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The Triflic Acid-Mediated Cyclization Reactions of *N*-Cinnamoyl-1-Naphthylamines

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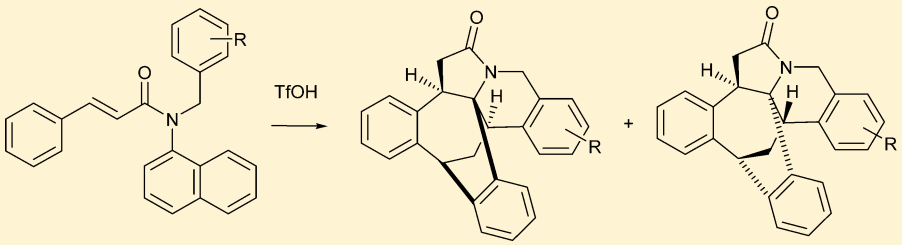
Supporting Information



ABSTRACT: *N*-Cinnamoyl-1-naphthylamines undergo a cyclization reaction with triflic acid to form 4-phenyl-3,4-dihydro-1*H*-naphth[1,8-*bc*]azepin-2-ones and 4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-ones. However, the *N*-benzyl analogues also undergo a unique cascade reaction to form novel heptacyclic structures via a 1,2-addition followed by a 4-addition to the naphthalene. With an electron-rich *N*-benzyl substituent, the heptacycle is the sole product.

INTRODUCTION

An amine and one or more aryl groups are key structural features of many modulators of G-protein-coupled receptors. We are therefore interested in approaches to the synthesis of structures that have a unique special disposition of these functional groups in order to identify more potent and selective modulators. We have recently reported that *N*-benzylcinnamanilide (**2a**) reacts with triflic acid (TfOH) to form 1-benzyl-4-phenyl-2,4-dihydro-1*H*-quinoline-2-one (**3a**) (80% yield) and 2,5-diphenylbenzazepin-3-one **4a** (7% yield) (Scheme 1).[1] A further study of factors determining the course of the reaction, with particular emphasis on improving the yield of the benzazepinone, has recently been published.[2]

This paper describes the results obtained from investigating the TfOH-mediated cyclization of *N*-cinnamoyl-1-naphthylamines, for which either a six-membered cyclization onto the 2-position or a seven-membered cyclization onto the 8-position could occur.

RESULTS AND DISCUSSION

The *N*-substituted-*N*-cinnamoyl-1-naphthylamines required for this study were readily prepared in high yield by the alkylation of *N*-cinnamoyl-1-naphthylamine[3] with KOt-Bu and the appropriate alkyl halide. The results of the TfOH-mediated cyclizations of the *N*-alkyl derivatives are shown in Table 1. Previously, it had been reported that **5a** was photolytically converted to **6a** in 12% yield;[3] no other products were reported, and **5b** did not react. In contrast, the reaction of **5a** with TfOH (Table 1, entry 1) gave mainly the six-membered cyclization product **6a** (78% yield) together with only a small amount of the seven-membered **7a** (11% yield). However, the *N*-methyl analogue **5b** (entry 2) gave a higher yield of seven-membered product **7b** (26% yield), though six-membered cyclization to **6b** (70% yield) still predominated. Increasing the size of the *N*-alkyl group to *n*-butyl (**5c**; entry 3) gave yet again an incremental increase in the yield of the seven-membered product **7c** (45% yield), and the isopropyl analogue **5d** (entry 4) gave seven-membered **7d** as the major product (62% yield). Thus, it would appear that increasing the bulk of the N-substituent favors seven-membered cyclization. Interestingly, whereas the ^{1}H NMR spectra of **6a**−**c** at ambient temperatures were time-averaged through facile conformational mobility, the spectrum of **6d** was poorly resolved. However, upon cooling to −30 °C, an ^{1}H NMR spectrum of two conformers for **6d** was obtained. In contrast, the ^{1}H NMR spectra of **7a**−**c** were poorly resolved at ambient temperatures, but again, upon cooling to −30 °C, well-resolved spectra of two conformers were obtained. For **7d**, a well-resolved ^{1}H NMR spectrum of two conformers was obtained at ambient temperatures.

The expected products from the cyclization of *N*-benzyl-substituted **5e** (entry 5) were **6e**, **7e**, and **8**, the latter formed via cyclization onto the benzyl group. From the TLC of the reaction mixture, it appeared that three products were formed. From a separation using a SiO_2 column, the least polar product was identified as **7e** (32% yield). The most polar fraction from the SiO_2 column gave a product that had the same molecular weight as **5e** (14% yield) and showed nine aliphatic protons in the ^{1}H NMR spectrum due to CH_2, CH_2CH, and $CHCH_2CH$ fragments. In the aromatic area, 12 protons were observed, the multiplicities of which indicated the presence of three ortho-disubstituted benzene rings. From a detailed analysis of 2D ^{1}H,^{1}H NOESY, ^{1}H,^{13}C HMBC, and ^{13}C,^{13}C INADEQUATE spectra combined with initial molecular mechanics calculations,

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Scheme 1

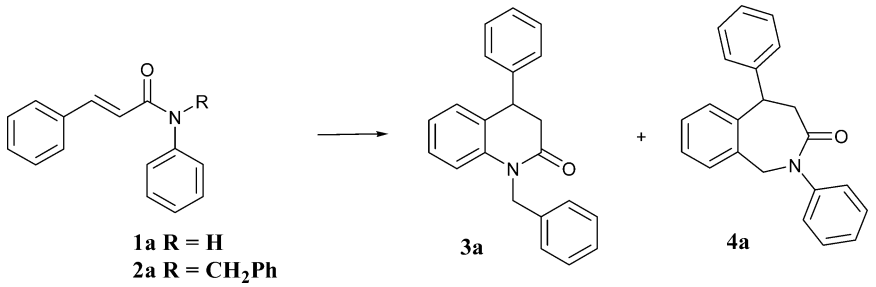
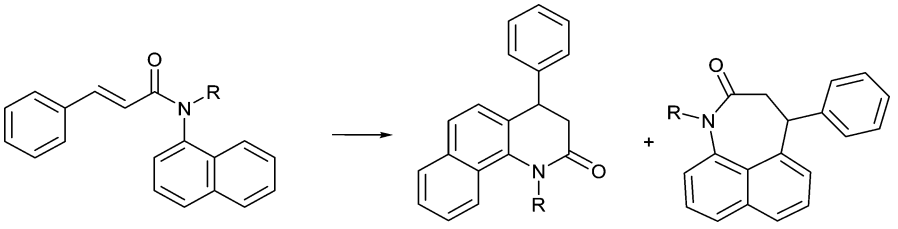


Table 1. Cyclization of *N*-Alkyl-*N*-cinnamoyl-1-naphthylamines



entry	amide	R	product	yield (%)	product	yield (%)
1	**5a**	H	**6a**	78	**7a**	11
2	**5b**	Me	**6b**	70	**7b**	26
3	**5c**	n-Bu	**6c**	47	**7c**	45
4	**5d**	i-Pr	**6d**	31	**7d**	62
5[a]	**5e**	Bn	**6e**	0	**7e**	0

[a]See the text.

the structure was assigned as **9e** (Table 2 and Figure 1). Further quantum-mechanical calculations were carried out using M06-2X/cc-pVTZ geometry optimizations, which have been shown to predict reliable molecular geometries in agreement with neutron and X-ray diffraction methods in the case of cyclic molecules, and gave the final geometry of **9e**.[4]

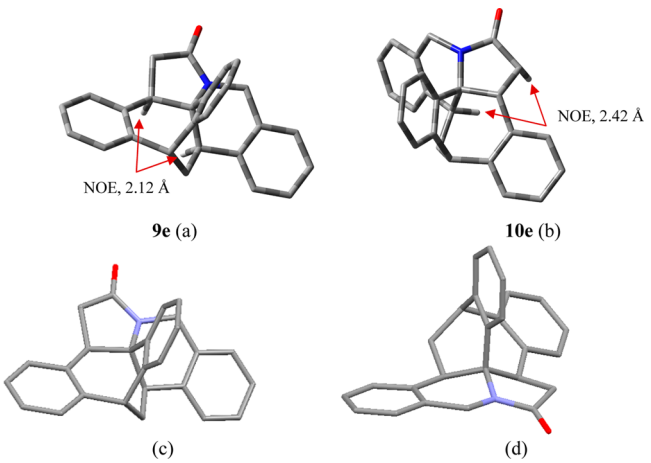
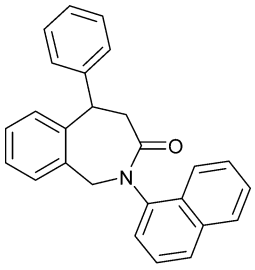


Figure 1. (a) Structure of **9e** from NMR/QM analysis. A strong NOE between the 8- and 19-CH protons is observed. The interproton distance of 2.16 Å is from M06-2X/cc-pVTZ IEFPCM($CHCl_3$) calculations. For comparison, the corresponding calculated distance in **10e** is 3.60 Å. (b) Structure of **10e** from NMR/QM analysis. A strong NOE between the 19-CH proton and a 9-CH_2 proton is observed. The interproton distance of 2.49 Å is from M06-2X/cc-pVTZ IEFPCM($CHCl_3$) calculations. For comparison, the corresponding distance in **9e** is 4.36 Å. (c, d) Two views of **9e** from the X-ray structure.



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The middle fraction contained two compounds that were readily separable by column chromatography on Al_2O_3. The more polar compound was identified as **6a** (12% yield). However, the less polar compound again had the same molecular weight as the starting material **5e** (10% yield) and gave ^1H and ^{13}C NMR spectra similar to those of **9e**. In a manner analogous to that for **9e**, the structure of this compound was established as **10e**, a diastereomer of **9e**, and the two structures **9e** and **10e** were distinguished on the basis of the NOEs observed (see Figure 1). The structure of **9e** was confirmed by single-crystal X-ray analysis (Figure 1). Satisfyingly, the calculated interproton distances between the 8-CH and 19-CH protons and between the 19CH proton and one of the 9-CH_2 protons are in close agreement with the values of 2.08 and 4.26 Å measured from the structure determined by X-ray analysis.

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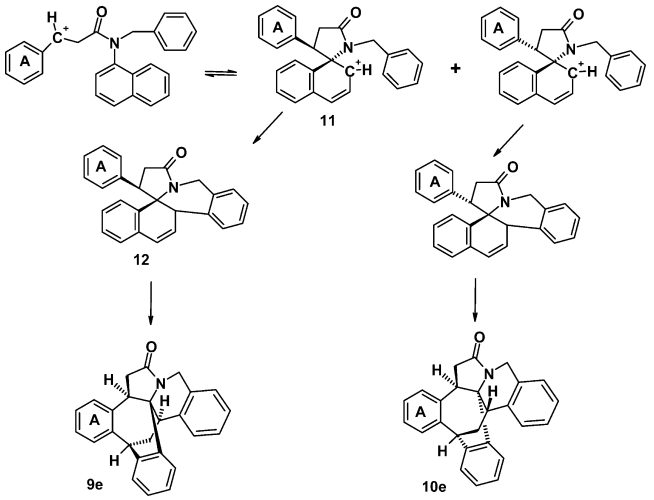
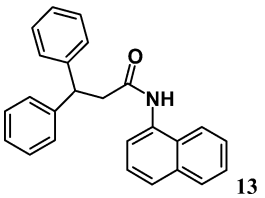
We believe that **9e** and **10e** are formed via initial addition of the carbocation to the 1-position of the naphthalene to form spiro carbocation intermediate **11**. This would bring the benzyl group into close proximity to the carbocation, which cyclizes to give the 1,2-dihydro derivative **12**. Under the strongly acidic conditions, the olefin is protonated to give yet another benzylic carbocation, which cyclizes onto the phenyl ring A to form the seven-membered ring in **9e**. The diastereomer **10e** would be formed by the alternative initial addition of the carbocation to the naphthalene.

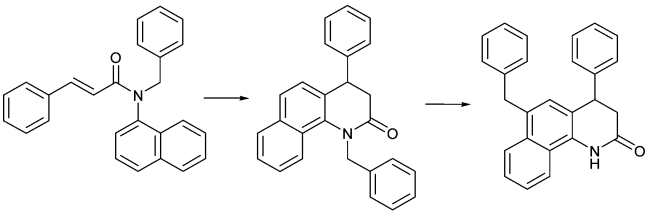


In order to test this hypothesis, **5a** was reacted with TfOH in benzene in an attempt to trap the NH-spiro intermediate related to **11**. However, the only products isolated were **13** (77% yield) and **6a** (19% yield). The structure of **13** was confirmed by an independent synthesis from 3,3-diphenylpropionyl chloride[5] and 1-naphthylamine.



If the proposed mechanism for the formation of **9e** and **10e** is correct, the introduction of electron-donating groups onto the benzyl group should facilitate the trapping of the initial carbocation **11** and result in a greater preference for the formation of the polycyclic amides. The results obtained with substituted benzyls are shown in Table 2. The reaction of 4-methyl-substituted **5f** (entry 2) with TfOH did indeed give the two polycycles **9f** and **10f** in higher yields (44% and 25% yields respectively) together with **6a** (22% yield). However, 3,5-dimethyl-substituted **5g** (entry 3) gave almost exclusively the polycycles **9g** (46% yield) and **10g** (39% yield). Surprisingly, from the reaction of 3,5-dimethoxy-substituted **5h** with TfOH (entry 4), none of the less polar polycycle and only a 10% yield of the more polar polycycle was obtained. Instead, products expected from a benzyl group with electron-withdrawing substituents were obtained, viz., **6h** (37% yield) and **7h** (30% yield). On the basis of the hypothesis that the 3,5-dimethoxybenzyl group is protonated by TfOH and thus acts more like an electron-withdrawing substituent, the cyclization using the weaker polyphosphoric acid (PPA) was investigated. PPA had previously been reported to promote the cyclization of cinnamanilide.[6] Satisfyingly, **9h** and **10h** were now obtained in reasonable yields of 46% and 27% respectively. A key feature in the ^{1}H NMR spectrum that defines the assignment of the stereochemistry is the chemical shifts of the 11-CH protons, which for **9e**–**h** appear at δ 4.67–4.76 and 4.93–4.99, whereas for **10e**–**h** they appear at δ 4.56–4.65 and 5.20–5.38.

Following the successful cyclization of **5h** with PPA, the cyclizations of other cinnamoylnaphthylamines were investigated. In contrast to the literature,[7] PPA-mediated cyclization of **5a** gave **7a** (10% yield) in addition to **6a** (82% yield), very similar to the results obtained with TfOH (Table 1, entry 1). However, PPA-mediated cyclization of **5e** gave none of the polycyclic products **9e** and **10e**. Instead a complex mixture of products was obtained within an R_f band of 0.1 in multiple solvent systems. However, a product isolated through crystallization of a partially purified mixture from Et_2O was identified as **14**. In particular, the signal for the 5-CH proton was a singlet at δ 7.02, and NOEs were observed between the 7-CH proton and the benzylic CH_2 protons and between the 10-CH proton and the NH proton. From NMR comparisons and MS, it would appear that the other products are isomers of **14**, with the benzyl group at other positions on the naphthalene rings. None of these products were found in the reaction of **5e** with TfOH. We believe that these compounds are formed through cyclization to give **6e**. *N*-Debenzylation then gives a benzyl carbocation, which reacts intermolecularly to alkylate the naphthalene ring. Indeed **6e**, prepared from **6a** by *N*-benzylation, reacted with PPA to give a similar mixture of products.



CONCLUDING REMARKS

N-Alkyl-*N*-cinnamoyl-1-naphthylamines undergo a TfOH-mediated cyclization to give 4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-ones and 4-phenyl-3,4-dihydro-1*H*-naphth[1,8-*bc*]azepin-2-ones via cyclization onto the 2- and 8-positions of the naphthalene, respectively. Although cyclization onto the 2-position is inherently more favored, as the size of the *N*-alkyl group increases, relatively more of the azepinone is formed. However, *N*-benzyl analogues also undergo a unique cascade reaction to form a diastereomeric pair of novel heptacycles. The presence of electron-donating substituents on the benzyl group favors formation of the heptacycle.

EXPERIMENTAL SECTION

General Experimental. Commercial reagents and solvents were used as received, unless otherwise stated. Thin-layer chromatography was performed on aluminum plates precoated with silica gel 60 F_{254} and developed by exposure to UV light and/or potassium permanganate solution followed by heating. Flash chromatography was carried out on silica gel (32–70 μm). Proton and carbon NMR spectra were obtained in $CDCl_3$ at 400, 500, or 600 MHz and at 127 or 151 MHz, respectively. Chemical shifts (δ) are expressed in parts per million (ppm) and are referenced to the residual solvent peak. The

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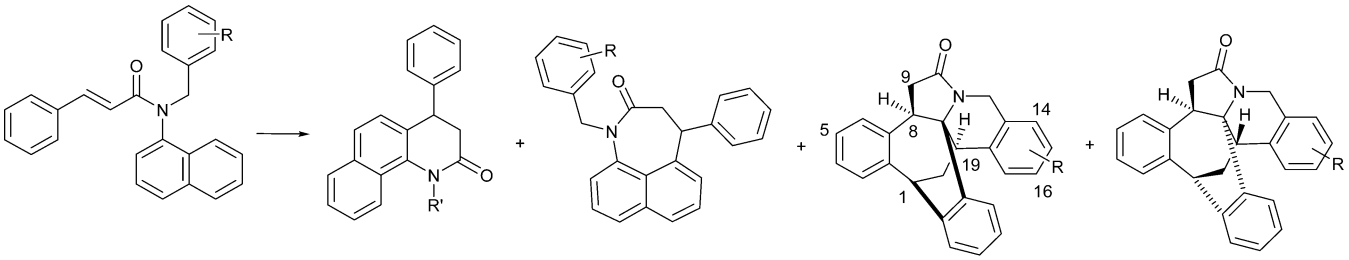
Table 2. Cyclization of *N*-(Substituted benzyl)-*N*-cinnamoyl-1-naphthylamines



5e-h **6a** R' = H, **6h** R' = 3,5-dimethoxybenzyl **7e-h** **9e-h** **10e-h**

entry	amide	R	acid	product	yield (%)	product	yield (%)	product	yield (%)	product	yield (%)
1	**5e**	H	TfOH	**6a**	12	**7e**	32	**9e**	14	**10e**	10
2	**5f**	4-Me	TfOH	**6a**	22	**7f**	0	**9f**	44	**10f**	25
3	**5g**	3,5-di-Me	TfOH	**6a**	0	**7g**	0	**9g**	46	**10g**	39
4	**5h**	3,5-di-OMe	TfOH	**6h**	37	**7h**	30	**9h**	10	**10h**	0
5	**5h**	3,5-di-OMe	PPA	**6a**	7	**7h**	16	**9h**	46	**10h**	27
6	**5e**	H	PPA[a]	**6a**	0	**7e**	0	**9e**	0	**10e**	0

[a]See the text.

following abbreviations are used to describe the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Gaussian resolution enhancement and zero filling were used for accurate measurements of J_{HH} couplings and for the analysis of overlapping signals. Low- and high-resolution mass spectra were recorded on a double-focusing magnetic sector mass spectrometer. Melting points are uncorrected.

***N*-Cinnamoyl-1-naphthylamine (5a).** Cinnamoyl chloride (2.5 g, 15 mmol) was added to a stirred suspension of 1-naphthylamine (2.1 g, 15 mmol) in EtOAc (150 mL) and *N*,*N*-dimethylaniline (2.5 mL, 20 mmol) at room temperature. A thick precipitate started to form, and after 2 h, the solid was collected, washed with Et_2O (2 × 50 mL), and dried to give **5a** (4.1 g, 83%) as a gray solid; mp 225−227 °C (MeOH) (lit. 225−227 °C[3]); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.16 (1H, d, J = 15.8 Hz), 7.41 (1H, t, J = 7.2 Hz), 7.46 (2H, t, J = 7.3 Hz), 7.52 (1H, t, J = 7.9 Hz), 7.56 (2H, ddt, J = 1.6, 7.5, 7.7 Hz), 7.64 (1H, d, J = 15.8 Hz), 7.66 (2H, d, J = 7.0 Hz), 7.77 (1H, d, J = 8.2 Hz), 7.91 (1H, d, J = 7.2 Hz), 7.95 (1H, dd, J = 1.6, 8.2 Hz), 8.15 (1H, d, J = 7.9 Hz), 10.20 (1H, s); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 120.9 (CH), 122.3 (CH), 122.5 (CH), 125.1 (CH), 125.6 (CH), 125.9 (CH), 127.8 (CH), 128.2 (CH), 129.0 (CH), 129.8 (CH), 133.5 (C), 133.7 (C), 134.9 (C), 140.3 (CH), 164.3 (C).

General Procedure for the Synthesis of *N*-Alkyl-*N*-cinnamoyl-1-naphthylamines 5b−h. *N*-Cinnamoyl-1-naphthylamine (1.4 g, 5.0 mmol), alkyl iodide (10 mmol) or benzyl bromide (5.0 mmol), and KBu^{t}O (0.55 g, 5.0 mmol) in THF (100 mL) were stirred and heated under reflux for 2 h. After the mixture was cooled, the THF was removed by rotary evaporation, and the residue was portioned between H_2O (50 mL) and EtOAc (100 mL). The EtOAc was separated, washed with brine (50 mL), and dried ($MgSO_4$). Removal of the solvent gave the crude product, which was either recrystallized from EtOAc/petroleum ether (PE) or purified by column chromatography on SiO_2, eluting with a solvent gradient from 1:2 DCM/PE to DCM.

*N-Methyl-N-cinnamoyl-1-naphthylamine (**5b**).* Isolated as a solid (97%), mp 102−103 °C (heptane) (lit. 87−89 °C[3]); R_f 0.6 (Et_2O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.48 (3H, s), 6.11 (1H, d, J = 15.5 Hz), 7.13−7.20 (5H, m), 7.40 (1H, dd, J = 1.1, 7.2 Hz), 7.53 (1H, dd, J = 7.3, 8.2 Hz), 7.55−7.58 (2H, m), 7.72 (1H, d, J = 15.5 Hz), 7.83−7.86 (1H, m), 7.92 (1H, d, J = 8.3 Hz), 7.94−7.98 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 37.6 (CH_3), 118.5 (CH), 122.8 (CH), 125.9 (CH), 126.1 (CH), 126.9 (CH), 127.6 (CH), 127.9 (CH), 128.6 (CH), 128.6 (CH), 128.9 (CH), 129.5 (CH), 130.5 (C), 134.8 (C), 135.2 (C), 139.9 (C), 142.1 (CH), 167.0 (C); FTIR (solid) 1650, 1613, 1396, 1365, 1084, 975, 776, 763, 700, 677, 651 cm^{-1}.

*N-n-Butyl-N-cinnamoyl-1-naphthylamine (**5c**).* Isolated as a solid (89%), mp 114−116 °C; R_f 0.6 (2:1 Et_2O/PE); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.90 (3H, t, J = 7.4 Hz), 1.26−1.43 (2H, m), 1.52−1.61 (1H, m), 1.63−1.72 (1H, m), 3.42 (1H, ddd, J = 5.1, 10.1, 13.2 Hz), 4.35 (1H, ddd, J = 6.0, 10.1, 13.2 Hz), 6.05 (1H, d, J = 15.5 Hz), 7.12−7.21 (5H, m), 7.37 (1H, dd, J = 1.0, 7.2 Hz), 7.50−7.58 (3H, m), 7.70 (1H, d, J = 15.5 Hz), 7.83−7.87 (1H, m), 7.90−7.96 (2H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9 (CH_3), 20.3 (CH_2), 30.4 (CH_2), 49.4 (CH_2), 118.9 (CH), 123.1 (CH), 125.6 (CH), 126.9 (CH), 127.1 (CH), 127.5 (CH), 127.9 (CH), 128.6 (CH), 128.6 (CH), 128.8 (CH), 129.4 (CH), 130.9 (C), 134.8 (C), 135.2 (C), 138.4 (C), 142.1 (CH), 166.6 (C); FTIR (solid) 1649, 1608, 1399, 1365, 1240, 1213, 980, 808, 781, 763, 706, 683, 534, 488 cm^{-1}; EI-MS m/z (relative intensity) 329 (19), 199 (52), 131 (100) 103 (31); HMRS (EI) M$^+$ calcd for $C_{23}H_{23}NO$ 329.17742, found 329.17729.

*N-Isopropyl-N-cinnamoyl-1-naphthylamine (**5d**).* Isolated as a solid (89%), mp 113−115 °C; R_f 0.5 (1:1 Et_2O/PE); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.95 (3H, d, J = 6.8 Hz), 1.38 (3H, d, J = 6.8 Hz), 5.16 (1H, heptet, 6.8 Hz), 5.90 (1H, d, J = 15.5 Hz), 7.04−7.07 (2H, m), 7.11−7.19 (3H, m), 7.36 (1H, dd, J = 1.0, 7.2 Hz), 7.49−7.55 (3H, m), 7.69 (1H, d, J = 15.5 Hz), 7.89−7.95 (3H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.0 (CH_3), 22.0 (CH_3), 48.5 (CH), 119.8 (CH), 124.0 (CH), 125.4 (CH), 126.7 (CH), 127.3 (CH), 127.8 (CH), 127.9 (CH), 128.4 (CH), 128.5 (CH), 129.1 (CH), 129.3 (CH), 132.9 (C), 134.5 (C), 135.3 (C), 135.6 (C), 141.8 (CH), 166.4 (C); FTIR (solid) 1642, 1589, 1571, 1376, 1345, 1234, 1129, 979, 784, 764, 709, 681, 653 cm^{-1}; EI-MS m/z (relative intensity) 315 (26), 185 (30), 172 (21), 131 (100), 103 (34); HMRS (EI) M$^+$ calcd for $C_{22}H_{21}NO$ 315.16177 found 315.16167.

*N-Benzyl-N-cinnamoyl-1-naphthylamine (**5e**).* Isolated as an oil (82%), mp 100−101 °C; R_f 0.4 (DCM); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.36 (1H, d, J = 14.0 Hz), 5.78 (1H, d, J = 14.0 Hz), 6.09 (1H, d, J = 15.5 Hz), 7.01 (1H, dd, J = 1.1, 7.2 Hz), 7.12−7.28 (10H, m), 7.38 (1H, dd, J = 7.3, 8.3 Hz), 7.51−7.58 (2H, m), 7.79 (1H, d, J = 15.5 Hz), 7.89 (1H, d, J = 8.3 Hz), 7.95 (1H, dd, J = 1.7, 7.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 52.9 (CH_2), 118.5 (CH), 122.8 (CH), 125.5 (CH), 126.8 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.4 (CH), 128.6 (CH), 129.0 (CH), 129.2 (C), 129.4 (CH), 129.6 (CH), 130.7 (C), 134.8 (C), 135.1 (C), 137.7 (C), 142.8 (CH), 166.8 (C); FTIR (solid) 1653, 1611, 1494, 1380, 1352, 1226, 980, 779, 765, 682, 530, 434 cm^{-1}; EI-MS m/z (relative intensity) 363 (58), 233 (89), 131 (100), 103 (40); HMRS (EI) M$^+$ calcd for $C_{26}H_{21}NO$ 363.16177, found 363.16210.

*N-4-Methylbenzyl-N-cinnamoyl-1-naphthylamine (**5f**).* Isolated as a solid (90%), mp 153−154 °C; R_f 0.6 (1:1 Et_2O/PE); ^{1}H NMR

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($CDCl_3$, 500 MHz) δ 2.31 (3H, s), 4.29 (1H, d, J = 14.0 Hz), 5.80 (1H, d, J = 14.0 Hz), 6.08 (1H, d, J = 15.5 Hz), 7.00 (1H, dd, J = 1.0, 7.2 Hz), 7.06 (2H, d, J = 7.8 Hz), 7.11−7.21 (7H, m), 7.38 (1H, dd, J = 7.3, 8.2 Hz), 7.51−7.58 (2H, m), 7.78 (1H, d, J = 15.5 Hz), 7.82−7.85 (1H, m), 7.89 (1H, d, J = 8.3 Hz), 7.93−7.96 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.2 (CH_3), 52.6 (CH_2), 118.6 (CH), 122.9 (CH), 125.5 (CH), 126.8 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.6 (CH), 128.9 (CH), 129.1 (CH), 129.4 (CH), 129.5 (CH), 130.7 (C), 134.8 (C), 135.2 (C), 137.1 (C), 137.8 (C), 142.6 (C), 166.7 (C); FTIR (solid) 1652, 1609, 1379, 1350, 1227, 983, 781, 766, 680, 538, 478, 450 cm^{-1}; EI-MS m/z (relative intensity) 377 (85), 247 (93), 131 (100), 105 (90), 103 (46); HMRS (EI) M^+ calcd for $C_{27}H_{23}NO$ 377.17742, found 377.17765.

*N-3,5-Dimethylbenzyl-N-cinnamoyl-1-naphthylamine (**5g**).* Isolated as a solid (83%), mp 120−121 °C; R_f 0.6 (1:1 Et_2O/PE); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.23 (3H, s), 4.24 (1H, d, J = 14.0 Hz), 5.79 (1H, d, J = 14.0 Hz), 6.09 (1H, d, J = 15.5 Hz), 6.85 (2H, s), 6.88 (1H, s), 7.03 (1H, dd, J = 0.7, 7.2 Hz), 7.12−7.22 (5H, m), 7.39 (1H, t, J = 7.8 Hz), 7.51−7.58 (2H, m), 7.78 (1H, d, J = 15.5 Hz), 7.83 (1H, d, J = 7.8 Hz), 7.89 (1H, d, J = 8.3 Hz), 7.94 (1H, dd, J = 1.6, 8.1 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.3 (CH_3), 52.8 (CH_2), 118.6 (CH), 122.9 (CH), 125.5 (CH), 126.8 (CH), 127.1 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.6 (CH), 128.9 (CH), 129.1 (CH), 129.5 (CH), 130.7 (C), 134.8 (C), 135.2 (C), 137.6 (C), 137.8 (C), 137.9 (C), 142.6 (CH), 166.7 (C); FTIR 1651, 1609, 1402, 1379, 1204, 977, 807, 777, 763, 698, 546, 527, 438 cm^{-1}; EI-MS m/z (relative intensity) 391 (86), 261 (100), 131 (74), 119 (63), 103 (33); HMRS (EI) M^+ calcd for $C_{28}H_{25}NO$ 391.19307, found 391.19337.

*N-3,5-Dimethoxybenzyl-N-cinnamoyl-1-naphthylamine (**5h**).* Isolated as a solid (85%), mp 115−117 °C; R_f 0.7 (Et_2O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.69 (6H, s), 4.28 (1H, d, J = 14.2 Hz), 5.79 (1H, d, J = 14.2 Hz), 6.09 (1H, d, J = 15.5 Hz), 6.35 (1H, t, J = 2.3 Hz), 6.40 (2H, d, J = 2.3 Hz), 7.10 (1H, dd, J = 1.0, 7.2 Hz), 7.12−7.21 (5H, m), 7.40 (1H, dd, J = 7.3, 8.2 Hz), 7.50−7.57 (2H, m), 7.76 (1H, d, J = 15.5 Hz), 7.80−7.83 (1H, m), 7.89 (1H, d, J = 8.3 Hz), 7.92−7.95 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 53.0 (CH_2), 55.4 (CH_3), 99.9 (CH), 107.2 (CH), 118.5 (CH), 122.8 (CH), 125.6 (CH), 126.8 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.6 (CH), 128.6 (CH), 129.0 (CH), 129.6 (CH), 130.7 (C), 13.8 (C), 135.1 (C), 137.8 (C), 140.0 (C), 142.7 (CH), 160.7 (C), 166.8 (C); FTIR (solid) 1656, 1593, 1383, 1201, 1146, 1055, 979, 828, 780, 766, 700, 532, 442 cm^{-1}; EI-MS m/z (relative intensity) 423 (69), 293 (100), 292 (76), 151 (52), 131 (91), 103 (43); HMRS (EI) M^+ calcd for $C_{28}H_{25}NO_3$ 423.18290, found 423.18267.

General Procedure for the TfOH-Mediated Cyclization. Triflic acid (10-fold excess) was added to a stirred solution of the amine in $CHCl_3$ (1 mmol/10 mL), and the reaction mixture was heated under gentle reflux until no starting material was present by TLC. The reaction mixture was cooled to room temperature, and water (20 mL) was added. The mixture was basicified with an excess of solid K_2CO_3 until CO_2 evolution ceased. The product was extracted into EtOAc (3 × 50 mL), dried ($MgSO_4$), concentrated in vacuo, and purified by column chromatography on SiO_2 and/or Al_2O_3.

*Reaction of N-Cinnamoyl-1-naphthylamine (**5a**). (a). With TfOH in $CHCl_3$.* Following the general procedure for cyclization, **5a** (0.54 g, 2.0 mmol) was heated under reflux for 2 h in $CHCl_3$. TLC showed two products, a major one (R_f 0.5, Et_2O) and a minor one (R_f 0.4, Et_2O). Purification by column chromatography on SiO_2, eluting with 2% EtOAc/DCM, gave 4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-one (**6a**) (0.42 g, 78%). Mp 195−196 °C (EtOAc/PE) [lit. 201 °C (benzene)]; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.04 (1H, dd, J = 7.2, 16.0 Hz), 3.12 (1H, dd, J = 6.6, 16.0 Hz), 4.47 (1H, t, J = 6.9 Hz), 7.12 (1H, d, J = 8.4 Hz), 7.19−7.34 (5H, m), 7.49−7.54 (2H, m), 7.58 (1H, ddd, J = 1.3, 6.9, 8.2 Hz), 7.84 (1H, d, J = 8.0 Hz), 7.93 (1H, d, J = 8.3 Hz); 8.86 (1H, s); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 38.9 (CH_2), 42.6 (CH), 119.9 (CH), 122.2 (C), 122.6 (C), 123.4 (CH), 126.2 (CH), 126.7 (CH), 127.3 (CH), 127.8 (CH), 128.0 (CH), 128.7 (CH), 129.0 (CH), 132.1 (C), 133.3 (C), 141.8 (C), 171.0 (C); FTIR (solid) 1671, 1376, 811, 767, 745, 707, 670, 563, 498, 454, 422 cm^{-1}; EI-MS m/z (relative intensity) 273 (100), 244 (13), 230 (25), 196 (21); HMRS (EI) M^+ calcd for $C_{19}H_{15}NO$ 273.1148, found 273.1147. Further elution with 10% EtOAc/DCM gave 4-phenyl-3,4-dihydro-1*H*-naphth[1,8-*bc*]azepin-2-one (**7a**) (0.06 g, 11%). Mp 209−221 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.28 (1H, dd, J = 1.5, 14.7 Hz), 3.40 (1H, ddd, J = 1.8, 7.1, 14.7 Hz), 4.83 (1H, d, J = 7.1 Hz), 6.97 (C10−H, dd, J = 1.3, 7.5 Hz), 7.06 (C2′−H, C6′−H, d, J = 7.6 Hz), 7.12 (C4′−H, t, J = 7.6 Hz), 7.16−7.23 (2H, m), 7.4 (C6−H, C9−H, t, J = 7.6 Hz), 7.68 (C8−H, dd, J = 1.3, 8.1 Hz), 7.83 (C7−H, dd, J = 1.4, 8.2 Hz), 8.74 (1H, brs); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 42.5 (CH_2), 47.3 (CH), 118.3 (CH), 124.4 (C), 125.8 (CH), 126.0 (CH), 126.7 (CH), 127.8 (CH), 128.5 (CH), 129.0 (CH), 129.3 (CH), 134.2 (C), 136.5 (C), 137.8 (C), 142.1 (C), 173.6 (C); FTIR (solid) 1677, 1406, 1263, 830, 768, 745, 726, 698, 568 cm^{-1}; CI-MS (m/z, relative intensity) 302 ($M + Na^+$, 11), 274 (MH^+ 100), 273 (46), 230 (18), 220 (19), 202 (18), 85 (16); HMRS (CI) MH^+ calcd for $C_{19}H_{16}NO$ 274.1232, found 274.1231.

(b). With TfOH in Benzene. Following the general procedure for cyclization, **5a** (0.54 g, 2.0 mmol) was heated under reflux for 2 h in benzene (10 mL). TLC showed two products, a major one (R_f 0.5, Et_2O) and a minor one (R_f 0.4, Et_2O). Purification by column chromatography on SiO_2, eluting with 1% EtOAc/DCM, gave 3,3-diphenylpropionyl-1-naphthylamine (**13**) (0.54 g 77%). Mp 191−192 °C; ^{1}H NMR ($CDCl_3$ 500 MHz) δ 3.22 (2H, d, J = 7.9 Hz), 4.67 (1H, d, J = 7.9 Hz), 6.96 (1H, d, J = 8.4 Hz), 7.00−7.40 (14H, m), 7.64 (2H, t, J = 8.0 Hz), 7.90 (1H, d, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 44.4 (CH_2), 48.0 (CH), 121.0 (CH), 121.7 (CH), 125.6 (CH), 126.0 (CH), 126.2 (CH), 126.9 (CH), 127.5 (C), 127.9 (CH), 128.5 (CH), 129.0 (CH), 132.1 (C), 134.0 (C), 143.6 (C), 170.2 (C); FTIR (solid) 1650, 1596, 1537, 1493, 1396, 1276, 796, 769, 742, 698 cm^{-1}; EI-MS m/z (relative intensity) 352 (25) 351 (100), 167 (81), 165 (69), 143 (53), 115 (62), 86 (32), 84 (55); HMRS (EI) M^+ calcd for $C_{25}H_{21}NO$ 351.1623, found 351.1613. Further elution with 2% EtOAC/DCM gave **6a** (0.10 g, 19% yield) identical to that obtained before.

(c). With PPA. A solution of **5a** (0.54 g, 2.0 mmol) in $CHCl_3$ (10 mL) was stirred and heated with PPA (10.0 g) in an open flask to 120 °C for 2 h, allowing the $CHCl_3$ to distill off. The reaction mixture was cooled, treated with ice (20 g), and then partitioned between DCM (50 mL) and water (20 mL). The organic layer was separated, and the aqueous layer was further extracted with DCM (2 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification by column chromatography on SiO_2, eluting with 2% EtOAc/DCM, gave 4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-one (**6a**) (0.44 g, 82%). Further elution with 10% EtOAc/DCM gave 4-phenyl-3,4-dihydro-1*H*-naphth[1,8-*bc*]azepin-2-one (**7a**) (0.055 g, 11%).

*Reaction of N-Methyl-N-cinnamoyl-1-naphthylamine (**5b**).* Following the general procedure for cyclization, **5b** (0.80 g, 2.5 mmol) was heated under reflux for 1.5 h. Purification by column chromatography, eluting with DCM, gave **6b** (0.56 g, 70%). Mp 107−109 °C (lit. an oil[8]); R_f 0.5 (Et_2O); ^{1}H NMR ($CDCl_3$ 500 MHz) δ 2.99 (1H, dd, J = 5.5, 14.9 Hz), 3.03 (1H, dd, J = 6.7, 14.9 Hz), 3.55 (3H, s), 4.32 (1H, t, J = 6.1 Hz), 7.10−7.16 (3H, m), 7.28 (1H, d, J = 7.3 Hz), 7.33 (2H, t, J = 7.4 Hz), 7.47−7.55 (2H, m), 7.59 (1H, d, J = 8.3 Hz), 7.86 (1H, dd, J = 1.3, 8.1 Hz), 7.96 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 37.9 (CH_3), 40.2 (CH_2), 42.5 (CH), 123.7 (CH), 125.1 (CH), 125.6 (CH), 125.6 (C), 125.8 (CH), 125.9 (CH), 127.3 (CH), 127.9 (CH), 128.9 (CH), 129.0 (CH), 129.6 (C), 134.4 (C), 138.4 (C), 140.7 (C), 172.5 (C); FTIR 1674, 1510, 1488, 1433, 1390, 1371, 1313, 1188, 1107, 817, 742, 709, 680 cm^{-1}; EI-MS m/z (relative intensity) 287 (100), 244 (42), 210 (16); HMRS (EI) M^+ calcd for $C_{20}H_{17}NO$ 287.1305, found 287.1298. Further elution with 2% EtOAC/DCM gave **7b** (0.20 g, 26%) as an oil. R_f 0.3 (Et_2O); ^{1}H NMR ($CDCl_3$ 400 MHz, −30 °C; a 3:17 ratio of conformers, only data for the major conformer are presented) δ 3.15 (3H, s), 3.21 (1H, dd, J = 6.7, 14.2 Hz), 3.34 (1H, dd, J = 1.4, 14.2 Hz), 4.88 (1H, d, J = 6.3 Hz), 7.13 (2H, d, J = 7.2 Hz), 7.20−7.34 (4H, m), 7.41 (1H, d, J = 6.3 Hz), 7.48 (1H, t, J = 7.1 Hz), 7.55 (1H, t, J = 7.8 Hz), 7.80 (1H, dd, J = 0.6, 8.1 Hz), 7.88 (1H, dd, J = 1.0, 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, −30 °C) δ 39.3 (CH), 42.0 (CH_2), 48.0 (CH_3), 121.6

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(CH), 125.7 (CH), 125.9 (CH), 126.9 (CH), 127.1 (C), 127.2 (CH), 128.2 (CH), 128.3 (CH), 128.6 (CH), 129.5 (CH), 135.4 (C), 137.8 (C), 140.3 (C), 141.9 (C), 172.0 (C); FTIR (film) 1656, 1575, 1432, 1385, 1282, 1116, 1077, 909, 824, 731, 698 cm^{-1}; EI-MS *m/z* (relative intensity) 287 (64), 259 (28), 244 (100), 182 (23); HMRS (EI) M^+ calcd for $C_{20}H_{17}NO$ 287.1305, found 287.1306.

*Reaction of N-n-Butyl-N-cinnamoyl-1-naphthylamine (**5c**).* Following the general procedure for cyclization, **5c** (0.76 g, 2.0 mmol) was heated under reflux for 2 h. Purification by column chromatography, eluting with 3:1 DCM/PE, gave **6c** (0.36 g, 47%) as an oil. R_f 0.55 (2:1 Et_2O/PE); ^1H NMR ($CDCl_3$ 500 MHz) δ 0.72 (3H, t, *J* = 7.3 Hz), 1.02−1.15 (2H, m), 1.26−1.38 (2H, m), 2.91 (1H, dd, *J* = 4.6, 14.9 Hz), 3.07 (1H, dd, *J* = 9.2, 14.9 Hz), 3.95−4.04 (1H, m), 4.16−4.24 (1H, brm), 4.31 (1H, dd, *J* = 4.6, 9.2 Hz), 7.06 (1H, d, *J* = 8.2 Hz), 7.24 (2H, d, *J* = 7.3 Hz), 7.29 (1H, dt, *J* = 1.8, 7.3 Hz), 7.33−7.37 (2H, m), 7.45−7.52 (2H, m), 7.57 (1H, d, *J* = 8.3 Hz), 7.85 (1H, dd, *J* = 1.5, 8.6 Hz), 7.91 (1H, d, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.7 (CH_3), 20.2 (CH_2), 30.4 (CH_2), 40.2 (CH_2), 42.2 (CH), 48.7 (CH_2), 123.5 (CH), 124.9 (CH), 125.4 (CH), 125.7 (CH), 125.8 (CH), 125.8 (C), 127.3 (CH), 128.3 (CH), 128.8 (CH), 128.9 (CH), 131.6 (C), 134.1 (C), 137.3 (C), 140.3 (C), 172.9 (C); FTIR (film) 1670, 1390, 1289, 1223, 816, 749, 736, 698 cm^{-1}; EI-MS *m/z* (relative intensity) 329 (100), 286 (29), 273 (71), 244 (34), 230 (21); HMRS (EI) M^+ calcd for $C_{23}H_{23}NO$ 329.17742, found 329.17762. Further elution with DCM gave **7c** (0.34 g, 45%) as a solid. Mp 105−107 °C; ^1H NMR ($CDCl_3$ 400 MHz, −30 °C; a 1:3 ratio of conformers, only data for the major conformer are presented) δ 0.75 (3H, t, *J* = 7.3 Hz), 1.04−1.45 (4H, m), 3.23 (1H, dd, *J* = 6.7, 14.0 Hz), 3.32−3.45 (2H, m including 3.35 (1H, dd, *J* = 1.8, 14.0 Hz)), 3.83−3.93 (1H, m), 4.89 (1H, d, *J* = 6.0 Hz), 7.20 (2H, d, *J* = 7.3 Hz), 7.22−7.42 (5H, m), 7.48 (1H, t, *J* = 8.0 Hz), 7.52 (1H, t, *J* = 8.0 Hz), 7.90 (1H, dd, *J* = 0.6, 7.7 Hz), 7.87 (1H, dd, *J* = 1.2, 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, −30 °C) δ 14.2 (CH_3), 20.6 (CH_2), 30.2 (CH_2), 41.5 (CH_2), 47.9 (CH), 51.1 (CH_2), 121.8 (CH), 125.5 (CH), 125.6 (CH), 126.8 (CH), 127.4 (CH), 127.9 (C), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.9 (CH), 135.7 (C), 137.7 (C), 139.1 (C), 141.8 (C), 171.4 (C); FTIR (solid) 1659, 1573, 1437, 1404, 1221, 827, 773, 740, 698 cm^{-1}; EI-MS *m/z* (relative intensity) 329 (100), 286 (48), 273 (29), 258 (46), 244 (52), 243 (59), 230 (71), 167 (34), 127 (24); HMRS (EI) M^+ calcd for $C_{23}H_{23}NO$ 329.17742, found 329.17735.

*Reaction of N-Isopropyl-N-cinnamoyl-1-naphthylamine (**5d**).* Following the general procedure for cyclization, **5d** (0.32 g, 1.0 mmol) was heated under reflux for 2 h. Purification by column chromatography, eluting with 3:1 PE/Et_2O, gave **6d** (0.10 g, 31%) as an oil. ^1H NMR ($CDCl_3$ 400 MHz, −30 °C) δ 0.69 (1.2H, d, *J* = 6.6 Hz), 1.4 (1.8H, d, *J* = 6.6 Hz), 1.95 (1.2H, d, *J* = 6.8 Hz), 2.09 (1.8H, d, *J* = 6.8 Hz), 2.75 (0.6H, dd, *J* = 3.2, 14.8 Hz), 2.94 (0.6H, t, *J* = 14.8 Hz), 3.00 (0.4H, dd, *J* = 5.7, 15.1 Hz), 3.24 (0.4H, dd, *J* = 2.1, 15.1 Hz), 4.04 (0.4H, heptet, *J* = 6.7 Hz), 41.4 (0.6H, heptet, *J* = 6.7 Hz), 4.27 (0.4H, d, *J* = 3.9 Hz), 4.37 (0.6H, dd, *J* = 3.2, 15.0 Hz), 6.74 (0.6H, d, *J* = 8.4 Hz), 7.02 (0.6H, brs), 7.21−7.62 (7.2H, m), 7.75 (0.4H, d, *J* = 8.2 Hz), 7.86 (0.6H, d, *J* = 7.6 Hz), 7.90−8.00 (1.6H, m); ^{13}C NMR ($CDCl_3$, 100 MHz, −30 °C) δ 18.9 (CH_3), 19.9 (CH_3), 22.7 (CH_3), 22.9 (CH_3), 39.7 (CH_2), 40.7 (CH), 42.7 (CH), 42.8 (CH_2), 56.1 (CH), 57.0 (CH), 123.4 (CH), 123.5 (CH), 124.6 (CH), 124.8 (CH), 125.2 (CH), 125.8 (CH), 125.8 (CH), 126.1 (CH), 126.2 (CH), 127.0 (CH), 127.1 (CH), 127.7 (CH), 127.9 (CH), 128.6 (CH), 129.0 (CH), 129.2 (CH), 129.3 (CH), 130.4 (C), 130.8 (CH), 133.2 (C), 133.8 (C), 134.3 (C), 139.0 (C), 140.2 (C), 140.3 (C), 173.1 (C), 174.4 (C); FTIR (film) 1671, 1407, 1380, 1284, 1238, 1125, 816, 770, 752, 732, 696, 612, 431 cm^{-1}; EI-MS *m/z* (relative intensity) 315 (63), 273 (100), 244 (22), 230 (29), 196 (27); HMRS (EI) M^+ calcd for $C_{22}H_{21}NO$ 315.1618, found 315.1618. Further elution with 2:1 PE/Et_2O gave **7d** (0.20 g, 62%) as an oil. ^1H NMR ($CDCl_3$ 500 MHz) δ 0.97 (2.25H, d, *J* = 6.84 Hz), 1.10 (0.75H, d, *J* = 6.8 Hz), 1.25 (2.25H, d, *J* = 6.7 Hz), 1.56 (0.75H, d, *J* = 6.5 Hz), 2.72 (0.25H, d, *J* = 12.8 Hz), 3.12 (0.75H, dd, *J* = 6.8, 13.9 Hz), 3.35 (0.75H, dd, *J* = 1.3, 13.9 Hz), 3.40 (0.25H, t, *J* = 12.2 Hz), 3.95 (0.75H, heptet, *J* = 6.8 Hz), 4.51 (0.25H, heptet, *J* = 6.7 Hz), 4.65 (0.25H, d, *J* = 11.6 Hz), 4.79 (0.75H, d, *J* = 6.2 Hz), 6.79 (0.25H, d, *J* = 7.0 Hz), 7.00−7.50 (0.75H, brm), 7.15−7.47 (8.25H, m), 7.69 (0.25H, d, *J* = 7.9 Hz), 7.76 (0.75H, d, *J* = 8.4 Hz), 7.81 (0.75H, d, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.5 (CH_3), 20.7 (CH_3), 22.5 (CH_3), 22.7 (CH_3), 41.9 (CH_2), 44.8 (CH_2), 48.0 (CH), 48.5 (CH), 53.5 (CH), 54.2 (CH), 122.4 (CH), 123.0 (CH), 124.7 (CH), 124.9 (CH), 125.0 (CH), 125.4 (CH), 126.6 (CH), 126.8 (CH), 127.7 (CH), 127.7 (CH), 128.0 (CH), 128.2 (CH), 128.6 (CH), 128.9 (CH), 129.1 (CH), 129.8 (CH), 135.3 (C), 135.7 (C), 138.0 (C), 138.7 (C), 141.1 (C), 142.0 (C), 146.8 (C), 171.3 (C), 172.9 (C); FTIR (film) 1658, 1574, 1434, 1401, 1381, 1259, 826, 768, 733, 697 cm^{-1}; EI-MS *m/z* (relative intensity) 315 (73), 272 (36), 244 (39), 231 (37) 230 (100), 229 (58); HMRS (EI) M^+ calcd for $C_{22}H_{21}NO$ 315.1618, found 315.1606.

*Reaction of N-Benzyl-N-cinnamoyl-1-naphthylamine (**5e**). (a). With TfOH.* Following the general procedure for cyclization, **5e** (0.72 g, 2.0 mmol) was heated under reflux for 2 h in $CHCl_3$. TLC showed no **5e** but revealed three potential products at R_f 0.7, 0.5, and 0.3 (Et_2O). Purification by column chromatography, eluting with 2% EtOAc/DCM, gave 1,4-diphenyl-3,4-dihydro-1*H*-naphth[1,8-*bc*]-azepin-2-one (**7e**) (0.23 g, 32%) as a solid. Mp 75−77 °C; ^1H NMR ($CDCl_3$, −20 °C) δ 2.98 (0.25H, d, *J* = 12.9 Hz), 3.33 (0.75H, dd, *J* = 6.8, 13.7 Hz), 3.52 (0.75H, d, *J* = 13.7 Hz), 3.59 (0.25H, t, *J* = 12.9 Hz), 4.43 (0.75H, d, *J* = 16.1 Hz), 4.75 (0.25H, d, *J* = 11.6 Hz), 4.91−5.05 (1.75H, m including 4.95 (0.75H, d, *J* = 6.8 Hz) and 4.99 (0.75H, d, *J* = 16.1 Hz)), 5.33 (0.25H, d, *J* = 15.7 Hz), 6.82 (0.25H, d, *J* = 7.3 H), 7.19 (1.5H, t, *J* = 7.0 Hz), 7.23−7.51 (12.25H, m), 7.73 (0.75H, d, *J* = 7.9 Hz), 7.77 (0.75H, dd, *J* = 2.0, 7.1 Hz), 7.87 (0.5H, d, *J* = 7.8 Hz); ^{13}C NMR ($CDCl_3$, −20 °C) δ 41.7 (CH_2), 43.7 (CH_2), 47.8 (CH), 47.9 (CH), 55.2 (CH_2), 55.9 (CH_2), 121.2 (CH), 121.8 (CH), 124.9 (CH), 125.1 (CH), 126.7 (CH), 126.7 (CH), 126.8 (CH), 127.6 (CH), 127.7 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.9 (CH), 129.7 (CH), 135.2 (C), 135.7 (C), 137.7 (C), 138.0 (C), 138.2 (C), 139.7 (C), 139.8 (C), 141.0 (C), 141.8 (C), 171.5 (C), 173.0 (C); FTIR (solid) 1665, 1434, 1388, 825, 768, 729, 697 cm^{-1}; EI-MS *m/z* (relative intensity) 364 (29), 363 (100), 272 (27), 244 (43), 230 (94); HMRS (EI) M^+ calcd for $C_{26}H_{21}NO$ 363.1618, found 363.1613. Further elution with 2−4% EtOAc/DCM gave a fraction that NMR proved to be a mixture of compounds. These were readily separated by chromatography on Al_2O_3 (basic, Brockman I), eluting with 25% PE/DCM, to give (1*S*,8*R*,19*S*,20*S*)- and (1*R*,8*S*,19*R*,20*R*)-11-azaheptacyclo-[17.7.1.$0^{2,7}$.$0^{8,20}$.$0^{11,20}$.$0^{13,18}$.$0^{21,26}$]heptacosa-2(7),3,5,13,15,17,21,23,25-nonaen-10-one (**10e**) as a solid (0.06 g, 8%). Mp 205−207 °C; ^1H NMR ($CDCl_3$) δ 2.05 (20-CH, 1H, ddd, *J* = 3.6, 9.1, 12.7 Hz), 2.69 (9-CH, 1H, dd, *J* = 12.3, 16.3 Hz), 3.06 (20-CH, 1H, ddd, *J* = 3.2, 9.6, 12.7 Hz), 3.11 (9-CH, 1H, dd, *J* = 8.2, 16.3 Hz), 3.59 (8-CH, 1H, dd, *J* = 8.9, 12.1 Hz), 3.76 (19-CH, 1H, t, *J* = 9.3 Hz), 4.05 (1-CH, 1H, t, *J* = 3.2 Hz), 4.56 (12-CH, 1H, d, *J* = 16.7 Hz), 5.38 (12-CH, 1H, d, *J* = 16.7 Hz); 7.01−7.43 (12H, m); ^{13}C NMR ($CDCl_3$) δ 33.4 (CH), 35.2 (CH_2), 39.7 (CH_2), 40.5 (CH_2), 47.8 (CH), 49.3 (CH), 63.6 (C), 121.8 (CH), 126.0 (CH), 126.5 (CH), 127.2 (CH), 127.3 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.9 (CH), 129.1 (CH), 131.5 (C), 136.0 (C), 138.8 (C), 139.1 (C), 140.1 (C), 141.4 (C), 174.7 (C); FTIR (solid) 1693, 1439, 1390, 752, 699 cm^{-1}; EI-MS *m/z* (relative intensity) 364 (27), 363 (100); HMRS (EI) M^+ calcd for $C_{26}H_{21}NO$ 363.1618, found 363.1628. Further elution with DCM gave **6a** (0.060g, 11%), identical to that obtained previously. Further elution of the initial SiO_2 column with 10% EtOAc/DCM gave (1*R*,8*R*,19*R*,20*R*)- and (1*S*,8*S*,19*S*,20*S*)-11-azaheptacyclo-[17.7.1.$0^{2,7}$.$0^{8,20}$.$0^{11,20}$.$0^{13,18}$.$0^{21,26}$]-heptacosa-2-(7),3,5,13,15,17,21,23,25-nonaen-10-one (**9e**) (0.10 g, 14%) as a solid. Mp 223−224 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ 2.48 (9-CH, 1H, dd, *J* = 12.9, 15.5 Hz), 2.86 (20-CH, 1H, ddd, *J* = 3.9, 6.6, 10.5 Hz), 3.03 (9-CH, 1H, dd, *J* = 7.6, 15.7 Hz), 3.07 (20-CH, 1H, dd, *J* = 10.4, 12.3 Hz), 3.64 (19-CH, 1H, dd, *J* = 3.4, 10.2 Hz), 3.86 (8-CH, 1H, dd, *J* = 7.6, 12.7 Hz), 4.09 (1-CH, 1H, d, *J* = 6.3 Hz), 4.80 (12-CH, 1H, d, *J* = 17.9 Hz), 4.99 (12-CH, 1H, d, *J* = 17.9 Hz), 6.93−6.98 (1H, m), 7.01−7.21 (9H, m), 7.21−7.25 (2H, m); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 32.4 (20-CH_2), 35.8 (9-CH_2), 42.8 (12-CH_2), 44.5 (19-CH),

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46.5 (1-CH), 50.7 (8-CH), 65.4 (20-C), 125.1 (22-CH), 125.5 (25-CH), 126.4 (15,17-CH), 126.9 (14-CH), 127.0 (23-CH), 127.2 (4,16-CH), 127.4 (5-CH), 128.2 (3-CH), 128.3 (24-CH), 129.2 (6-CH), 130.5 (13-C), 133.9 (21-C), 135.0 (7-C), 136.7 (18-C), 143.3 (26-C), 143.9 (2-C), 174.1 (10-C); FTIR (solid) 1685, 1492, 1449, 1397, 773, 747, 722 cm^{-1}; EI-MS *m/z* (relative intensity) 364 (27), 363 (100), 362 (31); HMRS (EI) M^+ calcd for $C_{26}H_{21}NO$ 363.1618, found 363.1609.

(b). With PPA. A solution of **5e** (0.72 g, 2.0 mmol) in $CHCl_3$ (10 mL) was stirred and heated with PPA (10.0 g) in an open flask to 120 °C for 2 h, allowing the $CHCl_3$ to distill off. The reaction mixture was cooled, treated with ice (20 g), and then partitioned between DCM (50 mL) and water (20 mL). The organic layer was separated, and the aqueous layer was further extracted with DCM (2 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography on SiO_2. The elution with DCM gave only partial separation, and three fractions were collected. From the first fraction, trituration with Et_2O gave 6-benzyl-4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-one (**14**) as a white solid. Mp 174−176 °C; ^1H NMR ($CDCl_3$, 600 MHz) δ 3.02 (3-CH, dd, *J* = 6.5, 15.9 Hz), 3.13 (3-CH, dd, *J* = 16.0, 6.7 Hz), 4.30 (Ph−CH, d, *J* = 16.0 Hz), 4.37 (Ph−CH, d, *J* = 16.0 Hz), 4.44 (4-CH, t, *J* = 6.6 Hz), 7.02 (5-H, s), 7.11 (2H, d, *J* = 7.3 Hz), 7.13−7.33 (8H, m), 7.47 (8-H, ddd, *J* = 8.5, 6.9, 1.1 Hz), 7.55 (9-H, ddd, *J* = 8.5, 6.9. 1.2 Hz), 7.94 (10-H, d, *J* = 8.5 Hz), 7.97 (7-H, d, *J* = 8.5 Hz), 8.83 (1H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 39.0 (3-CH_2), 39.0 (Ph-CH_2), 42.5 (4-CH), 120.2 (10-CH), 121.7 (4a-C), 123.0 (10a-C), 125.5 (7-CH), 126.2 (4′-CH), 126.4 (8-CH), 127.3 (4″-CH), 127.8 (2″-CH), 128.0 (5-CH), 128.5 (2′-CH), 128.6 (3′-CH), 129.1 (3″-CH), 131.1 (10b-C); 131.9 (6a-C), 132.0 (6-C), 140.6 (1′-C), 141.7 (1″-C), 170.7 (2-C═O); FTIR (solid) 3279, 1666, 1493, 1472, 1459, 1390, 1253, 1150, 767, 745, 726, 699, 678, 568, 492, 457 cm^{-1}; EI-MS *m/z* (relative intensity) 364 (24), 363 (100); HRMS (EI) M^+ calcd for $C_{26}H_{21}NO$ 363.1623, found 363.1620. NMR and MS analysis of the mixed fractions were consistent with their being mixtures of isomers of **14**.

*Reaction of N-4-Methylbenzyl-N-cinnamoyl-1-naphthylamine (**5f**).* Following the general procedure for cyclization, **5f** (1.1 g, 3.0 mmol) was heated under reflux in $CHCl_3$ (30 mL) for 2 h. Purification by column chromatography on SiO_2, eluting with 2% EtOAc/DCM, gave a product mixture (0.50 g) that was repurified by column chromatography on Al_2O_3, eluting with 1:1 PE/DCM, to give (1*S*,8*R*,19*S*,20*S*)- and (1*R*,8*S*,19*R*,20*R*)-14-methyl-11-azaheptacyclo[17.7.1.$0^{2,7}$.$0^{8,20}$.$0^{11,20}$.$0^{13,18}$.$0^{21,26}$]-heptacosa-2-(7),3,5,13,15,17,21,23,25-nonaen-10-one (**10f**) (0.27 g, 25%). Mp 240−241 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.04 (1H, ddd, *J* = 3.5, 9.1, 12.6 Hz), 2.23 (3H, s), 2.67 (1H, dd, *J* = 12.4, 16.4 Hz), 3.04 (1H, ddd, *J* = 3.0, 9.6, 12.6 Hz), 3.10 (1H, dd, *J* = 8.8, 16.4 Hz), 3.57 (1H, dd, *J* = 9.0, 12.1 Hz), 3.72 (1H, t, *J* = 9.2 Hz), 4.03 (1H, t, *J* = 2.8 Hz), 4.52 (1H, d, *J* = 16.5 Hz), 5.33 (1H, d, *J* = 16.5 Hz), 6.89−6.98 (3H, m), 7.01−7.04 (1H, m), 7.18 (1H, t, *J* = 7.3 Hz), 7.21−7.31 (5H, m), 7.38 (1H, d, *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.2 (CH_3), 33.3 (CH), 35.2 (CH_2), 39.7 (CH_2), 40.3 (CH_2), 47.8 (CH), 49.2 (CH), 63.6 (C), 121.8 (CH), 125.8 (CH), 126.5 (CH), 126.9 (CH), 127.2 (CH), 127.7 (CH), 127.8 (CH), 128.5 (C), 128.6 (CH), 128.8 (CH), 129.1 (CH), 136.0 (C), 136.7 (C), 138.8 (C), 138.9 (C), 140.2 (C), 141.4 (C), 174.7 (C); FTIR (solid) 1645, 1608, 1446, 754, 736, 585, 527 cm^{-1}; EI-MS *m/z* (relative intensity) 377 (93), 247 (21), 246 (22), 131 (55), 86 (62), 84 (97), 51 (100); HRMS (EI) M^+ calcd for $C_{27}H_{23}NO$ 377.1774, found 377.1773. Further elution with DCM gave **6a** (0.18 g, 22%). Further elution of the SiO_2 column with 10% EtOAc/DCM gave (1*R*,8*R*,19*R*,20*R*)- and (1*S*,8*S*,19*S*,20*S*)-14-methyl-11-azaheptacyclo[17.7.1.$0^{2,7}$.$0^{8,20}$.$0^{11,20}$.$0^{13,18}$.$0^{21,26}$]-heptacosa-2-(7),3,5,13,15,17,21,23,25-nonaen-10-one (**9f**) (0.48 g, 44%) as an oil. ^1H NMR ($CDCl_3$, 500 MHz) δ 2.26 (3H, s), 2.80−2.89 (1H, m), 2.97−3.10 (2H, m), 3.61 (1H, dd, *J* = 3.5, 10.2 Hz), 3.84 (1H, dd, *J* = 7.7, 12.7 Hz), 4.05 (1H, d, *J* = 6.2 Hz), 4.72 (1H, d, *J* = 17.7 Hz), 4.95 (1H, d, *J* = 17.7 Hz), 6.89−7.25 (11H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.4 (CH_3), 32.5 (CH_2), 35.7 (CH_2), 42.5 (CH_2), 44.3 (CH), 46.5 (CH), 50.7 (CH), 65.3 (C), 125.1 (CH), 125.4 (CH), 126.9 (CH), 127.0 (CH), 127.1 (CH), 127.3 (C), 127.3 (CH), 128.1 (CH), 129.1 (CH), 133.9 (C), 135.0 (C), 136.4 (C), 136.5 (C), 143.2 (C), 143.8 (C), 174.0 (C); FTIR (film) 1695, 1403, 741 cm^{-1}; EI-MS *m/z* (relative intensity) 377 (43), 363 (59), 362 (100); HRMS (EI) M^+ calcd for $C_{27}H_{23}NO$ 377.1774, found 377.1757.

*Reaction of N-3,5-Dimethylbenzyl-N-cinnamoyl-1-naphthylamine (**5g**).* Following the general procedure for cyclization, **5g** (1.2 g, 3.0 mmol) was heated under reflux in $CHCl_3$ (30 mL) for 2 h. Purification by column chromatography on SiO_2, eluting with 1:3 PE/DCM, gave (1*S*,8*R*,19*S*,20*S*)- and (1*R*,8*S*,19*R*,20*R*)-13,15-dimethyl-11-azaheptacyclo[17.7.1.$0^{2,7}$.$0^{8,20}$.$0^{11,20}$.$0^{13,18}$.$0^{21,26}$]-heptacosa-2-(7),3,5,13,15,17,21,23,25-nonaen-10-one (**10g**) (0.47 g, 39%). R_f 0.5 (10% Et_2O in DCM); mp 238−240 °C; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.73 (1H, ddd, *J* = 3.4, 9.9, 13.0 Hz), 2.21 (3H, s), 2.22 (3H, s), 2.70 (1H, dd, *J* = 12.1, 16.4 Hz), 3.09 (1H, dd, *J* = 8.8, 16.0 Hz), 3.12 (1H, ddd, *J* = 3.4, 9.1, 12.6 Hz), 3.57 (1H, dd, *J* = 8.8, 12.0 Hz), 3.74 (1H, t, *J* = 10.6 Hz), 4.01 (1H, t, *J* = 3.2 Hz), 4.62 (1H, d, *J* = 16.6 Hz), 5.20 (1H, d, *J* = 16.6 Hz), 6.78 (1H, s), 6.81 (1H, s), 7.03−7.07 (1H, m), 7.17 (1H, dt, *J* = 1.0, 7.3 Hz), 7.23 (1H, dd, *J* = 1.3, 7.4 Hz), 7.25−7.33 (4H, m), 7.42 (1H, d, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.6 (CH_3), 22.5 (CH_3), 33.5 (CH), 35.3 (CH_2), 38.4 (CH_2), 41.0 (CH_2), 47.9 (CH), 49.8 (CH), 63.9 (C), 122.3 (CH), 124.6 (CH), 126.0 (CH), 127.2 (CH), 127.7 (CH), 129.0 (CH), 129.1 (CH), 131.1 (CH), 132.7 (C), 134.2 (C), 135.3 (C), 136.1 (C), 137.3 (C), 138.7 (C), 140.3 (C), 141.5 (C), 174.5 (C); EI-MS *m/z* (relative intensity) 392 (25), 391 (70), 376 (100); HRMS (EI) M^+ calcd for $C_{28}H_{25}NO$ 391.1931, found 391.1938. Further elution with DCM + 4% Et_2O gave (1*R*,8*R*,19*R*,20*R*)- and (1*S*,8*S*,19*S*,20*S*)-13,15-dimethyl-11-azaheptacyclo[17.7.1.$0^{2,7}$.$0^{8,20}$.$0^{11,20}$.$0^{13,18}$.$0^{21,26}$]-heptacosa-2-(7),3,5,13,15,17,21,23,25-nonaen-10-one (**9g**) (0.55 g, 46%). Mp 160−162 °C; R_f 0.4 (10% Et_2O in DCM); ^1H NMR ($CDCl_3$, 500 MHz) δ 2.19−2.35 (9H, m including 2.20 (3H, s) and 2.31 (3H, s)), 2.94 (1H, dd, *J* = 7.4, 15.6 Hz), 3.37 (1H, t, *J* = 12.9 Hz), 3.77−3.88 (1H, m), 4.00 (1H, m), 4.67 (1H, d, *J* = 17.7 Hz), 4.93 (1H, d, *J* = 17.7 Hz), 6.77 (1H, s), 6.84 (1H, s), 7.02−7.30 (8H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.6 (CH_3), 23.0 (CH_3), 35.4 (CH_2), 38.3 (CH_2), 42.0 (CH_2), 44.5 (CH), 47.8 (CH), 53.0 (CH), 63.9 (C), 124.9 (CH), 124.9 (CH), 125.5 (CH), 127.0 (CH), 127.1 (CH), 127.6 (CH), 128.3 (CH), 128.9 (CH), 129.3 (CH), 130.2 (C), 131.3 (CH), 132.8 (C), 133.8 (C), 134.8 (C), 135.7 (C), 137.0 (C), 142.1 (C), 144.8 (C), 174.3 (C); FTIR (solid) 1690, 1393, 851, 751, 740, 590, 506 cm^{-1}; EI-MS *m/z* (relative intensity) 392 (30), 391 (100), 376 (39), 246 (18), 178 (22), 84 (26), 51 (29); HRMS (EI) M^+ calcd for $C_{28}H_{25}NO$ 391.1931, found 391.1943.

*Reaction of N-3,5-Dimethoxybenzyl-N-cinnamoyl-1-naphthylamine (**5h**). (a). With TfOH.* Following the general procedure for cyclization, **5h** (1.27 g, 3.0 mmol) was heated under reflux in $CHCl_3$ (30 mL) for 6 h. Purification by column chromatography on SiO_2, eluting with DCM, gave 1-(3,5-dimethoxybenzyl)-4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-one (**6h**) (0.47 g, 37%) as an oil. R_f 0.8 (Et_2O); ^1H NMR ($CDCl_3$, 500 MHz) δ 2.98 (1H, dd, *J* = 4.9, 14.6 Hz), 3.07 (1H, dd, *J* = 9.2, 14.6 Hz), 3.64 (6H, s), 4.27 (1H, dd, *J* = 4.9, 9.2 Hz), 5.12 (1H, d, *J* = 15.1 Hz), 5.31 (1H, d, *J* = 15.1 Hz), 6.23 (2H, d, *J* = 2.2 Hz), 6.30 (1H, t, *J* = 2.2 Hz), 7.01 (1H, d, *J* = 8.3 Hz), 7.07 (2H, d, *J* = 6.7 Hz), 7.24−7.32 (3H, m), 7.44−7.49 (2H, m), 7.56 (1H, d, *J* = 8.3 Hz), 7.81−7.85 (1H, m), 7.95−7.99 (1H, m); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 38.8 (CH_2), 42.5 (CH), 52.2 (CH_2), 55.3 (CH_3), 99.6 (CH), 105.7 (CH), 123.7 (CH), 125.2 (CH), 125.5 (CH), 125.7 (C), 125.8 (CH), 126.2 (CH), 127.2 (CH), 128.2 (CH), 128.9 (CH), 128.9 (CH), 131.2 (C), 134.2 (C), 137.7 (C), 140.4 (C), 140.4 (C), 160.7 (C), 172.7 (C); FTIR (film) 1665, 1641, 1599, 1489, 1416, 1131, 823 cm^{-1}; EI-MS *m/z* (relative intensity) 423 (100), 272 (37); HRMS (EI) M^+ calcd for $C_{28}H_{25}NO_3$ 423.1829, found 423.1810. Further elution with DCM + 5% MeOH gave 1-(3,5-methoxyphenyl)-4-diphenyl-3,4-dihydro-1*H*-naphth[1,8-*bc*]azepin-2-one (**7h**) (0.38 g, 30%). Mp 131−132 °C; R_f 0.5 (Et_2O); ^1H NMR ($CDCl_3$ 400 MHz, −30 °C; a 3:7 ratio of conformers) δ 2.97 (0.3H, d, *J* = 12.7 Hz), 3.27 (0.7H, dd, *J* = 6.7, 13.5 Hz), 3.49 (0.7H, d, *J* = 13.5 Hz), 3.58 (0.3H, t, *J* = 12.7 Hz), 3.70 (1.8H, s), 3.76 (4.2H, s), 4.20 (0.7H, d, *J* = 16.1 Hz), 4.75 (0.3H, d, *J* = 11.0 Hz), 4.75−5.02 (1.7H, m), 5.26 (0.3H, d,

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J = 15.8 Hz), 6.25−6.45 (3H, m), 6.81 (0.6H, d, J = 7.0 Hz), 7.03−7.60 (8.7H, m), 7.59−7.81 (1.0H, m), 7.87 (0.7H, d, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, −30 °C) δ 41.9, 43.7, 48.0, 55.5, 56.5, 98.4, 104.2, 104.8, 121.6, 125.0, 125.4, 125.6, 125.7, 126.8, 127.0, 127.8, 127.9, 128.3, 128.7, 129.1, 129.7, 135.1, 135.5, 137.7, 139.9, 140.5, 141.2, 141.8, 146.4, 160.6, 160.7, 171.3, 172.9; FTIR (solid) 1667, 1597, 1200, 1158, 824, 768, 751, 702 cm^{-1}; EI-MS m/z (relative intensity) 423 (100), 273 (60), 230 (22); HRMS (EI) M$^+$ calcd for $C_{28}H_{25}NO_3$ 423.1829, found 423.1828.

(b). With PPA. A solution of **5h** (1.27 g, 3.0 mmol) in $CHCl_3$ (10 mL) was stirred and heated with PPA (10.0 g) in an open flask to 110 °C for 2 h, allowing the $CHCl_3$ to distill off. The reaction mixture was cooled, treated with ice (20 g), and then partitioned between DCM (50 mL) and water (20 mL). The organic layer was separated, and the aqueous layer was further extracted with DCM (2 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography on SiO_2, initially eluting with 1:1 PE/ether, to give **7h** (0.21 g, 16%); further elution gave **6a** (0.10 g, 7%). Increasing the polarity to 1:3 PE/ether gave (1*S*,8*R*,19*S*,20*S*)- and (1*R*,8*S*,19*R*,20*R*)-13,15-dimethoxy-11-azaheptacyclo[17.7.1.0^{2,7}.0^{8,20}.0^{11,20}.0^{13,18}.0^{21,26}]-heptacosa-2(7),3,5,13,15,17,21,23,25-nonaen-10-one (**10h**) (0.34 g, 27%). Mp 183−185 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.64 (1H, ddd, J = 3.4, 97, 13.2 Hz), 2.69 (1H, dd, J = 12.2, 16.4 Hz), 3.07 (1H, dd, J = 8.6, 15.9 Hz), 3.32 (1H, ddd, J = 3.4, 8.8, 12.2 Hz), 3.54 (1H, dd, J = 8.4, 12.2 Hz), 3.69 (3H, s), 3.73−3.75 (4H, m including 3.74 (3H, s)), 3.97 (1H, t, J = 3.4 Hz), 4.56 (1H, d, J = 16.6 Hz), 5.21 (1H, d, J = 16.6 Hz), 6.23 (1H, d, J = 2.4 Hz), 6.26 (1H, d, J = 2.4 Hz), 7.00−7.04 (1H, m), 7.17−7.31 (H, m), 7.40 (1H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 31.4 (CH), 35.3 (CH_2), 38.3 (CH_2), 41.0 (CH_2), 48.1 (CH), 49.6 (CH), 55.1 (CH_3), 55.4 (CH_3), 63.7 (C), 97.8 (CH), 101.2 (CH), 119.8 (C), 122.1 (CH), 126.1 (CH), 127.2 (CH), 127.5 (CH), 127.6 (CH), 129.0 (CH), 129.1 (CH), 134.6 (C), 136.2 (C), 139.0 (C), 140.2 (C), 142.0 (C), 158.8 (C), 159.5 (C), 174.8 (C); FTIR (solid) 1694, 1589, 1394, 1201, 1149, 760 cm^{-1}; EI-MS m/z (relative intensity) 423 (100), 177 (80); HRMS (EI) M$^+$ calcd for $C_{28}H_{25}NO_3$ 423.1829, found 423.1827. Further elution with ether gave (1*R*,8*R*,19*R*,20*R*)- and (1*S*,8*S*,19*S*,20*S*)-13,15-dimethoxy-11-azaheptacyclo[17.7.1.0^{2,7}.0^{8,20}.0^{11,20}.0^{13,18}.0^{21,26}]-heptacosa-2-(7),3,5,13,15,17,21,23,25-nonaen-10-one (**9h**) (0.59 g, 46%). Mp 241−243 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.25 (1H, ddd, J = 4.9, 7.4, 12.4 Hz), 2.35 (1H, dd, J = 12.9, 15.8 Hz), 2.92 (1H, dd, J = 7.4, 15.8 Hz), 3.45 (1H, ddd, J = 2.2, 10.1, 12.4 Hz), 3.68−3.77 (7H, m, including 3.74 (3H, s) and 3.75 (3H, s)), 3.97 (1H, dd, J = 2.4, 4.9 Hz), 4.62 (1H, d, J = 17.8 Hz), 4.96 (1H, d, J = 17.8 Hz), 6.24 (1H, d, J = 2.0 Hz), 6.29 (1H, d, J = 2.0 Hz), 7.02 (1H, d, J = 7.5 Hz), 7.05 (1H, d, J = 7.5 Hz), 7.11−7.19 (5H, m), 7.28 (1H, d, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 35.5 (CH_2), 37.6 (CH_2), 41.9 (CH_2), 42.3 (CH), 48.1 (CH), 2.9 (CH), 55.2 (CH_3), 55.4 (CH_3), 63.7 (C), 97.8 (CH), 101.6 (CH), 119.1 (C), 125.0 (CH), 125.3 (CH), 126.9 (CH), 127.0 (CH), 128.2 (CH), 129.0 (CH), 129.2 (CH), 132.2 (C), 132.8 (C), 134.8 (C), 142.5 (C), 145.3 (C), 159.1 (C), 159.4 (C), 174.3 (C); FTIR (solid) 1697, 1606, 1586, 1394, 1206, 1147, 744 cm^{-1}; EI-MS m/z (relative intensity) 423 (48), 202 (54), 191 (48), 178 (51), 177 (100), 151 (30); HRMS (EI) M$^+$ calcd for $C_{28}H_{25}NO_3$ 423.1829, found 423.1820.

1-Benzyl-4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-one (6e). Following the general procedure for the alkylation of *N*-alkyl-*N*-cinnamoyl-1-naphthylamines **5b−h**, but with heating under reflux for 4 h, **6a** (1.44 g, 5.3 mmol) gave 1-benzyl-4-phenyl-3,4-dihydro-1*H*-benzo[*h*]quinolin-2-one (**6e**), which was purified by column chromatography on silica, eluting with 1:1 DCM/PE, and isolated as a white solid (1.5g, 79% yield). Mp 141−143 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.95 (1H, dd, J = 4.8, 14.7 Hz), 3.07 (1H, dd, J = 9.6, 14.7 Hz), 4.20 (1H, dd, J = 4.8. 9.6 Hz), 6.99 (1H, d, J = 8.3 Hz), 7.10−7.11 (4H, m), 7.15−7.20 (3H, m), 7.24−7.31 (3H, m), 7.40−7.49 (2H, m), 7.56 (1H, d, J = 8.3 Hz), 7.84 (1H, dd, J = 1.6, 8.5 Hz), 7.94 (1H, d, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 40.4 (CH_2), 42.4 (CH), 52.3 (CH_2), 123.7 (CH), 125.1 (CH), 125.4 (CH), 125.7 (C), 125.7 (CH), 127.2 (CH), 127.2 (CH), 127.8 (CH), 128.2 (CH), 128.3 (CH), 128.9 (CH), 128.9 (CH), 131.4 (C), 134.1 (C), 137.7 (C), 138.0 (C), 140.3 (C), 172.7 (C); FTIR (solid) 1676, 1376, 1281, 819, 771, 752, 723, 689, 672, 660 cm^{-1}; EI-MS m/z (relative intensity) 363 (100), 272 (32); HMRS (EI) M$^+$ calcd for $C_{26}H_{21}NO$ 363.1618, found 363.1615.

Quantum-Mechanical Calculations. All of the quantum mechanical calculations were carried out using Gaussian 09.[9] Geometry optimizations were performed using M06-2X/cc-pVTZ calculations. The "nosymm" keyword of Gaussian 09 was employed in order to carry out QM calculations with the symmetry of molecules disabled. For DFT geometry optimizations of **9e** and **10e**, the ultrafine numerical integration grid (with 99 radial shells and 590 angular points per shell) was used, combined with the "verytight" convergence condition (requesting the root-mean-square forces to be smaller than 1 × 10^{-6} hartree bohr^{-1}). Additional frequency calculations were also undertaken in order to verify that the optimized geometries correspond to true minima. Chloroform solvent effects were used in all of the quantum-mechanical calculations using the reaction field method IEFPCM.[10]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra of all novel compounds and the crystallographic data for **9e** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org. CCDC 953621 contains the supplementary crystallographic data for **9e**. These data can be obtained free of charge via the Internet at http://www.ccdc.cam.ac.uk/conts/retrieving.html or from The Cambridge Crystallographic Data Centre (12 Union Road, Cambridge CB2 1EZ, U.K.; Tel (+44)1223 336 408; E-mail: deposit@ccdc.cam.ac.uk).

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Notes

The authors declare no competing financial interest.

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