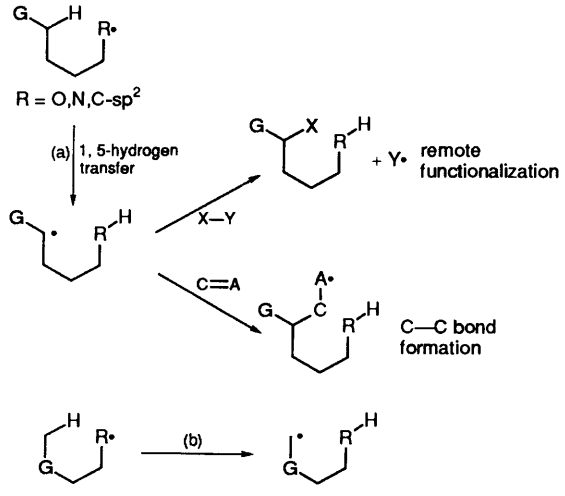
Radical Translocation Reactions across Amides. 1,5-Hydrogen-Transfer Reactions of *o*-Iodobenzamides and *N*-(*o*-Iodobenzyl) Amides

Dennis P. Curran* and Hongtao Liu
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, USA

Radicals derived from *N,N*-disubstituted *o*-iodobenzamides undergo rapid 1,5-hydrogen-transfer reactions. The regioselectivity of these reactions is coupled to the rotamer population of the starting iodobenzamide, and the products vary with changing amide substituents. Related 1,5-hydrogen-transfer reactions are observed for *N*-alkyl-*N*-(*o*-iodobenzyl)-benzamides and -acetamides.

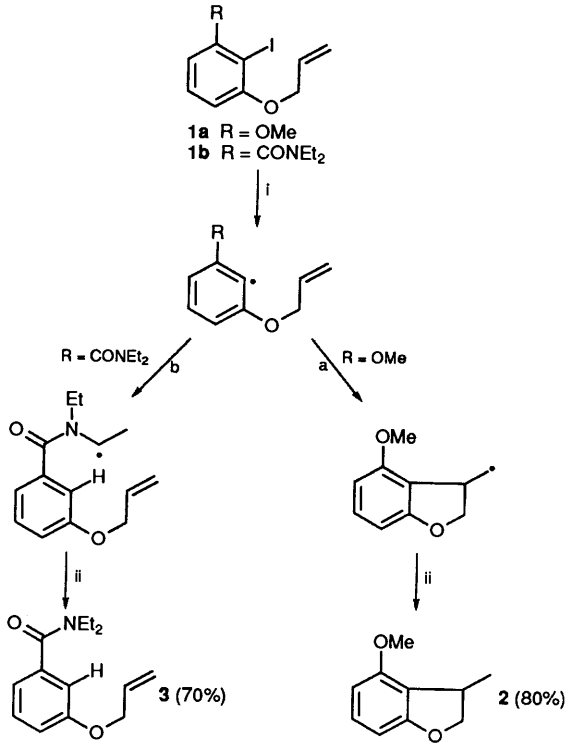
The development and synthetic application of radical-translocation reactions[1] have expanded very rapidly over the last few years.[2,3] In these reactions, radicals are generated at favourable sites and then 'translocated' to new sites prior to carbon–carbon bond-forming reactions. Though not the only kind of radical translocation, 1,5-hydrogen-transfer reactions are probably the most useful and powerful (Scheme 1). These



Scheme 1 **(a)** Radical translocation with '*exo*-oriented' groups (G). **(b)** Radical translation with '*endo*-oriented' groups (G).

reactions allow the indirect yet selective use of omnipresent carbon–hydrogen bonds as radical precursors, and they can now be conducted by using modern experimental techniques for radical reactions. Heteroatom-centred radicals were traditionally used as hydrogen abstractors for 'remote functionalizations' (the conversion of a C–H bond into a C–heteroatom bond), and these radicals can now be used for translocation as well.[4] Of newer vintage is the use of reactive carbon-centred radicals as hydrogen abstractors.[1,2,5] These reactions are typically conducted under standard conditions for generation of carbon-centred radicals (such as by the tin hydride and related methods). Rate and selectivity in the hydrogen-transfer step are imposed by the nature of the precursor and product radicals and by the structure of the substrate. To weaken the target C–H bond, substrates for radical translocations often bear a radical-stabilizing group (G), which can be located either exo (Scheme 1a) or endo (Scheme 1b) relative to the cyclic transition state for H-transfer. Such groups (G) have included allyl, benzyl, carbonyl, cyano, oxy, and even simple alkyl.[1–5]

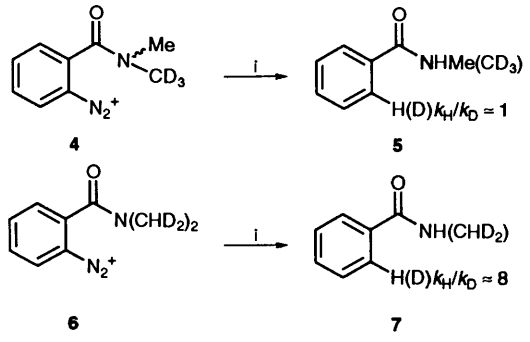
α-Amidoyl radicals are an important class of radicals that have been exploited for a number of synthetic purposes[6,7] in the wake of pioneering work by Hart.[8] Such radicals can be generated from a limited set of radical precursors including α-thio- or -selenophenyl amides, or α-amino thiohydroxamates. The predecessors of these compounds are usually imides or amino acids. α-Benzamidoyl radicals are an important sub-class of nitrogen-substituted radicals, and several observations in the literature suggested that 1,5-hydrogen-transfer reactions might be among the easiest ways to generate such radicals. Our interest in such reactions was sparked by a report of Snieckus and co-workers in 1985 (Scheme 2).[9] They observed that aryl



Scheme 2 Observations of Snieckus and co-workers. *Reagents:* i, $Bu_3Sn^•$; ii, Bu_3SnH.

radical cyclization of aryl methyl ether **1a** occurred smoothly under standard conditions to give the benzofuran **2** in 80% yield. In contrast, the cyclization of the related diethylamide **1b** under the same conditions provided exclusively the directly reduced product **3** in 70% yield. We suspected that the latter cyclization failed because it was superseded by the 1,5-hydrogen-transfer reaction shown in Scheme 2. This suspicion was later confirmed by Snieckus and Sloan,[10] who studied the reduction of compound **1b** with Bu_3SnD. That such a hydrogen transfer could be faster than an (already fast[11]) aryl radical cyclization encouraged us.

Related hydrogen-transfer reactions have been known since 1954,[12] and in the past they have usually been observed upon treatment of diazonium salts derived from *o*-aminobenzamides with copper powder (Scheme 3).[13] In such reactions, the



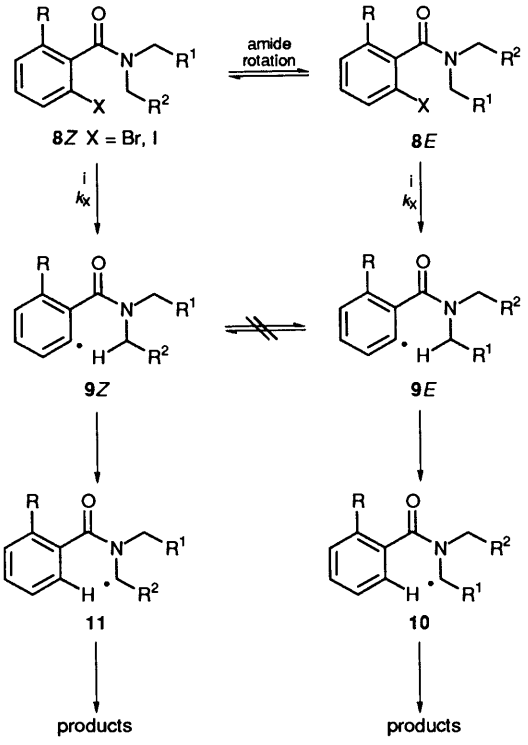
Scheme 3 Observations of Cohen and co-workers. *Reagent:* i, Cu.

electron-rich amidoalkyl radical that is produced upon 1,5-hydrogen transfer has a very short lifetime. It is rapidly oxidized to an acyliminium ion, and a net *N*-dealkylation usually ensues. In a classic series of mechanistic experiments reported in 1968,[14] Cohen *et al.* observed that copper-promoted decomposition of mono-deuteriomethylated diazonium salt **4** occurred to give compound **5** with an apparent isotope effect of ~1; however, when both *N*-methyl groups contained deuterium, a large deuterium-isotope effect (~8) was observed (see **6** ⟶ **7**). They explained the differences in isotope effects by suggesting that 1,5-hydrogen-transfer reactions of the aryl radicals derived from substrates **4** and **6** were faster than rotation of the amide C–N bond. Thus, the lack of an isotope effect with compound **4** simply reflects the 1/1 rotamer population of the precursor, while with substrate **6** the 'true' isotope effect is observed. Later, Grimshaw *et al.* studied the cyclizations of related benzanilide radicals, and they also showed that these cyclizations were faster than amide rotations.[15] Very recently, Esker and Newcomb observed that reactions of certain carbamoyloxy radicals also depend on C–N rotamer populations.[4c]

With today's knowledge of rate constants, we can further generalize the conclusions of Cohen and Grimshaw to provide the scenario in Scheme 4. Aryl radicals are very reactive, and their solution lifetimes probably cannot exceed *ca.* 10^{-5} s.[16] Amide rotamers interconvert in solution with lifetimes on the order of 10^{-1} to 10^{-2} s.[17] Since these numbers are so widely separated, it seems safe to conclude that aryl radicals such as **9** cannot live long enough to rotate and therefore that radicals **9***E* and **9***Z** are not interconvertible during their lifetimes. This means that 1,5-hydrogen-transfer ractions of unsymmetrical disubstituted primary amides **8** ($R^1 \neq R^2$) will depend on the rotamer population of the radical precursor (**8***E*/**8***Z*) and the rate of radical generation k_X. Since it seems likely that most rotamers **8***E* and **8***Z* will form radicals at very similar rates, this means that the rotamer population of the precursors will be the overriding factor that determines the products of 1,5-hydrogen-transfer reactions. In Scheme 4, rotamer **8***E* leads only to radical **10** while **8***Z* leads to isomeric radical **11**.

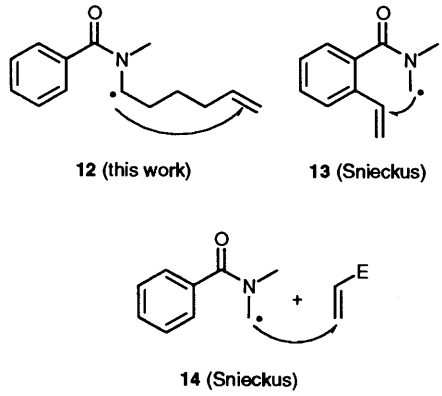
We now describe in complete detail the results of a study of 1,5-hydrogen-transfer reactions of *o*-iodobenzamides. A few of these results have previously been reported in a joint communication with the Snieckus group.[18] Structures **12–14**

* Use of non-standard *E*/*Z* stereochemical designators: the *E*/*Z* usage follows the CAP rules except for substrate **34a**, whose priorities would reverse *E*/*Z* designations.



Scheme 4 Hydrogen-transfer selectivity is dictated by starting rotamer ratio. *Reagent:* i, $Bu_3Sn^•$.

illustrate three different motifs for subsequent reactions of translocated radicals in these substrates. We report herein on applications of the first motif whereby a radical generated on one of the nitrogen substituents cyclizes to an acceptor on the same nitrogen substituent (see structure **12**). Snieckus and co-

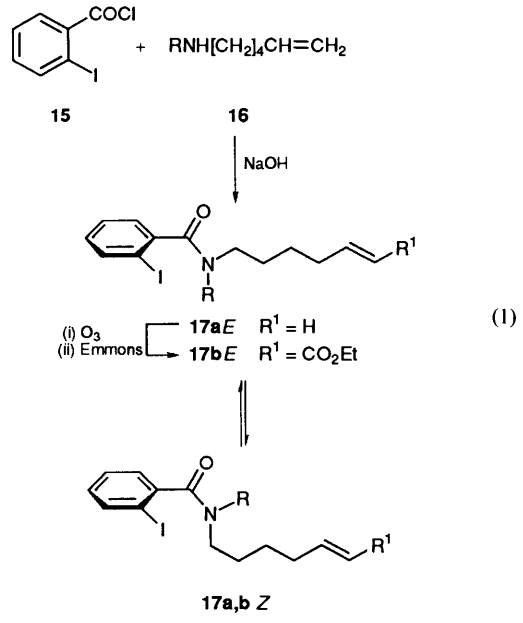


Motifs for subsequent reaction of translocated radicals

workers have studied the complementary approach whereby cyclization occurs to an acceptor on the aryl ring (see structure **13**) and they have also studied bimolecular reactions (see structure **14**). The chemistry of all these radicals is fascinating. Even though the synthetic usefulness of substrates like **12** is currently limited by problems of oxidation and rotamer population, our work sheds light on potential solutions to these problems. Finally we report briefly on results with related *N*-(*o*-iodobenzyl)-acetamide and -benzamide radicals, which show more immediate synthetic potential for conducting similar transformations. In a separate paper,[19] we reverse the locations of the aryl ring and the translocating C–H bond, and this leads to a new way to prepare and elaborate carbonyl-substituted radicals.

Results and Discussion

Many of the substrates used in this study have the general *o*-iodobenzamide structure **17** shown in eqn. (1). One of the amide side chains bears a radical acceptor five atoms away from a potential site of radical translocation, while the nature of the other side chain (R) is widely varied to alter the rotamer preference of **17** from >90% *E* to 100% *Z*. We refer to the



(1)

rotamer with R and the amide oxygen *cis* as *Z*, and that with the R and the amide oxygen *trans* as *E*.* Most of the amides **17a** (R^1 = H) were prepared by Schotten-Baumann acylation of the appropriate secondary amine **16** with *o*-iodobenzoyl chloride **15**. Preparations of the secondary amines **16** were achieved by standard methods that are presented in the Experimental section and discussed in the Thesis of H. Liu.[20] Amides **17b** with more activated acceptors proved crucial for successful cyclizations, and these were prepared from compound **17a** by ozonolysis and Wadsworth–Horner–Emmons olefination. The double bonds of such ester-substituted alkenes prepared in this work are *E*. All of the *o*-iodobenzamides **17** also showed chemical shift non-equivalence of geminal protons on the amide side chains due to slow rotation of the *N*-aryl bond on the NMR time scale. Such processes have been observed on many occasions,[17a–c] and the ^{1}H NMR spectra of relatively simple structures **17** at room temperature can be quite complex when the effects of restricted rotation about the amide (O)C–N and (O)C–Ar bonds are combined. The effects of the two processes can usually be differentiated since the amide C–N rotation is an *E*/*Z* isomerization and the (O)C–Ar bond rotation is an enantiomerization. Both processes are sufficiently rapid at room temperature so that all the coumpounds behave as homogeneous substances on chromatographic analysis and purification. In structures **17**, the planes of the aryl ring and the amide group are twisted by approximately 90° in the ground state;[5k] however, for the sake of simplicity, most of the amides are drawn in standard 'flat' representations.

Symmetrical amides **18a** and **18b** are crucial benchmark substrates for this work because they provide information on the expected behaviour of unsymmetrical substrates with the amide oxygen and the translocating side chain. Scheme 5 summarizes our observations with these substrates. Reduction of terminal alkene **18a** under Stork's conditions[21] in *tert*-butyl alcohol with sodium cyanoborohydride and 10% tributyltin chloride (catalytic method) provided a crude reaction mixture that consisted mainly of the dealkylated product **19a**; no cyclization product was observed. Monosubstituted primary amide **19a** probably arises by 1,5-hydrogen transfer of aryl radical **21a** to give radical **22a**. However, rather than cyclizing, radical **22a** is apparently oxidized to acyliminium ion **23a**, which evolves to dealkylated amide **19a** *via* hydrolytic work-up. We encountered this type of dealkylation with several other substrates (see below), though we still do not understand how the oxidation from radical **22** to ion **23** occurs under these ostensibly reducing conditions. Though radical **22** is a powerfully reducing radical,[22] it is not clear what reduction is coupled with its oxidation.

Reduction of substrate **18b** bearing an improved radical acceptor gave completely different results. When we treated diester **18b** (0.01 mol dm^{-3} in benzene) with 2 mol equiv. of tin hydride (standard method), we obtained a very clean, crude reaction mixture containing a single product. This product was isolated in 84% yield, and its structure was assigned as *cis*-5-*exo* cyclization product **20b**. The *cis* relative configuration of the cyclopentane substituents of compound **20b** was assigned by analogy with the results of related substrates (see below). These experiments show that 1,5-hydrogen-transfer reactions of radicals such as **21** occur efficiently to generate amidoyl radicals **22**, and we can estimate that $k_{1,5}$ must be $> 10^7$ s^{-1}.† They also show that amidoyl radicals are both nucleophilic and very easily oxidized. Electrophilic radical acceptors are a prerequisite for trapping of radical **22** prior to its apparent oxidation to iminium ion **23** by unknown oxidants.

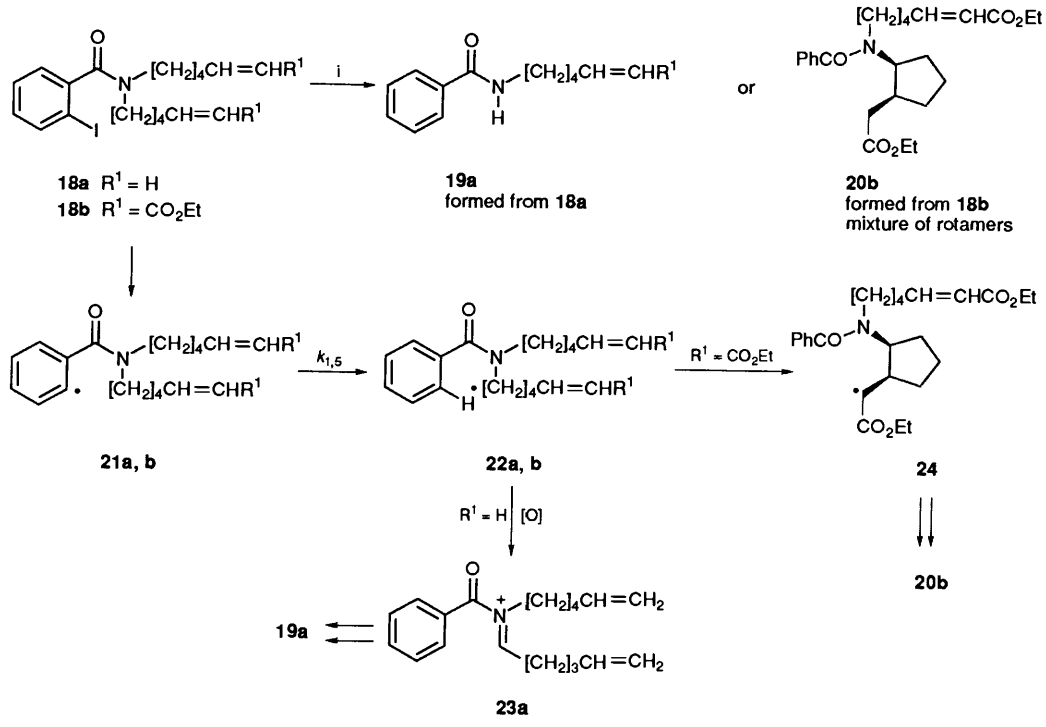
Prior to investigating unsymmetrical amide substrates, we briefly tested the ability of an ester connection to promote a 1,5-hydrogen-transfer reaction [eqn. (2)]. Benzoate esters, like monosubstituted primary benzamides, exist exclusively in the *syn* configuration[24] with respect to C=O and OR, and according to the analysis in Scheme 4 they should be reluctant to suffer 1,5-hydrogen transfer. This predicted reluctance is confirmed by the experiments shown in equation (2). Reduction of iodobenzoate ester **25a** by the catalytic method provided only the unsubstituted benzoate **26a**. To ensure that compound **26** did not arise from successful 1,5-hydrogen transfer followed by failed cyclization, we prepared the more activated acceptor **25b**. To give the aryl radical even more lifetime, we reduced diester **25b** by syringe-pump addition of tributyltin hydride (syringe-pump method) in benzene. This experiment provided reduced product **26b** in 47% yield alongside the solvent adduct **27b** (27%).[25] Since aryl radical lifetimes in benzene are limited by the rate of addition of these radicals to benzene, the isolation of adduct **27b** shows that the intermediate radicals have a maximum lifetime in this experiment. Despite this, there is no evidence for 1,5-hydrogen transfer.

The results of these experiments suggest that, like their amide counterparts, ester linkages do not rotate during the lifetime of aryl radicals. Because esters favour *syn* geometry, essentially all the radicals are generated in the wrong conformation for 1,5-hydrogen transfer, and none occurs. These results ensure that 1,5-hydrogen-transfer reactions of monosubstituted primary amides will fail because these amides also exist preferentially in *syn* conformations and their barriers to interconversion are even higher than those of esters.

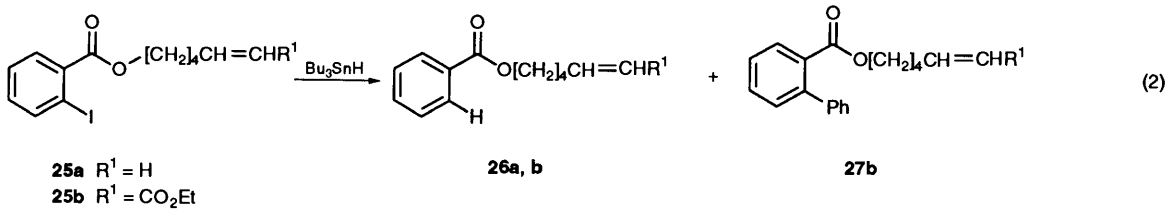
To probe the behaviour of disubstituted primary amides that

* The *E*/*Z* usage follows the CAP rules except for substrate **34a**, whose priorities would reverse *E*/*Z* designations.

† The rate constant for the reaction of tributyltin hydride with phenyl radical is estimated at $k_H = 4 \times 10^8$ dm^3 mol^{-1} s^{-1} at 80 °C (see footnote 7 in ref. 23).



Scheme 5 *Reagent:* i, Bu_3SnH



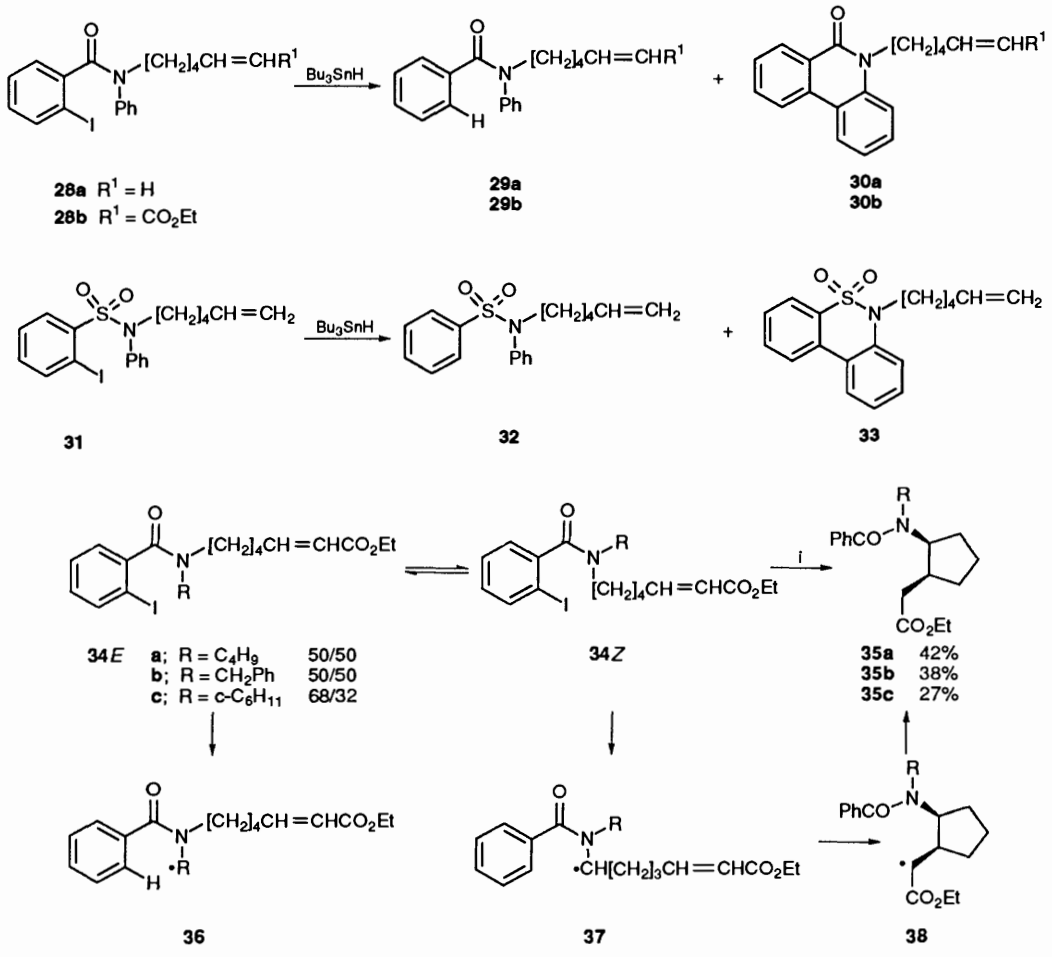
favour an *E* conformation, we selected the benzanilides **28a** and **28b** [eqn. (3)]. Though perhaps not widely appreciated, it has long been known that most anilides favour conformations with the amide oxygen and the *N*-phenyl group *trans*.[26] In the ^{1}H NMR spectrum of compound **28a** in $CDCl_3$, we were able to locate two resonances for the hydrogens of the methylene group adjacent to the nitrogen: a major resonance at δ 3.94 (88%) and a minor one at δ 3.44 (12%). We tentatively assign these resonances to **28a***E* and **28a***Z* (not shown). The *E*/*Z* rotamer ratio is expected to increase in benzene (the solvent for the radical translocation),[27] and indeed we could not locate resonances of the minor isomer in the ^{1}H NMR spectrum of compound **28a** recorded in this solvent. We conclude that, under the conditions of the radical reduction, amide *E*/*Z* ratios for **28a**, **b** are > 88/12.

Reduction of iodobenzoate **28a** by the syringe-pump method provided the directly reduced product **29a** in 19% yield and the phenanthridone **30a** (35%). Likewise, reduction of amido ester **28b** by the syringe-pump method provided compounds **29b** (15%) and **30b** (36%). We obtained very similar results when we reduced substrates **28a** and **28b** by the catalytic method. Phenanthridones **30a**, **b** result from a 1,6 (*ortho*) cyclization of the aryl radical derived from iodide **28a** to the *N*-phenyl group followed by oxidative re-aromatization. Related cyclizations have been observed by Grimshaw[15] and Togo.*[,28] Reduced substrate **29** must have been formed by direct hydrogen transfer from tin hydride to the aryl radical; had 1,5-hydrogen transfer occurred, 5-*exo* cyclization would have followed (see below). The behaviour of substrates **28a**, **b** is fully consistent with the model in Scheme 4. All the chemistry occurs between the aryl radical and the *E*-substituent (Ph); the translocating *Z*-substituent is ignored.

We also briefly investigated the behaviour of the *o*-iodobenzenesulfonyl analogue **31**, as shown in eqn. (4). Pines has observed that radicals derived from *o*-diazonium benzenesulfonamides perform 1,5-, 1,6-, and even 1,7-hydrogen transfers.[13d] After reduction of iodide **31** by the catalytic method, we isolated reduced product **32** in 20% yield alongside cyclic sulfonamide **33**, which we isolated in 54% yield. Given that compound **33** was the major product, we did not try to ascertain if 1,*n*-hydrogen-transfer reactions intervened in the formation of compound **32**. Though these *N*-phenyl amides and sulfonamides do not appear to be useful radical translocating groups, the aryl radical cyclizations do hold potential for heterocycle synthesis.

We next studied the behaviour of a series of substrates **34a–c** that we expected to exist with significant populations of both *E* and *Z* rotamers (Scheme 6). *E*/*Z* rotamer ratios were determined by integration of appropriate resonances in the ^{1}H NMR spectra. For the *N*-butyl and *N*-benzyl amides **34a** and **34b**, the *E*/*Z* ratios were close to 50/50. For the *N*-cyclohexyl amide **34c** the *E*/*Z* ratio was assigned as 68/32. That the

* While Togo reports a quantitative yield of a phenanthridone derived from 1,6-cyclization, Grimshaw (ref. 15) obtains mixtures of products derived from 1,6- and 1,5 (*ipso*) cyclization. In our system, the low total yields (< 60%) suggest that 1,5-cyclization might also have occurred. The so-formed spirocyclohexadienyl radical might not be reduced by tin hydride due to its stability, and it cannot directly re-aromatize. It may therefore have decomposed by unknown pathways.



Scheme 6 *Reagent:* i, Bu_3SnH

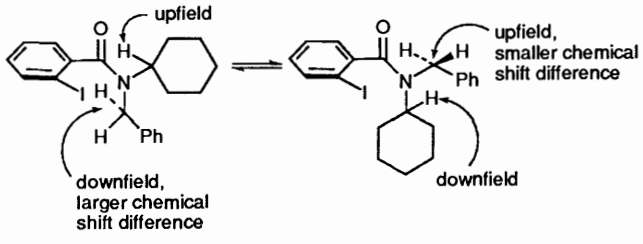
E isomer was favoured at equilibrium was suggested by both analogy to the related *N*-isopropyl compound[17g] and by chemical-shift trends in the ^1H NMR spectrum of a closely related model compound.*

In contrast to the clean, high-yielding reduction of symmetric substrate **18b** (Scheme 5), reductions of amido esters **34a–c** by the standard method gave rather complex mixtures containing one major product and a number of minor products. From each mixture, careful medium-pressure liquid chromatography (MPLC) purification provided the pure major product **35a–c** in yields of 42, 38 and 27%. These yields compare quite well with the predicted yields of the reactions, 42%, 42% and 27%, that we obtain by multiplying the % *Z* rotamer of substrate **34** by the isolated yield from the symmetrical substrate **18b** (84%).

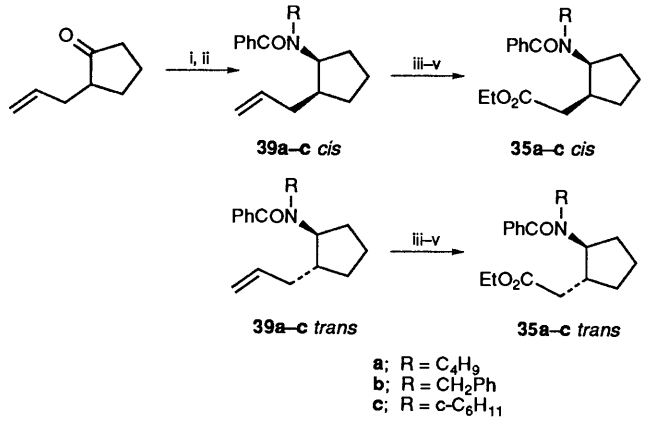
These results are consistent with the scenario in Scheme 6. Rotamers **34***Z* evolve by abstraction of iodine and rapid 1,5-hydrogen transfer to give radicals **37**, which in turn cyclize to radicals **38** and abstract a hydrogen to form compounds **35**. Rotamers **34***E* also suffer abstraction of iodine and 1,5-hydrogen transfer, but now the so-formed radicals **36** apparently evolve by a number of competing pathways to provide the unidentified minor products formed in these reactions. While we could not isolate and characterize any of these minor products, we did learn by comparison of the crude ^1H NMR spectra of the reactions with those of authentic samples that the directly reduced products are not formed in significant amounts in these reactions. This suggests that 1,5-hydrogen transfers are rapid in both rotamers, even though we isolate products from only one of them. Apparently, the concentration of tin hydride present in these reactions (< 0.02 mol dm^{-3}) is not sufficient to trap radicals **36** by hydrogen transfer, and these proceed by other pathways (oxidation? radical/radical reactions?). The failure of tin hydride to trap radicals at these concentrations is unusual, but it is precedented for other types of stabilized radicals such as benzyl and allyl.†

To verify structures and stereochemistry of adducts **35**, we prepared them by the independent route shown in Scheme 7. Reductive amination[30] of 2-allylcyclopentanone with the appropriate amine provided mixtures of stereoisomeric secondary amines, which were directly treated with benzoyl

* Owing to the complexity of the ^1H NMR spectrum of compound **34c**, its rotamer ratio could not be directly deduced. We used instead the simpler model shown below, substituting a benzyl group for the translocating side chain. When these two groups are present together (structure **34b**), the rotamer ratio is 50/50. Trends for the model compound are summarized below, and details are in the Experimental section.



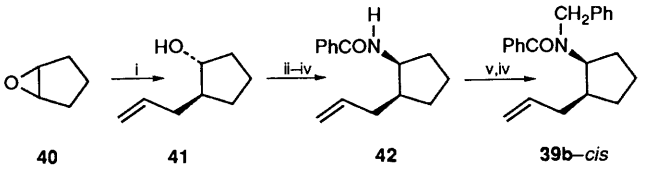
† Benzyl radicals are 50 times less reactive than alkyl radicals towards tin hydride. As concentrations approach 0.02 mol dm^{-3}, rates of H-transfer to such stabilized radicals can fall below the solution limit (ref. 29).



Scheme 7 *Reagents:* i, RNH_2, $NaBH_3CN$; ii, PhCOCl; iii, O_3; iv, Jones' reagent; v, $(ClCO)_2$, EtOH

chloride to provide amides **39a–c**-*cis* and -*trans*. At this stage, the stereoisomers were separable, and the following isolated ratios of products were obtained: 46/54; 47/53; 44/56. These six products were then individually subjected to ozonolytic cleavage, Jones oxidation, and esterification. In each case, the minor isomer corresponded to the product formed in the radical reactions of Scheme 6.

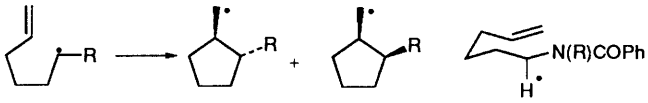
While these syntheses confirmed the general structures of the adducts, the low *cis*/*trans* selectivity in the reductive amination made configurational assignments uncertain. To secure a stereochemical assignment, **39b**-*cis* was prepared in a stereochemically defined manner as shown in Scheme 8.



Scheme 8 *Reagents:* i, CH_2=$CHCH_2MgCl$; ii, phthalimide, Ph_3P, DEAD; iii, NH_2NH_2; iv, PhCOCl; v, $LiAlH_4$

Opening of cyclopentene oxide **40** with allylmagnesium chloride provided *trans* alcohol **41**,[31] which was converted into *cis* amide **42** by a sequence of Mitsunobu displacement with phthalimide,[32] imide cleavage and benzoylation. Reduction of the benzoyl group to a benzyl group and rebenzoylation then provided **39b**-*cis*, thus confirming its stereochemistry. Similarities in the spectra of the series of structures **35** and **39** assured the consistency of the *cis*/*trans* assignments in the other two substrates.

The high *cis* selectivity observed in these cyclizations was unexpected. While more complex hexenyl radicals often show highly stereoselective cyclizations,[33] simple 1-substituted hex-5-enyl radicals like those shown below usually show low to moderate levels of selectivity. For example, when R = alkyl, moderate *cis* selectivity is usually observed,[34] while when R = *O*-alkyl or *O*-silyl,[35] moderate *trans* selectivity is observed. Substrates with R = ester or ketone usually give low selectivities.[36] The formation of the *cis* products is consistent with Beckwith's chair-like model, as shown below, but in light of the cited precedents, the reasons for the high *cis* selectivity are not clear. Experiments described below suggest the benzamide group is the crucial stereo-directing element.

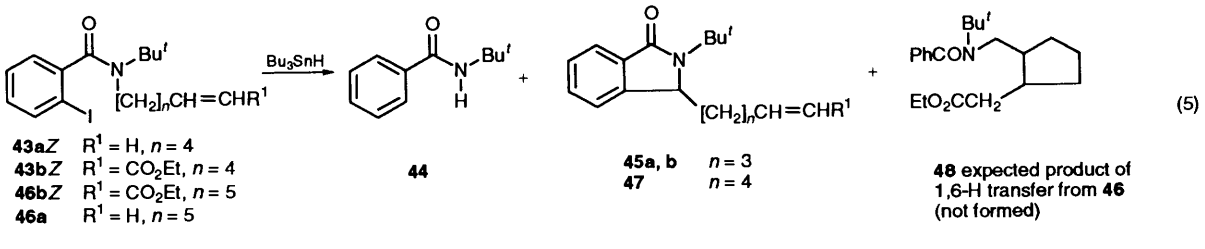


Cyclization stereoselectivities

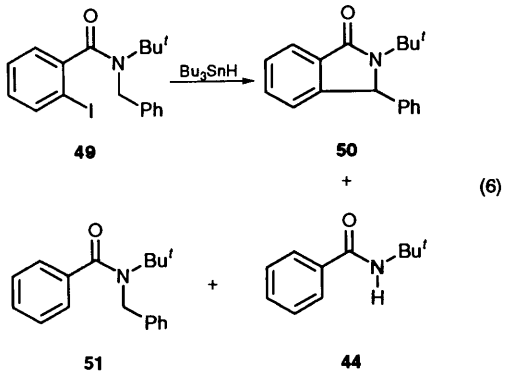
It is well known that *N*-*tert*-butyl amides strongly favour the *Z* rotamer,[17] so we selected substrates **43a**, **b** to represent unsymmetrical amides in which the translocating side chain is always favourably disposed for 1,5-hydrogen transfer [eqn. (5)]. The observations with these substrates did not follow expectations. Reductions of both iodides **43a** and **43b** provided very similar results when conducted by either the syringe-pump method or the catalytic method. In each case, a mixture of the dealkylated monosubstituted primary amide **44** and a new product **45** was formed in a ratio close to 1/1. In neither case was there evidence for formation of the directly reduced product. In the reduction of ester **43b**, there was also no evidence for formation of any of the expected 5-*exo* cyclization product. Since the reactions of compounds **43a** and **43b** were so similar, we studied in more detail only the products from compound **43a**. Reduction of compound **43a** by the catalytic method followed by purification by MPLC provided compound **44** in 41% isolated yield and bicyclic lactam **45a** in 38% isolated yield.

The formation of relatively large amounts of *N*-dealkylation products in the *tert*-butyl amides caused us to wonder about the origin of these products. We have proposed that they arise by 1,5-hydrogen transfer, followed by oxidation and hydrolysis. By this mechanism, an aldehyde should accompany the *N*-dealkylated product in equal yield, but we observed only small amounts of aldehydes in these experiments. An alternative mechanism for fragmentation involves 1,6-hydrogen transfer followed by β-elimination of the amidyl radical. This route seems unlikely because β-fragmentations of amidyl radicals are not fast. However, we tested the possibility for 1,6-hydrogen transfer by preparing and reducing the homologous substrate **46**. This reduction gave *N*-(*tert*-butyl)benzamide **44** (24%) and the isoindolinone **47** (37%). The expected product of 1,6-hydrogen transfer, compound **48**, was not observed. We conclude that the *N*-dealkylation products result from 1,5- and not 1,6-hydrogen transfer.

To probe the generality of the cyclization to form products like **45**, we prepared iodide **49** and reduced it under both the catalytic and syringe-pump procedures. The results of these experiments are summarized in eqn. (6). In addition to formation of the cyclic product **50** (46%) and the monosubstituted amide **44** (31%), we also isolated small but significant amounts of the directly reduced product **51** (9%). If amide **44** is produced by hydrolysis of an acyliminium ion, then its accompanying product should be benzaldehyde. We therefore analysed the crude reaction mixtures for the presence of



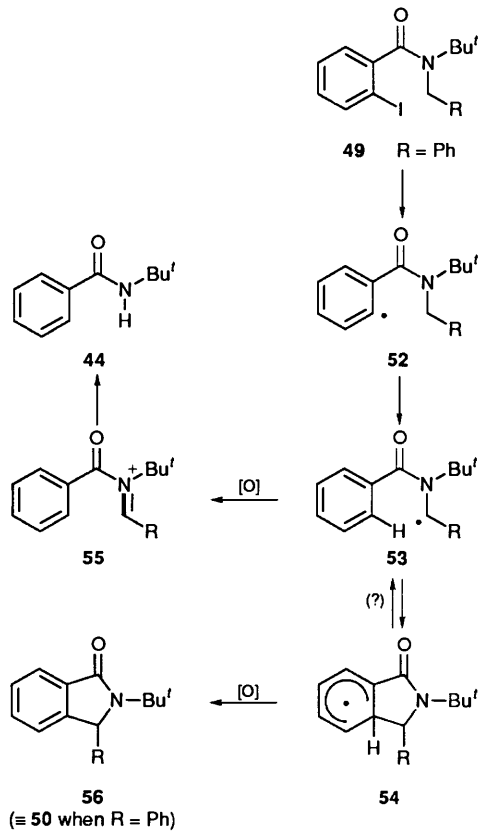
benzaldehyde by both GLC and ^1H NMR spectroscopy. While we did clearly detect benzaldehyde, its estimated yield (2–4%) was always considerably lower than the yield of amide **44**.



We propose the partial mechanism shown in Scheme 9 for the reactions of these *N-tert*-butyl amides. Initial radical **52** undergoes relatively rapid 1,5-hydrogen transfer to give amidoylalkyl radical **53**. Unfortunately, the presence of the *tert*-butyl group completely alters the subsequent behaviour of radical **53** relative to its symmetric counterpart shown in Scheme 5. Radical **53** shows no evidence of cyclization to the side chain (even with the activated acceptor **43b**), and it instead partitions between cyclization to radical **54** and oxidation, ultimately to give *tert*-butylbenzamide **44** (presumably) through acyliminium ion **55**.*[38] Conversion of radical **54** into product **56** (≡ **50** when R = Ph) again requires an oxidation.[25] Neither pathway involves a net reduction; however, no reaction occurs with azoisobutyronitrile (AIBN) in the absence of tin hydride, and when reactions were conducted with only catalytic amounts of tin hydride they stopped after partial conversion. For example, when compound **49** was treated with 10% tributyltin hydride, the reaction stopped after about 8% conversion. Finally, the bromide analogue of iodide **49** (which should be more difficult to reduce than the iodide) gave about the same product ratios when reduced under the standard conditions. These experiments suggest that neither tributyltin halide nor the starting halide is the oxidant for radicals **53** or **54**. When reductions of iodide **49** were conducted at lower concentrations (0.02 mol dm^{-3}), compound **44** actually became the major product (**50**/**44** ≈ 1/15); however, this reaction was less clean than those conducted at higher concentrations (≥ 0.2 mol dm^{-3}), and yields were not determined. The origin of the changing ratios of products **50**/**44** is unclear, though the changes suggest that the cyclization of radical **53** may be reversible.

While substrates **43**, **46** and **49** do seem to undergo reasonably efficient 1,5-hydrogen transfer, the presence of the *tert*-butyl substituent completely derails the 5-*exo* cyclization, to the benefit of dealkylation and addition to the aromatic ring. While the dealkylation pathway is observed as a minor one with other substrates, the formation of products such as compounds **45**, **47** and **50** is unique to the *tert*-butyl system. If the formation of dealkylation products could be suppressed, then this might be an excellent way to make benzo-fused lactams by radical translocation.

Though the results with all the substrates are quite consistent with the rotamer model that we proposed at the outset of the work (Scheme 4), a system that appears to have high preparative potential for conducting acylamino radical cyclizations by radical translocation did not emerge. Therefore, to close the study, we briefly investigated the related *o*-iodobenzyl amide structural motif [equation (7)]. In this class of substrate, the abstracting radical is located in one nitrogen substituent and the target C–H bond is in the other. Like the substrates in Scheme 6, substrate **57** will exist as two rotamers that will not interconvert during the lifetime of an aryl radical; however, unlike the substrates in Scheme 6, 1,5-hydrogen transfer is geometrically feasible in both rotamers.



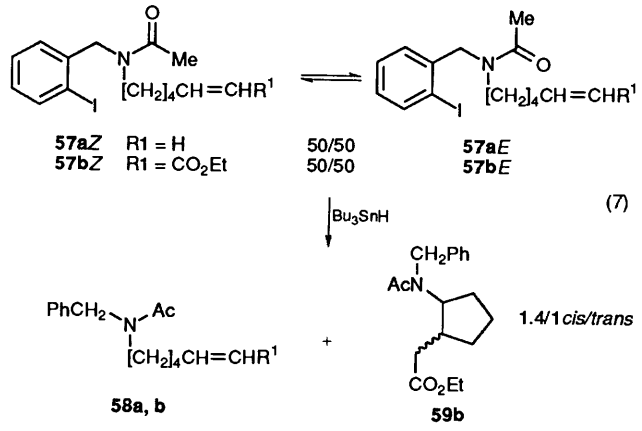
Scheme 9

N-(*o*-Iodobenzyl)acetamides **57a**, **b** were readily prepared (see Experimental section), and their *E*/*Z* rotamer ratios were close to 50/50 [eqn. (7)]. Reduction of amide **57a** by the catalytic method provided the directly reduced product **58a** in 65% isolated yield. While there were also small amounts of several minor products in the reaction, we could not obtain any in pure enough form to characterize. Reduction of amido ester **57b** gave a clean reaction mixture consisting of directly reduced product **58b** (30% isolated yield) and a 1.4/1 *cis*/*trans* mixture of cyclized products **59b** (61% isolated yield). We tentatively assign the stereochemistry of the major isomer as *cis*. We do not know whether product **58b** arises from failed hydrogen transfer or failed cyclization; however, differences in the behaviour of compounds **57a** and **57b** again underscore the need for reactive radical acceptors to observe cyclizations with these radicals.

The low cyclization stereoselectivity in this substrate is striking, especially when compared with the results in Schemes 5 and 6. It occurred to us that the different stereoselectivities in Schemes 5 and 6 compared with equation (7) might arise because the translocation reactions generated radicals in different conformations. If radical cyclization were faster than conformational interconversion, then ostensibly the same radicals could give different stereoisomers on cyclization.

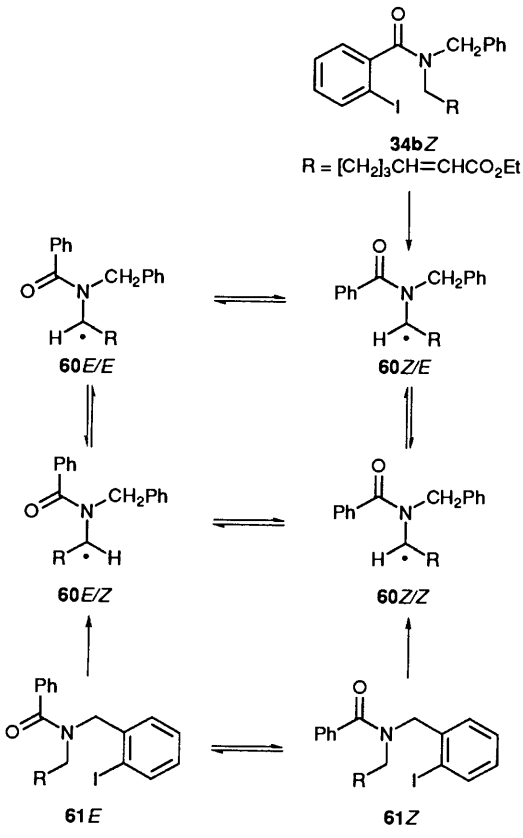
Our substrates present us with an opportunity to generate

* At this point, we cannot rule out formation of compound **56** through cyclization of cation **55**; however, this possibility seems less likely since related acyliminium ions are stable (ref. 37).

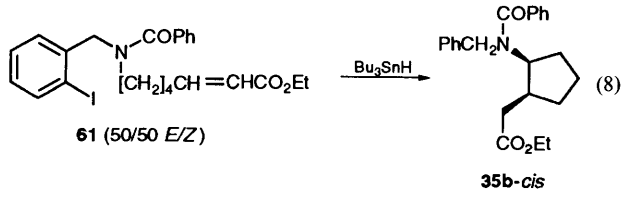


selectively rotational isomers of aminoalkyl radicals and to probe for the first time whether the stereochemistry of the products depends on the initial conformation of the radical. The ideas behind the planned experiment are summarized in Scheme 10. We envisage that the *N*-benzylbenzamide radical **60** can exist as one of four possible geometric isomers (*E*/*E*, *E*/*Z*, *Z*/*E*, *Z*/*Z*) because both the amide C–N bond and the N–C• bond[39] are expected to have significant barriers to rotation. However, unlike the aryl radicals, it is conceivable that these radicals could interconvert during their lifetimes. Relatively stable amidoalkyl radicals are expected to have much longer lifetimes than aryl radicals (perhaps as long as 10^{-2} to 10^{-3} s under these conditions). Either the radical N–C• bond or the amide C–N bond may rotate under these conditions. Resonance delocalization of the N-atom lone pair with the radical is expected to reduce the barrier to amide rotation.* Starting from the *N*-benzyl-*o*-iodobenzamide **34b***Z*, the potential equilibration in Scheme 10 should be entered exclusively at radical **60***Z*/*E*. In contrast, starting from a rotameric mixture of the *N*-(*o*-iodobenzyl)benzamide **61***E*/*Z* we can enter the equilibrium through radicals **60***Z*/*Z* (50%) and **60***E*/*Z* (50%). Will substrates **34b** and **61** give the same products on reduction? Isomers **61***E*/*Z* (50/50) were readily prepared (see Experimental section) and then reduced with tributyltin hydride [eqn. (8)]. From this reduction, we isolated a single product **35b**-*cis* in 51% yield after MPLC. Compound **35b**-*cis* was identical in all respects with that obtained by the reduction of iodo amide **34b**. There was no evidence for formation of either the directly reduced product or the *trans* isomer.

That reductions of isomers **34b** and **61** form the same product **35b** suggests that the formation of *cis*/*trans* mixtures from the amide **57b** [equation (7)] is due to the presence of the acetamide functional group as opposed to the (*cis*-selective) benzamide functional group. Though the results do not permit an unambiguous conclusion to be drawn about the interconversion in Scheme 10, the simplest scenario is that equilibrations of radical **60** shown in Scheme 10 are faster than cyclization. In this scenario, precursors **34b** and **61** then effectively generate the same radical(s). Less likely is the possibility that different, non-equilibrating radicals are generated on the reductions of compounds **34b** and **61**, but that these radicals coincidentally all cyclize with exclusive *cis* selectivity. Because the yields are not quantitative, other, even less likely scenarios cannot be



Scheme 10 Selective generation of amidoalkyl radical conformers



entirely ruled out.† At present, interpretation of the stereoselectivity differences between the benzamide [equation (8)] and acetamide [equation (7)] radicals is not possible. Do these substances cyclize through the same rotamer(s) and simply have different *cis*/*trans* selectivities, or do they cyclize through a different rotamer (or mixture of rotamers)? While it is intuitively reasonable that rapid radical cyclizations could be faster than the rotational isomerizations shown in equation (8), our stereochemical probe provides no evidence for this.

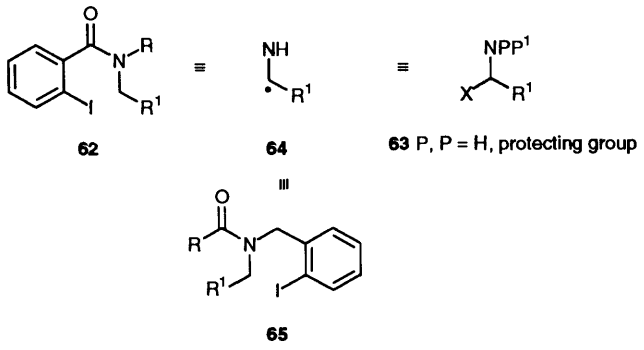
Conclusions.—The results of this study strongly support the initial premise that the reactions of *o*-iodobenzamides would depend significantly on the rotamer ratio of the radical precursor. Aryl radicals cannot suffer amide-bond rotations during their lifetimes. The yields of radical translocation products vary directly with the amide rotamer population all the way from zero for amides that prefer *E* isomers, through moderate (27–42%) for amides that exist as *E*/*Z* mixtures, to high (74–85%) for *Z* amides and symmetrical amides. Though we have not conducted good kinetic experiments, the results

* For example, it is quite clear that radicals of the type shown below can manage to rotate ester and amide bonds during their lifetime. See: ref. 40, and references therein.

† For example, starting from compound **61**, partitioning between radicals **60***Z*/*Z* and **60***E*/*Z* should occur in a ratio of ~ 50/50. Since the yield of adduct **35b**-*cis* is only 51%, we cannot rule out the possibility that this product comes only through one of the two pathways and that the other pathway leads exclusively to decomposition or un-isolated products.

suggest that all of the 1,5-hydrogen-transfer reactions of these aryl radicals are fast; $k_{1,5}$ is probably 10^7 s^{-1} or greater.

From the synthetic perspective, the class of radical-translocation reactions represented by Scheme 11 does not appear



Scheme 11 Reagents for synthon **64**

to hold as much potential as we had hoped. We had initially planned to identify a group R in substrates **62** that was easy to introduce and remove and that enforced formation of the *Z* amide rotamer required for radical translocation. Such a reagent **62** would then be the synthetic equivalent of a less readily available reagent **63** that generates radicals adjacent to primary amines **64**. The efficiency of 1,5-hydrogen transfer is not a problem, as is best exemplified by the excellent results with the symmetrical substrate **18b** (Scheme 5). Unfortunately, substrate **18b** is like a dialkylcuprate in that only one of its two reactive functional groups is operated on. Further, the detachment of the reacting group from the unreacting one does not appear to be easy. However, symmetrical amides obviate the rotamer problem, and they should be quite useful in the kinds of processes that have been investigated by Snieckus (see structures **13** and **14**). The *tert*-butyl amides were selected for their high preference for the *Z* rotamer, and indeed they appear to undergo efficient 1,5-hydrogen-transfer reactions. Unfortunately, these *tert*-butyl groups disturb the normal reactivity pattern of the radical, and new pathways are followed [equations (5) and (6)]. Though the dealkylation pathway is a nuisance, the pathway involving cyclization back to the aromatic ring could possibly be developed into a useful transformation.

Though we have investigated only two examples, the radical-translocation reactions of *N*-(*o*-iodobenzyl) amides **65** [equations (7) and (8)] appear to hold considerably more promise. In these reactions, starting rotamer populations are not a concern since hydrogen transfer can occur in either rotamer. Furthermore, the residual nitrogen substituents in the product (acyl and benzyl) could be removed by standard methods to liberate primary amines. In elegant extensions of our work on radical-translocation reactions of *o*-iodobenzyl ethers,[1,2] De Mesmaeker has generated radicals adjacent to secondary amines,[5c] and Ito has observed efficient 1,5-hydrogen-transfer reactions in tertiary amines bearing *o*-iodobenzyl groups.[41] Thus, the *o*-iodobenzyl group is emerging as a generally useful group for radical-translocation reactions of ethers, amides and amines.

Experimental

General.—All reactions were run under nitrogen. Solvents used were dried as follows: tetrahydrofuran (THF), diethyl ether and benzene were distilled under nitrogen from sodium–benzophenone. Methylene dichloride, dimethyl sulfoxide (DMSO) and triethylamine were distilled from calcium hydride. DMSO was stored over molecular sieves. Triethylamine was stored over potassium hydroxide pellets. MPLC was performed with Kieigel 60 (230–400 mesh ASTM) silica gel or on a prepacked EM lobar LiChroprep Si/60 column with a differential refractometer (Waters R401) as the detector. NMR spectra were recorded on a Bruker WH-300 (300 MH_3) instrument and mass spectra were recorded on a Varian CH5-DF instrument.

Synthesis of Radical Precursors.—N-(*Hex*-5-*enyl*)*hex*-5-*enamide* **16** (R = CH_2=$CH[CH_2]_3CO$) (*standard acylation procedure*). To a solution of hex-5-enoic acid (4.560 g, 40 mmol) in benzene (130 cm^3) at 25 °C was added oxalyl dichloride (23.27 g, 182 mmol). After the reaction mixture had been stirred for 12 h, the solvent and excess of oxalyl dichloride were removed. The acyl chloride was obtained as a pale yellow oil, which was used directly for the next reaction.

To a mixture of hex-5-enylamine (3.937 g, 40 mmol) and aq. sodium hydroxide (3.120 g, 78 mmol, in 6 cm^3) at 0 °C was added a solution of the above hex-5-enoyl chloride in THF (6 cm^3) very slowly. After the addition was complete, the reaction mixture was stirred for 12 h. Water (45 cm^3) was added and the reaction mixture was extracted with diethyl ether (3 × 80 cm^3). The combined organic layers were washed successively with water (2 ×) and brine (1 ×), and dried over magnesium sulfate. Purification by flash column chromatography [hexanes–EtOAc (2:1)] afforded the title amide (6.010 g, 75%); $\delta_H(CDCl_3)$ 5.70 (2 H, m), 5.42 (1 H, br), 5.00 (4 H, m), 3.24 (2 H, m), 2.2–2.0 (6 H, m), 1.79–1.62 (2 H, m) and 1.58–1.35 (4 H, m); ν_{max}(thin film)/cm^{-1} 3293, 3078, 2932, 2861, 1643, 1553, 1439 and 910; *m*/*z* 196, 154, 141, 126, 114, 98, 87, 69 and 55 (Found: M^+, 196.1701. $C_{12}H_{21}NO$ requires *M*, 196.1701).

Di(*hex*-5-*enyl*)*amine* **16** (R = CH_2=$CH[CH_2]_4$) (*standard LAH reduction*). To a suspension of lithium aluminium hydride (LAH) (1.366 g, 36 mmol) in anhydrous diethyl ether (12 cm^3) was added a solution of the above amide (6.0 g, 30 mmol) in THF (12 cm^3) at such a rate as to maintain gentle reflux. The addition was complete in 1 h. The mixture was then refluxed for 15 h. Water (4 cm^3) was added to the above, strongly stirred, mixture very slowly at 0 °C, and the mixture was stirred for another 30 min. Then cold aq. sodium hydroxide (9 g, 225 mmol in 22 cm^3) was added. The aqueous phase was extracted with EtOAc (5 × 30 cm^3). The combined organic layers were washed successively with water (3 × 10 cm^3) and brine (30 cm^3), and dried over magnesium sulfate. Concentration gave the title amine as a clear oil (5.101 g, 100%), $\delta_H(CDCl_3)$ 5.80 (2 H, m), 4.94 (4 H, m), 2.59 (4 H, t, *J* 7.2), 2.10–1.92 (4 H, m) and 1.59–1.30 (8 H, m); ν_{max}(thin film)/cm^{-1} 3076, 2930, 2859, 1642, 1456 and 911.

N,N-*Di*(*hex*-5-*enyl*)-2-*iodobenzamide* **18a**. Compound **18a** was prepared following the standard acylation procedure by using the above amine (5.100 g, 30 mmol) and 2-iodobenzoyl chloride **15** (9.595 g, 36 mmol). Purification by MPLC [hexanes–EtOAc (6:1)] afforded amide **18a** (6.705 g, 54%), $\delta_H(CDCl_3)$ 7.80 (1 H, d, *J* 7.8), 7.36 (1 H, m), 7.17 (1 H, dd, *J* 0.7 and 7.6), 7.04 (1 H, m), 5.86–5.74 and 5.74–5.58 (2 H, m), 5.08–4.82 (4 H, m), 3.76 (1 H, m), 3.19 (1 H, m), 3.02 (2 H, m), 2.13 (2 H, m), 1.89 (2 H, m), 1.75 (2 H, m), 1.66–1.32 (4 H, m) and 1.20 (2 H, m); ν_{max}(thin film)/cm^{-1} 2932, 2859, 1638, 1585, 1475, 1423, 910 and 772; *m*/*z* 411, 370, 342, 231, 203, 105 and 77 (Found: M^+, 411.1059. $C_{19}H_{26}INO$ requires *M*, 411.1059).

N,N-*Bis*[(E)-6-*ethoxycarbonylhex*-5-*enyl*]-2-*iodobenzamide* **18b** (*general ozonolysis and olefination procedure*). A solution of compound **18a** (1.644 g, 4.0 mmol) in CH_2Cl_2–MeOH (60 cm^3; 5:1) was ozonized at −78 °C. Ozonolysis was terminated when the solution became blue. The solution was bubbled with air until it became colourless. Then dimethyl sulfide (1 cm^3) was added, and the reaction mixture was allowed to warm to 25 °C before being diluted with water (15 cm^3) and extracted with diethyl ether (3 × 30 cm^3). The combined ether layers were

washed successively with water (3 ×) and brine (1 ×), and dried over $MgSO_4$. Concentration afforded the dialdehyde, which was used for the next step without purification.

Olefination. To a suspension of sodium hydride (60%; 0.4000 g, 10 mmol) in THF (10 cm^3) was added 'triethyl phosphonoacetate' (ethyl diethoxyphosphorylacetate) (2.240 g, 10 mmol). The reaction mixture was stirred until evolution of gas had ceased. Then a solution of the above dialdehyde in THF (5 cm^3) was added, and the reaction mixture was stirred for 5 h, diluted with water (20 cm^3) and extracted with diethyl ether (3 × 40 cm^3). The combined organic layers were washed successively with water (3 ×) and brine (1 ×), and dried over magnesium sulfate. Purification by flash column chromatography [hexanes–EtOAc (2:1)] gave diester **18b** as an oil (0.5600 g, 25% from **18a**), $\delta_H(CDCl_3)$ 7.80 (1 H, d, *J* 7.8), 7.37 (1 H, m), 7.16 (1 H, dd, *J* 1.3 and 7.5), 7.05 (1 H, m), 6.96 (1 H, td, *J* 7.0 and 15.6), 6.81 (1 H, td, *J* 6.9 and 14.6), 5.84 (1 H, d, *J* 14.6), 5.77 (1 H, d, *J* 15.6), 4.24–4.08 (4 H, m), 3.84–3.72 (1 H, m), 3.26–3.12 (1 H, m), 3.12–2.98 (2 H, m), 2.28 (2 H, m), 2.04 (2 H, m) 1.83–1.71 (2 H, m), 1.71–1.50 (4 H, m), 1.50–1.32 (1 H, m), 1.28 (6 H, t, *J* 7.1) and 1.32–1.19 (1 H, m); $\delta_H([^2H_6]DMSO$; 373 K) 7.85 (1 H, dd, *J* 0.9 and 7.6), 7.43 (1 H, m), 7.19 (1 H, dd, *J* 1.6 and 7.6), 7.13 (1 H, m), 6.94–6.82 (1 H, m), 6.82–6.71 (1 H, m), 5.92–5.80 (1 H, m), 5.80–5.64 (1 H, m), 4.12 (4 H, q, *J* 7.1), 3.43 (2 H, br), 3.00 (2 H, br), 2.37–2.22 (2 H, m) 2.07–1.98 (2 H, m), 1.75–1.60 (2 H, m), 1.60–1.43 (5 H, m) and 1.22 (7 H, m); ν_{max}(thin film)/cm^{-1} 2936, 2863, 1719, 1638, 1585, 1425, 1308, 1169 and 771; *m/z* 555, 510, 442, 402, 184, 146, 105 and 77 (Found: M^+, 555.1483. $C_{25}H_{34}INO_5$ requires *M*, 555.1482).

Hex-5-enyl 2-iodobenzoate **25a**. To a solution of 2-iodobenzoic acid (4.960 g, 20 mmol) in pyridine (64 cm^3) at 0 °C were added benzenesulfonyl chloride (7.064 g, 40 mmol) and hex-5-en-1-ol (2.003 g, 20 mmol). The reaction was stirred for 1 h, and was then diluted with water (20 cm^3), and extracted with diethyl ether (3 × 70 cm^3). The combined organic layers were washed successively with water (3 ×) and brine (1 ×), and dried over magnesium sulfate. The excess of pyridine was removed by distillation at atmospheric pressure. Purification by flash column chromatography [hexanes–EtOAc (15:1)] gave ester **25a** as a clear oil (3.734 g, 57%), $\delta_H(CDCl_3)$ 7.99 (1 H, dd, *J* 0.9 and 7.9), 7.78 (1 H, dd, *J* 1.7 and 7.8), 7.40 (1 H, m), 7.14 (1 H, m), 5.81 (1 H, m), 5.01 (2 H, m), 4.34 (2 H, t, *J* 6.6), 2.12 (2 H, m), 1.80 (2 H, m) and 1.33 (2 H, m); ν_{max}(thin film) 3071, 2934, 2858, 1728, 1639, 1583, 1562, 1385, 740 and 686; *m/z* 330, 315, 276, 248, 203, 121, 104, 82, 76 and 54 (Found: M^+, 330.0118. $C_{13}H_{15}IO_2$ requires *M*, 330.0117).

(E)-6-*Ethoxycarbonylhex-5-enyl 2-iodobenzoate* **25b**. Compound **25a** (2.798 g, 8.5 mmol) was ozonized to the corresponding aldehyde following the general ozonolysis procedure. Purification by flash column chromatography [hexanes–EtOAc (6:1)] afforded the aldehyde as a clear oil (2.788 g, 89%), $\delta_H(CDCl_3)$ 9.79 (1 H, m), 7.99 (1 H, d, *J* 7.9), 7.78 (1 H, dd, *J* 1.7 and 7.7), 7.39 (1 H, m), 7.14 (1 H, m), 4.31 (2 H, t, *J* 6.5), 2.54 (2 H, m) and 1.81 (4 H, m); ν_{max}(thin film)/cm^{-1} 3020, 2953, 2724, 1716, 1558, 1352, 957 and 750.

Wittig olefination. Compound **25b** was prepared following the general olefination procedure for compound **18b** by using the above aldehyde (2.224 g, 6.7 mmol). Purification by flash column chromatography [hexanes–EtOAc (15:1)] gave iodide **25b** as a clear oil (1.730 g, 65%), $\delta_H(CDCl_3)$ 8.0 (1 H, dd, *J* 0.9 and 8.9), 7.77 (1 H, dd, *J* 1.6 and 7.7), 7.41 (1 H, m), 7.15 (1 H, m), 6.96 (1 H, td, *J* 6.9 and 15.7), 5.84 (1 H, m), 4.35 (2 H, t, *J* 6.3), 4.18 (2 H, q, *J* 7.1), 2.28 (2 H, m), 1.80 (2 H, m), 1.65 (2 H, m) and 1.28 (3 H, t, *J* 7.1); ν_{max}(thin film)/cm^{-1} 3061, 2939, 2850, 1717, 1583, 1560, 1464, 1388, 857 and 746; *m/z* 402, 356, 248, 231, 108, 76 and 55 (Found: M^+, 402.0328. $C_{16}H_{19}IO_4$ requires *M*, 402.0328).

N-*Phenylhex-5-enamide*. To a vigorously stirred solution of aniline (14.00 g, 150.3 mmol, distilled from CaH_2) in benzene (20 cm^3) at 0 °C was added a solution of hex-5-enoyl chloride (6.550 g, 50.1 mmol) in benzene (2.5 cm^3) very slowly. The reaction mixture was stirred for 10 h at 25 °C. Water (25 cm^3) was added, and the benzene layer was separated. The aqueous phase was extracted with diethyl ether (3 × 40 cm^3). The combined organic layers were washed successively with water (1 ×) and brine (1 ×), and dried over magnesium sulfate. The excess of aniline was removed by distillation at atmospheric pressure. Purification by flash column chromatography [hexanes–EtOAc (6:1)] afforded the pure title amide (7.764 g, 82%), $\delta_H(CDCl_3)$ 7.66 (4 H, m), 7.09 (1 H, t, *J* 7.4), 5.80 (1 H, m), 5.03 (2 H, m), 2.36 (2 H, t, *J* 7.4), 2.14 (2 H, m) and 1.83 (2 H, m); ν_{max}(thin film)/cm^{-1} 3298, 3138, 3074, 2932, 1661, 1601, 1545, 1443, 1254, 754 and 693; *m/z* 189, 135, 93 and 77 (Found: M^+, 189.1154. $C_{12}H_{15}NO$ requires *M*, 189.1154).

N-(*Hex-5-enyl*)*aniline*. Prepared following the standard LAH reduction procedure with the above amide (7.564 g, 40.0 mmol) and LAH (1.671 g, 40.4 mmol). The title amine was obtained as a clear oil after purification by flash column chromatography [hexanes–EtOAc (40:1); Al_2O_3, basic] (6.701 g, 96%), $\delta_H(CDCl_3)$ 7.18 (2 H, m), 6.69 (1 H, t, *J* 7.5), 6.61 (2 H, d, *J* 7.7), 5.83 (1 H, m), 5.01 (2 H, m), 3.60 (1 H, br), 3.12 (2 H, t, *J* 6.9), 2.11 (2 H, m) and 1.58 (4 H, m); ν_{max}(thin film)/cm^{-1} 3410, 3052, 2930, 2857, 1603, 1507, 1478, 1321, 749 and 693; *m/z* 175, 132, 106, 93 and 77 (Found: M^+, 175.1361. $C_{12}H_{17}N$ requires *M*, 175.1361).

N-(*Hex-5-enyl*)-2-*iodo*-N-*phenylbenzamide* **28a**. Prepared following the standard acylation procedure by using the above amine (1.750 g, 10 mmol) and 2-iodobenzoyl chloride **15** (3.990 g, 15 mmol). Purification by flash column chromatography [hexanes–EtOAc (15:1)] afforded the title amide as a clear oil (3.387 g, 84%), $\delta_H(CDCl_3)$ 7.65 (1 H, d, *J* 7.8), 7.41 (2 H, m), 7.08 (5 H, m), 6.81 (1 H, dt, *J* 1.6 and 7.4), 5.79 (1 H, m), 4.96 (2 H, m), 3.94 (2 H, t, *J* 6.8), 2.08 (2 H, m) and 1.59 (4 H, m); ν_{max}(thin film)/cm^{-1} 3067, 2967, 2932, 2858, 1647, 1595, 1495, 1394, 1304, 1014, 698 and 766; *m/z* 405, 323, 231, 203, 105 and 77 (Found: M^+, 405.0590. $C_{19}H_{20}INO$ requires *M*, 405.0590).

N-(*Hex-5-enyl*)-N-*phenylbenzenesulfonamide* **32**. To a solution of hex-5-enylamine **16** (R = H) (0.875 g, 5 mmol) in pyridine (10 cm^3) at 0 °C was added benzenesulfonyl chloride (1.766 g, 10 mmol) dropwise. After the addition was complete, the reaction mixture was refluxed for 10 h. Excess of pyridine was removed by distillation at atmospheric pressure. Water (10 cm^3) was added, and the mixture was extracted with EtOAc (3 × 25 cm^3). The combined organic layers were washed successively with 10% hydrochloric acid (2 ×), water (2 ×) and brine (1 ×), and dried over magnesium sulfate. Purification by flash column chromatography [hexanes/EtOAc (10:1)] gave the title sulfonamide (1.621 g, 100%), $\delta_H(CDCl_3)$ 7.57 (3 H, m), 7.45 (2 H, t, *J* 7.2), 7.28 (3 H, m), 7.03 (2 H, m), 5.73 (1 H, m), 4.73 (2 H, m), 3.54 (2 H, m), 2.00 (2 H, m) and 1.47 (4 H, m); ν_{max}(thin film)/cm^{-1} 3069, 2936, 2864, 1639, 1595, 1491, 1446, 1350, 914 and 760; *m/z* 315, 272, 246, 174, 141, 107 and 77 (Found: M^+, 315.1292. $C_{18}H_{21}NO_2S$ requires *M*, 315.1293).

N-(*Hex-5-enyl*)-2-*iodo*-N-*phenylbenzenesulfonamide* **31**. To a solution of the above sulfonamide **32** (1.571 g, 5.0 mmol) in THF–Et_2O [(1:1) 100 cm^3] at −60 °C was added a solution of butyllithium in hexanes (1.53 mol dm^{-3}; 3.9 cm^3, 6.0 mmol) very slowly. After the addition was complete, the mixture was stirred at −60 °C for 8 h. A solution of iodine (1.524 g, 6.0 mmol) in THF (10 cm^3) was added dropwise. The reaction mixture was allowed to warm to 25 °C. Water (20 cm^3) was added, and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 40 cm^3). The combined organic layers were washed successively with saturated aq. $Na_2S_2O_3$ (1 ×), water (2 ×) and brine (1 ×), and dried over magnesium sulfate. Purification by flash column chromatography [hexanes–EtOAc (15:1)] afforded iodide **31** (2.105 g,

96%), $\delta_H(CDCl_3)$ 8.03 (1 H, dd, *J* 1.0 and 7.7), 7.82 (1 H, dd, *J* 1.6 and 7.9), 7.23 (6 H, m), 7.08 (1 H, dt, *J* 1.6 and 7.8), 5.71 (1 H, m), 4.92 (2 H, m), 3.86 (2 H, t, *J* 6.9), 2.00 (2 H, m) and 1.47 (4 H, m); ν_{max}(thin film)/cm^{-1} 3067, 2932, 2860, 1640, 1593, 1491, 1449, 1335, 912 and 762; *m/z* 441, 372, 267, 203, 174, 106 and 77 (Found: M$^+$, 441.0258. $C_{18}H_{20}INO_2S$ requires *M*, 441.0260).

N-*Butylhex-5-enamide*. Prepared following the standard acylation procedure with hex-5-enoic acid (1.710 g, 15 mmol) and butylamine (3.291 g, 45 mmol). Purification by flash column chromatography [hexanes/EtOAc (2:1)] afforded the title amide (1.910 g, 75%), $\delta_H(CDCl_3)$ 5.76 (1 H, m), 5.43 (1 H, br), 4.98 (2 H, m), 3.23 (2 H, m), 2.17–2.02 (4 H, m), 1.72 (2 H, m), 1.52–1.40 (2 H, m), 1.40–1.23 (2 H, m) and 0.91 (3 H, t, *J* 7.1) ν_{max}(thin film)/cm^{-1} 3287, 3078, 2926, 2865, 1641, 1549, 1439 and 910; *m/z* 169, 154, 127, 115, 97, 86, 73, 69, 60, 57 and 44 (Found: M$^+$, 169.1467. $C_9H_{19}NO$ requires *M*, 169.1467).

N-*Butyl*-N-(*hex-5-enyl*)-2-*iodobenzamide*. The requisite amine was prepared following the standard LAH procedure with the above amide (1.901 g, 11.2 mmol) and LAH (0.4690 g, 12.4 mmol). Concentration gave the amine **16** (R = Bu) (1.490 g, 86%), which was used for next step without purification.

To a solution of the amine (1.490 g, 9.6 mmol) and triethylamine (2.020 g, 20 mmol) in CH_2Cl_2 (20 cm^3) at 0 °C was added a solution of 2-iodobenzoyl chloride **15** (3.997 g, 15 mmol) in CN_2Cl_2. The reaction mixture was stirred for 8 h. The reaction mixture was diluted with water (20 cm^3), and extracted with diethyl ether (3 × 30 cm^3). The combined organic layers were washed with water (3 ×) and brine (1 ×), and dried over $MgSO_4$. Purification by flash column chromatography [hexanes–EtOAc (6:1)] gave the amide (1.681 g, 44%), $\delta_H(CDCl_3)$ 7.80 (1 H, m), 7.36 (1 H, m), 7.17 (1 H, m), 7.04 (1 H, m), 5.89–5.60 (1 H, m), 5.09–4.83 (1 H, m), 3.78 (1 H, m), 3.22 (1 H, m), 3.08 (2 H, m), 2.13 and 1.91 (2 H, m), 1.84 and 1.62 (2 H, m), 1.62–1.33 (4 H, m), 1.30–1.08 (2 H, m), 0.98 and 0.76 (3 H, t, *J* 7.3).

N-*Butyl*-N-[(E)-6-*ethoxycarbonylhex-5-enyl*]-2-*iodobenzamide* **34a**. Compound **34a** was prepared following the general ozonolysis/Wittig procedure with the above amide (0.9650 g, 2.5 mmol). Purification by flash column chromatography [hexanes–EtOAc (3:1)] afforded compound **34a** (0.5780 g, 51%), $\delta_H(CDCl_3)$ 7.80 (1 H, d, *J* 8.0), 7. 37 (1 H, m), 7.18 (1 H, d, *J* 7.6), 7.05 (1 H, m), 6.98 and 6.82 (1 H, m), 5.85 and 5.71 (1 H, d, *J* 15.7), 4.18 (2 H, q, *J* 7.1), 3.67 (1 H, m), 3.20 (1 H, m), 3.08 (2 H, m), 2.26 and 2.08 (2 H, m), 1.82–1.72 (2 H, m), 1.72–1.50 (2 H, m), 1.50–1.35 (2 H, m), 1.35–1.11 (5 H, m) and 0.98 and 0.76 (3 H, t, *J* 7.3); ν_{max}(thin film)/cm^{-1} 2934, 2867, 1719, 1638, 1425, 1306, 1269 and 750; *m/z* 457, 421, 344, 316, 304, 231, 203, 105 and 77 (Found: M$^+$, 457.1118. $C_{20}H_{28}INO_3$ requires *M*, 457.1116).

N-*Benzylhex-5-enamide*. Prepared following the standard procedure with hex-5-enoic acid (1.250 g, 11.0 mmol) and benzylamine (2.954 g, 27.5 mmol). Purification by flash column chromatography [hexanes–EtOAc (3:1)] afforded the title amide (1.638 g, 73%), $\delta_H(CDCl_3)$ 7.28 (5 H, m), 5.75 (1 H, m), 5.67 (1 H, br), 5.00 (2 H, m), 4.40 (2 H, d, *J* 5.6), 2.22 (2 H, t, *J* 7.4), 2.11 (2 H, m) and 1.84 (2 H, m); ν_{max}(thin film)/cm^{-1} 3281, 3033, 2930, 2863, 1644, 1551, 1454 and 698; *m/z* 203, 174, 160, 149, 106, 91, 79, 65 and 41 (Found: M$^+$, 203.1310. $C_{13}H_{17}NO$ requires *M*, 203.1310).

N-*Benzyl*-N-(*hex-5-enyl*)-2-*iodobenzamide*. The requisite amine was prepared following the standard LAH procedure with the above amide (1.638 g, 8.1 mmol) and LAH (0.4590 g, 12.0 mmol). Concentration gave the amine (1.354 g, 88%), which was used for the next step without purification.

The amide was prepared following the above procedure with the amine (1.354 g, 7.2 mmol), pyridine (2.373 g, 30 mmol), and 2-iodobenzoyl chloride **15** (3.992 g, 15 mmol). Purification by flash column chromatography afforded the title amide (2.090 g, 62%), $\delta_H(CDCl_3)$ 7.82 (1 H, m), 7.49–7.01 (8 H, m), 5.80 and 5.64 (1 H, m), 4.93 (2 H, m), 5.12 and 4.48 (1 H, m), 4.37 (1 H, m), 3.92 and 3.00 (2 H, m), 2.08 and 1.86 (2 H, m), 1.72 (1 H, m), 1.60–1.30 (2 H, m) and 1.11 (1 H, m); ν_{max}(thin film)/cm^{-1} 3029, 2930, 2859, 1640, 1473, 1423 and 747; *m/z* 419, 378, 350, 336, 292, 248, 231, 203, 105, 91 and 59 (Found: M$^+$, 419.0746. $C_{20}H_{22}INO$ requires *M*, 419.0746).

N-*Benzyl*-N-[(E)-*ethoxycarbonylhex-5-enyl*]-2-*iodobenzamide* **34**. Compound **34b** was prepared following the general ozonolysis–Wittig procedure with the above amide (1.050 g, 2.5 mmol). Purification by flash column chromatography [hexanes–EtOAc (3:1)] afforded compound **34b** (0.8000 g, 65%), $\delta_H(CDCl_3)$ 7.80 (1 H, m), 7.49–7.00 (8 H, m), 6.90 and 6.78 (1 H, m), 5.80 and 5.73 (1 H, d, *J* 15.5), 5.08 and 4.54–4.26 (2 H, m), 4.18 (2 H, q, *J* 7.0), 3.90 and 2.99 (2 H, m), 2.23 (1 H, m), 1.98 (1 H, m), 1.73 (1 H, m), 1.55 (2 H, m), 1.29 (3 H, t, *J* 7.0) and 1.20 (1 H, m); ν_{max}(thin film)/cm^{-1} 2934, 1717, 1638, 1453, 1269 and 746; *m/z* 491, 446, 417, 378, 364, 338, 318, 290, 260, 231, 105, 91 and 77 (Found: M$^+$, 491.0960. $C_{23}H_{26}INO_3$ requires *M*, 491.0959).

N-*Cyclohexylhex-5-enamide*. Prepared following the standard acylation procedure with hex-5-enoic acid (1.710 g, 15 mmol) and cyclohexylamine (4.461 g, 45 mmol). Purification by flash column chromatography [hexanes–EtOAc (2:1)] afforded the title amide (2.106 g, 72%), $\delta_H(CDCl_3)$ 5.75 (1 H, m), 5.25 (1 H, m), 4.99 (2 H, m), 3.77 (1 H, m), 2.12 (4 H, m), 1.71 (2 H, m), 1.66 (5 H, m), 1.35 (2 H, m) and 1.10 (3 H, m); ν_{max}(thin film)/cm^{-1} 3291, 2934, 2855, 1634 and 1551; *m/z* 195, 141, 98, 83, 69, 56 and 41 (Found: M$^+$, 195.1623. $C_{12}H_{21}NO$ requires *M*, 195.1623).

N-*Cyclohexyl*-N-(*hex-5-enyl*)-2-*iodobenzamide*. The requisite amine was prepared following the standard LAH procedure with the above amide (2.100 g, 10.8 mmol) and LAH (0.449 g, 11.8 mmol). Concentration gave the amine, which was used for the next step without purification.

The amide was prepared following the above procedure with the amine (10.8 mmol), triethylamine (2.171 g, 21.5 mmol), and 2-iodobenzoyl chloride **15** (4.317 g, 16.2 mmol). Purification by flash column chromatography [hexanes–EtOAc (6:1)] afforded the title amide (2.840 g, 64%), $\delta_H(CDCl_3)$ 7.80 (1 H, m), 7.32 (1 H, m), 7.18 (1 H, m), 7.03 (1 H, m), 5.82 and 5.60 (1 H, m), 4.91 (2 H, m), 4.36 and 3.48 (1 H, m), 3.25–2.82 (2 H, m), 2.20–2.00 (2 H, m), 2.00–1.75 (3 H, m), 1.75–1.58 (2 H, m), 1.58–1.28 (6 H, m) and 1.20–0.80 (3 H, m); ν_{max}(thin film)/cm^{-1} 3071, 2932, 2855, 1632, 1585, 1313 and 752; m/z 411, 328, 285, 231, 139, 105, 81 and 55 (Found: M$^+$, 411.1059. $C_{19}H_{26}INO$ requires *M*, 411.1059).

N-*Cyclohexyl*-N-[(E)-6-*ethoxycarbonylhex-5-enyl*]-2-*iodobenzamide* **34c**. Compound **34c** was prepared following the general ozonolysis–Wittig procedure with the above amide (1.027 g, 2.5 mmol). Purification by flash column chromatography [hexanes–EtOAc (3:1)] afforded compound **34c** (0.7050 g, 58%), $\delta_H(CDCl_3)$ 7.81 (1 H, m), 7.38 (1 H, m), 7.20 and 7.15 (1 H, m), 7.04 (1 H, m), 6.96 and 6.75 (1 H, m), 5.83 and 5.67 (1 H, d, *J* 15.8), 4.18 (2 H, q, *J* 7.2), 4.39 and 3.50 (1 H, m), 3.24–2.80 (2 H, m), 2.30 and 2.00 (2 H, m), 1.98 and 1.12 (11 H, m), 1.28 (3 H, t, *J* 7.2) and 1.22–0.80 (3 H, m); ν_{max}(thin film)/cm^{-1} 3051, 2928, 1717, 1653, 1559 and 1456; *m/z* 483, 438, 370, 356, 330, 310, 232, 203, 170, 105 and 77 (Found: M$^+$, 483.1277. $C_{20}H_{30}INO_3$ requires *M*, 483.1272).

N-(tert-*Butyl*)*hex-5-enamide*. Prepared following the standard acylation procedure by using hex-5-enoic acid (5.8 g, 50 mmol) and *tert*-butylamine (7.3 g, 100 mmol). Purification by flash column chromatography [hexanes–EtOAc (5:1)] afforded the title amide (7.5 g, 89%), $\delta_H(CDCl_3)$ 5.78 (1 H, m), 5.24 (1 H, br), 4.96 (2 H, m), 2.12 (4 H, m), 1.73 (2 H, m) and 1.38 (9 H, s); ν_{max}(thin film)/cm^{-1} 3308, 3076, 2969, 1672, 1551, 1454, 1364,

1227 and 912; *m/z* 169, 115, 84, 69, 58 and 49 (Found: M^+, 169.1467. $C_{10}H_{19}NO$ requires *M*, 169.1467).

N-(tert-*Butyl*)*hex*-5-*enylamine* **16** (R = Bu^t). Prepared following the standard LAH procedure with the above amide (0.8450 g, 5.0 mmol). Concentration gave the title amine as a yellow oil (0.6340 g, 83%), $\delta_H(CDCl_3)$ 5.79 (1 H, m), 4.97 (2 H, m), 2.54 (2 H, t, *J* 6.7), 2.05 (2 H, m), 1.43 (4 H, m) and 1.09 (9 H, m); ν_{max}(thin film)/cm^{-1} 3277, 3078, 2969, 2930, 2859, 1362, 1233 and 910; *m/z* 155, 140, 99, 86, 58 and 54 (Found: M^+, 155.1674. $C_{10}H_{21}N$ requires *M*, 155.1674).

N-(tert-*Butyl*)-N-(*hex*-5-*enyl*)-2-*iodobenzamide* **43a**. Prepared following the standard acylation procedure by using the above amine (0.2400 g, 1.5 mmol) and 2-iodobenzoyl chloride **15** (0.7800 g, 3.0 mmol). Purification by MPLC [hexanes–EtOAc (7:1)] yielded iodide **43a** (0.4610 g, 80%), $\delta_H(CDCl_3)$ 7.79 (1 H, d, *J* 7.8), 7.35 (1 H, m), 7.21 (1 H, dd, *J* 1.4 and 7.4), 7.01 (1 H, m), 5.61 (1 H, m), 4.86 (2 H, m), 3.22 (1 H, m), 2.94 (1 H, m), 1.91 (2 H, m), 1.57 (9 H, s), 1.38 (2 H, m) and 1.09 (2 H, m); ν_{max}(thin film)/cm^{-1} 3071, 2970, 1638, 1588, 1397, 1300, 1250, 1013, 910 and 774; *m/z* 385, 370, 342, 328, 288, 260, 231, 203, 105, 76 and 57 (Found: M^+, 385.0902. $C_{17}H_{24}INO$ requires *M*, 385.0903).

N-(tert-*Butyl*)*hept*-6-*enamide*. Prepared following the standard acylation procedure by using hept-6-enoic acid (3.840 g, 30 mmol) and *tert*-butylamine (6.582 g, 90 mmol). Purification by flash column chromatography [hexanes–EtOAc (4:1)] gave the title amide (4.918 g, 90%); $\delta_H(CDCl_3)$ 5.79 (1 H, m), 5.22 (1 H, br), 4.94 (2 H, m), 2.19 (4 H, m), 1.62 (2 H, m), 1.38 (2 H, m) and 1.34 (9 H, s); ν_{max}(thin film)/cm^{-1} 3310, 3071, 2962, 2854, 1647, 1453, 1363, 1226 and 1031; *m/z* 183, 128, 115, 83, 72 and 58 (Found: M^+, 183.1623. $C_{11}H_{21}NO$ requires *M*, 183.1623).

N-(tert-*Butyl*)*hept*-6-*enylamine*. Prepared following the standard LAH procedure by using the above amide (4.658 g, 25.5 mmol). Concentration afforded the title amine as a clear oil (4.213 g, 98%), $\delta_H(CDCl_3)$ 5.79 (1 H, m), 4.96 (2 H, m), 2.52 (2 H, t, *J* 7.0), 2.04 (2 H, m) and 1.40 (6 H, m); ν_{max}(thin film)/cm^{-1} 3315, 3078, 2928, 2875, 1641 and 1541; *m/z* 169, 154, 86, 74 and 58 (Found: M^+, 169.1831. $C_{11}H_{23}N$ requires *M*, 169.1830).

N-(tert-*Butyl*)-N-(*hept*-6-*enyl*)-2-*iodobenzamide* **46a**. Compound **46a** was prepared following the standard acylation procedure by using 2-iodobenzoyl chloride **15** (2.389 g, 9 mmol) and the above amine (1.014 g, 6 mmol). Purification by flash column chromatography [hexanes–EtOAc (10:1)] gave iodide **46a** as a clear oil (2.296 g, 100%), $\delta_H(CDCl_3)$ 7.80 (1 H, m), 7.36 (1 H, m), 7.24 (1 H, m), 7.03 (1 H, m), 5.68 (1 H, m), 4.91 (2 H, m), 3.20 (1 H, m), 2.95 (1 H, m), 1.88 (2 H, m), 1.58 (9 H, s), 1.35 (2 H, m), 1.12 (2 H, m) and 0.94 (2 H, m); ν_{max}(thin film)/cm^{-1} 3073, 2930, 2857, 1646, 1561, 1462, 1363, 1015, 910 and 773; *m/z* 399, 384, 356, 342, 316, 288, 260, 203, 105, 77 and 55 (Found: M^+, 399.1060. $C_{18}H_{26}INO$ requires *M*, 399.1059).

N-(tert-*Butyl*)*benzylamine*. Prepared following the standard LAH procedure with *N*(*tert*-butyl)benzamide **44** (1.750 g, 10 mmol). Concentration gave the title amine (1.222 g, 75%), $\delta_H(CDCl_3)$ 7.32 (5 H, m), 3.73 (2 H, s) and 1.18 (9 H s); ν_{max}(thin film)/cm^{-1} 3310, 3064, 3028, 2963, 1544, 1477, 1363 and 1027; *m/z* 162, 122, 105, 77, 57 and 51 (Found: M^+, 162.1283. $C_{11}H_{16}N$ requires *M*, 162.1283).

N-*Benzyl*-N-(tert-*butyl*)-2-*iodobenzamide* **49**. Compound **49** was prepared following the standard acylation procedure by using 2-iodobenzoyl chloride **15** (1.998 g, 7.5 mmol) and the above amine (1.221 g, 5.5 mmol). Purification by flash column chromatography [hexanes–EtOAc (15:1)] gave iodide **49** (1.188 g, 55%), $\delta_H(CDCl_3)$ 7.76 (1 H, d, *J* 8.0), 7.21 (7 H, m), 6.93 (1 H, dt, *J* 2.0 and 7.4), 4.57 (1 H, d, *J* 17.7), 4.41 (1 H, d, *J* 17.7) and 1.56 (9 H, s); ν_{max}(thin film)/cm^{-1} 3050, 2967, 1640, 1397, 1260, 1225, 1017, 970 and 750; *m/z* 393, 378, 336, 231, 203, 105, 91, 77 and 57 (Found: M^+, 393.0591. $C_{18}H_{20}INO$ requires *M*, 393.0590).

N-*Benzyl*-N-(tert-*butyl*)-2-*bromobenzamide*. Prepared following the standard acylation procedure by using 2-bromobenzoyl chloride (0.6580 g, 3 mmol) and the above amine (0.326 g, 2 mmol). Purification by flash column chromatography [hexanes–EtOAc (8:1)] gave the title bromide as an oil (0.602 g, 87%), $\delta_H(CDCl_3)$ 7.49 (1 H, d, *J* 7.9), 7.20 (8 H, m), 4.56 (1 H, d, *J* 17.1), 4.43 (1 H, d, *J* 17.1) and 1.56 (9 H, s).

N-(*Hex*-5-*enyl*)*acetamide*. Prepared following the standard acylation procedure by using hex-5-enylamine (0.990 g, 10 mmol) and acetyl chloride (2.355 g, 30 mmol). Purification by flash column chromatography [hexanes–EtOAc (5:1)] afforded the title amide (1.286 g, 91%), $\delta_H(CDCl_3)$ 5.77 (1 H, m), 5.26 (1 H, br), 4.94 (2 H, m), 3.23 (2 H, m), 2.05 (2 H, m), 1.96 (3 H, s) and 1.45 (4 H, m); ν_{max}(thin film)/cm^{-1} 3289, 3080, 2932, 2860, 1650, 1561, 1431, 1367 and 910; *m/z* 141, 126, 100, 82, 72, 60 and 55 (Found: M^+, 141.1154. $C_8H_{15}NO$ requires *M*, 141.1154).

N-(*Hex*-5-*enyl*)-N-(2-*iodobenzyl*)*acetamide* **57a**. To a refluxing mixture of the above amide (0.3530 g, 2.5 mmol), finely powdered sodium hydroxide (0.350 g, 8.75 mmol), potassium carbonate (0.700 g, 5 mmol), and tetrabutylammonium hydrogen sulfate (85 mg, 0.25 mmol) in benzene (2 cm^3) was added a solution of 2-iodobenzyl chloride **15** (0.9470 g, 3.75 mmol) in benzene (1 cm^3). The reaction mixture was refluxed for 4 h, quenched with water (5 cm^3), and extracted with diethyl ether (3 × 30 cm^3). The combined organic layers were washed successively with water (2 × 20 cm^3) and brine (20 cm^3), and dried over magnesium sulfate. Purification by flash column chromatography [hexane–EtOAc (3:1)] afforded iodide **57a** (0.768 g, 84%); $\delta_H(CDCl_3)$ 7.84 (1 H, m), 7.33 (1 H, m), 7.04 (2 H, m), 5.76 (1 H, m), 4.98 (2 H, m), 4.63 and 4.41 (2 H, s), 3.36 and 3.19 (2 H, t, *J* 7.7), 2.20 and 2.02 (3 H, s), 2.08 (2 H, m), 1.58 (2 H, m) and 1.38 (2 H, m); ν_{max}(thin film)/cm^{-1} 3069, 2930, 2859, 1649, 1565, 1423, 1358, 1013, 912 and 648; *m/z* 357, 316, 246, 230, 217, 188, 90 and 55 (Found: M^+, 357.0589. $C_{15}H_{20}INO$ requires *M*, 357.0590).

N-[(E)-6-*Ethoxycarbonylhex*-5-*enyl*]-N-(2-*iodobenzyl*)*acetamide* **57b**. Compound **57b** was prepared following the general ozonolysis–olefination procedure by using amide **57a** (1.440 g, 4.0 mmol). Purification by flash column chromatography [hexanes–EtOAc (2:1)] gave compound **57b** (1.390 g, 81%), $\delta_H([^2H_6]DMSO, 363\ K)$ 7.85 (1 H, d, *J* 7.8), 7.36 (1 H, m), 7.12 (1 H, d, *J* 6.8), 7.03 (1 H, m), 6.83 (1 H, td, *J* 6.8 and 15.8), 5.80 (1 H, td, *J* 1.6 and 15.8), 4.47 (2 H, s), 4.11 (2 H, q, *J* 7.1), 3.26 (2 H, t, *J* 7.0), 2.21 and 2.08 (3 H, s), 2.20 (2 H, m), 1.54 (2 H, m) 1.42 (2 H, m) and 1.21 (3 H, t, *J* 7.1); ν_{max}(thin film)/cm^{-1} 3058, 2934, 2860, 1719, 1651, 1431, 1269 and 752; *m/z* 429, 384, 302, 260, 246, 217, 155, 90 and 81 (Found: M^+, 429.0802. $C_{18}H_{24}INO_3$ requires *M*, 429.0801).

N-(*Hex*-5-*enyl*)*benzamide* **19a**. Prepared following the standard acylation procedure by using hex-5-enylamine (1.485 g, 15 mmol) and benzoyl chloride (3.163 g, 22.5 mmol). Purification by flash column chromatography [hexanes–EtOAc (2:1)] afforded the amide **19a** (2.370 g, 78%), $\delta_H(CDCl_3)$ 7.71 (2 H, d, *J* 6.9), 7.40 (3 H, m), 6.07 (1 H, br), 5.79 (1 H, m), 4.94 (2 H, m), 3.43 (2 H, m), 2.05 (2 H, m), 1.60 (2 H, m) and 1.51 (2 H, m); ν_{max}(thin film)/cm^{-1} 3316, 2932, 2859, 1640, 1543, 1311 and 696; *m/z* 203, 162, 148, 134, 122, 105, 77 and 55 (Found: M^+, 203.1310. $C_{13}H_{17}NO$ requires *M*, 203.1310).

N-(*Hex*-5-*enyl*)-N-(2-*iodobenzyl*)*benzamide*. Prepared following the procedure for compound **57a** by using the above amide (1.624 g, 8 mmol) and 2-iodobenzyl chloride (3.029 g, 12 mmol). Purification by flash column chromatography [hexanes–EtOAc (3:1)] afforded the title amide (2.859 g, 85%), $\delta_H(CDCl_3)$ 7.83 (1 H, m), 7.48–7.21 (7 H, m), 7.00 (1 H, m), 5.85–5.58 (1 H, m), 5.08–4.80 (2 H, m), 4.81 and 4.46 (2 H, br), 3.45 and 3.16 (2 H, br), 2.12 and 1.89 (2 H, m), 1.70 (1 H, m), 1.51 (2 H, m) and 1.20 (1 H, m); ν_{max}(thin film)/cm^{-1} 3061, 2859, 1638, 1419, 1013 and 748; *m/z* 419, 378, 364, 350, 334, 292, 217,

105 and 77 (Found: M^+, 419.0746. $C_{20}H_{22}INO$ requires *M*, 419.0746).

N-[(E)-6-*Ethoxycarbonylhex*-5-*enyl*]-N-(2-*iodobenzyl*)*benzamide* **61E**. Compound **61***E* was prepared following the general ozonolysis–olefination procedure by using the above amide (1.676 g, 4.0 mmol). Purification by flash column chromatography [hexanes–EtOAc (4.5 : 1)] gave compound **61***E* (1.415 g, 72%), δ_H([$^2H_6$]DMSO; 363 K) 7.85 (1 H, dd, *J* 0.9 and 7.7), 7.42 (6 H, m), 7.32 (1 H, dd, *J* 1.4 and 9.1), 7.04 (1 H, m), 6.77 (1 H, td, *J* 6.9 and 15.6), 5.76 (1 H, d, *J* 15.6), 4.57 (2 H, s), 4.11 (2 H, q, *J* 7.1), 3.26 (2 H, t, *J* 7.2), 2.10 (2 H, m), 1.54 (2 H, m), 1.32 (2 H, m) and 1.22 (3 H, t, *J* 7.1); ν_{max}(thin film)/cm^{-1} 3015, 2963, 1717, 1638, 1419, 1302, 1267 and 750; *m*/*z* 491, 446, 418, 386, 378, 364, 217, 105, 90 and 77 (Found: M^+, 491.0956. $C_{23}H_{26}INO_3$ requires *M*, 491.0957).

Radical Reductions.—Ethyl cis-2-[N-*benzoyl*-N-(6-*ethoxycarbonylhex*-5-*enyl*)*amino*]*cyclopentylacetate* **20b** (*standard procedure*). A solution of iodide **18b** (110.0 mg, 0.2 mmol), tributyltin hydride (132.0 mg, 0.4 mmol), and AIBN (4.0 mg, 0.02 mmol) in degassed benzene (20 cm^3) was refluxed for 8 h. The solvent was removed on an aspirator. Then wet diethyl ether (20 cm^3) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.3–0.4 mmol) were added. The mixture was heated gently for 5 min, and then filtered through a short silica gel column. Purification by MPLC [hexanes–EtOAc (3.5 : 1)] afforded diester **20b** as an oil (72.5 mg, 84%), δ_H([$^2H_6$]DMSO; 363 K) 7.40 (3 H, m), 7.30 (2 H, m), 6.78 (1 H, td, *J* 6.8 and 15.6), 5.76 (1 H, d, *J* 15.6), 4.21–4.08 (5 H, m), 3.36 (1 H, m), 3.00 (1 H, m), 2.42 (1 H, m), 2.35 (1 H, dd, *J* 11.0 and 15.4), 2.26 (1 H, dd, *J* 9.4 and 15.4), 2.09 (2 H, m), 1.94 (2 H, m), 1.78 (2 H, m), 1.62–1.40 (4 H, m) and 1.40–1.18 (8 H, m); δ_C($CDCl_3$) 173.1 (s), 172.4 (s), 166.5 (s), 148.3 (d), 137.7 (s), 129.0 (d), 128.4 (d), 126.2 (d), 121.6 (d), 66.0 (d), 65.9 (t), 65.8 (t), 60.1 (t), 39.1 (d), 35.4 (t), 31.9 (t), 31.6 (t), 29.6 (t), 25.2 (t), 23.7 (t), 15.2 (q) and 14.2 (q); ν_{max}(thin film)/cm^{-1} 3058, 2936, 2866, 1719, 1632, 1445, 1365, 1176 and 704; *m*/*z* 429, 384, 324, 276, 230, 170, 122 and 105 (Found: M^+, 429.2515. $C_{25}H_{35}NO_5$ requires *M*, 429.2515).

(E)-6-*Ethoxycarbonylhex*-5-*enyl benzoate* **26b** *and* (E)-6-*ethoxycarbonylhex*-5-*enyl* 2-*phenylbenzoate* **27b** (*syringe-pump method*). Iodide **25b** (201.0 mg, 0.5 mmol) was dissolved in degassed benzene (5 cm^3), and the solution was heated to reflux. A solution of tributyltin hydride (330.0 mg, 1.0 mmol) and AIBN (10.0 mg, 0.05 mmol) in degassed benzene (10 cm^3) was added to the refluxing solution by use of a syringe pump. The whole addition was completed in 8 h. After the addition was completed, the solution was refluxed for another 8 h. Benzene was removed on an aspirator. Then wet diethyl ether (50 cm^3) and DBU (1.0 mmol) were added to the above residue. The mixture was stirred for 5 min in a warm water-bath, and was filtered through a short silica gel column. Purification by MPLC [hexanes–EtOAc (20 : 1)] gave products **26b** (66.0 mg, 47%) and **27b** (45.0 mg, 26%). Compound **26b**: δ_H($CDCl_3$) 8.04 (2 H, d, *J* 7.2), 7.56 (1 H, t, *J* 7.5), 7.44 (2 H, t, *J* 7.8), 6.96 (1 H, td, *J* 6.7 and 15.7), 5.85 (1 H, m), 4.33 (2 H, t, *J* 6.3), 4.18 (2 H, q, *J* 7.2), 2.28 (2 H, m), 1.81 (2 H, m), 1.64 (2 H, m) and 1.28 (3 H, t, *J* 7.2); δ_C($CDCl_3$) 166.4 (s), 148.2 (d), 132.7 (d), 130.2 (s), 129.4 (d), 128.2 (d), 121.7 (d), 64.4 (t), 60.0 (t), 31.5 (t), 28.1 (t), 24.4 (t) and 14.1 (q); ν_{max}(thin film)/cm^{-1} 3030, 2943, 1716, 1652, 1600, 1452, 1314 and 715; *m*/*z* 230, 171, 154, 121, 105, 77 and 71 [Found: *m*/*z*, 230.0943. $C_{14}H_{14}O_3$ requires ($M - C_2H_5OH$): 230.0943]; compound **27b**: δ_H($CDCl_3$) 7.82 (1 H, dd, *J* 1.3 and 7.4), 7.53 (1 H, dt, *J* 1.4 and 7.6), 7.38 (7 H, m), 6.85 (1 H, td, *J* 6.9 and 15.7), 5.76 (1 H, m), 4.20 (2 H, q, *J* 7.2), 4.02 (2 H, t, *J* 6.2), 2.05 (2 H, m) and 1.32 (7 H, m); δ_C($CDCl_3$) 169.1 (s), 166.7 (s), 148.6 (d), 142.3 (s), 141.6 (s), 132.9 (s), 131.2 (d), 130.7 (d), 129.9 (d), 128.4 (d), 128.1 (d), 127.3 (d), 121.6 (d), 64.7 (t), 60.2 (t), 31.7 (t), 27.8 (t), 24.6 (t) and 14.3 (q); ν_{max}(thin film)/cm^{-1} 3063, 2951, 1717, 1653, 1450, 1367, 983 and 777; *m*/*z* 352, 306, 181, 108, 84 and 49 (Found: M^+, 352.1675. $C_{22}H_{24}O_4$ requires *M*, 352.1675).

N-(*Hex*-5-*enyl*)-N-*phenylbenzamide* **29a** *and* 5-(*Hex*-5-*enyl*)-*phenanthridin*-6(5H)-*one* **30a** (*catalytic procedure*). A solution of iodide **28a** (81.0 mg, 0.2 mmol), sodium cyanoborohydride (25.1 mg, 0.4 mmol), tributyltin chloride (6.6 mg, 0.02 mmol), and AIBN (4.0 mg, 0.02 mmol) in degassed *tert*-butyl alcohol (5.5 cm^3) was refluxed for 8 h. The reaction mixture was quenched with 10% aq. hydrochloric acid (5 cm^3), and extracted with diethyl ether (3 × 30 cm^3). The combined organic layers were washed successively with water (2 ×) and brine (1 ×) and dried over magnesium sulfate. Concentration and purification by MPLC [hexane–EtOAc (15 : 1)] gave compounds **29a** (11.0 mg, 19%) and **30a** (19.0 mg, 39%): compound **29a**: δ_H($CDCl_3$) 7.14 (10 H, m), 5.77 (1 H, m), 4.96 (2 H, m), 3.92 (2 H, t, *J* 7.5), 2.06 (2 H, m) and 1.57 (4 H, m); ν_{max}(thin film)/cm^{-1} 3063, 2928, 2857, 1647, 1595, 1494, 1392, 912 and 765; *m*/*z* 276, 231, 197, 105, 84, 77 and 49 (Found: M^+, 276.1624. $C_{19}H_{21}NO$ requires *M*, 276.1623); compound **30a**: δ_H($CDCl_3$) 8.55 (1 H, d, *J* 7.6), 8.27 (2 H, m), 7.74 (1 H, m), 7.55 (2 H, m), 7.34 (2 H, m), 5.83 (1 H, m), 5.02 (2 H, m), 4.40 (2 H, t, *J* 6.9), 2.17 (2 H, m), 1.83 (2 H, m) and 1.62 (2 H, m); δ_C($CDCl_3$) 161.7 (s), 138.5 (d), 137.2 (s), 133.7 (s), 132.4 (d), 129.6 (d), 128.9 (d), 128.0 (d), 125.8 (s), 123.5 (d), 122.3 (d), 121.6 (d), 119.6 (s), 115.2 (d), 114.9 (t), 42.7 (t), 35.6 (t), 27.0 (t) and 26.4 (t); ν_{max}(thin film)/cm^{-1} 3073, 2928, 2855, 1647, 1609, 1585, 1437, 1313, 748 and 725; *m*/*z* 277, 260, 209, 195, 178 and 84 (Found: M^+, 277.1466. $C_{19}H_{19}NO$ requires *M*, 277.1467).

N-(*Hex*-5-*enyl*)-N-*phenylbenzenesulfonamide* **32** *and* 6-(*Hex*-5-*enyl*)*dibenzo*[c,e][1,2]*thiazine* 5,5-*dioxide* **33**. Compounds **32** and **33** were prepared following the catalytic procedure by using iodide **31** (88.0 mg, 0.2 mmol). Purification by MPLC [hexanes–EtOAc (30 : 1)] yielded products **33** (34.0 mg, 54%) and **33** (13.0 mg, 20%): compound **32**: δ_H($CDCl_3$) 7.95 (3 H, m), 7.69 (1 H, dt, *J* 1.4 and 7.7), 7.56 (1 H, t, *J* 7.8), 7.49 (1 H, t, *J* 7.2), 7.34 (2 H, m), 5.61 (1 H, m), 4.87 (2 H, m), 3.91 (2 H, t, *J* 7.5), 1.97 (2 H, m) and 1.50 (4 H, m).

Ethyl cis-[2(N-*benzoyl*-N-*butylamino*)*cyclopentyl*]*acetate* **35a**. Compound **35a** was prepared following the standard procedure by using iodide **34a** (92.0 mg, 0.2 mmol), tributyltin hydride (132.0 mg, 0.4 mmol), and AIBN (4.0 mg, 0.02 mmol). Purification by MPLC [hexanes–EtOAc (7 : 1)] afforded compound **35a** (27.7 mg, 42%), δ_H([$^2H_6$]DMSO; 373 K) 7.40 (3 H, m), 7.29 (2 H, m), 4.16 (1 H, m), 4.08 (2 H, q, *J* 7.1), 3.32 (1 H, ddd, *J* 6.6, 9.8 and 14.0), 3.01 (1 H, ddd, *J* 5.6, 9.9 and 14.0), 2.45 (1 H, m), 2.40 (1 H, m), 2.32 (1 H, m), 1.98 (2 H, m), 1.80 (2 H, m), 1.62–1.38 (4 H, m), 1.20 (3 H, t, *J* 7.1), 1.15 (2 H, m) and 0.77 (3 H, t, *J* 7.3); δ_C($CDCl_3$) 173.1 (s), 172.4 (s), 137.8 (s), 128.9 (d), 128.3 (d), 126.1 (d), 60.4 (d), 60.3 (t), 39.1 (d), 35.5 (t), 31.8 (2 C, t), 29.5 (t), 23.8 (t), 20.0 (t), 14.2 (q) and 13.6 (q); ν_{max}(thin film)/cm^{-1} 3059, 2957, 2868, 1730, 1634, 1445, 1363 and 785; *m*/*z* 331, 244, 226, 202, 178, 135, 105 and 77 (Found: M^+, 331.2147. $C_{20}H_{29}NO_3$ requires *M*, 331.2147).

Ethyl cis-[2-(N-*benzoyl*-N-*benzylamino*)*cyclopentyl*]*acetate* **35b**. Compound **35b** was prepared following the standard procedure by using iodide **34b** (98.0 mg, 0.2 mmol), tributyltin hydride (132.0 mg, 0.4 mmol), and AIBN (4.0 mg, 0.02 mmol). Purification by MPLC [hexanes–EtOAc (6 : 1)] afforded compound **35b** (27.0 mg, 37%), δ_H([$^2H_6$]DMSO; 360 K) 7.35 (7 H, m), 7.19 (3 H, m), 4.76 (1 H, d, *J* 16.7), 4.35 (1 H, d, *J* 16.7), 4.30 (1 H, m), 4.10 (2 H, q, *J* 7.1), 2.50 (1 H, m), 2.48 (1 H, dd, *J* 5.4 and 16.4), 2.32 (1 H, dd, *J* 10.8 and 16.4), 1.90–1.60 (4 H, m), 1.51 (1 H, m), 1.33 (1 H, m) and 1.21 (3 H, t, *J* 7.1); δ_C($CDCl_3$) 173.3 (s), 173.0 (s), 138.5 (s), 137.4 (s), 129.3 (d), 128.7 (d), 128.5 (d), 128.4 (2 C, d), 127.2 (d), 60.5 (t), 60.3 (d), 39.2 (d), 35.6 (t), 31.7 (t), 29.4 (t), 23.8 (t) and 14.4 (q); ν_{max}(thin film)/cm^{-1} 3029, 2955, 2870, 1730, 1636, 1446, 1354 and 1190; *m*/*z* 364, 320, 274,

260, 212 and 105 [Found: M^+, 364.1913. $C_{23}H_{26}NO_3$ requires ($M - 1$), 364.1913].

Compound **35b** was also prepared following the standard procedure by using iodide **61** (98.0 mg, 0.2 mmol), tributyltin hydride (132.0 mg, 0.4 mmol), and AIBN (4.0 mg, 0.02 mmol). Purification by MPLC [hexanes–EtOAc (6:1)] afforded ester **35b** (37.3 mg, 51%).

Ethyl cis-[2-(N-*benzoyl*-N-*cyclohexylamino*)*cyclopentyl*]-*acetate* **35c**. Compound **35c** was prepared following the standard procedure by using iodide **34c** (242.0 mg, 0.5 mmol), tributyltin hydride (332.0 mg, 1.0 mmol), and AIBN (10.0 mg, 0.05 mmol). Purification by MPLC [hexanes–EtOAc (5:1)] afforded compound **35c** (46.5 mg, 26%), $\delta_H([^2H_6]DMSO$; 363 K) 7.38 (3 H, m), 7.31 (2 H, m), 4.12 (2 H, q, *J* 6.7), 3.78 (1 H, m), 3.40 (1 H, m), 2.62–2.41 (3 H, m), 2.13–1.80 (5 H, m), 1.80–1.35 (8 H, m), 1.26 (3 H, t, *J* 6.7) and 1.04 (3 H, m); $\delta_C(CDCl_3)$ 173.4 (s), 171.6 (s), 138.0 (s), 128.4 (d), 127.9 (d), 125.0 (d), 59.5 (t), 59.4 (d), 56.0 (d), 39.6 (d), 34.8 (t), 32.6 (t), 31.7 (t), 30.6 (t), 25.1 (t), 25.0 (t), 24.5 (t) and 13.8 (q); ν_{max}(thin film)/cm^{-1} 2931, 2858, 1732, 1622, 1446 and 1372; *m/z* 357, 312, 274, 252, 228, 204, 170, 122, 105 and 77 (Found: M^+, 357.2306. $C_{22}H_{31}NO_3$ requires *M*, 357.2304).

N-(tert-*Butyl*)*benzamide* **44** *and* 2-(tert *butyl*)-3-*oxo*-1-(*pent*-4-*enyl*)-1,2-*dihydroisoindole* **45a**. Compounds **44** and **45a** were prepared following the catalytic procedure by using iodide **43a** (76.0 mg, 0.2 mmol). Purification by MPLC [hexanes–EtOAc (15:1)] yielded products **44** (15.0 mg, 41%) and **45a** (19.0 mg, 38%): Compound **44**: $\delta_H(CDCl_3)$ 7.73 (2 H, dd, *J* 1.0 and 7.4), 7.41 (3 H, m), 5.93 (1 H, br) and 1.47 (9 H, s); ν_{max}(thin film)/cm^{-1} 3325, 3064, 2965, 1643, 1538, 1451, 1312, 936 and 846; *m/z* 177, 162, 122, 105, 77 and 57 (Found: M^+, 177.1574. Calc. for $C_{11}H_{15}NO$: M, 177.1574). Compound **45a**: $\delta_H(CDCl_3)$ 7.75 (1 H, d, *J* 8.5), 7.47 (1 H, m), 7.39 (1 H, m), 7.32 (1 H, d, *J* 7.5), 5.64 (1 H, m), 4.92 (2 H, m), 4.80 (1 H, m), 2.0 (4 H, m), 1.59 (9 H, s), 1.24 (1 H, m) and 0.8 (1 H, m); $\delta_C(CDCl_3)$ 169.4 (s), 145.8 (s), 138.1 (d), 133.9 (s), 131.1 (d), 127.8 (d), 123.1 (d), 121.4 (d), 115.1 (t), 60.1 (d), 55.2 (s), 34.5 (t), 33.5 (t), 28.7 (q) and 21.4 (t); ν_{max}(thin film)/cm^{-1} 3077, 2930, 2870, 1675 and 1535; *m/z* 257, 242, 201, 188, 146, 132, 84, 77, 57 and 49 (Found: M^+, 257.1780. $C_{17}H_{23}NO$ requires *M*, 257.1780).

N-(tert-*Butyl*)*benzamide* **44** *and* 2-(tert-*butyl*)-1-(*hex*-5-*enyl*)-3-*oxo*-1,2-*dihydroisoindole* **47**. Compounds **44** and **47** were prepared following the catalytic procedure by using iodide **46a** (160.0 mg, 0.4 mmol). Purification by MPLC [hexanes–EtOAc (15:1)] gave compounds **44** (12.0 mg, 24%) and **47** (39.0 mg, 37%): Compound **47**: $\delta_H(CDCl_3)$ 7.74 (1 H, d, *J* 7.7), 7.48 (1 H, m), 7.39 (1 H, d, *J* 7.9), 7.31 (1 H, m), 5.68 (1 H, m), 4.9 (2 H, m), 4.79 (1 H, m), 1.98 (4 H, m), 1.59 (9 H, s) and 1.29 (4 H, m); ν_{max}(thin film)/cm^{-1} 3076, 2930, 2870, 1678, 1535, 1383, 1217, 912 and 731; *m/z* 271, 256, 215, 188, 179, 132, 105 and 77 (Found: M^+, 271.1936. $C_{18}H_{25}NO$ requires *M*, 271.1936).

N-(tert-*Butyl*)*benzamide* **44**, 2-(tert-*butyl*)-3-*oxo*-1-*phenyl*-1,2-*dihydroisoindole* **50**, *and* N-*benzyl*-N-(tert-*butyl*)*benzamide* **51**. Compounds **44**, **50** and **51** were prepared following the syringe-pump technique by using iodide **49** (159.0 mg, 0.4 mmol), tributyltin hydride (264.0 mg, 0.8 mmol), and AIBN (8.0 mg, 0.04 mmol). Purification by MPLC [hexanes–EtOAc (9:1)] gave compounds **44** (25.0 mg, 31%), **50** (50.0 mg, 46%), and **51** (10.0 mg, 9%): compound **50**: $\delta_H(CDCl_3)$ 7.79 (1 H, m), 7.28 (7 H, m), 7.01 (1 H, m), 5.66 (1 H, s) and 1.45 (9 H, s); $\delta_C(CDCl_3)$ 170.0 (s), 146.7 (s), 141.0 (s), 132.0 (s), 131.5 (d), 129.0 (d), 127.9 (d), 127.9 (d), 126.3 (d), 123.1 (d), 122.5 (d), 65.0 (d), 56.0 (s) and 28.6 (q); ν_{max}(thin film)/cm^{-1} 3036, 2974, 1668, 1559, 1454, 1366, 1223, 928 and 748; *m/z* 265, 250, 193, 165, 153, 132, 104, 91, 77 and 57 (Found: M^+, 265.1467. $C_{18}H_{19}NO$ requires *M*, 265.1467); compound **51**: $\delta_H(CDCl_3)$ 7.34 (10 H, m), 4.60 (2 H, s) and 1.50 (9 H, s); ν_{max}(thin film)/cm^{-1} 3030, 2963, 1633, 1559, 1495, 1367, 972 and 789; *m/z* 267, 252, 210, 105, 91, 77, 57 and 51 (Found: M^+, 267.1622. $C_{18}H_{21}NO$ requires *M*, 267.1623).

N-*Benzyl*-N-(*hex*-5-*enyl*)*acetamide* **58a**. Compound **58a** was prepared following the catalytic procedure by using iodide **57a** (71.0 mg, 0.2 mmol). Purification by MPLC [hexanes–EtOAc (3:1)] gave amide **58a** (30.0 mg, 65%), $\delta_H(CDCl_3)$ 7.26 (5 H, m), 5.76 (1 H, m), 4.97 (2 H, m), 4.59 and 4.51 (2 H, s), 3.35 and 3.18 (2 H, t, *J* 7.6), 2.17 and 2.10 (3 H, s), 2.03 (2 H, m), 1.53 (2 H, m) and 1.36 (2 H, m); ν_{max}(thin film)/cm^{-1} 3031, 2930, 2859, 1645, 1495, 1423, 1360, 912, 731 and 698; *m/z* 231, 95, 83, 69 and 58 (Found: M^+, 231.1623. $C_{15}H_{21}NO$ requires *M*, 231.1623).

N-*Benzyl*-N-[(*E*)-6-*ethoxycarbonylhex*-5-*enyl*]*acetamide* **58b** *and ethyl* cis- *and* trans-[2-(N-*acetyl*-N-*benzylamino*)*cyclopentyl*]*acetate* **59b**-cis/trans. Compounds **58b** and **59b**-*cis*/*trans* were prepared following the standard procedure by using iodide **57b** (86.0 mg, 0.2 mmol), tributyltin hydride (132.0 mg, 0.04 mmol), and AIBN (4.0 mg, 0.02 mmol). Purification by MPLC [hexanes–EtOAc (2:1)] gave amido esters **58b** (18.0 mg, 30%), **59b**-*cis* (23.0 mg, 38%) and **59b**-*trans* (14.0 mg, 23%): compound **58b**: $\delta_H(CDCl_3)$ 7.38–7.12 (5 H, m), 6.87 (1 H, m), 5.79 (1 H, m), 4.59 and 4.51 (2 H, s), 4.16 (2 H, m), 3.36 and 3.19 (2 H, t, *J* 7.2), 2.20 (2 H, m), 2.17 and 2.11 (3 H, s), 1.58 (2 H, m), 1.42 (2 H, m) and 1.28 (3 H, m); ν_{max}(thin film)/cm^{-1} 2932, 1715, 1646, 1466, 1446, 1266, 1180 and 981; *m/z* 303, 260, 190, 155, 120, 113, 106, 99, 91, 85 and 77 (Found: M^+, 303.1834. $C_{18}H_{25}NO_3$ requires *M*, 303.1834); compound **59b**-*trans*: $\delta_H(CDCl_3)$ 7.40–7.20 (3 H, m), 7.15 (2 H, d, *J* 7.3), 4.57 (1 H, d, *J* 18.1), 4.32 (1 H, d, *J* 18.1), 4.12 (2 H, m), 2.73 (1 H, m), 2.38 (1 H, dd, *J* 6.2 and 15.2), 2.30–2.10 (2 H, m), 2.01 (3 H, s), 1.82–1.64 (4 H, m), 1.40 (2 H, m) and 1.26 (3 H, t, *J* 7.1); ν_{max}(thin film)/cm^{-1} 2955, 2872, 1728, 1647, 1414, 1375 and 731; *m/z* 303, 260, 216, 170, 150, 124, 106, 91 and 43 (Found: M^+, 303.1834. $C_{18}H_{25}NO_3$ requires *M*, 303.1834).

Independent Syntheses of Products.—N-(2-*Allylcyclopentyl*)-*butylamine* (*standard reductive amination procedure*). To a solution of butylamine (4.380 g, 60 mmol) in methanol (25 cm^3) were added aq. 5 mol dm^{-3} HCl (4 cm^3, 20 mmol), 2-allylcyclopentanone (1.240 g, 10 mmol), and sodium cyanoborohydride (0.4410 g, 7 mmol). After the reaction mixture had been stirred for 72 h, conc. HCl was added at 0 °C until pH < 2 for the solution. Most of methanol was removed under reduced pressure, and the residue was washed with diethyl ether (3 ×). Solid NaOH was added to the aqueous phase at 0 °C until ph > 10. The aqueous phase was extracted with diethyl ether (3 × 30 cm^3). The combined ether layers were washed successively with water (3 ×) and brine (1 ×) and dried over magnesium sulfate. Concentration gave the title amine as a clear oil (1.500 g, 83%), $\delta_H(CDCl_3)$ 5.78 (1 H, m), 4.99 (2 H, m), 3.17 (1 H, m), 2.64–2.30 (4 H, m), 2.20–1.00 (11 H, m) and 0.8 (3 H, m); ν_{max}(thin film)/cm^{-1} 2934, 2872, 1653, 1558, 1458 and 1379.

cis- *and* trans-N-(2-*Allylcyclopentyl*)-N-*butylbenzamide* **39a**. Compound **39a** was prepared following the standard acylation procedure by using the above amine (1.507 g, 8.3 mmol) and benzoyl chloride (1.405 g, 10 mmol). Purification by MPLC [hexanes–EtOAc (7:1)] afforded stereoisomers **39a**-*cis* (0.7250 g, 31%) and **39a**-*trans* (0.8460 g, 36%): compound **39a**-*cis*: $\delta_H([^2H_6]DMSO$; 363 K) 7.38 (3 H, m), 7.26 (2 H, m), 5.74 (1 H, m), 5.00 (2 H, m), 4.21 (1 H, m), 3.43 (1 H, m), 2.97 (1 H, m), 2.18 (1 H, m), 2.05 (1 H, m), 1.95 (3 H, m), 1.74 (2 H, m), 1.60–1.28 (4 H, m), 1.14 (2 H, m) and 0.79 (3 H, t, *J* 7.3); ν_{max}(thin film)/cm^{-1} 3069, 2957, 2872, 1634, 1418, 1360 and 700; *m/z* 285, 242, 178, 105, 77 and 57 (Found: M^+, 285.2093. $C_{19}H_{27}NO$ requires *M*, 285.2093); compound **39a**-*trans*: $\delta_H([^2H_6]DMSO$; 363 K) 7.41 (3 H, m), 7.28 (2 H, m), 5.71 (1 H, m), 4.94 (2 H, m), 3.70 (1 H, m), 3.21 (2 H, m), 2.18 (1 H, m), 2.06 (1 H, m), 1.88–1.67 (4 H,

m), 1.67–1.40 (4 H, m), 1.30–1.00 (3 H, m) and 0.84 (3 H, t, *J* 7.3); ν_{max}(thin film)/cm^{-1} 3061, 2957, 2868, 1634, 1420, 1362 and 700; *m/z* 285, 242, 178, 105 and 77 (Found: M$^+$, 285.2093).

cis-[2-N-*Benzoyl*-N-*butylamino*)*cyclopentyl*]*acetic acid* (*oxidation procedure*). Amide **39a**-*cis* (0.7000 g, 2.5 mmol) was ozonized following the standard procedure. The intermediate aldehyde was used for the next step without purification.

To a solution of the aldehyde in acetone (3 cm^3) at 0 °C was added Jones' reagent (1.5 cm^3). The reaction was monitored by TLC. The reaction mixture was diluted with water (10 cm^3), and extracted with diethyl ether (3 × 30 cm^3). The combined ether layers were washed successively with water (3 ×) and brine (1 ×), and dried over magnesium sulfate. Concentration gave the acid (0.6500 g, 86%), δ_H($CDCl_3$) 7.34 (5 H, m), 4.21 (1 H, m), 3.00 (2 H, m), 2.50 (1 H, m), 2.31 (1 H, m), 2.00–1.80 (5 H, m), 1.62 (1 H, m), 1.41 (3 H, m), 1.12 (2 H, m) and 0.90 (3 H, m); ν_{max}(thin film)/cm^{-1} 3600–2500 br, 1723, 1595, 1445, 1367 and 754; *m/z* 303, 274, 260, 244, 178, 135 and 74 (Found: M$^+$, 303.1834. $C_{18}H_{25}NO_3$ requires *M*, 303.1834).

Authentic sample of compound **35a**-cis. A solution of the above acid (0.6500 g, 2.1 mmol) and oxalyl dichloride (1.252 g, 9.9 mmol) in benzene (10 cm^3) was stirred for 5 h. Concentration afforded the acyl chloride, which was used for esterification without purification.

To a solution of ethanol (0.160 g, 4.2 mmol) and pyridine (0.240 g, 3.0 mmol) in CH_2Cl_2 (5 cm^3) at 0 °C was added a solution of the acyl chloride in CH_2Cl_2 (1 cm^3). The reaction mixture was stirred for 4 h, quenched with water (10 cm^3), and extracted with diethyl ether (3 × 15 cm^3). The combined ether layers were washed successively with water (3 ×) and brine (1 ×), and dried over magnesium sulfate. Purification by MPLC [hexanes–EtOAc (5:1)] afforded compound **35a**-*cis* as a clear oil (0.5230 g, 75%).

trans-[2-N-*Benzoyl*-N-*butylamino*)*cyclopentyl*]*acetic acid.* Prepared following the oxidation procedure by using amide **39a**-*trans* (1.200 g, 4.2 mmol). Concentration afforded the acid (0.9930 g, 78%), δ_H($CDCl_3$) 7.36 (5 H, m), 3.60–3.30 (1 H, m), 3.20–2.90 (2 H, m), 2.60–2.20 (2 H, m), 2.05–1.85 (2 H, m), 1.85–1.50 (3 H, m), 1.42 (3 H, m), 1.07 (1 H, m), 0.95 (3 H, m) and 0.81–0.60 (2 H, m); ν_{max}(thin film)/cm^{-1} 3600–2500 br, 1723, 1593, 1423 and 752; *m/z* 303, 244, 202, 178, 141, 105 and 77 (Found: M$^+$, 303.1834. $C_{18}H_{25}NO_3$ requires *M*, 303.1834).

Ethyl trans-[2-N-*benzoyl*-N-*butylamino*)*cyclopentyl*]*acetate* **35a**-trans. Compound **35a**-*trans* was prepared following the procedure for **35a**-*cis* by using the above *trans*-acid (0.9930 g, 3.3 mmol). Purification by MPLC (hexanes–EtOAc (6:1)] afforded compound **35a**-*trans* as a clear oil (0.885 g, 81%), δ_H([$^2H_6$]DMSO; 363 K) 7.41 (3 H, m), 7.28 (2 H, m), 4.04 (2 H, q, *J* 7.1), 3.73 (1 H, m), 3.20 (2 H, m), 2.42–2.17 (2 H, m), 2.05 (1 H, m), 2.12–1.60 (4 H, m), 1.60–1.40 (4 H, m), 1.30–1.10 (2 H, m), 1.18 (3 H, t, *J* 7.1) and 0.84 (3 H, t, *J* 7.3).

(2-*Allylcyclopentyl*)*benzylamine.* Prepared following the standard reductive amination procedure by using 2-allylcyclopentanone (1.240 g, 10 mmol), benzylamine (6.140 g, 60 mmol) and sodium cyanoborohyride (0.441 g, 7 mmol). Concentration gave the title amine (1.526 g, 72%), δ_H($CDCl_3$) (5 H, m), 5.78 (2 H, m), 4.99 (2 H, m), 3.80 (1 H, d, *J* 13.2), 3.69 (1 H, d, *J* 13.2), 2.71 (1 H, m), 2.20 (2 H, m) and 2.20–1.20 (7 H, m); ν_{max}(thin film)/cm^{-1} 3027, 2953, 2870, 1639, 1452 and 700.

cis- *and* trans-N-(2-*Allylcyclopentyl*)-N-*benzylbenzamide* **39b**. Compounds **39b** were prepared following the standard acylation procedure by using the above amine (1.526 g, 7.2 mmol) and benzoyl chloride (1.517 g, 10.8 mmol). Purification by MPLC [hexanes–EtOAc (7:1)] afforded amides **39b**-*cis* (0.985 g, 43%) and **39b**-*trans* (1.102 g, 48%): compound **39b**-*cis*: δ_H([$^2H_6$]-DMSO; 363 K) 7.35 (8 H, m), 7.20 (2 H, d, *J* 7.1), 5.80 (1 H, m), 5.04 (2 H, m), 4.88 (1 H, d, *J* 16.4), 4.31 (1 H, d, *J* 16.4), 4.33 (1 H, m), 2.24 (1 H, m), 2.08 (2 H, m), 1.88–1.25 (4 H, m) and 1.49–1.24 (2 H, m); ν_{max}(thin film)/cm^{-1} 3031, 2953, 2872, 1636, 1435, 1414 and 1348; *m/z* 319, 212, 105, 91 and 77 (Found: M$^+$, 319.1936. $C_{22}H_{25}NO$ requires *M*, 319.1936).

cis-[2-(N-*Benzoyl*-N-*benzylamino*)*cyclopentyl*]*acetic acid.* Prepared following the oxidation procedure by using amide **39b**-*cis* (0.900 g, 2.8 mmol). Concentration gave the product (0.7350 g, 79%).

Authentic sample of compound **35b**-cis. Compound **35b**-*cis* was prepared following the procedure for **35a**-*cis* by using the above acid (0.735 g, 2.2 mmol). Purification by MPLC [hexanes–EtOAc (5:1)] afforded compound **35b**-*cis* as a clear oil (0.640 g, 80%).

trans-[2-(N-*Benzoyl*-N-*benzylamino*)*cyclopentyl*]*acetic acid.* Prepared following the oxidation procedure by using amide **39b**-*trans* (1.000 g, 3.2 mmol). Concentration gave the title product (0.6710 g, 79%).

Ethyl trans-[2-(N-*benzoyl*-N-*benzylamino*)*cyclopentyl*]-*acetate* **35b**-trans. Compound **35b**-*trans* was prepared following the procedure for **35a**-*cis* by using the above acid (0.671 g, 2.0 mmol). Purification by MPLC [hexanes–EtOAc (5:1)] afforded ester **35b**-*trans* (0.5710 g, 78%).

N-(2-*Allylcyclopentyl*)*cyclohexylamine.* Prepared following the standard reductive amination procedure by using 2-allylcyclopentanone (1.240 g, 10 mmol), cyclohexylamine (5.940 g, 60 mmol), and sodium cyanoborohyride (0.441 g, 7 mmol). Concentration gave the title amine (1.640 g, 79%), δ_H($CDCl_3$) 5.74 (1 H, m), 4.94 (2 H, m), 3.16 and 2.72 (1 H, m), 2.34 (1 H, m), 2.18 (2 H, m) and 2.00–0.80 (17 H, m); ν_{max}(thin film)/cm^{-1} 2930, 2855, 1653, 1558, 1449 and 752.

cis- *and* trans-N-(2-*Allylcyclopentyl*)-N-*cyclohexylbenzamide* **39c**. Compounds **39c** were prepared following the standard acylation procedure by using the above amine (1.714 g, 8.2 mmol) and benzoyl chloride (1.382 g, 9.8 mmol). Purification by MPLC [hexanes–EtOAc (7:1)] afforded compounds **39c**-*cis* (0.7990 g, 31%) and **39c**-*trans* (1.000 g, 39%): compound **39c**-*cis*: δ_H([$^2H_6$]DMSO; 363 K) 7.38 (3 H, m), 7.22 (2 H, m), 5.81 (1 H, m), 4.95 (2 H, m), 3.79 (1 H, m), 3.26 (1 H, m), 2.32 (2 H, m), 2.08 (2 H, m), 1.85–1.52 (10 H, m), 1.40 (2 H, m) and 1.00 (3 H, m); ν_{max}(thin film)/cm^{-1} 3027, 2931, 2859, 1635, 1495, 1363 and 910; *m/z* 311, 228, 204, 122, 105, 77 and 55 (Found: M$^+$, 311.2250. $C_{21}H_{29}NO$ requires *M*, 311.2249); compound **39c**-*trans*: δ_H($CDCl_3$) 7.40–7.23 (5 H, m), 5.72 (1 H, m), 4.98 (2 H, m), 3.42 and 3.10 (1 H, m), 2.91 and 2.50 (1 H, m), 2.61 and 2.31 (2 H, m), 2.00–1.32 (15 H, m) and 1.32–0.90 (2 H, m); ν_{max}(thin film)/cm^{-1} 3071, 2932, 2857, 1634, 1443, 1319 and 700; *m/z* 311, 268, 254, 242, 228, 204, 122, 105, 77 and 55 (Found: M$^+$, 311.2249).

cis-[2-N-*Benzoyl*-N-*cyclohexylamino*)*cyclopentyl*]*acetic acid.* Prepared following the oxidation procedure by using amide **39c**-*cis* (0.70 g, 2.3 mmol). Concentration afforded the acid (0.4500 g, 60%), δ_H($CDCl_3$) 7.39 (3 H, m), 7.28 (2 H, m), 3.79 (1 H, m), 3.41 (1 H, m), 2.61–2.40 (4 H, m), 2.12–1.80 (5 H, m), 1.80–1.35 (6 H, m) and 1.00 (4 H, m); ν_{max}(thin film)/cm^{-1} 3600–2500 br, 2933, 2859, 1719, 1636, 1577, 1445 and 701; *m/z* 329, 272, 246, 228, 204, 164, 122, 105 and 77 (Found: M$^+$, 329.1990. $C_{20}H_{27}NO_3$ requires *M*, 329.1991).

Authentic sample of compound **35c**-cis. Compound **35c**-*cis* was prepared following the procedure for **35a**-*cis* by using the above acid (0.4500 g, 1.4 mmol). Purification by MPLC [hexanes–EtOAc (6:1)] afforded compound **35c**-*cis* as a clear oil (0.3350 g, 67%).

trans-[2-N-*Benzoyl*-N-*cyclohexylamino*)*cyclopentyl*]*acetic acid.* Prepared following the oxidation procedure by using amide **39c**-*trans* (1.000 g, 3.2 mmol). Concentration afforded the acid (0.7500 g, 71%), δ_H($CDCl_3$) 7.31 (5 H, m), 3.54–2.82 (2 H, m), 2.80–2.50 (2 H, m), 2.40–2.10 (2 H, m), 2.00–1.40 (10 H, m) and 1.40–0.90 (5 H, m); ν_{max}(thin film)/cm^{-1} 3600–2500 br, 2932, 1720, 1636, 1559, 1456 and 700; *m/z* 329, 311, 280, 265,

238, 212, 162 and 84 (Found: M^+, 329.1991. $C_{20}H_{27}NO_3$ requires M, 329.1991).

Ethyl trans-[2-N-*benzoyl*-N-*cyclohexylamino*)*cyclopentyl*]-*acetate* **35c**-trans. Compound **35c**-*trans* was prepared following the procedure for **35a**-*cis* by using the above acid (0.750 g, 2.3 mmol). Purification by MPLC [hexanes–EtOAc (6:1)] afforded compound **35c**-*trans* as a clear oil (0.6680 g, 81%), $\delta_H([^2H_6]DMSO$; 363 K) 7.38 (3 H, m), 7.24 (2 H, m), 4.05 (2 H, q, J 7.1), 3.35 (1 H, m), 3.18 (1 H, m), 2.80 (1 H, m), 2.46 (1 H, m), 2.10–2.00 (1 H, m), 2.00–1.80 (4 H, m), 1.80–1.60 (6 H, m), 1.60–1.42 (3 H, m), 1.18 (3 H, t, J 7.1) and 1.05 (3 H, m); ν_{max}(thin film)/cm^{-1} 2958, 2857, 1732 and 1633; m/z 228, 204, 170, 122, 105, 77 and 55 (Found: M^+, 357.2306. $C_{22}H_{31}NO_3$ requires M, 357.2304).

trans-2-*Allylcyclopentanol* **41**. To a solution of allylmagnesium chloride (75 cm^3, 150 mmol) in diethyl ether (125 cm^3) was added cyclopentene oxide **40** (4.206 g, 50 mmol). The reaction mixture was refluxed for 8 h, then was cooled to 0 °C, and excess of allylmagnesium chloride was destroyed by careful addition of water (50 cm^3). The aqueous phase was extracted with diethyl ether (3 × 100 cm^3). The combined ether layers were washed successively with water (3 ×) and brine (1 ×) and dried over magnesium sulfate. Purification [hexanes–EtOAc (3:1)] afforded the alcohol **41** as a clear oil (4.914 g, 78%), $\delta_H(CDCl_3)$ 5.80 (1 H, m), 4.98 (2 H, m), 3.82 (1 H, m), 2.25–2.10 (1 H, m), 2.10–1.92 (1 H, m), 1.90–1.45 (5 H, m), 1.38 (1 H, m) and 1.20 (1 H, m); ν_{max}(thin film)/cm^{-1} 3335, 2953, 1439, 1345 and 910.

cis-2-*Allylcyclopentylamine*. To a solution of phthalimide (2.950 g, 20 mmol) and triphenylphosphine (5.250 g, 20 mmol) in THF (90 cm^3) were added alcohol **41** (2.520 g, 20 mmol) and a solution of diethyl azodicarboxylate in THF (5 cm^3) simultaneously. The mixture was stirred for 72 h, and then the solvent was removed under reduced pressure. The resulting semisolid was dissolved in methanol (100 cm^3), and hydrazine (1 cm^3) was added carefully. The reaction mixture was refluxed for 10 h, and cooled to 25 °C. Conc. HCl (3 cm^3) was added, and the reaction mixture was refluxed for 10 h. The solvent was removed under reduced pressure, to give a yellow solid. The solid was washed with 0.4 mol dm^{-3} HCl (4 × 25 cm^3). The combined aqueous solution was washed successively with CH_2Cl_2 (7 × 20 cm^3) and diethyl ether (3 × 20 cm^3). The aqueous phase was neutralized with 5 mol dm^{-3} NaOH and extracted with diethyl ether (5 × 30 cm^3). The combined ether layers were washed successively with water (3 ×) and brine (1 ×) and dried over magnesium sulfate. Concentration gave the *cis*-amine (1.526 g, 61%), which was used for the next step without purification.

cis-N-(2-*Allylcyclopentyl*)*benzamide* **42**. Compound **42** was prepared following the standard acylation procedure by using the above amine (1.250 g, 10 mmol) and benzoyl chloride (2.108 g, 15 mmol). Purification by flash column chromatography [hexanes–EtOAc (5:1)] afforded compound **42** (1.570 g, 69%), $\delta_H(CDCl_3)$ 7.74 (2 H, d, J 7.1), 7.44 (3 H, m), 6.05 (1 H, d, J 6.8), 5.82 (1 H, m), 5.00 (2 H, m), 4.53 (1 H, m), 2.30–1.80 (5 H, m), 1.80–1.50 (3 H, m) and 1.40 (1 H, m); ν_{max}(thin film)/cm^{-1} 3296, 3069, 2957, 2872, 1634, 1539, 1491 and 694; m/z 229, 187, 161, 148, 122, 105, 93, 77, 67 and 51 (Found: M^+, 229.1467. $C_{15}H_{19}NO$ requires M, 229.1467).

cis-N-(2-*Allylcyclopentyl*)*benzylamine*. Prepared following the standard LAH procedure by using amide **42** (0.6870 g, 3.0 mmol) and LAH (0.137 g, 3.6 mmol). Concentration gave the title amine (0.5200 g, 81%), $\delta_H(CDCl_3)$ 7.30 (5 H, m), 5.78 (1 H, m), 4.95 (2 H, m), 3.80 (1 H, d, J 13.2), 3.69 (1 H, d, J 13.2), 3.08 (1 H, m), 2.70 (1 H, m), 2.24 (1 H, m) and 2.10–1.20 (7 H, m); ν_{max}(thin film)/cm^{-1} 3027, 2954, 2870, 1634, 1452, 910 and 758; m/z 214, 200, 186, 172, 146, 132, 106 and 91 [Found: $(M - H)^+$, 214.1596. $C_{15}H_{20}N$ requires $(M - 1)$ 214.1596).

Authentic sample of compound **39b**-cis. Compound **39b**-*cis* was prepared following the standard acylation procedure by using the above amine (0.22 g, 1.0 mmol), benzoyl chloride (0.420 g, 3.0 mmol), and triethylamine (0.6070 g, 6.0 mmol). Purification by MPLC [hexanes–EtOAc (6:1)] afforded compound **39b**-*cis* as a clear oil (0.24 g, 75%).

Acknowledgements

We thank the National Institutes of Health for funding this work. We also thank Dr. Elaine S. E. Owen and Mr. Hosung Yu for helpful comments on the manuscript.

References

1 D. P. Curran, D. Kim, H. T. Liu and W. Shen, *J. Am. Chem. Soc.*, 1988, **110**, 5900.
2 Leading reference: D. P. Curran and W. Shen, *J. Am. Chem. Soc.*, 1993, **115**, 6051.
3 D. P. Curran, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Flemming, Pergamon Press, Oxford, 1991, vol. 4, p. 779.
4 Recent leading references: (*a*) V. H. Rawal, V. Krishnamurthy and A. Fabre, *Tetrahedron Lett.*, 1993, **34**, 2899; (*b*) S. Kim and J. S. Koh, *Tetrahedron Lett.*, 1992, **33**, 7391; (*c*) J. L. Esker and M. Newcomb, *Tetrahedron Lett.*, 1992, **33** 5913; (*d*) Z. Cekovic and D. Ilijev, *Tetrahedron Lett.*, 1988, **29**, 1441.
5 (*a*) D. C. Lathbury, P. J. Parsons and I. Pinto, *J. Chem. Soc., Chem. Commun.*, 1988, 81; (*b*) A. D. Borthwick, S. Caddick and P. J. Parsons, *Tetrahedron Lett.*, 1990, **31**, 6911; (*c*) D. Denenmark, P. Hoffmann, T. Winkler, A. Waldner and A. De Mesmaeker, *Synlett*, 1991, 621; (*d*) A. De Mesmaeker, A. Waldner, P. Hoffmann, P. Hug and T. Winkler, *Synlett*, 1992, 285; (*e*) D. Denenmark, T. Winkler, A. Waldner and A. De Mesmaeker, *Tetrahedron Lett.*, 1992, **33**, 3613; (*f*) A. D. Borthwick, S. Caddick and P. J. Parsons, *Tetrahedron*, 1992, **48**, 10655; (*g*) D. P. Curran, D. Kim and C. Ziegler, *Tetrahedron*, 1991, **47**, 6189; (*h*) D. P. Curran, A. C. Abraham and H. Liu, *J. Org. Chem.*, 1991, **56**, 4335; (*i*) D. P. Curran and H. Yu, *Synthesis*, 1992, 123; (*j*) D. P. Curran, K. V. Somayajula and H. Yu, *Tetrahedron Lett.*, 1992, **33**, 2295; (*k*) D. P. Curran and N. DeMello, *J. Chem. Soc., Chem. Commun.*, 1993, 1314.
6 Reviews: C. P. Jasperse, D. P. Curran and T. L. Fevig, *Chem. Rev.*, 1991, **91**, 1237; D. P. Curran, *Synthesis*, 1988, 417, 489; B. Giese, *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, 1986.
7 D. H. R. Barton, N. Ozbalik and J. C. Sarma, *Pure Appl. Chem.*, 1988, **60**, 1551; P. M. Esch, H. Hiemstra, R. F. deBoer and W. N. Speckamp, *Tetrahedron*, 1992, **48**, 4659.
8 Selected references to early work: D. A. Burnett, J.-K. Choi, D. J. Hart and Y.-M. Tsai, *J. Am. Chem. Soc.*, 1984, **106**, 8201; D. J. Hart and Y.-M. Tsai, *J. Am. Chem. Soc.*, 1984, **106**, 8209; J. K. Choi and D. J. Hart, *Tetrahedron*, 1985, **41**, 3959; M. D. Bachi, A. De Mesmaeker and N. De Stevenart-De Mesmaeker, *Tetrahedron Lett.*, 1987, **28**, 2887; A. L. J. Beckwith and D. R. Boate, *Tetrahedron Lett.*, 1985, **26**, 1761; J.-K. Choi, D.-C. Ha, D. J. Hart, C.-S. Lee, S. Ramesh and S. Wu, *J. Org. Chem.*, 1989, **54**, 279.
9 K. Shankaran, C. P. Sloan and V. Snieckus, *Tetrahedron Lett.*, 1985, **26**, 6001.
10 C. P. M. Sloan, MSc. Thesis, University of Waterloo, 1987. We thank Professor V. Snieckus for informing us of these results.
11 A. N. Abeywickrema and A. L. J. Beckwith, *J. Chem. Soc., Chem. Commun.*, 1986, 464.
12 D. H. Hey and D. G. Turpin, *J. Chem. Soc.*, 1954, 2471.
13 (*a*) A. H. Lewin, A. H. Dinwoodie and T. Cohen, *Tetrahedron*, 1966, **22**, 1527; (*b*) D. H. Hey, G. H. Jones and M. J. Perkins, *J. Chem. Soc., Perkin Trans 1*, 1972, 1170; (*c*) T. Cohen, K. W. Smith and M. D. Swerdloff, *J. Am. Chem. Soc.*, 1971, **93**, 4303; (*d*) S. H. Pines, R. M. Purick, R. A. Reamer and G. Gal, *J. Org. Chem.*, 1978, **43**, 1337.
14 T. Cohen, C. H. McMullen and K. Smith, *J. Am. Chem. Soc.*, 1968, **90**, 6866.
15 J. Grimshaw, R. J. Haslett and J. Trocha-Grimshaw, *J. Chem. Soc., Perkin Trans. 1*, 1977, 2448; J. Grimshaw and R. J. Haslett, *J. Chem. Soc., Perkin Trans. 1*, 1980, 657.
16 J. C. Scaiano and L. Stewart, *J. Am. Chem. Soc.*, 1983, **105**, 3609.
17 (*a*) W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, 1970, **70**, 517; M. Oki, (*b*) *Top. Stereochem.*, 1983, **14**, 1; (*c*) *Applications of Dynamic NMR Spectroscopy*, UCH, Deetfield Beach, 1985; (*d*) K. Spaargareh,

P. K. Korver, P. J. van der Haak and Th. J. de Boer, *Org. Magn. Reson.*, 1971, **3**, 605; (*e*) L. M. Jackman, T. E. Kavanagh and R. C. Haddon, *Org. Magn. Reson.*, 1969, **1**, 109; (*f*) R. F. C. Brown, L. Radom, S. Sternhell and I. D. Rae, *Can. J. Chem.*, 1968, **46**, 2577; (*g*) A. H. Lewin, M. Frucht, K. V. J. Chen, E. Benedetti and B. Di Blasio, *Tetrahedron*, 1975, **31**, 207; (*h*) A. H. Lewin and M. Frucht, *Org. Magn. Reson.*, 1975, **7**, 206.
18 V. Snieckus, J.-C. Cuevas, C. P. Sloan, H. Liu and D. P. Curran, *J. Am. Chem. Soc.*, 1990, **112**, 896.
19 D. P. Curran, H. Yu and H. Liu, *Tetrahedron*, in press
20 H. Liu, PhD Thesis, University of Pittsburgh, 1991.
21 G. Stork, R. Mook, Jr., S. A. Biller and S. D. Rychnovsky, *J. Am. Chem. Soc.*, 1983, **105**, 3741.
22 D. D. M. Wayner, D. J. McPhee and D. Griller, *J. Am. Chem. Soc.*, 1988, **110**, 132.
23 S. A. Glover and J. A. Warkentin, *J. Org. Chem.*, 1993, **58**, 2115.
24 Leading reference: K. B. Wiberg and M. W. Wong, *J. Am. Chem. Soc.*, 1993, **115**, 1078.
25 W. R. Bowman, H. Heaney and B. M. Jordan, *Tetrahderon*, 1991, **47**, 10119.
26 T. H. Siddall and C. A. Prohaska, *J. Am. Chem. Soc.*, 1966, **88**, 1172; A. J. R. Bourn, D. G. Gillies and E. W. Randall, *Tetrahedron*, 1966, **22**, 1825; K. Nagarajan, M. D. Nair and P. M. Pillai, *Tetrahedron*, 1967, **23**, 1683.
27 J. P. Chupp and J. F. Olin, *J. Org. Chem.*, 1967, **32**, 2297.
28 H. Togo and O. Kikuchi, *Heterocycles*, 1989, **28**, 373.
29 S. T. Autrey, M. D. Alnajjar, D. A. Nelson and J. A. Franz, *J. Org. Chem.*, 1991, **56**, 2197; allyl radicals: G. Stork and M. E. Reynolds, *J. Am. Chem. Soc.*, 1988, **110**, 6911.
30 R. F. Borch, M. D. Bernstein and H. D. Durst, *J. Am. Chem. Soc.*, 1971, **93**, 2897.
31 T. Wakamatsu, H. Nakamura, Y. Nishikimi, K. Yoshida, T. Noda, M. Taniguchi and Y. Ban, *Tetrahedron Lett.*, 1986, **27**, 6071; U. Sunay and B. Fraser-Reid, *Tetrahedron Lett.*, 1986, **27**, 5335.
32 L. S. Hegedus and J. M. McKearin, *J. Am. Chem. Soc.*, 1982, **104**, 2444.
33 D. C. Spellmeyer and K. N. Houk, *J. Org. Chem.*, 1987, **52**, 959; A. L. J. Beckwith and C. H. Schiesser, *Tetrahedron*, 1985, **41**, 3925.
34 A. L. J. Beckwith, C. J. Easton, T. Lawrence and A. K. Serelis, *Aust. J. Chem.*, 1983, **36**, 545.
35 G. E. Keck and A. M. Tafesh, *Synlett*, 1990, 257.
36 D. P. Curran and C.-T. Chang, *J. Org. Chem.*, 1989, **54**, 3140.
37 T. Cohen and J. Lipowitz, *J. Am. Chem. Soc.*, 1964, **86**, 2515.
38 Related 1,5-radical cyclizations to aromatic rings: C. M. Camaggi, R. Leardini and P. Zanirato, *J. Org. Chem.*, 1977, **42**, 1570; J. J. Kohler and W. N. Speckamp, *Tetrahedron Lett.*, 1977, 631.
39 I. MacInnes, J. C. Walton and D. C. Nonhebel, *J. Chem. Soc., Chem. Commun.*, 1985, 712.
40 D. P. Curran and J. Tamine, *J. Org. Chem.*, 1991, **56**, 2746.
41 M. Murakami, M. Hayashi and Y. Ito, *J. Org. Chem.*, 1992, **57**, 793.

Paper 3/06654A
Received 4*th November* 1993
Accepted 10*th February* 1994