Inhibitors of Acyl CoA:Cholesterol Acyltransferase

Wayne Vaccaro,* Cindy Amore, Joel Berger, Robert Burrier, John Clader, Harry Davis, Martin Domalski, Tom Fevig,† Brian Salisbury, and Rosy Sher

Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, New Jersey 07033-0539

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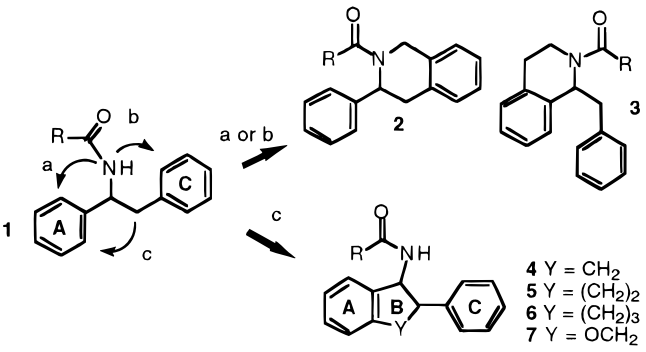
Conformational restriction of previously disclosed acyclic diphenylethyl)diphenylacetamides led to the discovery of several potent inhibitors of acyl CoA:cholesterol acyltransferase (ACAT). *cis*-[2-(4-Hydroxyphenyl)-1-indanyl]diphenylacetamide (**4a**) was the most potent ACAT inhibitor identified (IC_{50} = 0.04 μM in an *in vitro* rat hepatic microsomal ACAT assay, ED_{50} = 0.72 mg/kg/day in cholesterol-fed hamsters).

Introduction

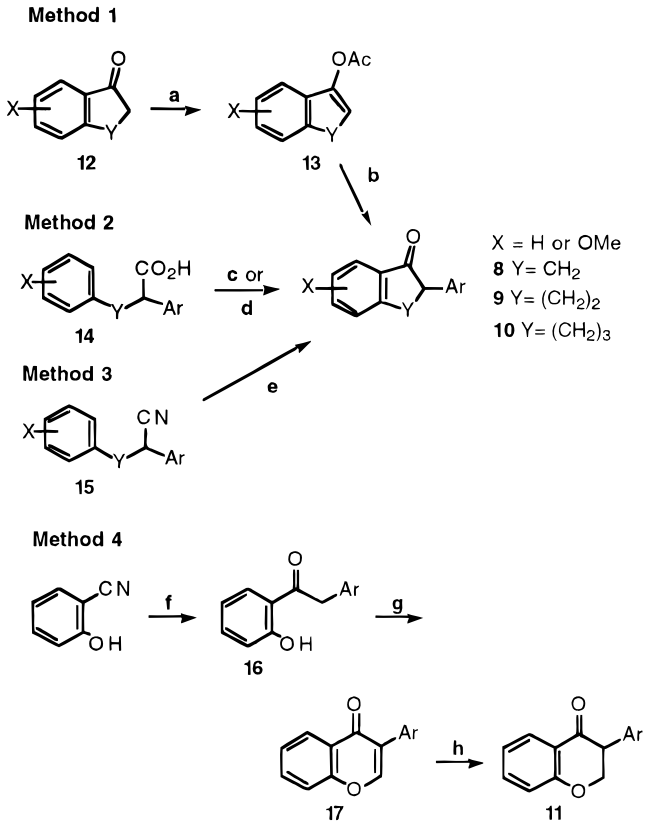
The enzyme acyl CoA:cholesterol acyltransferase (ACAT, EC 2.3.1.26) is intimately involved in the absorption of cholesterol. Inhibition of ACAT has been shown to reduce the absorption of dietary cholesterol, lower plasma lipid levels, and prevent the progression of atherosclerotic lesions in animal models.[1] We recently disclosed that amides such as **1** are potent inhibitors of ACAT.[2] Part of our research program has been directed toward the use of conformationally restricted analogs of **1** as potential inhibitors of ACAT. A previous publication from these laboratories describes the ACAT inhibition of tetrahydroisoquinolines **2** and **3**, constructed by conformational restriction of **1** *via* arrows a or b.[3] We have since discovered that conformational restriction of **1** as depicted *via* arrow c leads to a series of compounds, **4**−**7**, that are also inhibitors of ACAT. The chemistry and ACAT inhibition of **4**−**7** are the subject of this paper and are described below.



Chemistry

The requisite 2-aryl ketones **8**−**11** were prepared as depicted in Scheme 1. In method 1, conversion of **12** to the enol acetate **13** followed by palladium-mediated arylation[4] provided ketones **9** and **10**. Alternately, cyclization of the appropriate acid[5] **14** or nitrile **15** provided ketones **8** and **9** (methods 2 and 3). In method 4, the 2-arylbenzopyran **11** was prepared by a sequence involving the addition of a suitably substituted benzyl Grignard reagent[6] to 2-cyanophenol to provide **16**. Subsequent cyclization with dimethylformamide dimethyl acetal supplied **17**.[7] 1,4-Reduction of **17** with diisobutylaluminum hydride gave benzopyran **11**.[8]

Scheme 1. Preparation of 2-Aryl Ketones **8**−**11**[a]



[a] (a) Isopropenyl acetate, *p*-TSA(cat.); (b) ArBr, $Pd(OAc)_2$, (*o*-toluoyl)$_3$P, *n*-Bu_3SnOMe, $PhCH_3$; (c) (1) $(COCl)_2$, (2) $AlCl_3$, CH_2Cl2; (d) $MeSO_3H/P_2O_5$, $CHCl_3$, reflux; (e) NaCl, $AlCl_3$, neat, 180 °C; (f) (1) $ArCH_2MgCl$, THF, (2) H_2O, HCl, Δ; (g) $(MeO)_2CHNMe_2$, PhH, Δ; (h) (1) DiBAH, THF, −78 °C, (2) $Na_2SO_4(H_2O)_{10}$.

Cis amides of **4**−**7** were derived from ketones **8**−**11** as shown in Scheme 2. In method 5, ketones **9** or **11** were converted to the corresponding oximes **18** with hydroxylamine.[9] Treatment of **18** with diphenylphosphoryl chloride at low temperature presumably phosphorylates the oxime oxygen first; upon warming a phosphorus O to N rearrangement occurs to provide the phosphinylimine **19**.[10] Reduction of **19** with diisobutylaluminum hydride afforded the cis phosphonamide **20**, with complete stereocontrol. Hydrolysis of **20** provided the cis amine **21**. Acylation of **21** afforded the cis amides **5** or **7**. In method 6, sodium borohydride reduction of **9** or **10** followed by acid-catalyzed elimina-

† Present address: Hoechst Marion Roussel Inc., 2110 E. Galbraith Rd., Cincinnati, OH 45215.

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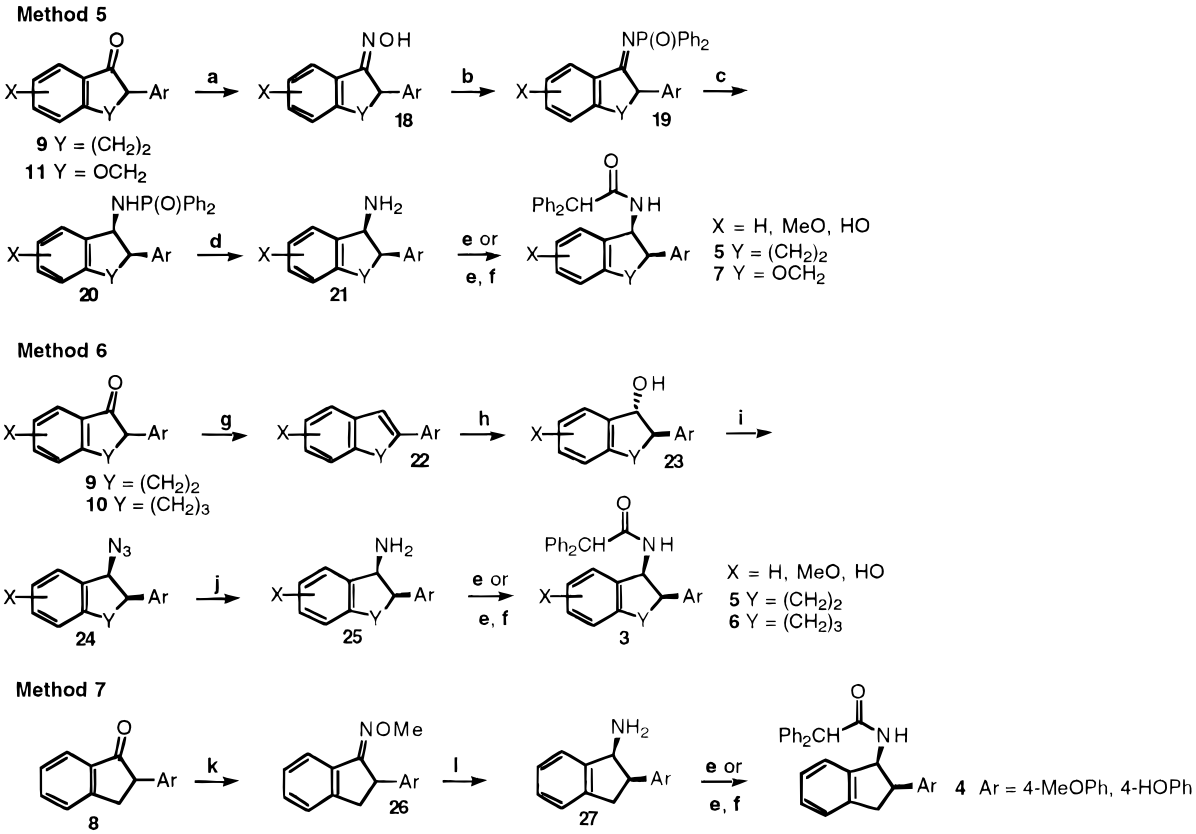
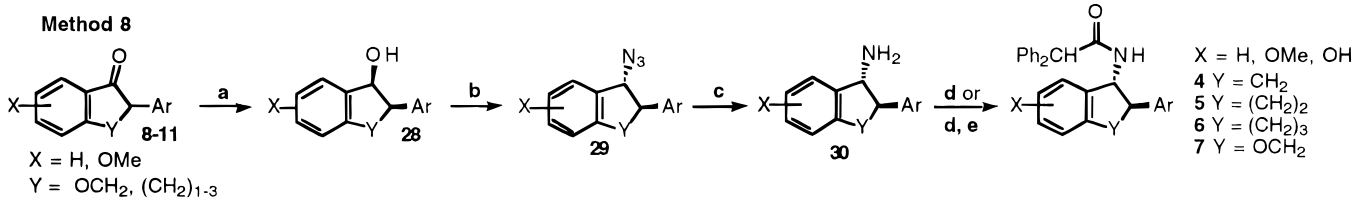
Scheme 2. Preparation of Cis Amides **4**−**7**[a]



[a] (a) NH_2OH·HCl, NaOAc, MeOH, H_2O; (b) Ph_2PCl, Et_3N, CH_2Cl_2, −78 °C room temperature; (c) (1) DiBAH, THF, −78 °C room temperature, (2) $Na_2SO_4(H_2O)_{10}$, −78 °C; (d) (1) 6 N HCl/MeOH, (2) ^-OH; (e) $Ph_2CHCOCl$, Et_3N, CH_2Cl_2 or Ph_2CO_2H, HOBT, EDCl, CH_2Cl_2; (f) (1) BBr_3, CH_2Cl_2, (2) $NaHCO_3$ (saturated), MeOH; (g) (1) $NaBH_4$, MeOH, room temperature, (2) *p*-TSA, toluene, reflux; (h) (1) BH_3THF, THF, 0 °C, (2) $^-OH/H_2O_2$; (i) $(PhO)_2P(O)N_3$, DEAD, Ph_3P, THF, −20 °C to room temperature; (j) H_2, 10% Pd/C, EtOAc/MeOH; (k) NH_2OMe·HCl, NaOAc, MeOH; (l) (1) BH_3THF, reflux, (2) H^+, (3) ^-OH.

Scheme 3. Preparation of Trans Amides **4**−**7**[a]

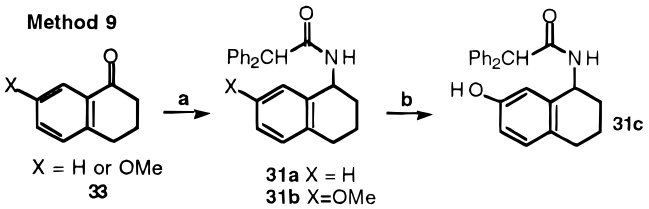


[a] (1) DiBAH, THF, −78 °C to room temperature, (2) $Na_2SO_4(H_2O)_{10}$, −78 °C; (b) $Ph_2P(O)N_3$, DEAD, Ph_3P, THF, −20 °C to room temperature; (c) H_2, 10% Pd/C, EtOAc/MeOH; (d) $Ph_2CHCOCl$, Et_3N, CH_2Cl_2 or Ph_2CO_2H, HOBT, EDCl, CH_2Cl_2; (e) (1) BBr_3, CH_2Cl_2, (2) $NaHCO_3$ (saturated), MeOH.

tion of the resulting alcohols gave olefin **22**. Hydroboration and subsequent oxidation of **22** supplied the trans alcohol **23** as the exclusive product. Conversion of alcohol **23** to the corresponding azide **24** with inversion of configuration was achieved using diphenyl phosphorazidate under Mitsunobu conditions.[11] Hydrogenation of **24** followed by acylation of the resulting amine **25** furnished the cis amides **5** or **6**. In method 7, conversion of **8** to the oxime ether **26** followed by borane reduction gave **27** as a 10:1 cis:trans mixture. This mixture was acylated to give amide **4**. Pure cis **4** was isolated by recrystallization or chromatography.

The preparation of trans amides **4**−**7** is shown in Scheme 3. Diisobutylaluminum hydride reduction of ketones **8**−**11** furnished the cis alcohol **28** with complete stereocontrol (method 8). Diphenyl phosphorazidate displacement of the alcohol **28** yielded the trans azide **29**. Hydrogenation of **29** supplied the trans amine **30**. Acylation of **31** provided trans amides **4**−**7**.

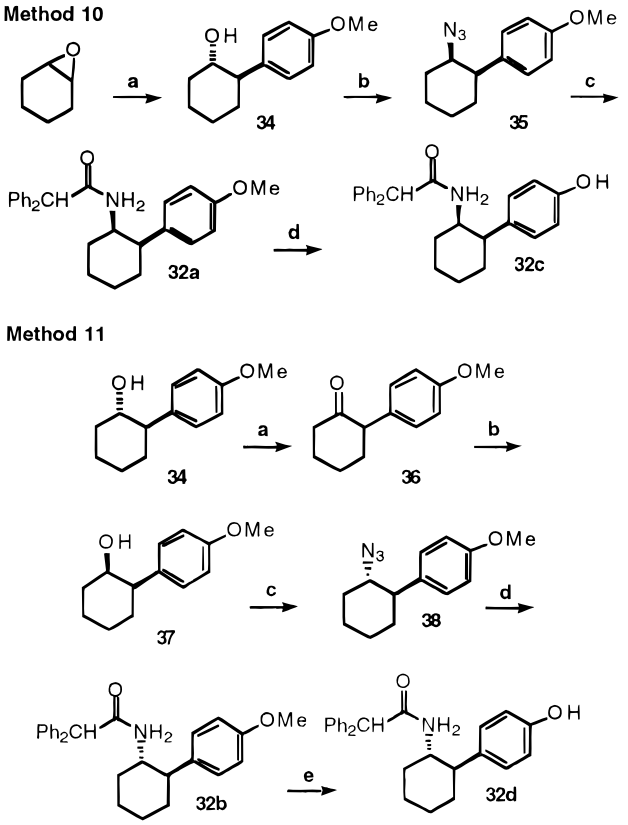
Scheme 4. Preparation of **31a**−**c**[a]



[a] (1) NH_2OH·HCl, NaOAc, MeOH, H_2O, (2) H_2, Pd/C, (3) $Ph_2CHCOCl$, Et_3N; (b) (1) BBr_3, CH_2Cl_2, (2) $NaHCO_3$ (saturated), MeOH.

The tetrahydronaphthyl and cyclohexyl derivatives **31** and **32** were prepared to ascertain whether both aryl rings A and C of **5** are required for ACAT inhibition (Schemes 4 and 5). Conversion of **33** to the corresponding oxime followed by hydrogenation and acylation provided compounds **31a**,**b** (method 9). Boron tribromide demethylation of **31b** furnished the phenol **31c**.

Scheme 5. Preparation of **32a**−**d**[a]



[a] Method 10: (a) *p*-MeOPhLi, BF_3Et_2O, THF; (b) DEAD, Ph_3P, $(PhO)_2P(O)N_3$; (c) (1) H_2, 10% Pd/C, (2) $Ph_2CHCOCl$, Et_3N; (d) (1) BBr_3, CH_2Cl_2; (2) $NaHCO_3$ (saturated), MeOH. Method 11: (a) DCC, DMSO, pyridine, TFA, CH_2Cl_2; (b) (1) DiBAH, THF, (2) $Na_2SO_4(H_2O)_{10}$; (c) DEAD, Ph_3P, $(PHO)_2P(O)N_3$; (d) (1) H_2, Pd/C, (2) $Ph_2CHCOCl$, Et_3N; (e) (1) BBr_3, CH_2Cl_2, (2) $NaHCO_3$ (saturated) MeOH.

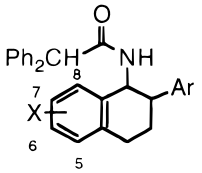
The cis stereochemistry of **32a**,**c** was established by Lewis acid-promoted ring opening of cyclohexene oxide with a suitably substituted aryllithium reagent to give trans alcohol **34** (method 10).[12] Azide displacement of the alcohol **34** provided the cis azide **35**. Hydrogenation and acylation of **35** gave **32a**. Subsequent demethylation gave **32c**.

The trans stereochemistry of **32b**,**d** was fixed as shown in method 11. Oxidation of alcohol **34** to the ketone **36** and subsequent diisobutylaluminum hydride reduction gave a 1:1 mixture of cis:trans alcohols which were separable by silica gel chromatography to give pure cis alcohol **37**. Previously we had achieved complete stereocontrol in the reduction of 2-aryltetralones under these same conditions (Scheme 3). Azide displacement with inversion of the secondary alcohol of **32** provided the trans azide **38**. Reduction and acylation of the resulting amine furnished **32b**. Boron tribromide demethylation afforded **32d**. Acyclic amides **1a**−**j** which were required for comparison with the conformationally restricted series **4**−**7** were prepared as previously described.[2]

Biology

ACAT inhibition was determined *in vitro* with rat hepatic microsomes, and *in vivo* activity was assessed in cholesterol-fed hamsters as previously reported.[2,3] Our earlier studies found that while a variety of functionalized amides **1** inhibited ACAT *in vitro*, only

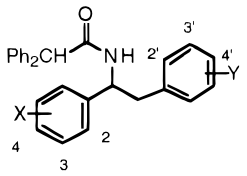
Table 1. ACAT Inhibition of Conformationally Restricted Analogs **5**



compd	X	Ar	inhib at 10 μM (%), cis/trans	IC_{50} (μM), cis/trans	LCE[a] rdn at 50 mpk (%), cis/trans
5a	H	2-$PhOCH_3$	55/53	−/−	−/0
5b	H	2-PhOH	75/71	2.7/4.0	−/0
5c	H	3-$PhOCH_3$	89/75	1.8/1.4	0/0
5d	H	3-PhOH	77/98	1.8/0.7	0/0
5e	H	4-$PhOCH_3$	13/51	−/−	0/0
5f	H	4-PhOH	91/93	0.35/0.7	16/58
5g	H	4-$PhNH_2$	−/91	−/0.7	−/57
5h	H	4-pyridyl	−/94	−/0.9	−/39
5i	5-OCH_3	Ph	12/41	−/−	−/−
5j	5-OH	Ph	80/61	1.4/−	0/0
5k	6-OCH_3	Ph	44/3	−/−	−/−
5l	6-OH	Ph	87/92	0.9/0.9	45/0
5m	7-OCH_3	Ph	25/28	−/−	−/−
5n	7-OH	Ph	84/94	2.4/1.3	38/78
5o	8-OH	Ph	−/68	−/−	−/20
5p	7-OCH_3	4-$PhOCH_3$	−/65	−/−	−/0
5q	7-OH	4-PhOH	88/98	3.5/0.4	0/97

[a] LCE: liver cholesterol esters (hamster).

Table 2. ACAT Inhibition of Acyclic Compounds **1**



compd	X	Ar	inhib at 10 μM (%)	IC_{50} (μM)	LCE[a] rdn at 50 mpk (%)
1a	H	4-OCH_3	92	1.6	65
1b	4-OCH_3	H	88	1.5	69
1c	3-OCH_3	H		1.5	0
1d	3-OCH_3	4-OCH_3		2.4	0
1e	4-OCH_3	4-OCH_3	40		32
1f	H	4-OH	92	0.8	0
1g	4-OH	H	95	1.0	69
1h	3-OH	H	88		19
1i	3-OH	4-OH			0
1j	4-OH	4-OH	97		40

[a] LCE: liver cholesterol esters (hamster).

those compounds where the amide moiety was diphenylacetamide (R = Ph_2CH) and at least one of the aryl rings A or C was appropriately substituted with polar functionality were active *in vivo*. These observations were found to carry over to the conformationally restricted series **4**−**7** as well. Our studies of the ACAT inhibition of conformationally restricted analogs of **1** commenced with diphenylacetamides **5** where Y = $(CH_2)_2$, hereafter referred to as the (6,6) series (Table 1). *In vitro* ACAT activity was found to be more sensitive to the type and positioning of polar substituents in the (6,6) series than in the acyclic series. Conformationally restricted analogs **5e**,**k** substituted with methoxy groups at sites determined to be optimal for ACAT inhibition in the acyclic series were found to be less active *in vitro* than their acyclic counterparts **1a**,**b** (Table 2). None of the methoxy-substituted conformationally restricted analogs were active *in vivo*. *In vivo* activity was achieved by

Table 3. Effect of Aryl Rings A and C on ACAT Activity

Cmpd	X	Stereo	% Inhibn. (10 μM)	IC_{50} (μM)	% LCE Rdn[a] (50 mpk)
31a	H	--	37	--	--
31b	OMe	--	63	--	0
31c	OH	--	51	--	--
32a	OMe	cis	77	3.0	+20
32b	OMe	trans	100	0.1	0
32c	OH	cis	80	3.0	0
32d	OH	trans	94	0.6	0

[a] LCE: liver cholesterol esters (hamster).

substitution of the aryl rings with other polar functionalities (OH, NH_2, and pyridyl). The preferred sites of hydroxyl substitution in the conformationally restricted (6,6) series for both *in vivo* and *in vitro* inhibition were determined to be at the 4- and 7-positions as illustrated by compounds **5f**,**m**. These results were somewhat suprising since the corresponding acyclic phenols **1f**,**h** were essentially devoid of *in vivo* activity. To our satisfaction, placement of hydroxyl groups at both the 4- and 7-positions provided compound **5q**, the most active compound identified in the (6,6) series ($ED_{50} = 7$ mg/kg/day). The corresponding diphenolic acyclic compound **1i** was not active *in vivo*.

The results of a study to determine whether both aryl groups A and C of **5** are necessary for ACAT activity are presented in Table 3. Although the tetrahydronaphthyl (**31**) and cyclohexyl (**32**) derivatives were found to have modest to excellent activity *in vitro*, none was active *in vivo*. When the B ring is a 6-membered carbocycle, both aryl rings A and C appear to be required for *in vivo* activity.

Encouraged by our findings in the (6,6) series, we next directed our efforts to the modification of the B ring by ring contraction ((6,5) series), ring expansion ((6,7) series), and the addition of heteroatoms. As in the (6,6) series, both methoxy and hydroxy analogs were active *in vitro*, but only hydroxy-substituted compounds were active *in vivo*. Comparison of the ACAT activity of a representative number of B ring-modified diphenylacetamides **4**−**7** is presented in Table 4. Varying the size of the B ring has little effect on *in vitro* activity but a profound effect on the *in vivo* activity. The trans carbocyclic analogs **4**−**6** have similar *in vivo* activity, but the *in vivo* activity of the corresponding cis compounds is highly dependent on the size of the B ring. 2D COSY and NOESY NMR studies were employed to determine the solution structures of the compounds in Table 4. These studies suggest that the amide moiety is pseudoequatorially oriented in compounds that have significant *in vivo* activity. Requirements for the orientation of the C ring are less stringent. Both pseudoaxial and pseudoequatorial alignments seem to be permitted, but the pseudoaxial orientation is preferred.

We postulated that the incorporation of heteroatoms into the B ring of the (6,6) series may alter the alignment of the amide and C ring to orientations similar to those observed in the potent ACAT inhibitor

Table 4. Comparison of (6,5), (6,6), and (6,7) Series

compd	X	stereo	orientation[a] amide	orientation[a] aryl	ACAT inhib at 10 μM (%)	IC_{50} (μM)	LCE[b] rdn at 50 mpk (%)
4	CH_2	cis	pe	pa	99	0.1	91
		trans	pe	pe	99	0.23	52
5f	$(CH_2)_2$	cis	pa	pe	91	0.35	16
		trans	pe	pe	93	0.7	58
6	$(CH_2)_3$	cis	pa	pe	75		0
		trans	pe	pe	96	0.3	61
7	OCH_2	cis	pe	pa	94	2.7	0
		trans	pe	pe	95	1.4	0

[a] Pe = pseudoequatorial, pa = pseudoaxial. [b] LCE: liver cholesterol esters (hamster).

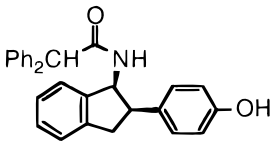
4 (cis isomer). The benzopyrans **7** were prepared to test this theory, and their structures were assigned by 2D COSY and NOESY NMR (Table 4). We were pleased to find that the cis benzopyran **7** does indeed have a pseudoequatorial amide and pseudoaxial C ring as in cis **4**. Although both benzopyrans **7** were active *in vitro*, neither was active *in vivo*. The observed differences in the *in vivo* activity of these compounds may be due to differences in metabolism or drug delivery. Throughout this study we have observed that *in vivo* activity in the conformationally restricted series is highly dependent upon both the site and type of polar substitution.

The most active compound of the (6,5) series, cis **4,** was resolved on a small scale by chiral HPLC (Chiracel OD column) and a preparative scale by fractional recrystallization of the di-*p*-toluoyl tartrate salt of the corresponding amine (method 12, Experimental Section). Enantiomeric purity of **4a**,**b** was determined by chiral HPLC comparisons with the racemate cis **4**. Virtually all of the ACAT activity was found to reside in enantiomer **4a** ($ED_{50} = 0.72$ mg/kg/day, Table 5).

Conclusion

A series of conformationally restricted analogs of previously reported acyclic amides **1** were evaluated as ACAT inhibitors. In both series *in vitro* activity was only slightly affected by variation of the amide functionality or substitution on the A and C rings.

Table 5. ACAT Inhibition of Enantiomers of Cis **4**



compd	IC_{50} (μM)	LCE[a] rdn (%) at 5 mg/kg/day	LCE[a] rdn (%) at 1 mg/kg/day
(±)-**4**	0.10	−63	−27
(+)-**4a**	0.04	−88	−73
(−)-**4b**	13.0	0	0

[a] LCE: liver cholesterol esters (hamster).

Additionally, in the conformationally restricted series, orientation of the amide and C ring, as well as deletion of either the A or C ring, had insignificant effects on the *in vitro* activity. However, in both series only diphenylacetamides where at least one of the aryl rings A or C is appropriately substituted with polar functionality are potent inhibitors *in vivo*. *In vivo* activity in the conformationally restricted series was found to be more sensitive to the site and type of polar substitution than was the acyclic series. NMR studies of the conformationally restricted series determined that a pseudoequatorially oriented amide moiety is necessary for *in vivo* activity in compounds with 5-, 6-, and 7-membered B rings. Requirements for the alignment of the C ring are less stringent. Both pseudoaxial and pseudoequatorial orientations are allowed, but pseudoaxial is preferred. Additionally, in the conformationally restricted series, both A and C rings were found to be required for *in vivo* activity.

Consideration and combination of the above observations led to the design of *cis*-*N*-[2-(4-hydroxyphenyl)-indan-1-yl]diphenylacetamide (**4**), a potent inhibitor both *in vitro* and *in vivo*. All of the *in vivo* activity of cis **4** was found to reside in one enantiomer, **4a** (IC_{50} = 0.04 μm in an *in vitro* rat hepatic microsomal assay, ED_{50} = 0.72 mg/kg/day in cholesterol-fed hamsters), the most potent compound identified by this study. Thus, preparation of conformationally restricted analogs of **1** has resulted in an increase in *in vivo* potency and has provided insight into the structural features required for *in vivo* activity.

Experimental Section

Reagents were used as received unless stated otherwise. Anhydrous solvents were purchased from Aldrich Chemical Co. Melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were taken on Varian 200, 300, 400, and 500 spectrometers and are reported in ppm downfield from internal tetramethylsilane. Elemental analyses were carried out on a Leemann Labs CE440 elemental analyzer or a Fissions EA 1108 CHNS instrument. IR spectra were obtained on a Perkin Elmer 1320 or Nicolet MA-1 FT infrared spectrophotometer. TLC was performed on Merck silica gel plates (60F F_{254}, 250 μm) and are reported as R_f (solvent system used to develop plate), method of visualization (UV, Ce stain (dipping TLC plate into a mixture of $CeSO_4$ (4 g), concentrated H_2SO_4 (10 mL), and H_2 (190 mL) and heating on a hot plate), or I_2 (TLC plate shaken with I_2-impregnated silica gel)). Chromatography was performed on Selecto Scientific 40 μm flash silica gel (32−63).

Biological Methods. Acyl CoA:cholesterol *o*-acyltransferase inhibition was determined *in vitro* with rat hepatic microsomes, and *in vivo* activity was assessed in cholesterol-fed hamsters as previously reported.[2,3]

Chemical Methods: Preparation of Acyclic Compounds 1. Preparation and physical data for acyclic compounds **1a**−**j** were previously reported.[2]

Preparation of 2-Aryl Ketones 8−11. Method 1: 2-Phenyl-6-methoxytetralone (9a). A 1 L round bottom flask was flamed-dried and cooled to room temperature under nitrogen. The enol acetate of 6-methoxytetralone (**13**)[13] (13.02 g, 60 mmol), tri-*n*-butyltin methoxide (17 mL, 60 mmol), palladium acetate (0.134 g, 60 mmol), tri-*o*-tolylphospine (0.365 g, 1.2 mmol), bromobenzene (5.2 mL, 50 mmol), and anhydrous toluene (200 mL) were added, and the mixture was heated to 100 °C overnight.[4] The mixture was cooled to room temperature, transferred to an Erlenmeyer flask, diluted with 5 vol of ethyl acetate (1500 mL), and treated with aqueous KF (2.5 M, 250 mL). The mixture was rapidly stirred overnight and vacuum filtered. The filtrate was transferred to a separatory funnel, washed with water and brine, dried over sodium sulfate, and concentrated onto silica gel. The resulting free flowing powder was loaded onto a chromatography column prepacked with silica gel and 15% EtOAc/hexane. Elution with 15−50% EtOAc/hexane gave an oil which was rechromatographed with 100% CH_2Cl_2. The resulting product was further purified by recrystallization from EtOAc to provide 8.3 g (49%) of the title compound. ^{1}H NMR (200 MHz, $CDCl_3$): 8.09 (1H, d, J = 8.8 Hz, C^8-*H*), 7.28 (5H, m, Ar), 6.87 (1H, dd, J = 2.6, 8.8 Hz, Ar), 6.73 (1H, d, J = 2.6 Hz, Ar), 3.88 (3H, s, OCH_3), 3.77 (1H, t, J = 7.4 Hz, C(O)C*H*), 3.03 (2H, m), 2.41 (2H, m). MS (CI): 253 (M^+, 100). HRMS (EI): $C_{17}H_{16}O_2$, calcd, 252.1150; found, 252.1149. IR (KBr): 3059, 3032, 2937, 2914, 2870, 1673, 1598, 1495, 1340, 1266, 1248, 1230, 1101, 1020, 856, 701 cm^{-1}. CHN: calcd for $C_{17}H_{16}O_2$ C = 80.93, H = 6.39; found C = 81.01, H = 6.50. Mp: 116−117 °C. TLC: R_f = 0.30 (100% CH_2Cl_2), UV, Ce.

The following compounds were prepared in similar fashion.

2-Phenyl-5-methoxytetralone (9b). ^{1}H NMR (400 MHz, $CDCl_3$): 7.66 (1H, d, J = 9.0 Hz, C^8-*H*), 7.33 (2H, m, Ar), 7.26 (2H, m, Ar), 7.18 (2H, m, Ar), 6.78 (1H, d, J = 8.9 Hz, Ar), 3.87 (3H, s, OCH_3), 3.81 (1H, m, C(O)C*H*), 3.16 (1H, dt, J = 4.9, 12.8 Hz), 3.0 (1H, m), 2.42 (2H, m). MS (EI): 252 (M^+, 100), 161 (61), 148 (62), 120 (29). CHN: calcd for $C_{17}H_{16}O_2$ C = 80.93, H = 6.39; found C = 80.79, H = 6.45. Mp: 82−83 °C. TLC: R_f = 0.33 (20% EtOAc/hexane), UV, Ce. Purification: SiO_2 chromatography (10% EtOAc/hexane), further purified by recrystallization from EtOAc/hexane. Yield: 54%.

2-Phenyl-7-methoxytetralone (9c). ^{1}H NMR (300 MHz, $CDCl_3$): 7.60 (1H, d, J = 2.8 Hz, C^8-*H*), 7.21 (7H, m, Ar), 3.86 (3H, s, OCH_3), 3.80 (1H, t, J = 8.2 Hz, C(O)C*H*), 3.01 (2H, m), 2.43 (2H, m). MS (EI): 252 (M^+, 100), 161 (54), 150 (39), 120 (53). CHN: calcd for $C_{17}H_{16}O_2$ C = 80.93, H = 6.39; found C = 80.88, H = 6.34. Mp: 74−75 °C. TLC: R_f = 0.35 (15% EtOAc/hexane), UV, Ce. Purification: recrystallization from EtOAc. Yield: 49%.

2-(4-Methoxyphenyl)-7-methoxytetralone (9d). ^{1}H NMR (300 MHz, $CDCl_3$): 7.50 (1H, d, J = 2.8 Hz, C^8-*H*), 7.03 (4H, m, Ar), 6.81 (2H, d, J = 8.7 Hz, Ar), 3.77 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 3.66 (1H, t, J = 8.0 Hz, C(O)C*H*), 2.92 (2H, m), 2.31 (2H, m). MS (CI): 283 (M^+, 100). CHN: calcd for $C_{18}H_{18}O_3$ C = 76.57, H = 6.43; found C = 76.80, H = 6.39. Mp: 92−93 °C. TLC: R_f = 0.21 (15% EtOAc/hexane) UV, Ce. Purification: recrystallized from EtOAc. Yield 50%.

2-(4-Methoxyphenyl)benzosuberone (10). ^{1}H NMR (200 MHz, $CDCl_3$): 7.62 (1H, dd, J = 1.6, 7.6 Hz, Ar), 7.33 (5H, m, Ar), 6.91 (2H, m, Ar), 4.04 (1H, dd, J = 10.4, 6.0 Hz, CH_2CHPh), 3.81 (3H, s, OCH_3), 3.07 (2H, m), 2.16 (3H, m), 1.85 (1H, m). MS (CI): 267 (M^+,100). HRMS (EI): calcd for $C_{18}H_{18}O_2$, 266.1307; found, 266.1293. IR (neat): 3061, 3001, 2935 (s), 2861, 2834, 1734, 1684 (s), 1645, 1605, 1512 (s), 1452, 1396, 1358, 1300, 1248 (s), 1207, 1180, 1108, 1034, 980, 958, 825, 800, 766, 737, 673, 649 cm^{-1}. TLC: R_f = 0.41 (15% EtOAc/hexane), Ce stain. Purification: SiO_2 chromatography (10% EtOAc/hexane). Yield: 45%, clear oil.

2-(4′-Aminophenyl)tetralone (9e). 4-Bromoaniline (12.3 g, 71.2 mmol) was added to a suspension of *p*-anisaldehyde (8.66 mL, 71.2 mmol) and anhydrous magnesium sulfate (17.1 g, 142.4 mmol) in ether (150 mL). The mixture was stirred overnight and vacuum filtered. The filtrate was concentrated

to 21.8 g (105%) of a light yellow solid. NMR confirmed consumption of the aldehyde and the formation of (4-bromoanilino)-4′-methoxybenzylidene which was used without further purification.

A mixture of the enol acetate of 1-tetralone **13** (19.2 g, 102 mmol), (4-bromoanilino)-4′-methoxybenzylidene (21.8 g, 75.2 mmol), bis(tri-*o*-tolylphosphine)palladium chloride (0.59 g, 0.75 mmol), tributyltin methoxide (29.3 mL, 102 mmol), and toluene (300 mL) was heated to 100 °C overnight (~18 h).[4] The reaction mixture was cooled to room temperature, diluted with 5 vol of EtOAc (1500 mL), and treated with a solution of KF (150 mL, 2.5 M in water). The two-phase mixture was rapidly stirred overnight. The mixture was vacuum filtered, and the filter cake was well washed with EtOAc. The filtrate was concentrated onto silica gel (~2 g of SiO_2/mmol of enol acetate). The resulting free flowing powder was poured onto a chromatography column prepacked with silica gel and 50% EtOAc/hexane. Elution with the 50% EtOAc/hexane provided 4.04 g of the title compound and 4.64 g of the imine of the title compound.

The imine (4.26 g, 12 mmol) was dissolved in ethyl acetate (150 mL). Water (3.24 mL, 180 mmol) and p-toluenesolfonic acid (3.42 g, 18 mmol) were added.[14] A white precipitate formed immediately. After ~2 h the precipitate was collected *via* vacuum filtration and washed well with ethyl acetate. The filter cake was transferred to a Erlenmeyer flask and partitioned between ethyl acetate (100 mL) and saturated $NaHCO_3$ (100 mL). When all of the solid had dissolved, the mixture was transferred to a separatory funnel, washed with saturated $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated to give 2.93 g of 2-(4-aminophenyl)tetralone (**9e**). The overall yield was 6.96 g (39%). ^{1}H NMR (200 MHz, $CDCl_3$): 8.09 (1H, d, J = 7.2 Hz, Ar), 7.49 (1H, app dt, J = 1.6, 7.4 Hz, Ar), 7.29 (2H, m, Ar), 6.97 (2H, d, J = 8.4 Hz, Ar), 6.66 (2H, d, J = 8.4 Hz, Ar), 3.70 (1H, t, J = 7.8 Hz, C(O)C*H*CH_2), 3.06 (2H, m, PhCH_2CH_2), 2.38 (2H, m, CH_2CH_2CH_2). IR (neat): 3448, 3360, 3224, 3020, 2932, 2863, 1729, 1678, 1615, 1453, 1432, 1263, 1185, 1028, 824 cm^{-1}. TLC: R_f = 0.24 (50% EtOAc/hexane), Ce stain.

The ketone was found to be somewhat unstable and was used immediately without further purification for the preparation of *trans*-[2-(4-aminophenyl)-1,2,3,4-tetrahydronaphthyl]-diphenylacetamide (**5g**) as described in method 8.

Method 2, Procedure c: 2-(4′-Methoxyphenyl)tetralone (9f). A dry 500 mL round bottom flask containing 2-(4-methoxyphenyl)-4-phenylbutyric acid **(14)**[15] (27.86 g, 103.1 mmol) was purged with nitrogen. The reaction flask was equipped with an oven-dried condensor, and the apparatus was allowed to cool under a stream of nitrogen. Anhydrous benzene (300 mL) was added *via* cannula, and the mixture was cooled to 0 °C. Oxalyl chloride (44.97 mL, 515.3 mmol) was slowly added. The nitrogen inlet was replaced with a drierite (calcium sulfate)-filled drying tube. The cooling bath was removed, and the reaction mixture was allowed to stir at room temperature for 1 h. The reaction mixture was then heated to reflux for 1 h, and the condensor was replaced with a short path distillation head. The solvent and excess oxalyl chloride were removed by distillation. The pot residue was dried on a vacuum pump for 2 h, purged with nitrogen, dissolved in anhydrous methylene chloride (600 mL), and cooled to 0 °C. Anhydrous aluminum chloride (15.12 g, 113.41 mmol) was added. TLC (20% EtOAc/hexane, Ce stain) indicated that the reaction was complete in <10 min. The reaction mixture was poured into an Erlenmeyer flask containing rapidly stirring 1 M HCl (~1 L). The resulting solution was transferred to a separatory funnel and extracted with methylene chloride. The organic extracts were combined, washed with water, dried over anhydrous sodium sulfate, and concentrated to give 28 g of a yellow solid. Recrystallization from EtOAc/hexane provided 18.05 g (69%) of 2-(4-methoxyphenyl)tetralone (**9f**) as white crystals. ^{1}H NMR (200 MHz, $CDCl_3$): 8.08 (1H, dd, J = 1.4, 7.8 Hz, Ar), 7.50 (1H, dt, J = 1.6, 7.4 Hz, Ar), 7.31 (2H, m, Ar), 7.12 (2H, d, J = 8.6 Hz, Ar), 6.89 (2H, d, J = 8.6 Hz, Ar), 3.80 (3H, s, OCH_3), 3.75 (1H, t, J = 7.8 Hz, C(O)C*H*CH_2), 2.77 (2H, m, CH_2CH_2CH), 2.41 (2H, m, ArCH_2CH_2). MS (FAB): 252 (M$^+$, 95), 131 (79), 121 (65), 118 (100), 115 (21), 90 (70), 77 (10), 56 (62). HRMS (FAB): calcd for $C_{17}H_{16}O_2$, 252.1150; found, 252.1141. IR ($CDCl_3$): 3065, 3033, 3055, 2941 (m), 2838 (m), 1683 (s), 1610 (m), 1600 (m), 1513 (s), 1455 (m), 1434 (m), 1354, 1309 (m), 1300 (m), 1263 (m), 1247, 1233, 1180 (m) cm^{-1}. CHN: calcd for $C_{17}H_{16}O_2$ C = 80.93, H = 6.39; found C = 81.33, H = 6.74. Mp: 107−107.5 °C, clear cubic crystals. TLC: R_f = 0.14 (10% EtOAc/hexane), UV, Ce stain.

The following compounds were prepared in similar fashion.

2-(3-Methoxyphenyl)tetralone (9g). ^{1}H NMR (300 MHz, $CDCl_3$): 8.12 (1H, d, J = 6.5 Hz, Ar), 7.52 (1H, app t, J = 6.1 Hz, Ar), 7.31 (3H, m, Ar), 6.78 (3H, m, Ar), 3.80 (3H, s, OCH_3), 3.8 (1H, t, J = 7.9 Hz, C*H*Ar), 3.08 (2H, m, CH_2CH_2CH), 2.45 (2H, m, ArCH_2CH_2). MS (EI): 253 (M$^+$, 100), 252 (M$^+$, 56). IR (KBr): 2990, 2940, 1679, 1601, 1491, 1464, 1453, 1426, 1303, 1268, 1244, 1226, 1172, 1033, 790 cm^{-1}. CHN: calcd for $C_{17}H_{16}O_2$ C = 80.93, H = 6.39; found,C = 80.67, H = 6.58. Mp: 86−87 °C. TLC: R_f = 0.40 (20% EtOAc/hexane), UV, Ce stain. Purification: recrystallization from CH_2Cl_2/hexanes. Yield: 90%.

2-(2-Methoxyphenyl)tetralone (9h). ^{1}H NMR (300 MHz, $CDCl_3$): 8.14 (1H, d, J = 6.3 Hz, Ar), 7.52 (1H, app t, J = 7.4 Hz, Ar), 7.34 (4H, m, Ar), 6.95 (2H, m, Ar), 4.08 (1H, dd, J = 12.3, 4.7 Hz, COC*H*Ar), 3.77 (3H, s, OCH_3), 3.06 (2H, m, CH_2CH_2CH), 2.51 (1H, m, ArCH_2CH_2), 2.30 (1H, m, ArCH_2-CH_2). CHN: calcd for $C_{17}H_{16}O_2$ C = 80.93, H = 6.39; found C = 80.68, H = 6.28. HRMS: calcd for $C_{17}H_{16}O_2$, 252.1150; found, 252.1150. MS (CI): 253 (M$^+$, 100), 235 (10), 145 (11). TLC: R_f = 0.40 (20% EtOAc/hexane). Purification: required no further purification. Yield: 95%, oil.

2-(4-Methoxyphenyl)-1-indanone (8). A solution of 40% aqueous KOH (489 g, 8.73 mol, in 863 mL of water) was diluted with 95% ethanol (2.2 L) and added to a room temperature solution of benzaldehyde (489 mL, 4.82 mol) and (4-methoxyphenyl)acetonitrile (598 mL, 4.41 mol) in 95% ethanol (1.5 L). The mixture was stirred for 1.5 h at room temperature. The resulting crystals were collected by suction filtration, washed with water and cold 95% ethanol, and air-dried to provide 999.4 g (96.3%) of 3-phenyl-2-(4-methoxyphenyl)acrylonitrile as white crystals. ^{1}H NMR (200 MHz, $CDCl_3$): 7.9 (2H, d), 7.65 (2H, d), 7.5 (4H, m), 7.0 (2H, d), 3.9 (3H, s). Mp: 92−94 °C.

Sodium borohydride (2.59 g, 68.1 mmol) was slowly added in portions over 10 min to a 60−70 °C suspension of 3-phenyl-2-(4-methoxyphenyl)acrylonitrile (16.0 g, 68.1 mmol) in absolute ethanol (200 mL). The mixture was stirred at 60−70 °C for an additional 2 h before cooling to ambient temperature and quenching the reaction with water. The resulting solution was diluted with water, acidified with concentrated HCl, and extracted with ether. The etheral extracts were combined, washed with water and brine, dried over anhydrous sodium sulfate, and concentrated to give 15.9 g (98.4%) of 3-phenyl-2-(4-methoxyphenyl)propionitrile as a solid which could be used without further purification. Alternately, the product can be isolated by dilution of the crude reaction mixture with several volumes of water and collection of the resulting precipitate by suction filtration (99%). ^{1}H NMR (200 MHz, $CDCl_3$): 7.3 (3H, m), 7.15 (4H, m), 6.9 (2H, d), 3.95 (1H, dd), 3.8 (3H, s), 3.1 (2H, m). MS (EI): 237 (M$^+$, 20), 146 (98), 91 (100). Mp: 66−67 °C.

A solution of KOH (673 g, 12.0 mol) in water (2.1 L) was added to a room temperature solution of 3-phenyl-2-(4-methoxyphenyl)propionitrile (933 g, 3.94 mol) in ethylene glycol (9 L). The resulting solution was refluxed overnight. The reaction mixture was cooled to room temperature, diluted with water, and extracted with ether. The aqueous phase was acidified with concentrated HCl and extracted with ether. The latter etheral extracts were combined, washed with brine, dried over anhydrous sodium sulfate, and concentrated. The resulting residue was dissolved in methylene chloride and diluted with hexanes to induce crystallization. The crystals were collected by suction filtration, washed with hexane/ethyl acetate (5/1) followed by hexane, and air-dried to provide 944 g (93.7%) of 3-phenyl-2-(4-methoxyphenyl)propionic acid. Mp: 107−109 °C. ^{1}H NMR (200 MHz, $CDCl_3$): 7.23 (4H, m),

7.10 (2H, m), 6.84 (2H, d), 3.81 (1H, m), 3.78 (3H, s), 3.38 (1H, dd), 3.01 (1H, dd). MS (EI): 256 (M^+, 30), 165 (100), 137 (38), 91 (40).

Oxalyl chloride (55 mL, 0.63 mol) was added *via* syringe to a solution of 3-phenyl-2-(4-methoxyphenyl)propionic acid **14** (64.1 g, 0.25 mol) and dimethylformamide (3 drops) in dichloromethane (400 mL). The mixture was stirred overnight at room temperature, evaporated, diluted with dichloromethane, and evaporated again. The residue was dissolved in dichloromethane (100 mL) and added slowly over 5 h *via* dropping funnel to a 0 °C suspension of aluminum chloride (67.0 g, 0.50 mol) in dichloromethane (800 mL). Upon completion of addition, the mixture was stirred for an additional 15 min at 0 °C, poured into water, and extracted with ether. The ether extracts were combined, washed with dilute potassium carbonate solution and brine, dried over anhydrous sodium sulfate, and concentrated. The resulting residue was recrystallized from ethanol (3 mL/g) to give 51.3 g (86%) of 2-(4-methoxyphenyl)-1-indanone (**8**). Mp: 83−85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): 7.80 (1H, d), 7.63 (1H, t), 7.53 (1H, d), 7.51 (1H, d), 7.41 (1H, d), 7.11 (2H,d), 6.86 (2H, d), 3.84 (1H, m), 3.76 (3H, s), 3.66 (1H, m), 3.23 (1H,dd). MS (EI): 238 (M^+, 100), 178 (20), 165 (30). CHN: calcd for $C_{16}H_{14}O_2$ C = 80.65, H = 5.92; found C = 80.62, H = 5.81.

Method 2, Procedure d: 5-Bromo-8-methoxy-2-phenyltetralone (9i). A solution of bromine (3.0 g, 18.8 mmol) in CH_3Cl (25 mL) was dropwise added over 20 min to a solution of 2-phenyl-4-(3-methoxyphenyl)butyric acid (9.1 g, 33.6 mmol) in $CHCl_3$ (200 mL) at 0 °C.[16] The resulting mixture was stirred for 1.5 h. TLC (5% MeOH/CH_2Cl_2) indicated consumption of starting material. The solution was diluted with Et_2O, transferred to a separatory funnel, repeatedly washed with water, dried over Na_2SO_4, filtered, and concentrated to an oil. Chromatography on SiO_2 (30% EtOAc/hexane) was unsuccessful at removing unreacted starting material. Titraturation with hexane did remove unreacted starting material and afforded 2-phenyl-4-(2-bromo-3-methoxyphenyl)butyric acid (**14**) (10.4 g, 90%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): 7.28 (6H, m, Ar), 6.63 (1H, d, J = 3 Hz, Ar), 6.53 (1H, dd, *J* = 3.0, 8.9 Hz, Ar), 3.68 (3H, s, OC*H*$_3$), 3.54 (1H, t, *J* = 7.6 Hz, C*H*CO_2H), 2.59 (2H, m), 2.33 (1H, m), 2.05 (1H, m). MS (CI): 349 (M^+, 100), 331 (11), 305 (62). CHN: calcd for $C_{17}H_{17}O_3Br$ C = 58.46, H = 4.91; found C = 58.49, H = 4.89. Mp: 107−108 °C. TLC: R_f = 0.37 (5% MeOH/CH_2Cl_2), UV, Ce stain.

A 1/10 solution (90 g) of freshly prepared CH_3SO_3H/P_2O_5 was added to a room temperature solution of 2-phenyl-4-(2-bromo-3-methoxyphenyl)butyric acid (**14**) (7.83 g, 20.4 mmol) in $CHCl_3$ (300 mL).[5] The mixture was stirred at room temperature for 20 min and then refluxed for 1.5 h. The reaction mixture was cooled, poured into water, transferred to a separatory funnel, and extracted with $CHCl_3$. The extracts were combined, washed with $NaHCO_3$ (saturated), water, and brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on SiO_2 (30% EtOAc/hexane) to afford 5 g of a beige solid. Recrystallization from 30% EtOAc/hexane gave 5-bromo-8-methoxy-2-phenyltetralone (**9i**) (45%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 7.66 (1H, d, *J* = 9 Hz, Ar), 7.33 (2H, m, Ar), 7.27 (2H, m, Ar), 7.19 (2H, m, Ar), 6.79 (1H, d, *J* = 9.0 Hz, Ar), 3.87 (3H, s, OC*H*$_3$), 3.81 (1H, m), 3.17 (1H, dt, *J* = 4.9, 17.7 Hz), 3.00 (1H, m), 2.43 (2H, m). MS (CI): 333 (M^{2+}, 100), 331 (M^+, 97). CHN: calcd for $C_{17}H_{15}O_2Br$ C = 61.65, H = 4.57; found C = 61.76, H = 4.54. Mp: 101−102 °C. TLC: R_f = 0.47 (50% EtOAc/hexane), UV, Ce stain.

Method 3: 2-(4-Pyridyl)tetralone (9j). $NaOH_{aq}$ (50%, 30 mL) was added to a mixture of phenethyl bromide (13.23 mL, 97.0 mmol), 4-pyridylacetonitrile hydrochloride salt (15.0 g, 97 mmol), and triethylbenzylammonium chloride (0.34 g, 1.49 mmol). An exothermic reaction ensued, and the resulting mixture was rapidly stirred overnight. TLC indicated a mixture of starting nitrile and mono- and dialkylated products. The mixture was partitioned between ethyl acetate and water, transferred to a separatory funnel, and extracted with ethyl acetate. The organic extracts were combined, washed with water and brine, dried over sodium sulfate, and concentrated to a dark oil. The oil was vacuum distilled. The fractions distilling at 160−200 °C were combined to give 13.32 g (62%) of 2-(4-pyridyl)-4-phenylbutyronitrile (**15**) as a clear oil. ^{1}H NMR (200 MHz, $CDCl_3$): 8.64 (2H, dd, *J* = 1.6, 4.4 Hz, pyr), 7.28 (7H, m, pyr, Ph), 3.75 (1H, dd, *J* = 6.2, 9.0 Hz, CH_2CHCN), 2.85 (2H, t, *J* = 8.6 Hz, $PhCH_2CH_2$), 2.22 (2H, m, CH_2CH_2CH). MS (EI): 222 (M^+, 29), 131 (69), 118 (17), 105 (65), 92 (100), 77 (25), 65 (22), 51 (17). HRMS (EI): calcd for $C_{15}H_{14}N_2$, 222.1157; found, 222.1135. IR (neat): 3061, 3.28, 2934, 2862, 2243, 2169, 1649, 1597 (s), 1563, 1539, 1496, 1454, 1415, 1353, 1314, 1221, 1186, 1076, 1030, 993, 913, 818, 782, 749, 701 (s), 669, 641, 621, 601. CHN: calcd for $C_{15}H_{14}N_2$ C = 81.05, H = 6.35, N = 12.60; found C = 80.71, H = 6.26, N = 12.55. TLC: R_f = 0.22 (50% EtOAc/hexane), $KMnO_4$, UV.

4-Phenyl-2-(4′-pyridyl)butyronitrile (**15**) (0.61 g, 2.68 mmol) was placed in a 100 mL round bottom flask which had been flame-dried and cooled under a stream of nitrogen. Sodium chloride (3.13 g, 53.6 mmol) and aluminum chloride (14.29 g, 107.2 mmol) were added, and the flask was heated to 180 °C in an oil bath. The mixture became molten and was easily stirred. After 30 min a small aliquot was removed, dissolved in water, and made basic with 15% $NaOH_{aq}$. A small amount of ether was added. TLC analysis (100% EtOAc) indicated complete consumption of starting material and formation of one new product. The reaction mixture was cooled to 0 °C and poured cautiously into water; 15% $NaOH_{aq}$ was added until the reaction became clear and the solution was basic. The solution was transferred to a separatory funnel and extracted with ether. The ether extracts were combined, washed with water and brine, dried over sodium sulfate, and concentrated onto silica gel. The resulting free flowing powder was loaded onto a chromatography column prepacked with silica gel and 100% EtOAc. Elution with the same solvent provided 0.45 g (75%) of 2-(4-pyridyl)tetralone as a yellow solid. Recrystallization from benzene/hexane afforded slightly yellow needles. ^{1}H NMR (200 MHz, $CDCl_3$): 8.57 (2H, dd, *J* = 1.5, 4.5 Hz, pyridine-H), 8.08 (1H, dd, *J* = 1.5, 7.9 Hz, C^8-H), 7.53 (1H, dt, *J* = 1.5, 7.5 Hz, Ar), 7.33 (2H, m, Ar), 7.14 (2H, dd, *J* = 1.7, 4.5 Hz, pyridine-H), 3.79 (1H, t, *J* = 8.2 Hz, C(O)C*H*), 3.09 (2H, m), 2.44 (2H, m). MS (EI): 223 (M^+, 63), 194 (17), 131 (12), 118 (100), 93 (20), 90 (78), 51 (10). IR ($CDCl_3$): 3073, 3031, 2941, 2869, 1684, 1601, 1455, 1434, 1417, 1307, 1226 cm^{-1}. CHN: calcd for $C_{15}H_{13}NO$ C = 80.69, H = 5.87 N = 6.27; found C = 80.84, H = 5.91, N = 6.25. Mp: 87−90 °C. TLC: R_f = 0.13 (75% EtOAC/hexanes), UV.

Method 4: 2-(4-Methoxyphenyl)chromanone (11). Magnesium turnings (31 g, 1.2 mol) were stirred with an overhead stirrer for 48 h under nitrogen.[6] THF (150 mL) was added, and the dark suspension was cooled to 0 °C. 4-Methoxybenzyl chloride (52.2 mL, 0.38 mol) in THF (150 mL) was added dropwise *via* cannula over 20 min. The reaction mixture was stirred at 0 °C for 2 h before being transferred *via* cannula to a room temperature solution of 2-hydroxybenzonitrile (15 g, 0.13 mol) in THF (150 mL). The mixture was allowed to stir overnight. TLC (50% EtOAc/hex) indicated consumption of starting material. The mixture was cooled to 0 °C and the reaction quenched by the addition of water (50 mL) followed by concentrated HCl (100 mL). The resulting solution was refluxed for 4 h, cooled to room temperature, transferred to a separatory funnel, and diluted with EtOAc. The aqueous layer was discarded. The EtOAc layer was washed with water and brine, dried over anhydrous sodium sulfate, and concentrated to a dark oil. The oil was subjected to silica gel chromatography (10−50% EtOAC/hexanes) to provide a yellow solid. Recrystallization of the solid from 5% ether/hexanes (∼200 mL) afforded 27.9 g (90%) of 2-(4-methoxyphenyl)-2′-hydroxyacetophenone (**16**) as a white solid. MS (EI): 242 (M^+, 19), 121 (100). CHN: calcd for $C_{15}H_{14}O_3$ C = 73.46, H = 5.82; found C = 74.72, H = 6.01. Mp: 79−81 °C.

A solution of 2-(4-methoxyphenyl)-2′-hydroxyacetophenone (**16**) (5.24 g, 21.6 mmol) and dimethylacetamide dimethyl acetal (5.75 mL, 43.3 mmol) in benzene (30 mL) was refluxed for 18 h.[7] TLC indicated consumption of starting material. The solution was cooled to room temperature and concentrated in vacuo. The resulting solid was recrystallized from methanol to afford 4.8 g (88%) of 2-(4-methoxyphenyl)chromenone (**17**)

as white crystals. ^{1}H NMR (300 MHz, $CDCl_3$): 8.25 (1H, dd, J = 1.8, 8.0 Hz), 7.93 (1H, s), 7.61 (1H, m), 7.40 (4H, m), 6.91 (2H, d, J = 8.7 Hz), 3.77 (3H, s). MS (EI): 252 (M^+, 40), 242 (25), 121 (100). CHN: calcd for $C_{16}H_{12}O_3$ C = 76.18, H = 4.80; found C = 76.16, H = 4.69.

Diisobutylaluminum hydride (47.2 mL, 47.2 mmol, 1 M in THF) was slowly added to a −78 °C solution of 2-(4-methoxyphenyl)chromenone (**17**) (4.57 g, 18.1 mmol) in THF (50 mL).[8] The mixture was allowed to warm to room temperature overnight. The mixture was recooled to −78 °C and the reaction quenched by the slow addition of solid sodium sulfate decahydrate. The mixture was allowed to warm slowly to room temperature and vacuum filtered. The filter cake was well washed with ethyl acetate. The filtrate was concentrated to supply 3.86 g (84%) of a white solid. The solid was recrystallized form dichloromethane/methanol to provide 2-(4-methoxyphenyl)chromanone (**11**) as white crystals. ^{1}H NMR (300 MHz, $CDCl_3$): 7.89 (1H, dd, J = 1.7, 7.9 Hz), 7.43 (1H, s), 7.13 (2H, d, J = 8.8 Hz), 6.97 (2H, m), 6.82 (2H, d, J = 8.8 Hz), 4.57 (2H, m), 3.87 (1H, m), 3.72 (3H, s). MS (EI): 254 (M^+, 22), 134 (100), 121 (34). CHN: calcd for $C_{16}H_{14}O_3$ C = 75.58, H = 5.55; found C = 75.46, H = 5.48. Mp: 91−93 °C.

Preparation of Cis Amides 3, Methods 4−7. Method 5: *N*-[*cis*-2-(4-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5e). A mixture of 2-(4′-methoxyphenyl)tetralone (**9f**) (6.22 g, 24.7 mmol), hydroxylamine hydrochloride (5.14 g, 74 mmol), sodium acetate (6.1 g, 74 mmol), water (12 mL), and methanol (45 mL) was refluxed overnight.[9] TLC (15% EtOAc/hexane) indicated consumption of starting material. The reflux condensor was removed, and the temperature of the oil bath was increased. The reaction mixture was concentrated to ca. 50% of its original volume, diluted with water, and cooled to room temperature. A gummy residue separated from the reaction mixture (a number of oximes will crystallize at this point and can be isolated in essentially pure form by simple filtration and washing with water). The residue was partitioned between ethyl acetate and water, transferred to a separatory funnel, and extracted with ethyl acetate. The organic extracts were combined, washed with water and brine, dried over sodium sulfate, and concentrated onto silica gel (∼2 g/mmol of oxime). The resulting free flowing powder was poured onto a chromatography column packed with 15% EtOAc/hexane. Elution with 15% EtOAc/hexane provided 6.11 g (93%) of N-hydroxy-2-(4′-methoxyphenyl)tetralone oxime (**18**) as a white solid. Recrystallization from EtOAc/hexanes afforded 3.87 g of white crystals. ^{1}H NMR (200 MHz, $CDCl_3$): 8.03 (1H, d, J = 7.8 Hz, Ar), 7.26 (2H, m, Ar), 7.12 (3H, m, Ar), 6.81 (2H, d, J = 8.6 Hz, Ar), 4.76 (1H, t, J = 4.3 Hz, ArCH_2CH_2), 3.76 (3H, s, OCH_3), 2.64 (2H, m), 2.06 (2H, m). MS (EI): 267 (M^+, 53), 250 (45), 234 (45), 159 (18), 134 (26), 121 (100), 116 (41), 91 (28), 77 (25). IR (KBr): 3280, 3245, 3194, 3052, 2937, 2911, 2855, 2831, 1609, 1509, 1250, 1180, 1042, 961, 760 cm^{-1}. CHN: calcd for $C_{17}H_{17}NO_2$ C = 76.38, H = 6.41 N = 5.24; found C = 76.59, H = 6.72, N = 5.13. Mp: 124−125 °C. TLC: R_f = 0.15 (15% EtOAc/hexane), Ce stain.

Chlorodiphenylphosphine (3.98 mL, 22.2 mmol) was slowly added to a −78 °C solution of the oxime **18** (5.93 g, 22.2 mmol) and triethylamine (3.1 mL, 22.2 mmol) in methylene chloride (50 mL of each).[4] The reaction mixture was allowed to slowly warm to room temperature. TLC indicated complete consumption of starting material. The solution was diluted with ether and filtered through Celite to remove most of the amine hydrochloride. The filtrate was concentrated in vacuo to a foam. The foam was taken up in benzene, dried over sodium sulfate, and filtered through a cotton plug to remove any remaining amine hydrochloride. The clear yellowish solution was concentrated in vacuo to provide the phosphinylimine **19** as a white foam (11.48 g, ∼115% crude yield), which was used without further purification.

The crude phosphinylimine **19** (10.32 g, 22.9 mmol) was dissolved in dry THF (200 mL) and cooled to −78 °C. Diisobutlyaluminum hydride (68.6 mL, 68.6 mmol, 1 M in THF) was added slowly *via* syringe.[10] TLC (50% EtOAc/hexane) indicated that the reaction was complete in <10 min. The reaction was quenched at −78 °C by the addition of solid sodium sulfate decahydrate, and the mixture was allowed to warm slowly to room temperature The mixture was filtered, and the filter cake was well washed with THF. The filtrate was concentrated in vacuo to a yellowish solid (9.68 g, 93% crude yield). A portion of the solid was recrystallized from benzene/hexane to give the phosphonamide **20** as a fluffy white solid. ^{1}H NMR (300 MHz, $CDCl_3$): 7.76 (3H, m, Ar), 7.55 (2H, m, Ar), 7.44 (2H, m, Ar), 7.35 (3H, m, Ar), 7.23 (3H, m, Ar), 7.10 (1H, d, J = 7.2 Hz, Ar), 7.04 (2H, d, J = 8.7 Hz, Ar), 6.83 (2H, d, J = 8.6 Hz, Ar), 4.57 (1H, dt, J = 5.1, 10.5 Hz, PhCHCH$_2$), 3.81 (3H, s, OCH_3), 3.40 (1H, m), 2.99 (1H, dd, J = 5.7, 11.4 Hz), 2.83 (2H, m), 2.17 (1H, m), 2.04 (1H, m). MS (FAB): 454 (M^+, 100), 236 (55), 218 (88), 201 (93). IR (KBr): 3435, 3198, 3054, 2934, 2833, 1613, 1514, 1436, 1251, 1180, 1125, 1110 cm^{-1}. CHN: calcd for $C_{29}H_{28}NO_2P$ C = 76.80, H = 6.22, N = 3.09; found C = 76.60, H = 6.16, N = 2.89. Mp: 204−204.5 °C. TLC: R_f = 0.20 (50% EtOAc/hexane), Ce stain.

HCl (6 N, 100 mL) was added to a room temperature solution of the crude phosphonamide (8.68 g, 19.1 mmol) in methanol (300 mL). The mixture was stirred overnight. TLC (50% EtOAC/hexane) indicated the absence of starting material. The mixture was concentrated in vacuo. The resulting white residue was pertained between 3 N HCl and ethyl acetate, transferred to a separatory funnel, and extracted with ethyl acetate. The organic extracts were reserved. The aqueous layer was transferred to a Erlenmeyer flask and adjusted to pH ∼9 with Na_2CO_3 (saturated). The resulting solution was transferred to a separatory funnel and extracted with methylene chloride. The methylene chloride extracts were combined, washed with water, dried over sodium sulfate, and concentrated to an amber oil (2.73 g, 56%). TLC indicated that the original ethyl acetate extracts contained some of the desired amine. The extracts were combined, stirred with sodium carbonate (saturated), transferred to a separatory funnel, washed with sodium carbonate (saturated), water, and brine, and concentrated onto silica gel. The resulting free flowing powder was loaded onto a chromatography column packed with silica gel and 50% EtOAc/hexane containing 1% triethylamine. Elution with the same solvent system supplied 1.24 g of the desired *cis*-2-(*p*-methoxyphenyl)-1,2,3,4-tetrahydronaphthylamine (**21**). Total yield for the reaction was 3.97 g (82%) of an amber oil which solidified on standing to a light yellow solid and 71% overall yield from the starting ketone. ^{1}H NMR (300 MHz, $CDCl_3$): 7.41 (1H, m, Ar), 7.25 (5H, m, Ar), 6.99 (2H, d, J = 8.61 Hz, Ar), 4.18 (1H, d, J = 3.66 Hz, NCHCH), 3.89 (3H, s, OCH_3), 3.20 (1H, d, J = 12.8 Hz, ArCH_2), 3.03 (2H, m, ArCH_2CH$_2$), 2.40 (1H, ddd, J = 5.99, 12.5, 24.6 Hz, CH$_2$CHHCH), 2.01 (1H, ddd, J = 2.7, 2.9, 12.9 Hz, CH$_2$-CHHCH), 1.89 (2H, bs, NH$_2$). MS (CI): 254 (M^+, 68), 237 (100), 119 (13). IR (KBr): 2934, 2876, 2835, 1608, 1512, 1245, 1179, 1027, 763 cm^{-1}. TLC: R_f = 0.28 (5% MeOH/CH_2Cl_2), Ce stain.

Typically the amines were not fully characterized and were used directly as follows. Diphenylacetyl chloride (1.34 g, 5.82 mmol) was added to a 0 °C solution of *cis*-2-(*p*-methoxyphenyl)-1,2,3,4-tetrahydronaphthylamine (**21**) (1.23 g, 4.85 mmol) and triethylamine (1.01 mL, 7.28 mmol) in methylene chloride (10 mL). When TLC (5% MeOH/CH_2Cl_2, Ce stain) indicated consumption of the starting amine, the reaction mixture was diluted with water and methylene chloride and stirred until all the solids dissolved. The mixture was transferred to a separatory funnel, washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo to provide 2.58 g of an off-white solid. The solid was recrystallized from methylene chloride/hexanes to give 1.43 g (66%) of *N*-[*cis*-2-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (**5e**) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): 7.38 (1H, m, Ar), 7.16 (8H, m, Ar), 7.12 (1H, m, Ar), 7.01 (2H, d, J = 8.7 Hz, Ar), 6.95 (2H, m, Ar), 6.87 (2H, m, Ar), 6.83 (2H, d, J = 8.7 Hz, Ar), 5.67 (2H, m, NH, NCHCH), 4.75 (1H, s, Ph$_2$CH), 3.84 (3H, s, OCH_3), 3.34 (1H, ddd, J = 11.6, 7.8, 3.9 Hz, CHCHCH$_2$), 2.87 (2H, m, ArCH_2CH$_2$), 2.13 (1H, m, CH$_2$-CHHCH), 1.68 (1H, m, CH$_2$CHHCH). MS (CI): 476 (M^{28+}, 19), 448 (M^+, 100), 237 (23), 212 (13). IR (KBr): 3307, 2934, 1641, 1538, 1513, 1243 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19,

H = 6.53, N = 3.13; found C = 83.39, H = 6.37, N = 3.02. Mp: 215−215.5 °C. TLC: R_f = 0.29 (2% EtOAc/CH_2Cl_2), Ce.

In a similar manner the following amides were prepared.

***N*-[*cis*-2-(3-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5c).** Prepared from **9g**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.28 (11H, m, Ar), 6.94 (2H, m, Ar), 6.81 (3H, m, Ar), 6.66 (2H, m, Ar), 5.70 (2H, m, NC*H*, N*H*), 4.77 (1H, s, Ph_2CH), 3.76 (3H, s, OCH_3), 3.38 (1H, m), 3.05 (1H, m), 2.88 (2H, m), 2.02 (1H, m), 1.70 (1H, m). MS (CI): 448 (M^+, 100), 237 (47), 212 (36). IR (KBr): 3306, 3000, 2900, 1642, 1600, 1527, 1493, 1453 cm^{-1}. HRMS: calcd for $C_{31}H_{30}NO_2$, 448.2277; found, 448.2271. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 83.25, H = 6.08, N = 2.92. Mp: 138−139 °C. TLC: R_f = 0.54 (40% EtOAc/hexane) UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 98%.

***N*-(*cis*-2-Phenyl-5-methoxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5i).** Prepared from **9b**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.12 (4H, m, Ar), 7.09 (9H, m, Ar), 6.84 (2H, m, Ar), 6.71 (3H, m, Ar), 5.61(2H, m, N*H*C*H*), 4.64 (1H, s, Ph_2CH), 3.76 (3H, s, OCH_3), 3.24 (1H, m), 2.82 (1H, m), 2.52 (1H, m), 2.08 (1H, m), 1.52 (1H, m). CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 82.88, H = 6.39, N = 3.06. MS (CI): 448 (M^+, 100), 237 (34), 212 (18). Mp: 217−218 °C. TLC: R_f = 0.63 (40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 85%.

***N*-(*cis*-2-Phenyl-6-methoxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5k).** Prepared from **9a**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.31 (6H, m, Ar), 7.19 (6H, m, Ar), 7.10 (2H, m, Ar), 6.91 (1H, m, Ar), 6.74 (2H, m, Ar), 6.64 (1H, s, Ar), 5.61 (2H, m, N*H*, HNC*H*), 4.73 (1H, s, Ph_2CH), 3.81 (3H, s, OCH_3), 3.36 (1H, m), 2.85 (2H, m), 2.10 (1H, m), 1.67 (1H, m). MS (EI): 447 (M^+, 37), 237 (100), 167 (13), 91 (13). CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 82.90, H = 6.24, N = 2.92. IR (KBr): 3302, 2900, 1643, 1606, 1531, 1500, 1266 cm^{-1}. Mp: 188−189 °C. TLC: R_f = 0.51(40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 96%.

***N*-(*cis*-2-Phenyl-7-methoxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5m).** Prepared from **9c**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.29 (3H, m, Ar), 7.20 (6H, m, Ar), 7.05 (3H, m, Ar), 6.86 (6H, m, Ar), 5.67 (2H, m, N*H*C*H*), 4.74 (1H, s, Ph_2CH), 3.71 (3H, s, OCH_3), 3.37 (1H, m), 2.79 (2H, m), 2.13 (1H, m), 1.65 (1H, m). CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 83.19, H = 6.42, N = 3.00. MS (CI): 448 (M^+, 100), 237 (12). Mp: 198−199 °C. TLC: R_f = 0.56 (40% EtOAc/ hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 95%

Method 6: *N*-[*cis*-2-(2-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5a). Sodium borohydride (0.64 g, 17 mmol) was slowly added in small portions to a 0 °C solution of 2-(2-methoxyphenyl)tetralone **(9h)** (1.42 g, 5.6 mmol) in methanol (30 mL) (vigorous gas evolution). The reaction mixture was allowed to stir until gas evolution ceased (∼10 min). TLC (20% EtOAc/hexane) indicated complete consumption of starting ketone. The reaction was quenched by the addition of 3 N HCl (10 mL). Most of the solvent was removed in vacuo. The residue was partitioned between 3 N HCl and ethyl acetate. The mixture was transferred to a separatory funnel and extracted with ethyl acetate. The extracts were combined, washed with water and brine, dried over anhydrous sodium sulfate, and concentrated to give 1.33 g (93%) of 2-(2-methoxyphenyl)-1,2,3,4-tertahydroynaphth-1-ol as a clear oil. The clear oil (1.29 g, 5.1 mmol) was dissolved in toluene (75 mL). A catalytic amount of *p*-toluenesolfonic acid (0.2 g, 1.0 mmol) was added. The mixture was refluxed overnight. Water generated during the reaction was removed with the aid of a Dean−Stark trap. TLC (20% EtOAc/hexane) indicated consumption of the alcohol. The mixture was cooled to room temperature, diluted with ethyl acetate, transferred to a separatory funnel, and extracted with ethyl acetate. The extracts were combined, washed with saturated sodium carbonate, water, and brine, dried over anhydrous sodium sulfate, and concentrated to a slightly yellow liquid. Chromatography on SiO_2 (10% EtOAc/hexane) provided 1.0 g (84%) of 2-(2-methoxyphenyl)-3,4-dihydronaphthalene (**22**) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): 7.30 (2H, m, Ar), 7.13 (4H, m, Ar), 6.96 (2H, m, Ar), 6.65 (1H, s, C=C*H*), 3.85 (3H, s, OCH_3), 2.92 (2H, t, J = 8.32 Hz), 2.71 (2H, t, J = 3.2 Hz). Mp: 57−58 °C. MS (EI): 236 (M^+, 100), 202 (13), 121 (38). CHN: calcd for $C_{17}H_{16}O$ C = 86.40, H = 6.83; found C = 86.58, H = 7.06. TLC: R_f = 0.63 (20% EtOAc/hexane), UV, Ce.

Borane tetrahydrofuran complex (4.46 mL, 4.46 mmol, 1 M in THF) was added to a 0 °C solution of 2-(2-methoxyphenyl)-3,4-dihyronaphthalene (0.96 g, 4.46 mmol) in tetrahydrofuran (50 mL). The solution was allowed to warm to room temperature overnight (∼20 h). TLC (20% EtOAc/hexane) indicated complete consumption of the olefin. The solution was cooled to 0 °C, and 3 N sodium hydroxide (6.8 mL) was cautiously added (reaction foams vigorously) followed by the slow addition of 30% hydrogen peroxide (4.7 mL). The resulting mixture was allowed to stir overnight. The solution was transferred to a separatory funnel and extracted with ethyl acetate. The extracts were combined, washed with saturated sodium bicarbonate, water, and brine, dried over anhydrous sodium sulfate, filtered, and concentrated to provide 1.17 g (∼100%) of *trans*-2-(2-methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-ol (**23**) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): 7.60 (1H, d, J = 7.25 Hz, Ar), 7.26 (4H, m, Ar), 7.15 (1H, d, J = 7.1 Hz, Ar), 7.01 (1H, m, Ar), 6.95 (1H, d, J = 8.5 Hz, Ar), 4.90 (1H, d, J = 9.5 Hz, C*H*OH), 3.85 (3H, s, OCH_3), 3.46 (1H, m, C*H*Ar), 3.04 (1H, m), 2.74 (1H, m), 2.17 (2H, m), 2.04 (1H, m). MS (EI): 254 (M^+, 66), 236 (31), 120 (100). HRMS: calcd for $C_{17}H_{18}O_2$, 254.1306; found, 254.1306. TLC: R_f = 0.29 (20% EtOAc/hexane), UV, Ce.

Diethyl azodicarboxylate (0.21 mL, 1.34 mmol) was added dropwise *via* syringe to a solution of triphenylphosphine (0.3 g, 1.2 mmol) in tetrahydrofuran (10 mL).[11] After 15 min the solution was cooled to −78 °C and *trans*-2-(2-methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-ol (**23**) (0.23, 96 mmol) in tetrahydrofuran (2 mL) was slowly added *via* cannula. Diphenyl phosphorazidate (0.26, 1.2 mmol) was slowly added, and the mixture was allowed to warm to room temperature overnight. TLC (20% EtOAc/hexanes) indicated that the reaction had not gone to completion. The mixture was recooled to −78 °C. Additional triphenylphosphine (0.3 g, 1.2 mmol) was added. Diethyl azodicarboxylate (0.21 mL, 1.34 mmol) was added dropwise. After ∼15 min, diphenyl phosphorazidate (0.26, 1.2 mmol) was slowly added, and the mixture was allowed to warm slowly to room temperature (∼7 h). TLC (20% EtOAc/hexanes) indicated consumption of starting alcohol. The reaction mixture was concentrated onto enough silica gel that a free flowing powder resulted (∼2 g of SiO_2/mmol of alcohol). The powder was loaded onto a chromatography column packed with silica gel and 10% EtOAc/hexane. Elution with 10% EtOAc/hexane provide 0.223 g of a clear thick oil. This oil contained the desired *trans*-2-(*p*-methoxyphenyl)tetrahydronaphthyl 1-azide (**24**) (TLC: R_f = 0.42 (20% EtOAC/hexane), yellow, Ce stain) contaminated with an equal amount of the eliminated product, 2-(2-methoxyphenyl)-3,4-dihydronaphthalene. The azide and eliminated product were difficult to separate by chromatography. The mixture was used without further purification.

The mixture (0.223 g) was dissolved in ethanol (40 mL), purged with nitrogen, and treated with 5% palladium on carbon (0.035 g). This suspension was hydrogenated on a Parr apparatus under 55 psi of hydrogen overnight. TLC (20% EtOAc/hexane, Ce stain) indicated consumption of starting material. The mixture was filtered through Celite, and the filter cake was well washed with 25% MeOH/CH_2Cl_2 (300 mL). The filtrate was concentrated in vacuo onto silica gel. The resulting free flowing powder was placed onto a chromatography column packed with silica gel and 5% MeOH/CH_2Cl_2. Elution with 5% MeOH/CH_2Cl_2 provided 0.90 g (51% for two steps) of *cis*-2-(2′-methoxyphenyl)-1,2,3,4-tetrahydronaphthyl-1-amine (**25**) as a thick oil. The amine was directly acylated with diphenylacetyl chloride as described previously to provide *N*-[*cis*-2-(2-methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (**5a**). ^{1}H NMR (300 MHz, $CDCl_3$): 7.16 (18H, m, Ar), 5.89 (1H, m, N*H*), 5.57 (1H, m, NC*H*CH), 4.89 (1H, s, Ph_2CH), 3.70 (3H, s, OCH_3), 3.33 (1H, m, CHC*H*CH_2), 2.87 (2H,

m, ArCH_2CH$_2$), 2.13 (1H, m), 2.0 (1H, m, CH$_2$CH_2CH). MS (CI): 448 (M$^+$, 100), 237 (24), 212 (28). IR (KBr): 3267, 3080, 2970, 1647, 1494, 1240, 744 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 82.74, H = 6.33, N = 2.89. HRMS: calcd for $C_{31}H_{29}NO_2$, 448.2276; found, 448.2267. Mp: 215−216 °C. TLC: R_f = 0.50 (40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 95%.

Method 7: *cis-N*-[2-(4-Methoxyphenyl)indan-1-yl]diphenylacetamide. A solution of 2-(4-methoxyphenyl)-1-indanone (**8**) (0.60 g, 2.52 mmol), methoxylamine hydrochloride (0.63 g, 7.55 mmol), sodium acetate (0.62 g, 7.55 mmol), and methanol (30 mL) was stirred overnight at room temperature. The reaction mixture was diluted with water and extracted 50% ethyl acetate. The extracts were combined, washed with brine, dried over anhydrous sodium sulfate, and concentrated to obtain 0.67 g (100%) of 2-(4-methoxyphenyl)-1-indanone oxime methyl ether (**26**).

Borane (1.65 mL, 1.65 mmol, 1 M in THF) was added to 2-(4-methoxyphenyl)-1-indanone oxime methyl ether (**26**) (0.23 g, 0.86 mmol) at room temperature. The mixture was stirred at room temperature for 1 h, heated to reflux, and allowed to reflux overnight. The reaction mixture was cooled to room temperature and the reacyion quenched ethanol. When the bubbling ceased, 1 M NaOH was added and the mixture was heated to 70 °C and vigorously stirred for 2 h. The mixture was cooled to room temperature, diluted with water and saturated $NaHCO_3$, and extracted with ether. The extracts were combined, washed with saturated $NaHCO_3$ and brine, dried over anhydrous sodium sulfate, and concentrated to give 2-(4-methoxyphenyl)indanamine (**27**) (0.215 g, 100%) as a mixture of cis and trans isomers (ca. 10:1). MS (EI): 239 (M$^+$, 47), 222 (48), 121 (100).

Diphenylacetyl chloride (1.24 mL, 1.24 mmol, 1 M in CH_2Cl_2) was dropwise added to a room temperature solution of 2-(4-methoxyphenyl)indanamine (**27**) (0.197 g, 0.83 mmol, ca. 10:1 cis:trans) and triethylamine (0.23 mL, 1.64 mmol) in dichloromethane (10 mL). After 4 h the reaction was quenched with water and the mixture transferred to a separatory funnel and extracted with 50% ethyl acetate/hexane. The extracts were combined, washed with brine, dried over anhydrous sodium sulfate, and concentrated to a beige solid. The solid was purified by silica gel chromatography (20% ethyl acetate/hexanes) to provide 0.24 g of the *N*-[2-(4-methoxyphenyl)indan-1-yl]diphenylacetamide (**4**) as a 11:1 cis:trans mixture. Further purification by HPLC (silica gel, 20% EtOAc/hexane) provided the pure *cis-N*-[2-(4-methoxyphenyl)indan-1-yl]diphenylacetamide (**4**) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 7.23 (9H, m), 7.16 (1H, d, J = 7.6 Hz), 7.03 (2H, m), 6.98 (2H, m), 6.79 (2H, d, J = 8.6 Hz), 6.65 (2H, d, J = 8.7 Hz), 5.86 (1H, t, J = 8.6 Hz), 5.37 (1H, d, J = 8.7 Hz), 4.75 (1H, s), 3.91 (1H, dt, J = 3.4, 8.0 Hz), 3.78 (3H, s), 3.36 (1H, dd, J = 7.8, 16.2 Hz), 3.09 (1H, dt, J = 3.4, 16.2 Hz). CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 83.20, H = 6.28, N = 2.94. MS (CI): 434 (M$^+$, 100). Mp: 168−170 °C.

Preparation of Trans Amides 3. Method 8: *N*-[*trans*-2-(4-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5e). Diisobutylaluminum hydride (83.8 mL, 83.8 mmol, 1 M in THF) was dropwise added *via* syringe to a −78 °C solution of 2-(4-methoxyphenyl)tetralone (**9f**) (7.15 g, 27.94 mmol) in anhydrous tetrahydrofuran (150 mL). The reaction mixture was allowed to come to room temperature overnight. TLC (15% EtOAc/hexane, Ce stain) indicated complete consumption of starting material. The mixture was cooled to 0 °C and the reaction cautiously quenched with solid sodium sulfate decahydrate. The reaction mixture was allowed to stir overnight. The mixture was vacuum filtered, and the filter cake was well washed with THF. The filtrate was concentrated in vacuo to a thick clear oil. The oil was dissolved in methylene chloride and concentrated onto silica gel to give a free flowing white powder (∼2 g of SiO_2/mmol). The powder was loaded onto a chromatography column packed with silica gel and 20% EtOAc/hexanes. Elution with 20% EtOAc/hexane provided 5.96 g (83%) of a white solid. Recrystallization from EtOAc/hexane afforded 4.84 g (67%) of *cis*-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphthalen-1-ol (**28**) as white crystals. ^{1}H NMR (200 MHz, $CDCl_3$): 7.27 (6H, m, Ar), 6.94 (2H, m, Ar), 4.76 (1H, c, J = 2.9 Hz, HOCHCH), 3.83 (3H, s, OCH_3), 2.98 (3H, m), 1.93 (1H, m), 1.60 (1H, m). MS (EI): 254 (M$^+$, 20), 119 (100), 91 (80). IR (KBr): 3435, 2934, 2878, 2835, 1610, 1513, 1243, 1177, 1032, 737 cm^{-1}. CHN: calcd for $C_{17}H_{18}O_2$ C = 80.29, H = 7.13; found C = 80.17, H = 7.10. Mp: 89−90.5 °C, white solid. TLC: R_f = 0.18 (20% EtOAc/hexane) Ce stain, UV.

Triphenylphosphine (4.54 g, 17.3 mmol) was added to a −20 °C solution of 2-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphthalen-1-ol (**28**) (3.52 g, 13.84 mmol) in tetrahydrofuran (100 mL).[11] Diethyl azodicarboxylate (3.05 mL, 19.4 mmol) was added dropwise *via* syringe followed by the dropwise syringe addition of diphenyl phosphorazidate (3.72, 17.3 mmol). The mixture was allowed to warm to room temperature overnight. TLC (20% EtOAc/hexanes) indicated consumption of the starting alcohol. The reaction mixture was concentrated onto enough silica gel that a free flowing powder resulted (∼2 g of SiO_2/mmol of alcohol). The powder was loaded onto a chromatography column packed with silica gel and 20% EtOAc/hexane. Elution with 20% EtOAc/hexane provided 3.46 g of a clear thick oil. This oil contained the desired *trans*-2-(*p*-methoxyphenyl)-1,2,3,4-tetrahydronaphthyl 1-azide (**29**) (TLC: R_f = 0.42 (20% EtOAC/hexane), yellow, Ce stain) contaminated with a small amount of the eliminated product. The azide and eliminated product were difficult to separate by chromatography. The oil was generally used without further purification in the following procedure.

trans-2-(4-Methoxyphenyl)-1,2,3,4-tetrahydronaphthyl 1-azide (**29**) (3.42 g, 12.24 mmol) was dissolved in ethanol (150 mL), purged with nitrogen, and treated with 10% palladium on carbon (0.35 g). This suspension was hydrogenated on a Parr apparatus under 55 psi of hydrogen overnight. TLC (20% EtOAc/hexane, Ce stain) indicated consumption of starting material. The mixture was filtered through Celite, and the filter cake was well washed with 25% MeOH/CH_2Cl_2 (300 mL). The filtrate was concentrated in vacuo onto silica gel. The resulting free flowing powder was placed onto a chromatography column packed with silica gel and 5% MeOH/CH_2Cl_2. Elution with 5% MeOH/CH_2Cl_2 provided 1.99 g (51% for two steps) of *trans*-2-(4′-methoxyphenyl)-1,2,3,4-tetrahydronaphthylamine (**30**) as a thick oil which solidified on standing. ^{1}H NMR (300 MHz, $CDCl_3$): 7.72 (1H, d, J = 7.2 Hz, Ar), 7.31 (5H, m, Ar), 6.98 (2H, d, J = 8.7 Hz, Ar), 4.11 (1H, d, J = 9.6 Hz, NCHCH), 3.82 (3H, s, OCH_3), 3.06 (1H, m), 2.94 (1H, dt, J = 16.8, 4.2 Hz), 2.69 (1H, m), 2.11 (2H, m), 1.69 (2H, bs, NH_2). MS (CI): 254 (M$^+$, 35), 237 (100). MS (FAB): 254 (M$^+$, 34), 237 (100). IR (KBr): 3432, 3359, 3287, 3244, 3030, 3010, 2932, 2883, 2836, 1697, 1609, 1513, 1487, 1239, 1184, 1029, 909, 830, 754 cm^{-1}. TLC: R_f = 0.26 (5% MeOH/CH_2Cl_2), I_2, Ce stain.

Diphenylacetyl chloride (2.14 g, 9.28 mmol) was added to a 0 °C solution of *trans*-2-(*p*-methoxyphenyl)-1,2,3,4-tetrahydronaphthylamine (**30**) (1.96 g, 7.74 mmol) and triethylamine (1.62 mL, 11.6 mmol) in methylene chloride (100 mL). When TLC (5% MeOH/CH_2Cl_2, Ce stain) indicated consumption of the starting amine, the reaction mixture was diluted with water and methylene chloride and stirred until all the solids dissolved. The mixture was transferred to a separatory funnel, washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo to provide an off-white solid. The solid was recrystallized from methylene chloride/hexanes to give 2.92 g (84%) of *N*-[*trans*-2-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (**5e**) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): 8.60 (1H, d, J = 9.2 Hz, NH), 7.33 (2H, m, Ar), 7.26 (3H, m, Ar), 7.18 (2H, d, J = 8.52, Ar), 7.08 (6H, m, Ar), 6.92 (1H, d, J = 7.68, Ar), 6.80 (2H, d, J = 8.5 Hz, Ar), 6.66 (2H, d, J = 7.3 Hz, Ar), 5.17 (1H, t, J = 9.8 Hz, NCH), 4.82 (1H, s, PhCH), 3.75 (3H, s, OCH$_3$), 2.87 (3H, m), 2.08 (1H, m), 1.96 (1H, m). MS (CI, CH_4): 448 (M$^+$, 25), 236 (100), 212 (22), 167 (10), 121 (10). IR (KBr): 3254, 3085, 3061, 2915, 1644, 1512, 1239, 1038, 743 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 82.87, H = 6.41, N = 3.16. Mp: 251−252 °C. TLC: R_f = 0.29 (2% EtOAc/CH_2Cl_2), UV, Ce stain.

In a similar manner the following amides were prepared.

***N*-[*trans*-2-(3-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5c).** Prepared from **9g**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.03 (18H, m, Ar), 5.62 (1H, d, J = 10.0 Hz, N*H*), 4.90 (1H, s, Ph_2CH), 3.82 (3H, s, OCH_3), 2.95 (2H, m), 2.72 (1H, m), 2.11 (2H, m). MS (CI): 448 (M^+, 100), 236 (12). IR (KBr): 3275, 3052, 2940, 1659, 1550, 1520, 1460, 1275, 750, 700 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 83.33, H = 6.71, N = 3.07. Mp: 213−214 °C. TLC: R_f = 0.55 (40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 85%.

***N*-[*trans*-2-(2-Methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5a).** Prepared from **9h**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.17 (13H, m, Ar), 6.97 (2H, m, Ar), 6.87 (1H, d, J = 8.1 Hz, Ar), 6.77 (2H, m, Ar), 5.89 (1H, d, J = 9.2 Hz, N*H*), 5.58 (1H, t, J = 10.4 Hz, NC*H*CH), 4.89 (1H, s, Ph_2CH), 3.70 (3H, s, OCH_3), 3.34 (1H, m), 2.95 (2H, m), 2.20 (1H, m), 2.04 (1H, m). MS (CI):448 (M^+, 100), 236 (8). IR (KBr):3266, 3050, 2915, 1647, 1552, 1494, 1462, 1453, 1438, 1240 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 83.04, H = 6.57, N = 3.37. Mp: 216−217 °C. TLC: R_f = 0.51 (40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 77%.

***N*-(*trans*-2-Phenyl-5-methoxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5i).** Prepared from **9b**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.31 (2H, m, Ar), 7.11 (11H, m, Ar), 7.31 (2H, dd, J = 2.0, 7.9 Hz, Ar), 6.75 (1H, d, J = 7.9 Hz, Ar), 6.65 (2H, m, Ar), 5.53 (2H, m, N*HCH*), 4.79 (1H, s, Ph_2CH), 3.74 (3H, s, OCH_3), 2.85 (1H, m), 2.58 (2H, m), 2.02 (2H, m). MS (CI): 448 (M^+, 100), 237 (47), 212 (43). HRMS: calcd for $C_{31}H_{29}NO_2$, 447.2198; found, 447.2274. Mp: 238−239 °C. TLC: R_f = 0.52 (40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/EtOAc. Yield: 72%.

***N*-(*trans*-2-Phenyl-6-methoxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5k).** Prepared from **9a**. ^{1}H NMR (200 MHz, $CDCl_3$/DMSO): 8.51 (1H, d, J = 9 Hz, Ar), 7.25 (9H, m, Ar), 7.07 (4H, m, Ar), 6.86 (1H, d, J = 8 Hz, Ar), 6.64 (4H, m, Ar), 5.20 (1H, t, J = 9.7 Hz, NC*H*CH), 4.81 (1H, s, Ph_2CH), 3.71 (3H, s, OCH_3), 2.89 (3H, m), 2.03 (2H, m). MS (FAB): 448 (M^+, 10), 237 (100). IR (KBr): 3538, 3272, 2949, 2930, 1645, 1551, 1496, 1257, 698 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 82.89, H = 6.62 N = 2.94. Mp: 259−260 °C. TLC: R_f = 0.17 (2% EtOAc/CH_2Cl_2), Ce stain. Purification: slurried with a mixture of THF/MeOH/CH_2Cl_2, collected solid. Yield: not reported.

***N*-(*trans*-2-Phenyl-7-methoxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5m).** Prepared from **9c**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.27 (13H, m, Ar), 6.98 (2H, m, Ar), 6.75 (3H, m, Ar), 5.64 (2H, m, N*HCH*), 4.85 (1H, s, Ph_2CH), 3.66 (3H, s, OCH_3), 3.22 (1H, m), 2.80 (2H, m), 2.07 (2H, m). CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 82.96, H = 6.44, N = 3.29. MS (EI): 448 (M^+, 1), 236 (100), 167 (26), 91 (67). Mp: 266−268 °C. TLC: R_f = 0.50 (40% EtOAc/hexane), UV, Ce. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 85%.

***N*-[*trans*-2-(4-Methoxyphenyl)-7-methoxy-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5p).** Prepared from **9d**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.22 (7H, m, Ar), 6.95 (6H, m, Ar), 6.75 (4H, m, Ar), 5.55 (2H, m, N*HCH*), 4.86 (1H, s, Ph_2CH), 3.87 (3H, s, OCH_3), 3.66 (3H, s, OCH_3), 2.85 (1H, m), 2.64 (1H, m), 2.05 (2H, m), 1.55 (1H, m). MS (EI): 478 (M^+, 1), 266 (100), 121 (45). CHN: calcd for $C_{32}H_{31}NO_3$ C = 80.47, H = 6.54, N = 2.93; found C = 80.04, H = 6.60, N = 3.02. Mp: 258−259 °C. TLC: R_f = 0.10 (5% MeOH/CH_2Cl_2), UV, Ce stain. Yield: 94%.

***N*-[*trans*-2-(4-Pyridyl)-1,2,3,4-tetrahydronaphthyl]-diphenylacetamide (5h).** Prepared from **9j**. ^{1}H NMR (200 MHz, $CDCl_3$): 8.43 (2H, dd, J = 1.6, 4.5 Hz, pyridine), 7.12 (12H, m, Ar), 6.90 (4H, m, Ar), 6.27 (1H, d, J = 9.4 Hz, N*H*), 5.53 (1H, t, J = 10.1 Hz, CHC*H*N), 4.80 (1H, s, Ph_2CH), 2.79 (3H, m), 2.00 (2H, m). MS (FAB): 419 (M^+, 50), 208 (100), 167 (34). IR (KBr): 3268, 3061, 3028, 2925, 1646, 1547, 1495, 1453, 742 cm^{-1}. CHN: calcd for $C_{29}H_{26}N_2$ C = 83.22, H = 6.26, N = 6.69; found C = 83.43, H = 6.18, N = 6.65. Mp: 237.5−238 °C. TLC: R_f = 0.35 (100% EtOAc), I_2, UV. Purification: recrystallized from ethanol. Yield: 62%, white solid.

N-[*trans*-2-(4-Aminophenyl)-1,2,3,4-tetrahydronaphth-1-yl]-diphenylacetamide (5g). Diisobutylaluminum hydride (88 mL, 88 mmol, 1 M in THF) was dropwise added to a −78 °C solution of 2-(4′-aminophenyl)-1-tetralone (**9e**) in THF (200 mL). The mixture was allowed to come to room temperature overnight. TLC (50% EtOAc/hexane) indicated consumption of starting material. The solution was cooled to 0 °C and slowly treated with NaF (7.74 g, 352 mmol) and water (4.75 mL, 264 mmol). The mixture was stirred overnight and vacuum filtered, and the filter cake was well washed with ethyl acetate. The filtrate was concentrated onto silica gel (2 g of SiO_2/mmol of ketone). The resulting free flowing powder was poured onto a chromatography column packed with 50% EtOAc/hexane and silica gel. Elution with 50% EtOAc/hexane provided 5.76 g (82%) of 2-(4′-aminophenyl)-1,2,3,4-tetrahydronaphth-1-ol as a white solid. A portion was further purified by recrystallization from EtOAc/hexane. ^{1}H NMR (200 MHz, $CDCl_3$): 7.21 (6H, m, Ar), 6.71 (2H, d, J = 8.4 Hz, Ar), 4.73 (1H, d, J = 3.0 Hz), 2.58 (3H, m), 2.38 (1H, m), 1.91 (2H, m). IR ($CDCl_3$): 3567, 3459, 3388, 3026, 2936, 2881, 2839, 1622, 1517, 1491, 1455, 1434, 1455, 1385, 1271, 1183 cm^{-1}. CHN: calcd for $C_{16}H_{17}NO$ C = 80.30, H = 7.7.16; found C = 80.08, H = 7.46. MS (FAB): 240 (M^+, 66), 223 (100). Mp: 121.5−122.5 °C, white crystals. TLC: R_f = 0.16 (50% EtOAc/hexane), Ce stain.

Boc anhydride (6.36 g, 29.1 mmol) in dioxane (50 mL) was added to a solution of 2-(4′-amionophenyl)-1,2,3,4-tetrahydronaphth-1-ol (5.76 g, 24.1 mmol) and NaOH (1.63 g, 40.9 mmol) in a mixture of dioxane (100 mL) and water (50 mL). The mixture was allowed to stir overnight. TLC (50% EtOAc/hexane) indicated the presence of starting material. Additional NaOH (0.3 g, 7.5 mmol) and Boc anhydride (1.05 g, 4.81 mmol) were added. The reaction mixture was allowed to stir overnight. TLC (50% EtOAc/hexane) indicated consumption of starting material. Water was added to dissolve a precipitate that formed, and the mixture was transferred to a separatory funnel extracted with CH_2Cl_2. The extracts were combined, washed with water, dried over Na_2SO_4, and concentrated to give 8.26 g of a white solid. The solid was recrystallized from EtOAc/hexane to provide 7.31 g (90%) of 2-[4-[*N*-(*tert*-butoxycarbonyl)amino]phenyl]-1,2,3,4-tetrahydronaphth-1-ol as white crystals. ^{1}H NMR (200 MHz, $CDCl_3$): 7.27 (8H, m, Ar), 6.48 (1H, s, N*H*), 4.75 (1H, d, J = 2.8 Hz, HOC*H*), 3.01 (3H, m), 2.40 (1H, m), 1.93 (1H, m), 1.58 (3H, s, minor rotamer, $(CH_3)_3C$), 1.53 (3H, s, major rotamer, $(CH_3)_3C$). MS (CI, NH_3): 357 (M^{18+}, 100), 340 (M^+, 10), 322 (10), 301 (20), 283 (20), 266 (40), 222 (50). HRMS: $C_{21}H_{25}NO_3$ calcd, 339.1834; obsd, 339.1830. IR ($CDCl_3$): 3689, 3584, 3437 (m), 3006, 2980 (m), 2935, 2887, 1723 (s), 1614, 1590 (m), 1521 (s), 1503 (m), 1455, 1412 (m), 1392, 1369 (m), 1312 (m), 1254, 1216 (m), 1159 (s), 1054 cm^{-1}. CHN: calcd for $C_{21}H_{25}NO_3$ C = 74.31, H = 7.42, N = 4.13; found C = 74.50, H = 7.77, N = 4.18. Mp: 174.5−175 °C. TLC: R_f = 0.16 (15% EtOAc/hexane), UV, Ce stain.

Diethyl azodicarboxylate (4.39 mL, 27.9 mmol) was dropwise added to a 0 °C solution of 2-[4-[*N*-(*tert*-butoxycarbonyl)amino]-phenyl]-1,2,3,4-tetrahydronaphth-1-ol (7.28 g, 21.5 mmol) and triphenylphosphine (7.03 g, 26.8 mmol) in THF (100 mL). Diphenyl phosphorazidate (5.78 mL, 26.8 mmol) was dropwise added, and the mixture was allowed to stir overnight. TLC (15% EtOAc/hexane, Ce stain) indicated almost complete consumption of starting alcohol. The mixture was concentrated onto silica gel (∼2 g/mmol of tetralol). The resulting free flowing powder was loaded onto a chromatography column packed with silica gel and 15% EtOAc. Elution with 15−30% EtOAc/hexanes provided 7.78 g of the 2-[4′-[*N*-(*tert*-butoxycarbonyl)amino]phenyl]-1-azidotetralin which was used without further purification.

2-[4′-[*N*-(*tert*-butoxycarbonyl)amino]phenyl]-1-azidotetralin (7.78 g, 21.4 mmol) was dissolved in ethyl acetate (100 mL) and diluted with ethanol (100 mL). The resulting clear solution was purged with nitrogen; 10% palladium on carbon (∼1 g) was added, and the mixture was hydrogenated on a Parr apparatus (50 psi) overnight. TLC (10% EtOAC/hexane)

indicated consumption of the starting azide. The mixture was filtered through Celite, and the filter cake was well washed with 50% MeOH/CH_2Cl_2 (600 mL). The filtrate was concentrated to provide 7.64 g of a solid. Recrystallization from EtOAc/hexane yielded 4.93 g of the 2-[4′-[*N*-(*tert*-butoxycarbonyl)amino]phenyl]-1-aminotetralin as a white solid (68% for the two-step process). ^{1}H NMR (200 MHz, $CDCl_3/CD_3OD$): 7.45 (1H, m, C^8-H), 7.28 (2H, m, Ar), 7.12 (4H, m, Ar), 4.00 (1H, d, J = 9.4 Hz, H_2NCHCH), 3.38 (2H, bs, NH_2), 2.87 (2H, m), 2.56 (1H, m), 1.97 (2H, m), 1.45 (9H, s, $OC(CH_3)_3$). MS (FAB): 339 (M^+, 4), 322 (53), 266 (100), 251 (8). IR (KBr): 3432, 3241, 2978, 2937, 1728, 1601, 1541, 1493, 1315, 1237, 1158, 1049, 937, 773 cm^{-1}.

Diphenylacetyl chloride (1.37 g, 5.96 mmol) was added to a 0 °C solution of 2-[4-[*N*-(*tert*-butoxycarbonyl)amino]phenyl]-1-aminotetralin (1.68 g, 4.96 mmol) and triethylamine (1.04 mL, 7.45 mmol) in methylene chloride (20 mL). The mixture was allowed to stir overnight. TLC (10% MeOH/CH_2Cl_2, I_2) indicated an absence of starting material. The mixture was diluted with saturated NH_4Cl and methylene chloride, transferred to a separatory funnel, washed with saturated NH_4Cl and water, dried over Na_2SO_4, and concentrated to a very insoluble white solid (2.83 g 107%) which was employed without further purification.

The crude amide (2.63 g, 4.96 mmol) was dissolved in dioxane (50 mL), cooled to 0 °C, and treated with a saturated solution of HCl/dioxane (50 mL). The mixture was allowed to stir overnight. The solution was made basic with 2 N NaOH and solid NaOH, transferred to a separatory funnel, and extracted with ethyl acetate. The extracts were combined, washed with water and brine, dried over Na_2SO_4, and concentrated onto silica gel. The resulting free flowing powder was loaded onto a chromatography column prepacked with silica gel and 10% EtOAc/CH_2Cl_2. Elution with 10% EtOAc/CH_2Cl_2 provided 1.72 g (80%) of the title compound **5g** as a white solid. Recrystallization from ethanol afforded 0.90 g of white crystals. ^{1}H NMR (200 MHz, $CDCl_3$): 7.14 (14H, m, Ar), 6.80 (4H, m, Ar), 5.90 (1H, d, J = 9.6 Hz, NH), 5.49 (1H, t, J = 10.2 Hz, PhC*H*NH), 4.89 (1H, s, Ph_2CH), 2.91 (2H, m), 2.61 (3H, m), 2.05 (2H, m). MS (FAB): 433 (M^+, 20), 307 (7), 289 (5), 222 (100). IR (KBr): 3387, 3263, 3060, 3026, 2913, 1646, 1621, 1555, 1517, 1494, 1452, 746 cm^{-1}. CHN: calcd for $C_{30}H_{28}N_2O$ C = 83.30, H = 6.52, N = 6.48; found C = 83.13, H = 6.54, N = 6.41. Mp: 229.5−230.5 °C. TLC: R_f = 0.23 (10% EtOAc/methylene chloride), UV, Ce stain.

Preparation of Phenols 3: Preparation of *N*-[*trans*-2-(4-Hydroxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5f). Boron tribromide (15.6 mL, 15.6 mmol, 1 M in methylene chloride) was added *via* syringe to a 0 °C solution of *N*-[*trans*-2-(4-methoxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (**5e**) (2.79 g, 6.23 mmol) in methylene chloride (200 mL). When TLC (5% EtOAc/CH_2Cl_2, Ce stain) indicated consumption of starting material, the reaction was quenched with methanol followed by saturated sodium bicarbonate. The mixture was allowed to stir overnight. The solids were dissolved by the addition of water and methylene chloride. The solution was transferred to a separatory funnel, and the organic phase was washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo to a white solid. Recrystallization from EtOAc provided 1.94 g (72%) of the title compound **5f** as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): 7.71 (1H, bs, O*H*), 7.10 (10H, m, Ar), 6.75 (2H, m, Ar), 6.58 (2H, app d, J = 8.4 Hz, Ar), 5.68 (2H, m, N*H*), 4.96 (1H, s, Ph_2CH), 2.92 (2H, m, $ArCH_2CH_2$), 2.58 (1H, m, NCHC*H*), 2.04 (2H, m, CH_2CH_2CH). MS (SIMS): 434 (M^+, 62), 223 (52), 212 (54), 181 (21), 167 (61), 107 (100). HRMS (FAB): calcd for $C_{30}H_{27}NO_2$, 434.2120; obsd, 434.2106. IR (KBr): 3404, 3271, 3086, 3062, 2920, 1645, 1516, 1494, 1451, 1228, 830, 743 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.27, N = 3.23; found C = 83.05, H = 5.71, N = 3.12. Mp: 204−206 °C, white powder. TLC: R_f = 0.17 (5% EtOAc/CH_2Cl_2), Ce.

In a similar manner the following compounds were prepared.

***N*-[*cis*-2-(4-Hydroxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5f).** Prepared from cis **5e**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.39 (1H, m, Ar), 7.24 (8H, m, Ar), 7.14 (1H, m, Ar), 7.06 (1H, bs, O*H*), 6.96 (4H, m, Ar), 6.85 (2H, dd, J = 7.56, 1.92 Hz, Ar), 6.60 (2H, d, J = 8.46 Hz, Ar), 5.80 (1H, app d, J = 10.0 Hz), 5.71 (1H, major rotamer (5.73 ppm, d, J = 4.74 Hz), minor rotamer (5.70 ppm, d, J = 4.83 Hz), NC*H*CH), 4.79 (1H, s, Ph_2CH), 3.25 (1H, m, CHC*H*CH), 2.89 (2H, m), 2.08 (1H, m), 1.58 (1H, m). MS (CI): 62 (M^{28+}, 16), 434 (M^+, 100). IR (KBr): 3348, 3254, 2933, 1646, 1513, 1496, 1447, 1239, 736 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.88, H = 5.98, N = 3.16. Mp: 211.5−212 °C. TLC: R_f = 0.39 (50% EtOAc/hexane), Ce stain.

***N*-[*trans*-2-(3-Hydroxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5d).** Prepared from trans **5c**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.17 (11H, m, Ar), 6.99 (2H, m, Ar), 6.92 (1H, s, Ar), 6.82 (3H, m, Ar), 6.68 (1H, d, J = 7.5 Hz, Ar), 5.72 (1H, d, J = 9.7 Hz, N*H*), 5.55 (1H, t, J = 10.4 Hz, NC*H*CH), 4.92 (1H, s, Ph_2CH), 2.86 (1H, m), 2.74 (1H, m), 2.60 (1H, dt, J = 2.9, 12.0 Hz), 1.96 (1H, m), 1.83(2H, m). MS (CI): 434 (M^+, 100). IR (KBr): 3272, 1646, 1600, 1515, 1494, 1454, 698 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.73, H = 6.18, N = 2.91. Mp: 207−208 °C. TLC: R_f = 0.37 (40% EtOAc/hexane), UV, I_2. Purification: recrystallization from THF/hexane. Yield: 94%.

***N*-[*cis*-2-(3-Hydroxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5d).** Prepared from cis **5c**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.38 (1H, m, Ar), 7.19 (10H, m, Ar), 6.95 (2H, dd, J = 2.0, 8.0 Hz, Ar), 6.87 (2H, d, J = 6.6 Hz, Ar), 6.76 (1H, dd, J = 2.2, 7.7 Hz), 6.61 (1H, d, J = 7.9 Hz, Ar), 6.56 (1H, s, Ar), 5.76 (1H, app d, J = 10.0 Hz), 5.65 (1H, dd, J = 5.1, 10.7 Hz, NC*H*CH), 4.78 (1H, s, Ph_2CH), 3.28 (1H, m), 2.85 (2H, m), 2.10 (1H, m), 1.65 (1H, m). MS (CI): 434 (M^+, 82), 222 (82), 211 (83), 166 (100). IR (KBr): 3290, 3287, 3273, 3026, 1656, 1599, 1588, 1547, 1528, 1493, 1452, 1266, 1229, 741, 722, 699 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.96, H = 6.15, N = 3.08. Mp: 186−187 °C. TLC: R_f = 0.34 (40% EtOAc/hexane), UV, Ce stain. Purification: chromatography on SiO_2 (100% CH_2Cl_2), further purified by recrystallization from EtOAc/hexane. Yield: 67%.

***N*-[*trans*-2-(2-Hydroxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5b).** Prepared from trans **5a**. ^{1}H NMR (200 MHz, DMSO-d_6): 9.35 (1H, s), 8.52 (1H, d, J = 9.0 Hz, Ar), 7.29 (5H, m, Ar), 7.05 (9H, m, Ar), 6.76 (4H, m, Ar), 5.47 (1H, m, NC*H*CH), 4.88 (1H, s, Ph_2CH), 3.28 (1H, m), 2.80 (2H, m), 2.02 (2H, m). MS (CI): 434 (M^+, 100). IR (KBr): 3393, 3312, 3291, 3278, 1645, 1523, 1508, 1491, 753, 746, 702 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.81, H = 6.35, N = 2.99. Mp: 258−259 °C. TLC: R_f = 0.39 (40% EtOAc/hexane), UV, I_2. Purification: recrystallization from THF/hexane. Yield: 91%.

***N*-[*cis*-2-(2-Hydroxyphenyl)-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5b).** Prepared from cis **5a**. ^{1}H NMR (200 MHz, $CDCl_3$): 7.37 (1H, m, Ar), 7.18 (9H, m, Ar), 6.89 (7H, m, Ar), 6.36 (1H, d, J = 7.8 Hz, Ar), 6.03 (1H, m, NC*H*CH), 5.85 (1H, d J = 10.0 Hz, N*H*), 4.70 (1H, s, Ph_2CH), 3.62 (1H, m), 2.91 (2H, m), 1.98 (1H, m), 1.67 (1H, m). MS (FAB): 434 (M^+, 100), 223 (56), 166 (52). IR (KBr): 3408, 3295, 3278, 3274, 1647, 1515, 1494, 1454, 749, 700 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 83.27, H = 6.24, N = 3.16. HRMS: calcd for (M^+) $C_{30}H_{28}NO_2$, 434.2119; found, 434.2085. Mp: 267−268 °C. TLC: R_f = 0.50 (40% EtOAc/hexane), UV, Ce stain. Purification: recrystallization from CH_2Cl_2/hexane. Yield: 99%.

***N*-(*trans*-2-Phenyl-5-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5j).** Prepared from trans **5i**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.03 (18H, m, Ar), 5.52 (2H, m, NC*H*C*H*), 4.79 (1H, s, Ph_2CH), 3.82 (3H, m), 2.05 (2H, m). HRMS: calcd for $C_{30}H_{27}NO_2$, 433.2042; found, 433.2050. MS (CI): 434 (M^+, 100), 233 (17), 212 (76). Mp: 219−220 °C. TLC: R_f = 0.28 (40% EtOAc/hexane), UV, Ce stain. Purification: recrystallization from CH_2Cl_2/EtOAc. Yield: 71%.

***N*-(*cis*-2-Phenyl-5-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5j).** Prepared from cis **5i**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.20 (4H, m, Ar), 7.12 (5H, m, Ar), 6.97 (4H, m, Ar), 6.87 (2H, m, Ar), 6.75 (2H, m, Ar), 6.61 (1H, d, J = 7.8 Hz, Ar), 5.60 (2H, m, NC*H*C*H*), 4.66 (1H, s, Ph_2CH),

3.27 (1H, m), 2.76 (1H, m), 2.55 (1H, m), 2.10 (1H, m), 1.61 (1H, m). CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.94, H = 6.27, N = 3.36. HRMS: calcd for $C_{30}H_{27}NO_2$, 433.2042; found, 433.2050. MS (CI): 434 (M^+, 100), 212 (31). Mp: 210−211 °C. TLC: R_f = 0.35 (40% EtOAc/hexane), UV, Ce stain. Purification: recrystallization from CH_2Cl_2/hexane. Yield: 67%.

***N*-(*trans*-2-Phenyl-6-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5l).** Prepared from trans **5k**. ^{1}H NMR (200 MHz, DMSO/$CDCl_3$): 8.91 (1H, s, O*H*), 8.25 (1H, d, *J* = 9.2 Hz, N*H*), 7.16 (10H, m, Ar), 7.04 (3H, m, Ar), 6.76 (1H, d, J = 8.4 Hz), 6.68 (2H, m, Ar), 6.44 (2H, m, Ar), 5,19 (1H, t, *J* = 9.l7 Hz, NC*H*), 4.78 (1H, s, OCH_3), 2.84 (2H, m), 2.70 (1H, m), 2.52 (1H, m), 2.00 (1H, m). MS (FAB): 434 (M^+, 21), 223 (100). IR (KBr): 3397, 3169, 2926, 1639, 1582, 1534, 1495, 1249, 701 cm^{-1}. CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.27, N = 3.23; found C = 82.97, H = 6.00, N = 3.09. Mp: 248−250 °C, white crystals. TLC: R_f = 0.38 (10% EtOAc/CH_2Cl_2), Ce stain. Purification: recrystallized from CH_2Cl_2/MeOH. Yield: 87%.

***N*-(*cis*-2-Phenyl-6-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5l).** Prepared from cis **5k**. ^{1}H NMR (300 MHz, DMSO/$CDCl_3$): 8.40 (1H, d, *J* = 9.8 Hz), 7.23 (11H, m, Ar), 7.10 (2H, m, Ar), 6.92 (1H, *J* = 9.21 Hz), 5.54 (2H, m, Ar), 6.52 (2H, m, Ar), 5.29 (1H, dd, *J* = 4.8, 9.8 Hz), 4.78 (1H, PhC*H*), 3.15 (1H, m), 2.82 (2H, m), 2.34 (1H, m), 1.93 (1H, m). MS (EI): 434 (M^+, 16), 224 (100), 167 (19), 91 (12). CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.27, N = 3.23; found C = 81.68, H = 6.15, N = 2.97. Mp: 248−250 °C. HRMS: calcd for $C_{30}H_{27}NO_2$, 433.2042; found, 433.2027. IR (KBr): 3312, 3308, 3075, 3043, 2947, 1656, 1542, 1497, 1270, 701 cm^{-1}. Mp: 254−255 °C. TLC: R_f = 0.25 (40% EtOAc/CH_2Cl_2), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/hexane.

***N*-(*trans*-2-Phenyl-7-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5n).** Prepared from trans **5m**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.30 (3H, m, Ar), 7.13 (9H, m, Ar), 6.92 (2H, d, *J* = 6.2 Hz, Ar), 6.85 (1H, d, *J* = 8.2 Hz, Ar), 6.58 (3H, m, Ar), 6.50 (1H, d, *J* = 2.5 Hz, Ar), 5.55 (1H, m, NC*H*), 5.43 (1H, m, NCHC*H*), 4.79 (1H, s, Ph_2CH), 2.73 (2H, m), 2.52 (1H, m), 1.96 (2H, m). CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.75, H = 6.25, N = 3.34. HRMS: calcd for $C_{30}H_{27}NO_2$, 433.2042; found, 433.2041. MS (CI): 434 (M^+, 100). Mp: 220−222 °C. TLC: R_f = 0.15 (30% EtOAc/CH_2Cl_2), UV, Ce stain. Purification: recrystallized from CH_2Cl_2 /hexane. Yield: 66%.

***N*-(*cis*-2-Phenyl-7-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (5n).** Prepared from cis **5m**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.53 (1H, bs), 7.40 (3H, m, Ar), 7.28 (6H, m, Ar), 7.15 (2H, dd, *J* = 2.2, 7.7 Hz, Ar), 7.00 (3H, m, Ar), 6.78 (4H, m, Ar), 5.80 (1H, d, *J* = 10.4 Hz, NC*H*), 5.56 (1H, dd, *J* = 5.0, 10.0 Hz, NCHC*H*), 4.83 (1H, s, Ph_2CH), 3.29 (1H, m), 2.81 (2H, m), 2.10 (2H, m). CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.88, H = 6.21, N = 3.16. HRMS: calcd for $C_{30}H_{27}NO_2$, 433.2042; found, 433.2039. MS (CI): 434 (M^+, 100). Mp: 177−178 °C. TLC: R_f = 0.44 (40% EtOAc/CH_2Cl_2), UV, Ce stain. Purification: SiO_2 chromatography (40% EtOAc/hexane). Yield: 83%.

***N*-(*trans*-2-Phenyl-8-hydroxy-1,2,3,4-tetrahydronaphth-1-yl)diphenylacetamide (50).** Prepared from **9i** by method 8. ^{1}H NMR (300 MHz, $CDCl_3$): 7.26 (9H, m, Ar), 7.11 (5H, m, Ar), 6.87 (3H, m, Ar), 6.62 (1H, d, *J* = 7.4 Hz, Ar), 5.80 (1H, m, NC*H*), 5.56 (1H, dd, *J* = 6.6, 9.1 Hz, NCHC*H*), 4.92 (1H, s, Ph_2CH), 2.78 (1H, m), 2.66 (1H, m), 1.94 (2H, m), 1.53 (1H, m). CHN: calcd for $C_{30}H_{27}NO_2$ C = 83.11, H = 6.28, N = 3.23; found C = 82.88, H = 6.20, N = 3.43. MS (FAB): 434 (M^+, 52), 222 (100), 211 (79). Mp: 218−219 °C. TLC: R_f = 0.56 (5% MeOH/CH_2Cl_2), UV, Ce stain. Purification: SiO_2 chromatography (20% EtOAc/hexane). Yield: 61%.

***N*-[*trans*-2-(4-Hydroxyphenyl)-7-hydroxy-1,2,3,4-tetrahydronaphth-1-yl]diphenylacetamide (5q).** Prepared from trans **5p**. ^{1}H NMR (400 MHz, DMSO): 8.49 (1H, d, *J* = 9.2 Hz, N*H*), 7.32 (2H, m, Ar), 7.25 (3H, m, Ar), 7.12 (3H, m, Ar), 7.03 (2H, d, *J* = 8.2 Hz, Ar), 6.89 (1H, d, *J* = 8.2 Hz, Ar), 6.63 (4H, m, Ar), 6.57 (1H, d, J =8.4 Hz, Ar), 6.45 (1H, d, *J* = 2.1 Hz, Ar), 5.10 (1H, t, *J* = 9.5 Hz, C*H*N), 4.83 (1H, s, PhC*H*), 2.77 (2H, m), 2.68 (1H, m), 1.93 (2H, m). CHN: calcd for $C_{30}H_{27}NO_3$ C = 80.15, H = 6.05, N = 3.12; found C = 79.71, H = 6.04, N = 3.24. HRMS: calcd for $C_{30}H_{27}NO_3$: 450.2069 found 450.2075. MS (CI): 450 (M^+, 96), 239 (41), 212 (100). Mp: 246−247 °C. TLC: R_f = 0.16 (5% MeOH/CH_2Cl_2), UV, Ce stain.

***N*-[*cis*-2-(4-Hydroxyphenyl)-7-hydroxy-1,2,3,4-tetrahydronaphthyl]diphenylacetamide (5q).** Prepared from **9d** by method 5. ^{1}H NMR (400 MHz, DMSO): 8.34 (1H, d, *J* = 9.84 Hz), (2H, m, Ar), 7.22 (3H, m, Ar), 7.18 (3H, m, Ar), 7.02 (2H, d, *J* = 8.44 Hz, Ar), 6.92 (1H, d, *J* = 8.24 Hz, Ar), 6.59 (6H, m, Ar), 5.24 (1H, dd, *J* = 4.6, 9.8 Hz, NCHC*H*), 4.81 (1H, s, Ph_2CH), 3.04 (1H, m), 2.77 (2H, m), 2.24 (1H, m), 1.81 (1H, m). CHN: calcd for $C_{30}H_{27}NO_3$ C = 80.15, H = 6.06, N = 3.12; found C = 79.90, H = 6.01, N = 3.22. MS (FAB): 450 (M^+, 97), 238 (100), 211 (51). Mp: 244−245 °C. TLC: R_f = 0.17 (5% MeOH/CH_2Cl_2), UV, Ce stain.

***trans*-*N*-[2-(4-Hydroxyphenyl)indan-1-yl]diphenylacetamide (4).** Prepared from **8** by method 7. ^{1}H NMR (200 MHz, $CDCl_3$): 8.14 (2H, m), 7.74 (1H, d, *J* = 8 Hz), 7.51 (1H, d, *J* = 8 Hz), 7.24 (14H, m), 5.79 (2H, m), 4.95 (1H, s), 3.37 (2H, m), 3.18 (1H, m). CHN: calcd for $C_{29}H_{25}NO_2$ C = 83.03, H = 6.01, N = 3.34; found C = 82.71, H = 6.34, N = 3.21. Mp: 188−190 °C. MS (CI): 420 (M^+, 100), 208 (72).

***cis*-*N*-[2-(4-Hydroxyphenyl)indan-1-yl]diphenylacetamide (4).** Prepared from **8** by method 7.^{1}H NMR (400 MHz, $CDCl_3$): 7.17 (10H, m), 6.99 (2H, d, *J* = 7.5 Hz), 6.92 (2H, d, *J* = 7.6 Hz), 6.70 (2H, d, *J* = 8.6 Hz), 6.53 (2H, d, *J* = 8.6 Hz), 5.82 (1H, t, *J* = 8.2 Hz), 5.70 (1H, s), 5.40 (1H, d, *J* = 9.2 Hz), 4.74 (1H, s), 3.86 (1H, dt, *J* = 4.0, 7.8 Hz), 3.30 (1H, dd, *J* = 7.9, 16.2 Hz), 3.05 (1H, dd, *J* = 4.0, 16.2 Hz). CHN: calcd for $C_{29}H_{25}NO_2$ C = 83.03, H = 6.01, N = 3.34; found C = 83.15, H = 6.12, N = 3.07. MS (CI): 420 (M^+, 100). Mp: 136.5−139 °C.

***N*-[*cis*-6,7,8,9-Tetrahydro-6-(4-hydroxyphenyl)-5*H*-benzocyclohepten-5-yl]diphenylacetamide (6).** Prepared from **10** by method 6. ^{1}H NMR (200 MHz, $CDCl_3$): 7.19 (6H, m, Ar), 7.08 (2H, dt, *J* = 1.9, 6.6 Hz, Ar), 7.00 (6H, m, Ar), 6.60 (2H, d, *J* = 8.4 Hz, Ar), 6.51 (2H, d, *J* = 8.6 Hz, Ar), 5.33 (1H, d, *J* = 3.5 Hz, NCHCH), 4.84 (1H, s, Ph_2CH), 2.92 (1H, dt, *J* = 3.6, 11.4 Hz), 2.80 (1H, m), 2.41 (1H, m), 1.78 (4H, m), 1.55 (1H, m), 1.39 (1H, t, *J* = 11.6 Hz). MS (CI): 448 (M + 1, 100), 236 (72). IR (KBr): 3410, 3236, 3060, 3045, 3025, 2918, 2854, 1651, 1597, 1582, 1452, 1364, 1233, 1207, 822 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 83.46, H = 6.59, N = 3.08. Mp: 196.5−197.5 °C, white crystals. TLC: R_f = 0.11 (5% EtOAc/CH_2Cl_2), Ce, UV. Purification: SiO_2 chromatography (5−10% EtOAc/CH_2Cl_2), further purified by recrystallization from CH_2Cl_2/MeOH. Yield: 44%, white solid.

***N*-[*trans*-6,7,8,9-Tetrahydro-6-(4-hydroxyphenyl)-5*H*-benzocyclohepten-5-yl]diphenylacetamide (6).** Prepared from **10** by method 8. ^{1}H NMR (200 MHz, $CDCl_3$/CD_3OD): 7.26−6.66 (18H, m, Ar), 6.14 (1H, d, *J* = 9 Hz, N*H*), 5.40 (1H, t, *J* = 9.3 Hz, C*H*N), 4.61 (1H, s, PhC*H*), 3.69 (3H, s, OCH_3), 3.19 (1H, m), 2.94 (1H, m), 2.65 (1H, m), 2.44 (1H, m), 1.82 (3H, m). MS (FAB): 462 (M^+, 85), 307 (50), 289 (40), 250 (100), 212 (40). IR (KBr): 3464, 3295, 2930, 1648, 1550, 1513, 1248, 1034, 744 cm^{-1}. CHN: calcd for $C_{31}H_{29}NO_2$ C = 83.19, H = 6.53, N = 3.13; found C = 83.31, H = 6.53, N = 2.79. Mp: 235−235.5 °C, fluffy white solid. TLC: R_f = 0.43 (5% EtOAc/CH_2Cl_2), UV, Ce stain. Purification: chromatography (0−5% EtOAc/CH_2Cl_2), recrystallized from EtOH/EtOAc. Yield: 87%, white solid.

***N*-[*cis*-3-(4-Hydroxyphenyl)-3,4-dihydro-2*H*-benzopyran-4-yl]diphenylacetamide (7).** Prepared from **11** by method 5.^{1}H NMR (300 MHz, $CDCl_3$): 7.16 (9H, m), 6.94 (2H, m), 6.81 (6H, m), 6.48 (2H, d, *J* = 8.6 Hz), 5.61 (2H, m), 4.74 (1H, s), 4.38 (1H, dd, *J* = 3.0, 11 Hz), 3.97 (1H, dd, *J* = 10.9, 13.7 Hz), 3.36 (1H, m). MS (FAB): 436 (M^+, 100), 316 (15), 225 (25). CHN: calcd for $C_{29}H_{25}NO_3$ C = 79.98, H = 5.79, N = 3.22 found C = 79.97, H = 5.80, N = 3.31. Mp: 154−156 °C, white solid. TLC: R_f = 0.21 (5% EtOAc/CH_2Cl_2), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/MeOH.

***N*-[*trans*-3-(4-Hydroxyphenyl)-3,4-dihydro-2*H*-benzopyran-4-yl]diphenylacetamide (7).** Prepared from **11** by

method 8. ^{1}H NMR (300 MHz, $CDCl_3$): 7.23 (6H, m), 7.05 (5H, m), 6.85 (5H, m), 6.62 (2H, d, J = 8.4 Hz), 5.72 (2H, m), 4.98 (1H, s), 4.18 (2H, m), 2.94 (1H, dt, J = 4, 1, 10.0 Hz). MS (FAB): 436 (M^+, 54), 225 (25), 212 (51), 167 (100). CHN: calcd for $C_{29}H_{25}NO_3$ C = 79.98, H = 5.79, N = 3.22 found C = 79.61, H = 5.81, N = 3.38. Mp: 202−203 °C, white solid. TLC: R_f = 0.13 (5% EtOAc/CH_2Cl_2), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/MeOH.

***N*-(7-Hydroxy-1,2,3,4-tetrahydronaphthalen-1-yl)diphenylacetamide (31c).** Prepared from **31b**. ^{1}H NMR (200 MHz, $CDCl_3$): 7.25 (10H, m, Ar), 6.88 (1H, d, J = 8.2 Hz, Ar), 6.60 (2H, m, Ar), 5.85 (1H, m), 5.17 (1H, m), 4.97 (1H, s, PhC*H*), 2.61 (2H, t, J = 5.8 Hz), 2.00 (1H, m), 1.67 (3H, m). CHN: calcd for $C_{25}H_{23}NO_2$ C = 80.64, H = 6.49, N = 3.92; found C = 80.59, H = 6.45, N = 4.02. MS (FAB): 358 (M^+, 100), 212 (62). Mp: 150.5−151.5 °C. TLC: R_f = 0.19 (30% EtOAc/hexane), UV, Ce stain. Purification: SiO_2 chromatography (30−50% EtOAc/hexane), recrystallized from EtOAc/hexane.

***N*-[*cis*-2-(4-Hydroxyphenyl)cyclohexyl]diphenylacetamide (32c).** Prepared from **32a**. ^{1}H NMR (200 MHz, $CDCl_3$/CD_3OD): 7.25 (6H, m, Ar), 7.02 (2H, m, Ar), 6.76 (6H, m, Ar), 4.82 (1H, s, PhC*H*), 4.38 (1H, m), 2.79 (1H, m), 1.96 (1H, m), 1.62 (4H, m), 1.28 (1H, m), 1.01 (2H, m). CHN: calcd for $C_{26}H_{27}NO_2$ C = 81.01, H = 7.06, N = 3.63; found C = 81.12, H = 7.13, N = 3.75. MS (FAB):386 (M^+, 100), 190 (26), 174 (76), 167 (91). Mp: 207−208 °C. TLC: R_f = 0.14 (30% EtOAc/hexane), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/hexane.

***N*-[*trans*-2-(4-Hydroxyphenyl)cyclohexyl]diphenylacetamide (32d).** Prepared from **32b**. ^{1}H NMR (200 MHz, $CDCl_3$/CD_3OD): 7.19 (6H, m, Ar), 6.90 (4H, m, Ar), 6.69 (4H, m, Ar), 4.72 (1H, s, PhC*H*), 4.02 (1H, dt, J = 4.0, 11.4 Hz, $PhCHCH_2$), 2.12 (2H, m), 1.79 (3H, m), 1.28 (4H, m). CHN: calcd for $C_{26}H_{27}NO_2$ C = 81.01, H = 7.06, N = 3.63; found C = 80.95, H = 7.04, N = 3.85. MS (FAB): 386 (M^+, 100), 212 (21). Mp: 187−188 °C. TLC: R_f = 0.13 (30% EtOAc/hexane), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 57%.

Desaryl Derivatives 31 and 32. Method 9: *N*-(7-Methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)diphenylacetamide (31b). A mixture of 7-methoxytetralone (2.0 g, 11.3 mmol), hydroxylamine hydrochloride (2.4 g, 34 mmol), and sodium acetate (2.8 g, 34 mmol) in methanol (20 mL) and water (2 mL) was refluxed overnight. The reflux condensor was removed, and the reaction mixture was concentrated to approximately one-half of its original volume. Water (3 mL) was added, and the mixture was allowed to cool to room temperature. A precipitate formed and was collected *via* vacuum filtration. The precipitate was washed with water and hexanes and dried in vacuo to provide 2.1 g (97%) of 7-methoxytetralone 1-oxime as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): 7.95 (1H, bs, O*H*), 7.46 (1H, d, J = 2.8 Hz, Ar), 2.09 (1H, d, J = 8.4 Hz, Ar), 6.89 (1H, dd, J = 2.8, 8.4 Hz, Ar), 3.83 (3H, s, OCH_3), 2.82 (2H, t, J = 6.6 Hz), 2.71 (2H, t, J = 6.0 Hz), 1.86 (2H, m). CHN: calcd for $C_{11}H_{13}NO_2$ C = 69.09, H = 6.85, N = 7.32; found C = 68.94, H = 6.76, N = 7.31. MS (CI): 205 (M^+, 100). Mp: 85−86 °C. TLC: R_f = 0.16 (15% EtOAc/hexane), UV, Ce stain.

7-Methoxytetralone 1-oxime (1.85 g, 9.67 mmol) was placed in a Parr bottle, dissolved in a minimum of EtOAc (∼20 mL), diluted with methanol (∼100 mL), and purged with N_2; 10% Pd/C (0.20 g) was added, and the resulting suspension was placed in a Parr apparatus, purged with H_2, and shaken at 60 psi of H_2 overnight. TLC (15% EtOAc/hexane) indicated consumption of the oxime. The suspension was filtered through Celite, and the filter cake was well washed with methanol. The filtrate was concentrated to provide 1.55 g (91%) of 7-methoxy-1,2,3,4-tetrahydronaphthylamine as a yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): 6.98 (2H, m Ar), 6.74 (1H, dd, J = 2.8, 8.4 Hz, Ar), 3.96 (1H, t, J = 5.8 Hz, Ar), 3.80 (3H, s, OCH_3), 2.71 (2H, m), 1.97 (4H, m), 1.72 (2H, m). MS (CI): 178 (M^+, 26), 161 (100).

7-Methoxy-1,2,3,4-tetrahydronaphthylamine was acylated with diphenylacetyl chloride as previously described to provide *N*-(7-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)diphenylacetamide (**31b**) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): 7.30 (10H, m, Ar), 6.97 (1H, d, J = 8.4 Hz, Ar), 6.70 (2H, m, Ar), 5.82 (1H, m), 5.23 (1H, m), 4.97 (1H, s, PhC*H*), 3.66 (3H, s, OCH_3), 2.67 (2H, t, J = 5.8 Hz), 2.09 (1H, m), 1.72 (3H, m). CHN: calcd for $C_{25}H_{25}NO_2$ C = 80.83, H = 6.78, N = 3.77; found C = 80.67, H = 6.78, N = 3.98. MS (CI): 372 (M^+, 100), 212 (86), 161 (25). Mp: 154−155 °C. Purification: recrystallized from CH_2Cl_2/MeOH. TLC: R_f = 0.34 (30% EtOAc/hexane), UV, Ce stain.

***N*-(1,2,3,4-Tetrahydronaphthalen-1-yl)diphenylacetamide (31a).** Prepared from 1-tetralone as described in the preparation of **31b**. ^{1}H NMR (300 MHz, $CDCl_3$): 7.30 (10H, m, Ar), 7.11 (4H, m, Ar), 5.79 (1H, m, N*H*), 5.24 (1H, m, NC*H*), 4.96 (1H, s, PhC*H*), 2.74 (2H, t, J = 5.8 Hz), 2.07 (1H, m), 1.73 (3H, m). CHN: calcd for $C_{24}H_{23}NO$ C = 84.42, H = 6.79, N = 4.10; found C = 83.69, H = 6.75, N = 4.21. MS (EI): 341 (M^+, 1), 167 (38), 131 (100), 91 (27). HRMS: calcd for $C_{24}H_{24}NO$ (M^+), 342.2858; found, 342.1878. Mp: 147−149 °C. TLC: R_f = 0.25 (20% EtOAc/hexane), UV, Ce stain. Purification: recrystallized from EtOAc/hexane.

Method 10: *N*-[*cis*-2-(4-Methoxyphenyl)cyclohexyl]diphenylacetamide (32a). *t*-BuLi (200 mL, 340 mmol, 1.7 M in pentane) was added to a −78 °C solution of 4-methoxybromobenzene (21.3 mL, 170 mmol) in THF (500 mL).[12] After 30 min, a −78 °C solution of boron trifluoride etherate (20.9 mL, 170 mmol) in THF (100 mL) was added *via* cannula. Cylclohexane oxide (5.73 mL, 56.7 mmol) was added. After 15 min the reaction was quenched at −78 °C with saturated sodium bicarbonate, and the mixture was allowed to warm to room temperature. The resulting solution was transferred to a separatory funnel and extracted with ether (3×). The etheral extracts were combined, washed with water and brine, dried over sodium sulfate, and concentrated onto silica gel. The resulting free flowing powder was loaded onto a chromatography column prepacked with silica gel and 15% EtOAc/hexanes. Elution with 15−40% EtOAc/hexanes provided 3.71 g (32%) of *trans*-2-(4-methoxyphenyl)cyclohexan-1-ol (**34**) as a white solid. ^{1}H NMR (200 MHz, $CDCl_3$): 7.19 (2H, d, J = 8.9 Hz, Ar), 6.79 (2H, d, J = 8.9 Hz, Ar), 3.83 (3H, s, OCH_3), 3.59 (1H, m), 2.38(1H, m), 2.12(1H, m), 1.83(3H, m), 1.53(2H, m), 1.42(3H, m). CHN: calcd for $C_{13}H_{18}O_2$ C = 75.69, H = 8.80; found C = 75.84, H = 8.69, N = 3.63. MS (EI): 206 (M^+, 22), 147 (30), 121 (100), 91 (15). TLC: R_f = 0.29 (30% EtOAc/hexane), UV, Ce stain.

A portion of *trans*-2-(4-methoxyphenyl)cyclohexan-1-ol (**34**) was then converted to *cis*-2-(4-methoxyphenyl)cyclohexylamine and acylated with diphenylacetyl chloride as described in the preparation of **5a** to provide *N*-[*cis*-2-(4-methoxyphenyl)cyclohexyl]diphenylacetamide (**32a**). ^{1}H NMR (200 MHz, $CDCl_3$): 7.26 (6H, m, Ar), 6.99 (4H, m, Ar), 6.80 (4H, m, Ar), 5.21 (1H, d, J = 7.8 Hz), 4.84 (1H, s, PhC*H*), 4.40 (1H, m), 3.84 (3H, s, OCH_3), 2.85 (1H, m), 2.02 (1H, m), 1.71 (3H, m), 1.58 (2H, m), 1.29 (1H, m), 1.06 (1H, m). CHN: calcd for $C_{27}H_{29}NO_2$ C = 81.17, H = 7.32, N = 3.51; found C = 81.12, H = 7.10, N = 3.63. MS (CI): 400 (M^+, 100). Mp: 150−152 °C. TLC: R_f = 0.25 (30% EtOAc/hexane), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/MeOH.

Method 11: *N*-[*trans*-2-(4-Methoxyphenyl)cyclohexyl]diphenylacetamide (32b). Pyridine (1.02 mL, 12.60 mmol), trifluoracetic acid (0.49 mL, 6.30 mmol), and dicyclohexylcarbodiimide (8.67 g, 42.0 mmol) were sequentially added to a room temperature solution of *trans*-2-(4-methoxyphenyl)cyclohexan-1-ol (**34**) (2.17 g, 10.5 mmol) in a solution of DMSO (10 mL) and CH_2Cl_2 (20 mL) overnight. TLC analysis indicated that starting material remained. Additional pyridine (0.5 mL, 6.2 mmol), trifluoroacetic acid (0.25 mL, 3.3 mmol), and dicyclohexylcarbodiimide (2.0 g, 9.7 mmol) were sequentially added, and the mixture was stirred overnight. The reaction mixture was diluted with hexane, and filtered through a plug of silica gel eluting with 30% EtOAc/hexane. The filtrate was concentrated, taken up in ether, transferred to a separatory funnel, washed with water and brine, dried over sodium sulfate, and concentrated. The residue was chromatographed on silica gel (20% EtOAc/hexane) to give 1.99 g (93%) of 2-(4-methoxyphenyl)cyclohexanone (**36**). A portion was recrystallized from EtOAc/hexanes to provide white crystals.

^{1}H NMR (200 MHz, $CDCl_3$): 7.07 (2H, d, J = 8.6 Hz, Ar), 6.88 (2H, d, J = 8.8 Hz, Ar), 3.80 (3H, s, OCH_3), 3.57 (1H, dd, J = 8.4, 17.4 Hz), 2.50 (2H, m), 2.19 (2H, m), 1.89 (4H, m). CHN: calcd for $C_{13}H_{16}O_2$ C = 76.44, H = 7.90; found C = 76.16, H = 7.79. MS (CI): 205 (M^+,100).

2-(4-Methoxyphenyl)cyclohexanone (**36**) was converted to *trans*-2-(4-methoxyphenyl)cyclohexylamine and acylated with diphenylacetyl chloride as described in the preparation of **5e** (method 8) to provide *N*-(*trans*-2-(4-methoxyphenyl)cyclohexyl]-diphenylacetamide (**32b**). ^{1}H NMR (200 MHz, $CDCl_3$): 7.15 (8H, m, Ar), 6.89 (4H, m, Ar), 6.72 (2H, m, Ar), 5.21 (1H, d, J = 8.8 Hz), 4.75 (1H, s, PhC*H*), 4.08 (1H, m), 3.85 (3H, s, OCH_3), 2.15 (2H, m), 1.76 (3H, m), 1.31 (4H, m). CHN: calcd for $C_{27}H_{29}NO_2$ C = 81.17, H = 7.32, N = 3.51; found C = 80.80, H = 7.18, N = 3.65. MS (FAB): 192 (M^+, 100), 174 (52), 169 (90). Mp: 192.5−193 °C. TLC: R_f = 0.28 (30% EtOAc/hexane), UV, Ce stain.

***N*-[*trans*-2-(4-Hydroxyphenyl)cyclohexyl]diphenylacetamide (32d).** Prepared from **32b**. ^{1}H NMR (200 MHz, $CDCl_3$/CD_3OD): 7.19 (6H, m, Ar), 6.90 (4H, m, Ar), 6.69 (4H, m, Ar), 4.72 (1H, s, PhC*H*), 4.02 (1H, dt, J = 4.0, 11.4 Hz, $PhCHCH_2$), 2.12 (2H, m), 1.79 (3H, m), 1.28 (4H, m). CHN: calcd for $C_{26}H_{27}NO_2$ C = 81.01, H = 7.06, N = 3.63; found C = 80.95, H = 7.04, N = 3.85. MS (FAB): 386 (M^+, 100), 212 (21). Mp: 187−188 °C. TLC: R_f = 0.13 (30% EtOAc/hexane), UV, Ce stain. Purification: recrystallized from CH_2Cl_2/hexane. Yield: 57%.

Method 12: Preparation of Enantiomerically Pure *cis*-*N*-[2-(4-Hydroxyphenyl)indan-1-yl]diphenylacetamide (4a,b). A solution of 2-(4-methoxyphenyl)-1-indanone (**8**) (67.8 g, 285 mmol), methoxylamine hydrochloride (35.7 g, 427 mmol), sodium acetate (35.0 g, 427 mmol) and methanol (750 mL) was heated to 60−65 °C for 5 h, cooled to room temperature, and stirred overnight. The reaction mixture was diluted with water and extracted with 50% ethyl acetate/hexane. The extracts were combined, washed with brine, dried over anhydrous sodium sulfate, and concentrated to obtain 72.1 g (100%) of 2-(4-methoxyphenyl)-1-indanone oxime methyl ether.

Borane (700 mL, 700 mmol, 1 M in THF) was added to 2-(4-methoxyphenyl)-1-indanone oxime methyl ether (72.1 g, 285 mmol) at room temperature. The mixture was stirred at room temperature overnight, refluxed for 5 h, and cooled to room temperature. The reaction was quenched water. When bubbling ceased, the mixture was acidified to ca. pH 1 with concentrated HCl, heated to 50 °C, vigorously stirred at for 2 h, cooled to room temperature, and stirred for an additional 5 h. The resulting mixture was diluted with water and extracted with ether. The aqueous phase was basified to pH 9−10 with solid KOH and extracted with ether. The latter extracts were combined, washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was partially purified by dissolving in ethyl acetate and filtering through silica gel to give 2-(4-methoxyphenyl)indanamine (68 g, 100%) as a mixture of cis and trans isomers (ca. 10:1). MS (EI): 239 (M^+, 47), 222 (48), 121 (100).

2-(4-Methoxyphenyl)indanamine (68 g, cis:trans = 10:1) was dissolved in hot ethanol (2.5 L). A hot solution of di-*p*-toluoyl-D-tartaric acid (100 g) in ethanol (500 mL) was added, and the resulting solution was allowed to stand overnight. The resulting crystals were washed with ethanol and 50% ether/hexane and dried to provide 74 g (≥98% ee) of the tartrate salt corresponding to **4b** (determined by free basing the amine salt and subsequent HPLC analysis: Chiracel OD column, 15% 2-propanol/hexane, 1 mL/min, t_R = 10.28 min), 6:1 cis:trans. The filtrate was concentrated to ca. 500 mL, basified with aqueous sodium hydroxide, and extracted with ether. The extracts were combined, washed with brine, dried over anhydrous sodium sulfate, and concentrated. The residue was dissolved in hot ethanol (1 L) and treated with di-*p*-toluoyl-L-tartaric acid (55 g) in hot ethanol (700 mL), and the resulting solution was allowed to stand overnight. The resulting crystals were collected by suction filtration, washed with ethanol and 50% ether/hexane, and dried to provide 63 g (≥98% ee) of the tartrate salt corresponding to the active enantiomer **4a** (determined by free basing the amine salt and subsequent HPLC analysis: Chiracel OD column, 15% 2-propanol/hexane, 1 mL/min, t_R = 8.52 min), 13:1 cis:trans. The crystals were partitioned between ether and aqueous sodium hydroxide, transferred to a separatory funnel, and extracted with ether. The etheral extracts were combined, washed with aqueous sodium hydroxide and brine, dried over anhydrous sodium sulfate, and concentrated to provide 24.7 g (36%) of 2-(4-methoxyphenyl)indanamine. Total recovery: 24.7 g, 36% yield.

The resolved 2-(4-methoxyphenyl)indanamine (24.7 g, 103 mmol) was dissolved in dichloromethane and treated in the following order with 1-hydroxybenzotriazole (14.0 g, 103 mmol), diphenylacetic acid (26.3 g, 124 mmol), and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (25.7 g, 134 mmol). After 30 min the mixture was poured into water and extracted with 50% ethyl acetate/hexanes. The extracts were combined, washed with 1 M HCl, 1 M K_2CO_3, and brine, dried over anhydrous sodium sulfate, and concentrated. The residue was recrystallized from dichloromethane/hexane to provide 27.8 g of *cis*-*N*-[2-(4-methoxyphenyl)indan-1-yl]diphenylacetamide free of the corresponding trans isomer.

Boron tribromide (160 mL, 160 mmol, 1 M in dichloromethane) was dropwise added to a room temperature solution of *cis*-*N*-[2-(4-methoxyphenyl)indan-1-yl]diphenylacetamide (27.8 g, 64.2 mmol) in dichloromethane (500 mL). When TLC indicated that the starting material had been consumed, the mixture was poured into water and extracted with ether. The extracts were combined, washed with water, 10% $Na_2S_2O_3$, and brine, dried over anhydrous sodium sulfate, and filtered through a pad of silica gel, eluting with dichloromethane followed by 50% dichloromethane/ether. The filtrate was concentrated, and the resulting residue was recrystallized from 50% dichloromethane/hexane. The crystals were collected by suction filtration, washed with 5/1 hexane/ethyl acetate followed by hexanes, and dried to provide 24.7 g (92%) of *cis*-*N*-[2-(4-hydroxyphenyl)indan-1-yl]diphenylacetamide (**4a**) as white needles, 100% ee by HPLC comparison with racemate cis **4** (reversed phase ES-OVM column, 23% CH_3CN in 0.02 M phosphate buffer, **4a** t_R = 12.0 min, **4b** t_R = 9.38 min). ^{1}H NMR (400 MHz, $CDCl_3$): 7.16 (10H, m), 6.96 (2H, d, J = 8.2 Hz), 6.92 (2H, d, J = 8.1 Hz), 6.70 (2H, d, J = 8.4 Hz), 6.54 (2H, d, J = 8.5 Hz), 5.82 (1H, t, J = 8.6 Hz), 5.37 (1H, d, J = 9.2 Hz), 5.27 (1H, s), 4.74 (1H, s), 3.86 (1H, dt, J = 3.7, 7.9 Hz), 3.31 (1H, dd, J = 7.9 Hz, 16.2 Hz), 3.05 (1H, dd, J = 3.6, 16.4 Hz). Mp: 165.5−167.5 °C. MS (CI): 420 (M^+, 100). CHN: calcd for $C_{29}H_{25}NO_2$ C = 83.03, H = 6.01, N = 3.34; found C = 83.14, H = 5.67, N = 3.29. Optical rotation: 25.1 °C, concentrated 11.62 mg/2 mL of EtOH, +8.4°.

The opposite enantiomer *cis*-*N*-[2-(4-hydroxyphenyl)indan-1-yl]diphenylacetamide (**4b**) can be similarly prepared by using di-*p*-toluoyl-L-tartaric acid and di-*p*-toluoyl-D-tartaric acid in the reverse order. ^{1}H NMR (300 MHz, $CDCl_3$): 7.21 (10H, m), 7.02 (4H, m), 6.75 (2H, d), 6.56 (2H, d), 5.85 (1H, t), 5.38 (1H, d), 4.85 (1H, s), 4.74 (1H, s), 3.39 (1H, m), 3.36 (1H, dd), 3.08 (1H, dd). Mp: 164−165 °C.

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