydrofuran and reagent **2a**. The semicarbazone reagent **2d** was too insoluble in common solvents (MeCN, DMF, EtOAc, CH_2Cl_2, acetone, sulfolane) for effective coupling with alcohols. For one of the esters (**9b**) we obtained an X-ray crystal structure. The data show that the C=N double bond has the *E* geometry, and all the atoms lie close to a plane, except for the bromine, which is perpendicular to that plane.

The radical cyclizations were conducted by simultaneously adding toluene solutions[16] of Bu_3SnH and AIBN by double syringe pump to a refluxing solution of the substrate in the same solvent. At the end of the addition,

(13) *β*-(Phenylseleno) alcohols are easily made from alkenes: (see ref 14) or epoxides (see ref 15).

(14) For example, see the following: (a) Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1974**, 100. (b) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704−3706.

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(16) We have used PhH in one case (see structure **16a** and footnote †† in ref 1) in order to demonstrate that the reaction works also at the reflux temperature of this solvent. The solvent is incorrectly specified as PhMe in ref 2.

refluxing was continued for an arbitrary period—generally 2−3 h. In a few cases (entries 8 and 17) Ph_3SnH was used but without significant influence on the results.

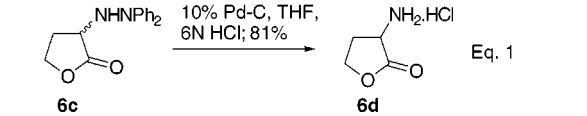
α-Phenylseleno derivatives may be used but, on the basis of limited experience (Table 1, cf. entries 13 and 14), we find that bromides give better results in the radical cyclization.

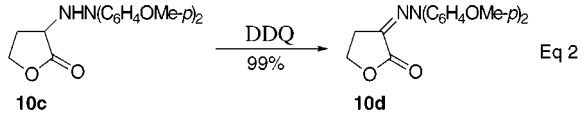
Reagent **2c** coupled smoothly with alcohol **13a**[17] (Table 1, entry 9) but, although dimethylhydrazones[18] and acylgermane dimethylhydrazones[19] cyclize satisfactorily, the radical cyclization step in the present case was not clean and was clearly inefficient; the reagent was not examined further. Bromides **8b** and **9b** gave even more complex mixtures on attempted radical cyclization (entries 3 and 4), and we conclude that glyoxylate-derived C═NNHC(O)NMe_2, C═NNHCO_2Me, and C═$NNMe_2$ groups are unsuitable as radical acceptors.[20]

Where the newly formed ring is produced on an existing cyclic structure, the ring fusion geometry[21] is cis for [3.3.0] and [4.3.0] systems (Table 1, entries 12−16, 18, and 19) but both cis and trans ring fused products are formed in the case of the [5.3.0] bicycle (entry 17). The acyclic starting materials of entries 6, 7, 8, and 10 gave isomer mixtures, and for the cis ring fused products (entries 12−19) both epimers at the position α to the carbonyl were obtained with little, if any, selectivity. In four cases (**12c**, **12c′**, **12c″**, **12c‴**; **15c**, ***exo*-18c**, ***endo*-18c**; ***exo*-23c**, ***endo*-23c**) the individual isomers could be separated, and tentative stereochemical assignments were made (except for **15c**) on the basis of NOE experiments (see Experimental Section).

Bromide **23b** gave two types of product: two isomers, tentatively identified as **23c′**, resulting from the typical cyclization, and another pair of isomers (***exo*-23c**, ***endo*-23c**) that are formed by 1,2-acyloxy migration[22] of the initial radical. The rearrangement affords a benzylic radical and is evidently faster than cyclization, since ***exo*/*endo*-23c** is the major product.

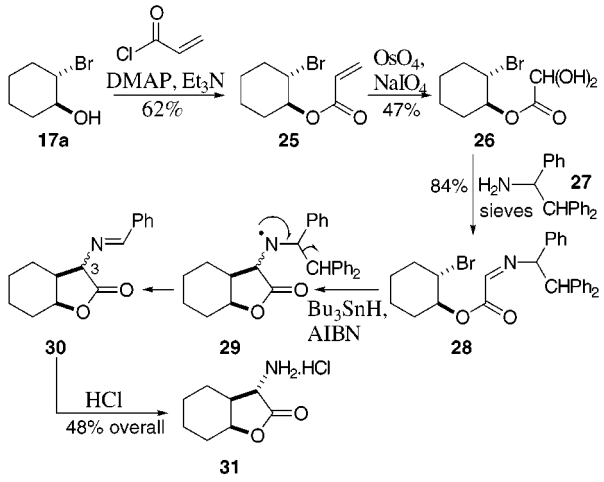
We have examined briefly various modifications to the α-hydrazino lactones[23] produced by the radical cyclization. Hydrogenation in an acidic medium served to convert **6c** into the corresponding α-amino lactone, which was trapped and isolated as the hydrochloride salt **6d** (eq 1). We also treated **10c** with DDQ (eq 2); however,





desaturation occurred more rapidly than oxidative removal of the *p*-methoxybenzene groups so that the α-hydrazono lactone (**10d**), rather than the product of simple de-arylation, was isolated.

Scheme 2



As a potential method of generating α-amino lactones by a route that does not involve hydrogenolysis (cf. **6c** → **6d**), we also examined the imino ester **28** (Scheme 2), which is so constituted that the initial radical cyclization product (see **29**) could lead directly to an imine (**29** → **30**) which would be expected to undergo easy hydrolysis. The required ester (**28**) was prepared in several straightforward steps, summarized in Scheme 2 (**17a** → **25** → **26** → **28**). In the event, bromide **28** behaved as expected and underwent radical cyclization to imines **30**, which were hydrolyzed to the desired α-amino lactone **31**, whose stereochemistry at C(3) was tentatively assigned as shown. Although **31** was obtained as a single isomer (after recrystallization), we assume, by analogy with our other results, that the precursor (**30**) was a mixture of C(3) epimers. We did not attempt to generalize the cyclization/hydrolysis process, however, as we were unable to prepare a reagent (comparable to **2a**) from **27** and glyoxylic acid; such a reagent would have given access to esters of type **28** in a single step by coupling with bromo alcohols.

Conclusion

Of the glyoxylic acid derivatives we have examined, the *N*,*N*-diphenylhydrazone appears to be the best, in terms of performance and ease of preparation, and the methodology summarized in Scheme 1 represents an easy route to α-hydrazino lactones. As illustrated in other work from this laboratory,[2,3] such compounds can be transformed into unusual amino acid derivatives. The *O*-benzyl oxime derivatives also cyclized satisfactorily. With one of the *N*,*N*-diphenylhydrazones we encountered a competing acyloxy radical rearrangement, which was facilitated by formation of a benzylic radical. We have also demonstrated an example of an unusual radical displacement (Scheme 2).[24]

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Experimental Section

General Procedures. Unless stated to the contrary, the general experimental procedures used previously[25] were followed. The symbols s′, d′, t′, and q′ used for ^{13}C NMR signals indicate zero, one, two, and three attached hydrogens, respectively. The ^{13}C signals for **C**H=N of the cyclization substrates were often not visible in APT spectra, but were observed in the broad band proton decoupled spectra.

(Diphenylhydrazono)acetic Acid (2a). This procedure differs from that reported[8] in the literature. Glyoxylic acid monohydrate (5.52 g, 60.0 mmol) was added to a stirred solution of commercial Ph_2NNH_2·HCl (13.2 g, 60.0 mmol) in water (720 mL). Stirring was continued for 2 h, and the precipitate was filtered off, washed with water, and dried under oil-pump vacuum to afford **2a** (13.9 g, 96%) as a gray powder: mp 201−203 °C (lit.[8] 200−202 °C); ^1H NMR (CD_2Cl_2, 300 MHz) δ 6.45 (s, 1 H), 7.15−7.25 (m, 4 H), 7.25−7.40 (m, 2 H), 7.40−7.55 (m, 4 H), 8.60−10.3 (br, 1 H).

[Di(4-Methoxyphenyl)hydrazono]acetic Acid (2f). Glyoxylic acid (0.8308 g, 9.025 mmol) was added to a stirred solution of **16** (2.2034 g, 9.025 mmol) in MeOH (15.0 mL), and stirring was continued overnight. Evaporation of the solvent and flash chromatography of the residue over silica gel (4 cm × 32 cm), using 60% EtOAc−hexane, gave **2f** (2.3901 g, 88%) as a crystalline solid.

Benzoylphenylhydrazonoacetic Acid (2g). Glyoxylic acid monohydrate (1.45 g, 20.0 mmol) was added to a magnetically stirred solution of N^1-benzoylphenylhydrazine hydrochloride[26] (5.0 g, 20.0 mmol) in water (300 mL). An extremely sticky residue was formed within 10 min of the addition, so the magnetic stirrer was replaced by a mechanical stirrer. After 12 h, the mixture was filtered to obtain **2g** (4.2759 g, 79%) as a crystalline solid.

General Procedure for Coupling of Alcohols with Reagents 2a or 2b. Glyoxylic acid diphenylhydrazone (**2a**) or glyoxylic acid *O*-benzyloxime (**2b**) (1.2 equiv) was added to a stirred mixture of the alcohol (1.0 equiv), DCC (1.32 equiv), and DMAP (0.12 equiv) in dry CH_2Cl_2. Stirring was continued for 12 h, and the mixture was then filtered. The insoluble material was washed with dry CH_2Cl_2 and the combined filtrates were evaporated to give a residue which was processed as described for the individual experiments.

2-Bromoethyl (Diphenylhydrazono)acetate (6b). The general procedure for coupling alcohols with **2a** was followed, using **2a** (1.21 g, 5.00 mmol), alcohol **6a** (0.685 g, 5.50 mmol), DCC (1.14 g, 5.50 mmol), and DMAP (61.0 mg, 0.50 mmol) in CH_2Cl_2 (25 mL). Flash chromatography of the residue over silica gel (3 cm × 30 cm), using 10% EtOAc−hexane, gave **6b** (1.39 g, 80%) as a crystalline solid: mp 102−104 °C; FTIR (CH_2Cl_2 cast) 1730, 1705, 1590, 1552 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.57 (t, J = 6.3 Hz, 2 H), 4.52 (t, J = 6.3 Hz, 2 H), 6.50 (s, 1 H), 7.15−7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 28.5 (t′), 63.8 (t′), 123.0 (d′), 126.2 (d′), 129.9 (d′), 141.9 (s′), 164.0 (s′); exact mass *m*/*z* calcd for $C_{16}H_{15}{}^{79}BrN_2O_2$ 346.0317, found 346.0326.

2-Bromoethyl [(Phenylmethoxy)imino]acetate (7b). The general procedure for coupling alcohols with **2b** was followed, using **2b** (1.790 g, 10.00 mmol), alcohol **6a** (1.370 g, 11.00 mmol), DCC (2.270 g, 11.00 mmol), and DMAP (122 mg, 1.00 mmol) in CH_2Cl_2 (50 mL). Flash chromatography of the residue over silica gel (4 cm × 30 cm), using 10% EtOAc−hexane, gave **7b** (2.371 g, 83%) as a pale yellow oil: FTIR (CH_2Cl_2 cast) 1727, 1598, 1497 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.57 (t, J = 6.3 Hz, 2 H), 4.56 (t, J = 6.3 Hz, 2 H), 5.32 (s, 2 H), 7.32−7.40 (m, 5 H), 7.58 (s, 1 H); ^{13}C NMR (CD_2Cl_2, 50.3 MHz) δ 28.8 (t′), 64.9 (t′), 78.2 (t′), 128.4 (d′), 128.7 (d′), 128.8 (d′), 136.6 (s′), 141.1 (d′), 161.5 (s′); exact mass *m*/*z* calcd for $C_{11}H_{12}{}^{81}BrNO_3$ 286.9980, found 286.9976.

2-Bromoethyl [Di(4-Methoxyphenyl)hydrazono]acetate (10b). The general procedure for coupling alcohols with **2a** was followed, using **2f** (2.321 g, 7.73 mmol), alcohol **6a** (1.0384 g, 8.50 mmol), DCC (1.7538 g, 8.50 mol), and DMAP (0.0944 g, 0.773 mmol) in CH_2Cl_2 (15 mL). Flash chromatography of the crude product over silica gel (4 cm × 32 cm), using 10% EtOAc−hexane, gave **10b** (2.7981 g, 89%) as a crystalline solid.

(*R,*R**)-2-Bromo-1-propylpentyl (Diphenylhydrazono)acetate (11b).** The general procedure for coupling alcohols with **2a** was followed, using **2a** (1.60 g, 6.67 mmol), alcohol **11a**[27] (930 mg, 4.45 mmol), DCC (1.38 g, 6.67 mmol), and DMAP (81 mg, 0.67 mmol) in CH_2Cl_2 (25 mL). Flash chromatography of the residue over silica gel (3 cm × 22 cm), using 5% EtOAc−hexane, gave **11b** (1.88 g, 98%) as a pale yellow oil.

(*R,*R**)-2-Bromo-1-propylpentyl [(Phenylmethoxy)imino]acetate (12b).** The general procedure for coupling alcohols with **2b** was followed, using **2a** (0.895 g, 5.00 mmol), alcohol **11a**[27] (1.15 g, 5.50 mmol), DCC (1.14 g, 5.50 mmol), and DMAP (61.0 mg, 0.50 mmol) in CH_2Cl_2 (25 mL). Flash chromatography of the residue over silica gel (3 cm × 30 cm), using 10% EtOAc−hexane, gave **12b** (1.85 g, 100%) as a colorless oil: FTIR (CH_2Cl_2 cast) 1744, 1722, 1597, 1497 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.90−0.98 (m, 6 H), 1.30−1.50 (m, 3 H), 1.57−1.87 (m, 5 H), 4.05−4.11 (m, 1 H), 5.15−5.20 (m, 1 H), 5.33 (s, 2 H), 7.30−7.44 (m, 5 H), 7.60 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 13.3 (q′), 13.7 (q′), 18.6 (t′), 20.9 (t′), 34.0 (t′), 36.8 (t′), 56.5 (d′), 76.3 (d′), 78.2 (t′), 128.5 (d′), 128.7 (d′), 135.9 (s′), 140.7 (d′), 161.3 (s′); exact mass *m*/*z* calcd for $C_{17}H_{24}{}^{81}BrNO_3$ 371.0919, found 371.0917.

2-Bromo-1-phenylethyl (Diphenylhydrazono)acetate (13b). The general procedure for coupling alcohols with **2a** was followed, using **2a** (265.5 mg, 1.106 mmol), alcohol **13a**[17] (244.7 g, 1.217 mmol), DCC (251.1 mg, 1.217 mmol), and DMAP (13.6 mg, 0.111 mmol) in CH_2Cl_2 (5.5 mL). Flash Chromatography of the residue over silica gel (1.7 cm × 35 cm), using first 20% EtOAc−hexane, and then 30% EtOAc−hexane, gave **13b** (357.1 mg, 76%) as a yellow oil.

2-Bromo-2-phenylethyl (Diphenylhydrazono)acetate (15b). The general procedure for coupling alcohols with **2a** was followed, using **2a** (281.4 mg, 1.172 mmol), alcohol **15a**[28] (259.2 mg, 1.290 mmol), DCC (266.1 mg, 1.290 mmol), and DMAP (14.3 mg, 0.117 mmol) in CH_2Cl_2 (5.9 mL). Flash Chromatography of the residue over silica gel (1.7 cm × 35 cm), using 20% EtOAc−hexane, and rechromatography, using 10% EtOAc−hexane, gave **15b** (387.0 mg, 78%) as a colorless solid.

A portion was recrystallized from MeOH (32% recovery): mp 105−107 °C.

3-Bromopropyl (Diphenylhydrazono)acetate (16b). The general procedure for coupling alcohols with **2a** was followed, using **2a** (1.21 g, 5.00 mmol), alcohol **16a** (497 μL, 5.50 mmol), DCC (1.14 g, 5.50 mmol), and DMAP (61 mg, 0.50 mmol) in CH_2Cl_2 (25 mL). Flash chromatography of the residue over silica gel (3 cm × 30 cm), using 10% EtOAc−hexane, gave **16b** (1.30 g, 72%) as a pale yellow oil: FTIR (CH_2Cl_2 cast) 1729, 1703, 1589, 1552, 1493 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.26 (quintet, J = 6.3 Hz, 2 H), 3.52 (t, J = 6.6 Hz, 2 H), 4.36 (t, J = 6.0 Hz, 2 H), 6.47 (s, 1 H), 7.16−7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 29.4 (t′), 31.5 (t′), 62.0 (t′), 122.1 (d′), 123.4 (d′), 125.9 (d′), 129.8 (d′), 141.8 (s′), 164.1 (s′); exact mass *m*/*z* calcd for $C_{17}H_{17}{}^{79}BrN_2O_2$ 360.0473, found 360.0475.

***trans*-2-Bromocyclohexyl (Diphenylhydrazono)acetate (17b).** The general procedure for coupling alcohols with

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2a was followed, using **2a** (1.21 g, 5.00 mmol), alcohol **17a**[29] (0.895 g, 5.00 mmol), DCC (1.14 g, 5.50 mmol), and DMAP (61 mg, 0.50 mmol) in CH_2Cl_2 (25 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using 5% EtOAc−hexane, gave **17b** (1.80 g, 90%) as a pale yellow oil: FTIR (CH_2Cl_2 cast) 1728, 1702, 1590, 1552, 1494 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22−1.54 (m, 3 H), 1.67−2.00 (m, 3 H), 2.12−2.27 (m, 1 H), 2.30−2.42 (m, 1 H), 4.01−4.10 (m, 1 H), 5.00−5.10 (m, 1 H), 6.50 (s, 1 H), 7.14−7.50 (m, 10 H); ^{13}C NMR (CD_2Cl_2, 50.3 MHz) δ 23.7 (t′), 25.9 (t′), 31.6 (t′), 36.1 (t′), 53.6 (d′), 76.3 (d′), 122.7 (d′), 124.3 (d′), 126.5 (d′), 130.4 (d′), 142.6 (s′), 163.7 (s′); exact mass *m*/*z* calcd for $C_{20}H_{21}{}^{79}BrN_2O_2$ 400.0786, found 400.0786.

***trans*-2-Bromocyclohexyl [(Phenylmethoxy)imino]-acetate (18b).** The general procedure for coupling alcohols with **2b** was followed, using **2b** (0.895 g, 5.00 mmol), alcohol **17a**[29] (0.970 g, 5.42 mmol), DCC (1.14 g, 5.50 mmol), and DMAP (61 mg, 0.50 mmol) in CH_2Cl_2 (25 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using 3% EtOAc−hexane, gave **18b** (1.50 g, 88%) as a colorless oil: FTIR (CH_2Cl_2 cast) 1744, 1724, 1598, 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.25−1.52 (m, 3 H), 1.70−1.95 (m, 3 H), 2.12−2.23 (m, 1 H), 2.33−2.41 (m, 1 H), 4.02−4.09 (m, 1 H), 5.03−5.10 (m, 1 H), 5.33 (s, 2 H), 7.33−7.45 (m, 5 H), 7.57 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 23.3 (t′), 25.5 (t′), 31.1 (t′), 35.6 (t′), 52.2 (d′), 77.1 (d′), 78.2 (t′), 128.5 (d′), 128.6 (d′), 128.7 (d′), 136.0 (s′), 141.0 (d′), 160.9 (s′); exact mass *m*/*z* calcd for $C_{15}H_{18}{}^{81}BrNO_3$ 341.0450, found 341.0453.

***trans*-2-(Phenylseleno)cyclohexyl (Diphenylhydrazono)-acetate (19b).** The general procedure for coupling alcohols with **2a** was followed, using **2a** (1.77 g, 7.37 mmol), alcohol **19a**[30] (2.06 g, 8.11 mmol), DCC (1.68 g, 8.11 mmol), and DMAP (89 mg, 0.74 mmol) in CH_2Cl_2 (40 mL). Flash chromatography of the residue over silica gel (4 cm × 30 cm), using 5% EtOAc−hexane, gave **19b** (2.99 g, 85%) as a pale yellow, viscous oil.

***trans*-2-Bromocyclopentyl [Benzoylphenylhydrazono]-acetate (20b).** The general procedure for coupling alcohols with **2a** was followed, using **2g** (0.192 g, 0.72 mmol), alcohol **20a**[31] (0.13 g, 0.78 mmol), DCC (0.162 g, 0.79 mmol), and DMAP (0.010 g, 0.08 mmol) in CH_2Cl_2 (30.0 mL). Flash chromatography of the crude product over silica gel (1.7 cm × 30 cm), using 2.5% MeOH−CH_2Cl_2, gave **20b** (0.1653 g, 56%) as an oil.

***trans*-2-Bromocyclopentyl (Diphenylhydrazono)acetate (21b).** The general procedure for coupling alcohols with **2a** was followed, using **2a** (667.0 mg, 2.76 mmol), alcohol **20a**[31] (500.0 mg, 3.0 mmol), DCC (800.0 mg, 3.0 mmol), and DMAP (37.0 mg, 0.30 mmol) in CH_2Cl_2 (10 mL). Flash chromatography of the crude product over silica gel (1.7 cm × 30 cm), using 10% EtOAc−hexane, gave **21b** (914.0 mg, 86%) as an oil: FTIR ($CHCl_3$ cast) 1727, 1701, 1667, 1651, 1551 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.50−2.53 (m, 6 H), 4.2−4.4 (m, 1 H), 5.3−5.6 (m, 1 H), 6.45 (s, 1 H), 6.91−7.72 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) (several expected signals were not observed) δ 21.8 (t′), 29.6 (t′), 34.7 (t′), 53.1 (d′), 82.4 (d′), 123.6 (d′), 130.0 (t′), 163.8 (s′); exact mass *m*/*z* calcd for $C_{19}H_{19}{}^{81}BrN_2O_2$ 388.0609, found 388.0609.

***trans*-2-Bromocycloheptyl (Diphenylhydrazono)acetate (22b).** The general procedure for coupling alcohols with **2a** was followed, using **2a** (168 mg, 0.070 mmol), alcohol **22a**[32] (150 mg, 0.77 mmol), DCC (158 mg, 0.77 mmol), and DMAP (8.5 mg, 0.07 mmol) in CH_2Cl_2 (5 mL). Flash chromatography of the crude product over silica gel (1.7 cm × 35 cm), using 10% EtOAc−hexane, gave **22b** (243.0 mg, 83%) as a light yellow oil: FTIR (CH_2Cl_2 cast) 1726, 1700, 1590, 1493, 1457 cm^{-1}; ^1H NMR (CD_2Cl_2, 300 MHz) δ 1.52−1.90 (m, 7 H), 1.92−2.21 (m, 2 H), 2.22−2.40 (m, 1 H), 4.31 (dt, J = 7.9, 3.7 Hz, 1 H), 5.3 (dt, J = 7.8, 3.2 Hz, 1 H), 6.53 (s, 1 H), 7.18−7.52 (m, 10 H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz) δ 22.6 (t′), 24.9 (t′), 27.9 (t′), 31.3 (t′), 35.2 (t′), 57.2 (d′), 80.3 (d′), 122.7 (d′), 124.3 (d′), 126.5 (d′), 130.3 (d′), 142.5 (s′), 163.5 (s′); exact mass *m*/*z* calcd for $C_{21}H_{23}{}^{81}BrN_2O_2$ 416.09225, found 416.09179.

***trans*-2-Bromo-2,3-dihydro-1*H*-inden-1-yl (Diphenylhydrazono)acetate (23b).** The general procedure for coupling alcohols with **2a** was followed, using **2a** (1.21 g, 5.00 mmol), alcohol **23a** (1.17 g, 5.50 mmol), DCC (1.14 g, 5.50 mmol), and DMAP (61 mg, 0.50 mmol) in CH_2Cl_2 (25 mL). After evaporation of the solvent, MeOH (10 mL) was added to the residue. The resulting precipitate was filtered off and washed with MeOH to give **23b** (1.80 g, 82%) as a crystalline solid: mp 159−161 °C; FTIR (CH_2Cl_2 cast) 1728, 1701, 1589, 1549, 1487, 1458 cm^{-1}; ^1H NMR (CD_2Cl_2, 360 MHz) δ 3.29 (dd, J = 17.1, 3.9 Hz, 1 H), 3.75 (dd, J = 17.1, 6.5 Hz, 1 H), 4.58−4.62 (m, 1 H), 6.43 (d, J = 3.2 Hz, 1 H), 6.48 (s, 1 H), 7.12−7.50 (m, 14 H); ^{13}C NMR (CD_2Cl_2, 50.3 MHz) δ 41.9 (t′), 50.8 (d′), 84.2 (d′), 122.8 (d′), 123.7 (d′), 125.3 (d′), 126.4 (d′), 126.6 (d′), 127.9 (d′), 130.1 (d′), 130.4 (d′), 138.8 (s′), 142.0 (s′), 164.0 (s′); exact mass *m*/*z* calcd for $C_{23}H_{19}{}^{81}BrN_2O_2$ 436.0609, found 436.0609.

***trans*-3-Bromotetrahydrofuran-2-yl (Diphenylhydrazono)acetate (24b).** NBS (1.48 g, 8.3 mmol) was added to a cooled (−15 °C, ice−salt) and stirred solution of dihydrofuran (**24a**) (0.5287 g, 7.54 mmol) and **2a** (1.99 g, 8.3 mmol) in THF (10 mL). The mixture was stirred for 2 h and then stored at −5 °C overnight. Evaporation of the solvent and flash chromatography of the residue over silica gel (1.7 cm × 34 cm), using 15% EtOAc−hexane, gave **24b** (2.12 g, 72%) as a foam: FTIR (CH_2Cl_2 cast) 1708, 1590, 1548, 1487, 1458 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 2.23−2.41 (m, 1 H), 2.61−2.81 (m, 1 H), 4.19−4.4 (m, 2 H), 4.42 (d, J = 5.4 Hz, 1 H), 6.43−6.57 (m, 2 H), 7.03−7.61 (m, 10 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) (several expected signals were not observed) δ 33.0 (t′), 44.9 (d′), 68.1 (t′), 96.2 (d′), 123.6 (d′), 130.5 (d′), 163.6 (s′); exact mass *m*/*z* calcd for $C_{18}H_{17}{}^{79}BrN_2O_3$ 388.0422, found 388.0422. The trans stereochemistry is assigned on the basis of mechanistic considerations and the value of the coupling constant for the OC**H**O proton (J = 5.4 Hz).

General Procedure for Radical Cyclization. The substrate was placed in a round bottom flask equipped with a Teflon-coated stirring bar and a reflux condenser sealed with a rubber septum. The system was flushed with Ar for 5−10 min, and dry PhMe was injected into the flask. The flask was placed in an oil bath preheated to 110 °C, and individual solutions of Bu_3SnH and AIBN in PhMe were injected simultaneously by syringe pump over 10 h. Refluxing was continued for an arbitrary period of 1−4 h after the addition. The reaction mixture was cooled, and the solvent was evaporated to give a residue which was processed as described for the individual experiments.

3-(2,2-Diphenylhydrazino)dihydro-2(3*H*)-furanone (6c). The general procedure for radical cyclization was followed, using **6b** (0.400 g, 1.15 mmol) in PhMe (70 mL), Bu_3SnH (500 μL, 1.86 mmol) in PhMe (10 mL), and AIBN (20 mg, 0.12 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using first 5% EtOAc−hexane (500 mL) and then 10% EtOAc−hexane, gave **6c** (234 mg, 75%) as a crystalline solid: mp 92−93 °C; FTIR (CH_2Cl_2 cast) 1774 cm^{-1}; ^1H NMR (CD_2Cl_2, 300 MHz) δ 2.30−2.53 (m, 2 H), 3.84−3.92 (m, 1 H), 4.14−4.24 (m, 1 H), 4.46 (td, J = 8.7, 3.2 Hz, 1 H), 4.70 (s, 1 H), 7.03−7.40 (m, 10 H), ^{13}C NMR (CD_2Cl_2, 75.5 MHz) δ 29.9 (t′), 55.8 (d′), 66.7 (t′), 120.7 (d′), 123.2 (d′), 129.6 (d′), 147.4 (s′), 175.9 (s′); exact mass *m*/*z* calcd for $C_{16}H_{16}N_2O_2$ 268.1212, found 268.1210.

Dihydro-3-[(phenylmethoxy)amino]-2(3*H*)-furanone (7c). The general procedure for radical cyclization was followed, using **7b** (0.315 g, 1.10 mmol) in PhMe (70 mL), Bu_3SnH (474 μL, 1.76 mmol) in PhMe (10 mL), and AIBN (30 mg, 0.18 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using first 10% EtOAc−hexane (700 mL) and then 30% EtOAc−hexane, gave **7c** (118 mg, 51%) as a colorless oil: FTIR (CH_2Cl_2 cast) 1774 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 2.22−2.42 (m, 2 H), 3.79 (td, J = 8.9, 1.8 Hz, 1 H), 4.18−4.26 (m, 1 H), 4.38 (td, J =

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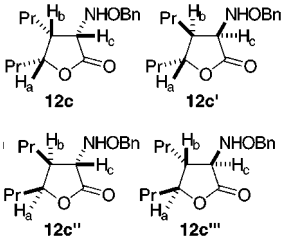
8.9, 3.8 Hz, 1 H), 4.71 (d, J = 11.8 Hz, 1 H), 4.76 (d, J = 11.8 Hz, 1 H), 6.12 (s, 1 H), 7.24−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 26.4 (t′), 59.1 (d′), 66.2 (t′), 77.1 (t′), 128.1 (d′), 128.5 (d′), 128.6 (d′), 137.2 (s′), 175.6 (s′); exact mass m/z calcd for $C_{11}H_{13}NO_3$ 207.0895, found 207.0896.

3-[2,2-Di(4-methoxyphenyl)hydrazino]dihydro-2(3*H*)-furanone (10c). The general procedure for radical cyclization was followed using **10b** (230 mg, 0.57 mmol) in PhMe (35 mL), Bu_3SnH (247.4 mg, 0.85 mmol) in PhMe (5 mL), and AIBN (9.30 mg, 0.057 mmol) in PhMe (5 mL). Flash chromatography of the crude product over silica gel (1.7 cm × 30 cm), using 20% EtOAc−hexane, gave **10c** (133.1 mg, 71%) as a crystalline solid.

3-(2,2-Diphenylhydrazino)dihydro-4,5-dipropyl-2(3*H*)-furanone (11c). The general procedure for radical cyclization was followed, using **11b** (0.494 g, 1.15 mmol) in PhMe (70 mL), Bu_3SnH (474 μL, 1.76 mmol) in PhMe (10 mL), and AIBN (30 mg, 0.18 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 28 cm), using 2% EtOAc−hexane, gave a crude fraction which contained a small amount of tributyltin residues (^{1}H NMR, 400 MHz). Further purification by flash chromatography over silica gel (1.6 cm × 28 cm), using 3% EtOAc−hexane, gave **11c** (330 mg, 82%) as a pale yellow oil, which was a 2:3:2:3 mixture (^{1}H NMR) of four chromatographically inseparable isomers.

(3α,4α,5α)-Dihydro-3-[(phenylmethoxy)amino]-4,5-dipropyl-2(3*H*)-furanone (12c), (3α,4α,5*β*)-Dihydro-3-[(phenylmethoxy)amino]-4,5-dipropyl-2(3*H*)-furanone (12c′), (3α,4*β*,5*β*)-Dihydro-3-[(phenylmethoxy)amino]-4,5-dipropyl-2(3*H*)-furanone (12c″), and (3α,4*β*,5α)-Dihydro-3-[(phenylmethoxy)amino]-4,5-dipropyl-2(3*H*)-furanone (12c‴).



The general procedure for radical cyclization was followed, using **12b** (0.407 g, 1.10 mmol) in PhMe (70 mL), Bu_3SnH (474 μL, 1.76 mmol) in PhMe (10 mL), and AIBN (30 mg, 0.18 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using 5% EtOAc−hexane, gave a crude fraction which contained a small amount of tributyltin residues (^{1}H NMR, 400 MHz). Further purification by flash chromatography over silica gel (1.6 cm × 24 cm), using 5% EtOAc−hexane, gave a 1:3:1:2 mixture (250 mg, 78% in all) of **12c**, **12c′**, **12c″**, and **12c‴** (as judged by ^{1}H NMR measurements). Flash chromatography of the mixture over silica gel (1.6 cm × 25 cm), using 3% EtOAc−hexane, gave four fractions, #1−#4. Each fraction was further purified by flash chromatography over silica gel (1 cm × 20 cm), using 2% EtOAc−hexane. Fractions #1, #2, #3, and #4 gave **12c**, **12c′**, **12c″**, and **12c‴**, respectively, as colorless oils.

Compound **12c** had the following characteristics: FTIR (CH_2Cl_2 cast) 1773 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.89−0.98 (m, 6 H), 1.29−1.61 (m, 7 H), 1.72−1.81 (m, 1 H), 2.52−2.60 (m, 1 H), 3.98 (dd, J = 7.6, 3.2 Hz, 1 H), 4.36−4.42 (m, 1 H), 4.72 (s, 2 H), 5.90 (s, 1 H), 7.27−7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 13.9 (q′), 14.5 (q′), 19.4 (t′), 20.9 (t′), 25.7 (t′), 32.4 (t′), 41.9 (d′), 63.7 (d′), 82.3 (d′), 128.1 (d′), 128.5 (d′), 128.6 (d′), 137.2 (s′), 174.6 (s′); exact mass m/z calcd for $C_{17}H_{25}NO_3$ 291.1834, found 291.1833. Irradiation of the $\mathbf{H}_a$ ^{1}H NMR signal for **12c** caused an NOE of 7.2% in the signal for $\mathbf{H}_b$ and 3.5% for the $\mathbf{H}_c$ signal.

Compound **12c′** had the following characteristics: FTIR (CH_2Cl_2 cast) 1773 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.92−0.99 (m, 6 H), 1.25−1.73 (m, 8 H), 2.11−2.20 (m, 1 H), 3.75 (dd, J = 8.5, 2.9 Hz, 1 H), 4.21−4.28 (m, 1 H), 4.70 (d, J = 11.6 Hz, 1 H), 4.75 (d, J = 11.6 Hz, 1 H), 6.02 (d, J = 2.7 Hz, 1 H), 7.28−7.40 (m, 5 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 14.0 (q′), 14.4 (q′), 19.5 (t′), 21.3 (t′), 29.0 (t′), 37.0 (t′), 44.1 (d′), 62.2 (d′), 76.3 (t′), 85.4 (d′), 128.4 (d′), 128.8 (d′), 137.6 (s′), 175.8 (s′); exact mass m/z calcd for $C_{17}H_{25}NO_3$ 291.1834, found 291.1827. Irradiation of the $\mathbf{H}_a$ ^{1}H NMR signal for **12c′** caused an NOE of 5% in the signal for the $\mathbf{H}_b$ and 0% for the $\mathbf{H}_c$ signal.

Compound **12c″** had the following characteristics: FTIR (CH_2Cl_2 cast) 1778 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 0.88−1.00 (m, 6 H), 1.25−1.65 (m, 8 H), 2.60−2.70 (m, 1 H), 3.36 (d, J = 10.5 Hz, 1 H), 4.49−4.56 (m, 1 H), 4.69 (d, J = 0.9 Hz, 2 H), 6.13 (s, 1 H), 7.28−7.40 (m, 5 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 14.0 (q′), 14.3 (q′), 19.5 (t′), 21.0 (t′), 30.3 (t′), 32.7 (t′), 40.6 (d′), 64.6 (d′), 77.4 (t′), 80.9 (d′), 128.3 (d′), 128.7 (d′), 129.1 (d′), 137.9 (s′), 175.4 (s′); exact mass m/z calcd for $C_{17}H_{25}NO_3$ 291.1834, found 291.1836. Irradiation of the $\mathbf{H}_a$ ^{1}H NMR signal for **12c″** caused an NOE of 13% in the signal for the $\mathbf{H}_b$ and 0% for the $\mathbf{H}_c$ signal.

Compound **12c‴** had the following characteristics: FTIR (CH_2Cl_2 cast) 1776 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.91−0.98 (m, 6 H), 1.30−1.72 (m, 8 H), 2.20−2.30 (m, 1 H), 3.41 (d, J = 9.9 Hz, 1 H), 4.02 (td, J = 8.5, 3.5 Hz, 1 H), 4.72 (d, J = 2.8 Hz, 2 H), 6.15 (s, 1 H), 7.27−7.38 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 13.9 (q′), 14.3 (q′), 18.9 (t′), 20.4 (t′), 34.2 (t′), 37.0 (t′), 42.7 (d′), 66.5 (d′), 76.9 (t′), 83.0 (d′), 128.0 (d′), 128.4 (d′), 128.7 (d′), 137.3 (s′), 175.1 (s′); exact mass m/z calcd for $C_{17}H_{25}NO_3$ 291.1834, found 291.1831. Irradiation of the $\mathbf{H}_a$ ^{1}H NMR signal for **12c‴** caused an NOE of 4% in the signal for the $\mathbf{H}_b$ and 5% for the $\mathbf{H}_c$ signal.

3-(2,2-Diphenylhydrazino)dihydro-5-phenyl-2(3*H*)-furanone (13c). The general procedure for radical cyclization was followed, using **13b** (364.2 mg, 0.861 mmol) in PhMe (54 mL), Bu_3SnH (0.35 mL, 1.29 mmol) in PhMe (7.5 mL), and AIBN (14.9 mg, 0.0911 mmol) in PhMe (7.5 mL). Flash chromatography of the residue several times over silica gel (1.7 cm × 35 cm), using 10% EtOAc−hexane, gave crude (^{1}H NMR) **13c** (192.1 mg, ca. 64%) as a yellow oil. Some of the material (86.5 mg, 0.251 mmol) crystallized from 5% EtOAc−hexane, and a portion was recrystallized from MeOH to give **13c** (9.4 mg, 35% recovery) as a mixture [ca. 1:1 (^{1}H NMR)] of two isomers.

3-(2,2-Diphenylhydrazino)dihydro-4-phenyl-2(3*H*)-furanone (15c). The general procedure for radical cyclization was followed, with the indicated modifications, using **15b** (250.3 mg, 0.592 mmol) in PhMe (37 mL), Bu_3SnH (0.24 mL, 0.89 mmol) in PhMe (5.25 mL), and AIBN (10.3 mg, 0.063 mmol) in PhMe (5.25 mL). The residue was dissolved in Et_2O (50 mL), and the solution was agitated for 40 min in a sonicator [Branson, model B-12, 80 W] with an aqueous solution of KF (515.9 mg, 8.88 mmol) in water (10 mL).[33] The precipitate of Bu_3SnF was filtered off and the ethereal phase of the filtrate was separated. The aqueous layer was washed with Et_2O and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.7 cm × 35 cm), using 10% EtOAc−hexane, gave the two individual isomers of **15c** (117.5 mg, 55.5 mg, 85% in all) as yellow oils, each of which was characterized spectroscopically, but we did not assign the stereochemistry to the individual isomers, as the observed $J_{\mathrm{CHN-CHPh}}$ values were comparable.

3-(2,2-Diphenylhydrazino)tetrahydro-2*H*-pyran-2-one (16c) and Propyl (Diphenylhydrazono)acetate (16c′). The general procedure for radical cyclization was followed, using **16b** (0.415 g, 1.15 mmol) in PhMe (70 mL), Bu_3SnH (474 μL, 1.76 mmol) in PhMe (10 mL), and AIBN (30 mg, 0.18 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using 5% EtOAc−hexane, gave **16c′** (66 mg, 20%) as a crystalline solid and **16c** (163 mg, 50%) as a colorless oil.

Compound **16c′** had the following characteristics: mp 83−84 °C; FTIR (CH_2Cl_2 cast) 1728, 1702, 1590, 1556, 1494 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.00 (t, J = 7.4 Hz, 3 H), 1.73 (sextet, J = 7.1 Hz, 2 H), 4.20 (t, J = 6.8 Hz, 2 H), 6.52 (s, 1 H), 7.12−7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 10.4

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(q′), 22.1 (t′), 66.3 (t′), 122.4 (d′), 124.3 (d′), 126.0 (d′), 130.0 (d′), 143.0 (s′), 164.8 (s′); exact mass *m/z* calcd for $C_{17}H_{18}N_2O_2$ 282.1368, found 282.1374.

Compound **16c** had the following characteristics: FTIR (CH_2Cl_2 cast) 1732 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.80−2.01 (m, 3 H), 2.22−2.37 (m, 1 H), 3.64−3.73 (m, 1 H), 4.27−4.37 (m, 2 H), 5.06 (s, 1 H), 7.00−7.31 (m, 10 H); ^{13}C NMR (CD_2Cl_2, 50.3 MHz) δ 21.6 (t′), 25.3 (t′), 55.7 (d′), 69.8 (t′), 120.6 (d′), 122.9 (d′), 129.5 (d′), 147.6 (s′), 171.7 (s′); exact mass *m/z* calcd for $C_{17}H_{18}N_2O_2$ 282.1368, found 282.1366.

(3α,3a*β*,7a*β*)- and (3α,3aα,7aα)-3-(2,2-Diphenylhydrazino)hexahydro-2(3*H*)-benzofuranone (17c). The general procedure for radical cyclization was followed, using **17b** (0.450 g, 1.12 mmol) in PhMe (70 mL), Bu_3SnH (474 μL, 1.76 mmol) in PhMe (10 mL), and AIBN (50 mg, 0.31 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using 3% EtOAc−hexane, gave **17c** (0.261 g, 72%) as a pale yellow oil which was a 1:1 mixture (^1H NMR) of isomers: FTIR (CH_2Cl_2 cast) 1773 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.10−1.90 (m, 8 H), 2.15−2.25 (m, 0.49 H), 2.48−2.68 (m, 0.69 H), 3.65 (dd, J = 6.2, 1.3 Hz, 0.41 H), 4.00 (dd, J = 6.2, 1.3 Hz, 0.42 H), 4.37−4.41 (m, 0.49 H), 4.48 (s, 0.91 H), 4.78 (dd, J = 12.2, 5.6 Hz, 0.34 H), 7.00−7.35 (m, 10 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 20.1 (t′), 21.4 (t′), 22.1 (t′), 23.1 (t′), 23.4 (t′), 25.3 (t′), 27.7 (t′), 29.0 (t′), 39.8 (d′), 41.1 (d′), 60.7 (d′), 63.3 (d′), 76.8 (d′), 78.2 (d′), 120.8 (d′), 121.1 (d′), 123.2 (d′), 123.4 (d′), 129.6 (d′), 129.7 (d′), 147.6 (s′), 147.9 (s′), 175.6 (s′), 176.2 (s′); exact mass *m/z* calcd for $C_{20}H_{22}N_2O_2$ 322.1681, found 322.1678.

(3α,3aα,7aα)-Hexahydro-3-[(phenylmethoxy)amino]-2(3*H*)-benzofuranone (*exo*-18c) and (3α,3a*β*,7a*β*)-Hexahydro-3-[(phenylmethoxy)amino]-2(3*H*)-benzofuranone (*endo*-18c).

exo-18c **endo-18c**

The general procedure for radical cyclization was followed, using **18b** (0.202 g, 0.595 mmol) in PhMe (40 mL), Bu_3SnH (240 μL, 0.893 mmol) in PhMe (5 mL), and AIBN (20 mg, 0.12 mmol) in PhMe (5 mL). Flash chromatography of the residue over silica gel (1.6 cm × 28 cm), using first 3% EtOAc−hexane (500 mL) and then 10% EtOAc−hexane, gave ***exo*-18c** (51 mg, 33%) as a crystalline solid and ***endo*-18c** (50 mg, 32%) as a colorless oil.

***exo*-18c** had the following characteristics: FTIR (CH_2Cl_2 cast) 1775 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 1.22−1.75 (m, 7 H), 1.95−2.03 (m, 1 H), 2.59−2.67 (m, 1 H), 3.56 (dd, J = 9.4, 2.6 Hz, 1 H), 4.50−4.58 (m, 1 H), 4.68 (s, 2 H), 6.11 (d, J = 2.3 Hz, 1 H), 7.25−7.39 (m, 5 H); ^{13}C NMR (CD_2Cl_2, 50.3 MHz) δ 21.2 (t′), 22.0 (t′), 24.7 (t′), 29.7 (t′), 37.2 (d′), 62.9 (d′), 77.36 (d′), 77.44 (t′), 128.2 (d′), 128.6 (d′), 129.0 (d′), 137.8 (s′), 175.4 (s′); exact mass *m/z* calcd for $C_{15}H_{19}NO_3$ 261.1365, found 261.1361.

***endo*-18c** had the following characteristics: mp 71.5−72.5 °C; FTIR (CH_2Cl_2 cast) 1774 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 0.93−0.40 (m, 3 H), 1.52−1.73 (m, 4 H), 2.13−2.26 (m, 1 H), 2.50−2.57 (m, 1 H), 4.11 (dd, J = 6.1, 4.0 Hz, 1 H), 4.41−4.45 (m, 1 H), 4.70 (s, 2 H), 5.91 (d, J = 3.5 Hz, 1 H), 7.30−7.40 (m, 5 H); ^{13}C NMR (CD_2Cl_2, 50.3 MHz) δ 20.1 (t′), 22.7 (t′), 23.3 (t′), 27.7 (t′), 39.3 (d′), 66.6 (d′), 76.80 (t′), 76.81 (d′), 128.3 (d′), 128.7 (d′), 128.8 (d′), 138.1 (s′), 174.8 (s′); exact mass *m/z* calcd for $C_{15}H_{19}NO_3$ 261.1365, found 261.1359. Irradiation of the $\mathbf{H}_a$ ^1H NMR signal for ***exo*-18c** caused an NOE of 8% in the signal for $\mathbf{H}_b$ and 1% for the $\mathbf{H}_c$ signal; in the case of ***endo*-18c**, the corresponding values were 12% and 11%, respectively.

(3α,3a*β*,7a*β*)- and (3α,3aα,7aα)-3-(2,2-Diphenylhydrazino)hexahydro-2(3*H*)-benzofuranone [19c (≡ 17c)]. The general procedure for radical cyclization was followed, using **19b** (500 mg, 1.05 mmol) in PhMe (70 mL), Bu_3SnH (370 μL, 1.37 mmol) in PhMe (10 mL), and AIBN (69 mg, 0.42 mmol) in PhMe (10 mL). Flash chromatography of the residue over silica gel (1.6 cm × 28 cm), using 3% EtOAc−hexane, gave **19c** (≡**17c**) (70 mg, 20%) as a pale yellow oil, which was a 1:1 mixture (^1H NMR) of isomers. The spectroscopic data were identical to those of **17c** obtained previously.

(3α,3a*β*,7a*β*)- and (3α,3aα,7aα)-3-(2-Benzoyl-2-phenylhydrazino)hexahydro-2*H*-cyclopenta[b]furan-2-one (20c). The general procedure for radical cyclization was followed, using **20b** (74.7 mg, 0.18 mmol) in PhMe (11.2 mL), Bu_3SnH (78.7 mg, 0.27 mmol) in PhMe (1.55 mL), and AIBN (3.1 mg, 0.02 mmol) in PhMe (1.6 mL). The solvent was evaporated and the residue was diluted with Et_2O (5 mL) and saturated aqueous KF (5 mL). The resulting mixture was stirred for 3.5 h and filtered through Celite using Et_2O. The aqueous layer was extracted with Et_2O, and the combined organic layers were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.7 cm × 30 cm), using 25% EtOAc−hexane, gave **20c** (29.5 mg, 49%) as an oil, which was a mixture [ca. 1:1 (^1H NMR)] of two isomers.

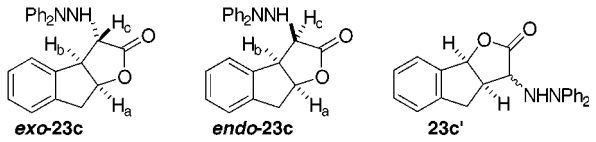
(3α,3a*β*,7a*β*)- and (3α,3aα,7aα)-3-(2,2-Diphenylhydrazino)hexahydro-2*H*-cyclopenta[b]furan-2-one (21c). The general procedure for radical cyclization was followed, using **21b** (100.0 mg, 0.26 mmol) in PhMe (16.0 mL), Bu_3SnH (113.0 mg, 0.39 mmol) in PhMe (2.2 mL), and AIBN (4.5 mg, 0.02 mmol) in PhMe (2.3 mL). The solvent was evaporated and the residue was diluted with Et_2O (5 mL) and saturated aqueous KF (5 mL). The resulting mixture was stirred for 4 h and filtered through Celite using Et_2O. The aqueous layer was extracted with Et_2O, and the combined organic layers were dried (Na_2SO_4) and evaporated to give **21c** (49.6 mg, 63%) as an oil, which was a mixture [ca. 1:1.4 (^1H NMR)] of two isomers: FTIR ($CHCl_3$ cast) 1767 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.30−2.11 (m, 6 H), 2.73−3.04 (m, 1 H), 3.42−3.53 (m, 1 H), 4.01 (d, J = 9.0 Hz, 1 H), 4.71−4.90 (m, 0.6 H), 5.03−5.24 (m, 0.5 H), 6.82−7.59 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.7 (t′), 23.9 (t′), 25.2 (t′), 31.3 (t′), 33.1 (t′), 33.2 (t′), 44.1 (d′), 44.5 (d′), 59.5 (d′), 63.7 (d′), 85.0 (d′), 86.1 (d′), 120.6 (d′), 120.7 (d′), 123.1 (d′), 129.3 (d′), 129.4 (d′), 147.1 (s′), 147.3 (s′), 175.3 (s′), 176.1 (s′); exact mass *m/z* calcd for $C_{19}H_{20}N_2O_2$ 308.1524, found 308.1521.

3-(2,2-Diphenylhydrazino)octahydro-2*H*-cyclohepta[b]-furan-2-one (22c). The general procedure for radical cyclization was followed, using **22b** (590 mg, 1.42 mmol) in PhMe (90 mL), Bu_3SnH (0.57 mL, 2.13 mmol) in PhMe (12 mL), and AIBN (22.9 mg, 0.14 mmol) in PhMe (12 mL). Flash chromatography of the crude product over silica gel (1.7 cm × 35 cm), using 15% EtOAc−hexane, gave **22c** (268.9 mg, 56%) as a mixture of four isomers, of which only one could be separated from the others. Two fractions were obtained from the chromatography; one (235.2 mg) consisted of three isomers and the other (33.7 mg) was a single isomer. The mixed fraction had the following characteristics: FTIR (CH_2Cl_2 cast) 1769 cm^{-1}; ^1H NMR (CD_2Cl_2, 300 MHz) δ 1.12−1.65 (m, 4.71 H), 1.65−2.16 (m, 4.74 H), 2.16−2.68 (m, 1 H), 2.86−3.0 (m, 0.19 H), 3.61−3.70 (m, 0.47 H), 4.03 (d, J = 7.8 Hz, 0.45 H), 4.12 (dt, J = 10.2, 4.3 Hz, 0.08 H), 4.5−4.64 (m, 0.89 H), 4.66−4.8 (m, 0.62 H), 4.92 (s, 0.14 H), 7.01−7.39 (m, 10 H); ^{13}C NMR (CD_2Cl_2, 75.5 MHz) δ 21.9 (t′), 22.2 (t′), 25.2 (t′), 25.6 (t′), 25.8 (t′), 27.1 (t′), 27.7 (t′), 28.8 (t′), 29.2 (t′), 30.3 (t′), 31.0 (t′), 31.2 (t′), 31.4 (t′), 31.5 (t′), 33.7 (t′), 45.7 (d′), 46.1 (d′), 50.8 (d′), 60.7 (d′), 62.1 (d′), 63.0 (d′), 81.4 (d′), 82.7 (d′), 83.8 (d′), 120.6 (d′), 120.7 (d′), 121.2 (d′), 123.0 (d′), 123.1 (d′), 123.5 (d′), 129.5 (d′), 129.6 (d′), 129.7 (d′), 147.4 (s′), 147.6 (s′), 148.0 (s′), 175.3 (s′), 175.4 (s′); exact mass calcd for $C_{21}H_{24}N_2O_2$ 336.1837, found 336.1832.

The single isomer had the following characteristics: FTIR (CH_2Cl_2 cast) 1777 cm^{-1}; ^1H NMR (CD_2Cl_2, 300 MHz) δ 1.48−1.95 (m, 9 H), 2.19−2.32 (m, 1 H); 2.34−2.47 (m, 1 H); 3.68 (dd, J = 6.3, 1.6 Hz, 1 H), 4.23 (d, J = 1.5 Hz, 1 H), 4.67 (dt, J = 10.1, 4.7 Hz, 1 H), 7.01−7.39 (m, 10 H), ^{13}C NMR (CD_2Cl_2, 75.5 MHz) δ 23.7 (t′), 24.2 (t′), 26.0 (t′), 27.3 (t′), 33.4 (t′), 47.1 (d′), 59.4 (d′), 84.8 (d′), 121.0 (d′), 123.2 (d′), 129.6 (d′), 147.5 (s′), 174.5 (s′); exact mass *m/z* calcd for $C_{21}H_{24}N_2O_2$ 336.1837, found 336.1834.

The use of Ph_3SnH gave a similar yield. However, it was found that the separation of the crude mixture was easier than in the case of Bu_3SnH.

(3α,3aα,8aα)-3-(2,2-Diphenylhydrazino)-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-b]furan-2-one (*exo*-23c), (3α,3a*β*,-8a*β*)-3-(2,2-Diphenylhydrazino)-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-b]furan-2-one (*endo*-23c) and (3a*R,8b*S**)-3-(2,2-Diphenylhydrazino)-3,3a,4,8b-tetrahydro-2*H*-indeno-[1,2-b]furan-2-one (23c′).**



The general procedure for radical cyclization was followed, using **23b** (0.500 g, 1.15 mmol) in PhMe (70 mL), Bu_3SnH (474 μL, 1.76 mmol) in PhMe (10 mL), and AIBN (30 mg, 0.18 mmol) in PhMe (10 mL). The solvent was evaporated and the residue was covered with 40% EtOAc−hexane and left to stand for 0.5 h. The precipitate was then filtered off and washed with 40% EtOAc−hexane (2 × 3 mL) to give a first crop of ***endo*-23c** (70.0 mg, 17%) as a crystalline solid. Evaporation of the filtrate and flash chromatography of the residue over silica gel (1.6 cm × 30 cm), using 5% EtOAc−hexane, gave a 1:1.2 mixture (67 mg) of ***exo*-23c** and **23c′** (as two isomers), pure ***exo*-23c** (100 mg, 24%) and pure ***endo*-23c** (90 mg, 22%), each of the three fractions being a crystalline solid.

The fraction containing ***exo*-23c** and **23c′** had the following characteristics: FTIR (CH_2Cl_2 cast) 1770 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 2.88−2.95 (m, 0.64 H), 3.20−3.50 (m, 2.35 H), 3.69 (dd, J = 6.0, 1.6 Hz, 0.29 H), 3.95 (t, J = 1.7 Hz, 0.47 H), 4.15 (d, J = 5.6 Hz, 0.49 H), 4.31 (dd, J = 7.9, 1.3 Hz, 0.33 H), 4.62 (d, J = 2.0 Hz, 0.49 H), 4.72−4.79 (m, 0.61 H), 5.56−5.63 (m, 0.77 H), 6.03 (d, J = 7.6 Hz, 0.25 H), 6.85−7.50 (m, 14 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 32.4 (t′), 36.2 (t′), 38.9 (t′), 44.1 (d′), 44.9 (d′), 51.3 (d′), 60.0 (d′), 63.0 (d′), 63.6 (d′), 84.8 (d′), 85.9 (d′), 86.6 (d′), 120.8 (d′), 120.9 (d′), 121.0 (d′), 123.3 (d′), 123.4 (d′), 123.5 (d′), 125.3 (d′), 125.6 (d′), 125.8 (d′), 126.2 (d′), 126.5 (d′), 127.4 (d′), 127.8 (d′), 128.7 (d′), 129.67 (d′), 129.70 (d′), 129.8 (d′), 130.3 (d′), 130.7 (d′), 138.5 (s′), 139.1 (s′), 140.2 (s′), 140.9 (s′), 142.7 (s′), 145.7 (s′), 147.3 (s′), 147.6 (s′), 147.7 (s′), 174.6 (s′), 174.9 (s′), 175.6 (s′); exact mass m/z calcd for $C_{23}H_{20}N_2O_2$ 356.1525, found 356.1522.

***Exo*-23c** had the following characteristics: mp 158−160 °C; FTIR (CH_2Cl_2 cast) 1771 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.33 (d, J = 3.3 Hz, 2 H), 3.97 (t, J = 1.5 Hz, 1 H), 4.17 (d, J = 5.8 Hz, 1 H), 4.56 (d, J = 1.8 Hz, 1 H), 5.59 (dt, J = 5.8, 3.4 Hz, 1 H), 6.82−7.40 (m, 14 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 38.6 (t′), 50.9 (d′), 63.4 (d′), 84.6 (d′), 120.5 (d′), 123.3 (d′), 125.0 (d′), 125.4 (d′), 127.6 (d′), 128.5 (d′), 129.6 (d′), 139.7 (s′), 140.3 (s′), 146.9 (s′); 174.9 (s′); exact mass m/z calcd for $C_{23}H_{20}N_2O_2$ 356.1525, found 356.1519.

***Endo*-23c** had the following characteristics: mp 183−185 °C; FTIR (CH_2Cl_2 cast) 1761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.21−3.37 (m, 2 H), 4.20 (dd, J = 8.1, 4.7 Hz, 1 H), 4.34 (dd, J = 8.1, 1.5 Hz, 1 H), 4.55 (s, 1 H), 5.17 (t, J = 4.7 Hz, 1 H), 7.03−7.40 (m, 14 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 38.6 (t′), 49.6 (d′), 60.6 (d′), 82.0 (d′), 121.5 (d′), 123.7 (d′), 125.0 (d′), 126.9 (d′), 128.4 (d′), 128.9 (d′), 129.5 (d′), 137.1 (s′), 140.9 (s′), 148.0 (s′), 174.5 (s′); exact mass m/z calcd for $C_{23}H_{20}N_2O_2$ 356.1525, found 356.1518. Irradiation of the $\mathbf{H}_a$ ^1H NMR signal for ***exo*-23c** caused an NOE of 6% in the signal for $\mathbf{H}_b$ and 0% for the $\mathbf{H}_c$ signal; in the case of ***endo*-23c**, the corresponding values were 6% and 3%, respectively.

(3α,3aα,6aα)- and (3α,3a*β*,6a*β*)-3-(2,2-Diphenylhydrazino)tetrahydrofuro[2,3-b]furan-2(3*H*)-one (24c). The general procedure for radical cyclization was followed, using **24b** (753.4 mg, 1.942 mmol) in PhMe (120 mL), Bu_3SnH (847.8 mg, 2.913 mmol) in PhMe (15 mL), and AIBN (32.0 mg, 0.1942 mmol) in PhMe (15 mL). Flash chromatography of the crude product over silica gel (1.7 cm × 34 cm), using 50% EtOAc−hexane, gave **24c** (285.0 mg, 47%) as a colorless oil, which was a mixture [ca. 1:1.4 (^1H NMR)] of two isomers: FTIR (CH_2Cl_2 cast) 1775 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.68−2.42 (m, 2 H), 3.18−3.30 (m, 1 H), 3.73−3.89 (m, 1 H), 4.0−4.18 (m, 2 H), 4.42−4.8 (br s, 1 H), 5.98 (d, J = 4.6 Hz, 0.53 H), 6.21 (d, J = 5.5 Hz, 0.37 H), 6.99−7.43 (m, 10 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 24.4 (t′), 30.3 (t′), 44.8 (d′), 45.0 (d′), 59.1 (d′), 62.4 (d′), 68.0 (t′), 69.4 (t′), 106.9 (d′), 108.2 (d′), 120.6 (d′), 120.8 (d′), 123.4 (d′), 129.5 (d′), 129.6 (d′), 146.9 (s′), 147.2 (s′), 173.0 (s′), 174.0 (s′); exact mass m/z calcd for $C_{18}H_{18}N_2O_3$ 310.1317, found 310.1309.

3-Aminodihydro-2(3*H*)furanone Hydrochloride (6d).[34] Hydrochloric acid (6 N, 0.8 mL) was added to a solution of **6c** (40 mg, 0.15 mmol) in THF (4 mL), followed by 10% Pd−C (20 mg), and the mixture was shaken under an atmosphere of H_2 for 3 h. The mixture was filtered through a small pad of Celite, which was washed with water, and the combined filtrates were evaporated. The ^1H NMR spectrum of the residue showed the amino lactone hydrochloride and $Ph_2NH{\cdot}HCl$. The residue was dissolved in water, and acetone was added to produce crystals (16.5 mg, 81%) of **6d**: mp 196−200 °C (decomp), (lit.[34] 201−203 °C); ^1H NMR (360 MHz, D_2O) δ 2.40−2.60 (m, 1 H), 2.79−2.91 (m, 1 H), 4.45−4.54 (m, 2 H), 4.61 (t, J = 9.7 Hz, 1 H).

Dihydro-2,3-furandione 3-Di(4-methoxyphenyl)hydrazone (10d). DDQ (30.9 mg, 0.1362 mmol) was added to a stirred solution of **10c** (29.8 mg, 0.09 mmol) in CH_2Cl_2 (2 mL) containing a small amount of water (0.15 mL). The reaction was complete within 5 min (TLC control, silica, 40% EtOAc−hexane). Saturated aqueous $NaHCO_3$ (10 mL) was added, and the mixture was extracted with CH_2Cl_2. The organic extract was washed with brine, dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (1.7 cm × 32 cm), using 40% EtOAc−hexane, gave **10d** (0.0294 g, 99%) as a crystalline solid: mp 160−161 °C; FTIR (CH_2Cl_2 cast) 1759, 1505 cm^{-1}; ^1H NMR (CD_2Cl_2, 400 MHz) δ 2.09 (t, J = 7.3 Hz, 2 H), 3.81 (s, 6 H), 4.15 (t, J = 7.3 Hz, 2 H), 6.87−7.19 (m, 8 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 26.9 (t′), 55.9 (q′), 64.7 (t′), 114.6 (d′), 124.8 (d′), 127.9 (s′), 138.0 (s′), 158.2 (s′), 168.9 (s′); exact mass m/z calcd for $C_{18}H_{18}N_2O_4$ 326.1266, found 326.1275.

***trans*-2-Bromocyclohexyl Propenoate (25).** Acryloyl chloride (986.6 mg, 10.9 mmol) was added slowly (over ca. 10 min) to a stirred and cooled (0 °C) solution of *trans*-2-bromocyclohexanol (**17a**[29]) (970.0 mg, 5.45 mmol), DMAP (18.3 mg, 0.8175 mmol), and Et_3N (1.1029 g, 10.9 mmol) in CH_2Cl_2 (35 mL). Stirring at 0 °C was continued for 2 h, and then saturated aqueous $NaHCO_3$ (15 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1.7 cm × 35 cm), using 10% EtOAc−hexane, gave **25** (783.1 mg, 62%) as a colorless oil: FTIR (CH_2Cl_2 cast) l726 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.13−2.42 (m, 8 H), 3.88−4.07 (m, 1 H), 4.81−5.02 (m, 1 H), 5.76−5.88 (m, 1 H), 6.08 (ddd, J = 17.2, 10.3, 1.5 Hz, 1 H), 6.31−6.48 (m, 1 H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.2 (t′), 25.4 (t′), 31.0 (t′), 35.5 (t′), 52.6 (d′), 75.8 (d′), 128.4 (d′), 131.0 (t′), 165.0 (s′); exact mass m/z calcd for $C_9H_{13}{}^{79}BrO_2$ 232.0098, found 232.0098.

***trans*-2-Bromocyclohexyl Dihydroxyacetate (26).** OsO_4 (2.5% w/w in *t*-BuOH, 4.0 mg, 0.016 mmol) was added to a stirred mixture of acrylate **25** (457.3 mg, 1.97 mmol), water (2.7 mL), and dioxane (8 mL). After 10 min, the mixture had become dark brown. $NaIO_4$ (1.264 g, 5.91 mmol) was then added portionwise over ca. 10 min, and the resulting mixture was stirred for 6 h. Brine (6.0 mL) was added, and the mixture was extracted with Et_2O. The combined organic extracts were washed with water and 10% aqueous $NaHSO_3$, dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (1.7 cm × 32 cm), using 15% EtOAc−hexane, gave **26** (235.4 mg, ca. 47%, assuming product is totally the dihydroxy acetate) as a colorless gum, which was used directly in the next step. The material was mainly the hydrate but

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contained (^{1}H NMR) a small amount (ca. 5 mol %) of the parent aldehyde (*trans*-2-bromocyclohexyl glyoxalate).

***trans*-2-Bromocyclohexyl [*N*-(1,2,2-Triphenylethyl)-formimidoyl]formate (28).** A solution of amine **27**[35] (2.9326 g, 10.8 mmol) in CH_2Cl_2 (10 mL) was added to a stirred solution of **26** (2.512 g, 10.8 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred overnight, and then evaporated. Flash chromatography of the residue over silica gel (4 cm × 32 cm), using 20% EtOAc−hexane, gave **28** (4.4311 g, 84%) as a foam: FTIR (CH_2Cl_2 cast) 1747, 1722 cm^{-1}; ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.24−2.43 (m, 8 H), 3.96−4.15 (m, 1 H), 4.78 (dd, J = 10.3, 3.2 Hz, 1 H), 4.90−5.01 (m, 1 H), 5.51 (t, J = 11 Hz, 1 H), 7.04−7.53 (m, 16 H); ^{13}C NMR (CD_2Cl_2, 100.6 MHz) δ 23.6 (t′), 23.7 (t′), 25.8 (t′), 25.9 (t′), 31.3 (t′), 31.4 (t′), 36.0 (t′), 36.1 (t′), 52.8 (d′), 52.9 (d′), 58.3 (d′), 58.4 (d′), 77.4 (d′), 77.5 (d′), 79.7 (d′), 79.9 (d′), 126.8 (d′), 127.0 (d′), 127.1 (d′), 127.9 (d′), 128.4 (d′), 128.6 (d′), 128.7 (d′), 128.8 (d′), 128.90 (d′), 128.93 (d′), 129.1 (d′), 129.20 (d′), 129.24 (d′), 140.8 (s′), 140.9 (s′), 141.5 (s′), 141.6 (s′), 142.1 (s′), 153.4 (s′), 153.6 (s′), 161.6 (s′), 161.9 (s′); exact mass m/z calcd for $C_{28}H_{28}{}^{79}BrNO_2$ 489.1303, found 489.1309.

(3α,3a*β*,7a*β*)- and (3α,3aα,7aα)-3-Aminohexahydro-2(3*H*)-benzofuranone Hydrochloride (31). The general procedure for radical cyclization was followed, using **28** (575.5 mg, 1.18 mmol) in PhMe (75 mL), Bu_3SnH (856.1 mg, 2.94 mmol) in PhMe (10 mL), and AIBN (20 mg, 0.12 mmol) in PhMe (10 mL). After evaporation of the solvent, hydrochloric acid (8 N, 10 mL) was added to the crude product and the solution was stirred for 1 h. The acidic solution was extracted with CH_2Cl_2, and the aqueous layer was evaporated under reduced pressure. To facilitate evaporation of HCl, EtOH (100%) was added periodically. After the evaporation, a yellow powder was obtained. This was dissolved in the minimum amount of EtOH, and Et_2O was then added until slight turbidity was observed. The mixture was kept at 5 °C overnight, to obtain **31**[36] as a white crystalline solid, which was recrystallized in the same way to give **31** (109.2 mg, 48%): mp 249−253 °C [(lit.[36b] 246 (decomp)]; FTIR (Microscope) 1775 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz) δ 0.98−1.93 (m, 7 H), 2.14 (d, J = 15.5 Hz, 1 H), 2.74−2.85 (m, 1 H), 4.48 (d, J = 6.5 Hz, 1 H), 4.68−4.77 (m, 1 H); ^{13}C NMR (CD_3OD, 100.6 MHz) δ 20.4 (t′), 22.6 (t′), 23.3 (t′), 27.7 (t′), 39.1 (d′), 56.2 (d′), 78.2 (d′), 173.9 (s′); exact mass m/z calculated for $C_8H_{13}NO_2$ (M − HCl) 155.0946, found 155.0945. The *N*-acetate was prepared[36b] and had mp 170−174 °C (lit.[36b] 174−175 °C).

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada and Merck Frosst for financial support. S.H. held an NSERC Undergraduate Summer Award, and V.B. was an undergraduate at École Nationale Supérieure de Chime de Rennes working on a research project at the University of Alberta.

Supporting Information Available: NMR spectra of new compounds and X-ray data for **9b**; both experimental procedures and characterization data for **2d**, **2e**, **2h**, **8b**, **9b**, **14b**, **13c**; and characterization data for **2f**, **2g**, **10b**, **11b**, **13b**, **15b**, **19b**, **20b**, **10c**, **11c**, **13c**, **15c**, **20c**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0013655

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