Asymmetric Induction in Allylic Amination

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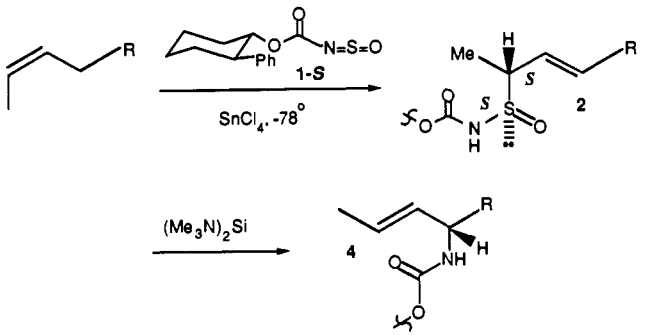
Abstract: Net allylic amination of *cis*-alkenes was accomplished by a two-step procedure that proceeded with excellent regio- and absolute stereochemical control in moderate to good chemical yield. Reaction of alkenes with the *N*-sulfinylcarbamate of *trans*-2-phenylcyclohexanol (**1**) in the presence of $SnCl_4$ provided allylic sulfinamides **2** with absolute stereochemical control at both sulfur and carbon stereocenters. Subsequent conversion of these adducts to allylic carbamates was achieved by treatment with hexamethyldisilazane where O silylation is followed by sigmatropic 2,3-rearrangement to form carbamate derivatives **4** of allylic amines. High levels of transmission of stereochemical integrity from the originally formed carbon stereocenter to that in the product bearing nitrogen were observed.

Through the efforts of a large number of research groups, there are now available a range of practical synthetic transformations that proceed with high levels of absolute stereochemical control in the formation of carbon stereocenters. The majority of these are reactions that effect carbon–carbon bond formation,[1] while a relatively smaller group are functional group transformations within an existing carbon framework.[2-4] Notably absent from this latter group were transformations that resulted in allylic oxidation of simple, unfunctionalized alkenes with practical levels of stereochemical control. Such reactions present unusual challenges as both regio- and geometric control need to be superimposed upon absolute stereochemical induction for such processes to be of value. This situation changed dramatically with our observations, first reported in 1987,[5] that the *N*-sulfinylcarbamate of our chiral auxiliary *trans*-2-phenylcyclohexanol underwent ene reactions with high levels of absolute stereochemical, geometric, and regiochemical control. At that time, we noted that these adducts could be successfully transformed to allylic alcohols by the well-precedented 2,3-rearrangement of derived sulfoxides (eq 1, Figure 1). We detail here our subsequent studies on parallel transformations of these same adducts that result in allylic amines (eq 2, Figure 1).



It occurred to us that the *N*-sulfinylcarbamate adducts could be transformed to intermediates that would undergo 2,3-rearrangement with the establishment of a new carbon–nitrogen bond if a second bond could be established between sulfur and nitrogen. Indeed, in 1988, Deleris, Dunogues, and Gadras reported that the adducts formed between alkenes and *N*-sulfinylsulfonamides undergo rearrangement with the formation of allylic amine derivatives[6] when treated with hexamethyldisilazane. The process is presumed to proceed by silylation of the sulfonamide oxygen with production of an intermediary imino species with a formal double bond between sulfur and nitrogen (Figure 2). Subsequent thermal rearrangement of this intermediate produces a species that is presumed to undergo fragmentation by attack of a nucleophile on silicon, forming the final allylic amine derivative.

We were delighted to find that, when the same procedure was applied to our chiral and enantiomerically enriched sulfonamide derivatives obtained from the ene reaction, allylic amine carbamates were produced in moderate to good yield and with transmission of absolute stereochemistry.[7] In Table I, we have provided a summary of the allylic amines produced by this technique. In all cases, the diastereomeric excess of the final carbamates before purification by recrystallization is on the order of 7:1, lower than that of the original sulfinamide ene adducts, which are generally produced with stereochemical control in excess of 95:5. Loss of stereochemical integrity could occur by stereomutation of the ene adducts, a process that we have observed to occur at room temperature. Further, incomplete transmission of stereochemistry in the sigmatropic 2,3-rearrangement could also contribute to the decrease in diastereomeric ratio. However, we presume that the rearrangement is concerted, as otherwise loss of regiochemical control should also be observed, and for the cyclic alkenes a concerted reaction must deliver the nitrogen to the same face from which the sulfur was attached and thus result in complete transmission of stereochemical integrity. Since the levels of control observed for both the cyclic and acyclic systems are comparable, we conclude that loss of control is the result of stereomutation of initial ene adducts. It does appear that the conditions that are used for silyation and rearrangement are at optimum.

The final product carbamates are almost invariably crystalline, and the level of stereochemical purity can be readily enhanced by recrystallization. In the majority of cases, levels of control of at least 95:5 can be achieved with chemical yields in excess of 50% for the overall process based on alkene. Obviously, the level of diastereomeric excess and the chemical yield are counterbalancing factors, and one can be sacrificed to further enhance the other. Notice that an acetate functionality is tolerated in the sequence (entries 6 and 7) although the ester suffers cleavage in the final stage that forms the carbamate. The conditions are, however, sufficiently mild that the carbamate **17** was not converted to a cyclic carbamate by intermolecular substitution of the alcohol functionality for the chiral auxiliary.

In all cases, resolution of the diastereomers of the products was obtained both by analytical HPLC and by ^{13}C NMR spectroscopy, although resolution of carbamates by the latter technique was generally poor. For example, a mixture of diastereomers of carbamate **9** was prepared by hydrolysis of the product carbamate and re-formation of the carbamate with use of racemic chiral auxiliary (Figure 3).[8] Many of the ^{13}C signals for the two

(1) For reviews, see: Morrison, J. D., Ed. *Asymmetric Synthesis*; Wiley: New York, 1983–1985; Vol. 1–5.
(2) For reviews, see: Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *Tetrahedron* **1981**, *37*, 3547.
(3) Pfenninger, A. *Synthesis* **1986**, 89.
(4) Midland, M. M. *Chem. Rev.* **1989**, *89*, 1553.
(5) Whitesell, J. K.; Carpenter, J. *J. Am. Chem. Soc.* **1987**, *109*, 2839–40. Whitesell, J. K.; Carpenter, J.; Yaser, H. *J. Am. Chem. Soc.* **1990**, *112*, 0000.
(6) Delenis, G., Dunognes, J.; Gadras, A. *Tetrahedron* **1988**, *44*, 4243.
(7) Some time ago, Sharpless investigated a system similar to ours that proceeds through ene reactions of a selenium species. Unfortunately, chemical yields were only moderate, and levels of induction were far below practical levels. See: Singer, S. P.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1449.
(8) Little kinetic selectivity was observed in re-formation of the carbamate, as a nearly 1:1 mixture of the two distereomers was obtained.

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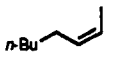
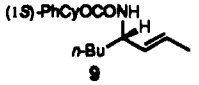
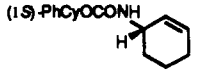
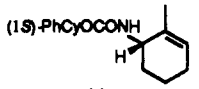
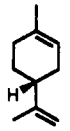
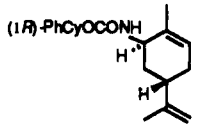
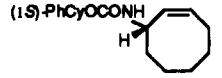
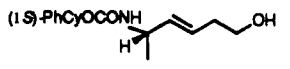
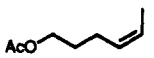
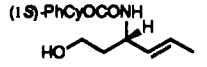
Table I. In all Cases Except for Reaction with (*R*)-Limonene, the (1*S*)-Enantiomer of *trans*-2-Phenylcyclohexanol Was Used as Auxiliary

entry	alkene	carbamate product	purified yield (%)[a]	d.e.[e] crude	d.e.[e] purified[b]
1		 **9**	75	–	10:1
2		 **10**	58	7:1	26:1
3		 **11**	33	7:1	>95:5
4		 **12**	38	7:1	>95:5[c]
5		 **13**	53	7:1	>95:5
6	 **14**[d]	 **15**	52	7:1	>95:5
7	 **16**	 **17**	46	12:1	>95:5

[a] Overall yield based on the *N*-sulfinylcarbamate of *trans*-2-phenylcyclohexanol. [b] Values reported as >95:5 represent the limit of detection by ^{13}C NMR spectroscopy. [c] Based on ^{13}C NMR spectral analysis of 2,3-rearrangement product before removal of siloxy group. [d] Contained 15% of trans isomer. [e] Diastereomeric excess.

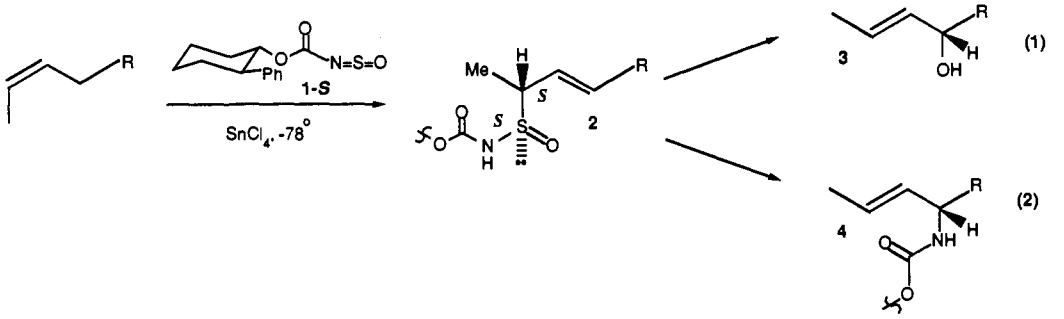


Figure 1.

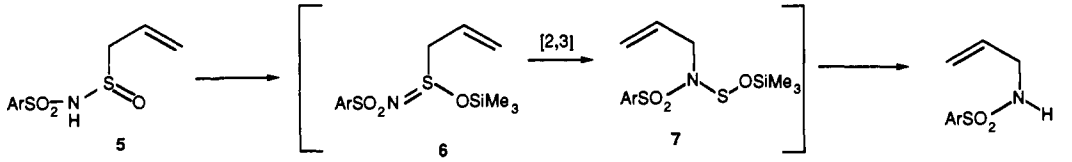


Figure 2.

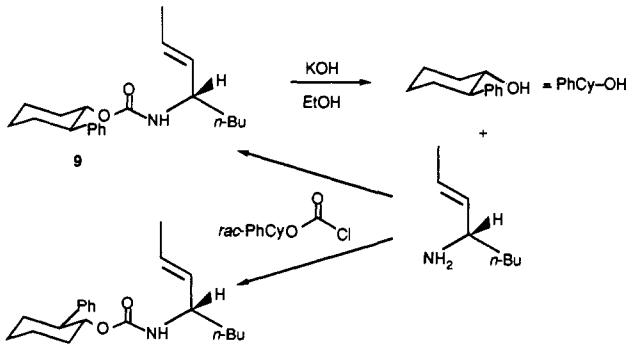


Figure 3.

diastereomers were coincident, and no pairs differed by more than δ 0.5. On the other hand, base-line resolution of these diastereomers was achieved on analytical HPLC analysis. This process of hydrolysis and reformation of the carbamates also confirms that the corresponding amines can be readily obtained from the carbamates.

The sigmatropic 2,3-rearrangement of the intermediate imino species is presumed to proceed through a transition state resembling that established for the corresponding rearrangements of sulfoxides.[9] Such an arrangement is illustrated in Figure 4, and the absolute stereochemistry of most product carbamates was assigned on that basis. An exception is that resulting from (*R*)-limonene, where all structural features were confirmed unambiguously by single crystal X-ray analysis.[10] It is clear that this rearrangement process is concerted on the basis of the levels

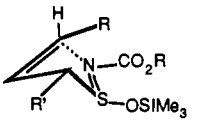


Figure 4.

of stereochemical transmission and regiochemical control observed from sulfonamide adducts to the final carbamates.

Conclusion

We have demonstrated quite practical and effective methods for functionalization of simple, *cis*-alkenes with the introduction of carbon,[11] oxygen,[5] and now nitrogen functionalities. These methods were the first and still remain the only practical techniques for the control of absolute stereochemistry in the allylic functionalization of such alkenes. As both enantiomers of our chiral auxiliary *trans*-2-phenylcyclohexanol are readily available,[12] these reactions represent an exceptionally versatile set of synthetic transformations for the control of absolute stereochemistry.

Experimental Section

Materials. Ether and tetrahydrofuran (THF) were distilled prior to use from a deep blue solution resulting from benzophenone and sodium. Benzene and methanol were stored over molecular sieves. Methylene chloride, pyridine, 1,2-dichloroethane and 1,1,1,3,3,3-hexamethyldisilazane (HMDZ) were distilled from calcium hydride and stored over molecular sieves. Thionyl chloride was distilled from calcium hydride under nitrogen immediately prior to use. Skelly B was stirred first with concentrated sulfuric acid and then with solid sodium carbonate, filtered through alumina, and distilled before use. All other solvents and reagents were used as obtained from commercial sources unless stated otherwise.

Procedure. Reactions were routinely carried out under dry nitrogen or argon atmospheres with magnetic stirring. Preparative chromatography was carried out with a Waters 6000 Å HPLC with two 7.8 mm × 60 cm Porasil A silica gel semipreparative columns and with a refractive index detector. Analytical HPLC was performed with a Waters 6000A HPLC pump with two 30-cm Porasil A silica gel analytical columns with a Waters 440 UV detector.

Spectra. ^{13}C NMR spectra were obtained with a Nicolet NT-360 spectrometer at 90 MHz or a General Electric QE-300 at 75 MHz. ^{1}H NMR spectra were obtained with a Nicolet NT-360 at 361 MHz or a General Electric QE-300 at 300 MHz. Unless otherwise stated, both carbon and proton NMR spectra were obtained in chloroform-*d*, and chemical shift values are reported in δ downfield shift from TMS as an internal standard. Compounds described as "clean by ^{13}C NMR spectroscopy" exhibited no impurities greater than 5%. IR spectra were obtained on dilute (5%) CH_2Cl_2 solutions with a Beckman Acculab 8 or a Perkin-Elmer 298 infrared spectrophotometer, with use of polystyrene's absorption at 1601 cm^{-1} as a reference. Low-resolution mass spectra in EI mode were recorded with a Bell and Howell Model 21-491 spectrometer at 70 eV and those in CI mode with a Finnigan-MAT 4023 GC/MS with methane. High-resolution mass spectra were recorded with a CEC 21-110B instrument in EI mode. Only *m/e* values greater than or equal to 40% of the base peak and *m/e* greater than or equal to 90 amu are reported. Optical rotations were measured with a Perkin-Elmer 141 polarimeter with use of the sodium D line. X-ray structures were determined by using a Syntex $P2_1$ autodiffractometer with a graphite monochromator.

General Procedure for the Preparation of *trans*-2-Phenylcyclohexyl *N*-Sulfinylcarbamate (1). To 1.0 g (4.6 mmol) of dried *trans*-2-phenylcyclohexyl carbamate in 50 mL of dry benzene at room temperature under nitrogen with rapid stirring were simultaneously injected over a 15-min period 0.53 mL (6.8 mmol, 1.5 equiv) of freshly distilled $SOCl_2$ and 0.72 mL (9.3 mmol, 2 equiv) of pyridine. Stirring was continued for 15 min after which the reaction was allowed to stand for 14 h. Moisture-free workup involved an initial Schlenk filtration under Ar to remove pyridinium salts followed by solvent and reagent removal under high vacuum. Note: Due to the high moisture sensitivity of the *N*-sulfinylcarbamate, solvent removal with a rotary evaporator is not recommended. The *N*-sulfinylcarbamate was used directly without further purification: ^{13}C NMR (90 MHz) δ 151.0 (s), 142.0 (s), 128.5 (d), 127.4 (d), 126.7 (d), 81.4 (d), 49.4 (d), 33.8 (t), 32.0 (t), 25.5 (t), 24.6 (t).

General Procedure for the Formation of Ene Adducts 2 of *N*-Sulfinylcarbamates and Alkenes. To the *N*-sulfinylcarbamate **1**, prepared as above from 1.0 g (4.6 mmol) of carbamate, in 8 mL of CH_2Cl_2 was added 5.4 mL (1.2 equiv) of a 1.0 M solution of $SnCl_4$ in CH_2Cl_2 at −78 °C under nitrogen. To this stirred mixture was added a precooled solution of an excess (>2 equiv) of alkene in 2 mL of CH_2Cl_2. The reaction was stirred at −78 °C for 20 min and then quenched by pouring into an Et_2O/H_2O mixture. The aqueous layer was extracted three times with 50-mL portions of EtOAc, and the combined organics were washed twice with saturated aqueous NaCl and dried over Na_2SO_4. Solvent removal in vacuo yielded the sulfinamide product, which was filtered through a short silica gel column with 1:1 EtOAc/Skelly B to remove any remaining tin salts. Note: A solution of $SnCl_4$ in CH_2Cl_2 proved to be less moisture sensitive and consequently gave consistently better results than anhydrous $SnCl_4$. The sulfinamide adducts of acyclic alkenes isomerize readily at room temperature. Further reactions should therefore be carried out immediately for these cases.

General Procedure for the Silylation and Rearrangement of Sulfinamide Adducts 2–4. To 1.30 mmol of the sulfinamide adduct was added 0.94 mL (3 equiv) of HMDZ in 3 mL of 1,2-dichloroethane. This mixture was stirred at room temperature under N_2 for 90 min, then at 50 °C for a further 90 min, and finally at reflux overnight. Solvent removal in vacuo followed by reagent removal under high vacuum afforded the product. (Note: These products are not particularly stable, and prompt hydrolysis is recommended.) To 1.1 mmol of the crude rearranged product were added 50 mL of a 3:1:1 $THF/H_2O/MeOH$ mixture and 235 mg (5 equiv) of LiOH. This mixture was stirred at room temperature for 3 h, after which time 200 mL of H_2O and 100 mL of EtOAc were added. The aqueous layer was extracted three times with 50-mL portions of EtOAc, and the combined organics were washed twice with saturated NaCl solution. The organic layers were dried over Na_2SO_4, and the solvent was removed in vacuo to afford the carbamate.

4-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-2(*E*)-octene (9). To 489 mg (1.30 mmol) of the ene adduct from *cis*-2-octene and **1** was added 0.94 mL (4.47 mmol) of HMDZ in 3 mL of 1,2-dichloroethane, and the rearrangement was carried out as above to yield 541 mg (93%) as a yellow oil: ^{13}C NMR (75 MHz) δ 156.1 (s), 142.7 (s), 131.7 (d), 128.1 (d), 127.1 (d), 126.3 (d), 126.2 (d), 79.2 (d), 64.2 (d), 50.0 (d), 34.1 (t), 33.5 (t), 32.4 (t), 28.0, (t), 25.6 (t), 24.5 (t), 22.2 (t), 17.4 (q), 13.8 (q), 0.2 (q); ^{1}H NMR (300 MHz) δ 7.30–7.10 (m, 5 H), 5.35 (br d, 2 H), 5.05 (ddd, J = 4.6, 10.7, 10.7 Hz, 1 H), 4.45–4.35 (m, 1 H), 2.75 (ddd, J = 3.5, 10.7, 10.7 Hz, 1 H), 2.30 (m, 1 H), 2.0–0.75 (m, 20 H), 0.15 (s, 9 H); IR 2940, 2860, 1700, 1220, 850 cm^{-1}. To 500 mg (1.1 mmol) of the crude rearranged product were added 50 mL of a 3:1:1 $THF/H_2O/MeOH$ mixture and 235 mg (5 equiv) of LiOH. Reaction and workup as above yielded 356 mg, purified by semipreparative chromatography to yield 275 mg (75%) of **9** as a viscous oil and a 10:1 ratio of diastereomers (by analytical HPLC analysis): ^{13}C NMR (75 MHz) δ 155.6 (s), 143.4 (s), 131.7 (d), 128.2 (d), 127.5 (d), 126.2 (d), 124.7 (d), 75.8 (d), 52.1 (d), 50.2 (d), 35.1 (t), 34.4 (t), 32.8 (t), 27.9 (t), 25.9 (t), 24.8 (t), 22.4 (t), 17.7 (q), 14.0 (q); ^{1}H NMR (300 MHz) δ 7.30–7.10 (m, 5 H), 5.20–4.95 (m, 2 H), 4.88 (ddd J = 4.5, 10.6, 10.6 Hz, 1 H), 4.17 (br d, 1 H), 3.86 (br s, 1 H), 2.62 (br dd, 1 H), 2.18 (br d, 1 H), 1.95–0.80 (m, 19 H); IR (cm^{-1}): 3440, 2920, 2860, 1695, 1595, 1480, 1205, 1095, 1020 cm^{-1}; MS, *m/e* 329 (M^+), 272, 159, 158, 142, 114, 91.

Preparation of a Mixture of Diastereomers of 4-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-2(*E*)-octene. To 1.0 g (3.04 mmol) of the carbamate **9** prepared as above were added 50 mL of 95% EtOH and 3.0 g (18 mmol) of KOH, and the mixture was heated at reflux for 48 h under N_2. The solution was then acidified with 5 N HCl and the EtOH removed in vacuo. Et_2O (100 mL) and H_2O (100 mL) were then added, and the aqueous layer was extracted twice with Et_2O to remove *trans*-2-phenylcyclohexanol. A 4 N NaOH solution was then added until a pH >10 was obtained, and the aqueous layer was extracted three times with Et_2O. Fractional distillation was used to remove the solvent, affording a brown oil. To this oil was added with stirring 1 equiv of racemic *trans*-2-phenylcyclohexyl chloroformate in 20 mL of Et_2O and 10 mL of saturated $NaHCO_3$, and stirring was continued at ambient temperature for 1 h. The organic layer was dried and concentrated, and semipreparative chromatography with 7:1 Skelly B/EtOAc was used to remove unreacted chloroformate, resulting in a solid showing a 1:1.1 ratio of diastereomers by analytical HPLC. Data for the diastereomer of **9**: ^{13}C NMR (90 MHz) δ 155.4 (s), 143.3 (s), 131.9 (d), 128.2 (d), 127.5 (d), 126.2 (d), 125.3 (d), 75.8 (d), 52.4 (d), 50.2 (d), 35.1 (t), 34.4 (t), 32.8 (t), 27.3 (t), 25.9 (t), 24.8 (t), 22.4 (t), 17.7 (q), 14.0 (q).

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(10) Whitesell, J. K.; Lynch, V. R.; Yaser, H. K. *Acta Crystallogr. C* **1990**, *in press*.
(11) Whitesell, J. K.; Bhattacharya, A.; Aguilar, D. A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 989. Whitesell, J. K.; Chen, H. H.; Lawrence, R. M. *J. Org. Chem.* **1985**, *50*, 4663. Whitesell, J. K.; Liu, C. L.; Buchanan, C. M.; Chen, H. H.; Minton, M. A. *J. Org. Chem.* **1986**, *51*, 551.
(12) Whitesell, J. K.; Lawrence, R. M. *Chimia* **1986**, *40*, 318.

1-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-2-cyclohexene (10). To 950 mg (2.74 mmol) of the recrystallized ene adduct prepared above was added 1.5 mL (7.13 mmol) of HMDZ in 3 mL of 1,2-dichloroethane, and the rearrangement was performed as above to yield a yellow oil: ^{13}C NMR (75 MHz) δ 155.9 (s), 142.7(s), 129.5 (d), 128.0 (d), 127.9 (d), 127.1 (d), 679.7 (d), 58.7 (d), 49.8 (d), 33.7 (t), 32.2 (t), 29.4 (t), 25.5 (t), 24.4 (t), 24.1 (t), 21.0 (t). This material was promptly hydrolyzed as above to give 711 mg (88%, 58% overall from carbamate) of **10** as a crystalline solid: mp 79–80 °C; ^{13}C NMR (CD_3OD, 75 MHz) δ 157.4 (s), 144.4 (s), 130.1 (d), 129.0 (d), 128.4 (d), 127.0 (d), 79.6 (d), 51.0 (d), 47.3 (d), 35.1 (t), 33.7 (t), 30.3 (t), 26.7 (t), 25.6 (t), 25.4 (t), 20.9 (t); ^{1}H NMR (300 MHz) δ 7.32–7.14 (m, 5 H), 5.71 (br d, 1 H), 5.27 (br d, 1 H), 4.87 (ddd, J = 10.4, 10.4, 4.5 Hz, 1 H), 4.31 (br d, 1 H), 3.98 (br s, 1 H), 2.62 (br m, 1 H), 2.20 (br s, 1 H), 2.00–1.11 (br m, 13 H); IR 3430, 3020, 2930, 2860, 1690, 1480, 1330, 1200, 1030 cm^{-1}; MS, m/e 299 (M^+), 158, 91. Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42: N, 4.68. Found: C, 76.22; H, 8.55; N, 4.72.

1-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-2-methyl-2-cyclohexene (11). To 670 mg (1.85 mmol) of the adduct prepared from 1-methylcyclohexene were added 1 mL (4.76 mmol) of HMDZ and 4 mL of 1,2-dichloroethane, and the standard rearrangement conditions were followed: ^{13}C NMR (300 MHz) δ 156.6 (s), 143.0 (s), 132.8 (s), 128.5 (d), 127.4 (d), 126.7 (d), 126.5 (d), 79.6 (d), 50.0 (d), 34.4 (t), 32.5 (t), 30.0 (t), 25.8 (t), 25.1 (t), 24.8 (t), 20.5 (t), 20.1 (q), 0.3 (q). This material was then hydrolyzed as above to give 426 mg (74%) of **11** as a crystalline solid: mp 108–109 °C; ^{13}C NMR (75 MHz) δ 155.8 (s), 143.3 (s), 133.3 (s), 128.1 (d), 127.6 (d), 126.2 (s), 125.8 (d), 75.9 (d), 50.5 (d), 48.9 (d), 34.1 (t), 32.9 (t), 29.5 (t), 25.9 (t), 25.9 (t), 25.1 (t), 24.9 (t), 20.9 (q), 18.3 (t); ^{1}H NMR (300 MHz) δ 7.32–7.13 (m, 5 H), 5.49 (br s, 1 H), 4.88 (ddd, J = 10.5, 10.5, 4.4 Hz, 1 H), 4.29 (br d, J = 10.5 Hz, 1 H), 3.82 (br d, 1 H), 2.58 (m, 1 H), 2.18 (m, 1 H), 1.98–1.10 (m, 16 H); IR 3440, 3030, 2940, 2860, 1700, 1490, 1210, 1070 cm^{-1}; MS, m/e 313 (M^+), 158, 154, 94, 91. Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.38; H, 8.85; N, 4.35.

[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-2-cyclooctene (13). To 1.42 g (3.77 mmol) of the sulfinamide prepared above were added 3 mL (14.3 mmol) of HMDZ and 5 mL of 1,2-dichloroethane. Standard reaction conditions were followed to afford 1.52 g (90%) of a yellow oil: ^{13}C NMR δ 156.0 (s), 142.8 (s), 131.1 (d), 128.7 (d), 128.1 (d), 127.2 (d), 126.3 (d), 79.5 (d), 59.5 (d), 50.0 (d), 35.8 (t), 34.2 (t), 32.3 (t), 29.2 (t), 26.5 (t), 26.2 (t), 25.9 (t), 25.7 (t), 24.6 (t), 0.1 (q). To this oil were added 50 mL of a 3:1:1 THF/MeOH/H_2O mixture and 1.0 g (23.4 mmol) of LiOH, and the reaction was allowed to stir at room temperature for 3 h. After the usual workup, the product was purified by semipreparative chromatography with 7:1 Skelly B/EtOAc to yield 777 mg (70%, 53% overall yield from carbamate) of **13**: mp 115–116 °C; ^{13}C NMR (75 MHz) δ 155.6 (s), 143.6 (s), 132.3 (d), 129.3 (d), 128.3, (d), 127.6 (d), 126.3 (d), 76.4 (d), 50.2 (d), 49.3 (d), 36.5 (t), 34.6 (t), 32.9 (t), 29.0 (t), 26.5 (t), 26.2 (t), 26.0 (t), 24.9 (t), 24.4 (t); ^{1}H NMR (300 MHz) δ 7.31–7.19 (m, 5 H), 5.57 (dd, J = 19, 8.0 Hz, 1 H), 5.01 (br s, 1 H), 4.87 (ddd, J = 11.0, 11.0, 3.9 Hz, 1 H), 4.33 (br s, 1 H), 2.66 (br t, 1 H), 2.30–1.20 (br m, 19 H); IR 3440, 3020, 2930, 2860, 1700, 1490, 1420, 1260, 1040, 890, 680 cm^{-1}; MS, m/e 327 (M^+), 158, 91.

1-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-2-methyl-5-isopropenylcyclohexene (12). To 460 mg (1.08 mmol) of the recrystallized ene adduct prepared above was added 1.5 mL (7.13 mmol) of HMDZ in 3 mL of 1,2-dichloroethane, and the rearrangement was performed as above to yield 550 mg (quantitative yield) of a yellow oil (single diastereomer by ^{13}C NMR): ^{13}C NMR (75 MHz) δ 156.4 (s), 148.9 (s), 142.7 (s), 130.6 (s), 128.2 (d), 127.6 (d), 127.1 (d), 126.3 (d), 108.6 (t), 79.8 (d), 60.2 (d), 49.9 (d), 34.6 (d), 33.7 (t), 32.3 (t), 30.3 (t), 25.6 (t), 24.5 (t), 20.7 (q), 20.1 (q); ^{1}H NMR (300 MHz) δ 7.35–7.12 (m, 5 H), 5.70 (br s, 1 H), 5.02 (ddd, J = 10.2, 10.2, 4.6 Hz, 1 H), 4.81 (s, 1 H), 4.69 (s,1 H), 4.34 (br s, 1 H), 2.76 (ddd, J = 9.5, 9.5, 4.6 Hz, 1 H), 2.36–1.00 (br m, 18 H), 0.19 (s, 9 H). This material was promptly hydrolyzed as above to yield 391 mg (96%; 38% overall yield from carbamate) of a crystalline solid, mp 53–54 °C. Carbamate (15%) and a second set of peaks mirroring the product and presumed to be the amide CON rotamer (10%) were visible by ^{13}C NMR analysis in addition to those for **12**: ^{13}C NMR (CD_3OD, 75 MHz) δ 158.0 (s), 150.2 (s), 144.4 (s), 133.2 (s), 129.0 (d), 128.5 (d), 127.2 (d), 126.2 (d), 109.3 (t), 77.1 (d), 51.3 (d), 50.5 (d), 36.2 (t), 35.4 (t), 35.2 (d), 33.8 (t), 31.7 (t), 26.9 (t), 25.8 (t), 21.2 (q), 21.1 (q); ^{1}H NMR (500 MHz) δ 7.28–7.13 (m, 5 H), 6.55 (s, 1 H), 5.85 (s,1 H), 4.93 (ddd, J = 10.6, 10.6, 4.4 Hz, 1 H), 4.74 (s, 1 H), 4.65 (s, 1 H), 3.28 (br s, 1 H), 2.72 (ddd, J = 11.6, 11.6, 3.8 Hz, 1 H), 2.28–1.26 (br m, 18 H); IR 3440, 2940, 2860, 1700, 1490, 1210, 1060, 1030 cm^{-1}; MS, m/e 353 (M^+), 159, 158, 134, 91.

3-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-4(*E*)-hexen-1-ol (17). To 3.0 g (7.1 mmol) of ene adduct were added 3 mL (14.3 mmol) of HMDZ and 7 mL of 1,2-dichloroethane, and the rearrangement was carried out as above to yield a yellow oil: ^{13}C NMR (90 MHz) δ 155.9 (s), 142.7 (s), 130.5 (d), 128.3 (d), 127.6 (d), 127.5 (d), 126.4 (d), 79.7 (d), 61.8 (t), 61.5 (d), 50.2 (d), 34.1 (t), 32.6 (t), 25.8 (t), 24.8 (t), 20.8 (q), 17.5 (q). This material was then hydrolyzed as above and passed through a bench-top column, with the product eluting with 1:1 Skelly B/EtOAc to yield 1.31 g (58%, 46% overall from carbamate) of a semicrystalline material that was recrystallized from Skelly B to give **16** that was free of both diastereomeric and regiochemical impurities by ^{13}C NMR: mp 70–71 °C; ^{13}C NMR (75 MHz) δ 156.5 (s), 143.3 (s), 130.8 (d), 128.3 (d), 127.5 (d), 126.3 (d), 125.9 (d), 76.5 (d), 58.9 (t), 50.0 (d), 49.0 (d), 38.1 (t), 34.3 (t), 32.7 (t), 25.9 (t), 24.8 (t), 17.7 (q); ^{1}H NMR (300 MHz) δ 7.37–7.15 (m, 5 H, 5.26 (br s, 2 H), 4.87 (br t, 1 H), 4.42 (br d, 1 H), 4.14 (br t, 1 H), 3.59 (br s, 1 H), 2.80–2.55 (m, 2 H), 2.20 (br d, 1 H), 1.98–1.20 (m, 14 H); IR 3620, 3430, 3060, 2980, 2940, 2860, 2300, 1700, 1490, 1420, 1250, 1050 cm^{-1}; MS, m/e 317 (M^+), 176, 159, 158, 130, 129, 126, 117, 114, 104, 98, 92, 91: HRMS for $C_{19}H_{27}NO_3$, calcd 317.1991, found 317.1992. Anal. Calcd for $C_{19}H_{27}NO_3$: C, 71.89 H, 8.57; N, 4.41. Found: C, 71.95; H, 8.78; N, 4.40.

5-[*N*-[[(*trans*-2-Phenylcyclohexyl)oxy]carbonyl]amino]-3(*E*)-hexen-1-ol (15). To 750 mg of sulfinamide adduct were added 2 mL (9.5 mmol) of HMDZ and 5 mL of 1,2-dichloroethane, and the rearrangement was carried out as above: ^{13}C NMR (75 MHz) δ 170.7 (s), 155.7 (s), 142.6 (s), 133.8 (d), 128.1 (d), 127.3 (d), 126.1 (d), 125.8 (d), 79.6 (d), 63.2 (t), 58.8 (d), 49.9 (d), 33.7 (t), 32.3 (t), 31.3 (t), 25.5 (t), 24.5 (t), 20.6 (q), 19.7 (q). This material was hydrolyzed as above to yield 356 mg (65%, 52% overall from carbamate) and recrystallized from Skelly B to give a product clean by ^{13}C NMR analysis: mp 121–122 °C; ^{13}C NMR (75 MHz) δ 157.7 (s), 144.8 (d), 135.1 (d), 128.6 (d), 128.2 (d), 127.2 (d), 126.6 (d), 77.2 (d), 62.5 (t), 51.3 (d), 47.7 (d), 36.5 (t), 35.4 (t), 33.9 (t), 26.9 (t), 25.8 (t), 21.0 (q); ^{1}H NMR (300 MHz) δ 7.32–7.15 (m, 5 H), 5.30 (br d, 1 H), 5.10 (br s, 1 H), 4.88 (ddd, J = 4.1, 10.5, 10.5 Hz, 1 H), 4.27 (br s, 1 H), 4.04 (br s, 1 H), 3.56 (d, J = 5.8 Hz, 2 H), 2.61 (m, 1 H), 2.18 (br d, 2 H), 1.97–1.00 (m, 12 H); IR 3610, 3440, 2940, 2860, 1700, 1490, 1420, 1260, 1040 cm^{-1}; MS, m/e 287 (M^+), 158, 129, 91. Anal. Calcd for $C_{19}H_{27}NO_3$: C, 71.89; H, 8.57; N, 4.41. Found: C, 71.94; H, 8.79; N, 4.51.

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Supplementary Material Available: Experimental details for the preparation of the sulfinamide adducts, detailed ^{13}C NMR spectral assignments, and structures (7 pages). Ordering information is given on any current masthead page.